Multiple Sclerosis and Falls – An Evolving Tale

Jacob J Sosnoff,[1] Robert W Motl[1] and Steven Morrison[2]

1. Associate Professor, Department of Kinesiology and Community Health, College of Applied Health Sciences, University of Illinois at Urbana-Champaign, Illinois, US; 2. Endowed Professor of Physical Therapy, Director of Research, School of Physical Therapy and Athletic Training, Old Dominion University, Norfolk, Virginia, US

Abstract

Falls are a common health concern in the multiple sclerosis (MS) community with one out of two individuals with MS reporting a fall in the previous 6 months. Falls often lead to physical injury and have been found to be associated with reduced participation and quality of life. These adverse consequences underscore the importance of identifying risk factors for falls in MS so that appropriate interventions can be designed and tested. Ongoing research has suggested that clinical disability, balance and gait impairment are related to past and future falls. The data also suggest that cognitive impairment is related to falls. Fortunately, it appears that these fall risk factors and falls per se can be reduced with targeted interventions in persons with MS. However, the most effective fall-prevention strategy in persons with MS has yet to be elucidated. Ultimately, the reduction of falls in persons with MS has the potential to improve participation and quality of life.

Keywords

Falls, multiple sclerosis, rehabilitation, balance, gait, cognition, participation

Disclosure: The authors have no conflicts of interest to declare.

Acknowledgements: This work was supported in part by a seed grant from the Consortium of Multiple Sclerosis Centers.

Received: 21 May 2013 **Accepted**: 25 June 2013 **Citation**: *European Neurological Review* 2014;9(1):44–8 *DOI:10.17925/ENR.2014.09.01.44*

Correspondence: Jacob J Sosnoff, University of Illinois at Urbana-Champaign, 301 Freer Hall, 906 South Goodwin Ave, Urbana, IL 61801, US. E: jsosnoff@illinois.edu

Multiple sclerosis (MS) is a chronic, often disabling, neurological disease, common among adults worldwide and in the US.[1] It has a heterogeneous geographical prevalence with higher rates reported in Central and Northern Europe, North America and Australia than for Asia, Africa and South America.[2] There are believed to be over 400,000 persons with MS in the US and 2.1 million worldwide. The majority of people with MS are typically diagnosed between 20 and 50 years of age, and women are affected two to three times more often than men. The exact cause of MS is not clear, but it is believed to result from a combination of genetic and environmental factors.[3]

This disease process involves intermittent bursts of focal inflammation across the central nervous system (CNS).[4] The inflammatory process results in the demyelination and transection of axons throughout the CNS. The resulting damage leads to conduction delays and blockage of action potentials along nerve axons.[4] This interference with neuronal conduction throughout the nervous system is associated with a heterogeneous array of functional impairments and symptoms including (but not limited to) muscle weakness, cognitive impairment, sensory disturbances, and a decline in postural control and gait function.[1]

Given these symptoms it is not at all surprising that falls are common in persons with MS. Indeed, over 50 % of persons with MS report falling over in a 6-month period.[5–8] Perhaps more alarming, the majority of those who do fall require medical attention for injuries.[9,6,10] For example, persons with MS are four times more likely to suffer a hip fracture brought about by a fall than age- and gender-matched peers without MS.[11] This elevated fracture risk stems from low bone mineral density and osteoporosis in persons with MS.[12,13] Lastly, persons with MS who have previously fallen report worse physical and psychological health status (i.e. health-related quality of life [QoL]) compared with nonfallers with MS.[7]

Falls can further have an adverse impact on fear of falling and falls self-efficacy and contribute to activity curtailment, physiological deconditioning, loss of independence and institutionalisation.[14,15] For instance, approximately 64 % of persons with MS have an increased fear of falling and, of those individuals, 83 % reported activity curtailment.[16] Another study documented that approximately 75 % of community-dwelling persons with MS who have fallen in the last 6 months self-reported activity restriction due to concerns about falling.[15] Recently, these self-reports of activity curtailment in persons with MS who have fallen were confirmed with objectively measured ambulatory physical activity (e.g. accelerometry). Specifically, persons with MS who had fallen in the last year had lower amounts of physical activity than persons with MS who had not fallen.[17]

