Falls in People with Multiple Sclerosis

Risk Identification, Intervention, and Future Directions

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Falls are highly prevalent in people with multiple sclerosis (MS) and result in a range of negative consequences, such as injury, activity curtailment, reduced quality of life, and increased need for care and time off work. This narrative review aims to summarize key literature and to discuss future work needed in the area of fall prevention for people with MS. The incidence of falls in people with MS is estimated to be more than 50%, similar to that in adults older than 80 years. The consequences of falls are considerable because rate of injury is high, and fear of falling and low self-efficacy are significant problems that lead to activity curtailment. A wide range of physiological, personal, and environmental factors have been highlighted as potential risk factors and predictors of falls. Falls are individual and multifactorial, and, hence, approaches to interventions will likely need to adopt a multifactorial approach. However, the literature to date has largely focused on exercise-based interventions, with newer, more comprehensive interventions that use both education and exercise showing promising results. Several gaps in knowledge of falls in MS remain, in particular the lack of standardized definitions and outcome measures, to enable data pooling and comparison. Moving forward, the involvement of people with MS in the design and evaluation of programs is essential, as are approaches to intervention development that consider implementation from the outset. *Int J MS Care.* 2020;22:247-255.

The incidence of falls in people with multiple sclerosis (MS) is high, and the consequences of falls are far-reaching for both the person and the health care system. This important topic has received increasing attention as researchers and health care professionals aim to identify the risk factors, context, and consequences and to use these data to develop theory-based interventions. This narrative review and position paper is written by members of the Special Interest Group on Mobility of Rehabilitation in Multiple Sclerosis (RIMS, the European network for best practice and research in MS) and aims to summarize the key literature in the area and to identify gaps in knowledge, challenges, and ways forward.

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Incidence of Falls

Falls are common in people with MS, with a large international data set demonstrating that 56% fall at least once within a 3-month period,[1] with 37% of individuals categorized as frequent fallers. Notably, people with MS fall more frequently, are more likely to experience injurious falls, and have different fall circumstances compared with their healthy peers.[2] Over a 6-month study period, 71% of people with MS reported falling versus 41% of healthy controls, with the MS group more likely to attribute their falls to tripping and distraction. Fall rates in people with MS are similar to those in community-dwelling stroke survivors (55%),[3] adults older than 80 years (50%),[4] and people with Parkinson disease (46%).[5]

Interestingly, there is a nonlinear association between falls and level of neurologic disability, with peaks in fall incidence occurring at Expanded Disability Status Scale (EDSS) scores 4.0 and 6.0,[6] with the highest rate

of recurrent falls occurring in those who do not yet use a mobility device.[7] Falls are not limited to people with MS who are ambulatory, and although there is less research evaluating falls in people with more advanced MS, studies show that wheelchair and scooter users also have a high incidence of falls (75%).[8] People with progressive MS have a higher incidence of falls,[1] and falls have been proposed as a critical incident that signifies a worsening of symptoms that requires clinical attention. Those restricting their activity and avoiding risky behaviors may have a lower fall rate, but this practice is not without consequences and is not a solution to fall prevention.[9]

A key consideration regarding the prevalence and incidence of falls is the way in which fall data are collected. There is a notable underestimation of number of falls by people with MS. Dibble et al[10] found that 6-month recall was 17% accurate, and 63% of responders underestimated the number of falls they had. This underestimation when retrospective recall is used is confirmed by Nilsagård et al,[11] who found that using retrospective recall, 34% were fallers, but using prospective diaries, 63% were. This consistent underestimation of number of falls when using retrospective recall led to recommendations that fall data be collected prospectively using diary-based methods.[12] However, the poor correlation between diary and electronic fall logging with a button push[13] suggests that a truly objective method of fall recording is required to advance this field.

