

Validation of the Fall Efficacy Scale- International, a measure of fear of falling, in people with multiple sclerosis

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Abstract:

Background: People with multiple sclerosis (MS) fall frequently and there is a paucity of clinically valid tools to measure the risk factors for falls.

Objective: To assess the unidimensionality of the 7-item Falls Efficacy Scale-International (FES-I), a measure of fear of falling and to determine if the 7-item FES-I predicts recurrent falls in people with MS.

Methods: Falls were counted prospectively for 6 months using fall calendars in 58 people with MS, aged 18-50 years with an Expanded Disability Status Scale (EDSS) score of 0-6. The FES-I was administered at baseline. Unidimensionality of the 7-item FES-I was assessed by confirmatory factor analysis. The relationship between FES-I score and future falls, after adjusting for recurrent falls in the past year was assessed by logistic regression.

Results: Fifty-four participants completed all assessments were included in the analysis. Goodness-of-fit indices confirmed a single factor solution for the 7-item FES-I (Discrepancy Chi-2, $p=0.101$; Tucker-Lewis Index: 0.953; Comparative Fit Index: 0.969; RMSEA: 0.098). There was a statistically significant association between fear of falling, and falls in the following 3 months, independent of recurrent falls in the past year (OR: 1.22 CI: 1.04-1.43, $p=0.016$).

Conclusion: The 7-item FES-I demonstrates good construct validity allowing the total score to be used as a measure of fear of falling in people with MS. Fear of falling, as measured by the 7-item FES-I, is associated with future recurrent falls independent of past recurrent falls in people with MS.

Keywords: Accidental Falls, Cohort Study, Fear, Multiple Sclerosis, Risk Factors, Validation

Chapter1: Literature Review and Rationale

Brief Overview of Multiple Sclerosis: Multiple sclerosis (MS) is a chronic progressive autoimmune disease of the Central Nervous System, and the most common neurological disease of young adults, (1) affecting 400,000 people in the U.S. (2) and over 2.5 million people worldwide. (3) The average of onset of MS is 30-35 years (4) and women are more likely to develop MS than men. (2) MS can produce lesions in the brain, brain stem, spinal cord, and optic nerves, leading to neurological dysfunction in any of these areas through demyelination and axonal loss. The natural history of MS can be categorized into several subtypes: (5) *Relapsing Remitting*, characterized as repeated exacerbation followed by periods of remission with partial or complete recovery, is the most common subtype of MS, affecting approximately 85% of all people with MS; *Primary progressive*, affecting approximately 15% of people with MS, and is characterized by gradual progression of impairment and disability from the onset; 50% of those starting with relapsing-remitting type of MS, develop *Secondary progressive* type, characterized by the relapsing-remitting pattern within a decade of diagnosis, which is followed by the progressive pattern of MS. Symptoms in MS vary widely and include cognitive impairment, loss of vision, spasticity and decreased strength, as well as loss of sensation and reduced coordination. (5, 6) Any of these impairments may increase the risk for falls.

Falls in People with Multiple Sclerosis: Several studies have found that people with MS fall frequently. Fifty-two to 70% of people with MS fall at least once within a period of 3 to 6 months. (7-11) Cattaneo et al. found that 54% of a sample of 50 people with MS in Italy reported falling one or more times in the prior two months. (7) In a U.S. cohort of 1,000

people with MS aged 45-90 years, Finlayson et al. found that more than 50% of people reported falling at least once in the previous six months, and more than 50% reported a history of at least one injurious fall at some time. (8) In a longitudinal prospective study from Sweden, Nilsagard et al. found that 48 people (63% of cohort) reported 270 falls. (10) Similarly, in a cross-sectional study of 474 people with MS from the U.S., Matsuda et al. found 58.2% of participants reported one or more falls in the previous 6 months. (1) More recently in a cohort of 150 participants, Gunn et al. found that 70% of the individuals fell at least once and during a three-month follow up period. (11)

In addition to single falls, recurrent falls and injurious falls are also common in people with MS. (1, 9, 11-13, 15) In 2013 prospective cohort study, Gunn et al. reported that 52.7% of the 150 participants fell twice or more during the three-month follow up period. (11) Coote et al., in a retrospective study from Ireland with 365 individuals, found that 17.8% of participants reported 2 or more falls during the previous three-month period. (12) Overall, nearly 50% of people with MS who suffer a single fall during a study period also experience recurrent (twice or more) falls. (7, 8, 11) Previous studies in older adults (13) and people with Parkinson's disease (14) have found that recurrent falls (≥ 2 falls within a year) are more clinically relevant, as they are likely to indicate worsened health condition. Effects of recurrent falls in people with MS are not known and warrant further investigation. In addition to recurrent falls, injurious falls are also common in people with MS. Matsuda et al. found that in a cohort of 455 people with MS 58.5% of participants reported an injurious fall and 18.9% of the participants required medical attention as a result of the injury. (1) In a sample of 195,417 veterans treated at Veterans Health Administration facilities, Cameron et al. found that female veterans with MS have three times the odds of an injurious fall

compared to female veterans without MS. (9, 15)

Together the results of these studies indicate a high prevalence of single, recurrent and injurious falls in people with MS. This high prevalence of falls in people with MS is comparable to the higher incidence and prevalence of falls in older adults (16) and further research is needed to understand the etiology and consequence of falls in this particular population. Falls, common in people with MS, are associated with severe injuries, including fractures and head trauma, reduced participation, loss of independence, placement in long-term care facilities, and death. If those at high risk for falls could be identified before they fall, clinicians could target interventions to prevent falls and fall-related injuries and disabilities.