One caveat to consider when reviewing the majority of research concerning consequences of falls in persons with MS is that all of the studies that support this disability-disuse cycle are cross-sectional in nature. Consequently, it is unclear whether falls truly lead to decreased activity and physiological deconditioning as proposed or rather falls are unrelated to activity, physiological deconditioning and QoL. Ideally, the best way to determine whether there is a strong relation between these variables in persons with MS would be to conduct longitudinal investigations. If such an association is noted, we would further propose that it is worthwhile to explore the possibility that physical activity promotion[18] can counteract the fall-related decline in physical activity and potentially minimise physiological deconditioning and reductions in QoL.

There is sufficient evidence to conclude that persons with MS are at elevated risk of falls compared with healthy individuals of a similar age and that falls seemingly have significant negative effect on QoL stemming from physical injury and reduction in participation. Such observations underscore the importance of identifying risk factors for falls in MS. The main risk factors, if modifiable, can become the focus of targeted interventions designed for reducing falls and the life-altering effects on secondary outcomes such as compromised QoL and/or participation.

Fall Risk Factors in Persons with Multiple Sclerosis

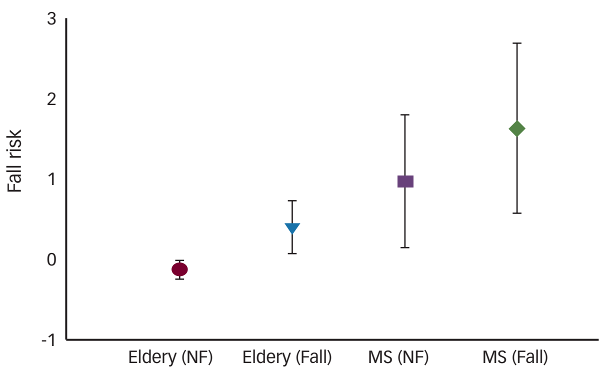
The first step to fall risk prevention in any given clinical population involves an understanding of those factors that can contribute to such occurrences. This is necessary for both identifying individuals at risk of future falls and also for providing information that can be used to design appropriate therapeutic interventions that target a reduction in fall occurrence. Such an approach has been widely adopted in the gerontology literature that serves as a backdrop for the discussion of falls risk and prevention in persons with MS.[19]

Accordingly, we highlight major observations from the well-developed and characterised falls literature among older adults, another population that has considerable risk of falls. One of the most important observations is that falls are preventable with interventions designed to target specific risk factors.[19,20] While previous studies have reported upward of over 400 potential fall risk factors for older adults,[21] the primary risk factors include sensorimotor function, general balance and walking ability.[22,23] Linked to these factors is the evidence that highlights that impairments in muscle strength and coordination are also strong predictors of falls in older adults.[21,24–27] Not surprisingly, interventions that target these specific factors have been the most widely developed and implemented. Overall, these interventions have been found to effectively reduced physiological falls risk and fall incidence in older adults.[19,20,24,27]

It is important to note that although the geriatric literature offers important insights in terms of falls in the older adult, there are notable differences between persons with MS and healthy older adults regarding specific risk factors leading to falls. For instance, assessment of falls risk using standard tools developed for geriatric populations such as the physiological profile assessment (PPA) illustrate that the overall risk of a future fall is greater for persons with MS than older adults (see *Figure 1*). Indeed, persons with MS without a fall history have a higher risk of falls even than older adults who have not fallen. This observation highlights the need to develop disease/patient specific falls risk models.

In comparison to our understanding of falls in the healthy older adult, much less is known about falls risk factors in persons with MS, particularly for those older individuals with this disease. While over 400 risk factors have been broadly identified with falls in general, only around 20 specific risk factors have been investigated in persons with MS.[28] The following discussion focuses on these factors, particularly those that are modifiable, as these could become the focus of interventions.

