

Comorbidity and Health-Related Quality of Life in People with Multiple Sclerosis

Sharon A. Warren, PhD; Karen V.L. Turpin, MSc; Sheri L. Pohar, PhD;
C. Allyson Jones, PhD; K.G. Warren, MD, FRCP(C)

*This study examined associations between comorbidity and health-related quality of life (HRQL) in people with multiple sclerosis (MS). Data were derived from the Canadian Community Health Survey (CCHS) Cycle 1.1, a cross-sectional survey conducted by Statistics Canada. A nationally representative sample of community-dwelling Canadians was interviewed to determine whether they had been diagnosed with various chronic conditions. Participants were also administered the Health Utilities Index Mark 3 (HUI3) questionnaire to evaluate HRQL. Of the 131,535 participants, 335 reported having MS. Comorbidities listed by at least 10% of respondents with MS were assessed for their relation to HRQL, with age, sex, education, marital status, income, and number of comorbidities included as covariates. Respondents averaged 1.6 comorbidities. Eight comorbidities were experienced by at least 10% of respondents: back problems (35%), nonfood allergies (29%), urinary incontinence (28%), arthritis (26%), hypertension (17%), chronic fatigue syndrome (16%), depression (16%), and migraine (14%). Differences in HRQL between people with and without urinary incontinence, arthritis, hypertension, chronic fatigue syndrome, and depression were either clinically important or statistically significant at the .05 level in bivariate analyses. Only urinary incontinence and depression, however, were negatively associated with HRQL in a multivariate analysis, which explained 26% of the variance. Lower levels of education and receiving social assistance were also negatively associated with HRQL, with social assistance contributing more to the variance in HRQL than either comorbidity. *Int J MS Care*. 2009;11:6–16.*

The term *quality of life* (QOL) is used to describe a subjective sense of well-being or global satisfaction with important aspects of daily life. *Health-related quality of life* (HRQL) is the term most often used to describe the QOL of people who are affected by an illness. It has been defined as “the value assigned to duration of life as modified by impairments, functional states, perceptions and social opportunities that are influenced by disease, injury, treatment or policy.”¹ HRQL is generally measured using one of two approaches: generic instruments (health profile and utility measures) and specific instruments (disease, population, function, or condition spe-

cific). Specific instruments, such as the Multiple Sclerosis Quality of Life (MSQOL-54) instrument,² measure those aspects of life whose quality is most likely to be affected by a specific disease. Generic health profile instruments, such as the Sickness Impact Profile (SIP), measure all aspects of QOL that might be affected by health and can therefore be used in any disease or general population. Generic utility measures, such as the Health Utilities Index (HUI) and the EuroQol-5 Dimension (EQ-5D), weight a person’s health status by the QOL that society associates with that level of health. Many HRQL instruments provide both an overall score and subscale scores for the dimensions of health they encompass.

Over the past 2 decades, HRQL instruments have been increasingly used to describe HRQL in people with multiple sclerosis (MS). Regardless of type of instrument employed, MS is consistently demonstrated to have a negative impact on HRQL. HRQL in people

From the Faculty of Rehabilitation Medicine (SAW, CAJ), and Northern Alberta Multiple Sclerosis Patient Care and Research Clinic (KVL, KGW), University of Alberta; and the Institute of Health Economics (SLP), Edmonton, Canada. Correspondence: Sharon Warren, PhD, Professor, Faculty of Rehabilitation Medicine, Room 3-48, Corbett Hall, University of Alberta, Edmonton, Alberta, Canada T6G 2G4; e-mail: sharon.warren@ualberta.ca.

with MS is often lower than in people with other diseases³ and is considerably lower than in the general population.^{4,5} Research has also explored factors that may influence HRQL, including sociodemographic characteristics, disease features, and treatment modalities. One factor that has not received much attention for its possible impact on HRQL is comorbidity—that is, having another disease or diseases besides MS. Comorbidity is common among the general population and has been shown to negatively affect HRQL in people with a variety of illnesses, including cancer⁶ and diabetes.⁷ Limited available research suggests that comorbidity is also common in people with MS and negatively affects their HRQL. Turpin et al.⁸ examined factors associated with HRQL in people with relapsing-remitting MS, as measured by the generic Short Form Health Status Survey (SF-36). They found that poor physical HRQL was associated with the presence of musculoskeletal and respiratory comorbid conditions, and that poor mental HRQL was associated with the presence of headaches, digestive system problems, and kidney, bladder, or urinary problems. In addition, some reports indicate that comorbidity has a negative impact on disability outcome in terms of ambulation. For example, Marrie⁹ found that vascular, musculoskeletal, gastrointestinal, visual, or mental comorbidity increased the risk of ambulatory disability, as measured by the Performance Scales (PS) in the North American Research Committee on Multiple Sclerosis (NARCOMS) Registry.

