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Depression in Multiple Sclerosis: A Longitudinal Analysis

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Abstract

High rates of depression are documented in persons with multiple sclerosis (MS), but few studies examine depression over time. This analysis considered data from 607 persons with MS over a seven-year period as part of an ongoing longitudinal study of quality of life in chronic illness. Latent growth curve analysis was used to examine trajectories in depression and the effects of covariates such as age, time since diagnosis of MS, type of MS, and functional limitations on the extent to which depression changed over the study period. The results of the analysis indicated that depressive symptoms fluctuated over time for individuals but did not show a tendency to an overall significant increase or decrease for the group as a whole. Younger age, longer time since diagnosis of MS, progressive forms of MS and greater extent of functional limitation were predictive of greater depressive symptoms at Time 1. With the exception of functional limitation, which showed an association with depression at all time periods, these variables did not predict the changes in depressive symptoms over time. Gender was not a significant predictor of changes in depressive symptoms, nor did women have higher rates of depression as expected from previous research. The results of this analysis indicate the importance of screening for depression in all persons with MS.

Multiple sclerosis (MS) is a chronic demyelinating disease of the central nervous system that affects women 2–3 times more often than men (Noonan, Kathman & White, 2002). A higher incidence of depressive symptoms and major depressive disorder in persons with MS is well documented, and reported in both large community surveys (Chwastiak et al., 2002; Patten, Beck, Williams, Barbui, & Metz, 2003) and studies of persons with MS (Sadovnick et al., 1996). Depressive symptoms are associated with reduced quality of life for persons with MS (Fruehwalk, Loeffler-Stastka, Eher, Saletu & Baumhackl, 2001; Lobentanz et al., 2004) and with an increased risk of suicide (Faber, 2003; Sadovnick, Eisen, Paty, & Ebers, 1991).

An important unresolved issue is whether depressive symptoms remain stable or fluctuate over time because most studies on this topic are cross-sectional. Therefore, additional longitudinal studies to describe the course of depressive symptoms and associated risk factors are warranted (Ehde & Bombardier, 2005). Learning more about the trajectory of depressive symptoms over time has implications for identification and treatment of depression in persons with MS. In particular, the influence of gender, age at MS onset, and severity of MS on the association between MS course and depression need further study (Zabad, Patten, & Metz, 2005).

To respond to these issues, the purpose of this study was to explore the trajectory of depressive symptoms over a seven-year time period in a sample of persons with MS. We examined the correlations between the characteristics of change in depressive symptoms and the moderating

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effects of age, gender, functional limitations and time since diagnosis of MS on individual trajectories. We addressed the following specific research questions:

1. What are the patterns of change in depressive symptoms over time?
2. Do covariates such as age, type of MS, years since diagnosis of MS, and functional limitation at Time 1 impact the trajectory of depression over time?
3. What are the correlations between characteristics of change in functional limitations and depressive symptoms over the seven-year time period after accounting for the effects of age, gender, and years since diagnosis of MS?

Background

Ehde & Bombardier (2005) note the importance of distinguishing depressive symptoms from a clinical diagnosis of major depressive disorder. Many studies of individuals with MS use instruments such as the Beck Depression Inventory (BDI) (Beck, Ward, Mendelson, Mock & Erbaugh, 1961) and the Center for Epidemiological Studies Depression Scale (CES-D) (Radloff, 1977) designed as screening tools to measure depressive symptoms. These measures have suggested cut-off points for scores, above which symptoms are considered clinically significant. In this paper, the term *depressive symptoms* is used to describe the results of studies that use these instruments, and *major depressive disorder (MDD)* is used when referring to studies that report a diagnosis consistent with American Psychiatric Association (APA) diagnostic criteria for MDD from the *Diagnostic and Statistical Manual of Mental Disorders, 4th Edition* (DSM-V).