Risk factors for falls in people with Multiple Sclerosis: Several risk factors for falls have been identified. A recent meta-analysis found that an increase risk for falls was statistically significantly associated with balance impairment, cognitive dysfunction, progressive MS and use of mobility aid. (17) While several others risk factors such as spasticity, gait, fear of falling, MS status and continence, were reported in this analysis, variation in study methodologies did not allow for quantitative analysis. These risk factors for falls can be categorized as physiological, cognitive and psychological risk factors. Advanced disease (10, 18) , impaired limit of stability, (18) weakness of lower limbs(1), spasticity (1, 7, 10), poor gait, (7, 10, 18) and urinary incontinence (8) are some of the neurophysiologic risk factors. Fatigue, poor concentration and cognitive dysfunction (19) are cognitive risk factors associated with falls. Fear of falling and balance confidence are some of the psychological risk factors that have been associated with falls in people with MS. (8, 9, 20)

In addition to these physiological and psychological risk factors, a history of fall in the past year has also been found to be an accurate measure (sensitivity of 89% and specificity of 56%) of future risk for falls. (21)

Most of the prospective studies until now have primarily focused on assessment of physiological risk factor for falls in people with MS. Specifically, two studies by Hoang et al. (22) and Gunn et al. (23) showed that neurophysiologic risk factors for falls could be assessed using a validated clinical measure known as the Physiological Profile Assessment (PPA) fall risk score. (24) These studies found that cumulative assessment of balance, coordination and cognitive function could identify people with MS who are at increased risk of recurrent falls. While the effects of neurophysiologic and cognitive risk factors for falls are fairly well studied, very few studies have evaluated or focused on the effects of psychological risk factors. Thus, there is an opportunity to further understand the relationship between psychological risks and falls in people with MS. In addition, the physiological tests are often time consuming and take up to an hour to perform. (24) Thus, an easy to administer psychological assessment might be a more clinically relevant tool to identify people with MS who are at increased risk for falls.

Fear of Falling, a psychological risk factor for falls in people with MS: Tinetti et al. defined fear of falling as “lasting concern about falling that leads to an individual avoiding activities that he/she remains capable of performing” (25) . In addition to being an independent risk factor for falls among people with Parkinson’s disease (26) and older adults (27) , it is also a known risk factor for falls in people with MS. Finlayson et al. found that participants who reported fear of falling were more likely to report having fallen in the past 6 months

compared with participants who did not report this fear. (8) While some level of fear of falling could allow an individual to estimate their risk of falling and act to protect against falls, studies in older adults show that an increased level of fear of falling can lead to be activity restriction. (28) In addition, research has shown that fear of falling is not just a psychological sequel of the trauma of falling, since people who have not experienced a fall also report fear of falling. (29)

Two related but separate constructs have been used to measure fear of falling: 1) fall self-efficacy, and 2) balance confidence. (30) While the construct of fall self-efficacy is based on a person's belief in his or her ability to execute an action, (30, 31) the construct of balance confidence is based on a person's confidence to avoid a loss of balance during activities of daily living (31, 32) . Several validated questionnaires have been developed based on these psychological constructs and are frequently used to assess fear of falling in different populations. (31)

Standardized measure of fear of falling: The Falls Efficacy Scale-International (FES-I) is the gold standard measure of fear of falling in older adults. (33-35) The Falls Efficacy Scale was originally developed by Tinetti to measure perceived self-efficacy at avoiding falls during essential nonhazardous activities of daily living. The Falls Efficacy Scale was modified later by the Prevention of Falls Network Europe (ProFaNE) group led by Todd and Yardley to create the FES-I. The FES-I measures "concern" about falling, with concern being a term closely related to fear, but one that is less intense and emotional. (33) The FES-I, designed as a cross-cultural assessment tool, has demonstrated validity in four European countries. (36) It is available in 15 languages and has excellent measurement qualities in persons

with cognitive impairment. (37) Studies in older adults have shown good test-retest reliability, (36) concurrent validity with existing measures of fear of falling, (33) and demonstrated feasibility within the clinical setting. (38) The FES-I is available in two versions—a 16-item version (33) and a 7-item short version (35). Both of these versions have been used with older adults and found to predict future falls; (34) Delbaere et al. found that higher FES-I scores were associated with a significantly increased risk of an injurious or multiple falls. (27)

The first ten questions of the 16-item FES-I assess concern for falling during activities that have lower physical demand, e.g. cleaning the house, getting dressed, getting in and out of chairs, reaching up or bending down, answering a telephone call. The next six questions assess concern for falling while performing more physically demanding activities outside the house, e.g. walking on a slippery or uneven surface, going out to social events. Responses are recorded on a 4-point scale, where 1 is “not concerned at all” and 4 is “very concerned”.

The 7-item FES-I contains selected questions from the 16-item version. In particular, the 7-item FES-I has one rather than multiple questions relating to walking tasks. The seven questions cover concern for falls with the following tasks: (1) getting dressed or undressed, (2) taking bath or shower, (3) getting in/out of a chair, (4) going up or down stairs, (5) reaching for stuff above head or ground, (6) walking up or down a slope, and (7) attending a social event or gathering.

van Vliet et al. recently assessed the construct validity of the two different versions of the

FES-I in people with MS using item-response theory (which assesses the probability that an individual with a certain level of concern will answer each item in a given way to match that level of concern.) The authors found that the 7-item FES-I had better psychometric properties than the 16-item version. In other words, the questions in the 7-item FES-I assessed the level of concern to match the level of fear of falling in a person with MS. van Vliet et al. also found that people with MS who fell scored higher than the people with MS who do not fall on both of the FES-I scales. (39)