The definition of a faller is inconsistent in MS fall research. The number of falls needed to classify a person with MS as a faller range from one or more falls,[11,14,15] to two or more falls,[16-18] to three or more falls.[19] Likewise, a wide range of fall definitions are used, including "unexpected event that results in the person ending up on the ground, floor, or any lower surface"[20-22]; "unintentionally coming to the ground or other lower level and other than as a consequence of sustaining a violent blow, loss of consciousness, or sudden onset of paralysis as in stroke or epileptic seizure"[23]; or "any unexpected loss of balance that resulted in whole body contact with the ground."[24] Some studies fail to define a fall.[25,26] This heterogeneity in both fall definition and classification limits comparison between studies and data pooling. One potential way to overcome these discrepancies in faller classifications used is to report fall data as fall rate per person-year. Fall rate per person-year can be calculated using the following formula[27]: [fall rate = (total number of falls/total number of person-days [all participants]) × 365].

Consequences of Falls

Falls can have significant physical, social, and psychological consequences for the individual. In terms of physical impact, injurious falls in people with MS are common, with rates of 0.18 to 0.23 per person per year.[6,28] Most fall-related injuries are relatively minor, for example, sprains and contusions; however, the risk of serious injury is pervasive, with head injuries and fractures also reported by people with MS who have fallen.[28,29] A threefold higher risk of hip fracture than age- and sex-matched peers, with greater risk in those prescribed corticosteroids in the previous 6 months, was reported in a population-based cohort.[30] Injurious falls contribute to the high socioeconomic cost associated with MS as a result of increased health care use and decreased labor force productivity.[31,32] These high rates of injurious falls (42%-58%[2,19]) are much greater than rates of 23%[33] to 30% seen in the elderly,[34] and after stroke, where rates of 10% have been reported.[3]

The psychological impact of falls presents predominantly as a high level of fear of falling and associated activity modification in both those who have[35] and those who have not experienced an actual fall.[36] Fear of falling has multiple definitions that reflect a multidimensional construct with physiological, cognitive, and behavioral components.[37,38] Based on a cross-sectional study, people with MS with elevated fear of falling are less likely to participate in leisure-time physical activities.[39] This behavior might be explained as a protective mechanism. However, this protective response may result in some people with MS curtailing their activities inappropriately, resulting in further deconditioning and adversely affecting physical function and independence.[40] This adverse response should be avoided, especially due to the growing body of evidence highlighting the benefits of regular physical activity for people with MS.[41] Most concerning is that studies have consistently found that fallers have lower quality of life than nonfallers.[14,42] Lower quality of life is associated with higher socioeconomic costs and contributes significantly to the intangible costs and burden for the person with MS related to issues around self-care, pain, anxiety, and depression.[32] Nilsagård et al[43] qualitatively explored the context and impact of accidental falls in people with MS, with participants describing falls as limiting, restricting, and embarrassing.

Factors Associated with and Predictive of Falls

Understanding the factors associated with and predictive of falls can assist in the development of interventions and also identify those in need of treatment. There are many varied fall risk factors highlighted in the literature, confirming the complexity and individual nature of fall prevention. Broadly, fall risk can be considered in terms of physiological, personal, and behavioral risk factors.

The most frequently reported physiological risk is impaired balance. Two meta-analyses[44,45] that considered data from cross-sectional and prospective studies confirmed that balance is a risk factor for falls. In addition, other indicators of reduced postural control, such as reduced walking speed, increased static postural sway while standing, and the use of a mobility aid, were also identified as fall risk factors in those reviews. These findings are accompanied by prospective cohort studies in which reduced lower-limb strength,[16] reactive stepping,[18] and dual-task ability[17] were identified as risk factors for falls. Worth noting, although visual problems are often one of the first symptoms noticed by people with MS and good vision is essential for maintaining balance control, testing of known visual risk factors in other groups (such as edge contrast sensitivity) is not considered a predictor of falls in people with MS.[46] It is possible that other aspects of vision could be an issue for people with MS, but most risk factor studies in MS to date have not included specific visual tests. Nevertheless, visual function is integrated into the EDSS score and traditional balance tests such as the Berg Balance Scale and the Physiological Profile Assessment (PPA). A prospective study with 100 participants found that not having a visual problem (via self-report) was associated with a greater fall risk.[47] This finding may indicate that those with visual problems are inherently more cautious and have a resulting lower risk of falls.

