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Selected Health Behaviors Moderate the Progression of Functional Limitations in Persons with Multiple Sclerosis: Eleven Years of Annual Follow-Up

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Abstract

Background—Multiple sclerosis (MS), a chronic neurological disease typically diagnosed in young adulthood, presents with a wide variety of symptoms, impairments and functional limitations. Given the chronic, unpredictable and long-term nature of this disease, preserving function is essential.

Objective—The purpose of this study was to identify psychosocial and behavioral factors that might influence the trajectory of functional limitation through eleven years of longitudinal follow-up of a sample of persons with MS.

Methods—Participants (N=606) completed measures of health behaviors, related constructs and functional limitations annually over eleven years. Longitudinal measures of functional limitations were analyzed using random-effects regression that allows for study of individual differences in the trajectories of a measure. Using the best fitting quadratic growth model, we tested the within and between-person effects of Nutrition, Interpersonal Relationships, Exercise, Stress Management, Health Responsibilities, Spiritual Growth, Self-Rated Health and Barriers, controlling for Age, Year since Diagnosis and Year of Dropout, on Functional Limitations in the 11th year.

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Results—After adjusting for covariates, higher mean scores for Exercise and Self-Rated Health were related to lower levels of Functional Limitations in Year 11. Higher mean scores for Stress Management, Health Responsibilities and Barriers were related to higher levels of Functional Limitations in Year 11. Higher mean Exercise scores and lower mean Health Responsibilities scores were related to slower rates of progression of functional limitations in Year 11.

Conclusion—Findings suggest that the highly variable trajectory of functional limitations in MS may be extended and shaped through health behavior strategies.

Keywords

Multiple Sclerosis; functional limitations; health behaviors

Introduction

According to current estimates, approximately 400,000 persons in the United States and 2.5 million worldwide live with multiple sclerosis (MS) [1 http://ghr.nlm.nih.gov/condition/multiple-sclerosis, 2013). This immune-mediated disease is characterized by the destruction of the myelin insulating the axons thus interfering with electrical conduction within the nervous system where axon damage and death may also occur [2]. MS is typically diagnosed in young adulthood; over time varying patterns of demyelinating lesions produce virtually infinite symptom combinations, impairment, and functional limitation. Although there may be long periods of time with few or no symptoms, it is now recognized that the disease is neurologically active in most persons with MS most of the time.

The last twenty years have brought major advances in understanding of the pathological changes of MS alongside an array of new disease-modifying medications. However, limited information about how individual behaviors and choices may serve as potential *moderators of* the course of the disease-related limitations [3,4] results in a key question for those with MS as well as clinicians and researchers interested in developing interventions to preserve function [5], prevent disability and promote quality of life: What factors (other than the biological disease) influence the development of functional limitations? The primary purpose of this study was to identify psychosocial and behavioral factors that might influence the trajectory of functional limitation through eleven years of continual longitudinal follow-up of a sample (N=606) of persons with MS.

Background

Ideal studies assessing the potential moderating effects of health promoting behaviors on functional limitations would follow large samples of persons newly diagnosed with MS, consider type of MS and use of disease modifying medications, and assess the influence of multiple health behaviors on functional limitations over an extended period of time. While studies sharing all of these characteristics do not presently exist, there is a growing body of literature providing indirect support for the moderating effects of health behaviors. Experimental studies (typically with small samples and brief follow-up) provide limited evidence that specific health behaviors may moderate the trajectory of limitations. One systematic review of 27 studies concluded that evidence supports possible disease-modifying

effects of exercise or physical activity [5] and a second review of 54 studies found that while there was moderate evidence that exercise improved aerobic capacity and muscular strength, there was not consistent evidence that exercise-training programs improved mobility, fatigue or health related quality of life for persons with MS [6]. Similarly, two recent Cochrane reviews found little data to support specific dietary strategies as disease modifying therapies in MS [7,8].