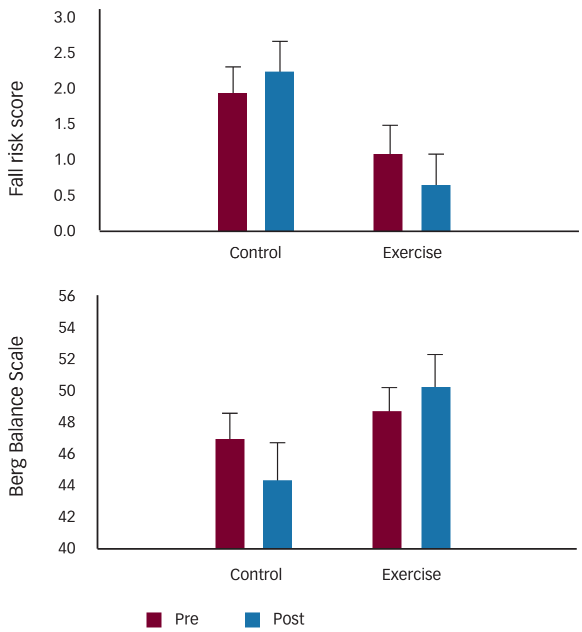
Figure 1: Physiological Fall Risk as a Function of Age, Fall and Disease Status



In one of the first and largest retrospective studies of 1,089 persons with MS, general balance and walking impairments, poor concentration and bladder incontinence were identified as the main correlates of fall incidence over a 6-month period.[8] A more recent retrospective study (n=447) cited that patient-reported mobility impairment, muscle weakness and balance problems were the main factors linked with falls in persons with MS.[22] Furthermore, this investigation observed that most falls occur during balance-challenging tasks, such as transfers and locomotion. While these studies have provided insight in terms of the risk factors leading to falls, a major limitation was the lack of any objective assessment of posture and gait, with both studies employing nonvalidated self-reported measures concerning balance and walking function.

To overcame this limitation, Sosnoff and colleagues[29] examined cross-sectional associations among demographic, clinical, walking and balance metrics and falls history in 52 ambulatory persons with MS.[29] Disease status was assessed by a neurologist with the Expanded Disability Status Scale (EDSS). Walking speed, coordination, endurance and postural control were quantified with an objective validated multidimensional mobility battery. Given that over half the participants fell in the previous year all individuals were further classified into faller and nonfallers based on their previous history. The results demonstrated that fallers, as a group, tended to be older, had a greater prevalence of assistive devices use, worse disability, decreased walking, endurance and impaired balance compared with nonfallers. Additionally, fallers had greater impairment in cerebellar, sensory, pyramidal and bladder/bowel subscales of the EDSS. Researchers have also focused on the association between gait impairment and falls. Specifically, one investigation quantified fluctuations in gait (e.g. gait variability) as a function of fall status in persons with MS.[30] The sample included 41 individuals with MS and 20 age- and sex-matched controls. Persons with MS were divided into two groups based on fall history (nonfallers and fallers). Overall, persons with MS had greater gait variability than controls as indexed by coefficient of variation and Fourier-based variability. Moreover, fallers with MS had greater Fourier-based variability than MS-nonfallers, whereas there was no difference between MS groups for traditional gait variability metrics. It was proposed that a contributing factor to the increased gait variability was impairments in dynamic balance. These observations highlight that gait impairment is related to fall status in MS and that interventions focusing on fall risk reduction should target balance and walking impairment.

Figure 2: Physiological Fall Risk Score and Berg Balance Scale Score as a Function of Group and Time



The mechanisms underlying gait and balance impairment and the association with falls are not well characterised. One of the few investigations examining neural correlates of falls in persons with MS reported that recurrent fallers with MS have greater lesion load of the brainstem and middle cerebellar peduncle than nonfallers.[31] Recently, Prosperini and colleagues,[32] utilising diffusion-tensor imaging, demonstrated that balance impairment is related to the disconnection between the spinal cord, cerebellum and cerebral cortex in a sample of 45 ambulatory persons with MS. This suggests that disruption in neural-information processing produces atrophy of the sensory motor cerebellar regions that are functionally connected with specific cortical areas.[32]