Although balance is impaired in MS fallers, a recent review found that clinical balance measures in isolation are poor at identifying future fallers.[48] This finding suggests that other factors are also important when identifying those at risk of falling and when designing treatments for preventing falls. Other MS symptoms related to falls include fatigue,[49] cognitive impairment,[50] spasticity,[11] and urinary incontinence,[22] although, again, the relationship may not be linear in nature. Similar to the literature in elderly populations, medications, in terms of quantity and class, are associated with higher fall rates in most studies published on this topic.[51,52] During the past decade, a variety of disease-modifying drugs have been introduced in MS. The challenge is to examine whether immunomodulatory drugs differ when examining falls in the MS community. This issue was partly addressed by Comber et al,[52] who investigated the effect of medication use on falls in MS. They reported increased odds of being a faller for participants taking medications categorized as genitourinary and sex hormones or centrally acting muscle relaxant medications.

When considering personal factors associated with and predictive of falls, reduced balance confidence[53] and reduced fall self-efficacy[54] have been shown to be predictive of future falls in people with MS, with concerns about falling being associated with changes in postural control in fallers.[55] Other personal factors that have also been highlighted as contributing factors for falls in MS are unrealistic appraisal of ability, poor organization/planning of activities, adjustment/replacement of activities, and emotional adaption through awareness and acceptance of limitations.[29,56] Gunn et al[57] examined physiological risk and perceived risk in 416 people with MS and found that approximately 50% of individuals had disparities between their physiological risk (using the PPA) and perceptual risk (using the Falls Efficacy Scale [international]) of falls, with most having a perceived risk greater than their physiological risk. It is hypothesized that those with excessive perceptual risk may be at increased likelihood of fear of falling and associated activity curtailment, whereas those with excessive physiological risk may engage in risk-taking behaviors through an unrealistic appraisal of ability.[58]

Understanding the environmental context of falls will improve management of falls in MS. Studies suggest that falls most often occur inside the home, in the morning or afternoon, and during general mobility without the execution of any other specific task.[6,29,59] It is likely that the circumstances associated with falls differ among those who are ambulant or wheelchair users, with one study suggesting that most falls occur during transfers for wheelchair users.[60]

An additional method to uncover risk factors for falls in MS is to ask individuals what they attribute their falls to. According to Matsuda et al,[29] people with MS attribute their falls to trips/slips, fatigue, failing to use an assistive device when needed, rushing, and not paying attention. Similarly, Peterson et al[61] found that poor balance, lower-extremity malfunction, and use of assistive devices were the leading causes of falls. More recently,

Gunn et al[6] reported that one-third of falls were associated with feeling fatigued and/or loss of balance, with tripping, legs giving way, and being distracted each accounting for 10% of falls.

Although cognitive impairment in isolation has been identified as an independent risk,[50] difficulty with dual tasking has also been shown to be associated with falls in people with MS.[62,63] Those who prioritize cognitive tasks over walking are at greater risk of falling,[64] which similarly has been found in other populations,[65] resulting in strategies such as balance first or slow down and concentrate.[66]

The proliferation of factors associated with and predictive of falling has led to several authors investigating multivariate risk prediction models using prospective study designs to identify those at future risk of falls, and hence treatment. Models included simple clinical variables such as the EDSS score, Ashworth score, and fine motor control assessed using the Nine-Hole Peg Test.[67] Some of these models require instrumented tools such as gait analysis devices, strength assessment using the Biodex Multipoint System, and the PPA.[16,19,67] Regarding clinical utility, these fall risk prediction models have varying levels of sensitivity (69%-71%) and specificity (70%-88%), with 80% sensitivity regarded as an important cutoff level for fall screening tools.[68] Only two studies included the area under the receiver operating characteristic curve, reporting values of 0.71[19] and 0.73,[16] suggesting moderate and acceptable levels of discriminative ability because the values are greater than 0.7.[69] Despite these many well-designed multivariable studies, Cameron et al[49] advocate identifying those at risk of future falls by simply asking about fall history. A fall in the past year was the best predictor of falls or injurious falls in the following 6 months. However, limitations of this approach are that 1) predicting future falls based on previous falls requires the person to fall at least once (and, therefore, experience the negative consequences associated with this) and 2) people with MS with memory deficits might not report accurately. Asking a simple question also relates to the recent emphasis on patient-reported outcomes, with a previous study demonstrating that self-report measures have higher levels of discriminative ability than performance-based measures,[22] although they did not report corresponding measures of clinical utility.