Prospective natural history studies of persons with MS tend to have larger samples and longer follow-ups, but most have addressed only biological (e.g. age, gender) or clinical (duration of MS) variables that provide only limited explanatory power for the progression of functional limitations [9,10,11,12,13]. In a widely cited study conducted before the advent of disease-modifying medications, Weinshenker and colleagues found that 50% of persons with MS require the use of an assistive device for walking 15 years after diagnosis and 10% require a wheelchair to support mobility [14]. Recently published studies with assessments over five to eleven years have explicated more nuanced changes in functional limitations, disability and quality of life (3,15,16). In one study, those with the lowest disease severity at the initiation of the study experienced the greatest increases in disability and decreases in quality of life over time (15). Other investigators (3,16) reported measures of walking, manual dexterity, activities of daily living and cognition reflecting deterioration over time while indicators of mood, social functioning and emotional well being remained stable or improved.

To date, only a few cross-sectional studies have considered health-promoting behaviors, continuing behavioral, cognitive, and emotional efforts to sustain and improve health and well being [17], as potential moderators of the progression of functional limitations [18,19]. For example, D'hooghe and colleagues found that participants (N=1,372) with relapsing onset MS who reported more frequent health promoting behaviors (physical activity, nutrition and spiritual growth) had a reduced risk of reaching an Expanded Disability Status score of 6 (requiring a cane for mobility) compared to a reference group [19].

The few prospective longitudinal studies to date assessing health behaviors and functional limitations in MS have had relatively small samples, limited length of follow-up (6 months to 5 years) and have assessed the impact of a single health behavior over time. In a 6-month longitudinal study with 276 persons with MS, Motl and McAuley found that change in physical activity was associated with changes in function, quality of life and selected symptoms [20,21]. Stuifbergen and colleagues followed a large sample of persons with MS (N=606) for five years and reported that rates of change in functional limitation correlated negatively with rates of exercise behavior and quality of life ratings [4].

The study reported here extends the follow-up of the sample from that earlier study [4] to an 11-year time period and explores the impact of multiple health behaviors (physical activity, healthy eating, stress management, supportive interpersonal relationships, health responsibility and spiritual growth) as moderators of the progression of functional limitation. Specifically, this study aims to test the within-person and between-person effects of health behaviors on functional limitations over an 11-year period. Two hypotheses were proposed:

1. Healthy behaviors are related to lower functional limitations levels within any given year; and

2. Healthy behaviors, averaged across time, are related to lower functional limitations levels and to a slower rate of progression in functional limitations at the end of the 11-year time period.

Methods

This longitudinal study followed a large sample of community residing persons with physician-diagnosed MS over an eleven-year period. Participants completed self-report measures of health behaviors, related constructs and functional limitations annually through a mailed survey. The study design was consistent with the IOM recommendations for longitudinal studies with persons with MS, as it did not rely on a small sample from specific subpopulations (e.g. clinic or support group), did not focus on a single issue, and included groups of persons with MS who may have markedly different limitations [22].

Data Collection Procedures

Study information and consents for this longitudinal study were mailed to 749 persons with MS who had participated in an earlier cross-sectional study [23]. Those who returned questionnaires (N=621; 84%) were enrolled in the longitudinal study and received study surveys over each of the following eleven years. Participants received two follow-up reminders and a new questionnaire if they did not respond in 30 days. The annual surveys were not sent to those requesting removal from the study, those who had died and those who were lost to follow-up. During the 11 waves of data collection reported here, response rates ranged from 83.1 to 89.6 % of eligible respondents. All aspects of this study were reviewed and approved by The University of Texas at Austin Institutional Review Board.

Measures

Barriers—Individual perceptions of the intrapersonal, interpersonal, and environmental factors that inhibit health-promoting behaviors were measured by the Barriers to Health-Promoting Activities for Disabled Persons Scale [24]. This 18-item scale asks respondents to indicate on a 4-point scale, from 1 (*never*) to 4 (*routinely*), how often the listed barriers keep them from taking care of their health. Higher scores indicate more perceived barriers. In addition, there is evidence the tool discriminates between disabled and non-disabled individuals in terms of barriers to health promoting activities. Cronbach's alpha for the barriers scale in our sample ranged from .82 to .90 across the 11 time points.

