AN INVESTIGATION OF ACCIDENTAL FALLS IN PEOPLE WITH MULTIPLE SCLEROSIS

By

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At no time during the registration for the degree of Doctor of Philosophy has the author been registered for any other University award without prior agreement of the Graduate Committee.

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1. **Gunn, H.,** Freeman, J., Marsden, J. F., Haas, B., Creanor, S., & Zaijeck, J. (2012). Risk factors associated with falls in multiple sclerosis. Plymouth Hospitals Trust Annual Research Conference, Plymouth, UK
2. **Gunn, H**., Endacott. R., Haas, B., Marsden, J. F., & Freeman, J. (2015). Developing a falls management intervention for people with MS: A nominal group study. RIMS annual conference, Milan, Italy

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3. **Gunn H**, Creanor S, Haas B, Marsden JF, Freeman J. Risk factors for falls in multiple sclerosis: an observational study. Mult Scler. 2013; 19(14):1913–22.
4. **Gunn H**, Creanor S, Haas B, Marsden J, Freeman J. Frequency, characteristics and consequences of falls in multiple sclerosis: findings from a cohort study. Arch Phys Med Rehabil. 2014; 95(2):538–45.
5. Nilsagard Y, **Gunn H**, Freeman J, Hoang P, Lord S, Mazumder R, et al. Falls in people with MS-an individual data meta-analysis from studies from Australia, Sweden, United Kingdom and the United States. Mult Scler J. 2014; In print
6. **Gunn H**, Cattaneo D, Finlayson M, Freeman J. Home or away? Choosing a setting for a falls prevention program for people with multiple sclerosis. Int J MS Care. 2014; 16(4): 186-191.
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An investigation of accidental falls in people with multiple sclerosis

Abstract

More than 50% of people with MS fall in any six-month period. The importance of developing a suitable falls management programme has been identified by people with MS and professionals. This thesis aimed to develop a model for an MS falls intervention. The studies employed a systematic approach to evaluate the risk factors for falls and to identify the optimal programme content, format and structure.

Methods

The thesis comprises two sections; the first involving a systematic review and an observational study of falls risk factors (n=148). Part two included a second systematic review to inform programme content, and a nominal group study (n=36) to explore approach, format and structure from the perspective of key stakeholders.

Results

Part one identified the potential target group (people at key mobility transition stages and those with progressive MS), and mechanisms by which the intervention could act (the identification of specific risk factors associated with falls in MS). These include non-modifiable disease and demographic characteristics (e.g. MS classification and gender), and potentially modifiable clinical characteristics (including balance, mobility, continence issues and medication usage).

Part two identified that an MS specific falls programme should address falls and participation-related outcomes, incorporating educational activities and a programme of individually tailored gait, balance and functional training. The programme should use a collaborative approach; supporting participants to achieve sufficient intensity and duration of exercise and to integrate falls prevention strategies into their daily lives. The programme should enable participants to engage flexibly according to individual needs and preferences.

Conclusions

This thesis has identified specific risk factors associated with accidental falls in MS. The evaluation indicates that the success and sustainability of an MS falls programme requires that it is MS specific, employs a collaborative approach and moves away from the group-based, weekly format common to many generic falls programmes.

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1 Introduction and background

1.1 Introduction

Multiple sclerosis (MS) is a disorder of the central nervous system (CNS) characterised by episodic acute inflammatory demyelination and axonal loss with limited remyelination. It is the most common cause of neurological disability in young adults, affecting approximately 2.5 million individuals worldwide[1]. Research suggests that the most frequent symptoms experienced by people with MS include impairments in mobility and balance, fatigue, memory and other cognitive areas, visual symptoms, continence, and sensory disturbances including pain[2]. Falls are a significant issue in MS, with research demonstrating that more than 50% of people fall in any six-month period[3]. Problems that are commonly highlighted by people with MS as a result of falls include injuries, loss of confidence and difficulties sustaining usual life roles[4–6]. Guidance from the Royal College of Physicians (RCP)[7] recommends that more research should be carried out with the aim of reducing rates of falls in MS.

1.2 Pathology and clinical course of multiple sclerosis

The pathological processes associated with MS are the subject of much debate, and key aspects are well described in papers by Compston and Coles and Mahad and Lassman[8,9]. Mechanisms of damage include multiple auto-immune mediated attacks on CNS myelin, and axonal degeneration[10]. Inflammatory processes disrupt the integrity of the myelin sheath and neighbouring axons, leading to impaired saltatory conduction in affected neurons[11]. This can be accompanied by complete conduction block in some cases, which is thought to be linked to the release of neuro-toxic inflammatory exudates, including nitric oxide[12]. These changes can to some extent resolve as the inflammatory response diminishes, and there is some evidence of limited, although incomplete, remyelination in the earlier stages of MS[13]. Degenerative processes lead to gradually accumulating neuronal loss over time, and are thought to be associated with loss of trophic support from oligodendrocytes following the initial inflammatory processes[14]. The exact nature of the link between the processes of inflammation and degeneration are again the subject of considerable debate in the literature. However, it would appear that inflammatory episodes tend to be associated with more acute, relapsing presentations, and degenerative processes with more progressive disease courses[9,15] (Figure 1-1).

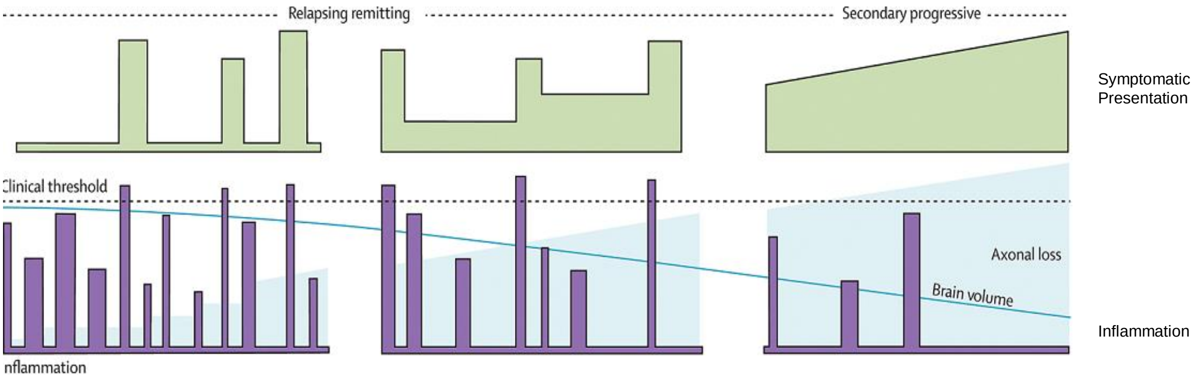


Figure 1-1 Pathological Processes in multiple sclerosis [8]

Diagnosis of MS uses specific criteria as originally laid down by McDonald et al and later revised[16]. Key aspects include evidence of multiple episodes of demyelination which are separate in both time and lesion location within the CNS. Most frequently, early lesions affect the optic nerves and spinal cord, and lead to symptoms of visual and sensory disturbance, pain and fatigue[11].

The presentation of MS can follow several different disease courses, as illustrated in Figure 1-2. The majority of people initially present with a relapsing-remitting course, with approximately 65% ultimately entering a secondary progressive phase[8]. Relapsing remitting MS is characterised by clearly defined periods where symptoms significantly worsen, followed by complete, or near complete symptom resolution[11]. Individuals with primary and secondary progressive MS tend to experience a gradual accumulation of disability over time, although the presence of fluctuations in symptoms (as against distinct relapses) have been described in both courses[17]. The precise relationship of the progressive and relapsing remitting courses is the subject of on-going research, and it is possible that different courses are actually linked to genetically heterogeneous sub-types of MS[18]. Benign MS is seen in approximately 10% of cases, and is described as a presentation in which individuals remain fully functional with little or no disability for a prolonged period following diagnosis[11]. Despite this initial course, some individuals will go on to develop more progressive symptoms, although there is conflicting evidence as to the frequency of this progression[19,20].

The clinical course of MS is extremely variable depending on MS sub-type, age of onset and the degree of involvement of sites within the CNS[21]. In several studies, a primary progressive presentation tended to be associated with more rapid initial accumulation of disability[22,23], although overall levels of disability were not significantly different in comparisons of individuals with primary progressive MS and those who had entered a secondary progressive phase[24]. This has led some authors to suggest that the presentation of a progressive course may be the most significant prognostic indicator in MS[25].

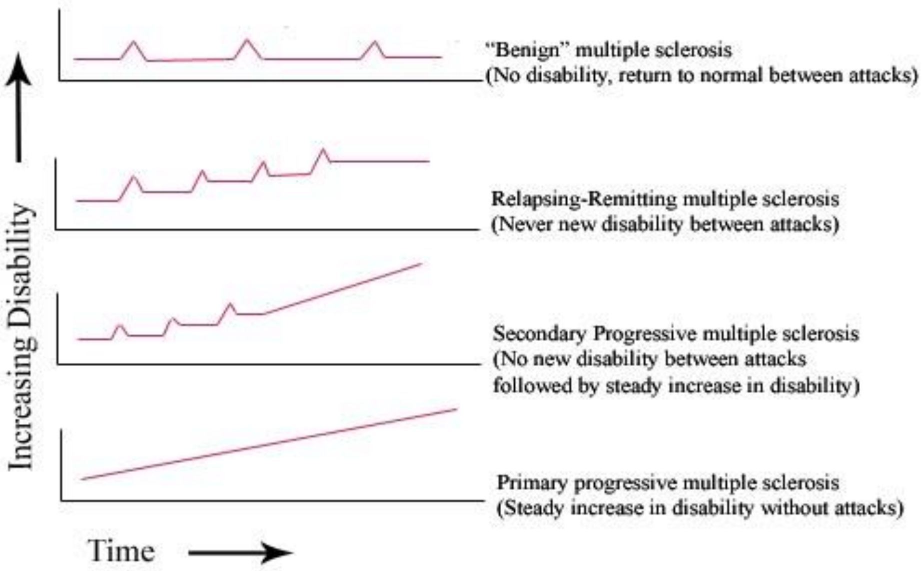


Figure 1-2: Multiple sclerosis sub-types [11]

Disease severity is usually classified using the Expanded Disability Status Score (EDSS)[26], which reflects the number of CNS functional systems involved as well as overall mobility status and independence. The EDSS has been criticised for poor validity and reliability as well as lack of responsiveness[27]. However, despite these limitations it remains widely used as a global measure of disability in MS[28]. When measured using the EDSS, the frequency of people at each stage demonstrates a bi-modal distribution, with peaks in numbers of people classified with EDSS scores of 1.0 and 6.5[29]. Longitudinal studies have demonstrated a non-linear progression through EDSS levels, with a relatively slow initial progression (median times spent at EDSS 1.0-1.5 of 4 years) prior to more rapid increase in EDSS score between levels 2.0 - 5.5, and subsequent slowing at level 6.0[22] . However, other natural history studies indicate median periods since diagnosis of 13+ years[30]; in clinical terms this suggests a high number of people living with significant impairments. This is supported by analysis of global disease burden, which indicates that years of life lived with a disability (as compared to premature mortality) contribute to more than 70% of the overall burden of MS[31]. For many people with MS and their families, MS related impairments may be associated with a range of activity limitations and participation restrictions[32]. MS is associated with poorer global measures of quality of life, engagement with work and leisure activities and increased reports of depression [33]. However, increased availability of therapies for disease modification and symptom management, alongside improved rehabilitation provision can significantly improve many aspects of function and self-efficacy [34,35].

The multiplicity of symptoms that may arise means that the physical, cognitive and psychological consequences of MS are wide ranging and variable. This thesis focusses on an investigation of accidental falls and hence a more detailed exploration of the key issues related to this aspect is now discussed.

1.3 Balance and mobility problems in multiple sclerosis

Changes in balance and mobility are frequently seen early in the course of MS; with up to 75% of people complaining of balance issues at some time in the disease course[36]. Studies have demonstrated altered postural responses in individuals with minimal impairments, including those where the impact of these changes may be sub-clinical. For example, Fjeldstad[37] and Martin[38] have both demonstrated that individuals with MS scored significantly worse in a range of laboratory-based balance and walking tests than age and sex-matched healthy controls, despite being assessed as having minimal levels of disability and no impairment to walking as judged by routine clinical assessments[38] and EDSS scoring[37]. Balance and mobility issues are often more pronounced in individuals with progressive MS sub-types[39]; however they remain an issue even for those with milder forms of MS.

1.3.1 Balance in multiple sclerosis

Postural stability is defined as the ability to maintain the body's centre of mass within the limits of the base of support[40]. A variety of laboratory and clinical measures have been used to evaluate postural stability in MS. Most frequently, stabilometry studies evaluate aspects of postural sway, centre of pressure (CoP) area, timing and scaling of postural responses. Responses under static conditions and secondary to internally and externally generated perturbations all provide data on aspects of postural stability and the potential mechanisms that may contribute to impairments.

Postural stability in static positions

The ability to maintain a static position is dependent on the integration of sensory and motor feedback and feed-forward to maintain equilibrium in a steady state. When maintaining a static position, people with MS demonstrate increased postural sway velocity and amplitude in both medio-lateral (ML) and antero-posterior (AP) directions, and have a greater CoP area than healthy controls (HC)[41–44]. Cattaneo[45] suggests that measures of total CoP area and velocity of sway measures are more sensitive measures of overall stability than maximal excursion values of ML and AP sway in people with MS, although his study findings demonstrated statistically significant differences in all measures when compared to HC. Directional postural sway has been investigated in significantly more depth in individuals with pure cerebellar ataxia, where both uni- and omni-directional increases in sway velocity and amplitude have been demonstrated[46–48]. In older people, increases in AP rather than ML sway have been demonstrated in individuals with self-reported balance impairments in several studies[49,50]. However, in a systematic review, only increases in ML sway amplitude and velocity were found to be predictive of recurrent falls[51]. One of the key issues impacting on the validity of findings relating to directional sway is the potential impact of stance width and foot position on postural sway patterns and magnitudes[48]. The lack of reporting of these aspects in MS studies makes interpretation of results challenging, and limits the conclusions that can be drawn.

A range of impairments have been highlighted as potentially contributing to altered postural stability in MS. Chung[52] found that measures of knee extensor torque and peak power asymmetry correlated with AP CoP variability in a study of 12 women with MS and an EDSS of 4 ± 1 (p<0.05), although there was no correlation with measures of ankle dorsi-flexor strength in the same study. CoP area and sway velocity have also been demonstrated to be greater in individuals with MS with higher spasticity as identified by soleus H-reflex amplitude[53]. However, further papers evaluating the interaction of spasticity and postural stability are scarce, both in MS or other pathologies. The impact of fatigue on postural stability has also been investigated in MS[54], with the authors concluding that inducing fatigue affected postural control in positions with a relatively small base of support (tandem stance), but not during quiet upright standing. This finding is supported by a study involving individuals post stroke[55], where increased exertion and self-reported fatigue were associated with increased postural sway measures during static double stance with feet 20cm apart, as well as during dynamic tasks.

More recently, lesions within the brainstem[56], spinal cord and cerebellum[57] have been found to be associated with altered balance and stability in MS, with the findings suggesting that different systems may be associated with postural stability under different sensory conditions. This links with a number of studies which have evaluated the specific contributions of visual, somatosensory and vestibular mechanisms to postural stability in MS[39,45,58,59]. Using variants of the sensory organisation test[60], Soyuer [39] demonstrated greater visual dependence in a steady stance test in subjects with MS who were assessed as having proprioceptive or vestibular loss, although it is not reported how these impairments were evaluated. Similarly, Cattaneo's 2007 study[45] found that MS subjects experienced significantly greater increases in postural sway and CoP area during steady stance tests with eyes closed than did HC. However, in this study, similar changes were also noted in sensory conditions where another sensory element was altered (e.g. during the steady stance on foam condition). This finding led the author to hypothesise that the deterioration in stability may be related to the need for simultaneous integration of information from multiple sensory systems to retain balance rather than purely demonstrating visual dependence. This theory is supported by other data from this study, which demonstrated further deterioration of postural stability in conditions where both visual and proprioceptive inputs were reduced, leaving vestibular input alone as the primary sensory mechanism.

However, it should be noted that in Cattaneo's study[45], nearly a third of subjects' stabilometry measures improved when one sensory input was altered. The authors hypothesise that this change may be associated with increased neuronal firing 'noise' as a result of the increased postural sway. This may lead to a loss of sensitivity in the interpretation of afferent inputs in test conditions with multiple sensory inputs. Therefore, by reducing the number of systems providing afferent input, more appropriate postural responses were possible. To date, insufficient research has been conducted to support this hypotheses.

The clinical significance of these alterations in measures of postural sway and CoP in MS is unclear. The available research suggests that such changes may not impact negatively on subjects' functional ability to maintain static postures in some conditions, particularly those with a relatively stable base of support (BoS). In a study by Frzovic[59], subjects with MS were able to maintain standing postures for a similar length of time to the HC subjects in all positions except tandem and single leg stance. Similarly, Daley and Swank[61] found that despite significantly abnormal measures of postural sway when compared to healthy controls, 69% of MS subjects were still fully ambulant, with 'minimal impairment in function' at worst (p669). Clinical measures of stability which include functional balance activities have been found to correlate poorly with stabilometry data[62–65], which also raises the question as to the link between altered control of postural stability as demonstrated in laboratory measures, and changes in function. One interpretation could be that some people with MS may be able to gradually compensate for some of the alterations in balance seen in laboratory based measures as a result of the relatively insidious nature of the changes over time. Another possible explanation could be limitations in the clinical outcome measures used to assess these deficits, as highlighted in other populations[66].

Dynamic stability

Dynamic stability is described as 'the ability to transfer weight within the base of support' ([65] page 279) in order to maintain balance. During self-generated perturbations, individuals utilise both anticipatory feed-forward and reactionary feedback postural response mechanisms in order to maintain stability and respond to the changing relationship between body segments and the centre of gravity (CoG)[67]. In measures of functional reach, arm raise and stepping activities, people with MS score significantly worse than HC in all aspects[38,42,59]. This change is seen in people with relatively low levels of disability (EDSS scores <2.5[38]). Evaluation of the mechanisms contributing to this change suggests that subjects have a tendency to reduce the degree of self-generated displacement during functional activities. This change is evidenced by Karst's study where significant reductions in CoP displacement were seen during reaching and leaning activities in standing even in individuals where static stabilometry measures were relatively normal in comparison to HC[42]. This change is similar to alterations seen in people following a stroke, where smaller displacements and increased velocity of the CoM were demonstrated during a reaching task when compared to HC[68]. These changes were also associated with increased variability in magnitude and velocity of displacement, an aspect not reported to date in MS.

Impairments in dynamic stability in MS have also been demonstrated during self-generated perturbations in sitting positions. In Lanzetta's study of trunk control in unstable sitting postures[65], displacement of the trunk in response to perturbation was significantly greater in both magnitude and velocity in subjects with MS when compared to HC. Velocity of displacement was found to be more discriminatory between the groups and tasks performed than magnitude of displacement, and instability was particularly apparent when activities involved head movements. This again would suggest a sensory component to the maintenance of stability, as maintenance of balance during head movement requires both visual and vestibular system input[40].

The maintenance of dynamic balance requires the ability to respond to externally generated perturbations as well as self-generated displacements. To respond effectively to an external perturbation, individuals need to be able to perceive and interpret the direction, magnitude and speed of displacements of the CoG relative to their BoS, and to generate a co-ordinated reaction of body segments that is appropriate in both timing and scaling[69]. In MS, significant issues are demonstrated in the ability to respond to external perturbations, with many individuals being unable to regain stability in response to a relatively small displacement, to the point of requiring external corrective intervention[45,59]. The mechanisms contributing to this impaired response were evaluated by Cameron[70] and Huisinga[71], with both studies suggesting that delayed postural response latencies are key factors associated with impairments in balance. In Cameron's study[70], subjects with MS demonstrated a large but very delayed automatic postural response to external perturbation, which correlated moderately strongly with latencies of somatosensory evoked potentials (SSEP) ($r=0.73$, $p<0.01$). Interestingly, the postural responses, despite being delayed demonstrated normal or excessive scaling relative to the velocity and amplitude of the perturbation. This contrasts with findings in subjects with pure cerebellar ataxia, where normal response time but inadequate scaling of velocity and amplitude of reaction is seen following external perturbation[72].

1.3.2 Gait changes in multiple sclerosis

Studies in MS have demonstrated a variety of changes in gait pattern and stability during walking activities, which reflect the frequency of issues reported by people with MS in this area[8]. People with MS tend to walk at slower speeds than HC[41,73], and have a decreased stride length and increased time spent in double limb support[38]. In EMG studies, these changes have been associated with altered muscle activation patterns, such as premature recruitment of gastrocnemius and delayed relaxation of tibialis anterior during stance phase, even in individuals with minimal functional impairments[74]. It could be postulated that these changes may be compensatory in nature as a strategy to increase stability by maintaining the CoM within the limits of the BoS[75]. This theory is supported by work by Remelius[76]; who demonstrated that people with MS (n=12, EDSS 4 (SD1.4)) showed smaller anterior displacements of the CoM in anticipation of walking, and an increased time to initiate walking when compared to HC.

Whilst decreasing displacement of the CoM will potentially increase stability, the strategy may impact on the energy expenditure associated with walking. This has been investigated by Motl[77], who demonstrated increased energy expenditure in subjects with MS relative to HC in a treadmill based study using accelerometers. Interestingly, while the MS subjects demonstrated lower activity counts per time period (suggesting they took fewer steps than the HC), the energy expenditure per count was higher. This may be due to increased variability and instability of their walking pattern, which would lead to increased displacement and thus higher readings from the accelerometer. The authors hypothesise that this may be associated with impairments such as spasticity and ataxia, however further research is needed to determine the possible contributory factors.

Walking activities in MS may also be associated with greater cognitive dependency. In a study of 18 people with MS and 18 HC using GAITrite analysis, Hamilton[78] found that the introduction of a cognitive task (digit span activity) led to significant decreases in walking speed and an increase in swing time variability in the MS subjects ($p < 0.05$), but not the HC. This work is supported by Delrue[79], who reported deteriorations in walking time and number of steps over a 30 metre walk with the addition of a serial seven subtraction task in 16 subjects with MS. However, when compared to a HC group, the only significant difference was in walking time. This finding is in agreement with work investigating dual task interference in older people, where walking time has been shown to be more closely correlated to functional performance and falls risk than other gait parameters[80–82].

1.4 Falls in people with neurological disorders

Studies demonstrate that people with neurological disorders are at least twice as likely to fall as age matched control individuals[83]. Increased falls rates have been shown in people with Parkinson's disease[84–86], stroke[87–89], spinal cord injury[90] and pure cerebellar ataxia[46], demonstrating that falls are an issue regardless of the nature, duration or pathology of the disorder.

1.5 Falls in multiple sclerosis

Research demonstrates that more than 50% of people with MS fall in any six-month period[3]. The mechanisms contributing to falls in MS are currently unclear. Few laboratory based studies of balance have included measurements of falls, and those which have tend to rely on simulated or proxy fall measures, which are known to correlate poorly to actual falls[91].

Falls in MS are associated with serious emotional and physical consequences, affecting activity levels, independence and quality of life[92]. People with MS have an increased risk of fracture relative to age-matched HC, and in particular, increased risk of fragility fractures (hip fracture Hazard Ratio 4.08 (95% CI 2.21- 7.56))[6]. This highlights the importance of managing falls risk and taking measures to reduce the potential for negative consequences through interventions such as osteoporosis management.

Research into the wider consequences of falls in MS is limited, however in older adults falls have shown to be associated with significant loss of independence and decreased quality of life[93]. There is some evidence to suggest that the experience of falling is also significant for individuals with MS. In a study by Peterson[92], which involved telephone interviews with 1064 individuals with MS, 63.5% reported fear of falling, of whom 82.6% reported activity curtailment associated with this fear. In agreement with similar studies in older people, the fear of falling was greater than the actual incidence of falls, which was 52.8% of the study sample. These findings are supported by a qualitative study involving people with MS[4], where respondents expressed feelings of anxiety and frustration associated with falls: 'I don't venture out on my own now because I can't, I'm frightened of falling over' (Interview 10 p16).

1.6 Falls in older people

While the evidence base relating to falls in people with neurological problems is relatively limited, there have been a large number of studies in older people[94]. Over 400 independent risk factors for falling have been identified in older adults[95], many of which are associated with impairments similar to those seen in MS. The key risk factors for falling identified, by analysis of over 30 risk factor studies carried out for inclusion in the NICE Clinical Guideline for the Management of Falls in Older People[96] are detailed below (Figure 1-3). As well as identifying risk factors that are independently associated with falls in older people, studies have also shown that the presence of multiple risk factors is associated with an increase in risk greater than the sum of individual factors[97].

Risk Factor	Number of studies reporting statistically significant differences in multivariate analysis	Number of studies reporting non statistically significant differences in multivariate analysis
Falls history	10	7
Mobility impairment	2	4
Visual impairment	3	8
Balance deficit	4	8
Gait deficit	3	6
Cognitive impairment	3	9
Fear	3	1
Environmental hazards	2	-
Muscle weakness	-	2
Incontinence	2	5

Figure 1-3: Risk factors for falling in older people[96]

The significant costs and consequences of falls in older people has led to substantial investment, both in service provision and in research funding, to support the development and evaluation of falls management interventions. Consequently, the evidence base in this area is now relatively robust[98]; with meta-analysis/review papers consistently supporting the use of programmes which specifically identify and address specific risk factors using targeted programmes which achieve high adherence and engagement[99]. This body of research is invaluable in informing the development and evaluation of falls programmes in other populations. It underlines the need to ensure that falls programmes are developed in a systematic manner, are based on the specific evidence for the patient group, and target individualized risk factors for falling[100].

1.7 Summary

Altered postural control is common in MS, and results in people being less able to respond effectively to internally and externally generated perturbations, resulting in loss of stability. There are a number of impairments that may contribute to altered postural control in MS, including deficits in sensory, motor and cognitive function. The exact nature of the factors contributing to the change in stability is unknown. However, slowed somatosensory evoked potentials and delayed but near-normal scaling and co-ordination of postural responses suggest this is an issue related to conduction speed rather than generation and control of responses.

Despite altered postural control mechanisms, many people with MS are able to maintain functional balance, and the correlation between stabilometry and clinical measures of balance is weak. In addition, it appears that several of the changes seen in balance response may be compensatory in nature, and hence it is important not to focus solely on associations with measurements of postural stability when investigating falls.

Falls are a significant issue in MS, and there is recognition that research and service development is needed in this area[7]. Due to the nature of MS, a wide range of physiological, psychological and environmental factors could lead to falls. Identification of the specific risk factors associated with falling is important to develop effective intervention strategies for people with MS.

1.8 Aim

This PhD project aims to provide the necessary evidence to inform the development of a model for an evidence-based MS falls management intervention. It is intended that the focus will be on systematically gathering robust evidence to gain a clear understanding of what is required to ensure that the programme is fit for purpose in terms of potential efficacy, acceptability to service users and providers, and sustainability within current models of UK service delivery.

The design and development of this project has been informed by the Medical Research Council (MRC) ‘Guidelines for developing and evaluating complex interventions’[101](Figure 1-4). This thesis covers the developmental stages of a longer term project. It is the intention to undertake post-doctoral work that will manualise, operationalise and then evaluate the intervention in a systematic manner.

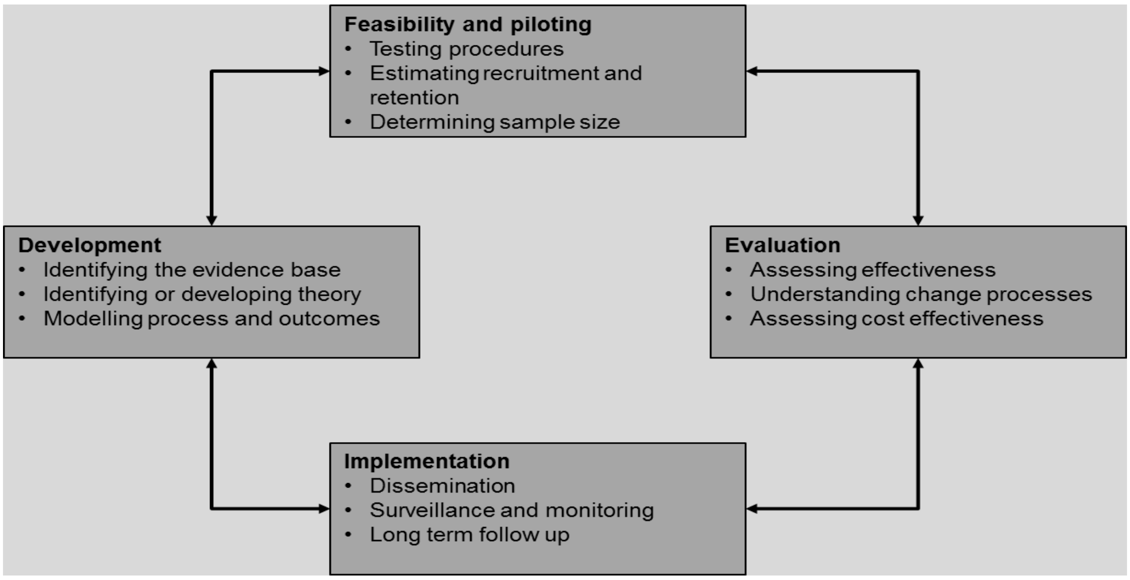


Figure 1-4: Stages in the development and evaluation of complex interventions[101]

The specific objectives of the programme of work within this thesis are to develop an MS falls intervention model by:

1. Evaluating the prevalence, characteristics and consequences of falls in MS
2. Identifying the risk factors associated with falling in people with MS
3. Recommending programme content on the basis of an evaluation of the existing evidence, to ensure the best chance of reducing falls rates.
4. Proposing the format and delivery of the intervention model based on users' and service providers' input, considering:
    a. acceptability for service users
    b. optimizing adherence and user participation
    c. ensuring sustainability

Part 1: Identification of risk factors for falls in multiple sclerosis

2 Systematic review one: Risk factors for falls in multiple sclerosis

2.1 Introduction

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. Due to the nature of MS, a wide range of physiological, psychological and environmental factors could contribute to falls risk. While some researchers have focused their attention on investigating factors affecting postural stability[42–44,70], others have evaluated specific risk factors for falling[3,102]. As discussed previously, postural stability measures correlate only weakly with falls risk. Therefore, the primary objective of this systematic review was to evaluate the risk factors associated with falls in people with MS, as described in the literature.

2.2 Methods

This systematic review was conducted using a written protocol developed by the author in collaboration with the supervisory team and 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 the key aspects of the systematic review, including inclusion and exclusion criteria, search strategy, methodological quality assessment, data extraction and analysis.

2.2.1 Search strategy

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, CINAHLplus and PsycINFO. Medical subject heading (MeSH) keywords and operators used were: ‘Multiple sclerosis AND accidental falls’ OR ‘multiple sclerosis AND postural balance’ NOT animals [mh].

Related terms ‘postural instability’, and ‘falls’ were also used in those sources where MeSH terms were not used. In addition, hand searches of reference lists and MS conference abstracts published over the past five 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), and where full text was available, were included within the review.

2.2.2 Study selection

Participants

This review examined articles evaluating any aspect of falls 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[103–105]. There is limited evidence relating to either population in MS; therefore all studies were included, 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 (e.g. those using functional measures equated to falls risk) were excluded on the basis of reported limitations in terms of the predictive validity of these measures, both within samples of elderly people[87,95,106,107], and those with MS[3]. Whilst it is recognised that prospective recording of falls is the gold standard[108], in order to ensure a comprehensive review in an area with a limited number of published articles, it was decided to evaluate all papers reporting falls incidence, either by prospective or retrospective reports.

Study designs

Randomised and quasi randomised controlled trials, controlled observational and cross-sectional design methodologies were eligible for inclusion. To ensure a comprehensive review, studies utilising alternative methodologies (e.g. qualitative studies) were also considered for inclusion where the article included appropriate participants and outcomes as outlined above.

Data extraction and screening

Articles were excluded if they were purely evaluations of outcome measures, or interventions which did not relate falls risk factors to falls frequency within the analysis. Abstracts were extracted and screened by the primary author (HG) to remove obviously irrelevant reports. Authors of five articles were contacted to request supplementary data; replies with sufficient data were received from three authors[5,45,109].

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

An assessment of study quality utilising the Newcastle-Ottawa Quality Assessment Scale (NOS)[110] was undertaken (appendix 7.1.1). The scale was adapted to ensure the wording was appropriate to the specific types of study being reviewed. One 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 eight stars. There is no validated cut-off for the NOS[110], however previous systematic reviews have used a score of ≥ six stars from a possible maximum of nine on the full scale[111]. Accordingly, a cut off of ≥ five stars was set for this review.