Mazumder et al[2] identified contextual differences in falls between middle-aged people with MS and controls. The authors found that healthy adults most often fall outdoors, whereas people with MS showed a higher rate of indoor falls. In addition, healthy adults were more likely to report falls due to a slippery surface, whereas people with MS were more likely to report falls due to a distraction or tripping, fatigue, or excess heat. This finding suggests that when fall prevention programs for people with MS are designed the unique risk factors for falling in this cohort need to be addressed.

Treatment

Given the complexity in causes and risk factors of falls in MS, a multifactorial approach seems to be the most appropriate strategy; however, much research to date considers exercise only. Two systematic reviews of interventions to reduce falls exist.[70,71] Sosnoff and Sung[70] identified ten studies, four of which were randomized controlled trials (RCTs) with a total of 524 participants. The increased focus on this topic resulted in 13 RCTs being included in a recently published Cochrane review.[71] In contrast, a systematic review of exercise interventions for fall prevention in older adults included 108 RCTs with 23,407 participants living in the community in 25 countries.[72] Most MS studies with exercise interventions included conventional balance, sensory-specific, and game-based exercises. Most trials demonstrated a reduction in actual falls and/or fall risk, most often with a concurrent improvement in balance and/or mobility. Despite these encouraging findings, firm conclusions could not be drawn due to the heterogeneity in study designs, small sample sizes, lack of assessor blinding, and limited use of prospective fall monitoring. The review authors highlight the need for additional knowledge regarding risk factors for falls in people with MS and suggest implementation of targeted multifactorial interventions examining both physiological and behavioral risk, as advocated by the International MS Falls Prevention Research Network (IMSFPRN).[73]

A related review concerning interventions to improve balance in people with MS[74] found that specificity is important (ie, balance and functional exercises had the largest effect on balance) and that dose of intervention is related to outcome. Sherrington et al[75] suggest that more than 50 hours of intervention is required to improve balance, yet, to our knowledge, no study in the MS field has examined an intervention program at this dose. The literature about older adults consistently finds that exercise interventions, although effective, are more

impactful as part of multiple-component or multifactorial interventions.[76]

Unfortunately, the strong evidence for multifactorial and multiple-component interventions in older fallers are sparsely replicated in MS. To date, only four multifactorial interventions have been published in MS.[26,77-79] Hugos et al[78] performed a retrospective evaluation of an existing exercise and education program for fall prevention in people with MS using the Free from Falls program for older adults with adaptations made for MS-specific symptoms such as fatigue. However, the retrospective nature of the study and the lack of a control group necessitates caution when interpreting these findings, which were a reduction in fall rates and improved balance performance and confidence. Sosnoff et al[26] evaluated a multifactorial approach based on the Safe at Home BAASE program.[80] Their pilot RCT of 34 participants compared four groups: waitlist control, home exercise alone, education targeting behavioral risk, and a combination of home exercise and education. The authors found a reduction in risk of falls for the groups engaged in an exercise component, although with mixed findings for the combined exercise and education arms. Limitations included underpowered sample size and lack of prospective fall monitoring before the intervention. Thus, further research examining multicomponent fall prevention interventions for people with MS is needed.

Interventions addressing personal and environmental factors associated with falls are lacking. For example, fear of falling and fall risk are not only associated with falls but are independent fall risk factors,[17,42,81] yet to date have had limited attention in interventions. The strong evidence from the older adult literature and our increasing understanding of the role of psychological and environmental aspects of falls in MS suggests that future interventions should address both aspects and be tailored to the individual risk factors and physiological/psychological profile. Therefore, we encourage future trials to investigate the efficacy of adding supportive features (eg, grab bars or handrails) in locations such as stairs and bathrooms in homes of people with MS. In addition, future research should examine the impact of fall prevention programs that include education around the use and training of walking aids or increasing awareness of the outdoor environment and situations that might lead to falls. Other environmental harm-minimization elements, such as fall monitoring devices or pressure sensors, also have not been addressed to date. Another element is that of harm minimization through fracture prevention via routine preventive bone density assessment and intervention to improve bone loss if it presents.