Self-Rated Health and Health Promoting Behaviors—A single item "How would you rate your overall health at the present time?" was used to measure self-rated health. Responses ranged from 1 (Poor) to 4 (Excellent) [25]. Health-Promoting Behaviors were operationalized with the Health-Promoting Lifestyle Profile II (HPLPII), a 52-item scale that assesses the frequency with which individuals report engaging in activities directed toward increasing their level of health and well-being. Responses are scaled from 1 (*never*) to 4 (*routinely*). This instrument has six subscales (Physical Activity, Spiritual Growth, Health Responsibility, Interpersonal Relations, Nutrition, and Stress Management). Reliability and

validity of the HPLPII have been supported in psychometric testing with a sample of 712 adults [26]. Evidence supports the use of the HPLP as a valid measure of health behavior in persons with MS [27]. Cronbach's alpha for the HPLPII Total and Subscales ranged from .75 to .95 over all measurement points.

Functional Limitations—This study used a self-report version of the Incapacity Status Scale (ISS) to provide a measure of functional limitations. A panel of international MS experts thoroughly evaluated this scale for use as an indicator of disability for MS, and Kurtzke has presented data supporting its construct validity [28]. Each of the 16 personal functions is rated on a 5-point scale, with 0 indicating normal or no difficulty with the activity and 4 indicating a complete inability to perform the activity. Total scores reflect limitations in a wide range of functions (ambulation, dressing, bathing, eating, fatigue, mood, cognition) and can range from 0 to 64. Total scores on the ISS were significantly related to performance measures of ambulation (r= −.49) and upper extremity coordination and control (r=−.57), and the pattern of change over time in most scores on the ISS self-report and performance measures of functioning was similar [4,29]. Cronbach's alpha for the total ISS score ranged from .82 to .88 across the time points.

Data Analysis

Longitudinal measures of functional limitations were analyzed using random-effects regression to study change in functional limitations over an 11-year period and test within-person and between-person effects of health promoting behaviors (Nutrition, Interpersonal Relationships, Exercise, Stress Management, Health Responsibilities, Spiritual Growth), self-rated health and barriers on characteristics that described change in functional limitations [30].

First, a growth model was developed to describe the form of change in functional limitations. To do this, four growth models were applied. The first assumed that scores did not change over time ("No Growth"). The second assumed that scores changed at a constant rate ("Linear Growth"). The third and fourth models allowed scores to change at a non-constant rate. Specifically, the third model used a quadratic function ("Quadratic Growth") that allowed scores to increase (or decrease) to a maximum (or minimum), followed by a decrease (or increase) [31]. The fourth model was based on an exponential function ("Exponential Growth") and included an asymptote so that scores could tend toward a stable level. An exponential growth model allows scores to increase (or decrease) initially and then level off to a stable level.

The four growth models were applied to the functional limitations scores. The year of measurement, denoted as *Year*, represented time. To study the effects of the predictors on functional limitations in the last year of measurement, Year was centered to the 11th year. Thus, Year was coded as Year = −10, −9, …, −1, 0. The intercept of a growth function represents the response at time = 0. Thus, for the models tested here, the intercept represents functional limitations at the 11th year. Given this centering of Year, it was possible to test the effects of health behaviors on the level of Functional Limitations at the last wave of data collection. Although not all individuals were measured in the 11th year, a random-effects

model makes it possible to estimate the effect of these variables on the predicted level of Functional Limitations in the 11th year.

Each model included random effects for the coefficients that defined the growth function. By including random effects in a model, the growth coefficients are unique to each individual [32]. Three indices of model fit, the AIC, AICC, and BIC, were used to compare the relative fit of the models and deviance tests were used to compare nested models. These indices do not require that the models are nested for comparisons. Smaller index values indicate better fitting models. The model with the smallest values across indices was taken as the best fitting growth model.

As is described in the Results section later, the Quadratic Growth model provided the best fit to Functional Limitations scores, and so this model is described in detail here (also see [31] [32] for depictions of quadratic growth models). The model included a random intercept, linear time effect, and quadratic time effect:

$$Y_{ij} = \beta_{0i} + \beta_{1i}\text{year} + \beta_{2i}\text{year}^2 + \varepsilon_{ij}$$

where y_{ij} is the Functional Limitations score in year j for individual i. The coefficient β_{0i} is the individual's expected level of Functional Limitations in Year 11 due to the centering of Year at the 11th year. The coefficient β_{1i} is the individual's expected linear rate of change in the 11th year. The interpretation of the linear time effect at the 11th year is due to the centering of Year. In a quadratic growth model, the rate of change is not constant over time as it is in a linear growth model, and the linear effect of time is the rate of change (i.e., the slope) in an outcome at a specific point in time [34]. Given the centering of Year at the 11th year, the linear time effect is the rate of change in functional limitations in the 11th year. We refer to this effect as the rate of progression in functional limitations in the 11th year. The coefficient β_{2i} and represents the rate of acceleration (or deceleration). If the quadratic effect is positive, then the curve is shaped upwards; if the effect is negative, then the curve is shaped downwards. Finally, ε_{ij} is the residual of the regression. The residuals were assumed to have an autoregressive pattern over time [33].