Although the majority of research points to impairments in walking and balance as the leading cause of falls, there is growing, albeit limited, evidence that cognitive function is also a significant factor in falls in persons with MS. In one of the first reports to document this association, 80 individuals with MS underwent a full neurophysiological screening and self-reported fall frequency. Overall, fall frequency was related to impaired verbal memory function when age was taken into account.[33] In general support of these findings, it has been demonstrated that older adults who have MS and are recurrent fallers (e.g. greater than two falls in the last 3 months) had reduced cognitive processing speed compared with single-event fallers.[34] Importantly, gait and balance function did not distinguish between recurrent and single-event fallers in this latter study. The possibility that cognitive function plays a role in fall prevalence is crucial since, as previously highlighted, most current fall prevention strategies do not target cognitive function.

Prospective investigations of fall risk in persons with MS have for the most part confirmed retrospective and cross-sectional research. For instance, one prospective study demonstrated that disability, walking function and spasticity were predictive of falls in 76 persons with MS over 9 months.[35] Another investigation revealed that muscle weakness, dynamic balance impairment and gait impairment were predictive of falls in women with MS.[36] Recently, balance metrics derived from a force platform have been predictive of future falls in persons with MS.[37] However, it is worth noting that these prospective investigations have not included measures of cognitive function, and so it remains to be seen whether cognitive dysfunction is predictive of future falls in persons with MS.

Overall, there is evidence that balance, walking impairment and muscle strength are consistently related to past and future falls in persons with MS,[28] and this generally parallels the observations reported for older adults in the gerontology literature. Consistent with the geriatric research[38,39] there is initial evidence that cognitive function is related to falls in persons with MS. This highlights those factors as significant targets for therapeutic interventions for reducing falls risk profile and incidence in MS. Indeed, there are data indicating that balance, walking impairment and muscle weakness can be modified with various interventions, including exercise training in persons with MS,[40–43] but there is limited evidence that such exercise interventions will decrease fall incidence in persons with MS.[44]

Fall-prevention Interventions in Multiple Sclerosis

With regards to falls, not all individuals with MS have the same risk, the same mechanism, or start falling at the same timepoint in the disease. Identification of those at greater risk is important. In general, several factors have been shown to predict falls (e.g. older age), but those of greatest clinical importance are the predictors that are potentially modifiable (e.g. balance factors, postural instability, altered gait).[45–47] Previous research has shown that although 'generic' falls risk tests have been developed for the elderly population, these are of limited use for differentiating falls risk in older people with neurological impairment as their hallmark balance and gait deficits are, in many cases, unique and more pronounced. In a recent report of the Quality Standards Subcommittee of the American Academy of Neurology it was stated that current "guidelines do not fully address the increased risk for falls in persons with chronic neurologic conditions, nor do they fully evaluate the effectiveness of methods to screen for those most at risk".[48] The problem of identifying good predictors for future falls is highlighted by the fact that one of the best indicators is two or more falls in the previous year.[49] However, this indicator provides no information of the underlying mechanism or reason, which leads to this adverse event. Thus it is critical to identify and determine the relationship among the factors that can predict the increased risk of falling for older persons with MS.

The identification of risk factors for falls in persons with MS that correspond with those reported for older adults has created the groundwork for the design and testing of targeted interventions aimed at reducing fall incidence.[44,50] Importantly, physiological risk factors for falls, including balance and walking dysfunction, and muscle weakness, are modifiable in community-dwelling older adults,[34] and persons with MS with targeted exercise training.[41] Indeed, a recent Cochrane review of 159 trials with nearly 80,000 older adult participants concluded that home-based exercise programmes focusing on these factors provide the most promising avenue for reducing fall risk and rate of falls.[19]

Despite the promise of physiologically targeted interventions, there have been few published investigations involving persons with MS. One RCT reported that supervised balance training (n=20) and motor control therapy (n=11) conducted in a rehabilitation setting led to a reduction in self-reported number of falls in the 1-month period after the intervention compared with a control group (n=10).[50] Another quasi-experimental study (i.e. nonrandomisation) observed that a 10-week community-based supervised physiotherapy intervention in persons with MS who utilised bilateral walking aid (n=111; mean age=55 years old) resulted in a decrease in fall incidence 3 months following the intervention compared with a control group.[7]