Gender and Depression

Major depressive disorder (MDD) affects twice as many women as men. The gender disparity is evident at the time of puberty (Kessler & Walters, 1998), and the reoccurrence rate appears similar for women and men (Kessler, McGonagle, Shao, & Nelson, 1994; Kovacs, Obronsky, & Sherrill, 2003; Simpson, Nee, & Endicott, 1997), indicating that women are more vulnerable to a first episode. Numerous factors are suggested for the gender disparity. Mood changes associated with times of hormonal change in women's lives support the potential contribution of the female endocrine system to the development of depression and may predispose women to be sensitive to psychosocial, biologic, and environmental factors associated with the disorder (Steiner, Dunn, & Born, 2003). Stressful life events are associated with depression (Kessler, 1997), and women may be more vulnerable to developing depression in association with these events (Maciejewski, Prigerson, & Mazure, 2001; Nazoo, Edwards, & Brown, 1997). Individual factors that may increase vulnerability to depression are a greater tendency of women to possess a cognitive style characterized by rumination (Nolen-Hoeksema, 2000), and the stronger relational orientation of women's personalities (Helgeson, 2002). Social role theories emphasize the contribution of chronic stress associated with female gender roles (Nolen-Hoeksema, 1990).

Depression and MS

As in the general population, MDD is more prevalent in women with MS (28%) than in men (8%) (Patten, Metz, & Reimer, 2000). The precise etiology of the elevated rate of depression in persons with MS is not known, and a combination of psycho-social, neurobiological, and disease-related factors is likely (Goldman Consensus Group, 2005). Dalton & Heinrichs (2005) suggest that depression in persons with MS may be a psychological reaction to the uncertainty of living with an unpredictable chronic condition. Others propose the contribution of MS-related cognitive deficits and resulting social stress and problems with occupational performance (Gilchrist & Creed, 1994). Recent stressful life events and chronic stress show

an association with depression in persons with MS (Pakenham, 1999; Patten et al., 2000). Social support has a protective effect, and women with MS in one study reported less support than men with MS (Gulik, 1994), perhaps contributing to higher rates of depression in women.

A direct or indirect association between MS-related neurobiological factors including altered immune function, CNS lesions, and abnormalities in hypothalamic functioning is suggested as a reason for the excess depression seen in persons with MS (Goldman Consensus Group, 2005). The results of studies that examine the association between neurobiological pathology and depressive symptoms have yielded inconclusive results (Siebert & Abernathy, 2005). Both lesions in the right temporal region of the brain and lesions in specific regions of the left side of the brain have been associated with a greater incidence of MDD (Benesova, Niedermayerova, & Havlikova, 2003; Feinstein et al., 2004). The role of disease modifying therapies such as interferon also has come under scrutiny. Feinstein (2000) concluded that although there is evidence of an increased risk of depressive symptoms with interferon use, methodological differences in the studies, especially in how depression is defined and measured, preclude a definitive conclusion about this association. Other factors that have been examined for an association with depression are age and severity, course and duration of MS.

Severity of MS—Numerous symptoms are associated with MS and may include muscle weakness, bladder and bowel malfunction, fatigue, vision loss and changes in mood (Schapiro, 2005). Male gender, age greater than 40 at onset of symptoms, frequent attacks in the first five years after disease, and a primary progressive course are factors associated with poorer outcomes (Kantarci & Weinshenker, 2005). The literature reveals conflicting findings about the relationship between severity of MS and depression. No significant relationship was found in some studies (Huber, Rammohan, Bornstein, & Christy, 1993; Gilchrist & Creed, 1994) while others reported that depressive symptoms were associated with greater deficits in physical functioning (Janssens et al., 2003; Lobentanz et al., 2004). In a study of 50 persons with MS (52% female) Galeazzi et al. (2005) found that both higher BDI scores and the risk for MDD increased as disease severity increased. This association was unchanged when adjusted for sex. A strong association was reported by Chwastiak et al. (2002) who found that persons with more severe MS were six times more likely than those reporting minimal severity to have scores on the CES-D above the cut-off for clinically significant depressive symptoms.