2.2.3 Synthesis

Following the eligibility and quality assessment stages, full data extraction of the included studies was undertaken using double data entry to minimise errors. Data extracted at this stage included more detailed demographic and MS classification data, method and results of risk factor measurements and detailed falls incidence data. Odds ratio (for categorical data) and weighted mean differences (for continuous data) and their 95% confidence intervals (95% CI) were extracted from the data or calculated for analysis where sufficient data was presented in the article or could be obtained from authors. Data were pooled in statistical meta-analysis using an inverse variance random effects Der Simonian-Laird meta-analysis using the 'meta package' for R[112,113] for any risk factors where comparable data for three or more studies could be extracted[114]. Each data set included in the meta-analysis was analysed for heterogeneity using the chi-squared statistic, setting a p value of 0.10[115]. Where statistical pooling was not possible or appropriate (e.g. in qualitative papers or those risk factors with insufficient numbers of data sets to allow comparison), findings are presented in narrative summary form.

2.3 Results

2.3.1 Studies

The electronic and hand searches yielded a total of 111 records (Figure 2-1). 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 falls incidence (n=38), or inappropriate methodologies (e.g. intervention trials (n=35)).

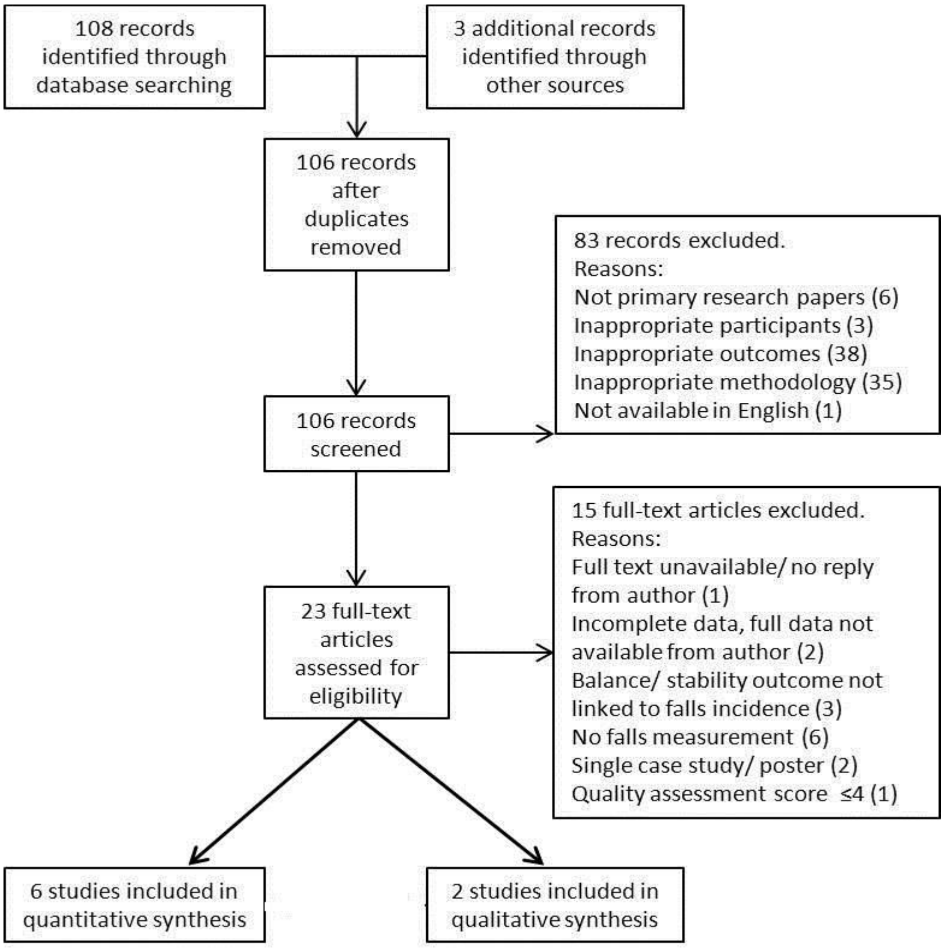


Figure 2-1 Study flowchart

2.3.2 Detailed review and assessment of methodological quality

Twenty-three articles were included in the detailed review. Of these, 14 did not fit the inclusion criteria. Nine lacked specific falls measurement; two had insufficient data to undertake the analysis, despite contacting the authors; there was no reply from one author; one article was a single case study and one a poster presentation.

Methodological quality was variable (Table 2-1). Only two studies recorded falls prospectively, and reporting periods varied considerably from between six months retrospective to one year prospective recording. Classification of falls and fallers was inconsistent and there was significant variation in the methods used to define fallers and non-fallers. Following detailed review and assessment of methodological quality one further article was excluded, leaving a final total of six quantitative and two qualitative papers.

2.3.3 Participants and fall rates

The final review comprised a total of 1929 participants. The six quantitative studies included a total of 1911 participants, whilst the qualitative studies included a total of 18 participants. Of the total participants, 1037 (53.75%) were classified as fallers. Of these 1019 were derived from the quantitative studies; all 18 participants in the qualitative studies were fallers. The quantitative data set comprised participants with an age range of 21-71 years, and 442 men (23.12%). The qualitative participants had an age range of 27-68 years; gender distributions were 50/50 for one study[116], but not detailed for the second[117]. A range of MS classification sub-types and severities were included in the studies, with various scales and cut-off values used to categorize disease severity (Table 2-1).

2.3.4 Risk factor measurements

Eighteen potential risk factors were evaluated (Table 2-2). There was limited consensus in the impairments included, with six of the 18 risk factors being measured in one study only. Those evaluated in three 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.

Study	Representativeness of the exposed subjects	Selection of comparison group	Method of evaluation of risk factor	Comparability of subjects	Assessment of outcome	Follow up period	Adequacy of follow up	Total NOS Score
Cattaneo 2002	*All able to walk with a cane (specific disease severity measure not included)	*	* Objective measure	*	Retrospective self-report	2 months	* all accounted for	5*
Finlayson 2006	*Aged ≥45 years MS severity not reported	*	Self-report	*	Retrospective self-report	*6 months	* all accounted for	5*
Kasser 2011	*EDSS 0-5.5, all women	*	*Objective measure	*	*Prospective Diary	*1 year	* 92/99 completed. No description of those lost	7*
Matsuda 2011	*Range of subtypes; MS severity not reported	*	Self-report	*	Retrospective self-report	*6 months	* all accounted for	5*
Nilsagard 2009	*EDSS 3.5-6.0	*	*Objective measure	*	* Prospective Diary	* 3 months	89% return rate. No description of those lost	6*
Soyuer & Erkorkmaz 2006	*EDSS ≤4.5	Healthy matched controls	*Objective measure	*	Retrospective self-report	*6 months	* all accounted for	5*

Exposed subjects = fallers; Comparison group = non-fallers EDSS = Expanded Disability Status Scale; Comparability determined by inclusion of EDSS/demographic data; * denotes rating - see appendix 7.1.1 for further information

Table 2-1: Methodological quality assessment: Newcastle-Ottawa quality assessment scale (NOS) for case control studies

Risk Factor/ Study Characteristic	Study					
	Cattaneo 2002	**Finlayson 2006**	**Kasser 2011**	**Matsuda 2011**	**Nilsagard 2009**	**Soyuer & Erkorkmaz 2006**
N =	50	1089	99	473	76	124
ADL[1]	Rivermead ADL					
Balance	Equiscale Test	Self-report	Limits of stability testing	Self-report	Berg Balance/ Four Square Step Test	Functional Reach
Cognition	[2]MMSE	Self-report		Self-report	Clock Drawing Test	MMSE
Continence		Self-report		Self-report	Self-report	
Dual Task					[3]TUG Cognitive	
Fatigue					Fatigue Severity Scale	
Fear of Falling		Self-report			Self-report	
Gait	Hauser Ambulation Index		GaitRITE analysis		[4]MSWS12	Tinetti Gait
Mobility	Rivermead Mobility					
Mobility Aid	Use of a cane	Wheelchair use		Use of walking aid/ wheelchair	Walking aid type and venue	
Motor Function	Motricity Index					Motricity Index
MS Status/ Disease severity		Self-report	[5]EDSS mild/ moderate/ severe		EDSS	
MS Classification				MS sub-type	MS sub-type	MS sub-type
Sensory disturbance			Sensory Integration Test		Birgitta Lindmark Motor Capacity E	
Spasticity	Modified Ashworth Scale- Gastrocnemius			Self-report	Modified Ashworth Scale: Sum	Ashworth
Strength				Self-report		
Visual issues				Self-report		

[1]ADL: Activities of Daily Living; [2]MMSE: Mini Mental Status Examination; [3]TUG: Timed Up and Go; [4]MSWS 12: The 12 Item MS Walking Scale; [5]Expanded Disability Status Scale

Table 2-2: Participants and fall rates

2.3.5 Meta-analysis

An OR with 95% CI was available (or calculable) for only six of the quantitative studies due to limitations in the data presented. Pooled meta-analysis was only feasible for four 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 2-3 with forest plots in Figure 2-2. Full data from all of the studies, including those which were not included in the meta-analysis, are available within appendix 7.1.2.

Risk Factor	**Balance Impairment**	**Use of a mobility aid**	**Cognition**	**Progressive MS**
Number of studies	4	4	3	3
Number of subjects	1412	1576	1239	596
Pooled OR	1.07	2.5	1.28	1.98
95% CI	1.04- 1.1	2.21- 2.83	1.2- 1.36	1.39-2.80
Heterogeneity (X^2)	0.01 (p= 0.9998)	0.28 (p= 0.9638)	0.0 (p= 0.9992)	1.22 (p=0.54)

OR = Odds Ratio; 95% CI = 95% Confidence Interval

Table 2-3: Pooled odds ratios

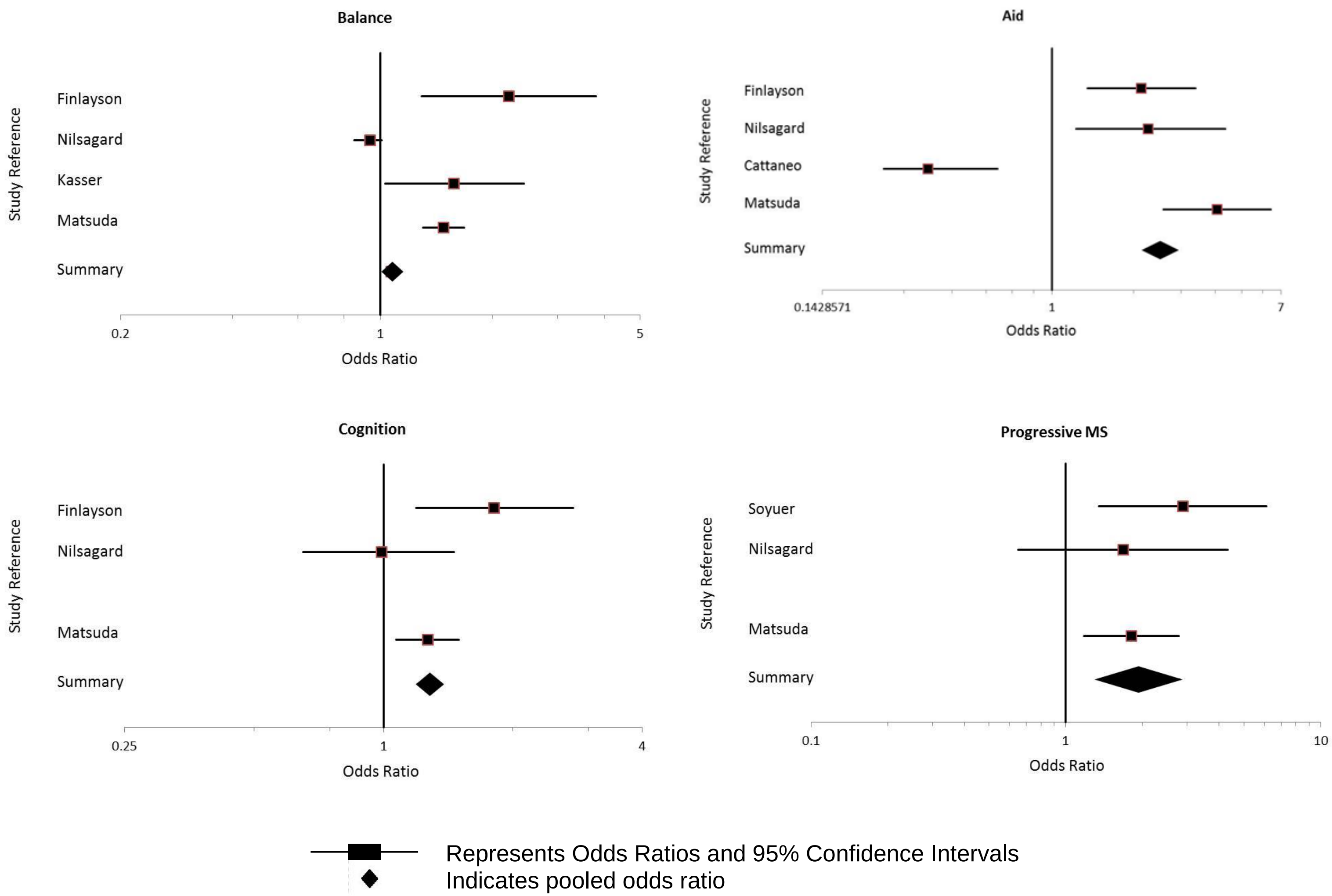


Figure 2-2: Forest plots

2.3.6 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 four studies which evaluated spasticity[3,39,102,118], three reported statistically significant differences between fallers and non-fallers. The fourth study[39] did not report a difference between fallers and non-fallers 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 between the studies, with different versions of the Ashworth and modified Ashworth Scale being used as well as differences in scoring methods (summation or averaging of scores). This may reflect the significant debate around the use and conduct of the Ashworth scale as a measure of spasticity[119,120].

Fear of falling

Fear of falling, as determined by self-report, was evaluated in two studies[3,121]. Odds Ratios of 1.74 (95% CI 1.32-2.31)[121] and 0.95 (95% CI 0.57-1.58)[3] were reported.

Gait

Measures of gait were undertaken in four studies[3,39,102,122], however the variation in methods of evaluation and data reporting precluded meta-analysis. Measurement instruments included laboratory-based analysis (n = 1), standardized generic walking tests (n=2) and MS specific walking tests (n=1). Whilst statistically significant differences in these measures were found between fallers and non-fallers in all studies, the predictive value of the walking tests to discriminate between fallers and non-fallers was poor[3].

MS status

MS status was objectively evaluated in two studies using the EDSS[3,122], although one[3] reported this as continuous data whilst the other[122] dichotomized their sample for analysis as either mildly (EDSS 0-2.5), or moderately affected (EDSS 3.0-5.5). A third article[121] 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 non-fallers.

Continence

Three studies included measures of continence within their evaluation[3,118,121]. Different self-report measures were used in each study to describe the degree that bladder and/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 <1.0.

Other risk factors

A range of other risk factors were evaluated within 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 one study[3], (OR 2.5 for each step on the Birgitta Lindmark motor capacity part E scale [123], 95% CI 1.36- 5.12), however the other studies did not demonstrate statistically significant differences between fallers and non-fallers, for any of these measures, with OR and 95% CI including values <1.0.

2.3.7 Qualitative papers

Two qualitative papers were reviewed within the analyses. One of the qualitative papers[116] interviewed six people with MS who had participated in a pilot program focusing on self-management of falls, whilst the other[117] followed up 12 participants from a quantitative falls risk factor study. All participants highlighted a range of factors that they felt were linked to falls; while many of these 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 falls avoidance strategies whilst undertaking 'risky' activities

2.4 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 1929 participants, 1037 (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.

2.4.1 Risk factors - key findings

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 falls risk.

The results of the 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, whilst the meta-analysis[3,118,121,122] has highlighted an association between balance and falling, the pooled odds ratios 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]. This suggests 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 predict falls 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 which may contribute to falls 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 which demonstrated to be key to the effective management of falls in other populations[100,124].

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 odds ratios 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[117], all aspects which may be affected by impairments in cognitive function. Within the quantitative papers, 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 MS[125]. A study by D'Orio (published after the completion of this systematic review)[126], 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 falls risk. This study also highlights the potential utility of alternative objective cognitive evaluations in studies investigating falls risk, such as the Symbol Digit Modalities Test[125], or Controlled Oral Word Associations Test[127].

Within the narrative review, several other potential risk factors for falling in MS have also been highlighted, including spasticity, gait disturbances, continence and fear of falling. The link between fear of falling and activity curtailment amongst people with MS has been previously highlighted by Peterson[92], who found that 63.5% of the 1064 participants in their sample reported fear of falling, and of these, 82.6% reported associated activity curtailment. In other populations, fear of falling has been identified as an independent risk factor for actual falls[93]. However, the two MS studies evaluating this issue presented conflicting results. This disparity may have arisen due to differences in the study samples: Participants in Matsuda's study which reported a link between fear of falling and falls were all over 45, with 56.19% of participants aged over 65 years[118]. In contrast, the age range of the participants in Nilsagard's study[3] was significantly lower (mean 50 years, range 25-75 years). 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[128].

This systematic review suggests that there are some similarities but also important differences in falls risk factors in people with MS when compared to other neurological conditions[129–134]. As with other groups, secondary issues such as deconditioning, medication use and environmental factors may also contribute to falls risk. However, to date, limited evaluation of these attributes has been undertaken. This, together with the wide range of evaluation methods used preclude meta-analysis.

2.4.2 Limitations of the review

The increased awareness of the importance of falls as an issue for people with MS is encouraging[7]. However, the relatively small number of studies and the variable methodological quality of the included papers means the findings should be interpreted with caution. For example, only two of the studies complied with European falls study guidelines for best practice[108] by recording falls incidence using a prospective falls diary system for the recommended three months minimum period; retrospective recall is known to be inaccurate and subject to bias in other populations[135]. Moreover, a variety of systems were used to classify fallers and non-fallers, including defining fallers as those who reported single falls, multiple falls or injurious falls. This is relevant as evidence from studies in other populations suggests the characteristics of occasional and frequent fallers are significantly different[103]. Currently the lack of reported data on these issues makes it impossible to know whether this is 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 make data pooling and comparison between studies problematic[136]. The results of this systematic review must be interpreted within this context

2.5 Summary and recommendations

Evidence in falls research with older people suggests that for interventions to be effective, they must be targeted to address the specific issues which have contributed to falls risk[137]. The findings of this review highlight that there is limited evidence indicating the factors associated with falls risk in MS. Meta-analysis indicates that generalised impairments in balance, mobility and cognitive function are associated with increased risk of falling, however, none of the measures used demonstrated robust predictive properties which could be used to target interventions to those at greatest risk. In addition, methodological issues associated with definitions and recording of falls limit the robustness of the existing evidence base.

The nature of MS emphasizes the diversity of factors that could be associated with falls risk, including the wide ranging neurological impairments and the unpredictable and evolving pattern of the disease course. For instance, clinical experience suggests that impairments which are common in MS, such as vestibular and cerebellar function[138,139] may be significant contributors to falls risk in people with MS.

The limitations associated with the existing evidence base suggest that further methodologically robust studies evaluating the risk factors for falls in MS are required prior to the development and evaluation of falls intervention programmes for this patient group. Undertaking this type of work prior to developing an intervention is strongly supported by guidance issued by the MRC which state that ‘a vitally important early task is to develop a theoretical understanding of the likely process of change by drawing on existing evidence and theory, supplemented if necessary by new primary research...’ [101]page 9. In the development of this research, study methodology and implementation should be informed by current best practice guidance relating to the use of standardized falls definitions, and the collection of prospective falls data. Similarly, 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 these to clinical practice.

3 Study one: Risk factors for falls in multiple sclerosis: an observational study

3.1 Introduction

This section will focus on the approach and methods used in study one to investigate the risk factors for falling in people with MS. An explanation of the research question, aims and objectives will be followed by a discussion of potential approaches to address the research question, and subsequent justification of the chosen strategy. The chapter will include an evaluation of the research method, including the plan of investigation, study participants, ethical considerations, and the methods used to ensure study quality.

3.2 Aims and objectives

Aim

This study aimed to identify the factors associated with increased falls risk in people with MS.

Objectives

- To evaluate the prevalence, characteristics and consequences of falls in MS
- To identify the risk factors associated with falling in people with MS
- To assess the clinical applicability of outcome measures which could be applied in the assessment of falls in people with MS
- To gather data to inform the development of an MS falls management intervention

3.3 Methods

3.3.1 Research approach

This quantitative cohort study, involved a one-off assessment of potential falls risk factors, followed by a three month follow up period of falls incidence data. The use of a cohort study is appropriate as it allows the researcher to develop an in-depth understanding of the nature of the problem, and to gather data to inform the development of subsequent interventions[140].

3.3.2 Participants

3.3.2.1 Study sample

Falls are typically associated with periods of activity involving standing and walking[5]; the sample was therefore recruited to comprise ambulant people with MS.

3.3.2.2 South West Impact of MS database

The majority of participants were registered on the South West Impact of MS (SWIMS) database; a patient-centred longitudinal study of disease course in people with MS, which is based in south-west England[30]. Individuals submit a range of self-reported postal assessments and information to the database every six months, including details of their overall health status, history of their MS and perceived levels of mobility and quality of life. At the time recruitment commenced, there were approximately 1300 people on this register. There were also a small number of participants who volunteered to participate in the project based on information they received through local MS groups and by word of mouth from other participants.

3.3.2.3 Participant selection and recruitment

Potential participants were selected from the SWIMS database according to the eligibility criteria and contacted by their neurologist via invitation letter. To ensure confidentiality, the database searches and distribution of contact letters was undertaken by the SWIMS database co-ordinator. Participants who made direct contact to volunteer after hearing about the study through local newsletters and whilst participating in other studies were sent the same information by the primary researcher (HG).

The invitation letter included a participant information sheet and stamped reply slip. To maximise the efficiency of the testing process, names of potential participants were generated from the SWIMS database in batches stratified by geographical area, and invitation letters sent to each group in turn. This enabled participants in each locality to be recruited at similar times, allowing blocks of testing to be carried out according to geographical location. By the completion of sampling, all those on the database who met the study inclusion / exclusion criteria were approached (numbers and details included in results section).

3.3.2.4 Inclusion / exclusion criteria

Individuals were eligible to participate if they had a confirmed diagnosis of MS (as against clinically isolated syndrome) as determined by McDonald's criteria[141], and an Expanded Disability Status Scale (EDSS)[26] score between 3.5 and 7 (indicating people who are likely to have some mobility impairment, but to be ambulant for at least a proportion of the time). The EDSS is recorded on the SWIMS database periodically; however, to ensure the EDSS score was up to date, a telephone version[28] was completed with each participant. Individuals were excluded if they were unable to effectively give informed consent to participate in the study, for instance due to cognitive impairment, using current best practice guidance to inform this decision[142] (Figure 3-1). Individuals with concurrent pathology which was likely to have a significant impact on their balance and stability (e.g. concurrent CNS disorder, lower limb amputation) were also excluded.

Guidance on Consent for Research[142]:

'While there are no standardized measures for determining capacity to consent, investigators may assess subjects on their abilities to understand and to express a reasoned choice concerning the:

-Nature of the research and the information relevant to his/her participation;
-Consequences of participation for the subject's own situation, especially concerning the subject's health condition; and
-Consequences of the alternatives to participation'.

(http://www.research.ucsf.edu/chr/guide/chrCogImp.asp accessed 18.06.12)

Figure 3-1: Informed consent guidance

3.3.2.5 Sample size

The required sample size was calculated as 150 participants. In the main analysis to identify the best linear combination of variables to predict fallers/non-fallers, a total of eight possible explanatory variables were considered. Based on Peduzzi[143], a sample size of 145 patients was determined to be sufficient for this type of analysis, assuming that the proportion of fallers (classified as those who have fallen in the three months following the assessment) was no lower than 55% (Figure 3-2). Although this could be considered a high rate of falling, previous MS studies have reported falls rates of 54% in two months[102] and 63% in three months[3] in samples with similar EDSS scores. Recruiting 150 participants allowed a 3% dropout rate, which was a conservative estimate based on previous research projects involving SWIMS participants, where the dropout rate was 1.7% over 2 years[144].

n= number of predictors(10/incidence)

n=8(10/.55) =145.45

Figure 3-2: Sample size calculation[143]

3.3.3 Predictor variables

Following the completion of the systematic review (chapter 2), a total of 8 predictor variables were highlighted for inclusion within the risk factor study. The choice of variables incorporated previously researched attributes where the measurements used lacked specificity and other attributes which could reasonably be considered as potential risk factors based on evidence from other populations and the attribute's prevalence in MS. Each of the chosen predictor variables is described here, along with a justification of the rationale for inclusion.

Predictor 1: Physiological attributes

In older people, impairments in balance, sensory and visual disturbances, strength and reaction times have been shown to be valid predictors of falls risk, with increased risk being associated with multiple impairments[145]. All of these key physiological attributes may be impaired in MS. The systematic review highlighted one previous study in MS which demonstrated an association between impaired proprioception and falls risk (OR 2.50, 95% CI 1.36-5.12)[3], and several other studies (which used generalised measures) identified balance impairment as a falls risk factor[118,121]. However, of the studies undertaken to date, only one[122] utilised a specific objective measure, and this relied on laboratory testing equipment.

The contribution of different visual impairments to falls in older people has been investigated, including visual acuity, edge-contrast sensitivity and depth perception[94]. Measures of edge-contrast sensitivity and depth perception have been consistently linked to falls risk[146], with studies demonstrating significant correlations between impairments in edge contrast sensitivity and recurrent falls (Hazard Ratio (HR) 2.09; 95% CI = 1.41-3.10)[147]. The contribution of visual impairments to falls risk in MS has not been evaluated to date, although the high incidence of visual impairment (approximately 80% report visual impairments at some point in their disease course) suggests this could be a significant contributing factor[148].

Lower limb (LL) weakness demonstrated a combined OR of 1.76 (95% CI 1.31-2.37) for any fall and 3.06 (95% CI 1.86-5.04) for recurrent falls, in a systematic review which included 13 studies in older people (n=6146)[149]. Although no studies of falls risk in MS have directly evaluated the contribution of weakness, the moderate correlation between knee extension torque and AP CoP variability as reported by Chung[52] may suggest a contribution of weakness to falls in MS.

Increased reaction time has been found to be an independent risk factor for falling in a range of older populations, including community dwelling individuals and residents of residential care facilities[94], suggesting its importance in people with a range of functional ability. Reaction time has not been included in studies evaluating falls risk in MS to date, however the presence of delayed somatosensory evoked potentials, and correspondingly slow reaction times in several studies[70,75] suggests this should be included.

Predictor 2: Ataxia

Up to 80% of people with MS report symptoms of ataxia at some point in their disease course[150]. However, there is no published research in MS which includes ataxia as a possible contributing factor to falls. In individuals with a diagnosis of primary ataxia, there is a high prevalence of falls, with one study demonstrating a significantly higher rate and frequency of falls in the ataxia group when compared to controls (93% vs 24% $P<0.01$)[46].

Predictor 3: Spasticity

Spasticity is frequently reported by people with MS[151]. Studies which have included spasticity as a potential risk factor for falls[3,39,102,118] have demonstrated variable results in the association between spasticity and falls risk. The two studies reporting odds ratios suggest a small increase in falls risk with higher levels of spasticity (OR 1.14 (95% CI 1.02-1.31)[3] and OR 1.32 (95% CI 1.14-1.52)[118]), whilst the two studies reporting alternative analyses demonstrated a non-significant trend for increased spasticity amongst participants who fell[39,102] . However, as highlighted previously in section 2.3.6, methodological issues preclude a definitive judgement about this.

Predictor 4: Fear of falling

Fear of falling and associated activity curtailment has been highlighted as an issue in MS[92]. However there is limited research investigating the contribution of fear of falling to falls risk itself, and findings of existing studies are equivocal[3,121]. In older people, the link between fear of falling and falls risk has been clearly demonstrated[93], with recommendations that a valid measure of fear of falling should be included in all assessments of falls risk[152].

Predictor 5: Cognitive function

Impairments in memory and thinking are commonly reported in MS, and evaluation has shown impairment in a range of cognitive processes[153]. Impaired cognitive function is a recognised risk factor for falls in older people, where global cognitive impairment, as well as specific issues in areas such as working memory and attention have been found to be associated with increased falls risk[99,154,155].The potential role of cognitive dysfunction as a contributing factor to falls risk in MS was highlighted in the systematic review (section 2.3.5), with pooled OR of 1.28 (95% CI 1.2-1.36). However issues with the use of self-report and the inclusion of generalised cognitive measures within existing studies suggest that evaluation of the specific contribution of attributes such as working memory and attention is warranted.

Predictor 6: Dual task interference

A systematic review of 15 studies examining the relationship between performance under dual task conditions and falls risk in older adults, demonstrated a pooled odds ratio of 5.3 (95% CI 3.1-9.1)[82]. A study by Hamilton[78], demonstrated significant declines in a range of gait performance measures in participants with MS relative to matched healthy controls. The degree of decline in dual task performance was related to levels of fatigue and self-reports of cognitive function, but not to disease severity or duration. Falls were not examined as a factor in this study, and indeed a history of falls in the preceding month was highlighted as an exclusion criterion.

Predictor 7: Autonomic dysfunction

Orthostatic hypotension is frequently cited as a risk factor associated with falls in older people, although there is conflicting evidence to support or refute this claim[137]. In MS, the reported frequency of autonomic dysfunction is variable[156]. However, studies have demonstrated significant differences in autonomic response relative to HC in up to two-thirds of participants[157]. On MRI evaluation, these changes were linked to presence of brainstem lesions; although there were no significant associations between abnormal autonomic responses (including orthostatic blood pressure response) and functional or EDSS groupings ($p > 0.05$). To date no MS studies have included measures of autonomic function in evaluations of postural stability or falls.

Predictor 8: Vestibular dysfunction

The association between vestibular impairment and postural stability has been investigated in older adults, where studies have demonstrated an increased incidence of vestibular dysfunction in individuals who sustained fall related fractures[158,159]. More recently, the inability to suppress the vestibular ocular reflex has been highlighted as a risk factor for falls in one study of older people (odds ratio=18; 95% confidence interval, 1.63–198.42)[160], although the small sample size of 38 individuals limits the generalizability. In MS, the prevalence of vestibular dysfunction has been reported to be as high as 70%[3], although the incidence of specific vestibular symptoms at any one time varies (between 7% and 15%[161,162] in published studies). Laboratory-based evaluations have found that a significant proportion of subjects with MS demonstrate abnormal responses to vestibular conditions during dynamic posturography testing[163], and that this was linked to impaired balance[45]. However, there have been no published studies to date which have evaluated the relationship between vestibular dysfunction and falls in MS, so this assertion remains speculative.

3.3.4 Plan of investigation

Assessment procedures

Assessment location

In a previous research workshop with people with MS, participants stated that sessions at local community hospitals would be preferable to home testing or alternative venues in future studies. Participants in this study were therefore invited to attend a one-off assessment session at a community hospital close to their home. The final distribution of assessment locations is shown in Figure 3-3, along with the dates of testing.

Assessment format

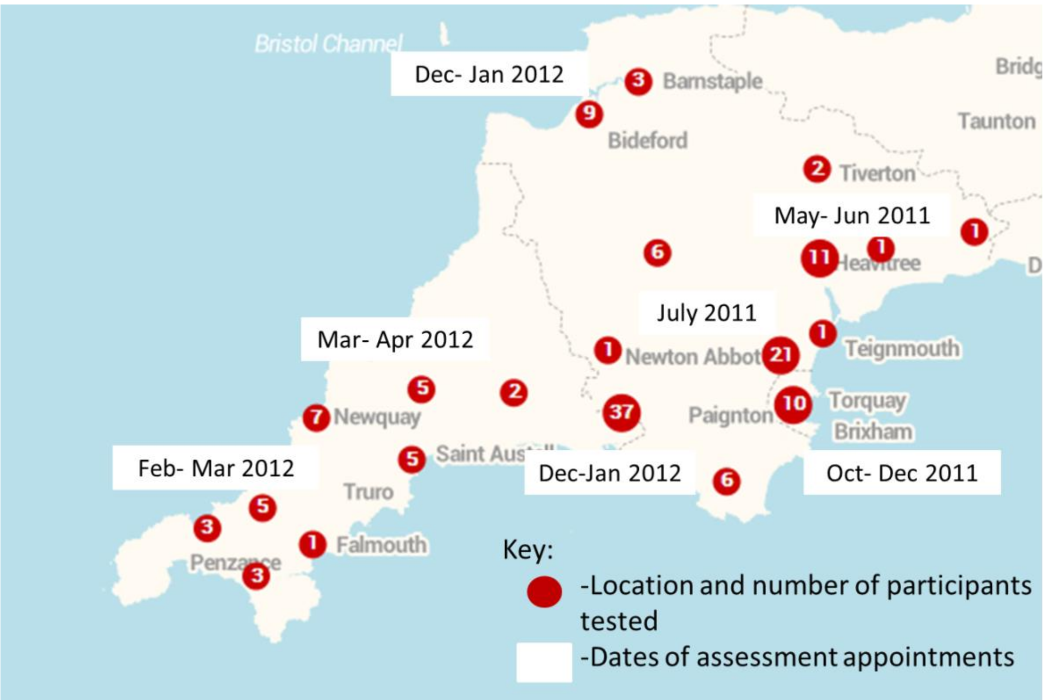


Figure 3-3: Assessment locations and assessment schedule

The participants of the research workshop considered that testing sessions lasting a maximum of 1.5 hours were acceptable in terms of time commitment and fatigue management; therefore the assessment battery for this study was designed in line with this. To minimise fatigue, the assessment protocol minimised unnecessary position changes, and varied the type of assessment throughout the process (questionnaire versus performance). Activities were always undertaken in the same order (appendix 7.2.1), as the potential benefit gained by minimising possible confounding of results through random test ordering was considered to be outweighed by the potentially negative impact of fatigue which may have resulted from multiple position changes. Pilot work on 10 non-MS individuals was undertaken to ensure that the assessment procedures were efficient and effective.

