Research Report

Identification of Risk Factors for Falls in Multiple Sclerosis: A Systematic Review and Meta-Analysis

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Background. Falls are a significant issue in people with multiple sclerosis (MS), with research demonstrating fall rates of more than 50%.

Purpose. The purpose of this study was to evaluate the risk factors associated with falling in people with MS.

Data Sources. Mixed search methods were used, including computer-based and manual searches. Additionally, hand searches of reference lists and conference abstracts were performed. All literature published from the source's earliest date to January 2012 was included; only full-text English-language sources (or those where a translation was available) were included.

Study Selection. Eligibility criteria specified articles evaluating any aspect of fall risk in adults with a confirmed MS diagnosis, where the incidence of falling as determined by prospective or retrospective participant report was included.

Data Extraction. Data were extracted independently by 2 reviewers using a written protocol and standardized extraction documentation. Detailed assessment of each article was independently undertaken by both reviewers, including assessment of study quality using an adaptation of the Newcastle Ottawa Scale plus extraction of key data (participant characteristics, fall incidence, and outcomes).

Data Synthesis. The final review comprised 8 articles with a total of 1,929 participants; 1,037 (53.75%) were classified as fallers. Eighteen different risk factors were assessed within the included studies. Meta-analysis demonstrated an increase in fall risk associated with impairments of balance and cognition, progressive MS, and use of a mobility aid. Narrative review of the qualitative articles and those factors where meta-analysis was not possible also was undertaken.

Limitations. Variation in assessment, analysis, and reporting methods allowed meta-analysis for only 4 factors.

Conclusion. There is limited evidence of the factors associated with fall risk in people with MS. Further methodologically robust studies are needed.

Multiple sclerosis (MS) is the most common cause of neurological disability in young adults, affecting approximately 2.5 million people worldwide.[1] Research suggests that the most frequent symptoms experienced by people with MS include fatigue; sensory disturbances, including pain; and impairments in mobility and balance, cognition, visual symptoms, and continence.[2] Falls are a significant issue in this group; with research demonstrating more than 50% of people falling in any 6-month period.[3] People with MS have an increased risk of fracture relative to non-MS age-matched populations and, in particular, an increased risk of fragility fractures, with a hip fracture hazard ratio of 4.08 (95% confidence interval [95% CI]=2.21–7.56).[4] These findings highlight the importance of managing fall risk and identifying measures to reduce the negative consequences of falls.

Although research into the wider consequences of falls in people with MS is limited, problems that are commonly highlighted include loss of confidence and difficulties sustaining the person's usual life roles.[5,6] This focus is in line with research findings in older adults, wherein falls and fear of falling are associated with significant loss of independence and decreased quality of life.[7,8] For people with MS, and therapists working with them, the ability to evaluate the key risk factors associated with falls could enable the identification of those at greatest risk, allowing appropriate targeting of interventions and resources to minimize falls.

Due to the nature of MS, a wide range of physiological, psychological, and environmental factors could lead to falls. Although some researchers have focused their attention on investigating factors affecting postural stability,[9–12] others have evaluated specific risk factors for falling.[3,13] The objective of this systematic review was to evaluate the risk factors associated with falling in people with MS, as described in the literature.

Method

The systematic review was conducted using a written protocol developed by the review authors in collaboration with a local university-based systematic review peer group. This review group included members with expertise in systematic reviews, information technology, meta-analysis, falls, and neurological rehabilitation. The protocol covered all key aspects of the systematic review, including inclusion and exclusion criteria, search strategy, methodological quality assessment, and data extraction and analysis. Copies of the protocol are available via the corresponding author.

Data Sources and Searches

Mixed search methods were used, including computer-based and manual searches. The electronic databases used were: MEDLINE, Cochrane Database of Systematic Reviews, AMED, EMBASE, British Nursing Index, CINAHL Plus, and PsycINFO. The following medical subject heading (MeSH) key words and operators used were: "Multiple Sclerosis AND accidental falls" OR "Multiple Sclerosis AND postural balance" NOT animals [mh] NOT humans [mh].