One limitation of previous fall-prevention interventions for persons with MS is that they have only involved supervised exercise training. However, this form of exercise is not widely accessible for the majority of persons with MS. Rather, most of these individuals would benefit from the convenience of a home-based rehabilitation programme. Recently, we have completed a pilot project that examined the efficacy and safety of a 12-week, home-based exercise programme on fall risk, balance and walking function in older adults with MS. In this study, 27 participants with MS, aged over 50 years and had a history of falling, were randomly assigned to the exercise (n=13) or wait list control group (n=14). Participants underwent fall risk assessment based on the PPA as well as measurement of balance (Berg Balance Scale [BBS]), and walking (timed 25-foot walk: T25FW) prior to and immediately following the 12-week intervention. The PPA is based on a standardised set of physiological assessments and provides an overall fall risk score ranging from +4 (very high risk) to –2 (very low risk). This score is based on the quantification of five main markers (vision, leg strength, proprioception, balance and cognition) compared with age and gender matched normative data. The outcome of the PPA is a valid marker of fall risk in older adults with and without disabilities.[24]

Overall, 22 participants (n=12 control; n=10 exercise) completed postintervention testing. As illustrated in *Figure 2A*, fall risk (i.e. PPA score) significantly decreased in the exercise group following the intervention, while there was an increase in fall risk in the control group over time. It is critical to note that a fall risk score of 1.0 indicates that there is a large probability that an individual will fall in the next year[40] suggesting that the exercise group had a much lower risk for falling in the near future.

The results presented in *Figure 2B* demonstrate that the decrease in fall risk coincided with an improvement in the clinical balance assessment (BBS) for the exercise group and a decrease in the control group. The control group further had worsened T25FW time (6.8±1.2 versus 7.7±1.6 second), while there was no change in the exercise group (6.6±1.1 versus 6.7±1.2 second).

Overall, these investigations suggest that fall risk and incidence can be reduced in persons with MS with targeted exercise programmes in a variety of settings (clinical, community and home based). It remains to be seen whether these reductions in fall risk and incidence immediately following the intervention results in increases in participation and improvements in QoL.

Falls and Multiple Sclerosis – Future Directions

Over the past decade, there has been a limited, albeit growing, amount of scientific interest concerning falls in persons with MS. Although predictors, consequences and preventive measures of falls in MS have been investigated, there are still several factors requiring clarification. For instance, only 20 fall risk factors have been directly examined in persons with MS,[51] a finding in stark contrast to the 400 factors that have been identified for healthy older adults.[5] Additionally, the majority of risk factors have been identified in cross-sectional investigations so the predictive capacity of these risk factors of future falls remains to be determined. As previously highlighted, the contribution of cognitive function to falls in persons with MS has not been extensively studied and has not been included in prospective investigations. This is important, given that current fall-prevention guidelines do not take cognitive function into account and may need to incorporate cognitive rehabilitative components to maximise success.[34]

Additionally, the most effective fall-prevention strategies for persons with MS have yet to be documented. It has recently been suggested that in order to maximise the effect of fall-prevention programmes for community-dwelling older adults the programmes should be multifactorial in nature rather than simply exercise based.[52] Multifactorial inventions often include management of fall risk factors, including but not limited to, suboptimal medication regimes, comorbidity, incontinence and environmental risk factors. Logically, this type of approach has much promise in persons with MS, but has as yet not been extensively tested.

One pilot investigation of nonexercise-based fall-risk management programme focusing on self-management principles indicated that participants who received the intervention decreased the fall-risk behaviours immediately following the intervention.[53] We are undertaking research to determine whether multifactorial fall-prevention approaches are more beneficial than exercise-based approaches for fall prevention in persons with MS.