Most studies evaluating HRQL in people with MS, however, list the presence of comorbidity as an exclusion factor; if comorbidities are examined, they are limited to those that could be consequences of having the disease. The literature consistently demonstrates negative relationships between depression and fatigue and HRQL in MS,¹⁰⁻¹³ although little is known about the extent to which having a diagnosis of depression or fatigue influences the impact of MS on HRQL. Nor has the extent to which having illnesses not likely to be consequences of MS such as cancer and diabetes influences the impact of MS on HRQL been established, although research has demonstrated that patients suffering from some combinations of diseases experience reduced HRQL¹⁴ or greater physical disability¹⁵ than would be expected from their separate effects. Whether HRQL varies by number of comorbidities has also not been established, despite evidence that HRQL decreases

as number of comorbidities increases in the general population.¹⁶⁻¹⁸ Other aspects of comorbidity and HRQL yet to be explored in detail include the interaction between comorbidity and sociodemographic factors and the relationship between comorbidity and specific dimensions of HRQL.

The present study was conducted to further explore the association between comorbidity and HRQL in people with MS. Comorbidity is an important factor to consider because it is potentially modifiable to achieve gains in HRQL. Information on the association between comorbidity and HRQL in MS may help health-care providers, patient advocates, and policy makers to choose among potential intervention strategies in the hope of achieving the greatest gains in HRQL.

Methods

Survey Design

This study used data from the Canadian Community Health Survey (CCHS) Cycle 1.1. Approval to access the survey data was obtained from Statistics Canada, and ethical approval of the study was obtained from the Health Research Ethics Board of the University of Alberta, where the research was conducted. The CCHS is a cross-sectional survey of the Canadian population over age 12 in which data are collected pertaining to utilization of health-care services, determinants of health, and health status.¹⁹ The survey excludes individuals living on crown or reserve lands and some remote areas of the country; it also excludes individuals living in various types of institutions and members of the Canadian Armed Forces. Nevertheless, the survey still represents approximately 98% of the community-dwelling population over age 12. A multistage stratified cluster design combined with random sampling methods is used to select a representative sample of the Canadian population to participate in the survey. Interviews are conducted either in person or by telephone. All information collected in the CCHS is either self-reported or reported by proxy. At the end of Cycle 1.1, a total of 131,535 respondents had been surveyed; the overall response rate was 84.7%.²⁰

Sample

Of the 131,535 respondents surveyed, 335 respondents reported having been diagnosed with MS by a health-care professional. This amounts to 0.22% of the community-dwelling Canadian population over age 12,

based on the extrapolation method used by Statistics Canada. This percentage translates into a prevalence rate of 240/100,000 as reported by Beck et al.,²¹ who included in their analysis subjects aged 18 and over who lived in one of the ten Canadian provinces, with the northern territories excluded. This rate is consistent with other estimates of MS prevalence in Canada, such as those derived from government health databases. The analysis for the present study was restricted to respondents over the age of 18 who provided complete data on the variables of interest (n = 302).

Measures

HRQL in the CCHS 1.1 was measured using the Health Utilities Index Mark 3 (HUI3),²² which falls within the category of generic utility instruments. The HUI3 addresses eight dimensions of health: vision, hearing, speech, ambulation, dexterity, emotion, cognition, and pain. Individuals are assigned to one of five or six levels of functioning for each dimension. Utility-based preference scores are assigned to each dimension level and then combined using a multiplicative utility function to arrive at an overall HRQL score. Overall HRQL scores range from -0.36 to 1.0 (-0.36 = worst possible health; 0.0 = dead; 1.0 = perfect health). Overall scores of 0.89 to 1.00 indicate no or mild impairment, 0.70 to 0.88 moderate impairment, and less than 0.70 severe impairment; negative scores indicate that society considers living in this health state to be less desirable than death. Single-dimension scores range from 0.0 to 1.0 (0.0 = no capacity; 1.0 = full capacity); scores of 0.89 to 1.00 indicate no or mild impairment, 0.70 to 0.88 moderate impairment, and less than 0.70 severe impairment. Although no "gold standard" exists, Drummond²³ has suggested that a difference between groups of at least 0.03 on the overall HUI3 score represents a minimal clinically important difference, and that categories of 0.03 to <0.06, 0.06 to <0.09, and ≥ 0.09 represent mild, moderate, and severe impact, respectively. A difference of at least 0.05 on single-dimension scores represents a minimal clinically important difference; categories of 0.05 to <0.10, 0.10 to <0.15, and ≥ 0.15 would represent mild, moderate, and severe impact, using the same extrapolation principle as for overall HUI3 score. Fisk et al.²⁴ examined the psychometric properties of the HUI3 compared with the EQ-5D and Short Form-6D (SF-6D), two other generic HRQL measures, concluding that the HUI3