3.3.5 Assessment measures

Demographic data related to falls risk were collected, followed by a battery of assessments related to the chosen eight predictor variables. Selection of an assessment measure for each predictor was based on current literature in MS, or in research including older people and other neurologically impaired groups where data specific to MS were unavailable. Measures were selected based on the following criteria:

1. Published validity and reliability data, preferably in studies with MS participants, or those with other neurological disorders
2. Should be feasible for use in a clinical environment in terms of both portability and cost
3. Should be appropriate for use in people with MS with a range of mobility levels, and should not generate excessive fatigue

Of the measures selected, only the Dual Task protocol, the Ashworth Scale and the Symbol Digit Modalities test have published psychometrics relating specifically to people with MS. The Brief Ataxia Rating Scale and Dynamic Visual Acuity tests have been evaluated in individuals with a range of cerebellar ataxias and vestibular dysfunction respectively. The other measures have been extensively evaluated in older people, and several have been utilised as measures in populations with neurological impairment. Ideally, psychometric and clinimetric data would be available for all measures in the MS population, however, the validation data in those not specifically tested with people with MS was considered sufficiently robust to warrant the use of the measure.

All assessments were carried out according to a written protocol which included standardised tester and participant instructions. Any variance from the protocol was noted for each participant, and considered during data analysis.

Predictor 1: Physiological Profile Assessment (PPA)

The PPA is a validated tool devised to provide a quantitative measure of key physiological risk factors for falls in older people[145]. The screening version of the tool includes the five measures found to be the most important discriminant measures of falls risk in a range of studies[103,146,164,165], with predictive accuracy greater than 75%[145]. Each element of the PPA comprises a single test which has been designed specifically for ease of administration for both participants and testers; the measures included are muscle strength, sensation, vision, balance and reaction time. Published reliability data for each measure demonstrate moderate to good reliability, with intraclass correlation coefficients (ICC) in the range of 0.5 to 0.7 in studies carried out with groups of older people[94]. Scores from each measure can be considered separately, or summed and weighted to give a total PPA risk score. Normative data are available on the PPA scores related to non-neurological populations, but to date there is no published data relating to individuals with specific neurological pathology.

Predictor 2: Brief Ataxia Rating Scale (BARS)

Measurement scales for ataxia have been developed for use in individuals with both primary and secondary cerebellar pathology; the recognised 'gold standard' assessment being the International Co-operative Ataxia Rating Scale (ICARS)[166]. The ICARS has been demonstrated to be a valid and reliable measure in individuals with a range of spinocerebellar ataxia (SCA) sub-types, Freidrichs ataxia and multi-system atrophy[167–169]. However, the scale includes 100 items and is both time consuming and fatiguing to complete[170]. In response, the BARS was developed as a quick, clinically applicable test for ataxia, using five aspects of the original ICARS which were demonstrated to be most appropriate in discriminant function analysis[171]. The BARS has been validated against existing ataxia rating scales in populations with a range of cerebellar ataxias[171], and assesses performance in five aspects of co-ordination, including upper and lower limb movements, gait, speech and ocular control. Each of the elements is a recognised stand-alone test for individual aspects of ataxia (e.g. visual issues, upper/lower limb dysmetria), however within the BARS, scores for each element are summed to give a total value. The maximum possible score is 30, with higher scores indicating greater disability.

Predictor 3: Ashworth scale

The measurement of spasticity is complex due to the multi-dimensional nature of its pathology[172]. The Ashworth scale has been extensively used as a measure of spasticity across a range of studies in people with a variety of neurological disorders[173]. Despite criticisms of its validity, it is recommended for use as an appropriate proxy measure of hypertonia[119]. In the literature a wide variety of test and scoring protocols have been published[174]. In this study the Ashworth scale was measured using the testing guidelines reported in Blackburn and Nuyens[175]. There are recognised problems associated with summed scoring of multiple muscles using the Ashworth scale[119]. Hence, individual measurements were taken of the gastrocnemius and soleus muscles on the leg which was reported by the individual as the leg with most stiffness, and each was scored individually.

Predictor 4: Falls Efficacy Scale (International) (FESi)

Whilst assessment of the psychological consequences and impact of falls using a standardised measure is widely recommended [96], there is no consensus over the measure that should be used[152]. The most commonly used measures are the Activities Specific Balance Confidence (ABC) Scale[176], CONFbal[177] and FESi[128]. In a systematic review of the properties of measures to assess the psychological outcomes of falling[178], the authors concluded that there was insufficient evidence to demonstrate the superiority of any particular measure, although all scales performed better than a simple global rating scale. However, the FESi has been recommended by the European Falls network ProFane as being the most feasible measure for clinical and research use due to the speed and simplicity of completion[108]. The FESi has also recently been validated for use in ambulant people with MS, demonstrating excellent internal reliability and construct validity[179]. The FESi produces a single score based on the summed total of the individual responses to the 16 questions; the maximum possible score is 64, with higher scores indicating a greater degree of anxiety.

Predictor 5: Symbol digit modalities test (SDMT)

The SDMT provides a fast, reliable measure which specifically evaluates areas of cognitive function which are likely to be relevant to falls risk including working memory and attention[180]. The psychometrics of the SDMT have been evaluated in people with MS, and include a sensitivity of 0.82, and specificity of 0.60[125]. Although other measures of cognitive function are available, the SDMT has been recommended as a measure of choice in MS cognitive screening due to its superior predictive validity and ease of administration[181]. In this study, the oral version of the SDMT was used, avoiding the potential issues of impaired writing ability influencing the score. Each participant response was recorded, and the total number of correctly identified symbols during the 90 second test period was calculated to give the test score. Previous studies have identified a cut-off score of 55 or lower as yielding a 72% classification accuracy for detecting cognitive impairment as measured by comprehensive neuropsychological testing batteries[125]. However for the purposes of this study, the SDMT scores were treated as a continuous measure.

Predictor 6: Dual task interference

A wide range of measures have been utilised within dual task interference studies. In a systematic review of measures of dual task performance as predictors of falls risk in older people, Beauchet[82] concluded that walking activities performed with and without complex verbal cognitive tasks were more accurate predictors of falls than simple cognitive tasks, the latter tending to demonstrate a ceiling effect. Similarly, standardised verbal cognitive tasks demonstrated greater reliability and sensitivity than motor tasks or non-standardised cognitive activities.

In this study, a 10 metre walk and serial 7 subtraction protocol which has been used in several studies investigating dual task interference in older people was selected[82]. This protocol has been shown to be easily utilised in a clinical environment and well tolerated by participants with a range of problems, including neurological disorders such as Parkinson's Disease[182]. Serial 7 subtraction protocols have also been shown to be sensitive to dual task issues in people with MS. Delrue[79] evaluated walking over a 30 metre course in 16 people with MS with and without serial 7 subtraction; the addition of the cognitive task led to a statistically significant difference between control and MS groups in walking time. However, no measures of falls risk or incidence were included in this study.

Data recording during the dual task activities included time taken to complete the 10 metre walk, number of steps taken, number of stops and number of calculations (total number and actual number correct). The measurement used in the main analysis was the percentage change in walking time between the two tasks, as used in other studies evaluating dual task interference[183,184].

Predictor 7: Orthostatic hypotension

Measurement of lying and standing blood pressure is a reliable, quick and non-invasive method of assessing autonomic function, which is applicable to the clinical environment and has been used in previous MS studies[157]. In line with British Hypertension Society (BHS) guidelines, blood pressure was measured after a minimum of 15 minutes in a supine position and recorded for at least two minutes after standing[185]. Any change in blood pressure and associated symptoms were noted. The test was considered positive if a drop of >20/10mmHg was noted after standing for at least one minute[186]. In this study a BHS validated digital sphygmomanometer was used (A&D Instruments, Oxfordshire). Whilst the potential for digital sphygmomanometers to be less accurate than manual devices is recognised[187], it was considered to be the most appropriate device in this situation where participant stability in standing is a potential issue.

Predictor 8: Dynamic visual acuity

Accurate evaluation of vestibular function is challenging, and many studies utilise laboratory based measures which are not practical in a clinical setting. However, studies have demonstrated that clinical measurements of DVA are both sensitive and specific indicators of vestibular dysfunction in individuals with a range of primary vestibular pathology[188], and are therefore sufficiently robust to use as outcome measures[189]. Dynamic visual acuity is dependent upon the interaction of smooth pursuit, opto-kinetic reflex (OKR) and vestibulo-ocular reflex (VOR) activity to achieve image stabilisation on the retina during motion through compensatory eye movements in the opposite direction to the perceived movement[190]. The precise interactions of the various reflexes is not fully understood, however, at speeds below 1.6^{0}/sec, smooth pursuit and OKR mechanisms appear to predominate, while at faster speeds ($>50^{0}$/sec) visual correction is primarily dependent on the VOR[191].

For this study, a testing protocol was used in line with those previously described in studies by Hillman[192]. The test procedure measured visual acuity under static and dynamic conditions, where the head was moved passively through a horizontal plane (Figure 3-4). Passive DVA tests have demonstrated to have greater sensitivity than active tests (P=<0.01), and horizontal testing has proven more sensitive than vertical testing in a number of studies[193,194]. Test position has not been shown to affect DVA score in people with vestibular pathology[195], therefore, for safety and comfort, the subject completed both tests in a sitting position. During the DVA test, the subjects' head was moved passively through a 40^{0} arc in a horizontal plane at a frequency of approximately 1.5Hz, equating to a maximum velocity of approximately 120^{0}/sec. Whilst slower than the speed used in some studies[196], 1.5Hz has been shown to have greater specificity than higher speeds up to 2 Hz, and to be more achievable in a clinical setting[189]. As maximum speeds of smooth pursuit are thought to be no greater than 100^0/sec[197], the 1.5Hz test frequency still ensured that the subjects were relying on VOR as the primary gaze stabilisation mechanism. To ensure appropriate speed and range of passive head movement was achieved, the dynamic test was conducted by the tester moving the subject's head through a range of motion indicated by a guide above the subject's head, whilst listening to a metronome set at the appropriate frequency through an ear piece to guide the movement velocity.

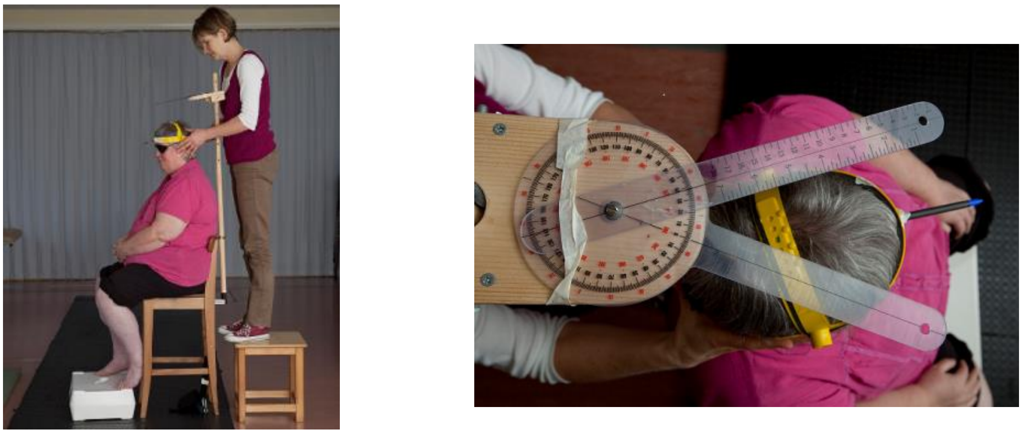


Figure 3-4: Set-up for dynamic visual acuity test

Visual acuity was measured using a Landolt C computer screen based testing protocol accessed through Freiburg Visual Acuity Test (FrACT) software, which is freely available via the internet[198]. The Landolt C test has the advantage of being less prone to issues related to cognitive capacity than traditional Snellen or E chart based tests[199]. The test procedure involved the subject verbally responding to the C prompts which were displayed on a laptop computer screen viewed from a distance of two metres. The FrACT software produced a readout of visual acuity after each test in both logMAR and decimal visual acuity scales[198], from which the Visual Acuity Score (VAS) (100-(50xlogMAR)) was calculated. The VAS has the advantage for data analysis purposes of not including negative numbers[200]. Each point on the VAS represents one standardised eye-chart letter, with deterioration of more than two lines (>10 points on the VAS) considered a significant loss of DVA in clinical settings[193].

3.3.6 Outcome variable: falls

Participants were asked about their falls history as part of the demographic and background data collection. Problems with the accuracy of retrospective falls recall[135,201] has led to the recommendation that falls data should be collected prospectively using daily diaries[108]. Therefore, the primary outcome variable for this study was incidence of falls as detailed through prospective falls recording methods. Falls were defined according to Lamb[108] (page 1619) as: ‘A slip or trip in which you lost your balance and landed on the floor or ground or lower level’; and near falls as ‘an occasion where you felt you were about to fall but did not actually fall’.

Following assessment, participants were asked to record falls data using a daily diary system for a three month period (appendix 7.2.2). The daily falls diary captured information on frequency of *actual* falls and *near* falls. For each *actual* fall, participants were asked to record standardised data in a format previously used by Nilsagard[3]. Detail was recorded about the time of day and activities being undertaken at the time of the fall, plus any related injuries, using tick-box and free text responses. Perceived rates of fatigue and hurrying were recorded using a four-point ordinal scale. For near falls, participants were asked to record the frequency of such events on a daily basis in the falls diary.

Participants received their falls diaries in a pre-prepared pack containing 84 daily diary sheets, completion instructions and reply paid return envelopes. The daily diary sheets were compiled into two-week batches, with a prompt and return envelope at the end of each batch to facilitate return of the diary sheets. Any participant whose diary returns fell behind schedule was followed up by a reminder telephone call or email. Participants were reminded a maximum of twice during the diary completion period. Diaries were reviewed immediately on return and participants were contacted to confirm falls data and clarify any aspects that were unclear. When participants recorded the activity associated with their fall as ‘other’, more detail was elicited during the follow-up contact. Participants were also asked further general questions about the perceived cause of the fall (appendix 7.2.3).

3.3.7 Ethical considerations

Ethical review

Ethical review was undertaken by the University of Plymouth Faculty of Health Education and Society Ethics Committee and the South-West (2) NHS Research Ethics Committee (10/H0203/66). NHS Trust Research and Development Approval was also gained for each assessment venue.

Informed consent

Written informed consent was gained from all participants using procedures detailed by the Council of Research and Ethics Committees (U.K.) and in accordance with the International Declaration of Helsinki[202].

Confidentiality

Initial invitation letters from the participants’ neurologists were distributed by the SWIMS co-ordinator to ensure confidentiality of potential participants. On recruitment to the study, participants were assigned a study identification number, which was used for all documentation, including the audio recordings of the SDMT and DTI responses. Original records identifying individual participant identification numbers remained accessible only to the primary researcher (HG), and were stored separately to other study records in a locked cabinet in accordance with data protection procedures.

Potential harm

Throughout the study, all possible precautions were taken to ensure participant safety and wellbeing. As fatigue can be an issue for people with MS, the testing procedure was developed to minimise unnecessary energy expenditure as described in section 3.3.4. Feedback was sought from the pilot participants to confirm the acceptability of the protocol.

As impairment in balance and mobility is common in people with MS[75], particular attention was paid to ensuring safety during any activities that could constitute a potential risk. Stand-by assistance, walking aids and chairs were available during standing and walking activities, and participants were free to sit down at any point if they felt unstable. All assessments were undertaken in community hospital venues, allowing access to medical assistance should a problem have occurred.

Data protection

All electronic data were stored on AES256 bit encrypted data sticks and password protected computers, in accordance with the Data Protection Act 1998 and Plymouth University data protection policy.

3.3.8 Data analyses

All data were entered directly onto Excel during the assessment. The data entry spread sheet was designed to minimize the potential for inaccuracies of data recording, and was trialled during the pilot phase of the study to ensure its utility and effectiveness. The accuracy of data entry was checked after each assessment. Any aspect of the assessment where participants were unable to provide data was recorded, including coding for each reason for non-completion.

Groupings: fallers and non-fallers

People were classified as fallers or non-fallers based on the prospective diary falls reports; participants were classed as fallers if they reported two or more falls during this period. This grouping is based on previous research in older people which suggests that individuals reporting single falls tend to have different characteristics to multiple fallers[145,203,204].

Missing data

There were no missing data in any of the self-report variables. Three of the eight predictor variables had individual missing data, which were excluded from analysis on a case-by-case basis.

Statistical methods

All statistical analyses were undertaken using IBM SPSS for windows version 20[205], using two-sided tests and 95% confidence intervals, with the significance level set at 5%. Where computational power allowed, exact significance levels were calculated, otherwise the Monte-Carlo approximation method was used.

Analysis of the characteristics and consequences of falls

For the analysis of falls frequency and related circumstances, all *actual* falls were included. As the data relating to the number of *actual* falls did not demonstrate a normal distribution, comparisons of the differences between the numbers of falls recorded by demographic and clinical characteristics were summarised using medians and interquartile ranges (IQR) and statistical analysis undertaken using the Mann-Whitney U test (for binomial variables such as gender) or Kruskal-Wallis tests for multiple category characteristics (such as MS classification and EDSS). The relationships between the number of *actual* falls and continuous characteristics (such as age and number of *near* falls) were analysed using Spearman's rho correlation (r_s).

The falls rate (*actual* falls) per person per year (PPY) was calculated in Excel using the formula[206], assuming a 90 day participation period:

$$Falls\ rate\ (PPY) = \frac{total\ number\ of\ actual\ falls}{total\ number\ of\ person\ days\ (all\ participants)} \times 365$$

The injury rate per person per year was similarly calculated.

Data relating to the circumstances associated with *actual* falls were summarised by calculating the frequency and percentage of the total number of falls recorded per categorical grouping (time of day, activities associated with the fall, perceived fatigue and hurrying).

Analysis of risk factor data

Data were summarised using frequencies and percentages, mean and standard deviation or median and inter-quartile range (IQR) as appropriate. Associations between categorical variables and falls grouping were analysed using Fisher's exact test. For continuous variables, the differences between the two falls groups were compared using independent two sample t tests (for normally distributed parametric data) or Mann Whitney U tests (for non-parametric data). To further explore possible associations between each factor and falls grouping, unadjusted odds ratios (and corresponding 95% confidence intervals (CIs)) were calculated.   Where data were categorical, OR were calculated for each category compared with the category indicating least impairment. Where individual categories had 0 values for one classification, sub-classifications were collapsed where appropriate, or OR calculations were not undertaken.

For the main statistical analysis, multi-variable logistic regression analysis, adjusting for disease severity as determined by EDSS score, was used to determine which combination of the eight predictor variables best discriminated between the two falls groups. Initially, forced entry was used to include all of the predictor variables plus the EDSS. Subsequently, backwards stepwise elimination was undertaken to develop a reduced model. The order of elimination was determined by evaluation of the Wald statistic for each predictor at each step alongside qualitative evaluation of the variables. This process is recommended above standard stepwise methods using solely significance-based decision-making to improve the stability and quality of the final model[207]. Further exploratory analyses of the component scores of variables included in the reduced model were undertaken to evaluate the relative contributions of each element to the overall performance of the retained predictor.

Goodness-of-fit of the final reduced model was assessed using the Hosmer and Lemeshow test and model performance assessed using analysis of the Receiver-Operating Characteristics (ROC) curve as a plot of the sensitivity and 1-specificity for all possible cut-off points[208]. The optimal cut-off point of the model (defined as the point that maximises sensitivity and specificity)[209] was determined using least-distance analysis distance ((1-Sn)2+(1-Spec)2) and confirmed by calculating the Youden index (defined as J =max {c Se(c)+ Sp(c)-1} [210](p458). The main assumptions of logistic regression were also investigated[211], using standard diagnostic methods.

3.3.9 Study quality

The 'STrengthening the Reporting of Observational studies in Epidemiology' (STROBE)[212] was used as a framework for the design, conduct and reporting of the study. Additional measures included the use of electronic data entry from the outset, which has been reported to increase recording accuracy whilst avoiding transcription error[213].

3.4 Results

3.4.1 Participant recruitment

A flow chart detailing participant recruitment and retention is included in

Figure 3-5. A total of 277 people were sent an invitation letter from the neurologist of persons registered on the SWIMS database. This represented all individuals registered with SWIMS who met the inclusion and exclusion criteria according to database searches carried out by the SWIMS co-ordinator. A total of 139 replies were received from this arm of recruitment, giving a response rate of 50%. A further 18 participants were recruited who made direct contact after having read about the study in the SWIMS newsletter, thus a total of 157 participants were screened for eligibility. Of these, seven participants were not eligible or withdrew; one of whom did so because she had been admitted to hospital with a fractured neck of femur following a fall.

Of the 150 people recruited, 148 completed at least two weeks of falls diary returns, enabling their data to be included in the final analysis. Two participants failed to complete any falls diary returns despite written and telephone prompts, and were therefore excluded from the analysis.

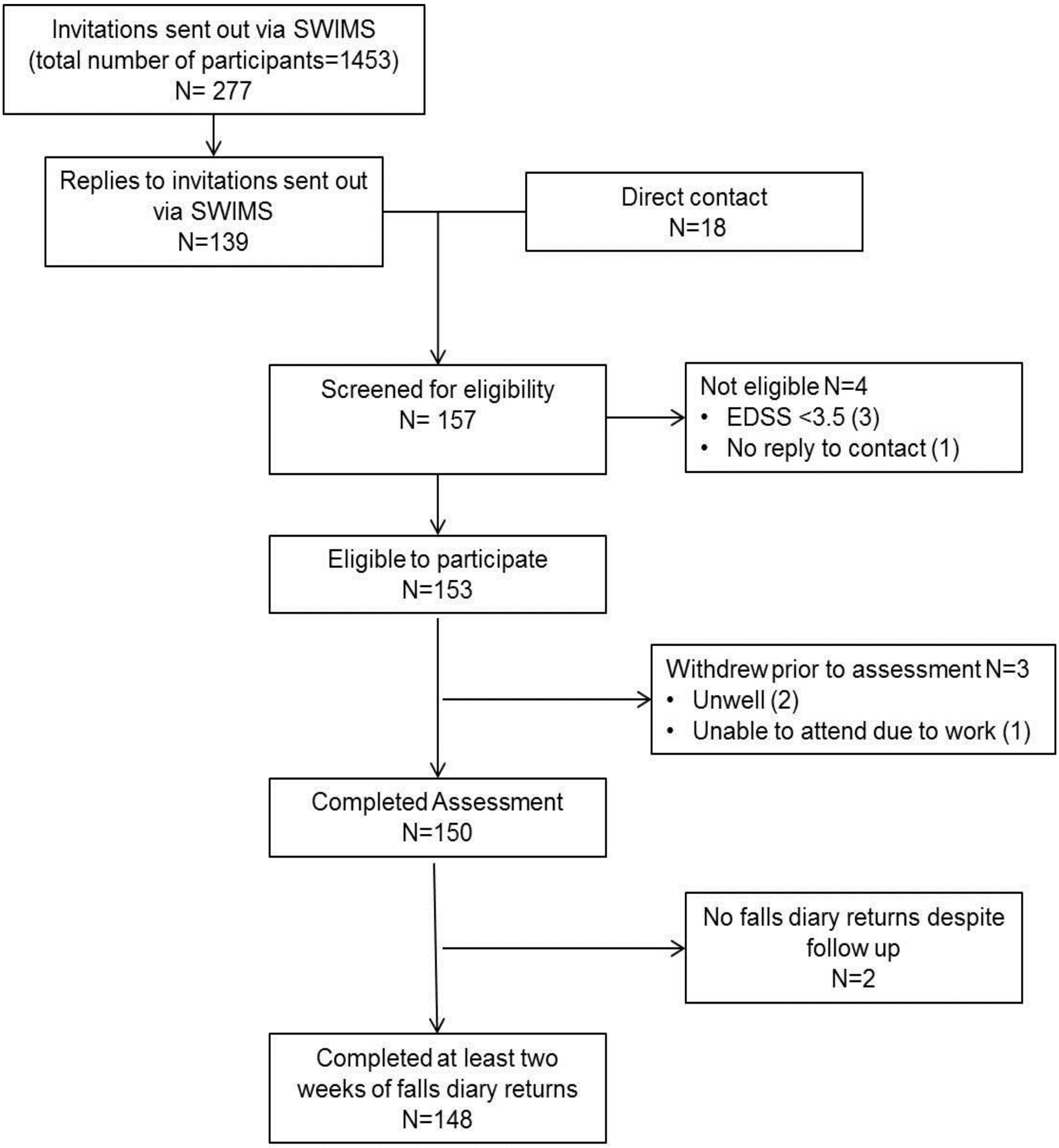


Figure 3-5 Participant Flow Diagram

3.4.2 Sample characteristics

Demographic and clinical characteristics

Table 3-1 details the demographic and clinical characteristics of the sample. This table includes data from non-participants as recorded in the SWIMS database to allow comparison to the wider population. The data for this comparison was obtained following consultation with the SWIMS principal investigator (Prof J Zaijeck), and all database interrogation was undertaken by the SWIMS database co-ordinator. The overall distribution of the study sample according to age and gender is broadly similar to those in the general MS population[214]. However, the non-respondents were, on average, significantly younger (p =0.005) and had been diagnosed with MS significantly more recently (p = 0.01) than those who chose to participate in the study.

In this comparison, for consistency between the two groups, MS classification is detailed using the data recorded from the SWIMS six-monthly questionnaire returns, rather than the MS classification recorded during the study. Fewer non-participants were recorded as having primary or secondary progressive MS compared to the participant group; although this difference was not statistically significant. Comparisons should however be treated with some caution as self-report data for disease classification was either missing or unknown in over 30% of non-participants and 12% of participants.

In line with the literature, disease severity as measured by the telephone EDSS reflects a bi-modal distribution, with higher frequencies in the 3.5 and 6.0 classifications[30]. As this data was only collected on recruitment to the study, data for non-participants is not available.

Characteristic		All (n= 295)	Participants (n=148)	Non Participants (n=147)	*p* value
Age, years, mean (SD)		55 (10)	58 (10)	53 (10)	0.005[a]
Gender n (%)					
	Female	238 (78)	114 (77)	116 (79)	0.697[b]
	Male	68 (22)	34 (23)	31 (21)	
Years since first symptoms, mean (SD)		-	23 (12)	Not available	-
Years since diagnosis, mean (SD)		14 (10)	17 (11)	13 (9)	0.01[a]
MS Classification n (%)*					
	Relapsing Remitting	86 (29)	43 (29)	43 (29)	0.581[c]
	Secondary Progressive	76 (26)	46 (31)	30 (20.6)	
	Primary Progressive	57 (19)	36 (25)	21 (14)	
	Benign	5 (2)	2 (1)	3 (2)	
	Combination	5 (2)	3 (2)	2 (1.4)	
	Unknown	21 (7)	9 (6)	12 (8)	
	Data missing	45 (15)	9 (6)	36 (25)	
EDSS, median (IQR)		-	5.5 (3)	-	
EDSS n (%)					
	3.5	-	26 (18)	Not available	-
	4	-	19 (13)		
	4.5	-	16 (11)		
	5	-	9 (6)		
	5.5	-	14 (9)		
	6	-	47 (32)		
	6.5	-	17 (11)		

a: *p* value from two-sample *t* test; b: *p* value from Mann-Whitney test; c: *p* value from Fisher's exact test; SD: Standard Deviation, IQR: Interquartile range; *classifications used by SWIMS

Table 3-1: Sample characteristics: comparison of participants and non-participants

3.4.3 Falls data

Falls diary returns

Of the 148 participants who completed at least two weeks of falls diaries, a total of 823 of a possible total of 888 falls diaries were returned (92.7%). Table 3-2 details diary return rates: as each falls diary recorded activity over a two week period, these are broken down by two-weekly intervals. The vast majority of participants (79%) recorded and returned falls data for the whole twelve week period, with around 10% recording activity for six weeks or less. Of the four participants who returned only two weeks of falls diaries (despite prompts and reminders), three recorded at least two falls during the two week period. The fourth participant did not record any falls.

	Number of returns	%
Total number of falls diaries returned (maximum possible =888)	823	92.7
Number of weeks of diaries returned		
2 weeks	4	2.7
4 weeks	1	0.7
6 weeks	6	4.1
8 weeks	4	2.7
10 weeks	16	10.8
12 weeks	117	79.1

Table 3-2: Falls diary return rates

Falls rates

Reporting of *actual* falls

From the total of 148 participants, 104 recorded *actual* falls during the diary data collection period. Within these 104 participants (70.3% of the total sample), the median number of falls was 3 (25^{th} and 75^{th} percentiles 1.25 and 6.75 respectively), with a range of 1-63 falls over the 12 week period. One third of the sample (49/148, 33%) reported between two and five *actual* falls, 13/148 (8.7%) reported between 6-10 falls and 16 (10.8%) reported ≥ 11 falls (Table 3-3).

Number of reported falls	N (n=148)	%
0	44	29.7
1	26	17.6
2-5	49	33.1
6-10	13	8.7
11 or more	16	7.4

Table 3-3: Reporting of *actual* falls

Falls rates

A total of 672 *actual* falls were recorded, which equates to a falls rate of 18.41 falls PPY when calculated including all 148 participants, or a falls rate of 26.20 falls PPY when calculated for only the 104 participants who recorded *actual* falls.

Reporting of *near* falls

With respect to *near* falls, a total of 3785 events were recorded by 128 participants (86% of the total sample). There was a moderate correlation between the number of *actual* and *near* falls recorded (r_s=0.47, 95% CI 0.34 to 0.59). Table 3-4 details the number of reported *near* falls relative to the number of reported *actual* falls. Sixty nine participants (46.6% of the total sample) recorded ≥11 *near* falls, with 13 of these (8.7% of the total sample) also reporting ≥11 *actual* falls. However, high numbers of *near* falls were also reported by participants across all the *actual* falls groups. Of particular interest is the group of individuals who reported relatively high numbers of *near* falls but relatively few *actual* falls, with 18 individuals (12% of the total sample) reporting ≥11 *near* falls but ≤1 *actual* fall.

Recorded *actual* falls N (%)		**Recorded *near* falls N (%)**				
	(Total N=148)	**0**	**1**	**2-5**	**6-10**	**≥11**
		20 (13.5)	**12 (8.1)**	**22 (14.9)**	**25 (16.9)**	**69 (46.6)**
0	**44 (29.7)**	13 (29.5)	7 (15.9)	4 (0.9)	7 (15.9)	13 (29.5)
1	**26 (17.6)**	4 (15.4)	3 (11.5)	6 (23.0)	8 (30.7)	5 (19.2)
2-5	**49 (33.1)**	2 (4.0)	2 (4.0)	11 (22.4)	8 (16.3)	26 (53.0)
6-10	**13 (8.7)**	1 (7.6)	0	0	0	12 (92.3)
≥11	**16 (10.8)**	0	0	1 (6.2)	2 (12.5)	13 (81.3)

Table 3-4: Numbers of reported actual and near falls

Association between clinical characteristics and number of *actual* falls

Analysis of the relationships between the number of *actual* falls and demographic and MS disease characteristics is summarised in Table 3-5. The correlation between age and number of falls was very weak (all participants correlation= -0.14 95% CI = -0.30 to 0.02). Amongst fallers, males fell significantly more frequently, than females. Those scoring EDSS >4.5 reported, on average, higher numbers of *actual* falls than people with other (lower or higher) EDSS scores, although the number of falls did not significantly differ between the seven EDSS score groups. Similarly, individuals who used a walking stick or elbow crutch reported more *actual* falls on average, than those who did not use an aid; although this did not reach statistical significance. Amongst fallers using a walking aid, there was no significant differences in the number of falls reported between the types of walking aid used (*p*= 0.09) (Table 3-5).