One explanation for the conflicting results may be the different measures of functional limitation used in the studies. Many of these studies assessed disease severity with the Expanded Disability Status Scale (EDSS) (Kurtzke, 1983), the most frequently used measure of functional limitation in persons with MS. The EDSS has been widely criticized for its lack of sensitivity to detect change, low interrater reliability (especially at the lower ends of the scale), and the skewed distribution and ordinal nature of the resulting scale scores. Because the EDSS predominantly measures ambulation, it does not reflect many other domains of MS impairment or limitation (Coulthard-Morris, 2000). Another reason for the conflicting results may be that participants in these studies often do not report extensive limitations, and the true extent of the association with depressive symptoms may not be apparent (Dalton & Heinrichs, 2005). Finally, concern has been raised about the possible overlap between the somatic complaints of depression measured on screening instruments and symptoms of MS that may confound the association between the two factors (Goldman Consensus Group, 2005).

Course Of MS—Few studies examine the association between disease course and depressive symptoms. Most persons with MS (60%) are initially diagnosed with relapsing-remitting MS (RRMS), in which clearly defined exacerbations of symptoms are followed by partial or complete recovery, and subsequently progress over a period of years to secondary-progressive MS (SPMS) characterized by a steady worsening of symptoms with or without occasional flare-ups and remissions (Kantarci & Weinshenker, 2005). Primary progressive MS (PPMS)

is characterized by progression of symptoms from the onset of the disease, and in one large study ($n = 1259$) accounted for 12% of MS cases (Kantarci et al., 1998). “Benign” MS is associated with an extended period – usually 15 years – during which the patient remains fully functional (Lublin & Reingold, 1996) and comprises approximately 17% of persons with MS (Pittock et al., 2004). While women make up the majority (80%) of persons with relapsing MS, they comprise approximately half of those with PPMS.

In one of the few studies to examine the association between disease course and depressive symptoms in 136 persons with MS, Zabad et al. (2005) found that those with PPMS had a lower lifetime risk of major depression compared with persons with relapsing forms of the disease. The authors posit that the later onset of illness in the PPMS group may mean that social support is well established, thus conferring a protective effect for depression risk. Alternatively, an increased inflammatory component of the relapsing forms of MS may be associated with greater depression (Zabad et al., 2005).

Age—Patten et al. (2003) note that the high correlation between age and duration of MS makes distinguishing this relationship difficult in cross-sectional analyses. Patten et al. (2000) reported that persons with MS under age 35 were significantly more likely to report a history of MDD than older individuals. However, in the Galeazzi et al. (2005) study, age was not associated with either a current or past episode of MDD. Compared with older individuals with MS ($M = 70$), younger persons ($M = 46$) scored significantly higher on a measure of depressive symptoms ($t(26) = 2.41, p < .05$), indicating that they experienced more of these symptoms (Kneebone, Dunmore, & Evans, 2003).

Duration of Symptoms of MS—Some cross-sectional studies report that longer time since MS diagnosis is associated with fewer depressive symptoms (Chwastiak et al., 2002; Pakenham, 1999). This may be a function of adaptation to illness and the development of coping techniques over time that mitigate the effect of illness on the development of depressive symptoms (Dalton & Heinrichs, 2005). However, Galeazzi et al. (2005) found no significant association between duration of illness and history of MDD including a current episode, although higher BDI scores were related to duration of illness. The relationship between higher BDI scores and duration of illness was non-significant after controlling for sex (Galeazzi et al., 2005). Patten et al. (2000) reported no significant difference in duration of illness (since onset of symptoms) for participants with a lifetime history of major depression and those without such history.

Stability of Depressive Symptoms Over Time—The limited data from longitudinal studies of depression in persons with MS do not provide a clear picture of the trajectory of depressive symptoms over time. Arnett and Randolph (2006) studied 53 persons with MS at two time points three years apart. Approximately half of the participants had scores in the mild-moderate range or above on the Beck Depression Inventory (BDI) at time 1, and mean scores did not significantly change between the two time points. Mean BDI scores also did not significantly change over the course of one year in a sample of 98 persons with MS (Schreurs, de Ridder, & Bensing, 2002). However, Amato et al. (1995) reported that mean scores on the Hamilton Rating Scale for Depression significantly increased between baseline and a second evaluation four years later in sample of 50 persons with MS. At the ten-year follow-up, the mean depression score for the remaining 45 participants was 14.22 compared with a mean score of 14.91 at the four-year follow-up (Amato, Ponziani, & Siracusa, & Sorbi, 2001). The small sample size of these studies, and the limited time of follow-up for most of them, precludes definite conclusions about depressive symptoms over time.