Fear of falling in People with Multiple Sclerosis: Fear of falling has been recognized as a risk factor for falling in people with MS in a few studies. (8, 40) The prevalence of fear of falling among people MS is 63.5%. (41) In addition, 82.6% of the individuals who reported fear of falling curtailed their activity because of the fear. (41)

The studies assessing the relationship between fear of falling and falls in MS have found inconsistent results. Finlayson et al. found that compared to people with MS who did not report fear of falling, people with MS who reported fear of falling had a 74% increase in odds (Confidence interval for the odds ratio was 1.32 to 2.31) of a fall. (8) Furthermore, in a cohort of 354 people with MS, Peterson et al. found a significant association between fear of falling and injurious falls that required medical attention. (9) In a cohort of 575 community-dwelling people with MS, Matsuda et al. found a significant association between concern for falling and single and recurrent falls. (8, 40)

To date, three studies have prospectively assessed fear of falling as a risk factor of falls in people with MS. Nilsagard et al. followed participants for three months and did not find fear

of falling to be associated with falls. (10) Two other studies have evaluated the association between fear of falling and future falls, including the assessment of recurrent falls. While the study by van Vliet et al. found that individuals who report recurrent fall within a 6-month period have a higher fear of falling, (39) Gunn et al. failed to confirm this association at a three-month follow-up. (11)

The variability in these findings may be due to lack of a precise measurement of fear of falling. (30) Most of these studies have used a single question to assess fear of falling, such as “Are you concerned about falling”. (8, 10, 40, 41) . Tinetti et al. proposed that a single question is imprecise due to variable threshold of fear for individuals. Thus, a multi-item questionnaire is better adapted to assess the self-perception of concern for fallings in different context. (42, 43)

Relationship between past falls, fear of falling and future falls in people with MS: Fear of falling and falls are interrelated. Studies in older adults have found that individuals who develop fear of falling are at risk for falls, and the ones who fall are at risk for developing fear of falling. (44) This results in a vicious cycle of risk of falls, fear of falling, and functional decline. (44) Given this interdependence between falls and fear of falling, it remains uncertain if fear of falling independently predicts recurrent falls in people with MS.

Rationale for the Thesis: In general, use of the total score of a rating scale to represent a single underlying construct assumes unidimensionality of the scale. (45) A lack of unidimensionality can lead to ambiguity and misinterpretation of the score. (46) While some of the psychometric properties of the 7-item FES-I are well established, a

comprehensive review of the literature did not reveal any goodness-of-fit indices to provide empirical evidence of the unidimensionality of the 7-item version of the FES-I scale. Unidimensionality allows the valid use of single score to represent the measure fear of falling and also allows the use the 7-item FES-I in a clinically meaningful way. In this study, we will first perform a confirmatory factor analysis on the 7-item FES-I. A single factor solution will support the unidimensionality of the questionnaires and allow the use of the total score to represent a certain level of fear of falling. As goodness-of-fit indices have never been reported, this thesis will complement the existing literature on validation studies of the 7-item FES-I in people with MS.

This thesis also addresses a significant gap in understanding the relationship between fear of falling and falls in people with MS. Past falls is a strong predictor of future falls among people with MS, as individuals who fell at least once in the past one year are more likely to fall in the future. (21) This phenomenon of an increased risk of recurrent falls due to falls in the past is also seen in other populations such as older adults and people with Parkinson's disease. (47) Thus, a presence of falls in the past year might considerably attenuate the relationship between fear of falling and future falls in people with MS. Furthermore, it remains unclear if demographic risk factors such as age, gender and disability status modify the relationship between fear of falling and future falls.

Three studies have prospectively assessed fear of falling as a risk factor of falls in people with MS, but none of these studies accounted for the effect of past falls on the relationship between fear of falling and future falls. Nilsagard et al. followed participants for three months and did not find fear of falling to be associated with future falls. (10) Two other

studies have evaluated the association between fear of falling and future falls, including the assessment of recurrent falls and found inconsistent results. van Vliet et al. found that individuals who report recurrent fall within a 6-month period have a higher fear of falling (39) , but Gunn et al. failed to confirm this association at a three-month follow-up. (23) In addition, to date only one cross-sectional study has assessed the relationship between fear of falling and injurious falls. This thesis aims to address these gaps in our current understanding of the relationship between fear of falling and future falls.

Given the clinical relevance of recurrent falls seen in other populations, (13, 14) and the uncertainty in the relationship between fear of falling and future falls, this study will evaluate the association between fear of falling and recurrent falls in people with MS. We hypothesize that people with MS who have increased fear of falling are at an increased risk for recurrent falls. This relationship will be assessed after adjusting for past fall, disability status, age and gender. The following directed acyclic diagram explores the relationships between the different variables we assessed in this thesis.

Specific Aims

Given the need for developing a valid clinically feasible tool to identify individuals at increased risk for falls, and to adequately assess fear of falling in people with multiple sclerosis, we will use data from the ongoing longitudinal cohort study, “Mechanisms of Imbalance and Falls in Multiple Sclerosis” (Michelle Cameron, PI) and address the following aims:

Aim 1.1) Using confirmatory factor analysis we will explore the underlying set of factors measured by the 7-item FES-I.

Hypothesis 1.1: A single first-order factor solution will be found for the 16-item FES-I and the 7-item scales. Goodness-of-fit indices will confirm a better model fit for the 7-item version of the FES-I.

Aim 1.2) Internal consistency of the 7-item FES-I will be measured to assess how closely the items in the questionnaires are related.

Hypothesis 1.2: The scale will have a high Cronbach’s alpha indicating a high inter-item reliability.