Dropout and Missing Data—Random-effects models allow for incomplete response data. If some data are missing, inference is valid if the data are missing at random. This assumption is less restrictive relative to complete-data methods, such as repeated-measures ANOVA, that require that data are missing completely at random [34]. Although annual measures of Functional Limitations were planned for an 11-year period, some individuals had incomplete data, and for some, the data were missing in a monotone fashion such that a participant missed a measurement year and provided no additional data in later years. For the remaining participants with incomplete data, the data were missing intermittently. Monotone patterns of missing data were addressed by creating a variable, henceforth called Year of Dropout, that was equal to the year at which a participant no longer provided additional data. Year of Dropout was equal to 0 if a participant dropped from the study after the first year, 1 if a participant dropped after the second year, and so on, up to a value of 10 to represent those who did not drop from the study by the 11th year. Lower scores indicated

earlier dropout times. Intermittently missing data were assumed to be missing at random [30, 35].

Predictor variables that were also measured annually were averaged across years to represent a participant's mean predictor response across the 11 years. We refer to these mean scores as the predictor mean scores. The predictor mean scores were included in the growth model at the second level to estimate the between-person effects of these variables. Some individuals were missing predictor variables in patterns that were similar to missing Functional Limitations scores. Thus, prior to creating the predictor mean scores, multiple imputation was applied to the data. Multiple imputation is valid if data are missing at random. A total of 30 imputed data sets were generated, following recommendations in Graham, Olchowski, and Gilreath [36]. Along with longitudinal measures of Functional Limitations, the imputation included Age, Years Since Diagnosis, Year of Dropout, and the longitudinal predictor variables. After the imputation, the person-level predictor means were created for inclusion in the data analyses.

To address the first aim to test within-person effects of health behaviors, annual health behavior measures were used as predictors of annual measures of Functional Limitations. To address the second aim to test the between-person effects of health behaviors, predictor mean scores were used as predictors of Functional Limitations levels in Year 11 and the rate of progression in Functional Limitations at Year 11. Both sets of analyses controlled for Age, Years Since Diagnosis and Year of Dropout. Health behavior measures were centered about the individual's predictor mean scores to allow estimation of the within-person effects [31]. Years Since Diagnosis was centered about the sample mean of 10.6 years, and Age was centered about the sample mean age at the first measurement year of 50.57 years. Two-tailed tests with $\alpha = .05$ were used to test these effects. PROC MIXED with SAS version 9.4 was used for the analysis.

Results

The sample used for the analyses and described below included 606 persons with MS (15 of the original participants were not included as they reported being mis-diagnosed with MS). At the start of the longitudinal study, the participants ranged in age from 21 to 81 (mean 50.57, SD=10.28). Consistent with most studies of persons with MS, the majority of participants were female (83%), white/non Hispanic (93%), and married (72%). In general the study participants were well-educated as 85% had completed high school and 35% had completed college. Participants had been diagnosed by a physician for an average of 13.4 years (SD 7.44) and 25% were currently employed full-time. (See Table I).

Among the growth models fitted to the longitudinal measures of Functional Limitations, the Quadratic Growth model had the lowest values for all fit indices. Deviance tests also indicated that this model was best-fitting. This model was selected to represent longitudinal measures of Functional Limitations. Maximum likelihood estimates with 95% confidence intervals are given in Table 2. These include estimates of the growth model's coefficients, effects of covariates (Age, Years Since Diagnosis, and Year of Dropout), within-person effects of the health behaviors on functional limitations over the 11-year period, and the

between-person effects of the health behaviors on Functional Limitations at Year 11 and on the rate of disease progression at Year 11.