was the most appropriate for MS studies because its scores were more highly correlated with clinical function measures like the Expanded Disability Status Scale (EDSS).²⁵ The HUI3 has also been shown to be responsive to changes in health status over time.²⁶

Participants in the CCHS 1.1 were asked about the presence or absence of the following chronic conditions in addition to MS: food allergies; nonfood allergies; asthma; back problems, excluding fibromyalgia and arthritis; arthritis or rheumatism, excluding fibromyalgia; hypertension; chronic bronchitis; emphysema or chronic obstructive pulmonary disease; diabetes; epilepsy; heart disease; cancer; effects of stroke; urinary incontinence; bowel disorder, such as Crohn's disease or colitis; Alzheimer's disease or other dementia; glaucoma; cataracts; thyroid condition; Parkinson's disease; chronic fatigue syndrome; and multiple chemical sensitivities. An "other" chronic condition category was used to cover conditions not included in this list. A chronic condition was considered to be present if it had been diagnosed by a health-care professional and had lasted or would be expected to last more than 6 months. The exception to self-report was depression, which was determined from the Composite International Diagnostic Interview Short Form for Major Depression (CIDI-SFMD), a validated instrument for the diagnosis of major depressive disorder in accordance with diagnostic criteria of the *Diagnostic and Statistical Manual of Mental Disorders* (Fourth Edition) (*DSM-IV*).²⁷

Analysis

Descriptive statistics were used to summarize socio-demographic characteristics of CCHS 1.1 respondents with MS that are commonly associated with negative health outcomes: age (years), sex, education (less than high school, high school, some postsecondary/college/trade school, university degree), marital status (not married or married/partnership), and income (receiving social assistance or not). Social assistance was used as a marker for income because the percentage of respondents who failed to report household income was large. Descriptive statistics were also used to summarize number of comorbidities experienced by respondents and the percentage experiencing each comorbidity.

Because of sample size considerations, only comorbidities that met the following criteria were assessed for their association with HRQL: 1) those experienced by

at least 10% of respondents with MS (ie, at least 30 people), and 2) those that exhibited clinically important differences in HRQL between groups (ie, at least a 0.03 difference between those with and without the comorbidity), regardless of whether the difference was significant when *t* tests were applied ($P < .05$). Analysis of covariance (ANCOVA) was used to assess the association between each comorbidity that met the inclusion criteria and overall HUI3 score, with age, sex, education, marital status, social assistance, other comorbidities, and number of comorbidities entered as covariates. ANCOVA was also used to assess the association between each comorbidity and single-dimension HUI3 scores, with the same covariates.

Sampling weights were applied to all analyses to account for the unequal probability of being selected into the survey. Bootstrap variance estimates were used to adjust for clustering and stratification²⁸ and to estimate 95% confidence intervals (CIs) and *P* values. *P* values were not corrected for multiple testing because all of the statistically significant differences were also clinically important, which suggests that they would not be due to chance. All analyses were performed using WESTVAR, version 4.2 (Westat, Inc, Rockville, MD), with bootstrap weights provided by Statistics Canada.