Aim 2) Determine if the subjects with MS who report increased fear of falling, as measured by the 7-item FES-I, have a higher risk for falls in the following 3 and 6 months. Our objective is to examine the predictive validity of the 7-item FES-I for 3 types of outcomes—multiple falls (≥ 2 falls) during the 3 and 6 months of follow up, and any injurious falls during the 6 month follow up. Associations will be assessed after controlling for confounding variables, such as past recurrent fall in the past year and demographic factors such as age, gender, and disability status.

Aim2.1) Determine if an increased fear of falling, as measured by FES-I, is associated with

higher risk of falls among People with Ms (PwMS).

Hypothesis2.1a. Subjects with MS with higher scores on the FES-I have higher odds of falling recurrently in the following 3 months.

Hypothesis2.1.b. Subjects with MS with higher scores on the FES-I has higher odds of falling recurrently (≥ 2 falls) in the following 6 months.

Hypothesis2.1.c. Subjects with MS with higher scores on the FES-I have higher odds of any injurious falls in the following 6 months.

Chapter 2: Journal Manuscript

Title: Fear of Falling and Recurrent Falls in People with Multiple Sclerosis: A Longitudinal Cohort Study

Introduction

People with multiple sclerosis (MS) fall frequently. Between 52 and 63% of people with MS fall at least once within a period of 3 to 6 months, (1-3) and recurrent falls are also common in people with MS. (4-6) Approximately 50% of people with MS who suffer a single fall during a study period also experience recurrent (two or more) falls. (1, 2, 7) Studies in older adults (8) and people with Parkinson's disease (9) have found that recurrent falls (≥ 2 falls within a year) are more clinically relevant than a single fall, as recurrent falls are likely to indicate worse health. Given the high prevalence of recurrent falls in people with MS, the risk for multiple falls in this population warrants further investigation.

While the risk factors for falls may be physiological or psychological, to date most studies have focused on assessing physiological fall risk factors and there is a paucity of research developing valid psychological predictors of falls in people with MS. Fatigue (5), fear of falling (2, 10, 11) and balance confidence are psychological factors associated with falls in people with MS.

Fear of falling is an independent risk factor for recurrent falls in older adults and people with Parkinson's disease. (8, 9) While some level of fear of falling could allow an individual to estimate their risk of falling and act to protect against falls, studies in older adults show

that greater fear of falling can lead to increased risk for falls. (12) In people with MS, fear of falling has been recognized as a risk factor for falls (2, 13) and at least one investigations reports a high prevalence of fear of falling in this population. (13) However, given the variability in measurement of fear of falling in the relatively small number of previous studies, (2, 10, 14) effect of fear of falling on the risk for falls in people with MS remains unclear.

Fear of falling and falls are interrelated. Older adults who develop fear of falling are at risk for falls, and the ones who fall are at risk for developing fear of falling. (15) This results in a vicious cycle of risk of falls, fear of falling, and functional decline. (15) Given this interdependence between falls and fear of falling, it remains uncertain if fear of falling independently predicts recurrent falls in people with MS.

The Falls Efficacy Scale-International (FES-I) is a valid and reliable measure of fear of falling in older adults (16-18) and recently, the psychometric properties of the FES-I were assessed in people with MS using item response theory. (19) The authors studied the original 16-item version and a 7-item version of the FES-I scale, and found that the 7-item FES-I had better psychometric properties in people with MS. (19) A higher total score on the 7-item FES-I indicated a higher level of fear of falling. In practice, use of the total score of a rating scale to represent a single underlying construct assumes unidimensionality of the scale. (20) A lack of unidimensionality can lead to ambiguity and misinterpretation of the score (21). A comprehensive review of the literature did not reveal any goodness-of-fit indices to provide empirical evidence of the unidimensionality of the 7-item FES-I.

In this study, we assessed the psychometric properties, particularly the unidimensionality, of the 7-item FES-I using confirmatory factor analysis and assessed the goodness-of-fit. We hypothesized that the 7-item FES-I would have a single-factor solution. We then explored the association between future falls and fear of falling, as measured by the FES-I. We hypothesized that the total score on the 7-item version of the FES-I would predict the risk for recurrent falls (≥ 2 falls) in people with MS, independent of past recurrent falls.

Methods

Human Subjects Protections: This study was approved by the Institutional Review Boards at the Portland VA Medical Center and the Oregon Health & Science University. All potential participants were given a verbal explanation of the experimental protocol and a detailed informed consent document, and were given an opportunity to ask questions. All participants gave written informed consent to participate in this study.

Participants: Fifty-eight persons with MS were recruited for a study of mechanisms of imbalance and falls in MS at an academic medical center and the affiliated Veterans Administration medical center in the Northwest USA. Potential subjects were recruited using flyers posted at the clinics of these centers, and by flyers and announcements at patient education programs and MS support groups. Of the 58 subjects who were recruited, 54 completed all aspects of this study and were included in this analysis. (Figure 2)

Inclusion and Exclusion Criteria: The subjects in this study met the following inclusion criteria: confirmed diagnosis of MS by McDonald criteria (22), any subtype of MS, including relapsing remitting, primary progressive, or secondary progressive, (23) between the ages

of 18 and 50 years, mild-to-moderate MS disability as defined by an Expanded Disability Status Scale (EDSS) score of ≤ 6.0 (24), willing and intellectually able to understand and to sign an informed consent and to adhere to protocol requirements, sufficient motor function to complete a written daily record of falls for 6 months, and community dwelling.

The following exclusion criteria were applied: a self-reported musculoskeletal or neurological condition other than MS, known to affect balance or gait, and be associated with falls, such as a lower-extremity joint replacement, peripheral neuropathy, vestibular disorder, alcoholism, stroke, or seizure; unable to follow directions in English; unhealed bone fractures or other conditions that put subjects at risk of injury during balance testing; and blindness (visual acuity corrected worse than 20/200).