Characteristic	Total	Non-fallers	Fallers	Recorded falls per person over 3 months (n=148)		Recorded falls per person (fallers only) over 3 months (n= 104)		
	(n= 148)	(n= 44)	(n= 104)	Med	IQR	Med	IQR	p
Age, years, mean (SD)[a]	58 (10.01)	59 (9.65)	57 (10.14)	-	-	-	-	-
Gender, n (%)[b]								
Female	114 (77)	34 (30)	80 (70)	1.5	0 to 6	2	1 to 5	0.02[d]
Male	34 (23)	10 (30)	24 (70)	2.5	0 to 4	4	2 to 16	
EDSS, n (%)[c]								
3.5	26 (17.6)	9 (35)	17 (65)	1	0 to 2	2	1 to 4	0.41[e]
4	19 (12.8)	5 (17)	14 (73)	1	0 to 4	2	1 to 6.5	
4.5	19 (12.8)	8 (42)	11 (58)	2	0 to 5	3	2 to 25	
5	9 (4)	2 (22)	7 (78)	3	0.5 to 8.5	4	2 to 10	
5.5	14 (9.4)	4 (29)	10 (71)	2.5	0 to 7	4	2 to 12	
6	47 (31.7)	14 (30)	33 (70)	2	0 to 4	3	1.5 to 7.5	
6.5	17 (11.5)	5 (29)	12 (71)	2	0 to 5.5	3.5	1 to 10	
MS Classification, n (%)[c]								
Relapsing Remitting	42 (28.4)	12 (29)	30 (71)	1.5	0 to 4	2.5	1 to 4	0.27[e]
Secondary Progressive	66 (44.6)	20 (30)	46 (70)	1	0 to 4	2	1 to 7	
Primary Progressive	37 (25)	11 (30)	26 (70)	2	0 to 6	4	2 to 8	
Other	3 (2.1)	1 (33)	2 (67)	6	3 to 6	6	3 to 6	
Mobility aids, n (%)[c]								
None	38 (25.7)	12 (32)	26 (68)	1	0 to 4	2.5	1 to 5	0.17[e]
Walking Sticks	76 (51.4)	23 (30)	53 (70)	2	0 to 5	4	2 to 9.5	
Elbow Crutch	13 (8.8)	4 (31)	9 (69)	2	0 to 7.5	7	1.5 to 9.5	
Walking Frame	21 (14.2)	5 (24)	16 (76)	2	0.5 to 3	2	1 to 3	

a: Spearman's rho correlation; b: Mann-Whitney U test; c: Kruskal-Wallis test; d: exact p value; e: Monte Carlo based p value

Table 3-5: Association between clinical characteristics and falls rates

Characteristics of falls

Reported circumstances of *actual* falls

Complete data about the circumstances and consequences of falls were available for 555 of the recorded 672 *actual* falls (Table 3-6). Of these 555 falls, the majority occurred during the day (n=404, 72.8%), with most (n=345, 62.2%) happening inside. 55% of falls were linked to the five specific activities described on the questionnaire, with the highest proportions linked to 'personal hygiene' activities (n=91, 16.4%). 'Working outdoor' activities were associated with 14.6% of falls (n=81). The largest proportion of falls (n=230, 41.5%) were associated with 'other' activities. Analysis of the free text details and responses to the telephone follow up (data available for 115 (50%) of 'other' entries), indicates that these falls were associated with general mobility functions such as standing, turning or walking (n=153, 27.7%), stair climbing (n=39, 7%) or transfers (n=38, 6.8%).

Circumstance		**Number of recorded *actual* falls (n=555)**	**% of recorded *actual* falls**
Time of day			
	Morning	207	37.3
	Afternoon	197	35.5
	Evening	111	20.0
	Night	27	4.9
	Missing or unclear	*13*	*2.3*
Location			
	Inside	345	62.2
	Outside	196	35.3
	Missing or unclear	*14*	*2.5*
Reported activities			
	Cleaning indoors	43	7.7
	Working in the kitchen	48	8.7
	Personal hygiene	91	16.4
	Physical/ leisure	43	7.7
	Working outdoors	81	14.6
	Other (based on free text details and telephone follow-up):		
	Standing, turning, walking (not linked to specific activity)	153	27.7
	Transfers	38	6.8
	Climbing stairs	39	7
	Missing or unclear	*19*	*3.4*

Table 3-6: Circumstances of *actual* falls

Perceived causes of falling (Table 3-7)

Almost one third of falls (n=154, 27.8%) were associated with the participants feeling ‘somewhat more’ fatigued than usual at the time of their fall, with a further 13.3% occurring when fatigue was ‘much more’ than usual (n=74). Analysis of self-reported hurrying at the time of falling showed the majority of falls occurred when participants perceived that they were either not hurrying at all, or were hurrying as usual (n=250, 45% and n=153, 27.6% of falls respectively).

In response to the general ‘cause of falling’ question asked during the telephone follow up of falls diary returns, the majority of falls where a specific cause was identified were associated with loss of balance (n=107,19.4% of falls), although tripping, legs giving way and being distracted were each reported as being associated with approximately 10% of falls. There were, however, a large number of non-responses to this question, predominantly as participants tended to identify that they felt the falls were probably due to a combination of several factors, or to external circumstances which they felt were beyond their control (for example being knocked off-balance by other people, or problems with assistive devices).

Perceived cause		**Number of recorded falls (n= 555)**	**% of recorded falls**
Fatigue			
	As usual	207	37.3
	Much more	74	13.3
	Not at all	72	13.0
	Somewhat more	154	27.8
	Missing or unclear	*48*	*8.6*
Hurrying			
	As usual	153	27.6
	Much more	18	3.2
	Not at all	250	45.0
	Somewhat more	78	14.1
	Missing or unclear	*56*	*10.1*
Attribution (based on telephone follow-up)			
	Trip	61	11.0
	Slip	8	1.4
	Vision	2	0.4
	Distracted	46	8.3

Perceived cause		Number of recorded falls (n= 555)	% of recorded falls
	Dizzy/Giddy/Faint	10	1.8
	Balance	107	19.4
	Legs gave way	48	8.7
	Not sure	3	0.5
	Missing, unsure or unclear	*269*	*48.5*

Table 3-7: perceived causes of falls

Consequences of falls

Of the 555 falls with complete data, 62 (11.2%) were associated with reports of injuries. Table 3-8 shows a breakdown of the frequency and type of injury. The majority of reported injuries were bruising, cuts/lacerations or sprains/strains. Six individuals required input from healthcare professionals as a consequence of falling: Three attended a hospital accident and emergency unit (A&E), and three sought input from their General Practitioner (GP). All of those who attended A&E were treated as day cases; two for checks following a head injury and one for treatment of a fractured finger.

Three participants were unable to get up from the floor after falling, despite not having sustained injuries. Of these, one individual reported being on the floor for over an hour before they were able to summon help, meeting the criteria for a 'long lie'[94(p10)].

Type of injury	Number reported	Associated health care required
Head Injuries	3	2 Hospital A&E attendances
Confirmed fracture	1	1 Hospital A&E attendance
Cuts and Lacerations	18	3 GP attendances
Sprains and Strains	13	-
Bruising	20	-
General (non-specific) injuries	7	-

Table 3-8: Consequences of falls

3.4.4 Analysis of falls risk factors

Classification of 'fallers' and 'non-fallers'

Of the 148 participants included in the analysis, 104 (70.3%) recorded at least one fall. Seventy eight participants (52.7% of the total sample) recorded two or more falls, thus meeting the pre-determined criteria to be classified as fallers within the analysis of risk factors (Table 3-9).

Falls Classification	Number of falls	N (n=148)	%
'Non faller'	0-1	70	47.3
'Faller'	2 or more	78	52.7

Table 3-9: Falls classification

3.4.4.1 Analysis of demographics and clinical characteristics as predictors of fall risk

Table 3-10 summarises the demographic and clinical characteristics of the participants categorised according to total sample and falls classification. Analysis of the association between each characteristic and risk of being classified a faller is also included, along with the associated odds ratios and 95% confidence intervals.

Characteristic	All Participants (n= 148)	Non-Fallers (n= 70)	Fallers (n= 78)	*p*-value	Odds Ratio (95% CI) (Fallers: Non-Fallers)
Age (years) mean (sd) [range]	57 (10) [33-84]	59 (10) [34-76]	57 (10) [33-84]	0.343[a]	0.98 (0.95 to 1.01)
Gender, n (%)					
Female	114	57 (50)	57 (50)	0.230[b]	Ref
Male	34	13 (38)	21 (62)		1.61 (0.74 to 3.53)
Self-reported MS Classification, n (%)					
Relapsing Remitting	42	21 (50)	21 (50)	0.192[b]	Ref
Secondary Progressive	66	35 (53)	31 (47)		0.89 (0.41 to 1.92)
Primary Progressive	37	13 (35)	24 (65)		1.85 (0.75 to 4.57)
Benign	2	0	2 (100)		[d]
Malignant	1	1 (100)	0		[d]
Bladder issues, n (%)					
None/Occasional	87	50 (57)	37 (43)	0.003[b]	Ref
Regular/Frequent	61	20 (33)	41 (67)		2.77 (1.40 to 5.48)
Use of any walking aid, n (%)					
No	38	19 (50)	19 (50)	0.710[b]	Ref
Yes	110	51 (46)	59 (54)		1.16 (0.55 to 2.42)
Previous falls (in the past 3 months), n (%)					
0		46	17	<0.001[b]	Ref
1		11	10		2.46 (0.89 to 6.83)
2 or more		13	51		10.62 (4.65 to 24.22)
EDSS, n (%)					
3.5	26	15 (58)	11 (42)	0.58[c]	Ref
4	19	10 (53)	9 (47)		1.23 (0.37 to 4.03)
4.5	16	6 (38)	10 (62)		2.27 (0.63 to 8.15)
5	9	3 (33)	6 (67)		2.73 (0.56 to 13.37)
5.5	14	5 (36)	9 (64)		2.45 (0.64 to 9.39)
6	46	23 (50)	24 (50)		1.42 (0.54 to 3.74)
6.5	17	8 (47)	9 (53)		1.53 (0.45 to 5.25)
Total number of medications, median (IQR)	5 (2 to 7)	4 (2 to 6)	5 (3,7)	0.278[c]	1.01 (0.92 to 1.12)
Self-reported prescribed medications, median (IQR)	3 (1 to 5)	2 (1 to 4)	4 (2,6)	0.029[c]	1.12 (0.99 to 1.26)
Self-reported OTC medications, median (IQR)	1 (0 to2)	1 (0 to2)	0 (0,1)	0.013[c]	0.79 (0.64 to 0.97)

OTC: over the counter; IQR: inter-quartile range; CI: confidence interval; [a] p-value from two-sample t-test, [b] p-value from Fisher's exact test, [c] p-value from Mann-Whitney test; [d] not calculable as 0 value in one group; Ref: reference category

Table 3-10: Demographic and clinical characteristics

Demographics and MS classification

No statistically significant associations were seen for any of the demographic and MS classification data when analysed by falls classification. Similarly, whilst odds ratios were greater than one for many of the characteristics, 95% CI crossed one in all cases. Of interest is the variation in OR for falling seen with EDSS level, which shows a non-linear pattern in the odds of falling, which steadily increases from EDSS 3.5-5.0, and then decreases at each step from 5.5 to 6.5.

There was an increased risk of falls associated with variability in MS status; this was regardless as to whether symptoms were reported as improving, variable or deteriorating. Of note, variable or improving symptoms were associated with higher OR for falling than deteriorating symptoms (OR 2.01, 95% CI 0.72-5.65 and OR 1.75, 95% CI 0.81-3.78 respectively).

MS symptoms

Participants were asked information relating to the severity of their MS related symptoms which were not assessed by any of the objective tests; this included continence issues and past and current visual issues. There was a significant association between falls classification and urinary continence issues, with the odds of being classified as a faller 2.77 times higher in those who reported having regular or frequent urinary continence issues (OR 2.77, 95% CI 1.4-5.48). There were no significant associations for any of the other characteristics, although fallers were more likely to report previous and current problems for every characteristic.

Use of mobility aids

Over 74% of the participants (n=110) reported using a walking aid at some time; the most frequent being a walking stick (n=76 (51.3%)). As expected given the EDSS scores of the participants, few used a scooter or wheelchair indoors, however 27% (n=40) used a scooter or wheelchair outside at least some of the time. Thirty-four percent (n=35) of the participants reported using at least one orthotic, with eight using more than one type of orthotic device. Table 3-11 summarises the types of device used.

Type of orthosis	Number of users (%)
Foot up	13 (8.7)
Ankle foot orthosis	8 (5.4)
Functional electrical stimulation	9 (6)
Hip flexion ankle foot orthosis	2 (1.3)
Other	11 (7.4)

Table 3-11: Orthotics used

Analysis of mobility aid and orthotic use by falls classification showed that fallers were more likely to use a walking aid or orthotic than non-fallers, although the differences were non-significant. The differences were similar for all types of walking aid; however the OR for each type of aid were only slightly above one and all 95% CI crossed one. Patterns of use were different for scooter and wheelchair use, with slightly fewer of the fallers reporting using a scooter or wheelchair either inside or outside. This difference was most apparent with outdoor use, where 21 (30%) of non-fallers but only 19 (24.4%) of fallers reported using a scooter or wheelchair for this purpose. Consequently, the OR associated with use of a scooter or wheelchair were both below one, (0.75 for outdoor use and 0.89 for indoor use) indicating a decreased risk of falls. However, the CI for both values crossed one, and the numbers of participants in the indoor group were extremely small.

Medication

Data were collected on both prescribed and over the counter medications, which included dietary supplements, herbal preparations and homeopathic remedies (Table 3-12). The majority of participants were taking at least one medication; only 14 participants (9.5%) took neither prescribed or over the counter products. The mean number of medications for the whole group was 4.78 (SD 3.5), with a mean of 1.32 (SD 1.82) for over the counter products and 3.45 (SD 2.84) for prescribed medications. Ten participants (12.8%) took more than 10 medications, six of whom were categorised as non-fallers and four as fallers.

When analysed according to falls frequency, there were significant differences between the two groups, with fallers taking more prescribed medications and fewer over the counter products ($p<0.05$)(Table 3-10). The OR for prescribed medication use showed that increased medication use was associated with a small increase in falls risk, with 95% CI just crossing one. The regression coefficient for this variable suggests that for every extra prescribed medication, the odds of falling increased by 0.12. For over the counter medication use, the OR and 95% CI were all less than one with over the counter medication users 0.79 times as likely to fall as non-users (95% CI 0.64-0.97). The regression co-efficient for this factor suggested that the odds of falling decreased by 0.23 per medication.

As the literature associated with falls in older people shows a significant link between risk of falling and use of four or more medications, the groups were categorised according to this cut-off point. The ORs were higher for users of four or more medications, and in particular for those taking four or more prescribed medications (OR 1.19 for one- three medications, 1.90 for four or more, 95% CI 0.46-3.05 and 0.75-4.85 respectively). Conversely, the odds of falling were lower when four or more over the counter products were used compared to lower levels of usage, although 95% CI crossed one for all values.

Total number of medications		**All Participants (n= 148)**	**Non-Fallers (n= 70)**	**Fallers (n= 78)**	***p*-value**	**Odds Ratio (95% CI) (Fallers: Non-Fallers)**
n (%)	0	14 (9)	8 (11.4)	6 (7.7)	0.47^b	ref
	1-3	44 (30)	23 (32.9)	21 (26.9)		1.21 (0.36-4.09)
	4 or more	90 (61)	39 (55.7)	51 (65.4)		1.74 (0.56-5.44)
Prescribed meds						
n (%)	0	25 (17)	14 (20)	11 (14.1)	0.27^b	Ref
	1–3	58 (39)	30 (42.9)	28 (35.9)		1.19 (0.46-3.05)

Total number of medications		All Participants (n= 148)	Non-Fallers (n= 70)	Fallers (n= 78)	*p*-value	Odds Ratio (95% CI) (Fallers: Non-Fallers)
	4 or more	65 (44)	26 (37.1)	39 (50)		1.90 (0.75-4.85)
OTC medications						
n (%)	0	65 (44)	24 (34.3)	41 (52.6)	0.07[b]	Ref
	1–3	65 (44)	35 (50)	30 (28.5)		0.50 (0.25-1.01)
	4 or more	18 (12)	11 (15.7)	7 (9.0)		0.37 (0.12-1.09)

OTC: over the counter; CI: confidence interval; [b] p-value from Fisher's exact test; ref: reference category for regression.

Table 3-12: Sub-group analysis of medication use

A range of different types of medications were reported to be taken; a summary is included in Figure 3-6 summarises the wide range of medications taken. The most frequent prescription medications were related to MS disease and symptom management, including antidepressants, spasticity and continence medication. Twenty-six participants (17.6%) were taking disease modifying medications, whilst 59 participants (39.9%) were taking medication for symptom management (such as neuropathic pain, fatigue and tremor). Of the over the counter medications, the most frequently reported were vitamin D, multi-vitamins, cod liver oil and evening primrose oil.

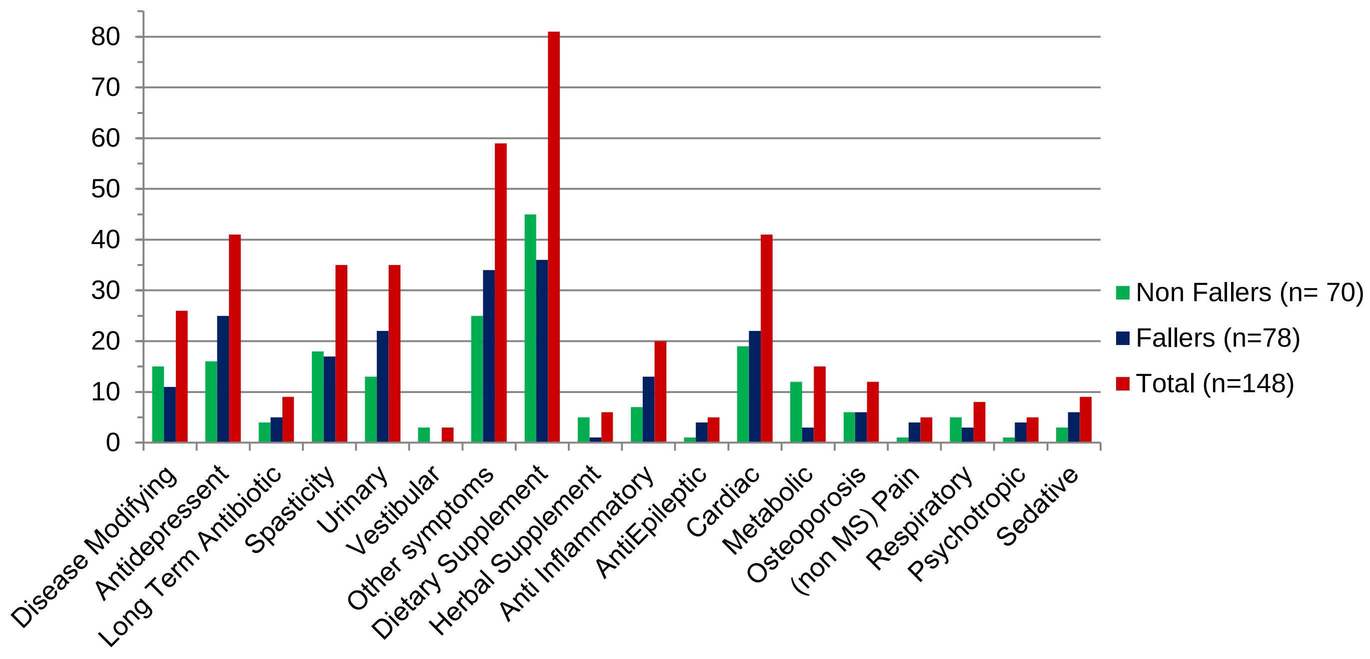


Figure 3-6: Types of medication used

Previous falls history

Participants were asked whether they had fallen in the three months preceding their assessment visit, using the standard definition of a fall as described in the study methods. Falls frequency was assessed by a simple 'did you fall once, or two or more times' question, in an attempt to minimise the variability associated with retrospective recall of falls[201]. Eighty-four (56.8%) participants reported at least one fall in the previous three months; with 64 of these (43.2%) reporting two or more falls. There were significant associations between retrospective falls history and the odds of falling during the prospective diary collection period ($p<0.0001$), with the odds of subsequent falls being 10.62 times greater for those who reported two or more falls in the preceding three months (95% CI 4.65-24.22).

Participants were asked about any injuries associated with their falls in the three months preceding the assessment; 49 (33.1%) reported injurious falls. Four participants (2.7%) reported confirmed fractures, all of whom were classified as fallers from the prospective data collection. Any previous fall-related injury was significantly associated with prospective odds of falling (OR 6.0, 95% CI 2.69-13.4).

3.4.4.2 Analysis of predictor variables

Overall performance and comparison of fallers/non-fallers

Scores for each of the predictor assessments are summarised in Table 3-13. The average scores for the variables previously validated as predictors of falls risk in other (non-MS) groups indicate relatively poor performance in this sample, regardless of falls classification. For example, the whole-sample average FESi score of 39.06 (SD 9.85) is significantly higher than the cut-off value of 23 which is predictive of falls classification in older adults[215]. Similarly, the PPA scores for the whole sample indicate increased falls risk in comparison to age matched non-MS individuals (the group providing the normative data upon which the PPA risk scores are calculated)[145]. For the other predictor variables, the whole-group sample scores reflect significant levels of impairment. The mean SDMT score of 43.56 (SD 13.13) is indicative of significant cognitive impairment in this sample[125]; similarly, there was a large average decrease in dual task performance of 30% (IQR -57 to -12). The whole-group Ashworth scores is broadly comparable to other MS studies of ambulant people[39], whilst the prevalence of abnormal blood pressure responses during the lying-standing task in our sample was relatively low in comparison with other studies (11% within this sample compared with 37% and 16% respectively[157,216]). The DVA scores also indicate poor performance in comparison to other groups; scores in 71 of the 148 participants (48% of the total sample) indicate a vestibular dysfunction as determined by a decrement of more than 10 points on the VAS[193].

Whilst evaluation of the predictor variables by falls classification indicates worse performance by fallers in all eight predictors, statistically significant differences were seen in only two; the PPA and the Ashworth score. These aspects are explored in more depth within the regression analysis.

Missing data

The levels of missing data were extremely low, with all participants managing to complete all elements of each test except the measures of DVA and Dual Task performance. Feedback from participants indicated that the test elements were challenging but reasonable, and no adverse effects were reported. Within the DVA, the most common reason for missing data was the severity of symptoms during the dynamic part of the test: For most participants who were unable to complete the task (n=8) this manifested as dizziness, and oscillopsia. Within the dual task performance assessment, three participants were unable to complete the task; one was unable to complete the 10 metre walk the second time due to fatigue; one participant became highly anxious when undertaking the cognitive task; and one participant was unable to understand the requirements of the cognitive task. As the dual task performance test included a significantly challenging cognitive element (serial seven subtractions), analysis of the correlation between cognitive impairment (using the SDMT score) and the participants' performance in the dual task assessment was undertaken (Spearman's rho). The relationship between these characteristics was negligible and non-significant ($r_s = 0.002$, $p = 0.98$).

Predictor	**All participants (n= 148)**	**Non-Fallers (n= 70)**	**Fallers (n= 78)**	***p*-value**
Ashworth score (median (IQR))	0 (0-1)	0 (0-1)	0.5 (0-2)	-
Ashworth score 0 (n (%))	89 (60)	50 (56)	39 (44)	0.004[c]*
Ashworth score 1 (n (%))	26 (18)	7 (27)	19 (73)	
Ashworth score 2+ (n (%))	33 (22)	13 (40)	20 (60)	
BP drop greater than 20/10 on standing (n (%))	16 (11)	7 (44)	9 (56)	0.80[c]
FESi (mean (SD))	37.06 (9.85)	35.77 (10.08)	38.22 (9.54)	0.13[b]
SDMT number correct (mean (SD))	43.56 (13.13)	45 (12.2)	42 (13.7)	0.10[b]
BARS (median (IQR)	8 (4 to 12)	6 (3 to 11)	8.5 (4 to 13)	0.11[a]
PPA (median (IQR))	2.25 (1.07 to 3.44)	1.68 (0.93 to 2.69)	2.85 (1.31 to 4.44)	<0.0001[a]*
Dual Task % change[i] (median (IQR))	-30 (-57 to -12)	-26.7 (-54 to -12)	-34.4 (-71 to -10)	0.52[a]
DVA change in visual acuity score[ii] (median (IQR))	9.5 (5 to 15.9)	-8.5 (5 to 15.5)	-10 (4.5 to 16.25)	0.88[a]

BARS: Brief Ataxia Rating Scale; BP: Blood Pressure; FESi: Falls Efficacy Score (international); PPA: Physiological Profile Assessment; SDMT: Symbol Digit Modalities Test; DVA: Dynamic Visual Acuity; IQR: interquartile range; SD: standard deviation; [a]:p-value from Mann Whitney U test; [b]:p-value from two-sample t-test; [c]:p-value from Fisher's exact test; *p<0.05; [i]: n=70/75; [ii]: n=67/73

Table 3-13: Analysis of predictor variable scores- fallers: non-fallers

Multiple regression analysis: full model

The initial regression model was developed using forced entry of all eight predictor variables, adjusting for the EDSS (considered as a continuous variable). Results are shown in Table 3-14; within this model only two predictor variables make significant contributions to the performance of the model: Ashworth score and PPA. For the Ashworth score, the odds ratios are non-linear, with a much higher OR of being classified as a faller for those assessed as Ashworth grade one (OR 7.88, 95% CI 2.16-28.80) than those classified as grade two or higher (OR 2.51, 95% CI 0.91-6.95). Increasing PPA score was associated with increased risk of being classified as a faller (OR 1.9, 95% CI 1.34-2.69).

Predictor	B	SE	Wald	df	p-value	Odds Ratio (95% CI) (Fallers: Non-Fallers)
Ashworth score 0 (n (%))	Ref	-	-	-	-	Ref
Ashworth score 1 (n (%))	2.064	0.661	9.74	1	0.002*	7.88 (2.16 to 28.8)
Ashworth score 2+ (n (%))	0.921	0.519	3.15	1	0.076	2.51 (0.91 to 6.95)
BP drop greater than 20/10 on standing (n (%))	0.216	0.619	0.12	1	0.727	1.24 (0.37 to 4.17)
FESi (mean (SD))	0.009	0.024	0.16	1	0.693	1.01 (0.96 to 1.06)
SDMT number correct (mean (SD))	0.005	0.02	0.05	1	0.819	1 .00(0.97 to 1.05)
BARS (median (IQR))	-0.06	0.063	0.82	1	0.364	0.944 (0.83 to 1.07)
PPA (median (IQR))	0.641	0.178	12.99	1	<0.001*	1.9 (1.34 to 2.69)
Dual Task % change[i] (median (IQR))	-0.003	0.003	1.24	1	0.266	1.00 (0.99 to 1.0)
DVA change in visual acuity score[ii] (median (IQR))	0.007	0.025	0.07	1	0.789	1.00 (0.96 to 1.06)
EDSS (median (IQR))	-0.207	0.258	0.65	1	0.421	0.81 (0.49 to 1.35)
Constant	-1.172	1.525	0.59	1	0.442	0.31

EDSS: Expanded Disability Status Scale; BARS: Brief Ataxia Rating Scale; BP: Blood Pressure; FESi: Falls Efficacy Score (international); PPA: Physiological Profile Assessment; SDMT: Symbol Digit Modalities Test; DVA: Dynamic Visual Acuity; IQR: interquartile range; SD: standard deviation; df: degrees of freedom; *p<0.05; B: regression coefficient; SE: Standard Error; df: degrees of freedom; [i]: n=70/75; [ii]: n=67/73;

Table 3-14: Regression analysis; full model

Exploratory component analysis: PPA

Exploratory analysis of the individual aspects of the multi-component PPA risk score demonstrates that the key contributing factors were postural sway and reaction time (all $p<0.006$, after adjustment for EDSS) (Table 3-15). Whilst the *p*-values for these elements indicate statistically significant differences between fallers and non-fallers (as discussed previously), the odds ratios for each individual element are extremely close to one.

PPA Element	Non-Fallers (n=70)	Fallers (n=78)	*p*-value	Univariate regression*					
				B	SE	Wald	df	p-value	Odds ratio (95% CI) (Fallers: Non-Fallers)
Strength (mean (SD))	22.6 (9.05)	23.22 (10.17)	0.972[b]	0.01	0.02	0.15	1	0.70	1.01 (0.97 to 1.04)
Sensation (median(IQR))	2.2 (1.2 to 4.4)	2.8 (1.4 to 5.5)	0.160[a]	0.09	0.06	2.40	1	0.12	1.09 (0.98 to 1.22)
Vision (median (IQR))	21 (20 to 21)	21 (18.75 to 21)	0.069[a]	-0.08	0.05	2.23	1	0.14	0.92 (0.83 to 1.03)
P-A sway-(max excursion, foam, eyes open, mm) (median (IQR))	38 (31 to 51.25)	51 (37 to 80.5)	0.001[a]	0.02	0.01	7.46	1	0.006	1.02 (1.01 to 1.03)
M-L sway (max excursion, foam, eyes open, mm) (median (IQR))	44 (29 to 76)	64 (39 to 105.5)	0.006[a]	0.01	0.004	8.47	1	0.004	1.01 (1.00 to 1.02)
Total sway area, mm (median (IQR))	1584 (922.5 to 4008.25)	2906 (1522.5 to 8142.75)	0.001[a]	0.00	0.00	8.73	1	0.003	1.00 (1.00 to 1.00)
Reaction time, milliseconds (median (IQR))	268 (238 to 301)	286 (257 to 381)	0.029[a]	0.01	0.002	7.74	1	0.005	1.01 (1.00 to 1.01)
PPA Risk Score (median (IQR))	1.68 (0.93 to 2.69)	2.85 (1.31 to 4.44)	<0.001[a]	0.43	0.12	13.82	1	<0.001	1.54 (1.23 to 1.93)

PPA: Physiological Profile Assessment; P-A: antero-posterior; M-L: medio-lateral; *: Adjusting for EDSS; B: regression coefficient; SE: Standard Error; df: degrees of freedom; OR: odds ratio; IQR: interquartile range; [a]:p-value from Mann Whitney U test; [b]: p-value from two-sample t-test

Table 3-15: Univariate regression of the Physiological Profile Assessment individual elements

Development of a reduced regression model

From the initial full logistic regression model, a reduced model was developed retaining only the significant predictor variables (Ashworth scale and PPA summed score) (Table 3-16). The EDSS was retained in the final model in accordance with the initial study protocol.

Predictor		B	S.E.	Wald	df	p-value	Odds ratio (95% CI) (Fallers: Non-Fallers)
	EDSS	0.304	0.196	2.40	1	0.121	0.74 (0.50 to 1.08)
	Ashworth score 0	Ref	-	-	-	-	Ref
	Ashworth score 1	1.252	0.522	5.75	1	0.016	3.50 (1.26 to 9.72)
	Ashworth score 2+	0.815	0.479	2.89	1	0.089	2.26 (0.88 to 5.78)
	PPA	0.494	0.131	14.31	1	<0.001	1.64 (1.27 to 2.12)
	Constant	0.113	0.894	0.02	1	0.899	1.12

EDSS: Expanded Disability Scale; PPA: Physiological Profile Assessment; B: regression coefficient; SE: Standard Error; df: degrees of freedom; OR: odds ratio; CI: confidence interval

Table 3-16: Regression analysis: reduced model

Goodness of fit

An overall indication of goodness of fit of the model was obtained through use of the Hosmer and Lemeshow goodness of fit statistic. For this model, the following results were obtained:

χ^2 5.892 df 8 p= 0.659

The non-significant result indicates that there is no evidence of lack of fit based on this statistic[217].

Model diagnostics

Diagnostics were run on the reduced model to check that the assumptions for logistic regression were satisfied[211]. Tests for linearity of the logit demonstrated that all interactions between predictor variable and Ln predictor variable were non-significant (p>0.05). Collinearity diagnostics demonstrated that the variance inflation factor (VIF) fell below one, and the related tolerance statistic (1/VIF) fell above the recommended threshold of 0.2 for all predictor variables[217] (appendix 7.2.4).

Validity of the model

Model performance was assessed using analysis of the Receiver-operating Characteristics (ROC) curve as a plot of the sensitivity and 1-specificity for all possible cut-off points (Figure 3-7)[208] (details in appendix 07.2.5). The area under the curve c statistic was 0.73 (SE 0.04, 95% CI 0.65-0.81 p<.0001), indicating a fair to good overall predictive ability[218]. Using both least distance ((1-Sn) 2+ (1-Spec) 2) and Youden index methods, the optimal cut-off point was determined to be 0.51 (Youden index 0.39). At this level the model demonstrated a sensitivity of 69% and a specificity of 70%. This is in comparison with the predictive validity of the best performing individual predictor (the PPA), where similar analysis yielded a c statistic of 0.67 (SE 0.04, 95% CI 0.58- 0.76 p<0.0001). For this predictor, the optimal cut-off point was determined to be 0.54 (Youden index 0.19), with a sensitivity of 56% and a specificity of 74%.

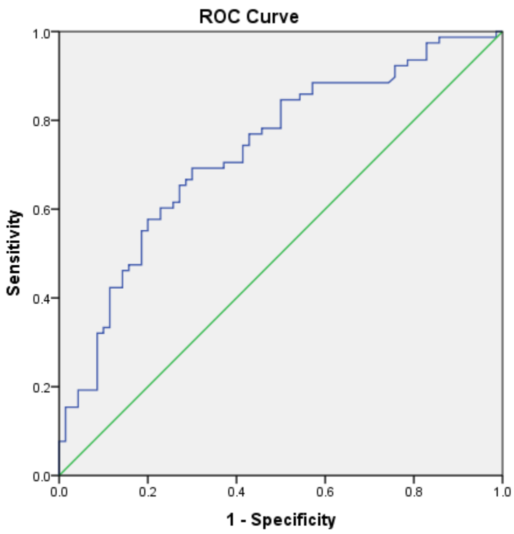


Figure 3-7: ROC curve for reduced regression model

Exploratory analysis: comparison of risk factor measurements according to number of recorded falls.