Related terms "postural instability" and "falls" also were used in those sources where MeSH terms were not used. In addition, hand searches of reference lists and MS conference abstracts published over the previous 5 years were performed. All literature published from their earliest date to January 2012 was included; only English-language sources (or those where a translation was available), where full text was available, were included in the review.

Study Selection

Participants. This review examined articles evaluating any aspect of fall risk in adults with a confirmed diagnosis of MS (as against clinically isolated syndrome). Falls studies in elderly people have suggested different risk factors for falling in individuals related to their levels of mobility or daily activity patterns.[14–16] There is limited evidence relating to either population in MS; therefore, we included all studies, regardless of mobility status.

Interventions/outcomes. Studies were included that evaluated potential risk factors (physiological, psychological, and environmental) against the incidence of falling as determined by prospective or retrospective participant report. Studies where risk of falls was inferred by proxy measures (eg, those using functional measures equated to fall risk) were excluded on the basis of reported limitations in terms of the predictive validity of these measures, both within samples of elderly people[17–20] and those with MS.[3] Although we were aware that prospective recording of falls is the gold standard,[21] to ensure a comprehensive review in an area with a limited number of published articles, we

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- eTable 1: Adapted Newcastle-Ottawa Quality Assessment Scale
- eTable 2: Methodological Quality Assessment: Newcastle-Ottawa Quality Assessment Scale (NOS) for Case Control Studies
- eTable 3: Complete Data Sets for Risk Factors Included in Meta-Analysis

evaluated all articles reporting fall incidence, either by prospective or retrospective reports.

Study designs. Randomized and quasi-randomized controlled trial, controlled observational, and cross-sectional design methods were eligible for inclusion. To ensure a comprehensive review, studies utilizing alternative methods (eg, qualitative studies) also were considered for inclusion where the article included appropriate participants and outcomes as outlined above.

Data Extraction and Quality Assessment

Articles were excluded if they were purely evaluations of outcome measures or interventions that did not relate fall risk factors to fall frequency within the analysis. Abstracts were screened by the primary author (H.J.G.) to remove obviously irrelevant reports. Authors of 5 articles were contacted to request supplementary data; replies with sufficient data to include the article in the review process were received from 3 authors.[22–24]

Using a written protocol and standardized data extraction forms, a more detailed assessment of each retrieved article was independently undertaken by 2 reviewers (H.J.G. and J.A.F.) to assess compliance of studies with the eligibility criteria. Data extracted at this stage included details of the study participants, outcomes, method, and measures of falls incidence. Discrepancies were resolved through discussion before a final decision was made on inclusion based on the consensus reached.

An assessment of study quality utilizing the Newcastle-Ottawa Quality Assessment Scale (NOS)[25] was undertaken (eTab. 1, available at ptjournal.apta.org). The scale was adapted to ensure the wording was appropriate to the specific types of study being reviewed: 1 criterion in the original version of the NOS (demonstration that outcome of interest was not present at the start of the study) was excluded from this review, as it was inappropriate given the nature of the topic, leaving a maximum available NOS score of 8 stars. There is no validated cutoff for the NOS[25]; however, a previous systematic review used a score of 6 or more stars from a possible maximum of 9 on the full scale.[26] Accordingly, a cutoff of 5 or more stars was set for this review.

Data Synthesis and Analysis

Following the eligibility and quality assessment stages, full data extraction of the included studies was undertaken using double data entry to minimize errors. Data extracted at this stage included more detailed demographic and MS classification data, method and results of risk factor measurements, and detailed fall incidence data. Odds ratios (ORs) (for categorical data) and weighted mean differences (for continuous data) and their 95% CI values were extracted from the data or calculated for analysis where sufficient data were presented in the article or could be obtained from authors. Odds ratios are a measure of risk that compare the relative likelihood of an event occurring between 2 groups.[27] An OR of 1 indicates no difference in odds (in this context, the odds of being classified as a faller) between the groups, and an OR greater than 1 indicates an increase in the odds for 1 group compared with the other.[28] Data were pooled in statistical meta-analysis using an inverse variance random-effects Der Simonian-Laird meta-analysis using the "meta" package for R[29,30] for any risk factors where comparable data for 3 or more studies could be extracted.[31] Each data set included in the meta-analysis was analyzed for heterogeneity using the chi-square statistic, with a P value of .10.[32] Where statistical pooling was not possible or appropriate (eg, in qualitative articles or those risk factors with insufficient numbers of data sets to allow

The Bottom Line

What do we already know about this topic?