Within-person effects of health behaviors

Adjusting for the effects of the covariates, higher Spiritual Growth scores was related to lower Functional Limitations within years and across the 11-year period. No other within-person effects were significant (Table 2).

Between-person effects of health behaviors

Adjusting for the effects of the covariates, higher mean scores for Exercise and Self-Rated Health were related to lower levels of Functional Limitations in Year 11. Higher mean scores for Stress Management, Health Responsibilities and Barriers were related to higher levels of Functional Limitations in Year *11*. Mean levels of Nutrition, Interpersonal Relationships and Spiritual Growth were not related to Functional Limitations in Year 11. With regard to the rate of Functional Limitation progression in Year 11, higher mean Exercise scores and lower mean Health Responsibilities scores were related to slower rates of progression of functional limitations in Year 11. No other between-person effects on the rate of disease progression in Year 11 were significant.

Discussion

This study sought to identify psychosocial and behavioral factors that might influence the trajectory of functional limitations for persons with MS. As expected, years since diagnosis and age were related to functional limitation. Only one health behavior, scores on the measure of spiritual growth, was significantly related to functional limitations consistently over the 11-year period. After adjusting for covariates, five of the eight health-related constructs examined in this study were significant predictors of the level of functional limitations at Year 11. However, the nature of the relationships varied. To our knowledge, the findings reported here are from one of the largest samples and lengthiest longitudinal studies of health promotion and functional limitations in persons with MS.

This analysis is more complex than our earlier work [4] as it examines a wider range of health promoting constructs and reveals a corresponding multifaceted set of relationships. With regard to the within person effects tested in Hypothesis I, scores on the measure of spiritual growth, were significantly related to functional limitations over the 11-year period. That is, from one year to the next, higher levels of spiritual growth were related to lower functional limitations. While use of positive attitudes to adapt may help stave off functional limitations, it is also possible that those who engage in more spiritual growth-related health behaviors (sample items: 'am aware of what is important to me in life' and 'feel connected to a force greater than myself') may perceive their growing impairments as less limiting.

Hypothesis 2 addressed whether health behaviors averaged across time were related to lower levels of functional limitation and the rate of change at the end of the 11-year time period. Consistent with the bulk of literature about health promoting behaviors and functional limitations in MS, the higher mean scores on exercise and self-rated health across the 11 years were related to lower levels of functional limitations at Year 11. By contrast, higher

stress management, health responsibility and barrier scores were associated with higher functional limitation scores. Perhaps, individuals with MS use stress management and health responsibility strategies to address or mitigate their functional limitations. In addition, exercise (higher) and health responsibility (lower) scores were associated with slower <u>rates</u> of functional limitation progression. Consistent with recent Cochrane reviews [7,8], self-reported nutrition behaviors had no effect on functional limitations at Year 11 or the rate of progression.

The variability of both the nature of limitations in MS and the course of the disease within and between individuals required the use of complex statistical procedures to accurately capture both the trajectory of functional limitations over time and the potential moderators. While many commonly used analyses assume linear rates of change, we found that change in functional limitations was best described in this sample with a quadratic function suggesting that the rate of change in functional limitation was not constant across time. Further, the random-effects regression analyses indicated individual differences in the coefficients that described change in functional limitations. These empirical findings are consistent with the widely reported clinical observation of the individualized, inconsistent, and unpredictable rate of change in functional limitations experienced by those with MS. The failure of earlier studies to identify strong clinical predictors of disease progression may be due, at least in part, to not incorporating non-linear rates of change and random effects models in the analyses.

Findings from this study must be interpreted with some caution as they rely on responses from a convenience sample of individuals who may be more interested in health behaviors than the general population of persons with MS. Participants had been diagnosed for varying amounts of time at the start of the study, thus the rates of change cannot be anchored to the time of diagnosis. As a large survey, this study relied on self-reports of functional limitations, health behaviors and related constructs. While there are limitations associated with this approach, these must be balanced with the feasibility of examining these constructs in a large geographically dispersed sample. In that sense, our findings are complimentary to focused assessments of health behaviors and functional performance using smaller samples [29]. In addition, the length of follow-up (11 years) exacerbated a challenge faced by all longitudinal studies, the attrition of participants. While there was a consistently high response rate from active participants, there was an expected loss of participants over time due to death and increasing impairment. The analysis of covariates demonstrates that in a longitudinal study of this nature it is important to account for the time at which participants end their participation.