Independent variables: Fear of falling was assessed using Falls Efficacy scale-International (FES-I) questionnaire. The scale measures concern for falling while performing activities that range from basic (e.g. getting dressed, getting in and out of chair, reaching up or bending down, answering a telephone call) to more physically demanding (e.g. walking on slope, going out to social events). Responses assess the level of concern about falling while performing each activity on a 4-point scale, where 1 is “not concerned at all” and 4 is “very concerned”. (16) The 16-item FES-I was administered and the responses to the items that comprised the 7-item FES-I (17) were used to calculate a 7-item FES-I score. In case of missing responses on the questionnaire, total scores were calculated using scoring criteria reported in earlier validation studies. (16, 17)

MS severity was assessed at baseline using the Expanded Disability Status Scale (EDSS),

which is based on a clinical neurological examination. (24) Each subject is assigned an EDSS step that ranges from 0 to 10. Step 0 indicates normal neurological function and Step 10 indicates death due to MS. Step 6 indicates “Intermittent or unilateral constant assistance (cane, crutch, or brace) required to walk about 100 meters with or without resting” and only subjects with an EDSS of ≤ 6.0 were included in this study.

Dependent variables: Recurrent falls were prospectively measured using fall calendars. At their baseline visit, all subjects were provided with monthly fall calendars to record their falls each day. A fall was defined as “any unexpected event that results in you ending up on the ground, floor, or any lower surface”. (25, 26) At the end of each month, subjects mailed back the month’s fall calendar. If the page was not received within 1 week after the end of the month, a research assistant phoned the subject to ask for the page to be sent in. Total fall counts were assessed for the 6 months following the baseline visit, and the variable was dichotomized as (1) recurrent fallers and (2) non-recurrent fallers. Individuals reporting at least 2 falls in 6 months were defined as recurrent fallers, and individuals reporting one or no falls were defined as non-recurrent fallers.

Statistical analysis: All analyses were performed using STATA version 12.1 (StataCorp, TX), and a significance level of 0.05 was set for all hypothesis testing. Descriptive statistics were performed to assess central tendency and variability of all measured variables. To compare means of continuous variables, Mann-Whitney U tests and t-tests were performed for non-parametric and parametric data, respectively. Ordinal variables were compared using Chi-square tests.

Distribution of the total FES-I scores, which was considered as a continuous variable, was assessed. Then the reliability and construct validity of the FES-I scales were assessed. To evaluate the reliability of the FES-I scale, Cronbach's alpha was calculated. Confirmatory factor analysis was used to assess the construct validity of the FES-I scale. Additionally, the unidimensional construct of the FES-I scale was evaluated using a confirmatory factor analysis (CFA) to assess whether empirical data fit the predefined hypothesized structure using structural equation modeling. Our *a priori* hypothesis was that the 16-item FES-I and the 7-item versions of the FES-I represent a single underlying construct. Commonly accepted confirmatory factor analysis fit indices (Chi-square, CFI, RMSEA, TLI) were used to assess the goodness-of-fit.

Logistic regression was performed to assess the relationship between total score on the FES-I scale and recurrent falls in the following 3 and 6 months. Odds ratios were reported as the measure of association between the score on the FES-I and recurrent falls. Relationships between FES-I score and future falls were tested, after adjustment for recurrent falls in the past year, EDSS score, age, and gender. In multivariate analysis, the effects of the confounding factors were assessed using the conventional criteria of 10% change in the estimate.

Results

Demographics and baseline characteristics: Fifty-four participants (93.1%) completed all of the baseline assessments and 6-month prospective fall counts and were included in the analysis. (Table 1) The mean age of the participants was 39.6 years and the female-to-male ratio was 2.2:1. 94.4% of the participants had relapsing-remitting MS and 5.6% had

secondary-progressive type. The mean EDDS score was 2.7, and ranged from 0 to 6. Forty-one (75.9%) participants reported at least one fall in the past year, and 34 (37.1%) reported 2 or more falls in the past year. In addition, 24 participants (44.4%) reported at least one injurious fall in the past year.

At baseline, there were some significant differences between the recurrent fallers and the non-recurrent fallers. (Table 2) Recurrent fallers had a higher mean score on the 7-item FES-I (12.1 versus 9.4, $p=0.01$). In addition, the mean EDSS score was higher for the recurrent fallers than for the non-recurrent fallers (3.1 versus 2.1, $p=0.01$). However, there were no statistically significant differences in the average age or gender distribution.

Unidimensionality of the 7 FES-I: For the 54 subjects who completed the study, the baseline mean score on the 7-item FES-I was 11.1 (4.4) and the range of the total score was 7 to 23. Scores on the 7-item FES-I were not normally distributed (7-item version: Kurtosis: 3.27) and were skewed to the right (7-item version: Skewness: 1.07). Cronbach's alpha was 0.91 for the 7-item FES-I scale indicating a high internal reliability.

The unidimensionality of the 7-item FES-I was assessed using confirmatory factor analysis with 52 subjects. (Two participants did not answer one question each and were therefore excluded from this analysis.) The goodness-of-fit indices for a one-factor solution are shown in Table 3. The χ^2 statistics ($p=0.101$), Tucker-Lewis Index (TLI) and Comparative Fit Index (CFI) were all greater than or equal to 0.95 for the 7-item FES-I, indicating that the 7-item version has a good fit for a unidimensional model.