People with multiple sclerosis (MS) experience frequent falls and report activity curtailment and loss of independence as a result of falls and fear of falling.

What new information does this study offer?

The study's findings indicate that certain factors—such as impairments of balance and cognition, progressive MS, and use of a mobility aid—may increase falls risk; however, methodological limitations and the paucity of the existing evidence base are significant limitations.

If you're a patient, what might these findings mean for you?

These findings suggest major factors that may contribute to the risk of falling. Further research is required to identify specific risk factors so that fall management programs can be further developed.

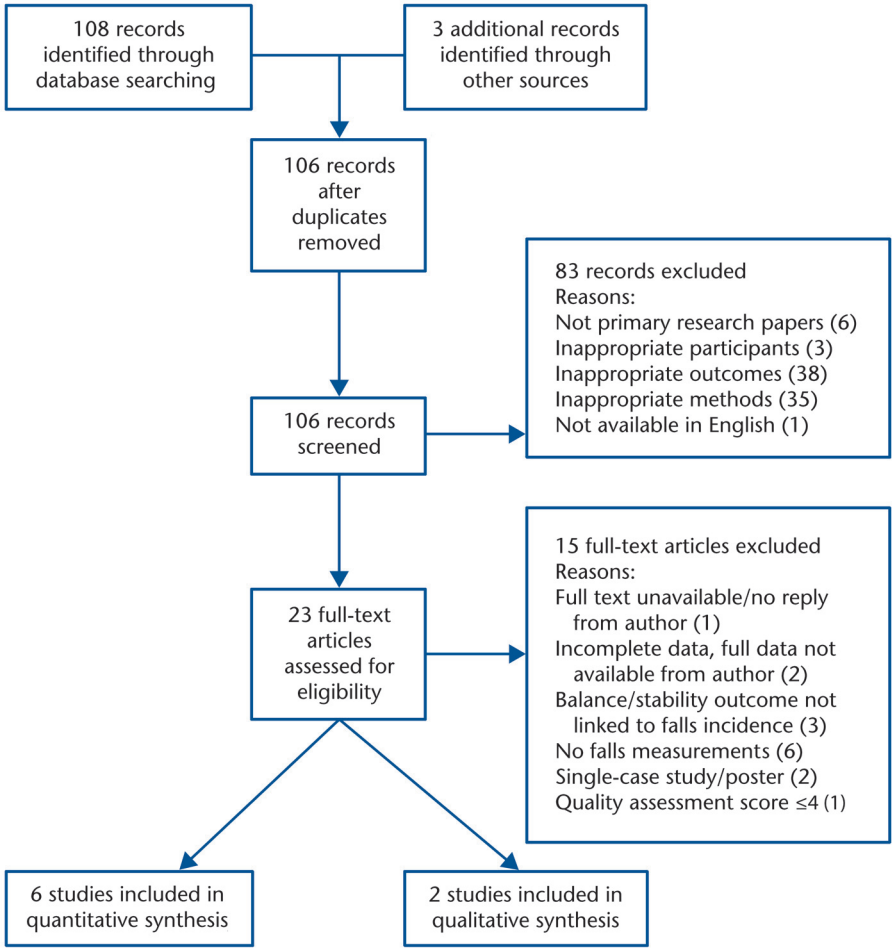

Figure 1.
Flow chart of studies screened for inclusion in the review.

comparison), findings are presented in narrative summary form.

Results

Studies

The electronic and hand searches yielded a total of 111 records (Fig. 1). Once duplicate records were removed, 106 records were screened for eligibility, and 83 records were excluded. The most common reasons for exclusion were articles not reporting fall incidence (n=38) and inappropriate methods (eg, intervention trials) (n=35).