Conclusion

Overall, findings suggest that there is considerable variability in how functional limitations are experienced among persons with MS. The unpredictable trajectory of MS illustrated here underscores the ongoing adaptation efforts required of persons with MS. While this descriptive longitudinal study identified health behaviors as statistical and temporal predictors of functional limitations, we are unable to directly address cause and effect. However, the findings from this study, when considered within the context of existing

evidence across multiple studies, suggest that strategically engaging in positive health behaviors may be a response that shapes the trajectory of functional limitations in MS.

Acknowledgments

References

1. National MS Society Multiple Sclerosis information sourcebook. New York: Information Resource Center and Library of the National MS Society; 2005.

2. Trapp BD, Peterson J, Ransohoff RM, Rudick R, Mork S, Bo L. Axonal transection in the lesions of multiple sclerosis. N Engl J Med. 1998; 338(5):278–285. [PubMed: 9445407]

3. Chruzander C, Johansson S, Gottberg K, Einarsson U, Fredrikson S, Holmqvist LW, Ytterberg C. A 10-year follow up of a population-based study of people with multiple sclerosis in Stockholm, Sweden: changes in disability and the value of different factors in predicting disability and mortality. J Neurol Sci. 2013; 332(1–2):121–127. [PubMed: 23896259]

4. Stuifbergen AK, Blozis SA, Harrison TC, Becker HA. Exercise, functional limitations, and quality of life: A longitudinal study of persons with multiple sclerosis. Arch Phys Med Rehabil. 2006; 87(7):935–943. [PubMed: 16813781]

5. Dalgas U, Stenager E. Exercise and disease progression in multiple sclerosis: can exercise slow down the progression of multiple sclerosis? Ther Adv Neurol Disord. 2012; 5(2):81–95. [PubMed: 22435073]

6. Latimer-Cheung AE, Pilutti LA, Hicks AL, Martin Ginis KA, Fenuta AM, MacKibbon KA, Motl RW. Effects of exercise training on fitness, mobility, fatigue, and health-related quality of life among adults with multiple sclerosis: a systematic review to inform guideline development. Arch Phys Med Rehabil. 2013; 94(9):1800–1828. [PubMed: 23669008]

7. Farinotti M, Vacchi L, Simi S, Di Pietrantonj C, Brait L, Filippini G. Dietary interventions for multiple sclerosis. Cochrane Database Syst Rev. 2012; 12:CD004192. [PubMed: 23235605]

8. Jagannath VA, Fedorowicz Z, Asokan GV, Robak EW, Whamond L. Vitamin D for the management of multiple sclerosis. Cochrane Database Syst Rev. 2010; (12):CD008422. [PubMed: 21154396]

9. Wollin JA, Spencer N, McDonald E, Fulcher G, Bourne M, Simmons RD. Longitudinal changes in quality of life and related psychosocial variables in Australians with Multiple Sclerosis. Int J MS Care. 2013; 15(2):90–97. [PubMed: 24453768]

10. Trojano M, Liguori M, Bosco Zimatore G, Bugarini R, Avolio C, Paolicelli D, Giuliani F, De Robertis F, Marrosu MG, Livrea P. Age-related disability in multiple sclerosis. Ann Neurol. 2002; 51(4):475–480. [PubMed: 11921053]

11. Confavreux C, Vukusic S, Adeleine P. Early clinical predictors and progression of irreversible disability in multiple sclerosis: An amnesic process. Brain. 2003; 126(Pt 4):770–782. [PubMed: 12615637]

12. Eriksson M, Andersen O, Runmarker B. Long-term follow up of patients with clinically isolated syndromes, relapsing-remitting and secondary progressive multiple sclerosis. Mult Scler. 2003; 9(3):260–274. [PubMed: 12814173]

13. Tremlett H, Paty D, Devonshire V. Disability progression in multiple sclerosis is slower than previously reported. Neurology. 2006; 66(2):172–177. [PubMed: 16434648]

14. Weinshenker BG, Bass B, Rice GP, Noseworthy J, Carriere W, Baskerville J, Ebers GC. The natural history of multiple sclerosis: a geographically based study. I. Clinical course and disability. Brain. 1989; 112(Pt 1):133–146. [PubMed: 2917275]