Fear of Falling measured by the 7-item FES-I scale as a predictor of recurrent falls:

The crude and adjusted odds ratios describing the relationship between fear of falling (as measured by the 7-item FES-I) and recurrent falls and injurious falls are shown in Table 4. In the bivariate analysis, we found that fear of falling was strongly associated with recurrent falls in the following 3 and 6 months. For each point increase in the total FES-I score, the odds of recurrent falls in the following 3 months and 6 months increased by 25% and 19%, respectively. The total score on the 7-item FES-I was predictive of recurrent falls, when adjusted for recurrent falls in the past year. At 3 months, a one-point increase in the total FES-I score increased the odds of recurrent falls by 22%, regardless of recurrent falls in the past year. Similarly, at 6 months, the odds of falling increased 14% for each one-point increase in the 7-item FES-I. We examined age, gender, and EDSS score as potential confounding factors separately and did not find them to confound the relationship between fear of falling as measured by the 7-item FES-I and falls in 3 and 6 months. In this multivariate analysis, the change between the adjusted and the crude odds ratio was less than 10%. Thus, we only adjusted for past recurrent falls in the final model.

We did not find a significant association between fear of falling and injurious falls in the following 6 months.

Discussion

Our analysis demonstrates that, in people with MS, the 7-item FES-I has a unidimensional fit and is a reliable measure of fear of falling. This is the first study to find that fear of falling predicts recurrent falls in the following 3 and 6 months, independent of falls in the past year.

Confirmation of a single-factor solution supports the findings of a previous study that the 7-item FES-I has good construct validity in people with MS. (19) The unidimensionality of the 7-item version of the scale justifies using the total score of the 7-item FES-I to represent the construct of fear of falling in people with MS. The fit indices evaluated in this study, including the chi square test of model fit (27), the comparative fit index and the Tucker-Lewis index support this unidimensionality. The RMSEA also supported a single-factor model, although the point estimate was greater than 0.05, the lower limit of the 90% confidence interval for the RMSEA was considerably smaller than 0.05, which is an acceptable indication of model fit. (28)

Our study addresses a significant gap in understanding of the relationship between fear of falling and falls in people with MS. Previous cross-sectional studies have shown an association between fear of falling and increase risk for falls in people with MS. (2, 13, 29) Ours is the only study to assess the effect of past falls on the relationship between fear of falling and risk of future falls in people with MS.

We assessed if previous falls modify the relationship between fear of falling and future falls, as past falls are a strong predictor of future falls among people with MS. (30) We found that fear of falling, as measured by the 7-item FES-I, is associated with falls in the following 3 and 6 months independent of past recurrent falls. The association between fear of falling and falls in the following 3 months is not affected by past recurrent falls. Although the association with falls in the following 6 months shows some change with adjustment for past recurrent falls, the point estimate of the odds ratio differ by less than 10% (14% as

compared to 19% increase in odds per point increase on the 7-item FES-I score) suggesting that past recurrent falls do not significantly influence this association. Initially, we forced age, gender, and EDSS score in the multivariate model to adjust for confounding factors. We found the estimated association did not change after adjusting for these variables, confirming that the variables were not confounding the relationship between fear of falling and falls in people with MS. Thus, age, gender and EDSS were not retained in the final model to avoid complex high dimensionality.

Three prior studies have assessed fear of falling as a risk factor for prospectively counted falls in people with MS. While Nilsagard et al. and Gunn et al. did not find fear of falling to be associated with falls in the following 3 months (3, 7), van Vliet et al. found that individuals who report recurrent falls within a 6-month period have a higher fear of falling. (19) This inconsistency among studies may be due to differences in how fear of falling was assessed or differences in the level of physical activity in these cohorts. Nilsagard et al., similar to all prior cross-sectional studies, used a single question to assess fear of falling. In contrast, our study used the 7-item version of the FES-I. Gunn et al. used the 16-item FES-I and van Vliet et al. used both the 16 and 7-item versions of the FES-I. Studies in older adults have found that a single-item question to assess fear of falling is less sensitive than a multi-item questionnaire. (31, 32) In addition, physical activity may mediate the relationship between fear of falling and future falls, (33) and the level of activity may have differed among these studies. Future studies should use multi-item scales to assess fear of falling in MS and should also include measures of physical activity to evaluate the impact of this variable on the relationship between fear of falling and falls in people with MS.

How fear of falling increases the risk of falls is unknown. The association between fear of falling and falls may reflect shared physiological risk factors, such as increased postural instability. (34, 35) Fear of falling may also result in curtailment of activity and subsequent deconditioning that then increases the risk for falls. (29, 36) Additional studies are needed to more fully understand this complex relationship.

The strengths of this study include prospective ascertainment of falls using daily calendars, thus minimizing information bias. Furthermore, a minimal loss to follow-up reduced the possibility of a differential bias (93.1% of the participants completed the study at six-month follow-up).

There were several limitations of our study that restricts the generalizability and interpretation of our results. The small sample size decreases the power of the study and the absence of the primary progressive type limits the generalizability of our results to all people with MS. In addition, the participants in our study were recruited for a study of balance and falls, which may explain why they reported a higher rate of falls than prior studies (72% vs. 50-63% during the 6-month follow-up). This raises a small possibility of differentially biasing the relationship between fear of falling and the outcome away from the null.

In conclusion, our study supports the use of 7-item version of the FES-I as a measure of fear of falling in people with MS, and that a higher score on the 7-item FES-I can identify individuals at an increased risk for future falls, whether they have or have not fallen in the past.

Chapter 3: Implications for Public Health and Clinical Practice

The U.S. Preventive Services Task Force (USPSTF) recommends assessment of potential risk factors to identify populations at-risk, and the prevention of adverse health conditions in that population. Often, the risk factors are targets for intervention. (1) Fear of falling has the potential to be used as an indicator for assessment of risk for falls in PwMS, and as a potential target for future fall-prevention programs. Similar to previous studies in older adults and people with Parkinson's disease (2, 3), this study confirms a significant association between fear of falling and increased risk of falls. We found that an increased fear of falling, as measured by the 7-item FES-I, increases the risk of falls within the following 3 months, regardless of a history of recurrent fall in the past one-year.