A study published since the development of the protocol for this study suggested that there may be distinct differences in falls risk characteristics between people with MS classified as non-fallers, single fallers and multiple fallers[118]. In addition, it is possible that there are differences in the characteristics of people who record the most frequent falls in comparison with those who record fewer falls. Therefore, to explore the validity of the *a prioi* decision to classify fallers as those who recorded two or more falls during the diary data collection period, and to explore the possible effect of falls incidence amongst fallers, the scores within each of the predictor variables were analysed according to frequency groupings.

A pragmatic decision was made to categorise the participants into four groups for this analysis: non fallers, single fallers and those recording 2-5, or ≥ 6 falls (Table 3-17). Normally distributed data were analysed using a one way ANOVA; *post hoc* analyses utilised independent t tests where any significant differences were identified. For non-parametric data, Kruskal-Wallis tests were undertaken; *post hoc* analyses used Mann-Whitney u tests. Because of the multiple analyses associated with the *post hoc* tests, a Bonferroni-adjusted significance level of p= 0.008 was used in this part of the evaluation to account for the increased possibility of a type-I error[219].

Predictor	0 falls (n=44)	1 fall (n=26)	2-5 falls (n=49)	≥6 falls (n=29)
Ashworth score (median (IQR))[a,d]	0 (0)	0 (0-2)	1 (0-2)	0 (0-1.5)
BP drop greater than 20/10 on standing (n (%))	5 (11)	2 (8)	3 (6)	6 (20)
FESi (mean (SD))[b]	34.45 (9.0)	37.6 (11.0)	36.2 (8.6)	43.2 (11.6)[c]
SDMT number correct (mean (SD))	44 (12.24)	47.6 (12.34)	41.4 (14.1)	43.9 (14.2)
BARS (median (IQR))	6.5 (4-11)	7 (2-11)	8 (4-12)	11 (5.5-13)
PPA (median (IQR))[a]	1.84 (0.95- 2.78)	1.68 (0.88- 2.53)	2.67 (1.20- 4.19)	2.99 (1.5-4.8)
Dual Task % change[i] (median (IQR))	-29.1 (-56 to -14)	-24.7 (-46 to -9)	-43.6 (-88 to -13)	-26.6 (-55 to -9.2)
DVA change in visual acuity ratio[ii] (median (IQR))	8.5 (5.8 to 16.3)	10.5 (5 to 15.3)	10.2 (1 to 17.5)	9.5 (6.3 to 14.4)
EDSS (median (IQR))	5.5 (3.5 to 6.5)	5 (4 to 6)	5.5 (4 to 6)	5.5 (4.5 to 6)

[i]: n=145; [ii]: n=140; [a:] *p*<0.05 (Kruskal Wallis test) [b:] *p*<0.05 (one way ANOVA); [c:] *p*>0.008 (independent *t* test); [d:] *p*>0.008 (Mann-Whitney U test);

Table 3-17: Analysis of predictor data grouped according to number of reported falls

In agreement with the main analysis, the results of this exploratory evaluation demonstrate statistically significant differences between the groups for the Ashworth score and the PPA risk score. *Post hoc* testing demonstrated these differences to lie between those reporting 0/1 fall and those reporting ≥2 falls, thus supporting the validity of the *a priori* hypothesis relating to falls classification (also illustrated by Figure 3-8 and Figure 3-9). There was no significant difference between non-fallers and those reporting a single fall for any of the predictors (Table 3-17). This exploratory analysis demonstrated that the mean FESi score in the group recording ≥ six falls was significantly higher than the score of those recording fewer falls (p<0.008). This is in contrast to the findings of the main analysis, where no significant differences between fallers and non-fallers were found for this predictor.

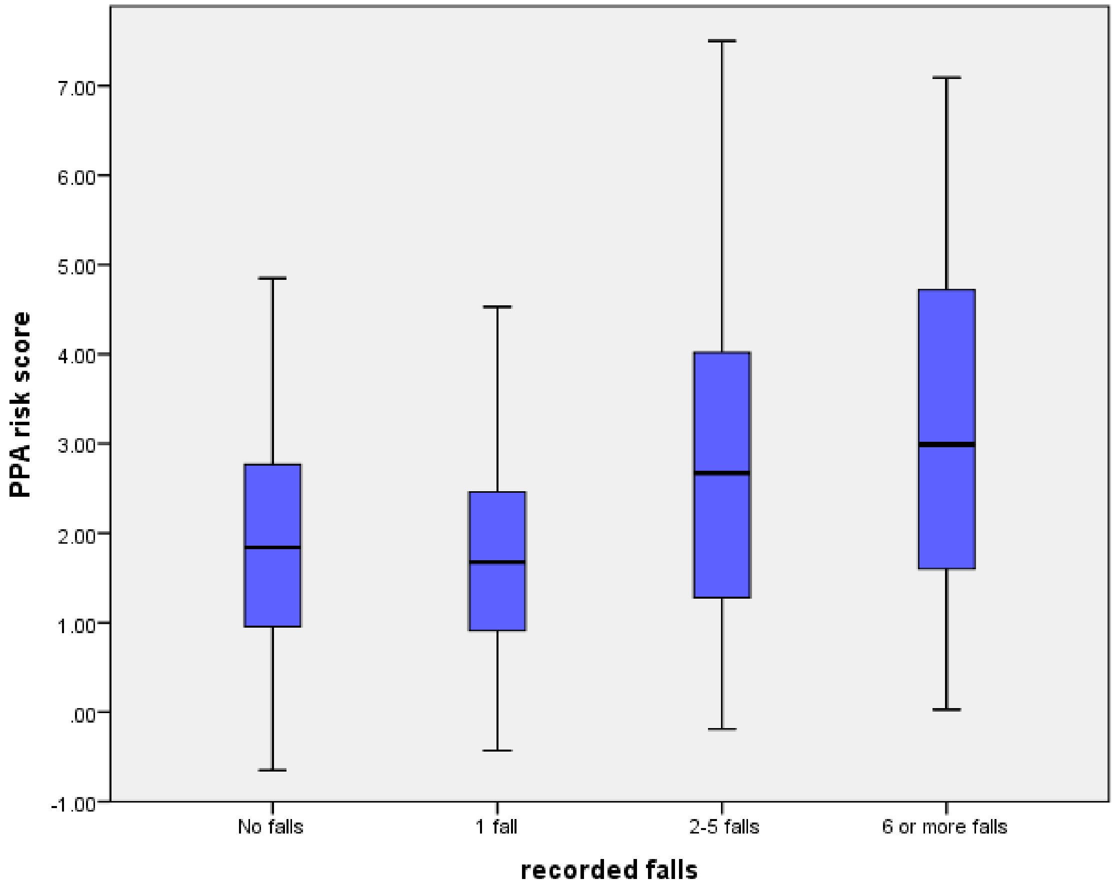


Figure 3-8: Evaluation of PPA risk score by frequency of reported falls

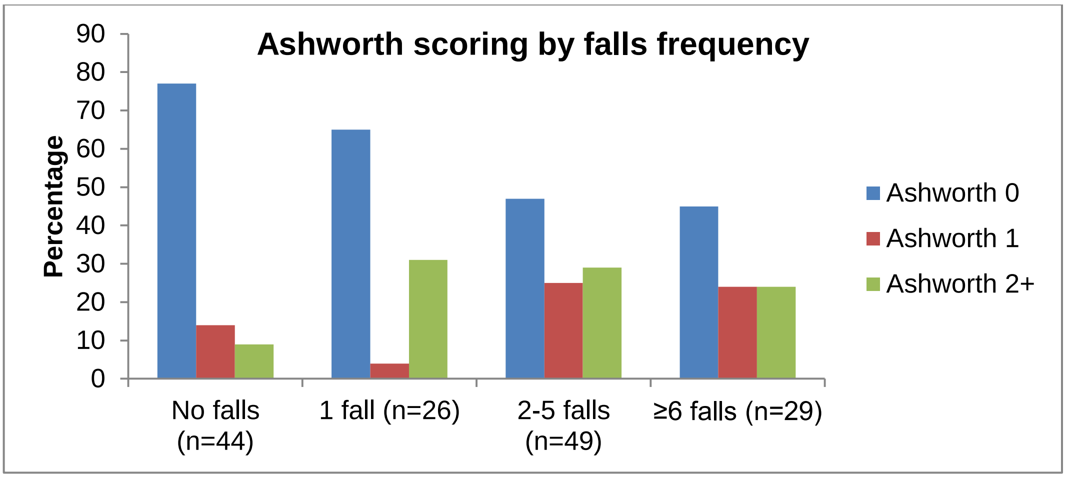


Figure 3-9: Evaluation of Ashworth score by frequency of reported falls

3.5 Discussion

This study evaluated the risk factors associated with falls in MS, utilising robust clinical outcome measures and prospective falls recording methods. A sample of 150 people with a confirmed diagnosis of MS and an EDSS of 3.5-6.5 were recruited, with 148 people returning sufficient falls diary data to be included in the final analysis.

3.5.1 Sample characteristics

The clinical characteristics of this sample were similar to the wider MS population, with a bi-modal peak in EDSS classification at levels 3.5 and 6.5, more women than men, and a higher proportion classifying themselves as having a progressive disease sub-type[30]. The majority of participants had been diagnosed with MS for at least 10 years (17 years (SD +/- 11), which is in line with other similar MS studies[19]. Given the recruitment criteria of EDSS ≥ 3.5, it is relatively unlikely that individuals with a more recent diagnosis would have been eligible to participate.

When compared to the non-respondents to the study invitation, the volunteer participants were, on average, older, and had been diagnosed with MS for longer than non-participants. Although the association between MS classification and participation in the study was not statistically significant, the percentage of individuals recruited to the final sample who were classified as having a progressive MS sub-type within the SWIMS database was much higher than those who chose not to reply to the invitation (>55% versus <35%). As a progressive MS classification has been previously highlighted as a risk factor for falling[220], this difference could reflect a recruitment bias within the study. Whilst all individuals who met the EDSS or mobility inclusion criteria within the SWIMS database were sent an invitation to attend, it may be the case that those individuals who had a specific interest in falls (possibly due to having experienced falls themselves) would be more likely to reply. The main action taken to minimise this potential effect was that all invitation and newsletter reports clearly stated that participation in the project was open to anyone with an appropriate level of mobility, regardless of whether they fell or not. However, due to confidentiality and data protection issues, it was not possible to follow up non-responders to investigate this further.

3.5.2 Characteristics and consequences of falls

Analysis of falls risk, falls rates and injury rates is important to enhance understanding of the impact of falls, as well as aid the development and evaluation of interventions[99,137]. This study demonstrated a prevalence of accidental falls of 70.3%, with 52.7% of the cohort reporting two or more falls in the three month period. This rate is high relative to other studies, where a prevalence of 50-60% for single falls over a similar time period have been reported[3,122]. This may be explained in part by the relatively high disability level of this sample, which includes individuals with EDSS scores ranging between 3.5 and 6.5, and more than 50% of the sample being classified as EDSS ≥5.5. The higher average age of the participants in this study (mean 57 (±10.14)) may also be a factor. In contrast, Kasser[122] recruited individuals with a mean age of 53 (±6) and EDSS ranging from 0-5.5, whilst Nilsagard's sample had a mean age of 50 (range 25-75), and EDSS ranging between 3.0 to 6.0[3]. The relatively large number of individuals with a higher EDSS score in this study could have affected the falls rate.

Variations in definitions of falls and falls reporting measures may also, at least in part, account for this discrepancy. Many previous studies used retrospective falls recall[102,118,121], a method known to be associated with significant under-reporting of falls[201]. Whilst this study was conducted according to best-practice guidelines in order to optimise the validity and reliability of the falls data[108], it is acknowledged that accuracy can also be problematic with prospective falls diaries[221]. Issues highlighted in the literature include the potential for participants to change aspects of their behaviour in response to their awareness of being observed, and variability in accuracy of falls reporting depending on the frequency of diary completion and return[135]. In this study, accuracy was optimised by asking participants to complete diaries on a daily basis, returning each two-week batch of forms as soon as they were completed. Non-returns were followed up within one month of the anticipated return date, and participants who failed to return any prospective falls diaries were excluded from the analysis.

A comparison of numbers of falls according to differing demographic and MS characteristics has not been previously reported. In this study, men reported a higher average number of *actual* falls than women, and the average number of *actual* falls increased with increasing EDSS score. This is particularly the case in individuals classified as EDSS 4.5-5.5, who are beginning to use a walking aid, but are not constantly reliant on it. Whilst no statistically significant differences were seen between the EDSS groups, interpretation is limited by the small numbers of participants at each EDSS level. Further research, using larger data sets of participants from across the EDSS spectrum, is required to clarify these findings. This may help to inform clinical practice with regard to the best time to target falls interventions.

This study provides evidence of the negative consequences following falls, thus underlining the urgent need to develop and evaluate falls interventions in MS[7]. The overall rate of reported injuries requiring medical attention was 0.18 injuries per person per year (PPY). In contrast, previous studies have reported injury rates of 0.23[5] and 0.03[222] PPY. This variation could in part be explained by differing study methodologies. The injury rates reported by Cameron[222] were ascertained through reviews of a centralised database reporting actual contact episodes with health professionals; whereas our study, and that of Peterson[5], used self-reported data, a method which may be associated with over-reporting of injurious falls[135]. The use of prospective recording of falls and a daily diary recording system in this study aimed to minimise any potential inaccuracies. However, it is acknowledged that a lack of corroboration of injurious falls events is a limitation. Several cases falls in this study were associated with a ‘long lie’. In the literature pertaining to older people there is recognition that being unable to get up from the floor for periods of more than one hour (the definition of a ‘long lie’[223]) is associated with a significant increase in morbidity[224]. At present, studies investigating this aspect have not been undertaken in MS, and the younger age of many of the study participants could suggest they were less vulnerable to the consequences of a long lie than older, potentially frailer individuals. However, this issue warrants further investigation. Similarly, whilst this study provides data relating to the physical consequences of falls, other important potential issues, such as the emotional and psychological impact of falling were not evaluated.

In this cohort, a range of activities were associated with falls, suggesting, as previously described, that falls are an 'ever present reality' for this group[116](page 151). The profile of activities associated with falls in this study highlights that many falls events were related to basic activities of daily living, such as personal hygiene (16.4% of falls) and domestic activities such as 'cleaning' (7.7%) and 'working in the kitchen' (8.7%). In contrast, Nilsagard's study[3] found physical or leisure activities were more frequently associated with falling. Participants were not given a specific definition of physical/ leisure activities in either study, therefore it is possible that differing perceptions may have contributed to this variance. However, other factors, such as the geographical location of the studies may also be significant. In qualitative research carried out by Nilsagard (based in Sweden), many participants reported that winter snow and ice were a key issue leading to falls and activity modification[117]; however this factor is likely to be much less of an issue in warmer areas. Research which evaluates these aspects in more depth across a range of locations may add to our understanding.

This study found that a quarter of falls (27.7%) are associated with general mobility tasks such as standing, turning and walking. Whilst the range of activities included in the diary sheets was not comprehensive, it was evident that the falls occurred across a range of circumstances, rather than being restricted to more energetic activities, or activities traditionally associated with perceptions of risk, such as working outdoors or physical or leisure activities. In the analysis of perceived cause of fall, there was variability in the causes that participants ascribed to their falls, although 'loss of balance' was most frequently mentioned. However, participants were often unable to identify any particular cause for why they fell, or attributed the fall to external influences. While the reliability (and hence validity) of this data, which was gathered by telephone follow-up calls, could be questioned, the findings are broadly in agreement with those of Peterson[225], whose study also highlighted the potentially complex interactions of environment, activity and impairments in MS. The data from this study appears to support Peterson's recommendation[225] that an educational element may be an important component of falls interventions in order to maximise falls self-efficacy by raising awareness of the likely causes of falls.

3.5.3 Risk factors for falling

Analysis was undertaken of the relationship between falls classification and the clinical characteristics of the participants, as well as performance in eight predictor measures which incorporated factors previously linked to falls in MS, but where the measures used in previous studies lacked specificity. Also included were those attributes with limited or no evaluation in MS, but which could reasonably be considered as potentially important based on the literature.

This evaluation demonstrated a significant increase in risk of falls with urinary continence issues, previous falls history and prescription medication usage. In contrast, use of over the counter medications (predominantly dietary supplements) was associated with a significant reduction in falls risk; this aspect has not been investigated in previous studies and would merit further evaluation - it is possible that other factors may be contributing to this association.

In contrast to others[3,102,121,226], the results did not show that either use of a walking aid or EDSS score was significantly associated with falls risk. However, a pattern was observed of increasing falls risk with EDSS progression from 3.5 to 5.5; the point on the scale just prior to transition from not using a walking aid to using a walking aid. This finding may reflect the clinical characteristics of the different study samples; compared to other similar research, participants in this study tended to have higher EDSS scores [3,122] and more people were in the progressive phase of the disease[3]. This could suggest that a key time for falls interventions programmes may be when people first start to consider using a walking aid. Equally, this finding could simply be an artefact of the EDSS classification scale, which is acknowledged to have important limitations[27]. For example, by definition, use of a walking aid requires that an individual is scored at ≥ EDSS 6.0, regardless of their walking ability/stability[26]. One possibility is that those scored as EDSS 6.0 were less at risk of falls than those scoring EDSS 4.0 - 5.5 because they actively chose to use a walking aid as a falls avoidance strategy. In this study, walking aid use alone was not predictive of falls risk. However, it is recognised that walking aid use was determined in a rather simplistic manner by self-report of the type of aid (if any) that participants used as their *main* walking aid. The conflicting findings between this study and others, plus the evident complexity of this issue suggest that this could be an area for more in-depth analysis in future studies. For instance, data relating to the type of walking aid (if any) being used at the time of any fall, consistency of use, source of provision of walking aids and whether any training had been undertaken in use of the aid may also improve the understanding of this potentially key aspect.

Despite participants exhibiting generally high levels of concern (mean FESi 37.06 (SD 9.85)), this study did not demonstrate fear of falling to be predictive of falls risk, which contrasts to the findings of others[92,121]. One potential explanation for these differences is the multi-dimensional and complex nature of fear of falling[227], which has raised some uncertainty as to the validity of fear of falling measures[228]. Factors such as age, role and social expectations may all contribute to the perception of, and response to falls, and may also partly account for the differences seen in people with MS compared to other populations[215,229]. Of note, when the data was explored in detail the FESi score of participants who fell frequently was significantly higher than those who did not. It could be theorised that this fear of falling may be an accurate perception of reality, and therefore an adaptive response rather than a predisposing factor for falls in this group. These issues require further exploration as it is likely to be an important consideration in the development of MS falls interventions.

In contrast to other MS studies[102,121], cognitive function was not significantly associated with falls risk in this study. This may be related to the aspects of cognitive function measured: previous studies used global measures of cognitive function such as the mini mental status examination[102] or self-report[121] whereas this study used the SDMT as a specific measure of attention and working memory. However, SDMT has been found to be associated with fall status in one recent paper published by Sosnoff[230]. As participants in Sosnoff's study had generally lower levels of MS severity (as measured by EDSS) and better balance performance (as measured by sway area) than the participants in this study it is possible that cognitive impairment is a more significant risk factor in these earlier stages of mobility impairment than later when other factors may be more important.

Similarly, differing methods in assessing dual task performance, including selection of mobility and cognitive tasks could account for some of the discrepancies between the results in this study and other literature[3,184,231]. The need to investigate the psychometrics and performance of differing dual task paradigms in MS has been identified as a priority[232], and it is possible that the test selection may, at least in part, account for these varying findings.   For example, the only study[3] to measure dual task performance published prior to the completion of this investigation used the timed-up-and-go (cognitive) test, which is a sit-to-stand, walk and turn task. This might be more demanding on balance mechanisms than the straight walk and return task used in this study. Subsequent studies have also used a variety of cognitive tasks, including alternate alphabet tasks[183], word naming tasks[184] or serial three subtractions[231]; with the results suggesting an average decrease in velocity amongst all participants of 11-

15%[183,184]. This contrasts with the median reduction in walking velocity of 30% (IQR -57-12) in this study. There are a number of possible explanations for this discrepancy, including differences in difficulty of the cognitive tasks between the studies, as arguably the cognitive task used in this study (serial seven subtractions) presents a more significant cognitive challenge. Different levels of cognitive function in study samples or different prioritisation of the physical and cognitive elements of the tasks between the groups (which may be related to the instructions given) may also be significant as these aspects are known to affect dual task performance in other groups[233].

This study investigated a range of new attributes that have not previously been objectively evaluated as falls risk factors in MS, namely ataxia, postural hypotension and vestibular dysfunction. This was considered important since all have been associated with falls in other non-MS samples[160,234]. However, this study did not demonstrate evidence that any of these attributes are significantly associated with falls risk in MS, although fallers did perform worse than non-fallers in each aspect.

After adjusting for EDSS, the final model for predicting falls risk included only two of the potential predictor measures, the Ashworth scale and the PPA. Spasticity, as measured by a lower limb total Ashworth score, has been shown to be associated with falls in previous MS studies[3]; however, the association was thought to be linear in nature, with falls risk increasing with each step on the Ashworth scale. In contrast, these findings demonstrate a non-linear relationship, with a score of one being associated with much higher odds of falling than a score of two or more. Whilst the limitations of the Ashworth scale as a measurement instrument are recognised[120], it is reasonable to postulate that the reduced stiffness seen with lower grades of spasticity may result in less stability (and therefore a higher risk of falls) in weaker lower limbs.

Prior to the completion of this study, the PPA had not previously been used in MS studies, although more recently Hoang has published in this area[231]. Exploratory analysis of the individual dimensions of the PPA assessment in this study suggests that changes to postural sway and delayed reaction time were key attributes, whilst sensory changes, strength and vision did not (individually) predict falls classification. The association between increased postural sway, delayed reaction time and falls status is perhaps not surprising given the known link between delayed postural response latency and balance performance as discussed in section 1.3.1. However, whilst the differences in scores between fallers and non-fallers were statistically significant for all measures of sway (M-L, A-P and total sway area) and reaction time, the odds ratios for each element were much lower than the odds ratio associated with the total PPA risk score. This is most likely to reflect the units of measurement used, as the PPA risk score odds ratios are based on a unit change in z score (i.e. standard deviation), whilst the sway measure and reaction time odds ratios represent the magnitude of change in odds associated with a one point change in the absolute unit of measurement (i.e. millimetres (sway) and milliseconds (recation time)) [145].

The PPA risk score alone was able to predict falls with a 'fair' level of accuracy, however, addition of the EDSS and Ashworth scale to the model improved the accuracy to 'good'[218]. The sensitivity and specificity of this final model were higher than for previously reported models in MS studies[3,231,235]; confirmation of this is required in future research as this has the potential to form the basis of work to develop an MS-specific falls risk assessment tool.

3.5.4 Strengths and limitations

Strengths of this study are the standardised measures used, which are clinically applicable. The decision to complete all aspects of data collection in a single, time limited session and to use relatively 'low-tech' outcome measures was made in an attempt to minimise fatigue for participants and to maximise the clinical applicability of the study. It is acknowledged that using these criteria limited the selection of measures which may have influenced the results. For example, the short-form PPA only includes one measure of balance (sway on foam, eyes open). Other studies have included alternative balance measures (e.g. maximal balance range and co-ordinated balance)[231], which could add detail to the specific aspects of balance performance which are affected by people at increased risk of falling. Similarly, measurement of spasticity at only the participant's self-reported worst ankle could have missed problems around other joints. In addition, some possible risk factors were not assessed at all, for example fatigue. Whilst other studies have reported no significant differences between fallers and non-fallers[117,231], the limitations of existing fatigue evaluation tools is a significant constraint to the effective analysis of this impairment[236,237].

Using recommended methods for defining and recording falls are a methodological strength of the study. One potential limitations is the measurement of EDSS using the telephone interview method as compared to the gold standard face-to-face method; although this pragmatic decision was made on the basis that this method has demonstrated excellent agreement with the original face-to-face version (intra-class correlation coefficient: 94.8%)[28]. Other potential limitations include concerns regarding the validity of the Ashworth scale as a measure of spasticity using the Ashworth scale[120] and potential inaccuracies associated with use of self-report diaries for falls data collection[108]. Using participant self-report to collect data on medication use may also have led to some inaccuracies; similarly, detailed information regarding medication dosages and participant adherence was not collected, hence these findings should be interpreted with caution.

3.6 Summary and recommendations

This study confirms the high prevalence of falls in people with MS, and highlights the significance of falls for this population. The results demonstrate that many people with MS experience frequent falls, which are often associated with routine daily activities, rather than the more 'dangerous' situations commonly associated with falls risk in health individuals. This study also adds detail about the physical consequences of falls for people with MS, including injuries requiring medical attention. Within the study, there was a pattern towards people who were classified as fallers being more likely to be male, to have a progressive disease classification, and to have an EDSS score around the threshold of transition to full-time walking aid use. Whilst these predictors were not statistically significant, the patterns provide an indication of those individuals who should be targeted for a falls intervention.

The analysis of falls risk factors highlighted key attributes linked to an increased risk of falls, including continence issues, spasticity, postural sway on an unstable surface and slower reaction time. The study has also demonstrated that other impairments not investigated previously, such as ataxia, vestibular dysfunction and postural hypotension, were not significant predictors of falls risk in this sample. This information is important to ensure that the development of future falls interventions targets key modifiable risk factors.

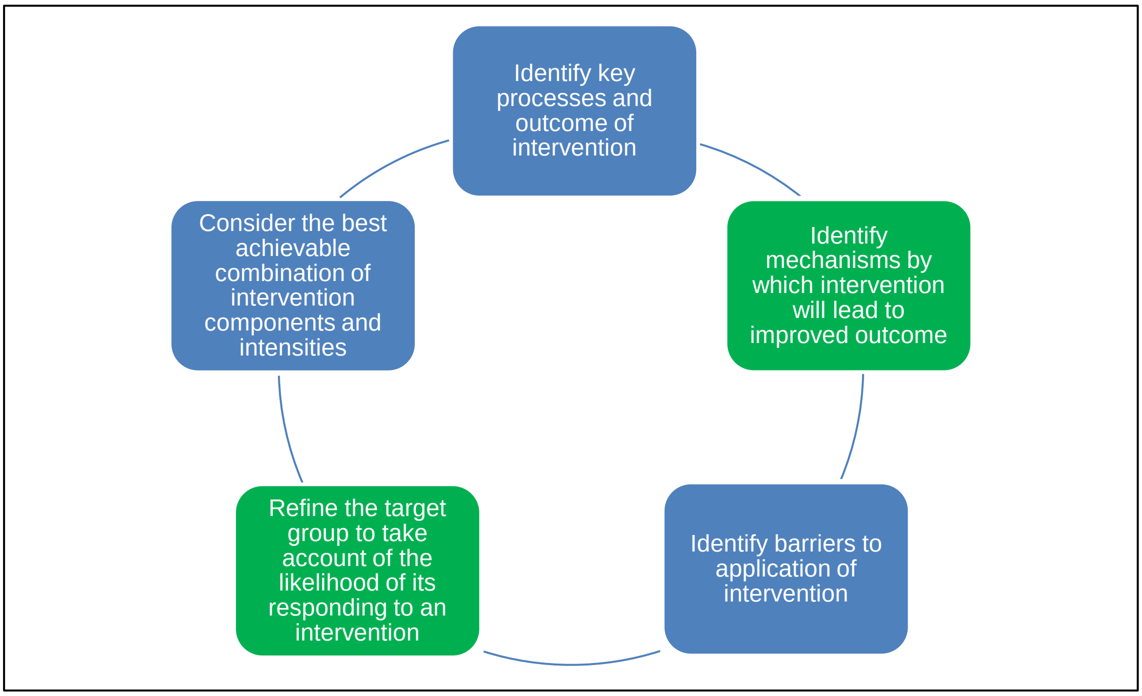
In this study, participants generally demonstrated high levels of concern about falling; however, this was seen throughout the sample and was not predictive of increased falls risk. Many of the recorded falls occurred during every day mobility tasks, suggesting that falls are an ever present reality for many people. These aspects must also be considered in the development of a falls intervention, potentially by the inclusion of educational strategies such as hazard identification and avoidance, activity modification and reduction of falls-related concern.

Part 2: Developing a falls management intervention for people with multiple sclerosis

Introduction

The need to develop an intervention to effectively manage falls in MS has been highlighted by both professionals[7], and people with MS[4,116]. This is supported by the findings of part one of this thesis and other research highlighting the high frequency of falls and incidence of injury, loss of function and resultant impact on quality of life[3,92,231,238]. Whilst several pilot studies have been undertaken[239–241], development of an evidence-based MS falls intervention has been constrained by the relatively limited condition-specific data to adequately inform the content and format of such a programme.

In a supplement to the MRC guidelines for developing and evaluating complex interventions[101], Campbell suggested specific tasks that should be undertaken in the programme design stages in order to optimise an intervention (Figure 1)[242]. Part one of this thesis has identified the potential target group for the intervention (people at key mobility transition stages and those with progressive MS), and potential mechanisms by which the intervention could lead to an improved outcome (the identification of specific risk factors associated with falls in MS). These include non-modifiable disease and demographic characteristics (such as MS classification and gender), and a number of potentially modifiable clinical characteristics (including balance, mobility, continence issues and medication usage). Part two of the thesis aims to address the specific programme content and design issues highlighted within Campbell's framework.



Green boxes: tasks addressed in thesis part 1, Blue boxes: tasks addressed in thesis part two

Figure 1: Tasks contributing to the development of a complex intervention (based on Campbell 2007)

Programme content

Programme content needs to target multiple sclerosis-specific risk factors

Whilst the MS specific evidence base is limited, investigations in other groups suggest that it is possible to develop cost effective interventions which reduce falls risk and rate, as well as improving activity and participation related outcomes[98]. Falls management in older people has been a fruitful area of research, and practice is now informed by a relatively strong evidence base[99]. In repeated large scale studies in this group, falls management programmes delivered in a range of settings and formats have demonstrated positive outcomes[99]. However, research in falls management for people with neurological conditions (e.g. stroke, Parkinson's disease), suggests that applying the evidence base developed in one area (older people) to another population may not lead to similarly positive outcomes[84,243,244]. It is currently unclear why these applied falls programmes appear to be ineffective. Potential explanations may include different mechanisms contributing to falls risk in these neurological conditions, differences in attitudes and responses to falls in different populations, or other as yet unknown factors.

However, these findings do suggest that when developing falls programmes, it is essential to consider the unique risk factors and characteristics of the programme users alongside an evaluation of condition-specific evidence of the effectiveness of intervention strategies.

Which risk factors?

Since completion of the systematic review (May 2012, chapter 2), and the observational study (December 2012, chapter 3), a number of studies evaluating falls risk in MS have been published. Therefore, it is necessary to synthesise the findings of part one of this thesis with this new literature to clarify which risk factor(s) the intervention should aim to address. Table 1 reviews the key findings from these three sources of evidence. This summary suggests that the potentially modifiable risk factors with the strongest evidence base are impaired balance, and mobility issues (including gait performance and use of assistive devices). It can be seen that other significant risk factors have also been identified which include cognitive issues, spasticity, fear of falling/balance confidence, continence and medication use. However, the multi-factorial nature of these risk factors suggests that more research is needed to understand the precise contribution of each to falls risk. For example, the relationship between continence issues and falls could be influenced by mobility status, whilst medication use is likely to be related to disease severity. Similarly, the specific elements of cognitive dysfunction which impact on falls risk are as yet unknown.

Identifying the relative contributions of component parts within a multi-factorial programme, and their contribution to overall effect, is particularly complex[245]. One way of addressing this is to systematically evaluate interventions targeted at specific risk factors in a step-wise manner, rather than targeting multiple risk factors at the outset. Additionally, whilst both single and multiple risk factor falls programmes for older people have demonstrated positive outcomes[99], adherence rates to programmes with a predominantly single focus are generally higher than multifactorial programmes[246]. Hence, although the data demonstrates that balance and mobility issues are both key falls risk factors in MS, after a critical review of the literature, it was decided that this stage of the project would focus on developing an intervention which primarily targeted balance in standing and walking.

The association between balance and mobility impairments in MS is complex (refer to chapter 1 discussion page 20). It is likely that there is a significant inter-relationship between the two aspects. However, studies show that impairments in balance (as quantified by laboratory-based measures) precede clinically observable changes in mobility[38,42]. Evidence also demonstrates that balance is amenable to change in MS[247], although it is currently unclear whether the magnitude change is sufficient to impact on falls. In other populations, balance programmes have been shown to be effective in decreasing falls[99,248,249], in contrast to programmes which target mobility alone (through general mobility interventions and walking programmes), which have tended to be either ineffective or to increase falls risk[99,100].