Results

Table 1 describes the CCHS 1.1 respondents with MS, including 95% CIs for continuous variables. The respondents' mean age was 48.7 years; majorities were female (68.3%) and married (71.0%). The largest percentage of respondents (42.9%) had achieved at least some postsecondary/college/trade school education, and 11.1% were receiving social assistance. Eight comorbidities were experienced by at least 10% of respondents: back problems (34.5%), nonfood allergies (29.2%), urinary incontinence (28.0%), arthritis (25.6%), hypertension (17.0%), chronic fatigue syndrome (16.4%), depression (16.3%), and migraine (14.2%). Only the comorbidities shown in Table 1 (urinary incontinence, arthritis, hypertension, chronic fatigue syndrome, and depression), however, were associated with clinically important differences in overall HUI3 score. The mean number of comorbidities reported by respondents was 1.6. Respondents' mean overall HUI3 score was 0.57. On single dimensions, the lowest mean HUI3 scores were observed for ambu-

Table 1. Sociodemographic characteristics, comorbidities, and mean HUI3 scores of respondents with multiple sclerosis

Variable	Value
Age, mean (95% CI), yr	48.7 (46.6–50.8)
Female, %	68.3
Education, %	
<High school	17.9
High school	19.0
Some postsecondary/college/ trade school	42.9
University degree	20.1
Married, %	71.0
Receiving social assistance, %	11.1
Urinary incontinence, %	28.0
Arthritis, %	25.6
Hypertension, %	17.0
Chronic fatigue syndrome, %	16.4
Depression, %	16.3
Comorbidities, mean (95% CI), No.	1.6 (1.3–1.9)
HUI3 score, mean (95% CI)	
Overall	0.57 (0.52–0.63)
Vision	0.93 (0.91–0.95)
Hearing	0.99 (0.98–0.99)
Speech	0.99 (0.98–1.00)
Ambulation	0.71 (0.65–0.77)
Dexterity	0.93 (0.90–0.96)
Emotion	0.93 (0.91–0.95)
Cognition	0.89 (0.86–0.92)
Pain	0.75 (0.69–0.80)

Abbreviations: CI, confidence interval; HUI3, Health Utilities Index Mark 3.

lation (0.71) and pain (0.75), both in the moderate impairment range. All other dimensions fell into the no or mild impairment range, with cognition close to the moderate impairment range (0.89).

Table 2 shows the findings of the ANCOVA analysis for overall HRQL. Regression coefficients are given for the continuous variables of age and number of comorbidities, and mean differences for all the categorical variables included in the analysis. No association was observed between either age or number of comorbidities and HRQL. Of the five comorbidities included in the analysis, urinary incontinence and depression were associated with the largest clinically important overall HRQL deficits. The adjusted mean difference in overall HUI3 score between respondents with and without urinary incontinence was -0.23 . In other words, on

Table 2. Results of ANCOVA analysis for overall HUI3 score

Variable	Regression coefficient or mean difference (95% CI)
Age	0.00 (−0.01 to 0.00)
Sex	
Female	−0.08 (−0.19 to 0.04)
Male	–
Education	
< High school	−0.21 (−0.43 to 0.01)
High school	−0.13 (−0.30 to 0.04)
Some postsecondary/college/trade school	−0.20 (−0.37 to −0.03) ^a
University degree	–
Marital status	
Not married	0.05 (−0.06 to 0.16)
Married/partnership	–
Receiving social assistance	
Yes	−0.33 (−0.48 to −0.19) ^a
No	–
Number of comorbidities	0.01 (−0.02 to 0.05)
Urinary incontinence	
Yes	−0.23 (−0.38 to −0.09) ^a
No	–
Arthritis	
Yes	−0.06 (−0.19 to 0.07)
No	–
Hypertension	
Yes	−0.06 (−0.20 to 0.07)
No	–
Chronic fatigue syndrome	
Yes	−0.08 (−0.28 to 0.13)
No	–
Depression	
Yes	−0.22 (−0.35 to −0.09) ^a
No	–

Abbreviations: ANCOVA, analysis of covariance; CI, confidence interval; HUI3, Health Utilities Index Mark 3.

^a*P* < .05 after adjusting for covariates.

average people with MS who had urinary incontinence had a HRQL score 0.23 points lower than the HRQL score of people without urinary incontinence, when all other comorbidities and other variables were controlled for. The adjusted mean difference for depression was −0.22. The deficits for both urinary incontinence and depression were in the severe impact range and were statistically significant, with each comorbidity making an independent contribution to HRQL. Arthritis, hypertension, and chronic fatigue syndrome were associated with overall HRQL deficits that were clinically important (in the moderate impact range). Of the

sociodemographic characteristics, sex, education, marital status, and social assistance were associated with clinically important overall HRQL deficits, but only education and social assistance were statistically significant. Of all 11 variables included in the ANCOVA analysis, social assistance was associated with the largest overall HRQL deficit (an adjusted mean difference of −0.33), placing it in the severe impact range. The adjusted *R*² statistic for the ANCOVA analysis was 0.26; that is, 26% of the variance in overall HRQL was explained by the ANCOVA model.