Previous studies have found that PwMS who develop fear of falling may curtail activities (4) leading to reduced mobility and physical deconditioning. Identification of individuals-at-risk can lead to prevention of future falls. Cognitive behavioral interventions, such as "A Matter of Balance" have been designed to reduce fear of falling in older adults. The program was found to significantly improve fall efficacy among participants who attended five or more two-hour sessions. (5) Given the strong association between fear of falling and falls in PwMS, this thesis provides further evidence and rationale for developing a cognitive behavioral fall prevention program targeting fear of falling in PwMS.

Professional organizations such as the American Academy of Neurology (AAN) issue guidelines to prevent falls among people with neurological disorders. (6) Results of this thesis confirm the association between fear of falling and future falls using a validated

standardized measurement and provides evidence on the basis of which the public health agencies and the professional organizations can assess fall-related studies in people with MS. Currently, the AAN Quality Standards Subcommittee's practice parameter guidelines recommends identification of screening tools that can be performed rapidly and easily in the office or at the bedside. (6) The 7-item Fall Efficacy Scale-International has the potential to be adapted in such a setting. The 7-item FES-I is a short and easy to administer tool that is available in multiple languages. The choices of words used in the FES-I accounts for cross-cultural differences. (7) Such user-friendly features of the FES-I scale enhances its clinical utility.

Furthermore, in a clinical setting, the Fall Efficacy Scale-International could be used by clinicians, specifically, rehabilitation specialists such as Physical Therapist and Occupational Therapists. Future studies could assess a cut-off point with the highest sensitivity and specificity to discriminate between individuals with high and low fear of falling in people with MS. In older adults, a score > 14 on the 7-item FES-I scale indicated higher concern for falling. (8) With a defined cut-off point in PwMS, FES-I has the potential to be used for identifying individuals who would be ideal targets of cognitive behavioral therapy programs and fall prevention strategies.

Finally, given the clinical feasibility and the reliability of the FES-I, it could be used as a patient-reported outcome measure (PROM), which has become an essential element within the clinical practice, the evaluation of health services delivery and even, drug trials. (9) Patient experiences, as measured by a PROM, provide a complementary perspective to the overall healthcare experience. Self-reported instruments such as the FES-I can serve as an

important surrogate physiological marker for intervention programs and prevention strategies. Overall, the FES-I can serve an important role in the identification of individuals at increased risk for falls, and potentially preventing adverse outcomes in this high-risk population.

Figures:

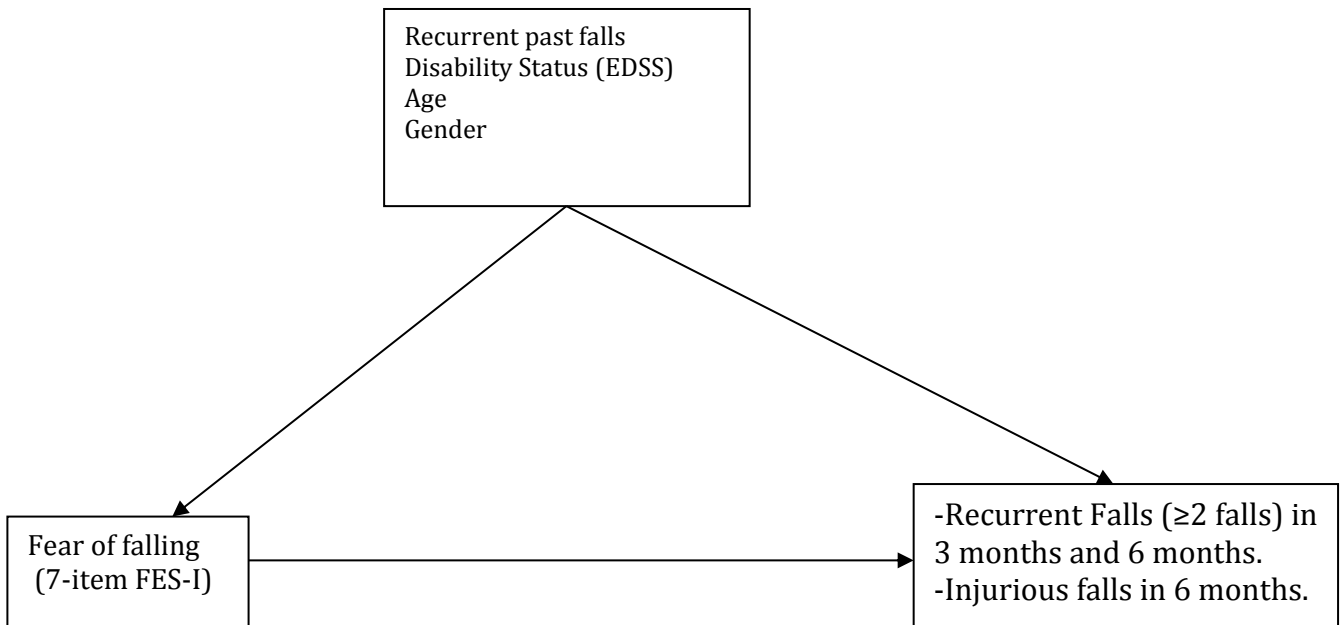


Figure 1: Directed acyclic graph (DAG) showing the relationship between fear of falling, recurrent falls, and injurious falls. Recurrent past falls, disability status, age, and gender are confounders.