Risk Factor	Systematic review findings (chapter 2)	Observational study findings (chapter 3)	Papers published since December 2012.
MS and patient characteristics (non- modifiable)			
▪ Progressive MS Classification	OR 1.98 (1.39-2.80)	→	↑[250,251a]
▪ Self-report deteriorating MS	↑[121]	-	↑[252]
▪ EDSS	↑	Non-linear relationship*	Non-linear relationship*[250]
▪ Gender: Male		→	↑[252]
Clinical characteristics (potentially modifiable)			
▪ Impaired balance	OR 1.07 (1.04-1.11)		
Stability during quiet stance	-	↑ PPA sway	↑ PPA sway[231]; posturography[253,254]
Stability during dynamic stance/tasks	-	-	↑ Posturography[253,254]; BBS[255] controlled stability[231]. → BBS[254]
▪ Impaired mobility			
Mobility aid use	OR 2.5 (2.21- 2.83)	→	↑ Number of aids[252];bilateral walking aid use[235]; any aid[251a]
Gait measurements	↑[39,102,117,122]	-	→ 25FWT, 6MWT[230]TUG[255]gait speed[253]; ↑ slower walking speed[251a]; DGI[255]
Dual task performance	→[117]	→	-
▪ Cognitive impairment	OR 1.28 (1.20-1.36)	→	↑ Self-report[252]; executive function[126,231]; processing speed[230] → no difference in 6 of 8 domains of cognitive function[256]
▪ Spasticity	↑[102,117,118]	Non-linear relationship*	-

Risk Factor	Systematic review findings (chapter 2)	Observational study findings (chapter 3)	Papers published since December 2012.
▪ Fear of falling/ balance confidence	↑[121]	→	↑ FESi[179,256]; ABC[255]
▪ Strength	↑[118]	→	→[231]
▪ Continence	↑[117,118,121]	↑	-
▪ Medication use			
Prescribed	-	↑	↑[257]
Over the counter		↑	
▪ Sensory disturbance	↑[122]	→ Proprioception	↑ Cutaneous sensation, → proprioception[235]
▪ Visual issues	-	→	-
▪ Postural hypotension	-	→	-
▪ Ataxia	-	→	-
▪ Vestibular dysfunction	-	→	-
▪ Reaction time		↑	→[231]

[1,2 etc.]: Numbers in superscript indicate study references; *statistically significant difference but non-linear association; ↑ significant difference between fallers and non-fallers; → No significant difference between fallers and non-fallers; OR: odds ratio in meta-analysis (95% confidence interval); [251a]: systematic review of 15 studies

Table 1: Summary of multiple sclerosis falls risk factors identified in part 1 of this thesis and other papers published since December 2012

Programme design issues

The clinical and cost effectiveness of a number of well-described evidence based falls interventions have raised concerns[152], with ongoing debate as to the optimal type, duration and delivery mode[258]. Research suggests that adherence and participant engagement may be key factors affecting the success of falls interventions[259,260]. It has been proposed that adherence issues may be exacerbated by differing attitudes to falls and falls management within different population groups[261–263]. Involving stakeholders integrally in the initial design of rehabilitation programmes can be pivotal to maximising adherence by optimizing the ecological validity of the programme[260,263,264].

Summary, aims and objectives

Based on the issues highlighted above, the following key principles were established to guide the development of a falls programme model, namely that it should:

1. Address MS condition-specific risk factors and issues
2. Use interventions based on best-available evidence
3. Promote high levels of adherence and engagement by involving service users and providers throughout the development process
4. Consider cost-effectiveness to optimise long-term sustainability

The aim of part two of this thesis was to develop a model for an MS specific falls management programme.

This aim was achieved by setting two specific objectives:

1. To recommend the content of an MS specific falls intervention model, informed by a comprehensive literature review of the MS evidence base.
2. To establish the most appropriate delivery methods and formats for the intervention model, through the use of a nominal group methodology.

4 Systematic review two: The effectiveness of interventions to improve balance and reduce falls in adults with multiple sclerosis

4.1 Introduction

This systematic review evaluated; (1) the evidence base for rehabilitation interventions where falls outcomes were measured and (2) evidence based rehabilitation interventions of balance that could be used to reduce falls in MS.

4.1.1 Review objectives:

- To evaluate the existing evidence base for interventions targeting falls in MS
- To develop recommendations for the specific content that should be included in a falls programme targeting balance as a falls risk factor for people with MS
- To evaluate the evidence relating to the optimal method of delivery of programmes targeting balance and/or falls in MS
- To identify the key issues that could affect the clinical and cost effectiveness of the rehabilitation programme, including adherence and participant satisfaction/ engagement.

4.1.2 Study inclusion criteria

The review was protocolised prior to its commencement, as follows:

Participants

This review examined articles evaluating any aspect of falls management and/or any balance intervention in adults with a confirmed diagnosis of MS (as against clinically isolated syndrome).

Interventions

Given the relatively limited evidence-base relating to falls management and balance rehabilitation in MS, this review aimed to be as comprehensive as possible. An evaluation of possible sources of data suggested that both grey literature and published papers were likely to include relevant information, and that a range of types of research paper were likely to be informative. For the falls management interventions, any intervention which identified management of falls in MS as a primary aim was included. For the interventions evaluating balance outcomes, papers were included if the prescribed intervention used any type of rehabilitation approach. Programmes which aimed to increase engagement in general physical activity (such as walking programmes) were not included.

Control/comparator measures

To ensure a comprehensive review, intervention studies were included regardless of whether there was a comparison measure or not.

Outcomes

Primary outcomes

Primary outcomes included falls incidence, measures of balance (as an identified risk factor for falls), and any measure of adherence to the interventions. Falls outcomes included prospective and retrospective self-report of falling and falls self-efficacy. Balance outcomes included direct measures of balance (such as posturography), and surrogate measures (such as Berg balance scale and functional reach).

Secondary outcomes

Secondary outcomes included any evaluation of participant satisfaction or other outcome related to the acceptability and utility of the intervention.

Study designs

Randomised and quasi randomised controlled trials, controlled observational and cross-sectional design methodologies were eligible for inclusion. To ensure a comprehensive review, studies utilising alternative methodologies (e.g. single group studies and primary qualitative research using recognised methods of data collection and analysis) were also considered for inclusion.

4.2 Search strategy

Mixed search methods were used including computer based and manual searches. The electronic databases searched were: Medline, Cochrane database of systematic reviews, AMED, Embase, British Nursing Index, CINAHLplus and PsycINFO. Medical subject heading (MeSH) keywords and operators used were: 'Multiple Sclerosis AND accidental falls' OR 'Multiple Sclerosis AND postural balance' OR 'Multiple Sclerosis AND exercise' OR 'Multiple Sclerosis AND physical/physio therapy' NOT animals [mh]. Related terms 'postural instability', 'balance' and 'falls' were also used in those sources where MeSH terms were not available. In addition, hand searches of reference lists and MS conference abstracts published over the past five years were performed. All literature published from their earliest date to January 2014 were included; only English language sources (or those where a translation was available), where full text details were available from either the original publication or through contact with the corresponding author, were included within the review.

4.3 Review methods:

Data extraction and screening

Abstracts were extracted and screened to remove obviously irrelevant reports. Subsequently, the inclusion and exclusion criteria were applied to the title and abstract of each identified citation. The full text was obtained for all papers that appeared to meet the criteria, and those for which a decision was not possible based on the information contained within the title and abstract alone. The full text of each paper was then assessed for adherence to the review criteria.

Risk of bias (quality) assessment

This review included a range of study types and methodologies and therefore a number of quality assessment tools were employed relevant to the methodologies used. Where insufficient detail was provided in the published paper to adequately assess the risk of bias, authors were contacted and asked to provide additional information.

For studies using designs which compared group outcomes, the Cochrane Risk of Bias tool [265] was used to critically appraise all papers. Studies with single group designs were appraised using the Downs and Black checklist of methodological quality[266,267]. Qualitative studies were evaluated using the Critical Appraisal Skills Programme (CASP) qualitative research appraisal tool[268] (appendices 7.3.1, 7.3.2. and 7.3.3).

All studies were evaluated independently by two reviewers (HG and local clinician S. Markevics), with discrepancies resolved through discussion before a final scoring decision was made. In accordance with the aim to be as comprehensive as possible, cut-off points were not set for methodological quality assessments. However, the findings of the assessment were taken into consideration when considering the inferences that could be drawn from the synthesis of the results.

Piloting

Prior to main screening, a pilot of the screening form, study quality checklist and data extraction form was undertaken to check both the review processes and documentation.

4.3.1 Data synthesis and analysis

Following the eligibility and quality assessment stages, data extraction was undertaken. This included detailed demographic and MS classification data, intervention data and the primary and secondary outcome measure results.

4.3.2 Evaluation of content

Falls interventions

Falls programme documentation was reviewed to establish the aims, content, format and structure of each. Comparisons between programmes was undertaken to establish commonalities and differences, enabling a summary of existing practice and provision.

Interventions with balance outcomes

The interventions in this section of the review exclusively used exercise modalities. As there was a wide variety of exercise types, analysis was undertaken using the sub-groupings defined by the ProFane group and used by Gillespie[99]:

- Strength Training
- Endurance Training
- Gait, balance and functional training
- 3D training (constant repetitive movement through all 3 spatial planes (e.g. Tai chi))
- General exercise programmes

In addition, one extra category was added (Active console games (e.g. Nintendo Wii®)) to reflect a growing area of practice which is used to improve balance and manage falls in other groups[269,270] and where a number of recent papers have been published in MS.

Evaluation of programme content was undertaken within each of the exercise sub-groups where interventions were broadly comparable (detailed below). Owing to the heterogeneity of exercise interventions included in the ‘general exercise’ group, analysis of content in this sub-group is limited to a general description of programmes included.

Strength and endurance training sub-group

Content analysis compared the type and intensity of training. The parameters based on the American College of Sports Medicine (ACSM)[271] guidelines for exercise intensity and duration as used by Sherrington[272] were used as a framework for analysis.

Gait, balance and functional training sub-group

Gait, balance and functional training interventions were defined as those using specific function-based activities to improve balance and stability. In older people, research suggests that the degree of challenge to balance and overall dosage are key factors influencing outcome[99], with the evidence indicating that programmes should achieve a minimum of 50 hours of highly challenging balance training over a six-month period to optimize falls risk reduction[100]. Therefore, within this sub-group, programmes were assessed according to their degree of challenge to balance according to the classification used by Sherrington[272], namely whether the interventions achieved one or more of:

- Movement of the centre of mass
- Narrowing of the base of support
- Minimising upper limb support

In accordance with Sherrington[272], interventions which achieved two out of three of these criteria were classified as 'moderately challenging' and three out of three as 'highly challenging' balance activities.

4.3.3 Evaluation of effect

Data was pooled for statistical meta-analysis using 'Revman 5'[115] for any interventions where comparable data for two or more studies using a controlled experimental methodology could be extracted[114]. For trials with multiple arms, only one pair-wise comparison was included in any analysis to avoid repeated counting of control group participants within the analysis[99]. The pragmatic decision was made to include the arm of each study with the most conservative effect size.

Due to the potentially small numbers of participants, and variability within the studies, random effects analysis was used[273]. For dichotomous outcome measures (e.g. falls classification), Mantel-Haenszel analysis was undertaken, whilst for continuous outcome measures generic inverse variance analysis was selected[115]. When varying units of analysis were used within the studies, the standardised mean difference (Hedges g) was used as the unit of analysis, however, where possible (when similar units of analysis were used), absolute mean differences are also reported to aid evaluation of the *clinical* significance of the pooled effect. Standard deviation of the mean change scores was imputed where this was not reported in the study data by using the Cochrane recommended method

$\sqrt{\frac{(n\text{T-1})SD^2\text{ preT} + (n\text{C-1})SD^2\text{ preC}}{n\text{T}+n\text{C-2}}}$, where T is the intervention group and C is the control group[115], with a conservative estimate of the correlation coefficient of 0.7. Validity of the selected coefficient was checked by running repeated sensitivity analyses using coefficients of 0.6-0.8, which showed minimal variation in the output. Each pooled data set was analysed for heterogeneity using a combination of visual inspection of the graphs along with consideration of the *chi*-squared statistic, setting a *p* value of 0.10[99,115].

Where statistical pooling was not possible or appropriate (e.g. in qualitative papers, single group pre/post study design papers or those outcomes with insufficient numbers of data sets to allow comparison), findings were presented in narrative summary form. For single group studies, simple adjusted Cohen's d effect sizes were calculated using the formula recommended by Beeson and Robey[274]: $d1 = \frac{\overline{\chi}\ A2 - \overline{\chi}\ A1}{S\ A1}$, where A2 and A1 designate post and pre-treatment periods respectively, and *S*A1 is the pre-treatment standard deviation. Interpretation was undertaken with an awareness of the potential inflation of effect sizes in small number single group studies[275,276].

4.3.4 Evaluation of treatment intensity and duration

Calculations of maximum treatment dose for each study were undertaken utilising the frequency and duration data from each study description, with an assumption that participants undertook all available sessions of the intervention. For the purposes of comparison, the optimal dose of 50 hours of intervention over a 26 week period as calculated by Sherrington[272] was used as the 'gold standard'. However, as the maximum duration of all of the included studies was 12 weeks, an adjusted value of 25 hours (1500 minutes) of intervention over the study period was classified as high dose in this context.

In order to explore the possible relationship between treatment dosage and outcome (as measured by effect size), correlation analyses were undertaken using Pearson's correlation, having first established normal distribution of the data by analysis of skewness, kurtosis and inspection of Q-Q plots[217]. An alternative method of undertaking this exploration, were sufficient data available, would be to undertake meta regression[115]. However, given the relatively small number of studies within this aspect of the review, correlation analysis was selected as a pragmatic choice[115]. Data were analysed according to total dose within the study period as undertaken within Sherrington's analysis[272]. However, owing to the range of intervention durations and number of short duration studies, a decision was made to also explore the relationship between treatment intensity in minutes of intervention per week, programme duration in weeks and effect size. Analyses were performed using Cohen's d estimate of effect size as this was available for the majority of studies.

4.3.5 Evaluation of programme format, adherence and engagement.

Assessment of programme format

Data were extracted and presented descriptively for each element of interest. This included programme venue, structure and leadership.

Assessment of adherence and engagement

Analysis of adherence and engagement was undertaken for all programmes where data was available. This included both quantitative and qualitative data. For the quantitative analysis, study attrition rates, session attendance and documented completion of home exercise or practice sessions is presented descriptively. An exploration of the relationship between adherence and key factors including type of activity, programme duration and use of supervision, falls frequency and related circumstances was undertaken using Fisher's exact test[217]. Analysis of the qualitative papers was undertaken using a pragmatic process to explore and develop key themes within the data as described by Braun and Clarke[277].

4.4 Results:

4.4.1 Search results

The search strategy returned a total of 529 results, which after initial screening was reduced to 97 papers with abstracts for review. On completion of the full screening process a total of 31 papers and documents were included in the final review (see Figure 4-1 and Figure 4-4 for details).

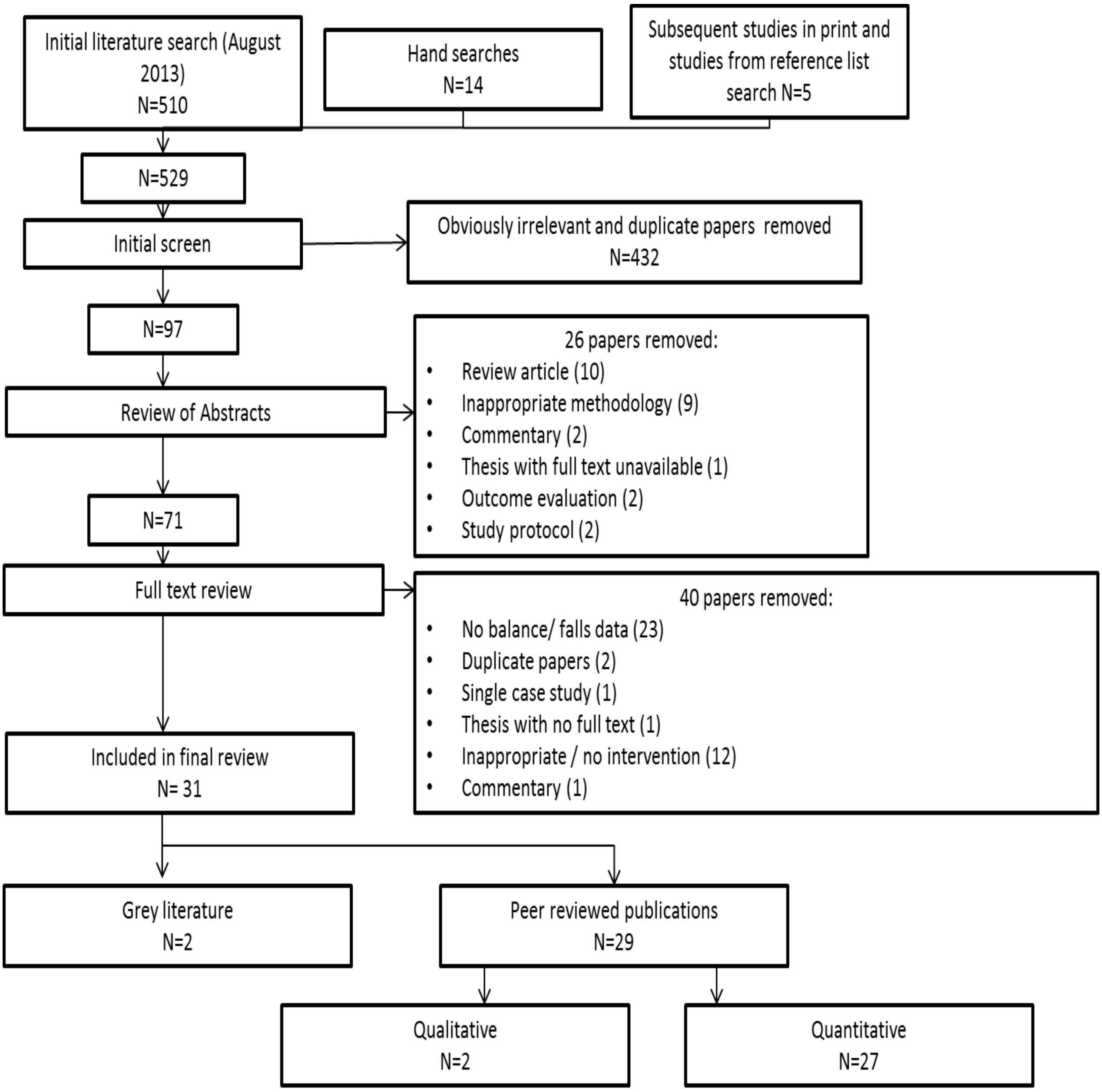


Figure 4-1: Review flowchart part one - summary of included/ excluded papers

4.4.2 Participants

Demographic characteristics

The review included a total of 1036 individuals, with 967 (93%) being included in the final analyses. Overall, 70% (n=596) of the 855 participants with reported demographic data were female. A variety of age reporting methods were used, however, most reported participant mean age. The lowest mean age was 34 (SD 9) years[278], whilst the highest was 60 (SD 6) years[239].

Clinical characteristics

The methods used to classify the types and presentations of MS were highly variable, however most studies reported the EDSS. Amongst the 16 studies using EDSS to classify disease severity, the lowest median EDSS was 3.5 (IQR 1.5-5)[279], whilst the highest was 5.98 (SD 0.43)[280]. The next most frequently used measure was disease duration, with means ranging from 7.7 (SD 4.1)[281] to 16 (range 4-28)[282] years in the seven studies reporting this. In the majority of these studies, it is not clear whether this classification is time since symptom onset or time since formal diagnosis.

Inclusion/exclusion criteria

A range of inclusion and exclusion criteria were reported. All studies included participants who were ambulant, although a range of cut-offs were used (ranging from ability to stand for 30 seconds and walk 6 metres[241] to ability to walk at least 100 metres[283]). The majority of studies excluded participants reporting a current or recent relapse or significant cognitive issues.

4.4.3 Study characteristics

Thirty-one separate data sources of data were included within the review. Of these, two (Coote 2013[235]/ Hogan 2013[284]) report different aspects of data analysis from the same study, therefore these papers were evaluated together. Hence the totals of different study types and data sources are as follows:

- Peer reviewed studies with a quantitative methodology: 26
- Peer reviewed studies with a qualitative methodology: 2
- Grey literature (non-peer reviewed): 2

Table 4-1 summarises the study methodologies included within the review; full details of individual studies are available in appendix 7.3.4.

Methodology	Studies
Two-group quantitative studies	
RCT two arms	Ahmadi 2010[278] Brichetto 2013[285] DeBolt 2004[286] Learmonth 2012[280] Lord 1998[282] Nilsagard 2013[283] Prosperini 2013[287] Sosnoff 2014[239] Stephens 2001[288] Tarakci 2013[289]
RCT multiple arms	Armutlu 2001[290] Broekmans 2011[291] Cakit 2010[281] Cattaneo 2007[241] Coote 2013[235]/ Hogan 2013[284]
Cross over design	Sabapathy 2011[292] Wiles 2001[293]
Single group quantitative studies	
Single group pre/ post-test design	Finlayson 2009[240] Finkelstein 2008[294] Freeman 2004[295] Huisinga 2012[296] Kileff 2005[297] Mills 2000[298] Prosperini 2010[279]
Multiple case studies	Freeman 2010*[299] Kasser 1999[300]
Qualitative studies	
1:1 semi structured interviews	Peterson 2010[116]
Focus group(s)	Learmonth 2013[301]
Grey literature	
Falls programme with evaluation	Frankel 2013[302]
Single group pre/ post-test design	Gutierrez 2005[303]

*Replicated single case studies which were also analysed as a group.

Table 4-1: Summary of study methodologies

4.4.4 Methodological quality

Comparator group studies

Seventeen studies which included comparator groups were included. A summary of the risk of bias analysis is included in Figure 4-2, with a detailed breakdown of the quality assessment for individual studies shown in Figure 4-3. Standards of reporting within the papers was variable, with the most frequently omitted methodological items relating to management of incomplete outcome data and outcome concealment. All but one paper reported all outcomes in their analyses, suggesting a relatively low reporting bias. As found in other reviews of rehabilitation trials, blinding of participants and personnel was variable[304].

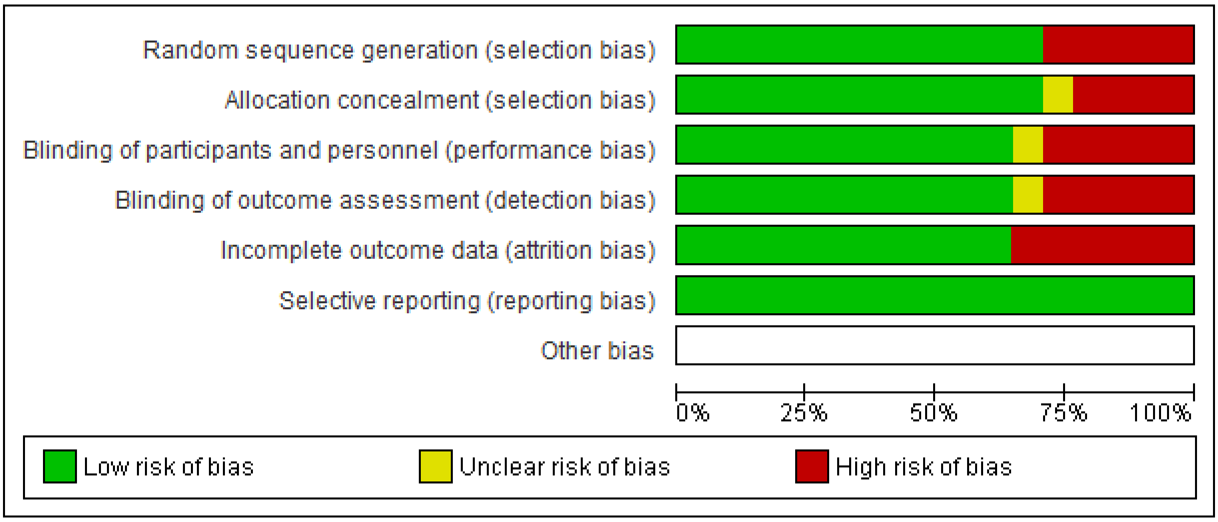


Figure 4-2: Risk of bias assessment- summary

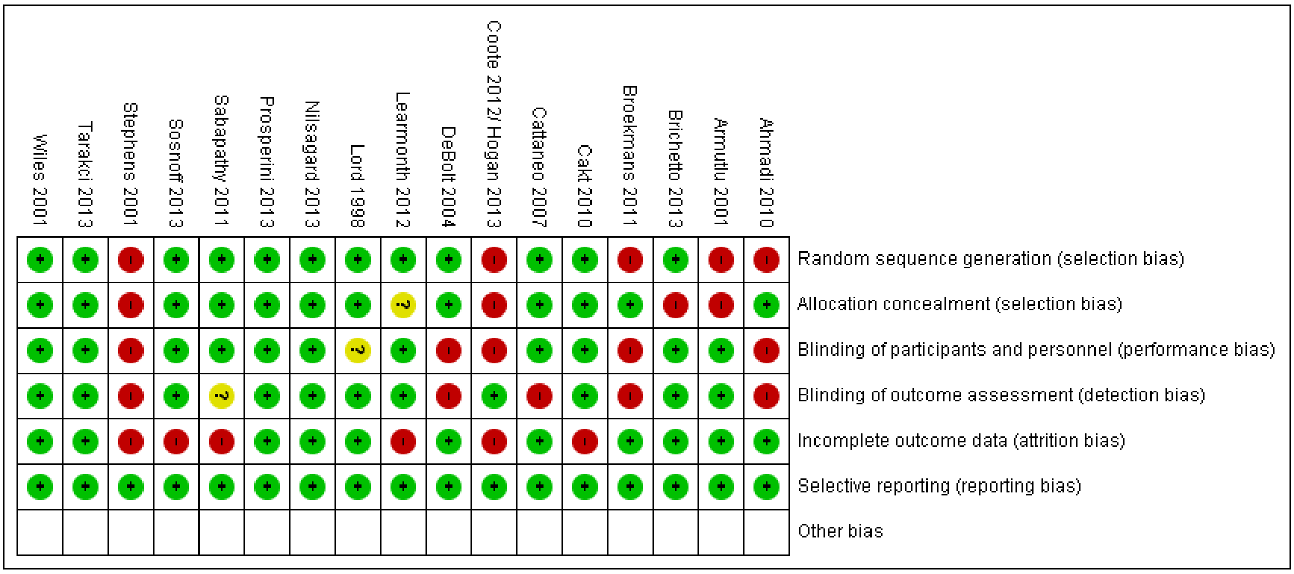


Figure 4-3: Risk of bias assessment- full details

Single group studies

Quality scores for the 10 single-group studies are summarised in Table 4-2. Scores ranged between 9 and 14, with a median score of 12 from a possible 27 points. The majority of studies were well reported; however, as would be expected with this methodology, the main issues were with study power and potential confounding due to lack of control groups. In addition, few studies documented blinding assessors and the majority of samples were drawn from convenience groups, potentially affecting external validity.

Downs and Black Criteria Scores by section (maximum possible scores in brackets):	Finkelstein 2008[294]	Finlayson 2009[240]	Freeman 2010[299]	Freeman 2004[295]	Gutierrez 2005[303]	Huisinga 2012[296]	Kasser 1999[300]	Kileff 2005[297]	Mills 2000[298]	Prosperini 2010[279]
Reporting (10)	8	8	8	8	9	7	7	8	7	9
External validity (3)	1	0	1	1	0	1	0	0	1	0
Internal validity: bias (7)	3	4	2	2	3	2	1	3	3	2
Internal validity: confounding (6)	1	2	1	1	0	1	1	1	1	1
Power (1)	0	0	0	0	0	0	0	0	0	0
TOTAL (27)	13	14	12	12	12	11	9	12	12	12

Table 4-2: Downs and Black quality assessment

Qualitative studies (Table 4-3)

Both qualitative studies scored a maximum 10 points in the quality assessment.

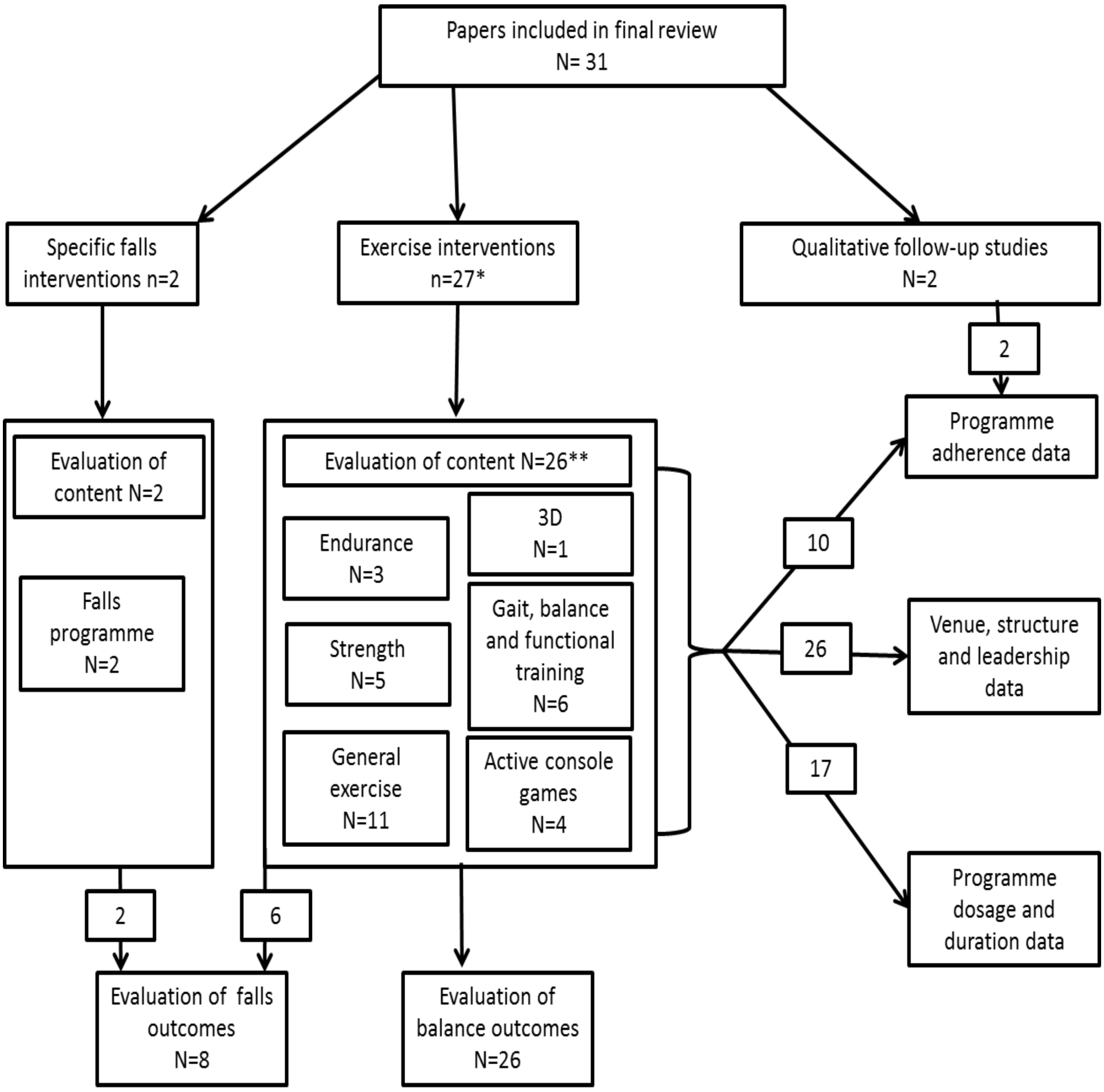
Question	Learmonth 2013[301]	Peterson 2010[116]
Was there a clear statement of the aims of the research?	1	1
Is a qualitative methodology appropriate?	1	1
Was the research design appropriate to address the aims of the research?	1	1

Question	Learmonth 2013[301]	Peterson 2010[116]
Was the recruitment strategy appropriate to the aims of the research?	1	1
Was the data collected in a way that addressed the research issue?	1	1
Has the relationship between researcher and participants been adequately considered?	1	1
Have ethical issues been taken into consideration?	1	1
Was the data analysis sufficiently rigorous?	1	1
Is there a clear statement of findings?	1	1
How valuable is the research?	1	1
Total	**10**	**10**

Table 4-3: Qualitative study quality assessment

4.4.5 Types of intervention

Papers were included that explored falls interventions, balance-focussed exercise interventions and those evaluating participant experiences of the included interventions. Figure 4-4 shows a breakdown of the papers according to intervention type. Of the 31 papers, the majority were evaluations of exercise interventions with balance outcomes, although six also evaluated falls-related outcomes.



*Two papers reported different outcomes for the same study; therefore content analysis only includes 26 studies; **some studies include >1 type of intervention

Figure 4-4: Review flowchart part two- types of intervention

4.4.6 Interventions addressing falls-related outcomes

Characteristics of studies

Eight peer reviewed studies evaluated falls outcomes as either a primary or secondary study aim. These studies included a total of 455 participants; where demographic data were reported 67.5% of the participants were female (n=206/305). The mean age of participants ranged from 47-60 years; all studies recruited across the age range with the exception of Finlayson[240], who initially set a lower age limit for inclusion of 55, but later reduced this to 40 following recruitment issues. A search of the grey literature highlighted one further falls programme with an associated programme evaluation.