Table 3 illustrates mean differences in single-dimension HRQL scores for each comorbidity, adjusted for all other variables. The largest clinically important and statistically significant deficit associated with urinary incontinence was in ambulation, with an adjusted mean difference in ambulation scores between respondents with and without this comorbidity of −0.26. In other words, on average people with urinary incontinence had an ambulation score that was 0.26 points lower than people without urinary incontinence when all other comorbidities and variables were controlled for. Urinary incontinence was also associated with clinically important and statistically significant deficits in vision (−0.08), dexterity (−0.12), and cognition (−0.11), and with a clinically important deficit in pain (−0.07). Arthritis was associated with a clinically important deficit in pain (−0.12). Hypertension was associated with clinically important deficits in vision (−0.05), ambulation (−0.08), and dexterity (−0.11), but with a higher cognition score (0.07) that was both clinically important and statistically significant. Chronic fatigue syndrome was associated with a clinically important deficit in ambulation (−0.05). Depression was most strongly associated with a deficit in pain (−0.16), followed by deficits in emotion (−0.14) and cognition (−0.13), all of which were clinically important and statistically significant. As might be expected from differences in overall HRQL, urinary incontinence and depression were associated with the greatest number of deficits in single health dimensions.

In summary, the overall HRQL scores of people with MS who also experienced either urinary incontinence or depression were substantially lower than the HRQL scores of those who did not. Urinary incontinence was associated with more single-dimension deficits than depression. Neither of the deficits in overall HRQL associated with these two comorbidities was

Table 3. Differences in single-dimension HUI3 scores by comorbidity

Dimension	Difference, mean (95% CI)				
	Urinary incontinence	Arthritis	Hypertension	Chronic fatigue syndrome	Depression
Vision	-0.08 ^a (-0.13 to -0.02)	-0.01 (-0.04 to 0.02)	-0.05 (-0.11 to 0.01)	0 (-0.05 to 0.06)	0.02 (-0.01 to 0.06)
Hearing	0 (-0.01 to 0.02)	-0.01 (-0.03 to 0.01)	-0.01 (-0.04 to 0.02)	0 (-0.03 to 0.02)	0 (-0.02 to 0.02)
Speech	-0.02 (-0.06 to 0.02)	-0.01 (-0.02 to 0.01)	-0.01 (-0.03 to 0.02)	0.01 (-0.01 to 0.04)	0.01 (0 to 0.03)
Ambulation	-0.26 ^a (-0.41 to -0.11)	-0.01 (-0.15 to 0.14)	-0.08 (-0.26 to 0.11)	-0.05 (-0.27 to 0.17)	-0.03 (-0.18 to 0.11)
Dexterity	-0.12 ^a (-0.22 to -0.01)	-0.01 (-0.09 to 0.06)	-0.11 (-0.24 to 0)	-0.02 (-0.15 to 0.11)	-0.03 (-0.13 to 0.07)
Emotion	-0.01 (-0.07 to 0.04)	-0.01 (-0.07 to 0.05)	-0.02 (-0.08 to 0.04)	-0.01 (-0.09 to 0.06)	-0.14 ^a (-0.23 to -0.05)
Cognition	-0.11 ^a (-0.18 to -0.05)	-0.03 (-0.09 to 0.03)	0.07 ^a (0.01 to 0.12)	-0.04 (-0.17 to 0.08)	-0.13 ^a (-0.22 to -0.05)
Pain	-0.07 (-0.21 to 0.07)	-0.12 (-0.28 to 0.04)	-0.01 (-0.16 to 0.14)	-0.04 (-0.17 to 0.15)	-0.16 ^a (-0.28 to -0.04)

Abbreviations: CI, confidence interval; HUI3, Health Utilities Index Mark 3.

^a*P* < .05 after adjusting for covariates.

as great as the deficit associated with receiving social assistance.

Discussion

Respondents in this study had a mean overall HRQL score (0.57) similar to that of people with MS residing in other countries that have been studied. Using the EQ-5D (a utility measure with an analogous scoring system), Kobelt et al. observed an average HRQL of approximately 0.55 among people with MS across a number of European countries²⁹ and 0.69 in the United States, which is still in the severe impairment range.³⁰

Although number of comorbidities has been associated with HRQL in other populations,¹⁶⁻¹⁸ it was not associated with HRQL among people with MS in this study. Using a different breakdown of the data, however, the mean overall HRQL score of respondents with no comorbidity (0.64) was 0.12 points higher than that of respondents with one or more comorbidities (0.52). This suggests that the presence of comorbidity was negatively associated with HRQL, even if number of comorbidities was not.