Method

Procedure

The data for this analysis were collected during an ongoing longitudinal study of health promoting behaviors and quality of life of individuals with MS (Stuifbergen, Blozis, Harrison, & Becker, 2006). Participants for the longitudinal study were initially recruited in 1999 from a group of individuals who had participated in an earlier cross-sectional survey. The 621 participants who consented to participate in the longitudinal study have received a questionnaire each year unless they requested to be dropped from the study, reported a change in diagnosis, died, or became too ill to participate or were lost to follow-up. The response rate to the annual survey (1999–2005) ranged from 85.3% to 89.6%. All phases of the study received institutional review board approval, and institutional review board approval was received prior to annual data collection.

Sample Characteristics

This analysis considered data from 607 persons who responded to the annual surveys (14 of the original 621 participants subsequently reported that they had been misdiagnosed with MS and were dropped from the analyses). At the start of the longitudinal study in 1999, the average age of respondents was 50.6 (SD = 10.28) and the mean time since diagnosis ranged was 13.3 years (SD = 7.4). Seventeen percent were male, and the majority (92.6%) reported their race as Caucasian. Most participants were married (72%) with at least 12 years of education (83.7%). Thirty-two percent were unemployed due to disability. The type of MS reported most frequently was relapsing-remitting MS (40%) followed by primary progressive (18%), secondary progressive (17%) and benign sensory (10%). The Time 1 mean score on a measure of functional limitations (M=18.36, SD=10.06) indicates that as a group this sample did not report extensive functional limitations. Initial mean scores on a screening instrument for depressive symptoms (Mean=10.01, SD=6.34) met the cut-off for clinical significance. At time 1, 41% of the sample had scores of 10 or greater on the CESD, indicating clinically significant depressive symptoms. There was no significant gender difference in either functional limitations or depressive symptoms at time 1.

Instruments

The survey instruments were in booklet form to facilitate completion in participants with fine motor limitations and a 14-point font enhanced readability. The following measures were used in this analysis:

Demographic Information—Information on age, ethnicity, education level, marital status, employment, and economic status was collected in a background information sheet at each data collection point.

MS Related Factors—Type of MS, duration of MS symptoms, and age at MS diagnosis were obtained from data collected during the first survey.

Depressive Symptoms—The self-rating ten-item Center for Epidemiological Studies Depression Scale (CESD-10) (Andresen, Malmgren, Carter, & Patrick, 1994) is a short version of the 20-item Center for Epidemiological Studies Depression Scale (CES-D) (Radloff, 1977). The CESD-10 is designed to screen for depressive symptoms in primary care settings. Items are rated on a four-point scale from “rarely or none of the time” (less than 1 time per day) to “most or all of the time” (5–7 days) regarding how often each item was experienced in the last week. Examples of items are “I was bothered by things that usually don’t bother me” and “I felt depressed.” Scores range from 0–30, and higher scores indicate greater depressive symptoms. A cut-off score of 10 is suggested to indicate symptoms that may be clinically

significant. Andresen et al. (1994) reported evidence for discriminant and convergent validity and a test-retest reliability coefficient of .71 for the CESD-10. The Cronbach alpha for the CESD-10 for this sample was .85 at Time 1.

Disease Severity—The Incapacity Status Scale (ISS) (Kurtzke, 1981) evaluates functioning related to the ability for various aspects of self-care, ambulation and vision. The ISS was adapted to a self-administered format from a structured interview for use in the longitudinal study (Stuifbergen & Becker, 2001). The ISS contains 16 items rated on a 5-point scale from 0 (normal functioning) to 4 (complete inability). Scores range from 0 – 64 with higher scores indicating greater perceived functional limitation. Kurtzke (1981) provided data supporting construct validity of the measure. Stuifbergen, Becker, Blozis, Timmerman and Kullberg (2003) reported internal consistency reliability (Cronbach alpha coefficients) of .83 and .89 for the adapted ISS in a sample of community-residing women with MS. The Cronbach alpha for the ISS for this sample was .88 at Time 1.