The studies included a range of methodologies and interventions; the two specific falls management programmes used education-focussed approaches whilst the six other studies used exercise-based interventions. As all of the exercise-based intervention studies also included balance outcomes, an evaluation of their content has been integrated into section 4.4.7 of this review.

Evaluation of content: Education-based interventions (Table 4-4 and Table 4-5)

Specific falls programmes:

1. Free from falls programme (National MS Society (NMSS) USA)[302,305].
2. Safe at home *BAASE* (behaviour, attitudes, activity, symptoms, environment) programme[240].

The main features of these two programmes are summarised in Table 4-5. Both resources are based on information used in falls programmes for older people, with the addition of MS specific considerations (such as MS specific risk factors and management strategies). Whilst the programme developed by Finlayson[240] reports tailoring the content according to MS specific falls risk factors, the 'Free from falls MS programme' appears to base its risk factor discussion on the whole range of potential MS symptoms.

Aims which are common to both resources include increasing fall awareness, action planning and signposting to useful resources. In addition, the 'Free from falls MS programme' includes a weekly group exercise session plus advice for home exercise practice. The exercise element 'takes an integrated approach to improving function in everyday activities'[305] (page 41) and includes exercises based around six elements:

- Centre of gravity training
- Multisensory training
- Postural strategy training
- Gait pattern enhancement and variation training

- Strength training
- Flexibility and range of motion

Both programmes emphasise the importance of group discussion and problem solving, with take home activities such as evaluating home hazards and developing fall action plans.

Study ID	Inclusion	Exclusion	Age (SD)	Gender	MS Status/ Classification	N	Intervention	Setting
Finlayson 2009[240]	Self- reported diagnosis of MS, at least one fall in the past year, at least occasional use of a mobility device	BTCOA raw score ≥ 9	56.7 (7.4)	5M 25F	MS diagnosed 16 years on average	30	12 hour manualized group educational program- 6 x 2hour sessions delivered by an OT	Group setting
Frankel 2013[302] (unpublished data)	Not reported	Not reported	Not reported	Not reported	Not reported	143	8 week programme including education and exercise awareness sessions.	Group setting

SD: standard deviation; N: number recruited; BTCOA: Blessed Test of Concentration, Orientation and attention; OT: occupational therapist; FES: Falls efficacy scale; BBS: Berg balance scale; ABC: Activities-specific balance confidence scale; M: Male; F: Female

Table 4-4: Characteristics of education interventions reporting falls outcomes

Programme	Country	Aims	Duration	Delivery method	Content	Outcome measures
Intervention packages						
Free from falls MS (based on Free from falls programme developed for older people by OASIS) (Frankel 2013) [302]	USA	Education Action planning Confidence Signposting Exercise	8 weeks	Face to face group sessions x8, 2 hours a week (16 hours total)	Education : 'fall awareness' Lecture, discussion and hand outs Exercise: 'Building better balance' Weekly 50 minute exercise session plus home exercises	ABC, BBS, TUG, 4SST, Confidence regarding falls (locally produced scale)
Safe at home BAASE (Finlayson 2009) [240]	USA	Increase knowledge of risk factors Increase knowledge and skills to manage falls and falls risk Modify current behaviours to reduce personal fall risk.	9 weeks	Face to face group sessions 6 x 2 hour sessions (12 hours total)	Education: Group discussions and activities, lectures and take-home exercises	Falls prevention and management questionnaire, falls prevention strategies survey, FES, number of falls

OASIS Institute, St Louis USA; BAASE: Behaviour, Attitudes, Activity, Symptoms and Environment; ABC: Activities –specific balance confidence scale; BBS: Berg balance scale; TUG: Timed up and go test; 4SST: Four square step test; FES: falls efficacy scale; N/A: not applicable

Table 4-5: Content summary - education-based falls programmes

Evaluation of effectiveness: Education and exercise-focussed programmes

Problems with the accuracy and variability of falls measurement have been widely recognised, leading to a series of recommendations by the European falls network ProFane in 2005[108]. This includes the need for a specific definition of falls, the use of prospective reporting methods using falls diaries and for falls data to be collected for a minimum of three months following the intervention period. The quality of falls recording and reporting in the studies in this review was generally low (Table 4-6); no study met all three of the ProFane recommendations. Only one study followed participants up at the end of the intervention period[240], and a range of reporting methods were used including retrospective recall (n=3), falls diaries (n=2) and the use of proxy measures inferring change in falls risk or falls self-efficacy (n=3).

Education-focussed programmes (Table 4-4)

'Safe at home BAASE' programme

Finlayson[240] included the 23 people who completed at least five of the six education sessions in the main analysis. Key outcomes included significant improvements in self-efficacy and self-management for falls, as determined by a mean improvement of nine points on the Falls Efficacy Scale (FES). Of note, the FES was rescaled from 0-10 to 0-100 for each item 'to increase response variability', and no detail is available as to how the change score equates to the original FES. This makes comparison of these results problematic. Qualitative analysis of interviews from a sub-group of the participants (n=6)[116] suggested that increased self-awareness was an important outcome, for instance being able to understand personal capabilities. This in turn assisted the development of individual falls management strategies.

Although detailed data on falls rates were not evaluated, eight of the 23 participants reported experiencing at least one fall during the programme, with the participants reporting 19 falls in total.

Outcomes were compared between the 23 participants who had attended at least 5/6 programmes, and four who did not complete the programme but had attended ≤ four sessions (classified as 'non-completers' and excluded from the main analysis). The results of this comparison demonstrated no significant difference between the groups. Whilst the authors acknowledge the small sample size, this does raise the question as to whether attendance at all the sessions was essential, since all participants received the educational information (in written format), regardless of whether or not they attended the group.

'Free from falls' programme

An unpublished evaluation of the 'Free from Falls' programme reported outcome data for participants completing the programme (N=143, data supplied by report author[302]). Immediately following the programme, a significant increase in the Activities Specific Balance Confidence (ABC) scale of 12 points was recorded. Significant improvement was also noted in self-reports of falls confidence as measured by a locally developed confidence scale, and participants reported a decrease in self-reported concern of falling and activity curtailment at six months (n=115). However, the method of data collection for this part of the evaluation was not reported.

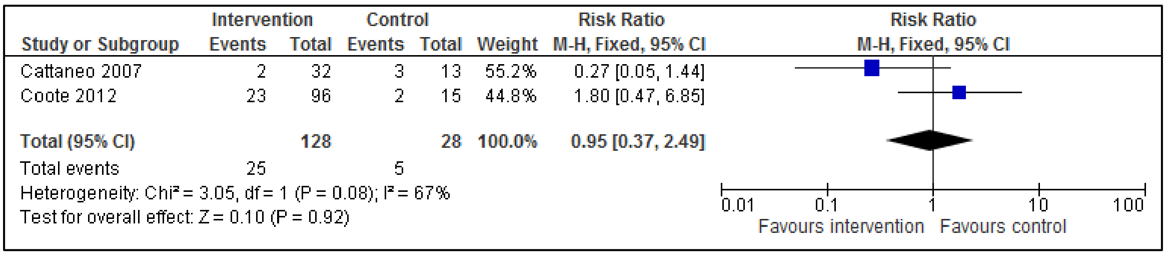
Study ID	Programme duration	Use of falls definition	Measurement of falls: Pre-intervention	Measurement of falls: During the intervention	Measurement of falls: Post-intervention	Falls proxy measures
Education-focussed programmes						
Finlayson 2009[240]	9 weeks	No	No	Self-report- collection method not stated	Retrospective recall at week 12	Falls prevention and management questionnaire, falls prevention strategies survey, FES
Frankel 2013[302]	8 weeks	No	None	None	None	ABC, self-reported confidence regarding falls, concern of falling and activity curtailment.
Exercise-focussed programmes						
Cattaneo 2007[241]	3 weeks	Yes	Retrospective recall- 1 month (1 or more falls)	Report of 1 or more falls during the intervention period	No	-
Coote 2013[235]	12 weeks	Yes	Retrospective recall- 3 months	None	Retrospective recall at week 12	-
Prosperini 2010[279]	6 weeks	No	No	No	No	Length of time and support needed to avoid falling- reported as risk of falls
Sosnoff 2014[239]	12 weeks	Yes	Retrospective recall- 3 months	Prospective self-report diary	No	-
Stephens 2001[288]	10 weeks	No	No	Prospective self-report diary	No	-
Wiles 2001[293]	8 weeks	No	No	No	No	Patient/Carer VAS concern re falls (0-100)

FES: Falls efficacy scale; ABC: Activities-specific balance confidence scale; VAS: Visual analogue scale

Table 4-6: Methods of falls reporting and evaluation

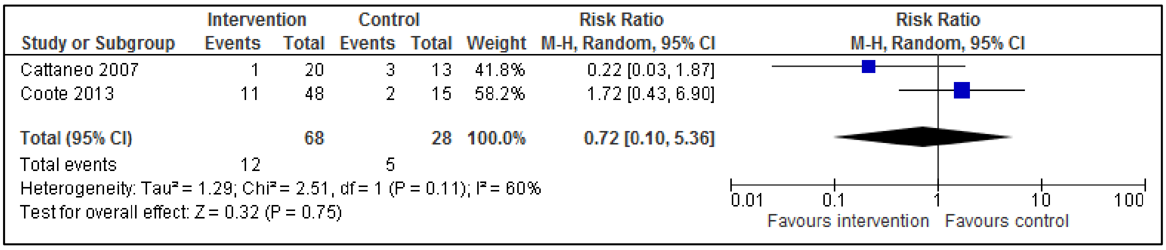
Exercise-focussed programmes (Table 4-7)

The six exercise-focussed studies are summarised in Table 4-7. Of these, falls incidence data allowing calculation of falls risk ratio was available for two[235,241]. Both studies included more than one intervention arm, however, data are presented in a pooled format in the meta-analysis to avoid duplicate entry of control group data[115]. Despite there being a statistically significant difference between the number of participants reporting falls pre and post intervention in both studies, the pooled risk ratio for the data indicates a small decrease in risk ratio with a high degree of variability (RR 0.95, 95% CI 0.37-2.49) (Figure 4-5). When analysing the same data but only including data from study arms where the intervention included activities classified as moderate-high challenge (Cattaneo[241] motor and sensory strategies only, Coote[235], group exercise training only) (Figure 4-6), the risk ratio is slightly more in favour of the intervention groups, however, the smaller sample size has the effect of further increasing the 95% CI (RR 0.72; 95% CI 0.10-5.36). The variety of interventions included in this analysis, wide confidence intervals, limited data, and varying methods of recording falls mean that the results should be interpreted with caution.



M-H: Mantel-Haenszel random effects model; df: degrees of freedom; CI: confidence interval

Figure 4-5: Forest plot of exercise interventions with falls outcomes (including all participants)



M-H: Mantel-Haenszel random effects model; df: degrees of freedom; CI: confidence interval

Figure 4-6: Forest plot of exercise interventions with falls outcomes (Including just participants in the moderate-high challenge study arms)

The other four studies in this section all reported positive outcomes in favour of the intervention, including a reduction in the reported numbers of fallers and lab based proxy measures of 'falls', as well as improvements in other falls-related outcomes such as falls self-efficacy measures.

Two studies reported falls data without sufficient detail to enable calculation of relative risk. Sosnoff[239] reports that fewer of the participants undertaking a home-based exercise programme reported falls during the intervention period compared to a waiting-list control group (50% compared to 94% respectively). However, despite documenting the definition of falls and methods of falls data collection, no falls data was reported. Similarly Stephens[288] reported a 34% decrease in falls from baseline and fewer falls in the intervention group (mean falls per person 3.17 ± 4.49) compared to the control group (4.83 ± 4.54 falls per person) during their 'Awareness Through Movement (ATM)' programme, although group differences were not significant. However, the reporting of falls data was incomplete, and no definition of falls or description of falls recording methods was reported.

The remaining two studies evaluated 'falls related' outcomes, using surrogate measures. Wiles[293] used a 0-100 visual analogue scale of participant and carer concern regarding falling, reporting statistically significant reductions for both following intervention. This study used a randomised crossover design with three conditions; outpatient physiotherapy, home-based physiotherapy and no physiotherapy, with eight-week washout periods between each condition. Prosperini[287] defined 'risk of falls' as the percentage of time participants used hand support whilst standing on a Freeman-like translating board under varying conditions, including eyes open and eyes closed in double and single stance. Following the visuo-proprioceptive training intervention there was a statistically significant decrease in hand support time required in the single leg stance condition for both eyes open and eyes closed conditions ($p<0.001$). Of note, the MS participants generally had a high level of balance performance, only differing significantly from healthy controls at baseline in the single leg stance conditions. This reflects the mild disease severity of the sample (median EDSS 3.5 (range 1.5-5.5)).

Study ID	Inclusion	Exclusion	Age (SD)	Gender	MS Status/ Classification	N	Intervention	Setting
Cattaneo 2007[241]	Ability to stand independently >30 seconds, ability to walk 6 metres	Berg Balance <53, subjects who had already received the prescribed Rx regime	46 (10.2)	13M 31F	Not specified (all sub types eligible)	50	Balance re-education: motor & sensory vs motor vs conventional therapy	Inpatient rehabilitation unit
Coote 2013[235]	Confirmed diagnosis of MS	Current relapse, steroid treatment within 3 months, pregnant at time of referral <18 years of age.	55 (10.75)	40M 70F	Mean time since diagnosis 15.35 years (SD 4)	111	Group physiotherapy vs yoga vs 1:1 physiotherapy	Community/ home setting
Prosperini 2010[279]	MS diagnosis with self-reported falls or fear of falling. Objective balance disturbance walking without aid or rest	Relapse within 2/12, severe visual disturbance, vestibular or otological issues, cardiac disease	40.3 (11.7)	16M 24F	EDSS median 3.5 (range 1.5-5.5)	40	Stabilometry based balance exercise including visual feedback and smooth pursuit	Laboratory
Sosnoff 2014[239]	Confirmed diagnosis of MS, able to walk 25 feet independently, age 50-75, relapse free 30 days, at least 1 fall in the past 12 months	Cognitive issues	60 (6.1)	6M 21F	EDSS median 5 (IQR 2.5)	27	Home exercise programme vs wait list control	Home based
Stephens 2001[288]	MS diagnosis, ability to stand independently without assistive device and walk 100ft with or without assistive device	<18, relapse <1/12, surgery <3/12	54 (10.05)	4M 8F	EDSS mean 4.75 (SD 1.1)	12	Awareness through movement vs educational class	University classroom
Wiles 2001[293]	Definite or probable MS, reported difficulties in walking. Able to walk >5metres with or without aid	No current relapse	47.2 (28-69)	15M 27F	EDSS mean 5.7 (range 4-6.5)	42	Hospital based physiotherapy vs home-based physiotherapy vs no therapy	Home/ physiotherapy department

M: male; F: female; N: number recruited; SD: standard deviation; x/12: time in months; IQR: inter-quartile range; VAS: visual analogue scale; Rx: treatment

Table 4-7: Characteristics of exercise interventions reporting falls outcomes

4.4.7 Interventions addressing balance outcomes

Study characteristics

Table 4-8 summarises the studies included in this section and documents the type of exercise interventions as categorised by Gillespie[99] (detailed in section 4.3.2). Four of the studies included multiple types of exercise intervention in different study arms.

Study ID	N	Strength	Endurance	General Exercise	3D Training	Functional Training	Active Console Games
Ahmadi 2010[278]	21			X			
Armutlu 2001[290]	26			X			
Brichetto 2013[285]	36						X
Broekmans 2011[291]	36	X					
Cakit 2010[281]	45		X	X			
Cattaneo 2007[241]	50			X		X	
DeBolt 2004[286]	37	X				X	
Finkelstein 2008	12			X			
Freeman 2004[295]	10			X			
Freeman 2010[299]	8			X			
Gutierrez 2005[303]	9	X					
Coote 2013[235]/ Hogan 2013[284]	111			X			
Huisinga 2012[296]	15	X					
Kasser 1999[300]	4						X
Kileff 2005[297]	8		X				
Learmonth 2012[280]	32					X	
Lord 1998[282]	23			X			
Mills 2000[298]	8				X		
Nilsagard 2013[283]	84						X
Prosperini 2010[279]	40					X	
Prosperini 2013[287]	36						X
Sabapathy 2011[292]	21	X	X				
Sosnoff 2014[239]	27					X	
Stephens 2001[288]	12			X			
Tarakci 2013[289]	110					X	
Wiles 2001[293]	42			X			
Totals	**863**	**5**	**3**	**11**	**1**	**6**	**4**

N: number recruited;

Table 4-8: Summary of exercise interventions evaluating balance as an outcome

Evaluation of intervention sub-types

1. Strength training

Study ID	Recruitment source	Clinical and demographic characteristics of sample			
		Mean age (SD)	N	Gender split	Clinical characteristics (SD)
Broekmans 2011[291]	Local volunteers	47.8 (10.6)	36	13M 23F	Mean EDSS 4.3 (0.2)
DeBolt 2004[286]	Volunteer participants	50.7 (7.8)	37	8M 29F	Mean EDSS 1-6
Gutierrez* 2005[303]	Convenience sample of local population	43.3 (12.1)	9	2M 7F	Mean EDSS 4.44 (1.67)
Huisinga 2012[296]	University medical centre	43.2 (10.1)	15	2M 13F	Mean EDSS 3.9 (1.5)
Sabapathy 2011[292]	Local volunteers recruited by poster	55 (7)	21	4M 12F	Variety of MS sub-types and severity (not specified)

EDSS: Expanded disability status scale; SD: standard deviation; M: Male; F: Female; *: Non peer-reviewed data (MSc thesis); N: number recruited;

Table 4-9: Clinical and demographic characteristics of participants (strength training interventions)

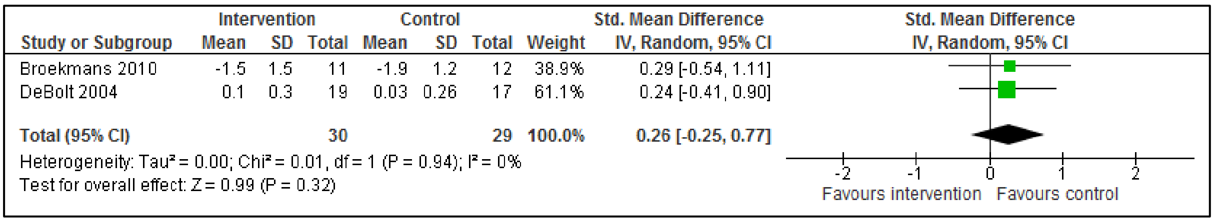
Content

Five studies utilised strength training protocols. These predominantly focussed on training for the lower limb and core, all included exercise to target these areas. In addition, one arm of Broekmnan's[291] study used electrical stimulation to supplement the strengthening intervention.

Using the Sherrington[272] definitions of intensity of strength training (based on ACSM guidelines[271]), none of the studies included an intensity of training which reached the classification threshold for high intensity training, and only two studies[291,303] could be classified as moderate intensity. The workload of the two studies which utilised quantifiable measures of repetition maximum[292,296]both fell below the ACSM recommended workload of 40% 1RM[271]. The remaining study[286] utilised bodyweight strength training, making classification of intensity using these parameters impossible. With the exception of DeBolt[286], all the programmes used seated weight machines, therefore the activities were unlikely to challenge participants' balance directly.

Effect

Of the five studies, only two included a control group. Four of the five showed an improvement in balance parameters following a period of strength training; however only two of the 'strengthening only' interventions showed statistically significant differences in balance measures[292,296]. A range of outcome measures were included, therefore meta-analysis of the two control-group studies is presented using standardised mean difference (SMD) (Figure 4-7). This analysis suggests a pooled SMD of 0.26 (95% CI -0.25-0.77). The effect size (d) of the single group studies was generally small (Table 4-10), possibly reflecting the lack of challenge to balance within the programme content as discussed above.



Std: standardised; IV: inverse variance; df: degrees of freedom; CI: confidence interval

Figure 4-7: Forest plot of strength training interventions

Study ID	Intervention	Measure	Design		Intensity	N	Mean pre	SD pre	Mean post	SD post	Mean change	*p*	effect size (*d*)
Broekmans 2011[291]	Resistance training +/- electrical stimulation compared with control	Functional reach (cm)▪	M	RT	**	11	31.7	1.5	30.2	1.8	-1.5	>0.05	-1.00
				RT(E)		10	29.7	1.9	32.7	1.4	3	<0.05	1.58
DeBolt 2004[286]	Home based functional exercise with weighted belt. Exercise targeted lower limbs and core	Accusway AP sway	M		*	19	0.477	0.253	0.382	0.212	-0.095	>0.05	0.38
Gutierrez 2005[303]	Weight machine based circuit targeting lower limbs and core	Force platform mean AP postural sway(mm), normal stance, eyes open	S		**	9	51	NR	50	NR	-1	>0.05	Not calculable
Huisinga 2012[296]	Weight machine and free weight circuit targeting lower limbs, upper limbs and core	Force platform postural sway root mean square of sway value (mm)	S		*	15	28.32	1.21	24.78	0.88	-3.54	<0.05	2.93
Sabapathy 2011[292]	Weight machine/ body weight/ free weight programme targeting lower limbs, upper limbs and core	Functional reach (cm)	S		*	5	35.8	14.2	41.3	5.2	5.5	<0.01	0.39

ACSM Intensity measures: ***High: training workload achieved >60% 1 repetition maximum (1RM); ** Moderate: training workload achieved 40-60% 1RM; *Low: training workload below moderate threshold; RT: resistance training only group; RT (E): Resistance training plus electrical stimulation; S: single group studies; M: multiple group studies; N: number analysed; SD: standard deviation; AP: anterior-posterior; NR: not reported. ▪results not reported in original paper- supplied by corresponding author on request.

Table 4-10: Summary of studies using strength training

Study ID	Intervention	Measure	Design	Intensity	N	Mean pre	SD pre	Mean post	SD post	Mean change	*p*	effect size (*d*)
Cakit 2010[281]	Cycling progressive resistance programme	Functional Reach (cm)	M	*	14	24.7	6.3	32	4.9	7.3	<0.01	1.16
Kileff 2005[297]	Progressive static cycling programme	Functional Reach (cm)	S	**	8	25.14	4.02	26.71	4.42	1.57	>0.05	0.39
Sabapathy 2011[292]	Endurance circuit: Seated, recumbent and arm cycling, cross trainer and treadmill	Functional Reach (cm)	S	**	11	38.6	5.9	40	5.3	1.4	>0.05	0.24

Intensity measures: ***High: training workload achieved >60% maximum heart rate (MHR) or Borg rate or perceived exertion (RPE) >15; ** Moderate: training workload achieved 40-60% MHR or RPE 11-14; *Low: training workload below moderate threshold; S: single group studies; M: multiple group studies; N: number analysed; SD: standard deviation

Table 4-11: Summary of studies using endurance training

2. **Endurance training**

Study ID	Recruitment source	Clinical and demographic characteristics of sample			
		Mean age (SD/range)	**N**	**Gender split**	**Clinical characteristics (SD)**
Cakit 2010[281]	Not stated	37.9 (10.43)	45	13M 20F	Mean time since diagnosis 7.7 yrs (4.1)
Kileff 2005[297]	Neurology outpatient clinics	45 (33-61)	8	8F	EDSS 4-6
Sabapathy 2011[292]	Local volunteers recruited by poster	55 (7)	21	4M 12F	Variety of MS classifications and severity

EDSS: Expanded disability status scale; SD: standard deviation; M: Male; F: Female; N: number recruited

Table 4-12: Clinical and demographic characteristics of participants (endurance training interventions)

Content

All three studies evaluating endurance programmes utilised gym-based interventions. Two studies[281,297] used static cycling whilst the third used a circuit including activities targeted at increasing endurance. Evaluation of intensity of training using the ACSM informed criteria as used by Sherrington[272] suggests that none of the programmes delivered a high intensity of endurance training. Two used moderate intensities of training. Of note, the only study to show a statistically and clinically significant change was the intervention using the lowest intensity of training[281]. However, the participants in this study were younger than those in the other two studies, which might have impacted on the results.

Effect

Of the three studies using endurance-based interventions, only one included a control group[281], and all had small sample sizes. All demonstrated improvements in mean balance measures following training; however the differences were statistically significant in one study[281], and effect sizes were small for the other two[292,297].

3. 3D training

Study ID		Clinical and demographic characteristics of sample			
	Recruitment source	Mean age (SD)	N	Gender split	Clinical characteristics (SD)
Mills 2000[298]	Not stated	range 42-56	8	3M 5F	All secondary progressive MS

EDSS: Expanded disability status scale; SD: standard deviation; M: Male; F: Female; N: number recruited

Table 4-13: Clinical and demographic characteristics of participants (3D training interventions)

Only one study[298] included an intervention which would be classified under ProFane guidelines[99] as utilising three-dimensional constant repetitive movement training. This study enrolled eight participants onto an eight week programme of tai chi supplemented by a home video to facilitate daily practice for a recommended 30 minutes a day, five days a week. Despite only two of the eight participants reporting an improvement in balance, objective measures showed a significant improvement in single leg balance time (p<0.05). However, a number of methodological issues, including lack of blinding and potential issues with the non-standard balance outcome measures used in the study mean that the findings should be interpreted with caution.

4. General exercise programmes

Study ID		**Clinical and demographic characteristics of sample**			
	Recruitment source	**Mean age (SD)**	**N**	**Gender split**	**Clinical characteristics (SD)**
Ahmadi 2010[278]	Not stated	34 (9.05)	21	21F	Not specified (all sub types eligible)
Armutlu 2001[290]	Outpatients	33.61 (range 23-45)	26	10M 16F	Mean EDSS 4.7 (range 3.5-5.5)
Cakit 2010[281]	Not stated	37.9 (10.43)	45	13M 20F	mean time since diagnosis 7.7 years (4.1)
Cattaneo 2007[241]	Convenience sample of inpatient MS rehab unit	46 (10.2)	50	13M 31F	Not specified (all sub types eligible)
Finkelstein 2008	12 consecutive patients who met the recruitment criteria	52 (4)	12	2M 10F	9 moderate MS, 2 mild, 1 severe (self-report)

Study ID	Recruitment source	Clinical and demographic characteristics of sample			
		Mean age (SD)	N	Gender split	Clinical characteristics (SD)
Freeman 2004[295]	Volunteer participants	50 (11.9)	10	2M 8F	EDSS mean 5 (range 3-6.5)
Freeman 2010[299]	Multiple centres recruited via usual referral routes	32-59	8	6M, 2F	5PP, 3RR
Hogan 2013[284]	Range of referral sources (e.g. self-referral, local clinicians and MS specialists)	55 (10.75)	111	40M 70F	Mean time since diagnosis 15.35 years (4)
Lord 1998[282]	Outpatients	53 (9.5)	23	5M 15F	Mean time since onset 16.15 years (range 4-28)
Stephens 2001[288]	Local MS support groups and physician practices	54 (10.05)	12	4M 8F	Mean EDSS 4.75 (1.1)
Wiles 2001[293]	Outpatients	47.2 (range 28-69)	42	15M 27F	Mean EDSS 5.7 (range 4-6.5)

EDSS: Expanded disability status scale; SD: standard deviation; PP: Primary Progressive MS; SP: Secondary Progressive MS; M: Male; F: Female; N: number recruited

Table 4-14: Clinical and demographic characteristics of participants (general exercise interventions)

Content

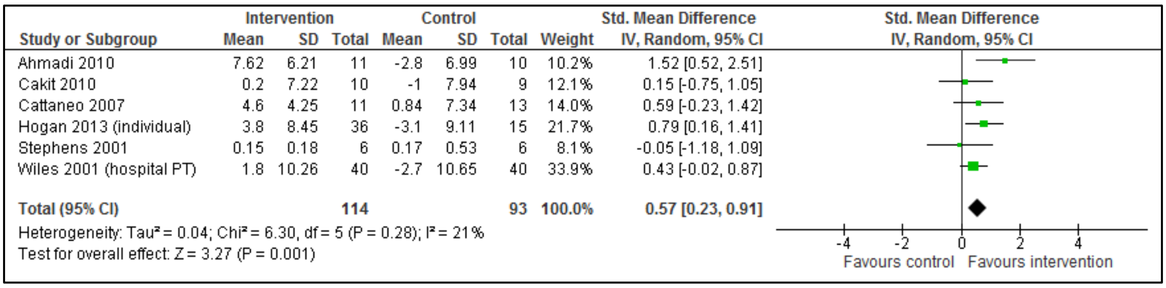
Eleven of the studies in the review utilised generic physical activity (e.g. yoga) or physical therapy interventions (e.g. exercise programmes). One study[284] had two different physical activity arms which are reported separately here, thus a total of 12 different groups were included in the final analysis. Table 4-15 details the interventions used in these studies.

Study ID	Intervention details	Types of general exercise interventions				
		Individual PT/ exercise (home or therapy department)	Group exercise	Awareness through movement	Yoga	Functional training
Ahmadi 2010[278]	Group yoga		x		x	
Armutlu 2001[290]	PNF/pressure splints and balance/ functional exercise	x				x
Cakit 2010[281] (home exercise programme group)	General strength and balance intervention	x				x
Cattaneo 2007 [241] (motor training group)	Balance/stability training on an unstable surface	x				x
Finkelstein 2008	Telerehabilitation based exercise programme	x				x
Freeman 2004[295]	Generalised group balance/mobility exercise group		x			x
Freeman 2010[299]	Core stability training	x				
Hogan 2013[284] (individual physiotherapy group)	Individualised physiotherapy	x				x
Hogan 2013[284] (yoga group)	Group yoga		x		x	
Lord 1998[282]	Individualised physiotherapy (task specific or neurodevelopmental)	x				x
Stephens 2001[288]	Awareness through movement classes		x	x		
Wiles 2001[293]	Home based and outpatient based physiotherapy	x				x

Table 4-15: Types of general exercise interventions

Effect

Meta-analysis was possible for six of the studies, yielding a pooled standardised mean difference of 0.57 (95% CI 0.23-0.91) (Figure 4-8). Within the single-group studies, the calculated effect size (Cohen's d) was somewhat smaller, ranging from 0.39 to 0.59.



Std: standardised; IV: inverse variance; df: degrees of freedom; CI: confidence interval; PT: physiotherapy

Figure 4-8: Forest plot of general exercise interventions

Study ID	Measure	Unit	N	Mean pre (SD)	Mean post (SD)	Change in mean	*P*	ES (d)
Armutlu 2001[290]	Anterior balance	CM	13	13.5 (20.4)	5.1 (0.97)	-8.4	<0.05	0.41
Finkelstein 2008	BBS	-	12	38.8 (11.1)	43.3 (9.9)	4.3	<0.001	0.39
Freeman 2004	BBS	-	10	45.9	49.9	4	0.02	-
Lord 1998[282] (facilitation group)	BBS	-	10	35 (16.4)	43.5 (11.1)	8.5	Not stated	0.52
Lord 1998[282] (NDT group)	BBS	-	10	39.1 (12.3)	46.3 (8.8)	7.2	Not stated	0.59

NDT: neurodevelopmental therapy; BBS: Berg balance scale; CM: centimetres; N: number analysed; SD: standard deviation; ES: effect size (Cohen's d)

Table 4-16: Effect sizes of general exercise interventions (single group studies)

5. Gait, balance and functional training

Study ID	Recruitment source	Clinical and demographic characteristics of sample			
		Mean age (SD)	N	Gender split	Clinical characteristics (SD)
Cattaneo 2007[241]	Convenience sample of inpatients- MS rehabilitation unit	46 (10.2)	50	13M 31F	Not specified (all sub types eligible)
Hogan 2013[284]	Range of referral sources (e.g. self-referral, local clinicians and MS specialists)	55 (10.75)	111	40M 70F	Mean time since diagnosis 15.35 years (4)
Learmonth 2012[280]	MS service register	51 (8)	32	9M 23F	Mean EDSS 5.98 (0.43)
Prosperini 2010[279]	Not stated	40.3 (11.7)	40	16M 24F	Variety of classifications EDSS median 3.5 (range 1.5-5.5)
Sosnoff 2014[239]	MS research database	60 (SD6.1)	27	6M 21F	Median EDSS 5 (IQR2.5)
Tarakci 2013[289]	Referred by local neurologist	40.57 (10.27)	110	35M 64F	Mean EDSS 4.29 (1.40)

EDSS: Expanded disability status scale; SD: standard deviation; M: Male; F: Female; N: number recruited

Table 4-17: Clinical and demographic characteristics of participants (gait, balance and functional training interventions)

Content

Of the six studies included, four provided detailed information of programme content[241,280,284,289], and further detail was available on the Sosnoff's[239] intervention through a related publication[306]. The studies used a range of exercise interventions (refer to Table 4-18). Balance training activities included tasks in lying, sitting and standing, and in some cases there was the addition of an unstable base of support as a progression option. All studies included options for exercise progression based on participant ability and safety. However, it is unclear whether the decision to progress an exercise was made by the participant, session leader or a combination of both. Three studies included strengthening and endurance activities in addition to balance training[239,280,289], possibly reducing the overall emphasis on balance practice within these programmes.