Detailed Review and Assessment of Methodological Quality

Twenty-three articles were included in the detailed review. Of these, 14 articles did not fit the inclusion criteria: 9 articles lacked specific falls measurements; 2 articles had insufficient data to undertake the analysis, despite contacting the authors; there was no reply from 1 author; 1 article was a single-case study; and 1 publication was a poster presentation. Methodological quality was variable (eTab. 2, available at ptjournal.apta.org). Only 2 studies recorded falls prospectively, and reporting periods varied considerably, from 6 months for retrospective recording to 1 year for prospective recording. Classification of falls and fallers was inconsistent, and there was significant variation in the methods used to define fallers and nonfallers. Following detailed review and assessment of methodological quality, an additional article was excluded, leaving a final total of 6 quantitative articles and 2 qualitative articles.

Participants and Fall Rates

The final review comprised a total of 1,929 participants. The 6 quantitative studies included a total of 1,911 participants, and the 2 qualitative studies included a total of 18 participants. Of the total participants, 1,037 (53.75%) were classified as fallers; of these, 1,019 were derived from the quantitative studies, and all 18 participants in the qualitative studies were classified as fallers. The quantitative data set comprised participants with an age range of 21 to 71 years and 442 men (23.12%). The

Table 1.

Risk Factors Measured[a]

Risk Factor/ Study Characteristic	Articles					
	Cattaneo et al, 2002[13]	Finlayson et al, 2006[39]	Kasser et al, 2011[40]	Nilsagard et al, 2009[3]	Soyuer et al, 2006[35]	Matsuda et al, 2011[36]
N	50	1,089	99	76	124	473
ADL	Rivermead ADL Scale					
Balance	Equiscale Test	Self-report	Limits of stability testing	Berg Balance Scale/ Four Square Step Test	Functional reach	Self-report
Cognition	MMSE	Self-report		Clock Drawing Test	MMSE	Self-report
Continence		Self-report		Self-report		Self-report
Dual task				TUG cognitive		
Fatigue				Fatigue Severity Scale		
Fear of falling		Self-report		Self-report		
Gait	Hauser Ambulation Index		GaitRITE analysis	MSWS-12	Tinetti gait scale	
Mobility	Rivermead Motor Assessment					
Mobility aid	Use of a cane	Wheelchair use		Walking aid type and venue		Use of walking aid/ wheelchair
Motor function	Motricity Index				Motricity Index	
MS status/ disease severity		Self-report	EDSS mild/moderate/ severe	EDSS		
MS classification				RR, PP, SP	RR, PP, SP	RR, PP, SP, PR
Proprioception			Sensory Integration Test	Birgitta Lindmark Motor Capacity Part E Scale		
Spasticity	Modified Ashworth Scale, gastrocnemius muscle			Modified Ashworth scale sum score	Ashworth scale	Self-report
Strength						Self-report
Visual issues						Self-report

[a] ADL=activities of daily living, MMSE=Mini-Mental Status Examination, TUG=Timed "Up & Go" Test, MSWS-12=12-Item Multiple Sclerosis Walking Scale, MS=multiple sclerosis, EDSS=Expanded Disability Status Scale, RR=relapsing remitting, PP=primary progressive, SP=secondary progressive, PR=primary relapsing.

Table 2.

Pooled Odds Ratios[a]

Risk Factor	Balance Impairment	Use of a Mobility Aid	Cognition	Progressive Multiple Sclerosis
No. of studies	4	4	3	3
No. of participants	1,412	1,576	1,239	596
Pooled OR	1.07	2.5	1.28	1.98
95% CI	1.04–1.10	2.21–2.83	1.20–1.36	1.39–2.80
Heterogeneity (χ^2)	0.01 (P=.9998)	0.28 (P=.9638)	0 (P=.9992)	1.22 (P=.54)

[a] OR=odds ratio, 95% CI=95% confidence interval.