Data Analysis

MPLUS 4.0 software was used to estimate latent growth curve (LGC) models (Muthen & Muthen, 2005). Compared to traditional repeated measures analysis of variance, LGC modeling is a more advantageous statistical technique for a number of reasons (Kline, 2005; Rakov & Marcoulides, 2006). First, this multivariate, structural equation modeling approach allows for the estimation of intraindividual trajectories of change in depression over time. Within a conventional ANOVA framework, these differences are typically treated as error variance. However, the flexibility of LGC techniques allows for the estimation of an extensive array of parameters such as linear and nonlinear effects and their corresponding variances and covariances. Second, LGC analysis allows the user to estimate measurement error. The underlying assumptions of conventional strategies such as ANOVA imply that the error variances associated with repeated measures are both equal and independent across individuals. Under many circumstances, these assumptions are often violated in behavioral and social research. By using LGC modeling, users can effectively model measurement error and thus more accurately estimate change over time.

LGC is also a favored strategy in longitudinal studies because of the way in which researchers can handle missing observations. A researcher analyzing longitudinal data with missing observations using conventional repeated measures ANOVA is limited to basic mean substitution (a limited estimate of the individual's score) or listwise deletion (dropping cases from the analyses that do not have all data points). In contrast, a program like MPLUS estimates missing data using full information maximum likelihood estimates (FIML). If a participant has valid data for at least 4 data points, FIML can be used to estimate missing data points, thus, allowing the researcher to make use of all available data.

When the LGC models were examined, four indicators of model fit were evaluated to determine the overall quality of the models. While there are numerous fit indices to choose from, the indices reported here have often been reported and recommended in the current SEM literature (Boomsma, 2000; McDonald & Ho, 2002). These indicators include chi-square values, the Tucker-Lewis Index (TLI), the comparative fit index (CFI), and the root-mean square error of approximation (RMSEA). Within an SEM framework, non-significant chi-square values are indicative of good model fit. However, because chi-square values are typically influenced by large sample sizes, other indices should be considered when fitting structural equation models (Kline, 2006). The TLI and CFI represent good fit model if the values are equal to .90 or higher. Values of .05 or less for the RMSEA represent adequate model fit (Bentler, 1990; Steiger, 1990).

Findings

Latent Growth Curve Models

A series of LGC models were examined to assess change in depressive symptoms. The analytical strategies involved three stages: 1) the estimation of LGC models to determine the trajectory of depression for an MS sample; 2) an analysis of additional models to address predictors or covariates of change in depression over time; and 3) the analysis of a time-covariant model that examined the impact of functional limitations on depression across all seven time points. We began the analysis by examining the most parsimonious model, which included a two factor LGC model of linear change in depression scores. The model is defined as follows:

$$Y_{ij} = \pi_{0j} + \pi_{1j}t_{ij} + r_{ij}$$

In this model, Y_{ij} reflects the depression score for each person (j) at time i . The intercept for person j is represented by π_{0j} and the individual slopes are represented by π_{1j} . Annual depression scores are represented by t_{ij} where i indicates the corresponding annual depression score for person j . The model was fitted to the data and while some indicators of fit are well within the acceptable ranges, ($\chi^2(23) = 69.04$, $p < .001$, CFI = .98, TLI = .98 and RMSEA = .06), the RMSEA is larger than the optimal value ($< .05$).

An examination of randomly selected empirical growth plots suggested that the trajectory of depression for the sample was nonlinear. Thus, the next step in the analysis involved fitting models to test for nonlinearity. While a two-factor linear model is the most parsimonious among LGC models, fitting such models is not the most ideal approach when the time intervals between outcome measures extend for longer periods of time. For this reason, the shape of the trajectory in depression scores may best be described as a function of nonlinearity (Du Toit & Cudeck, 2001). A three factor latent variable model that includes an intercept, conditional slope, and quadratic slope was tested. Figure 1 depicts the three-factor LGC model of trajectories of depression for the MS sample. The three-factor latent variable model was tested and the results yielded significant improvement in model fit: $\chi^2(18) = 21.578$, $p = .2512$, CFI = .998, TLI = .998 and RMSEA = .02. Table 1 depicts the standardized covariances among the slope, intercept, and quadratic latent variables. These estimates represent the relationship between individual differences in depression scores and the rate of change in depression over time. The covariance estimate associated with the intercept and slope suggest that depression rates start high and then taper off across time. The covariance between the conditional slope and the quadratic slope implies that higher depression scores at Time 1 were associated with a higher rate of decline in depression scores over time.