Another factor of previous research is that it has almost exclusively focused on ambulatory individuals. This focus ignores upward of a quarter of the persons with MS who are nonambulatory.[54,55] There is evidence that falls are quite common in the general wheelchair population with ~50 % reporting a fall.[56–58] In general, risk factors for falls in wheelchair users seem distinct from those observed in ambulatory populations.[57] Overall, this suggests that fall risk factors in nonambulatory individuals with MS are distinct from ambulatory individuals and that distinct fall prevention strategies are necessary in this segment of the MS community.

Conclusion

There is little doubt that persons with MS are at elevated risk for falls and that falls have significant negative effect on QoL stemming from physical injury and reduction in participation. Despite significant advances in understanding falls in persons with MS, there is still much research necessary for further identifying risk factors for falls in portions of the MS community (e.g. nonambulatory segments) and scientifically verifying various fall-prevention strategies. The reduction of falls in individuals with MS has the potential to ultimately improve participation and QoL, and have a major public health impact. ■

1. Noseworthy JH, Lucchinetti C, Rodriguez M, Weinshenker BG, Multiple sclerosis, *N Engl J Med*, 2000;343(13):938–52.
2. Koch-Henriksen N, Sorensen PS, The changing demographic pattern of multiple sclerosis epidemiology, *Lancet Neurol*, 2010;9(5):520–32.
3. Lassmann H, Bruck W, Lucchinetti CF, The immunopathology of multiple sclerosis: an overview, *Brain Pathol*, 2007;17(2):210–18.
4. Bjartmar C, Trapp BD, Axonal and neuronal degeneration in multiple sclerosis: mechanisms and functional consequences, *Curr Opin Neurol*, 2001;14(3):271–8.
5. Cattaneo D, De Nuzzo C, Fascia T, et al., Risks of falls in subjects with multiple sclerosis, *Arch Phys Med Rehabil*, 2002;83(6):864–7.
6. Matsuda PN, Shumway-Cook A, Bamer AM, et al., Falls in multiple sclerosis, *PM R*, 2011;3(7):624–32; quiz 632.
7. Coote S, Hogan N, Franklin S, Falls in people with MS who use a walking aid: Prevalence, factors and effect of balance and strengthening interventions, *Arch Phys Med Rehabil*, 2013;94(4):616–21.
8. Finlayson ML, Peterson EW, Cho CC, Risk factors for falling among people aged 45 to 90 years with multiple sclerosis, *Arch Phys Med Rehabil*, 2006;87(9):1274–9; quiz 1287.
9. Peterson EW, Cho CC, von Koch L, Finlayson ML, Injurious falls among middle aged and older adults with multiple sclerosis, *Arch Phys Med Rehabil*, 2008;89(6):1031–7.
10. Cameron MH, Poel AJ, Haselkorn JK, et al., Falls requiring medical attention among veterans with multiple sclerosis: a cohort study, *J Rehabil Res Dev*, 2011;48(1):13–20.
11. Bazelier MT, van Staa T, Uitdehaag BM, et al., The risk of fracture in patients with multiple sclerosis: the UK general practice research database, *J Bone Miner Res*, 2011;26(9):2271–9.
12. Dobson R, Ramagopalan S, Giovannoni G, et al., Risk of fractures in patients with multiple sclerosis: a population-based cohort study, *Neurology*, 2012;79(18):1934–5.
13. Dobson R, Ramagopalan S, Giovannoni G, Bone health and multiple sclerosis, *Mult Scler*, 2012;18(11):1522–8.
14. Finlayson ML, Peterson EW, Falls, aging, and disability, *Phys Med Rehabil Clin N Am*, 2010;21(2):357–73.
15. Matsuda PN, Shumway-Cook A, Ciol MA, et al., Understanding falls in multiple sclerosis: association of mobility status, concerns about falling, and accumulated impairments, *Phys Ther Mar*, 2012;92(3):407–15.