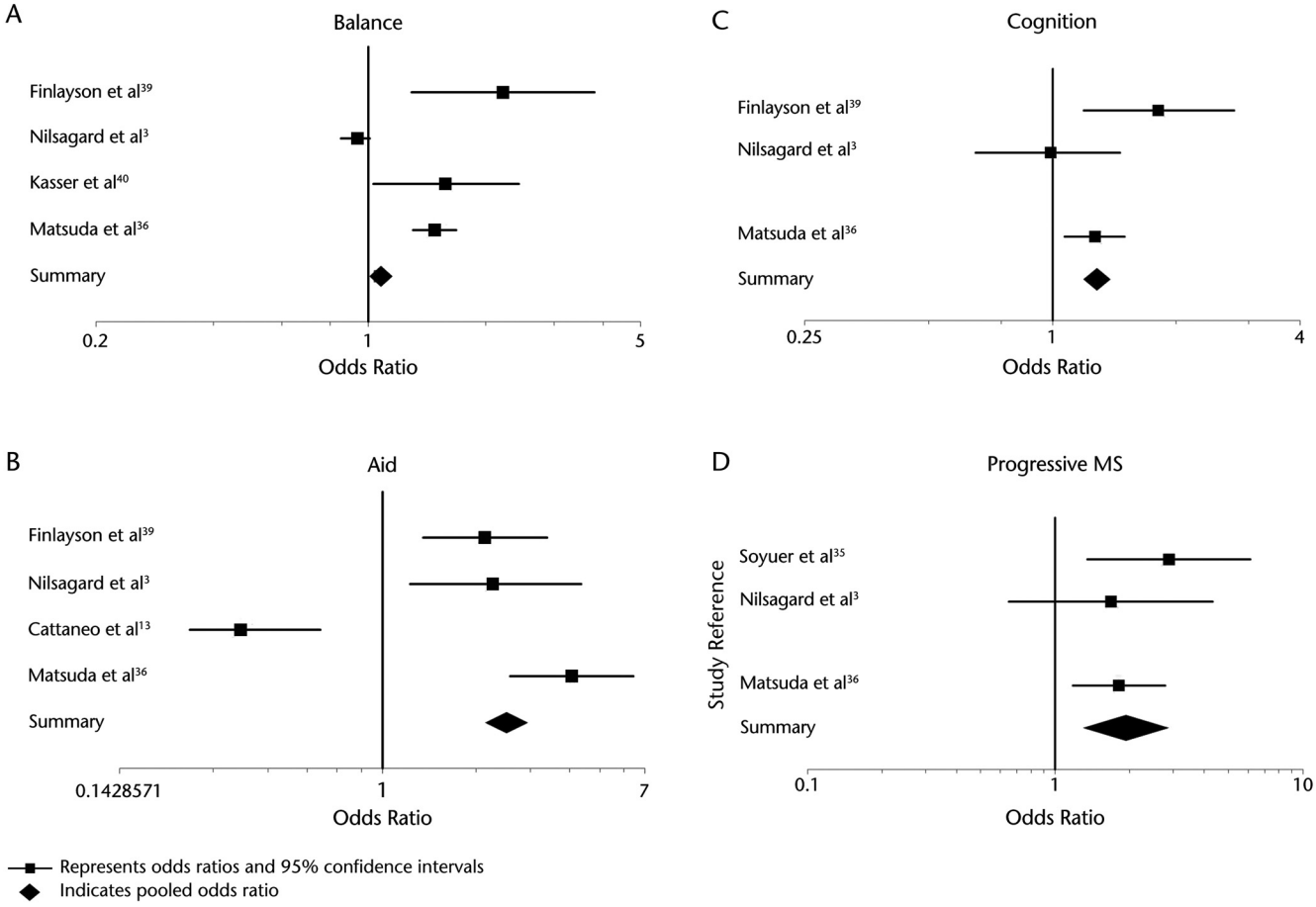

Figure 2.
Forest plots: (A) balance, (B) walking aid use, (C) cognition, and (D) progressive multiple sclerosis (MS) classification.

participants in the qualitative studies had an age range of 27 to 68 years; distributions of participants by sex were 50/50 for 1 study[33] but not detailed for the second study.[34] A range of MS classification subtypes and severities were included in the studies, with various scales and cut-off values used to categorize disease severity (eTab. 2).