Recent studies[82,83] have investigated the views and opinions of persons with MS in relation to what they would consider the optimal fall prevention program, highlighting their preference for practical, personalized interventions with peer interaction and ongoing support (either in groups or by other media). Balance/strength exercises and fall prevention/management techniques, as well as services regarding mobility aids and home modification from trained professionals (eg, occupational therapists and physiotherapists), might be included. Something remarkable is that people with MS recognize that personal factors, such as the competence of knowing and accepting their capacity to engage in activities, are crucial in preventing falls.

Gaps in Knowledge

To increase our understanding of falls in people with MS and, hence, their treatment, there are several gaps in knowledge that require attention. Balance impairment is associated with and predictive of falls, but our understanding of what particular postural control deficits are associated with falls is limited.[84,85] Determining what postural control deficit or what element of balance (eg, proprioceptive deficits, reduced strength, cognitive motor interference, or reaction time) is most associated with falls will allow more targeted and tailored approaches and could potentially increase the efficacy of exercise interventions.

In addition, our understanding of the protective versus predictive nature of these deficits and their contribution to falls is limited. For example, if an individual walks at a slower gait speed with a wider base of support, this may be a compensatory mechanism to increase stability. Therefore, attempts to normalize this pattern of gait, such as increasing speed, may be inherently disadvantageous to reducing fall risk. Similarly, if imbalance occurs due to fast walking speed, a reduction in gait speed may be seen as a positive outcome of intervention. Longitudinal observational studies of clinical measures and posturography should be implemented, with fall incidence assessed prospectively before and after assessment. Such investigations may enable more targeted rehabilitation strategies for fall prevention in people with MS.

An associated issue is the choice of balance measures used to establish fall risk. For example, people with

MS fall while standing, turning, and walking,[6,29] yet many balance measures capture balance with feet in a static position. Posturography seems promising as a fall risk tool,[86] but the static foot plate does not mirror the dynamic activities where falls occur, and access to this in many clinics is limited, with some systems requiring technical expertise. The use of sensor-based measures of balance during gait[87] may be an option worth pursing because it would allow the collection of ecologically valid postural control data, potentially in remote settings.

When conducting studies to evaluate multiple-component risk prediction tools, the model first needs to be developed, and it subsequently needs to be validated; none of the existing MS fall risk prediction tools have been validated to date. The model development study often tends to overestimate predictive ability of a model, either due to overfitting if the sample size is small or if there are too few outcome events relative to the number of predictor variables.[69] External validation applies the model and assesses its predictive performance for a new sample who were not involved in the model development study. Model impact studies are recommended after external validation to assess the effect on the change in behavior of clinicians, on cost-effectiveness, and on health outcomes.[88] In addition to including analysis of the traditional predictive values (eg, sensitivity, specificity, area under the curve), impact studies must also consider safety and efficiency.[89]

Arguably fall prevention interventions for people with MS are in their infancy, although the start is promising. One concern is the mismatch between the range of physiological and psychological risk factors and the predominance to date of exercise-only interventions; however, more recent interventions are acknowledging this and evaluate multiple-component and multifactorial interventions. Intervention development is complex, and for this multifactorial, variable, and individualized problem, the challenges will be many. Frameworks such as the Medical Research Council (MRC) development of complex interventions[90] may assist with this challenging process. An additional consideration as this field progresses is the need to articulate the theory behind the interventions, an aspect of intervention development for which the rehabilitation field has previously been criticized. It is essential that transparent dissemination of the development processes behind complex interventions occurs and that theoretical underpinnings and mechanisms of intended action are clearly articulated so that the intervention is developed in line with best practice.[91,92]

It is likely that a range of interventions considering either group or individual treatment, using face-to-face or remote methods and in-hospital, outpatient, and community settings, and with a range of international health care and social contexts will be needed; one size certainly will not fit all for the issue of falls in MS.

Challenges

One key challenge in pooling and comparing data is the lack of standardization of fall definitions, faller classifications, and fall outcomes to date. The use of frameworks such as Core Outcome Measures in Effectiveness Trials (COMET)[93] to develop and apply core outcome sets for MS fall interventions is recommended to overcome the current issue of multiple definitions, classifications, and outcomes. Most concerning is the limited input to date from people with MS in deciding study outcomes, which requires attention in future work.