Predictors of Change in Depression

We examined predictors in change of depression by regressing the intercept, conditional slope and quadratic slope on the predictors of interest. These findings suggest that high initial levels of depression were related to younger age ($-.188$), length of time since diagnosis of MS ($-.127$), type of MS ($-.098$), and extent of functional limitations at Time 1. Overall, these variables accounted for 25% of the variance in the intercept or initial depression scores. All predictors were significant except for gender. There is some evidence that women reported slightly higher levels of depression scores than men. However, gender was not a significant predictor of initial levels of depression nor did it appear to have an impact on intraindividual changes in depression over time.

Time-Covariate LGC Models

Our final research question pertains to whether or not change in functional limitations is related to change in depressive symptoms over time. The overall trend in depressive symptoms is

similar to the basic quadratic model. In other words, initial depression scores start at a high level and then slowly decline over time. However, in years when functional limitation levels increased, the trajectories of depressive symptoms may actually increase. This is indicated by the significant impact that each annual measurement of functional limitations has on the conditional and quadratic slope.

Discussion

We set out to evaluate changes in depressive symptoms over a seven-year period among person with MS and examine the moderators of change in these symptoms over time. Several factors about our large sample are worth noting: participants in studies of depression and MS are frequently drawn from specialty clinics. Ours was a convenience sample recruited through local chapters of the National MS Society in the southwestern United States, and persons who are members of the national organization may have different characteristics than a clinical population. It is also important to note that our participants entered this study at various times in their illness trajectory, and thus our Time 1 data are not baseline data at onset of MS but reflect differences in illness duration among participants.

Our first research question addressed change in depressive symptoms over time. Previous research studies with relatively small samples sizes have shown conflicting results about the stability of these symptoms over time. During the seven-year study period, depression scores in our sample (N=607) did not vary significantly, nor was the pattern of change linear. This indicates that depressive symptoms fluctuated over time for individuals but did not show a tendency to an overall increase or decrease for the group as a whole.

Our second research question asked if age, type of MS, years since MS diagnosis, and functional limitation at time 1 impacted the trajectory of depressive symptoms. Although younger age, longer duration of MS, progressive forms of MS and greater extent of functional limitation were predictive of greater depressive symptoms at time 1, with the exception of functional limitation these variables did not predict the changes in depressive symptoms over time. At all time periods, greater functional limitation was associated with greater depressive symptoms. Two potential mechanisms have been proposed for this association: adverse changes in functional status may trigger increased stress, or, alternatively, there may be a common physiological mechanism associated with both greater functional limitations and depressive symptoms. It is worth noting that our sample in general did not report extensive functional limitations on the ISS. However, the fact that greater extent of functional limitation predicted change in depressive symptoms during all time points has important implications for clinicians. The results of this analysis suggest that change in functional status, regardless of the amount, is associated with greater depressive symptoms. Initiation of contact with health professionals is often caused by exacerbation of symptoms, thus creating an opportunity for nurses to screen for the presence of depressive symptoms.

Our finding that younger age, progressive forms of MS, and greater duration of MS at time 1 were predictive of initial depressive symptoms finds mixed support in previous research findings. First, we confirm the findings of Patten et al. (2000) that younger age is associated with greater depressive symptoms. MS is usually diagnosed between the ages of 20 – 40, a time of life when people are actively engaged in work and family responsibilities. Having unpredictable and chronic symptoms coupled with the life-stage demands of early adulthood may influence levels of depressive symptoms through stress and coping mechanisms. Greater duration of MS at time 1 also was predictive of greater initial depressive symptoms, lending support to previous studies that reported this association. As neither age nor duration of MS affected changes in depression scores over the seven years, and scores tended not to greatly

vary over time, our findings suggest that all persons with MS should have depression screening as part of the early diagnostic process.