Risk Factor Measurements

Eighteen potential risk factors were evaluated (Tab. 1). There was limited consensus in the impairments included, with 6 of the 18 risk factors being measured in 1 study only. Those evaluated in 3 or more studies were balance (n=6), walking (n=4), cognition, (n=5), level of disease severity/MS status/MS classification (n=3), continence (n=3), spasticity (n=4), and use of a mobility aid (n=4). Potential risk factors were assessed using a range of methods, including objective measures, observational assessments, and self-report data. Where validated measures were used, there was significant variation in test procedure and reporting.

Meta-analysis

An OR with 95% CI was available (or calculable) for only 6 of the quantitative studies due to limitations in the data presented. Pooled meta-analysis was feasible for only 4 individual risk factors: impairments to balance (pooled OR=1.07, 95% CI=1.04–1.10), use of a mobility aid (pooled OR=2.5, 95% CI=2.21–2.83), cognitive impairments (pooled OR=1.28, 95% CI=1.2–1.36), and MS classification (progressive compared with relapsing remitting classifications, pooled OR=1.98, 95% CI=1.39–2.80). Data for these risk factors are presented in Table 2, with forest plots presented in Figure 2. Full data from all of the studies, including those that were not included in the meta-analysis, are presented in eTable 3 (available at ptjournal.apta.org).

Narrative Review

Variation in analysis and reporting methods, or the limited number of studies evaluating each risk factor, precluded meta-analysis for the majority of risk factors. A narrative

review of the results is presented here.

Spasticity

Of the 4 studies that evaluated spasticity,[3,13,35,36] 3 reported statistically significant differences between fallers and nonfallers. The fourth study[35] did not report a difference between fallers and nonfallers as measured by a single Ashworth scale rating, although it was not stated which muscle group was evaluated in this study. There was significant variation in assessment of spasticity among the studies, with different versions of the Ashworth scale and modified Ashworth scale being used, as well as differences in scoring methods (summation or averaging of scores). These findings may reflect the significant debate around the use and conduct of the Ashworth scale as a measure of spasticity.[37,38]

Fear of Falling

Fear of falling, as determined by self-report, was evaluated in 2 studies.[3,39] Odds ratios of 1.74 (95% CI=1.32–2.31)[39] and 0.95 (95% CI=0.57–1.58)[3] were reported.

Gait

Measures of gait were undertaken in 4 studies[3,13,35,40]; however, the variation in methods of evaluation and data reporting precluded meta-analysis. Measurement instruments included lab-based analysis (n=1), standardized generic walking tests (n=2), and MS-specific walking tests (n=1). Although statistically significant differences in these measures were found between fallers and nonfallers in all studies, the predictive value of the walking tests to discriminate between fallers and nonfallers was poor.[3]

MS Status

Multiple sclerosis status was objectively evaluated in 2 studies using the Expanded Disability Status Scale (EDSS),[3,40] although MS status was reported as continuous data in 1 study[3] and the sample was dichotomized for analysis as either mildly affected (EDSS score=0–2.5) or moderately affected (EDSS score=3.0–5.5) in the other study.[40] A third article[39] reported self-perception of MS status as "deteriorating" or "stable." In all studies, falls were associated with higher EDSS scores or self-reported deteriorating MS status, and statistically significant differences were noted between fallers and nonfallers.

Continence

Three studies included measures of continence within their evaluation.[3,36,39] Different self-report measures were used in each study to describe the degree that bladder or bowel problems interfered with daily life. All studies reported that continence was more problematic in participants who fell, although there was limited detail as to the specific problems experienced and 95% CI values included OR values of less than 1.0.