15. Wynia K, van Wijlen AT, Middel B, Reijneveld SA, Meilof JF. Change in disability profile and quality of life in multiple sclerosis patients: a five-year longitudinal study using the Multiple Sclerosis Impact Profile (MSIP). Mult Scler. 2012; 18(5):654–661. [PubMed: 21965423]

16. Giordano A, Ferrari G, Radice D, Randi G, Bisanti L, Solari A. POSMOS study. Self-assessed health status changes in a community cohort of people with multiple sclerosis: 11 years of follow-up. Eur J Neurol. 2013; 20(4):681–688. [PubMed: 23217086]

17. Pender, NJ. Health Promotion in Nursing Practice. Norwalk, CT: Appleton and Lange; 1987.

18. Stuifbergen A, Brown A, Phillips L. Predictors and moderators of the disablement process in persons with multiple sclerosis. NeuroRehabilitation. 2009; 24(2):119–129. [PubMed: 19339751]

19. D'Hooghe MB, Nagels G, DeKeyser J, Haentjens P. Self-reported health promotion and disability progression in multiple sclerosis. J Neurol Sci. 2013; 325(1–2):120–126. [PubMed: 23294496]

20. Motl RW, McAuley E. Longitudinal analysis of physical activity and symptoms as predictors of change in functional limitations and disability in multiple sclerosis. Rehabil Psychol. 2009; 54(2): 204–210. [PubMed: 19469611]

21. Motl RW, McAuley E. Pathways between physical activity and quality of life in adults with multiple sclerosis. Health Psychol. 2009; 28(6):682–689. [PubMed: 19916636]

22. Joy, JE.; Johnston, RB. Multiple sclerosis: Current status and strategies for the future. Washington, DC: National Academies Press; 2001.

23. Stuifbergen AK, Seraphine A, Roberts G. An explanatory model of health promotion and quality of life in chronic disabling conditions. Nurs Res. 2000; 49(3):122–129. [PubMed: 10882316]

24. Becker H, Stuifbergen AK, Sands D. Development of a scale to measure barriers to health promotion activities among persons with disabilities. Am J Health Promot. 1991; 5(6):449–454. [PubMed: 10171668]

25. Lawton MP, Moss M, Fulcomer M, Kleban MH. A research and service oriented multi-level assessment instrument. J of Gerontology. 1982; 37(1):91–99.

26. Walker, S.; Sechrist, K.; Pender, N. Health promoting lifestyle profile II. Omaha, NE: Author; 1995.

27. Stuifbergen A. Health-promoting behaviors and quality of life among individuals with multiple sclerosis. Sch Inq Nurs Pract. 1995; 9(1):31–50. [PubMed: 7777743]

28. Kurtzke JF. A proposal for a uniform minimal record of disability in multiple sclerosis. Acta Neurol Scand. 1981; 64(Suppl. 87):110–129.

29. Stuifbergen AK, Morris M, Becker H, Chen L, Lee HY. Self-report versus performance measure in gauging level of function in multiple sclerosis. Disabil Health J. 2014; 7(4):413–418. [PubMed: 25224981]

30. Hedeker, D.; Gibbons, RD. Longitudinal data analysis. John Wiley & Sons, Ltd.; 2006.

31. Raudenbush, SW.; Bryk, AS. Hierarchical Linear Models. 2nd. Thousand Oaks: Sage Publications; 2002.

32. Singer, JD.; Willett, JB. Applied longitudinal data analysis: Modeling change and event occurrence. Oxford University Press; 2003.

33. Chi EM, Reinsel GC. Models for longitudinal data with random effects and AR (1) errors. Journal of the American Statistical Association. 1989; 84:452–459.

34. Little, RJA.; Rubin, DB. Statistical analysis with missing data. 2nd. Hoboken, New Jersey: John Wiley & Sons, Inc.; 2002.