A more important issue may be the capacity of particular comorbidities to affect HRQL. Specifically, people with MS in this study who also reported urinary

incontinence, arthritis, hypertension, chronic fatigue syndrome, or depression had lower overall HRQL scores than those without these five comorbidities. Urinary incontinence and depression were associated with the greatest deficits in overall HRQL. Because the study was cross-sectional, it is not possible to draw definitive conclusions about the causal nature of associations between these two comorbidities and HRQL. In fact, urinary incontinence and depression are generally considered in the health-care community to be consequences of MS. Nevertheless, there may be some causal relationship between these conditions and HRQL; to the extent that urinary incontinence and depression cause a reduction in HRQL, addressing these particular comorbidities has the greatest potential to achieve improvements.

In this study, the mean overall HRQL score of people with urinary incontinence was 0.23 points lower than that of people without this comorbidity. Given that a difference of at least 0.09 indicates a severe impact, the gravity of this condition for affected patients is evident. Urinary incontinence was also reported by more respondents than any of the other comorbidities related to HRQL: 28.0%, compared with 16.3% for depression. The fact that urinary

incontinence was also the comorbidity associated with the largest number of single-dimension deficits (vision, ambulation, dexterity, cognition, and pain) reinforces the importance of its association with HRQL. People with urinary incontinence are likely to be struggling with more single-dimension health deficits than people with the comorbidities of arthritis, hypertension, chronic fatigue syndrome, or depression. Regardless of the causal nature of the association between urinary incontinence and HRQL, it is clear that people with urinary incontinence should be targeted for special attention because of their lower overall HRQL and multiple single-dimension scores.

The need to identify and treat urinary incontinence in patients with MS is receiving increasing attention in the health-care community. The results of this study justify research into new ways of combating urinary incontinence, for example, by neuromuscular stimulation and botulinum injections. In the meantime, health-care providers can ensure that they promote open communication with patients about urinary incontinence—often a sensitive subject—in addition to following published management guidelines,³¹ including therapies with some degree of proven effectiveness such as medications, bladder appliances, and pelvic floor exercises. Groups advocating for people with MS could promote strategies to reduce the impact of urinary incontinence on daily life. For example, Wollin and Spencer³² have observed a link between urinary incontinence and unemployment among people with MS. Negotiations with employers to allow reduced work hours, flexible bathroom breaks, and workstations close to bathroom facilities have all been suggested by the Multiple Sclerosis International Federation to help retain people with MS in the workforce.³³

The mean overall HRQL score of people with depression was 0.22 points lower than that of people without depression, again indicating a severe impact. In addition, depression was associated with deficits in multiple single-dimension scores: emotion, cognition, and pain. As with urinary incontinence, regardless of the causal nature of the relationship between depression and HRQL, it is clear that people with MS who are experiencing depression should receive special attention.

The results of this study reinforce the already recognized need among health-care providers to identify people with MS who are depressed and to treat these

patients with antidepressant medications and cognitive-behavioral therapies that have been shown to be effective. The association between depression and pain observed in this study supports emerging avenues of research on depression and the pain dimension of HRQL, promoted by a growing awareness of the prevalence of pain in patients with MS. Using a self-administered questionnaire that included the SF-36 and the Hospital Anxiety and Depression Scale (HADS), Kalia and O'Connor³⁴ recently found a positive correlation between bodily pain and depression/anxiety in MS patients. The literature reveals controversy over the direction of the relationship between depression and pain, with a tendency toward the assumption that pain is more likely to cause depression than the reverse. Nevertheless, evidence also exists suggesting that depression can predict pain. For example, Carroll et al.³⁵ found that depression was a strong predictor of neck and low back pain in the general population. Advocacy groups could raise awareness about the relationship between depression and pain and encourage research into the specifics of this relationship.