Other Risk Factors

A range of other risk factors were evaluated in the studies, including measures of sensory disturbance (n=2), dual task performance (n=1), and fatigue severity (n=1). Sensory disturbance was strongly associated with falls in 1 study[3] (OR=2.5 for each step on the Birgitta Lindmark Motor Capacity Part E Scale,[41] 95% CI=1.36–5.12); however, the other studies did not demonstrate statistically significant differences between fallers and nonfallers, with OR and 95% CI including values of less than 1.0.

Qualitative Articles

Two qualitative articles were reviewed in the analyses. In 1 qualitative study,[33] 6 people with MS who had participated in a pilot program focusing on self-management of falls were interviewed, whereas the other study[34] followed up 12 participants from a quantitative fall risk factor study. All participants highlighted a range of factors that they felt were linked to falls. Although many of these factors have been measured in quantitative risk factor studies, others such as endurance and temperature sensitivity have not been evaluated to date. One of the key areas raised by participants in both studies was the cognitive demands required of them in order to avoid and manage falls during daily activities. They described the need to prepare, plan, and specifically consider fall-avoidance strategies while undertaking "risky" activities.

Discussion

Knowledge of falls risk factors is essential to guide the development, implementation, and evaluation of falls management interventions. This systematic review has evaluated eight studies investigating risk factors for falls in people with MS. From a total number of 1,929 participants, 1,037 (53.75%) were classified as fallers. This figure highlights the significance of falls in MS, both for the potential to affect an individual's quality of life and the accompanying costs of managing falls-related injuries.

The results of the meta-analysis have highlighted that a progressive MS classification is a significant risk factor for falls, with those with a progressive classification 1.98 times more likely to fall than those with a relapsing-remitting classification. The narrative review has also identified the possible link between deteriorating MS status (as measured by clinician-rated EDSS or self-report) and fall risk.

The results of our meta-analysis support the notion that attributes such as altered balance and use of a mobility aid are associated with increased risk of falling in people with MS.

However, although the meta-analysis[3,36,39,40] has highlighted an association between balance and falling, the pooled OR values demonstrated only a small increase in the odds of falling for those with balance impairments; the use of a mobility aid was associated with far higher odds ratios. In addition, none of the balance measures demonstrated a sensitivity of greater than 0.56 in predicting falls.[3] These findings suggest that the use of balance measures alone is unlikely to be effective as a screening mechanism to identify individuals who are at risk of falling, and identifying which combination of factors best predicts fall risk is yet to be achieved. Furthermore, this review highlights that existing studies have focused on relatively broad issues, such as severity of MS and use of a mobility aid, in their attempt to identify potential risk factors. It could be argued that the use of a mobility aid may reflect the presence of multiple (and perhaps interacting) impairments that may contribute to fall risk rather than being a risk factor in its own right. Unfortunately, such broad descriptors fail to provide sufficient detail to guide the development of targeted management strategies, an approach that is demonstrated to be key to the effective management of falls in other populations.[42,43]

The meta-analysis also highlights the role that attributes such as cognitive impairment may have as risk factors for falls in people with MS, with combined OR values indicating that individuals with cognitive impairment are 1.28 times more likely to fall than those without cognitive impairment. This aspect is supported by qualitative data from people with MS who identified the importance of risk awareness, planning, and attention during task performance as key to preventing falls[34]—all aspects that may be affected by impairments in cognitive function. Within the quantitative articles, several of the cognitive measures utilized in the studies reviewed, such as self-report of memory, thinking and concentration issues, and the Mini-Mental Status Examination, have been criticized as being relatively generic and failing to evaluate key aspects of cognitive function that are commonly impaired in people with MS.[44] A recent study by D'Orio et al[45] (published after the completion of this systematic review) evaluating the impact of cognitive function on walking speed and falls suggests that more specific elements of cognition, including verbal memory and executive function, may contribute to fall risk. This study also highlights the potential utility of alternative objective cognitive evaluations, such as the Symbol Digit Modalities Test[44] or Controlled Oral Word Associations Test,[46] in studies investigating fall risk.