35. Molenberghs, G.; Kenward, MG. Missing data in clinical studies. West Sussex, England: John Wiley & Sons, Ltd.; 2007.

36. Graham JW, Olchowski AE, Gilreath TD. How many imputations are really needed? Some practical clarifications of multiple imputation theory. Prev Sci. 2007; 8(3):206–213. [PubMed: 17549635]

Table 1

Sample Demographics (N=606)

Characteristic	Mean +/−SD	Range	n (%)
Age	50.57 +/− 10.28	21–81	
Years of school completed	14.4 +/− 2.60	6–30	
Years since diagnosis	13.4 +/− 7.44	1–49 years	
Gender			
Female			502 (82.8)
Male			104 (17.2)
Marital Status			
Never Married			36 (5.8)
Married			436 (72.0)
Divorced			82 (13.5)
Widowed			22 (3.6)
Other			31 (5.2)
Race/Ethnicity			
Non-Hispanic White			561 (92.6)
Black			19 (3.1)
Asian American			1 (.2)
Hispanic			15 (2.5)
Other			10 (1.7)
Employment status			
Part or full-time employment			221 (36.4)
Unemployed due to disability			194 (32.1)
Retired/Laid Off			88 (14.5)
Other			103 (17.0)
Type of MS (Self-Report)			
Benign sensory			59 (9.7)
Relapsing-remitting			244 (40.3)
Primary-progressive			110 (18.1)
Secondary-progressive			107 (17.7)
Progressive-relapsing			65 (10.7)
Don't know			21 (3.5)

Table 2

Maximum Likelihood Estimates of Moderating Effects on Functional Limitations Across 11 Years (n=606)

Parameter	Estimate	95% CI	P-value
Growth Model Coefficients			
Intercept	21.83	(8.29, 35.38)	-
Year	1.26	(−0.82, 3.33)	0.23
Year^2	−0.01	(−0.07, 0.04)	0.62
Covariates			
Years since diagnosis	0.09	(0.01, 0.17)	0.02
Age	0.09	(0.03, 0.16)	0.01
Timing of Dropout	−1.30	(−2.28, −0.32)	0.01
Timing of Dropout by Year	−0.15	(−0.29, −0.01)	0.04
Between-Person Effects on Functional Limitations Level at Year 11			
Nutrition	0.08	(−0.11, 0.27)	0.41
Interpersonal Relationships	−0.01	(−0.29, 0.28)	0.97
Exercise	−0.77	(−0.96, −0.57)	<0.001
Stress Management	0.44	(0.18, 0.69)	<0.001
Health Responsibilities	0.43	(0.22, 0.64)	<0.001
Spiritual Growth	−0.19	(−0.44, 0.07)	0.16
Self-Rated Health	−4.15	(−5.77, −2.53)	<0.001
Barriers	0.53	(0.39, 0.67)	<0.001
Between-Person Effects on the Rate of Accumulation of Functional Limitations at Year 11			
Nutrition	0.00	(−0.02, 0.02)	0.88
Interpersonal Relationships	0.00	(−0.02, 0.03)	0.85
Exercise	−0.03	(−0.04, −0.01)	<0.001
Stress Management	0.00	(−0.02, 0.03)	0.76
Health Responsibilities	0.02	(0.00, 0.04)	0.02
Spiritual Growth	−0.01	(−0.03, 0.01)	0.47
Self-Rated Health	0.03	(−0.13, 0.18)	0.74
Barriers	0.01	(0.00, 0.02)	0.17
Within-Person Effects on Functional Limitations Over 11 Years			
Nutrition	0.07	(−0.04, 0.17)	0.19
Interpersonal Relationships	0.06	(−0.16, 0.27)	0.59
Exercise	−0.10	(−0.28, 0.09)	0.29
Stress Management	−0.02	(−0.18, 0.15)	0.85
Health Responsibilities	−0.04	(−0.27, 0.18)	0.69
Spiritual Growth	−0.24	(−0.43, −0.04)	0.02
Self-Rated Health	−0.93	(−2.23, 0.37)	0.15

Parameter	Estimate	95% CI	P-value
Barriers	0.09	(−0.01, 0.18)	0.06

Notes: P-values are for two-tailed hypothesis tests that a parameter is equal to zero vs. that it is not. A P-value is not provided for the Intercept of the growth model because we did not hypothesize that this value would differ from zero given that *Functional Limitations* cannot take on the value of 0. The Quadratic Growth model includes a first-order autoregressive covariance structure for the occasion-specific residuals.