16. Peterson EW, Cho CC, Finlayson ML, Fear of falling and associated activity curtailment among middle aged and older adults with multiple sclerosis, *Mult Scler*, 2007;13(9):1168–75.
17. Sosnoff JJ, Sandroff BM, Pula JH, et al., Falls and physical activity in persons with multiple sclerosis, *Mult Scler Int*, 2012;2012:315620.
18. Motl RW, Dlugonski D, Wojcicki TR, et al., Internet intervention for increasing physical activity in persons with multiple sclerosis, *Mult Scler*, 2011;17(1):116–28.
19. Gillespie LD, Robertson MC, Gillespie WJ, et al., Interventions for preventing falls in older people living in the community, *Cochrane Database Syst Rev*, 2012;9:CD007146.
20. Stel VS, Smit JH, Pluijm SM, Lips P, Balance and mobility performance as treatable risk factors for recurrent falling in older persons, *J Clin Epidemiol*, 2003;56(7):659–68.
21. Clark RD, Lord SR, Webster IW, Clinical parameters associated with falls in an elderly population, *Gerontology*, 1993;39(2):117–23.
22. Lord SR, Ward JA, Age-associated differences in sensori-motor function and balance in community dwelling women, *Age Ageing*, 1994;23(6):452–60.
23. Fasano A, Plotnik M, Bove F, Berardelli A, The neurobiology of falls, *Neurol Sci*, 2012;33(6):1215–23.
24. Lord SR, *Falls in older people: risk factors and strategies for prevention, 2nd ed*, Cambridge/New York: Cambridge University Press, 2007.
25. Lord SR, Menz HB, Tiedemann A, A physiological profile approach to falls risk assessment and prevention, *Phys Ther*, 2003;83(3):237–52.
26. Horak FB, Postural orientation and equilibrium: what do we need to know about neural control of balance to prevent falls?, *Age Ageing*, 2006;35(Suppl. 2):ii7–ii11.
27. Nutt JG, Horak FB, Bloem BR, Milestones in gait, balance, and falling, *Mov Disord*, 2011;26(6):1166–74.
28. Gunn HJ, Newell P, Haas B, et al., Identification of Risk Factors for Falls in Multiple Sclerosis: A Systematic Review and Meta-Analysis, *Phys Ther*, 2013;93(4):504–13.
29. Sosnoff JJ, Socie MJ, Boes MK, et al., Mobility, balance and falls in persons with multiple sclerosis, *PLoS One*, 2011;6(11):e28021.
30. Socie MJ, Sandroff BM, Pula JH, et al., Footfall Placement Variability and Falls in Multiple Sclerosis, *Ann Biomed Eng*, 2013;41(8):1740–47.
31. Prosperini L, Kouleridou A, Petsas N, et al., The relationship between infratentorial lesions, balance deficit and accidental falls in multiple sclerosis, *J Neurol Sci*, 2011;304(1–2):55–60.
32. Prosperini L, Sbardella E, Raz E, et al., Multiple Sclerosis: White and Gray Matter Damage Associated with Balance Deficit Detected at Static Posturography, *Radiology*, 2013;268(1):181–9.
33. D'Orio VL, Foley FW, Armentano F, et al., Cognitive and motor functioning in patients with multiple sclerosis: neuropsychological predictors of walking speed and falls, *J Neurol Sci*, 2012;316(1–2):42–6.
34. Sosnoff JJ, Balantrapu S, Pilutti LA, et al., Cognitive processing speed is related to fall frequency in older adults with multiple sclerosis, *Arch Phys Med Rehabil*, 2013;94(8):1567–72.
35. Nilsagard Y, Lundholm C, Denison E, Gunnarsson LG, Predicting accidental falls in people with multiple sclerosis—a longitudinal study, *Clin Rehabil*, 2009;23(3):259–69.
36. Kasser SL, Jacobs JV, Foley JT, et al., A prospective evaluation of balance, gait, and strength to predict falling in women with multiple sclerosis, *Arch Phys Med Rehabil*, 2011;92(11):1840–46.
37. Prosperini L, Fortuna D, Gianni C, et al., The diagnostic accuracy of static posturography in predicting accidental falls in people with multiple sclerosis, *Neurorehabil Neural Repair*, 2013;27(1):45–52.
38. Mirelman A, Herman T, Brozgol M, et al., Executive function and falls in older adults: new findings from a five-year prospective study link fall risk to cognition, *PLoS One*, 2012;7(6):e40297.