The issue of "dose" of intervention required to improve postural control is a challenge, and a fine balance between the optimal dose/duration and the practicalities involved in engaging with and delivering such a program needs to be considered. Evidence from a range of groups highlights sustained engagement as a major challenge to fall prevention interventions[94] and suggests that programs need to be easy to access, perform, and embed into a person's daily life for initial improvements to be sustained.[95] There are also significant resource implications in the provision of such interventions that may challenge existing models of health care. Supplementing face-to-face delivery with the provision of Web-based resources or telephone or e-mail contact to support engagement seems promising,[96] as do programs that embed a supported self-management approach.[80,97]

Perhaps the greatest challenge in reducing fall risk and, hence, falls is variability. Presentations and symptoms of MS (and thus fall risk factors) vary significantly between people and over time, which necessitates flexible intervention programs that can be individually targeted and that support people to be able to self-assess their changing symptoms and adjust their programs effectively on an ongoing basis. Additional variability in personal, environmental, and social factors means that programs need to be adaptable and responsive to needs and circumstances. Such programs require input from highly trained clinicians who are supported to use a wide range of skills and present feasibility and sustainabil-

ity issues for many models of health care delivery. For researchers, this degree of variability is also a significant challenge, particularly in achieving a high degree of flexibility in program provision while maintaining the degree of standardization and intervention fidelity necessary to ensure methodological rigor in clinical trials. Collaboration, nationally and internationally, will be vital for recruiting sufficient numbers of people to undertake the large-scale studies that are essential to develop a robust evidence base, although the variety of health care settings internationally adds another challenge.

The introduction of wearable electronic technology, worn on the body or embedded into mobile and portable solutions (smartphones, watches, etc), creates a new challenge for those investigating falls in people with MS. Although the potential of these devices to identify risk factors for falls is clear, their benefits are still to be verified. Importantly, these devices enable the research field to detect movement behavior of people with MS outside the laboratory and/or clinical facilities. This opportunity might uncover new "real-life" risk factors that were not previously considered.

Conclusion and Way Forward

It is probable that we cannot prevent all falls; however, our aim should be to prevent as many falls as possible. Falls that require medical attention are particularly burdensome for both the person and the health care system and might be prioritized; however, even minor falls may have a profound effect on well-being and on activity participation and, therefore, warrant intervention to prevent them.

PRACTICE POINTS

- Falls are prevalent in people with MS and have significant negative consequences. Clinicians should ask about falls at all stages of the condition and refer for appropriate interventions in a timely manner.
- Falls are multifactorial and complex, and there are many, varied risk factors. The most reliable predictor of future falls is a history of falls.
- Interventions should target physiological risk factors (eg, balance and strength impairments), personal risk factors (eg, fear of falling, matching physical ability to the task), and environmental risk factors (eg, use of appropriate assistive devices).

Falls are common and have a wide range of negative effects. Research to date suggests that there are a variety of physiological, personal, and environmental factors that contribute to falls for people with MS; a better understanding of these factors will lead to improved risk prediction tools and interventions for this cohort. Interventions to date have largely comprised exercise-only interventions; these show promise and suggest that challenging, functional balance programs targeting individual risk factors, which are structured to support people to engage at a high intensity over a long duration, are most likely to be effective. However, large-scale effectiveness trials are urgently required to determine the key components that should form the basis of MS fall exercise interventions, regardless of delivery method or health care setting.

Given the range of issues contributing to falls in MS, future interventions should consider other aspects of fall risk, particularly the psychological and MS-specific risk factors. This also necessitates a recognition that not all risk factors will be modifiable and that people will often choose to accept a degree of risk to maintain their participation in daily activities. Alongside assessing and optimizing modifiable individual fall risk factors, programs need to support people to develop effective, realistic strategies to manage fall risk while maintaining engagement; to recognize when changes to their strategies are required; and to access further support as necessary. As in other groups, perhaps the focus of programs should move away from emphasizing fall reduction and instead move toward approaches that aim to maximize "safe mobility."

The way forward is undoubtedly through collaboration: nationally, internationally, across disciplines, and with people with MS. A better understanding of this complex, individual, and multifactorial issue will assist in designing, evaluating, and implementing interventions to prevent or reduce falls for people with MS. □

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