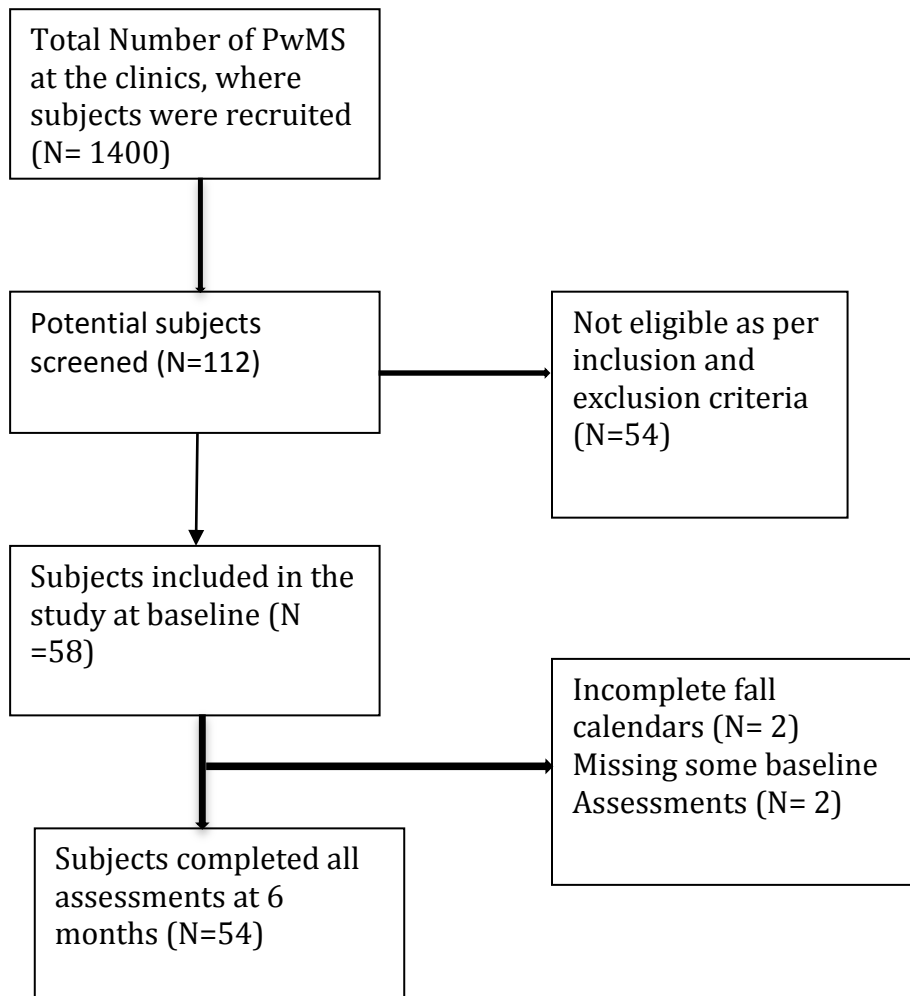


Figure 2: Study Design

PwMS = People with Multiple Sclerosis

Tables:

Table 1. Participant characteristics (n = 54 subjects)

Characteristic	Value
Age in years (Mean +/- SD)	39.6 (8.3)
Gender (Female:Male)	37:17 (2.2:1)
MS type	
Relapsing-Remitting	51 (94.4%)
Secondary Progressive	3 (5.6%)
Primary progressive	0 (0%)
EDSS Score (mean, range)	2.7 (0-6)
7-item FES-I score (Mean, SD, range)	11.1 (4.4), 7-23
Falls in past 1 year	
At least 1 fall	41 (75.9%)
No Falls	13 (24.1%)
Recurrent fall in past 1 year	
Fallers (>=2 falls)	34 (37.1%)
Non-recurrent Fallers (no or 1 fall)	20 (62.9%)
Subjects with at least 1 injurious fall	24 (44.4%)

Table 2. Characteristics of participants who are recurrent fallers and non-fallers at baseline. Recurrent fallers were defined as >=2 falls in the last year.

Characteristics	Non- recurrent fallers (n=20)	Recurrent fallers (n=34)	p-value
Age (years)	38.25 (+/-2.03)	40.4 (+/-1.32)	0.429
Gender, (Female:Male)	12:8	25:9	0.301
EDSS score	2.1 (1.5)	3.1 (1.4)	0.01
7-item version total FES-I score (Mean, SD)	9.4 (3.8)	12.1(4.4)	0.01

Table 3: Model fit statistics for confirmatory factor analyses comparing 16-items and 7-items to one-factor solution (n = 52 subjects)

Measure of fit	7-Items FES-I
Discrepancy χ^2 (df), <i>p</i> -value	21.041 (14), <i>p</i> = 0.101
Tucker-Lewis index (TLI)	0.953
Comparative Fit Index (CFI)	0.969
Root Mean Square Error of Approximation (RMSEA) (95% CI)	0.098 (0.0001, 0.180)

Table 4. Score on the 7-item FES-I and the risk of future recurrent falls.

	Unadjusted OR	OR adjusted for recurrent past falls in the past year
Recurrent falls in the following 3 months	1.25 (1.07-1.46; <i>p</i> = 0.004)	1.22 (1.04, 1.43; <i>p</i> = 0.016)
Recurrent falls in the following 6 months	1.19 (1.02, 1.38; <i>p</i> = 0.02)	1.14 (0.98-1.32; <i>p</i> = 0.092)
Injurious falls in the following 6 months	1.05 (0.93-1.19; <i>p</i> = 0.419)	0.99 (0.87-1.15; <i>p</i> = 0.97)

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Chapter 3

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