39. Segev-Jacubovski O, Herman T, Yogev-Seligmann G, et al., The interplay between gait, falls and cognition: can cognitive therapy reduce fall risk?, *Expert Rev Neurother*, 2011;11(7):1057–75.
40. Hayes HA, Gappmaier E, LaStayo PC, Effects of high-intensity resistance training on strength, mobility, balance, and fatigue in individuals with multiple sclerosis: a randomized controlled trial, *J Neurol Phys Ther*, 2011;35(1):2–10.
41. Motl RW, Pilutti LA, The benefits of exercise training in multiple sclerosis, *Nat Rev Neurol*, 2012;8(9):487–97.
42. Motl RW, Smith DC, Elliott J, et al., Combined training improves walking mobility in persons with significant disability from multiple sclerosis: a pilot study, *J Neurol Phys Ther*, 2012;36(1):32–7.
43. Snook EM, Motl RW, Effect of exercise training on walking mobility in multiple sclerosis: a meta-analysis, *Neurorehabil Neural Repair*, 2009;23(2):108–16.
44. Coote S, Hogan N, Franklin S, Falls in People With Multiple Sclerosis Who Use a Walking Aid: Prevalence, Factors, and Effect of Strength and Balance Interventions, *Arch Phys Med Rehabil*, 2013;94(4):616–21.
45. Michael YL, Lin JS, Whitlock EP, et al., Interventions to Prevent Falls in Older Adults: An Updated Systematic Review, US Preventive Services Task Force Evidence Syntheses, 2010.
46. Tinetti ME, Brach JS, Translating the fall prevention recommendations into a covered service: can it be done, and who should do it?, *Ann Int Med*, 2012;157(3):213–14.
47. Tinetti ME, Making prevention recommendations relevant for an aging population, *Ann Int Med*, 2010;153(12):843–4.
48. Thurman DJ, Stevens JA, Rao JK, Practice parameter: Assessing patients in a neurology practice for risk of falls (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology, *Neurology*, 2008;70(6):473–9.
49. Gunn H, Creanor S, Haas B, et al., Risk factors for falls in multiple sclerosis: an observational study, *Mult Scler*, 2013;19(14):1913–22.
50. Cattaneo D, Jonsdottir J, Zocchi M, Regola A, Effects of balance exercises on people with multiple sclerosis: a pilot study, *Clin Rehabil*, 2007;21(9):771–81.
51. Gunn HJ, Newell P, Haas B, et al., Identification of risk factors for falls in multiple sclerosis: a systematic review and meta-analysis, *Phys Ther*, 2013;93(4):504–13.
52. Day LM, Fall prevention programs for community-dwelling older people should primarily target a multifactorial intervention rather than exercise as a single intervention, *J Am Geriatr Soc*, 2013;61(2):284–5; discussion 285–6.
53. Finlayson M, Peterson EW, Cho C, Pilot study of a fall risk management program for middle aged and older adults with MS, *NeuroRehabilitation*, 2009;25(2):107–15.
54. Coote S, McKeown G, Shannon M, A profiling study of people with multiple sclerosis who access physiotherapy services in Ireland, *Int J MS Car*, 2010;12(3):115–21.
55. Einarsson U, Gottberg K, Fredrikson S, et al., Activities of daily living and social activities in people with multiple sclerosis in Stockholm County, *Clin Rehabil*, 2006;20(6):543–51.
56. Kirby RL, Ackroyd-Stolarz SA, Brown MG, et al., Wheelchair-related accidents caused by tips and falls among noninstitutionalized users of manually propelled wheelchairs in Nova Scotia, *Am J Phys Med Rehabil*, 1994;73(5):319–30.
57. Nelson AL, Groer S, Palacios P, et al., Wheelchair-related falls in veterans with spinal cord injury residing in the community: a prospective cohort study, *Arch Phys Med Rehabil*, 2010;91(8):1166–73.
58. Gavin-Dreschnack D, Nelson A, Fitzgerald S, et al., Wheelchair-related falls: current evidence and directions for improved quality care, *J Nurs Care Qual*, 2005;20(2):119–27.