Regarding the association between type of MS and depressive symptoms, our findings are in opposition to those of Zabad et al. (2005) who reported that progressive forms of MS were associated with lower rates of MDD. We found that progressive forms of illness were associated with greater depression. However, the depression measures were not equivalent as we used a screening tool to assess depressive symptoms rather than a clinical diagnosis of MDD. Our findings may also reflect our decision to create two illness course categories, non-progressive and progressive, for the purposes of data analysis. We combined primary progressive MS (PPMS) and secondary progressive MS (SPMS) into one category for analysis. However, persons with SPMS may share more characteristics with persons who report RRMS because most persons initially are diagnosed with RRMS and eventually progress to SPMS.

Our third research question addressed the correlations between characteristics of change in functional limitations and depressive symptoms after accounting for the effects of age, gender and years since MS diagnosis. We report that these variables did not influence the relationship between functional limitation and depressive symptoms over the seven-year study period. The finding that depressive symptoms were not more prevalent in women, and that gender did not influence the trajectory of depressive symptoms, deserves mention. Although there was a trend for women to have higher mean depression scores than men, this difference was not significant either at Time 1 or over the seven years, as might be expected based on most previous research. It may be that the experience of having a chronic illness in some way overrules the usual female predominance of depression. Or, our findings may reflect the fact that greater depression was associated with progressive forms of the illness, and a greater percentage of men than women in our sample had progressive forms of the illness. Finally, perhaps the men in our sample were in some way different from those recruited through specialty clinics.

Conclusion

We are unaware of other longitudinal studies with a comparable sample size that examines depressive symptoms over time in persons with MS. Our finding that 41% of the participants had initial CES-D scores meeting the threshold of clinical significance underscores the extent to which persons with MS are vulnerable to depression and associated adverse effects. The fact that depression was equally prevalent for women and men indicates that all persons with MS face multiple physical and emotional challenges associated with living with an unpredictable disease that has no cure. It is unclear if the association between functional limitations and depressive symptoms throughout the study period reflects the disease process itself or is related to situational factors. Further research is needed to clarify this association. Regardless of the cause of depressive symptoms, careful assessment by health professionals for depression in persons with MS and the timely initiation of appropriate treatment is important to maintain quality of life for these individuals.

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χ^2 = chi-square

CFI = Compative Fit Index

TLI = Tucker Lewis Index

RMSEA = Root Mean Square Error of Approximation

* $p < .05$

Figure 1.

Latent growth curve model of depression across seven time points, $\chi^2_{(18)} = 21.578$, $p = .2512$,
CFI = .998, TLI = .998, RMSEA = .02

χ^2 = chi-square

CFI = Compative Fit Index

TLI = Tucker Lewis Index

RMSEA = Root Mean Square Error of Approximation

* $p < .05$

Table 1
LGC Model of Depressive Symptoms with Functional Limitations as a Time-Varying Covariate

Parameter	Unstandardized Estimate	Standardized Estimate	Sig.
Growth Parameters			
Mean Intercept	11.496	2.329	p < .01
Mean Conditional Slope	-0.312	-0.201	n.s.
Mean Quadratic Slope	0.059	0.227	n.s.
Intercept Variance	21.588	0.886	p < .01
Conditional Slope Variance	2.381	0.988	p < .01
Quadratic Slope Variance	0.067	0.986	p < .01
Time Invariant Parameters			
Age at Time 1---> Intercept	-0.100	-0.207	p < .01
Length of Illness at Time 1---> Intercept	-0.089	-0.134	p < .05
Type of MS at Time 1---> Intercept	-0.992	-0.100	p < .05
Time Varying Parameters			
Limits at Time 1---> CESD Time 1	0.270	0.434	p < .01
Limits at Time 2---> CESD Time 2	0.294	0.462	p < .01
Limits at Time 3---> CESD Time 3	0.281	0.459	p < .01
Limits at Time 4---> CESD Time 4	0.280	0.457	p < .01
Limits at Time 5---> CESD Time 5	0.269	0.444	p < .01
Limits at Time 6---> CESD Time 6	0.276	0.439	p < .01
Limits at Time 7---> CESD Time 7	0.263	0.444	p < .01

Model: $\chi^2_{76} = 95.491$, $p = .0648$, $CFI = .992$, $TLI = .990$, $RMSEA = .02$