The importance of pain for respondents in this study was highlighted by the fact that pain was one of only two single health dimensions (the other being ambulation) that were scored in the moderate impairment range as part of overall HRQL. The impact of comorbidity was far greater on pain than on ambulation when data from the study were used to calculate overall HRQL scores for people with no comorbidity versus those with one or more comorbidities. The single-dimension pain score of people with no comorbidity was 0.88 (indicating only moderate impairment), compared with 0.65 (severe impairment) for those with one or more comorbidities. In other words, the pain score for people with comorbidity was 0.23 points lower than for people without comorbidity. On the other hand, the single-dimension ambulation score of people with no comorbidity was 0.69, compared with 0.74 for those with one or more comorbidities, a difference of only 0.05 points.

Interestingly, the mean overall HRQL of people with arthritis in this study was only 0.06 points lower than those without arthritis, but their single-dimension pain score was 0.12 points lower. Pain was the only single-dimension score whose difference between those with and without arthritis was clinically important. This may indicate that arthritis adds to any pain

already experienced as part of MS. Further research into the association between arthritis and HRQL may confirm that MS patients with arthritis should be targeted to identify problems with pain that could be effectively treated. The fact that arthritis was reported by the second-highest number of respondents, after urinary incontinence (25.6%), highlights the possible gains in HRQL that might be achieved by successfully controlling arthritis-related pain.

Little research is available indicating an association between hypertension and HRQL in patients with MS. The differences in overall HRQL and single-dimension scores for vision, ambulation, dexterity, and cognition observed in this study may all warrant further examination, especially the higher cognition score (mean difference of 0.07) in people with hypertension that was both clinically important and statistically significant. One possible explanation is that MS patients being treated with antihypertensive medication are receiving some benefit in terms of cognition. Hajjar et al.³⁶ have reported that lowering blood pressure with antihypertensive agents that cross the blood-brain barrier and affect the renin-angiotensin-aldosterone system (perindopril or losartan) or brain calcium metabolism (nitrendipine) provides protection against cognitive decline in patients who are cognitively intact. The literature indicates, however, that the impact of antihypertensive medication is more complex than this: some evidence exists that reduction in blood pressure does not always have a positive effect on cognition³⁷ and that its benefits may vary depending on patient age.^{36,38} Given the prevalence of cognitive decline in the MS population, screening for and appropriate treatment of hypertension may prove worthwhile, although it would be advisable to first try to obtain a better understanding of how such treatment might affect cognition across different categories of MS patients.

Chronic fatigue syndrome may not have been distinguished from MS-related fatigue by respondents in this study, making the difference observed in mean overall HRQL between those with and without this comorbidity difficult to interpret. It may simply reflect the impact of MS-related fatigue on HRQL found in previous research.¹⁰⁻¹³ Even if respondents made a distinction, because of the cross-sectional nature of the study, no definitive conclusion can be drawn about the causal nature of the association between chronic fatigue syndrome and HRQL. The deficit was relatively small

(-0.08), and ambulation was the only single health dimension for which a deficit was noted (also small, at -0.05). Also unclear is the direction of the latter relationship—that is, whether chronic fatigue syndrome contributes to walking problems or the reverse. Nevertheless, these findings suggest areas for further research. For example, it might be investigated whether the percentage of respondents reporting chronic fatigue syndrome would be similar in a study that clearly determined whether patients distinguished between this syndrome and MS-related fatigue and, if so, what the resulting clinical implications of having chronic fatigue syndrome might be.

Receiving social assistance (ie, having a low income) was associated with a greater overall HRQL deficit than any of the comorbidities included in this study, with the mean score of patients receiving social assistance being 0.33 points lower than that of those who were not. Lower education level was also associated with a deficit in HRQL, an observation that has also been reported by other researchers.³⁹ Income, education, and social class have been recognized as three of the most important determinants of health in the general population; gradients in life expectancy exist across these three variables in many developed countries.⁴⁰ Moreover, self-reported ratings of general health are substantially lower and chronic illnesses are more prevalent in the lowest income brackets compared with the highest.⁴¹ In patients with MS, low income may impede access to medical care; for example, it might prohibit purchasing expensive prescription medications, assistive devices, or even health-care services such as housekeeping or rehabilitation therapy not covered by health insurance that could enhance HRQL. As with comorbidities in this study, the causal nature of the association between social assistance and HRQL remains unclear. The reason for receiving social assistance is also unclear, although reduced employment opportunities among people with MS may be one factor. Lower employment levels have certainly been described in people with MS,^{39,42} and those with lower education levels may be particularly affected by physical inability to work. Regardless of the causal nature of the association between social assistance and HRQL, people with MS who are receiving social assistance clearly need to be targeted for special attention because of their lower overall HRQL scores. Iezzoni and Ngo⁴³ have called for research on how neurologists and other health-care