Within the narrative review, several other potential risk factors for falling in MS also have been highlighted, including spasticity, gait disturbances, continence, and fear of falling. The link between fear of falling and activity curtailment among people with MS has been previously highlighted by Peterson et al,[6] who found that 63.5% of the 1,064 participants in their study reported fear of falling and, of these participants, 82.6% reported associated activity curtailment. In other populations, fear of falling has been identified as an independent risk factor for actual falls[7]; however, the 2 MS studies evaluating this issue presented conflicting results. This disparity may have arisen due to differences in the study samples. Participants in the study by Matsuda and colleagues,[36] who reported a link between fear of falling and falls, were all over 45 years of age, with 56.19% of the participants aged over 65 years. In contrast, the age range of the participants in the study by Nilsagard et al[3] (mean age=50 years, range=25–75) was significantly lower. Given the known link between fear of falling and falls in older people, we recommend that this area should be evaluated further in future studies, using validated assessment measures such as the Falls Efficacy Scale.[47]

This systematic review suggests that there are similarities in fall risk factors in people with MS and other neurological conditions.[8,48,49] As with other groups, secondary issues such as deconditioning, medication use, and environmental factors also may contribute to fall risk. To date, however, these attributes have been evaluated in only 1 or 2 studies. This factor, together with the wide range of evaluation methods used, preclude meta-analysis.

The increased awareness of the importance of falls as an issue for people with MS is encouraging.[50] However, the relatively small number of studies and the variable methodological quality of the included articles mean the findings should be interpreted with caution. For example, only 2 of the studies complied with European fall study guidelines for best practice[21] by recording fall incidence using a prospective falls diary system for the recommended 3-month minimum period; retrospective recall is known to be inaccurate and subject to bias in other populations.[51] Moreover, a variety of systems were used to classify fallers and nonfallers, including defining fallers as those who reported single falls, multiple falls, or injurious falls. This finding is relevant, as evidence from studies in other populations suggests the characteristics of occasional and frequent fallers are significantly different. Currently, the lack of reported data on these issues makes it impossible to know whether these findings are also the case in people with MS. Finally, as

has been reported in other areas of MS research, significant variation in the methods used to assess and categorize risk factors, together with the wide range of outcome measures used and variation in reporting procedures, makes data pooling and comparison among studies problematic. The results of this systematic review must be interpreted within this context.

Conclusion and Recommendations

Falls are a significant issue affecting a large number of people with MS. Based on the existing body of evidence, it is not possible to clearly identify specific risk factors for falling in people with MS. Knowledge of these factors is important, as accurate identification of those most at risk has the potential to enable individuals to make informed decisions regarding their health and well-being, such as the need to modify potentially high-risk activities. The ability to assess risk accurately also will assist professionals in the targeting of management interventions. There is an urgent need for robust, clinically relevant research to support this developing area of practice. As highlighted by Platt, well-designed research that is conducted using sound methodological principles makes for "rapid and powerful progress."[52(p347)]

The nature of MS emphasizes the diversity of factors that could be associated with fall risk, including the wide-ranging neurological impairments and the unpredictable and evolving pattern of the disease course. For instance, clinical experience suggests that impairments that are common in people with MS, such as vestibular and cerebellar function,[53,54] may be significant contributors to fall risk in this population. We recommend that specific evaluation of these mechanisms should be included in future studies evaluating fall risk factors in MS.

In the development of future research evaluating fall risk in people with MS, we recommend that study methods and implementation should be informed by current best practice guidance relating to the use of standardized fall definitions and the collection of prospective fall data. We suggest that risk factor evaluation should use psychometrically validated, objective measures, which are widely used and have clinical applicability, to aid clinicians and researchers to compare study findings, synthesize the results, and relate them to clinical practice.

Miss Gunn, Mr Haas, Professor Marsden, and Dr Freeman provided concept/idea/research design. Miss Gunn and Dr Freeman provided writing. Miss Gunn provided data collection. Miss Gunn, Mr Newell, and Dr Freeman provided data analysis. Miss Gunn and Dr Freeman provided project management. Mr Haas, Professor Marsden and Dr Freeman provided consultation (including review of manuscript before submission).

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