providers can help ensure that patients have adequate income. Advocacy groups might promote retraining opportunities for those whose physical disabilities require a change in type of work and continue their efforts to achieve workplace modifications to accommodate disabilities associated with MS. Advocacy groups could also promote better social assistance packages for people with MS. The Multiple Sclerosis Society of Canada is currently engaged in a “Campaign for Income Security,” asking the federal government for policy changes to allow more people with MS to continue working and to ensure that they have a minimum income (Yves Savoie, President and Chief Executive Officer, Multiple Sclerosis Society of Canada, e-mail communication, May 6, 2008). This initiative recognizes that lower income may be due to the inability to work of not only people with MS but also their caregivers.

Limitations

The results of this study should be interpreted in light of certain limitations. The list of comorbidities included in the CCHS 1.1, and therefore available for assessment, was fixed. In addition, some categories were medical diagnoses, while others were organ-based dysfunction such as urinary incontinence that can be caused by many age- or disease-related conditions, including MS. Complicating the matter is that determination of the presence of MS and comorbidities was predominantly via self-report. Although questions regarding chronic conditions specified that they be diagnosed by a health-care professional, over- or under-reporting remains a possibility. The accuracy of self-reports of chronic conditions in the CCHS does not seem to have been studied. Research in other populations has demonstrated that agreement between patient and physician report varies across medical conditions.⁴⁴ Other researchers have found, however, that self-reports of chronic conditions are generally accurate,⁴⁵ and the NARCOMS Registry reports excellent agreement between patient self-reports and physician diagnoses in its database.⁴⁶ Participants in this study were representative of Canadians with MS in terms of age and sex⁴⁷; however, generalizability of the results is limited because the CCHS sampling frame does not capture those individuals who reside in institutions, which would represent about 5% of people with MS and those with the most severe disability.⁴⁸ The impact of

some comorbidities could not be examined because of sample size restrictions, and some examined associations that were clinically important but not statistically significant may have failed to reach significance because of a lack of power. In addition, there was no control for disability level, using an MS-specific tool such as the EDSS. Research indicates that as disability increases, physical HRQL decreases in patients with MS, but whether the same relationship exists between disability and mental HRQL is controversial.⁴⁹ Disability status may have accounted for some of the association between urinary incontinence and HRQL in this study, and some of the association between social assistance and HRQL, as unemployment is higher among the disabled. Disability status may or may not have accounted for some of the association between depression and HRQL, however, because depression can occur at any point along the MS disability continuum. Adjusting for age might partially control for disability, because the weight of evidence suggests that current age is highly correlated with disability level⁵⁰; however, age is not a guaranteed predictor of disability. Finally, longitudinal studies of people diagnosed with MS to determine the impact of preexisting comorbidities versus those that develop later, either independently or possibly as a result of MS (eg, urinary incontinence and depression), would help to clarify relationships between comorbidity and HRQL in MS, as would experimental studies assessing the impact of interventions that address these comorbidities on HRQL.

Practice Points

- The most common comorbidities found in this MS study population were back problems, nonfood allergies, urinary incontinence, arthritis, hypertension, chronic fatigue syndrome, depression, and migraine.
- The health-related quality of life of this sample was poorest in the areas of ambulation and pain, followed by cognition.
- Health-related quality of life was significantly worse in the presence of the comorbidities of urinary incontinence and depression.
- Health-related quality of life was also significantly worse for participants who reported receiving social assistance.

Conclusion

Urinary incontinence, depression, receiving social assistance, and lower education were associated with the greatest deficits in HRQL in this study. Clinicians should be aware of which patients have these particular comorbidities and sociodemographic characteristics, because their HRQL scores appear to be substantially lower than those who do not. Being sensitive to such patients' needs early in their care may reduce the potential impact of these factors on HRQL. Further research is needed on the nature and strength of associations between comorbidity, sociodemographic characteristics, and HRQL and the effectiveness of interventions to help maximize improvements in HRQL. □

Acknowledgments: The research and analysis in this study are based on data from Statistics Canada. The opinions expressed do not represent the views of Statistics Canada.

Financial Disclosures: Ms. Turpin has received lecture fees from Discovery Institute of Medical Education and EMD Serono. Dr. Pohar has received lecture fees from Pfizer and Rogers Communications. Drs. S. Warren, Jones, and K.G. Warren have no conflicts of interest to disclose.

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