Using Sherrington's classifications of degree of challenge[272], three[241,280,284] could be classified as providing 'highly challenging balance training'. Sosnoff[239] and Tarakci[289] met only two of the three criteria as their intervention data did not include information on the minimisation (or otherwise) of upper limb support. When undertaking this assessment it is recognised that the severity and type of MS symptoms could affect the validity of the Sherrington classification, as arguably, lower levels of challenge to balance could still represent a significant test to people with a greater level of mobility impairment. Nevertheless, two of the three studies which achieved a 'significant' challenge to balance[272] included people with a relatively long duration of MS[284] and higher EDSS levels[280].

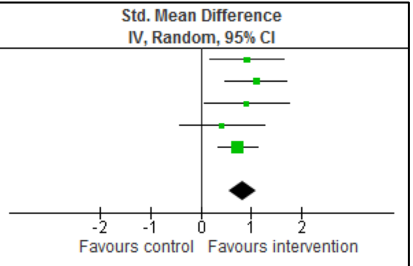
Effect

A total of 284 participants were included in the final analysis of effect. Five of the six studies included a control group, yielding a pooled sample for meta-analysis of 144 intervention and 98 control participants. Meta-analysis shows a pooled standardised mean difference (SMD) of 0.82 (95% CI 0.55-1.10). As all five studies used the Berg balance scale (BBS) as an outcome, calculation of pooled mean difference was also possible, (pooled mean difference 6.69 points on the BBS (95% CI 4.49-8.89)). Whilst Hogan[284] reported the largest effect size of all the studies, there are methodological concerns regarding their use of a patient preference randomised design; patients randomised to their preference may have a standardised effect size greater than those indifferent to group randomisation[307].

Study or Subgroup	Intervention Mean	Intervention SD	Intervention Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI
Cattaneo 2007	6.65	5.23	20	0.84	7.34	13	13.8%	0.92 [0.19, 1.66]
Hogan 2013 (group)	5.7	7.48	48	-3.1	9.11	15	20.0%	1.10 [0.49, 1.72]
Learmonth 2012	5.3	8.75	15	-3.8	10.86	10	10.5%	0.91 [0.07, 1.76]
Sosnoff 2014	1.6	2.95	10	-2.3	11.78	12	10.4%	0.42 [-0.43, 1.27]
Tarakci 2013	4.33	7.47	51	-2.13	9.84	48	45.2%	0.74 [0.33, 1.14]
Total (95% CI)			**144**			**98**	**100.0%**	**0.82 [0.55, 1.10]**

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 1.95$, df = 4 (P = 0.74); $I^2 = 0\%$

Test for overall effect: Z = 5.87 (P < 0.00001)



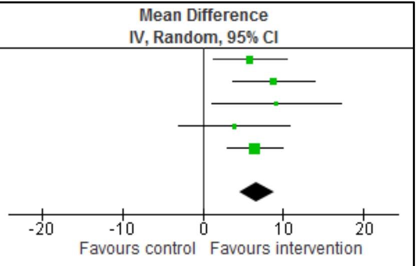
Std: standardised; IV: inverse variance; df: degrees of freedom; CI: confidence interval

Figure 4-9: Forest plot of gait, balance and functional training (standardised mean differences)

Study or Subgroup	Intervention Mean	Intervention SD	Intervention Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
Cattaneo 2007	6.65	5.23	20	0.84	7.34	13	22.9%	5.81 [1.21, 10.41]
Hogan 2013 (group)	5.7	7.48	48	-3.1	9.11	15	18.9%	8.80 [3.73, 13.87]
Learmonth 2012	5.3	8.75	15	-3.8	10.86	10	7.5%	9.10 [1.04, 17.16]
Sosnoff 2014	1.6	2.95	10	-2.3	11.78	12	10.2%	3.90 [-3.01, 10.81]
Tarakci 2013	4.33	7.47	51	-2.13	9.84	48	40.6%	6.46 [3.00, 9.92]
Total (95% CI)			**144**			**98**	**100.0%**	**6.69 [4.49, 8.89]**

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 1.79$, df = 4 (P = 0.77); $I^2 = 0\%$

Test for overall effect: Z = 5.95 (P < 0.00001)



Std: standardised; IV: inverse variance; df: degrees of freedom; CI: confidence interval

Figure 4-10: Forest plot of gait, balance and functional training (absolute mean differences)

Prosperini[279] compared a single group of MS participants to matched healthy controls, measuring balance using stabilometry. Following the training period, significant improvements were reported in the percentage of time using visual, proprioceptive and vestibular balance strategies (*p* all <0.001). However, these differences were only evident in tests undertaken in a monopodalic stance, and no difference was seen in measures of trunk sway before and after the training period. This could be associated with the low initial degree of trunk sway (mean 1.3 degrees, range 0.7-6.2) in the eyes closed condition. As with the 'falls' outcomes in this study (reported in section 4.4.6), this finding may be associated with the sample's low average disability scores (median EDSS 3.5, range 1.5-5.5).

Although it was not possible to undertake a detailed analysis of any associations between effect and degree of challenge provided by the training programme, visual comparison of the results is possible (see Table 4-18). From this table it can be seen that the SMD of all three of the programmes classified as providing a high degree of challenge is greater than those providing a moderate degree of challenge.

Study ID	Participant mobility level (SD)	SMD	Challenge assessment	Programme details												
				Standing balance	Walking	Side stepping	Sit-stand	Step ups	Single leg	Tandem walk/ stance	Calf raise	Stand on unstable base	Squat	Sensory retraining	Dual task	Functional training
Cattaneo 2007[241]	Able to stand >3 seconds, BBS <53	0.91	***	x								x		x	x	x
Hogan 2013[284]	GNDS range 3-4	1.10	***	x		x	x	x		x	x		x			x
Learmonth 2012[280]	Mean EDSS 6.14 (0.36)	0.91	***	x	x	x	x	x	x	x	x	x				
Prosperini 2010[279]	Mean EDSS 3.5 (1.5-5.5)	-	**	x										x		
Sosnoff 2014[239]	Mean EDSS 5. (3.5)	0.42	**	x	x					x			x			
Tarakci 2013[289]	Mean EDSS 4.38 (1.37)	0.74	**	x	x		x	x		x						x
	Challenge assessment (Sherrington 2008): Degree of challenge determined by whether interventions achieved one or more of: (1) Movement of the centre of mass; (2) Narrowing of base of support; (3) Minimizing upper limb support. Interventions achieving 2/3 = moderately challenging, 3/3 = highly challenging.															

SD: standard deviation; BBS: Berg balance scale; GNDS: Guys neurological disability scale; EDSS: Expanded disability status scale; SMD: Standardised Mean Difference

Table 4-18: Summary of programme content and level of challenge within gait, balance and functional training activities

6. Active console game interventions

Study ID	Recruitment source	Clinical and demographic characteristics of sample			
		Mean age (SD)	N	Gender split	Clinical characteristics (SD)
Brichetto 2013[285]	Outpatients of MS centre	42 (10.7)	36	14M 22F	Mean disease duration 11.5 years
Kasser 1999[300]	Volunteer participants	52 (5.2)	4	1M 3F	Range of sub types
Nilsagard 2013[283]	Swedish MS registry	49.7 (11.3)	84	20M 64F	Range of sub types
Prosperini 2013[287]	Volunteers of those regularly attending the hospital MS centre	36.2 (8.7)	36	11M 25F	Mean EDSS 3.25 (1.5-5)

EDSS: Expanded disability status scale; SD: standard deviation; M: Male; F: Female; N: number recruited

Table 4-19: Clinical and demographic characteristics of participants (active console game interventions)

Four studies (involving 160 participants) that used some form of active game intervention were included in the review. Three of these were comparison studies and the fourth was a multiple case series study.

Content

The three comparison group studies all used the Nintendo Wii balance board, and a similar range of games from the standard Wiifit+ package. As detailed in X: games included in the programme

Table 4-20, Nilsagard[283] ranked the games according to degree of difficulty, and Prosperini[287] included a description of task requirement for each of the games used.

Although the game choices were similar for all three studies, there was variation in the methods for game selection and inclusion. In Brichetto's study[285], games were randomly selected and presented to participants at each session. Conversely, in both other studies participants chose the games they played. No study documented the game choices or proportion of time spent playing each game.

Kasser's multiple case series study[300] used a PRO balance master to undertake activities requiring participants to adjust their centre of gravity to achieve movement of a cursor towards an on-screen target. As this system utilises two flush mounted 9x18' force plates, it was possible to alter the stance position, base of support (BoS) size and to include stepping around the BoS within the programme. Support surfaces could also be altered (e.g. by the insertion of a foam block) and sensory inputs manipulated. This is in contrast to the Wii based studies, where the 20 x 13' gaming board which sits above the ground surface precludes the majority of these types of programme modification.

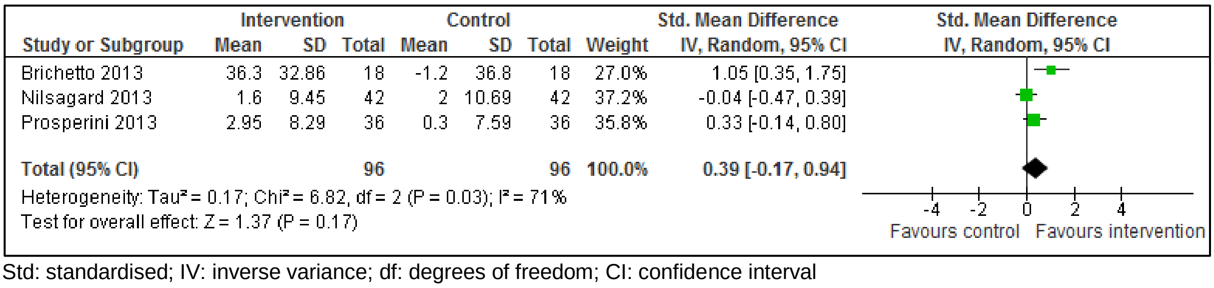
Game	Description of game requirements (from Prosperini 2013)[287]	Study reference		
		Brichetto 2013[285]	Nilsagard 2013[283]	Prosperini 2013[287]
'Easier' Games (Nilsagard) [283]				
Penguin slide	Weight transfer (lateral)		X	X
Ski Slalom	Weight transfer (lateral)	X	X	X ☑
Perfect 10	-		X	
Heading	Weight transfer (lateral)	X	X	X
Table tilt	Weight transfer (multi-directional)	X	X	X ☑
'More challenging' Games (Nilsagard) [283]				
Tightrope tension	Walk in place while maintaining 'balance'	X	X	X
Balance bubble	Weight transfer (multi-directional)		X	X
Snowboard slalom	-	X	X	
Skateboard arena	-		X	
Table tilt +	-		X	
Balance bubble +	-		X	
Other games				
Zazen	Static stance	X		X ☑
Method of game selection/ progression		Random allocation of games in each session	Progressed from easy to challenging games. Choice of game made by the participant.	Choice by the participant of any ☑ game for the first 4 weeks, then any game for the remaining 4 weeks.

X: games included in the programme

Table 4-20: Classification of active console game content

Effect

Meta-analysis was possible for three of the four studies which utilised active console game interventions[283,285,287] (Figure 4-11). As the studies utilised a variety of outcome measures for balance, standardised mean difference was calculated, with a pooled effect size of 0.39 (95% CI -0.17- 0.94).



Std: standardised; IV: inverse variance; df: degrees of freedom; CI: confidence interval

Figure 4-11: Forest plot of active console game interventions

The remaining study[300] utilised a multiple case study design. All four participants in this study showed improvements in dynamic balance as measured by the limits of stability test (range of improvement 10-64%); however, these results should be interpreted with caution due to methodological issues which include a lack of assessment of baseline stability.

4.4.8 Assessment of treatment dosage and duration (exercise intervention studies)

Seventeen studies reported sufficient data to calculate the dosage and duration of interventions. Using the recommended optimal dose of 50 hours of intervention over a six month period[272] as the gold standard and assuming full adherence, only six studies described maximum possible dosages that could achieve this level if they were continued for six months (Table 4-21).

Study ID	Maximum intensity per week (minutes)	Programme duration in weeks	Maximum dose in study period	Effect size (Cohen's d)	Study methodology	Intervention classification
Ahmadi 2010[278]	210	8	1680	0.94	Comparator	GE
Brichetto 2013[285]	180	4	720	1.02	Comparator	AC
Cattaneo 2007[241]	180	3	540	0.86	Comparator	GE/ GBF
Coote 2013[235]/ Hogan 2013[284]	60	10	600	0.6	Comparator	GBF
DeBolt 2004[286]	150	10	1500	0.38	Comparator	R
Freeman 2010[299]	110	8	880	1.21	Single	GE
Kileff 2005[297]	60	12	720	0.39	Single	E
Learmonth 2012[280]	120	12	1440	0.45	Comparator	GBF
Lord 1998[282]	170[b]	5-7[a]	1020[a]	0.52	Comparator	GE
Mills 2000[298]	210	8	1680	1.58	Single	3D
Nilsagard 2013[283]	30	12	360	-0.13	Comparator	AC
Prosperini 2013[287]	150	12	1800	0.27	Comparator	AC
Sabapathy 2011[292]	120	8	960	0.24	Comparator	E/S
Sosnoff 2014[239]	180	12	2160	0.39	Comparator	GBF
Stephens 2001[288]	190	10	1900	0.68	Comparator	GE
Tarakci2013[289]	180	12	2160	0.44	Comparator	GBF
Wiles 2001[293]	90	8	720	0.14	Comparator	GE

3D: 3D training; AC: active console games; GE: general exercise; GBF: gait, balance and functional training; E: endurance; S: strength; a: stated programme duration was 5=7 weeks, for analysis a mid-point of 6 weeks duration was assumed; b: mean dosage for both groups; yellow boxes indicate interventions likely to achieve the recommended dose if they were continued for 6 months with full adherence

Table 4-21: Evaluation of treatment dosage and duration

Analysis of the relationship between programme intensity (minutes /week) and effect size (Cohen's d), demonstrated a moderate positive correlation (*r*= 0.58, *p*= 0.02). In contrast, there was a moderate negative correlation between programme duration in weeks and effect size (*r*= -0.49, *p*= 0.05). There was a weak, non-significant correlation (*r*= 0.17, *p*= 0.51) between total dose over the study period and effect size.

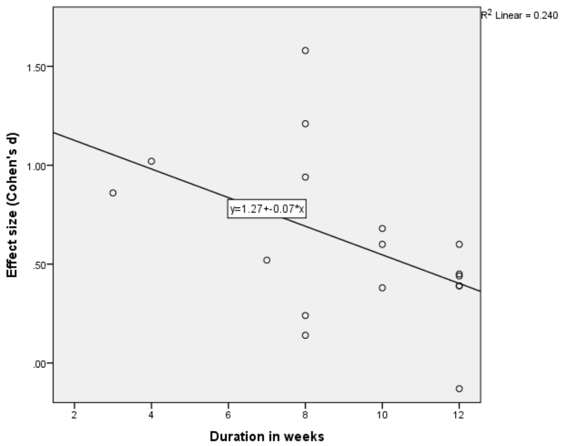


Figure 4-12: Correlation analysis: programme duration and effect size

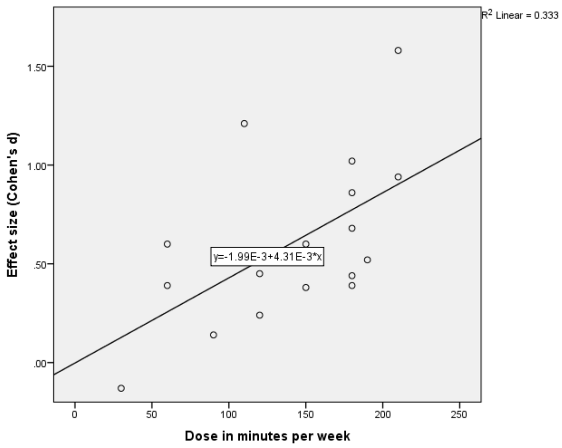


Figure 4-13: Correlation analysis: dose (minutes per week) and effect size

To explore the potential confounding when including single-group studies with potentially inflated effect sizes, a separate analysis was undertaken using only the data from comparator studies. In this analysis, the correlation between intensity (minutes per week) and effect size was *r*= 0.70 (*p*= 0.005) and duration was *r*= -0.56 (*p*= 0.04). The relationship between total study dose and effect size remained weak and non-significant (*r*= 0.15, *p*= 0.61).

4.4.9 Assessment of programme venue, structure and leadership

Publications were analysed for details of the programme venue, structure and leadership; data was available from 27 studies. Data extracted for each of the three categories was grouped to aid clarity of reporting (e.g. individual and group structures, general types of venue). Details are included in Table 4-22

Study ID	Intervention	Venue	Session Leader	Structure (group number)
Ahmadi 2010[278]	GE	Not stated	Yoga teacher familiar with MS	Group-combined (not stated)
Armutlu 2001[290]	GE	Physio department	Physiotherapist	Individual-supervised
Brichetto 2013[285]	BF	Rehabilitation unit	Not stated	Individual-supervised
Cakit 2010[281]	E	Not stated	Rehabilitation physician	Group-combined (small group)
Cattaneo 2007[241]	GE/GBF	In-patient rehabilitation unit	Physiotherapist	Individual-supervised
Coote 2013[235]/ Hogan 2013[284]	GBF	Not stated	Physiotherapist	Group-circuit (not stated)
DeBolt 2004[286]	R	Community sessions then home based	Not stated	Individual–independent
Finkelstein 2008[294]	GE	Home based	Physiotherapist	Individual-independent
Finlayson 2009[240]	Education	Not stated	Occupational Therapist	Group-combined (2-7)
Frankel 2013[302] (unpublished)	Education/GE	Not stated	Not stated	Group-combined (not stated)
Freeman 2010[299]	GE	Physiotherapy department plus home based	Physiotherapist	Individual-supervised
Freeman 2004[295]	GE	Local hospital physiotherapy department	Physiotherapist and assistant	Group-combined (10)
Gutierrez 2005[303] (unpublished)	R	Gymnasium	Trained fitness staff	Individual-supervised
Huisinga 2012[296]	R	Gymnasium	Certified trainers	Individual-supervised

Study ID	Intervention	Venue	Session Leader	Structure (group number)
Kasser 1999[300]	BF	Laboratory	Investigator	Individual (supervised)
Kileff 2005[297]	E	Physiotherapy department	Physiotherapist	Individual (supervised)
Learmonth 2012[280]	GBF	Community leisure centres	Physiotherapist and fitness instructor	Group- circuit (not stated)
Lord 1998[282]	GE	Not stated	Physiotherapist	Individual-supervised
Mills 2000[298]	3D	Home/centre	Tai chi instructor	Not stated
Nilsagard 2013[283]	BF	Physiotherapy outpatient department	Physiotherapist	Individual-supervised
Prosperini 2010[279]	GBF	Laboratory	Investigator	Individual-supervised
Prosperini 2013[287]	3D	Home based	Not stated	Individual-independent
Sabapathy 2011[292]	E/R	Community healthcare settings	Two exercise physiologists	Individual-supervised
Sosnoff 2014[239]	GBF	Home based with 3 follow ups	Certified exercise leader	Individual-independent
Stephens 2001[288]	GE	University	Feldenkrais practitioner	Group-combined (6)
Tarakci 2013[289]	GBF	Hospital rehabilitation unit	Physiotherapist	Group-combined (6-7)
Wiles 2001[293]	GE	Home/ physiotherapy department	Physiotherapist	Individual-supervised

3D: 3D training; AC: active console games; GE: general exercise; GBF: gait, balance and functional training; E: endurance; S: strength

Table 4-22: Summary of programme venue, structure and leadership data

Programme venue:

Programme venue data fell into five broad categories:

- Healthcare settings
- Community based (e.g. community centres, local gymnasium)
- Home-based programmes
- Combination of venues (e.g. external sessions initially followed by home-based sessions)
- Research setting (e.g. university laboratory or testing centre)

Nine of the 27 programmes were based in a healthcare setting (33%). These included physiotherapy departments, rehabilitation units and community healthcare clinics.

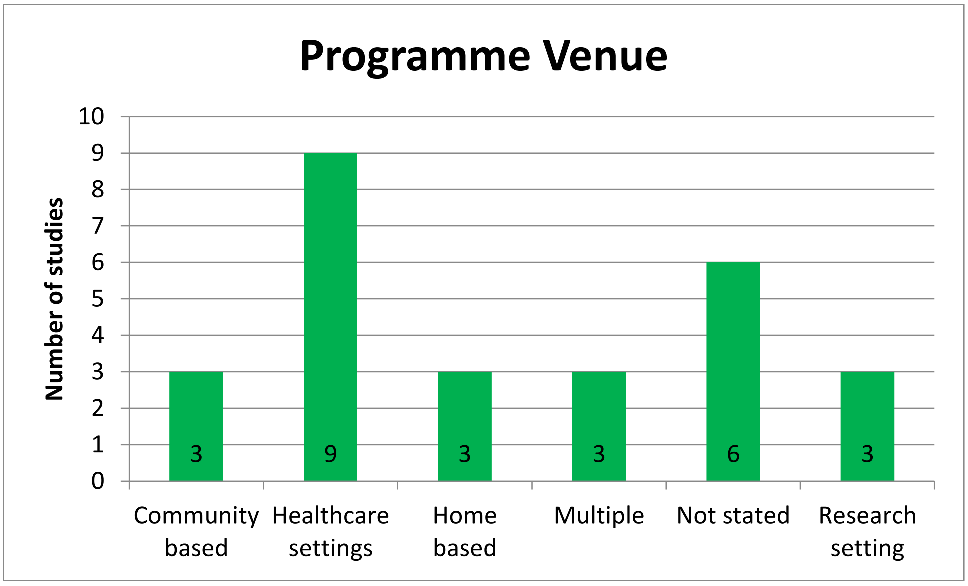


Figure 4-14: Programme venue

Programme structure

Programme structure was classified as group or individual formats and then sub-divided as detailed below:

- Individual
  - Supervised (one-to-one supervision throughout the programme)
  - Independent (initial instruction (+/- follow ups) then participant completes activities independently
- Group
  - Combined (all participants completing activities concurrently)
  - Circuit (participants completing activities independently in a group setting)

Data on group size was also extracted where this was available.

The participants worked individually in 17 of the 28 programmes (63%), predominantly undertaking activities with one-to-one ‘supervision’. Descriptions of the supervision format and role of the supervisor varied and included selection of exercises, physical assistance/facilitation, monitoring and progression of activities and feedback. The participants who undertook independent programmes usually received initial instruction and exercise prescription, followed by varying levels of review and progression of exercise.

The majority of programmes using group formats were structured to enable participants to undertake similar activities simultaneously. This included the two specific falls education programmes and five exercise-based programmes. Two other programmes used a circuit structure.

Few papers included data on group size, but where this was available; groups were small, even for the education-based programme. Minimum group size was two[240] (Finlayson 2009) and maximum group size was 10[295] (Freeman 2004).

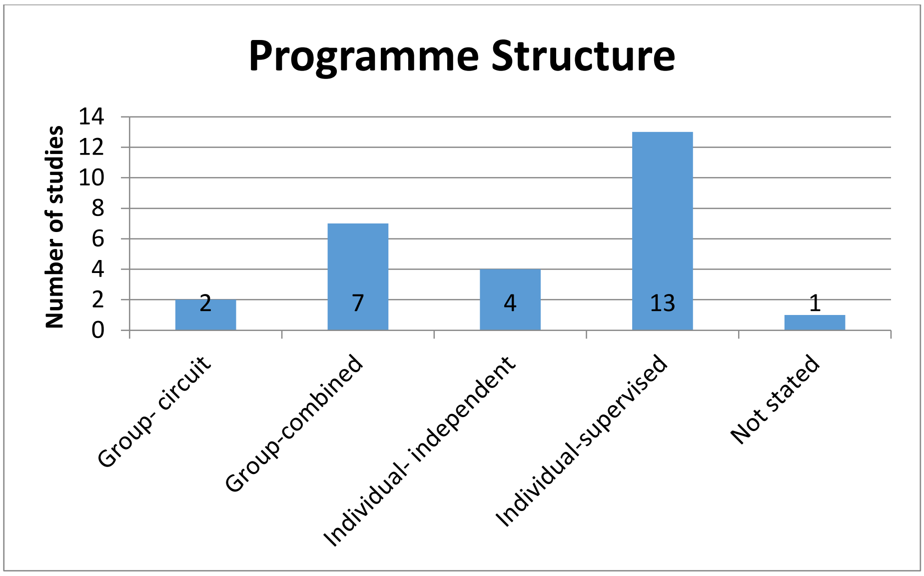


Figure 4-15: Programme structure

Programme leadership:

Programme leadership was classified according to four categories.

- Healthcare professional
- Researcher (profession not reported)
- Other professional (e.g. fitness instructor)
- Combined/multiple (e.g. healthcare professional with assistant, healthcare professional and fitness instructor)

Over half of the programme leaders were healthcare practitioners (n=15, 56%). The six ‘other’ programme leaders were all exercise professionals, including exercise physiologists, gym instructors and teachers of specific forms of exercise (e.g. Feldenkrais, tai chi, yoga).

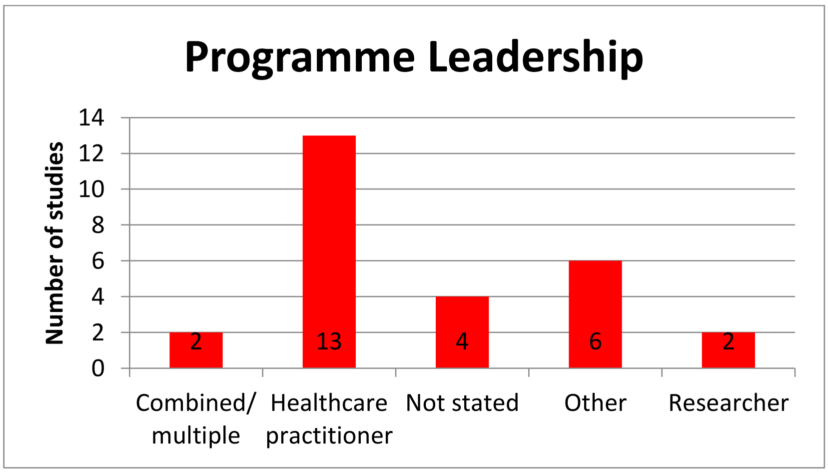


Figure 4-16: Programme leadership data

4.4.10 Assessment of programme attrition, adherence and engagement

Twelve papers were included, of which 10 are already included in the review of interventions on balance/falls outcomes (Table 4-23). Two additional papers explored factors affecting adherence to and engagement with exercise programmes (Table 4-24). Whilst 10 papers included measures of attrition and adherence, attrition data was available for 12 interventions, and adherence data for 13 interventions as several papers reported different study arms separately.

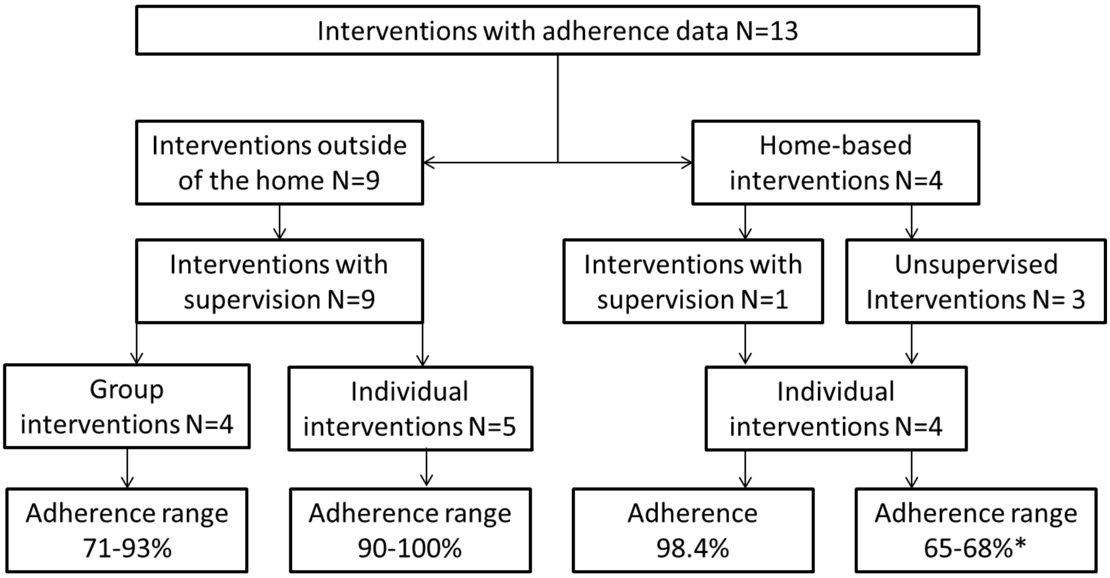
Quantitative analysis

Attrition

The attrition rate ranged from 0-33% with a median attrition rate of 18% (IQR7-22.5%) (n=12). In general small, single group studies tended to have lower attrition rates than larger, multiple group studies; however there were no significant associations between attrition rate and methodology (Fisher's exact test, $p>0.05$).

Adherence and engagement

Figure 2-17 summarises the adherence data as categorised according to type of intervention, venue of delivery and supervision level (refer to Table 4-23 for full data). Measurement methods included session attendance (determined by attendance lists), and session completion (using diary data).



*One study reported significant variability in adherence between individual participants (n=8) but not total or mean data to contribute to this summary

Figure 4-17: Summary of programmes reporting adherence data

Overall programme adherence was measured by comparing expected session attendance or home exercise completion to recorded session attendance or session completion. Using this method, reported adherence ranged from 65-100%. Further analysis explored the relationship between adherence and type of activity, programme duration and use of supervision. Whilst there were no statistically significant associations using Fisher's exact test (p >0.05), programmes taking place outside of the home tended to report higher adherence than home-based interventions. Adherence to group interventions ranged from 71-93% (n=4) compared to individually supervised activities (range 90-100%, n=5). However, given the potentially significant variation between individuals, mean adherence values should be interpreted with caution. This is illustrated by data from Mills' study[298], in which individual participants completed anywhere between 25-200% of the recommended level of home practice.

Study ID	Study type	Intervention	Initial N=	Attrition rate	Adherence measure	Adherence	Programme duration (weeks)	Home based	Supervision	Individual or group
Broekmans 2011[291]	RCT	Resistance training	36	8%	Session attendance	99%	20	N	Y	I
Finlayson 2009[240]	Single group	Educational programme	30	23%	Number completing 5/6 sessions	77%	9	N	Y	G
Gutierrez 2005[303]	Single group	Resistance training	9	0%	Session attendance	100%	8	N	Y	I
Mills 2000[298]	Single group	Tai chi	8	0%	Daily practice diaries (recommended 30' per day)	Adherence (relative to the recommendation) ranged from 25% to 200%	8	Y	N	I
Cakit 2010[281]	RCT	Cycling	15	7%	Session attendance	93%	8	N	Y	G
		Home exercise programme	15	33%	Session completion (diaries)	65%		Y	N	I
Coote 2013[235]/ Hogan 2013[284]	RCT	Group exercise	66	27%	Median session attendance	80%	10	N	Y	G
		Individualised physiotherapy	45	22%	Median session attendance	90%		N	Y	I
Learmonth 2012[280]	RCT	Group exercise programme	32	22%	Session attendance	71%	12	N	Y	G
Nilsagard 2013[283]	RCT	Supervised Wii sessions	84	17%	Number of sessions completed	99.9%	12	N	Y	I
Sosnoff 2014[239]	RCT	Home exercise programme	27	19%	Session completion (diaries)	68%	12	Y	N	I

Study ID	Study type	Intervention	Initial N=	Attrition rate	Adherence measure	Adherence	Programme duration (weeks)	Home based	Supervision	Individual or group
Wiles 2001[293]	RCT (crossover design)	Hospital Physiotherapy	42	7%	Sessions attended	94.20%	8 weeks per arm	N	Y	I
		Home Physiotherapy			Sessions completed	98.40%		Y	Y	I

': minutes; RCT: randomised controlled trial; N: No; Y: Yes; G: Group programme; I: Individual programme

Table 4-23: Quantitative programme attrition and adherence

Qualitative analysis

Two qualitative studies were included which were follow-ups of balance/ falls programmes. The studies included a total of 20 participants from the 60 recruited to the original studies[240,280].

Study ID	Learmonth 2013[301]	Peterson 2010[116]
Aim/Objective	To explore the experience of participating in a 12 week group exercise class	To explore changes in falls self-efficacy following participation in an educational programme
Design	Focus groups	Interviews
Recruitment	Participants to an exercise study[280]	Participants in a pilot falls management programme[240]
Age, mean (SD) or range	40-68	58-67
Gender	4M 10F	3M 3F
MS Status/Classification (mean (SD))	EDSS 6-6.5	All completed ADL independently

SD: standard deviation; M: male; F: female; ADL: activities of daily living; MSIS: MS impact scale; EDSS expanded disability status scale

Table 4-24: Qualitative evaluations of programme adherence and engagement

From the analysis of these papers, three key themes emerged relating to the participants' experience:

- Personal factors
- Programme structure and format
- Programme leadership and support

Personal factors

People identified a range of pragmatic and health-related reasons for participating in the programme. Engaging in an exercise based programme was a positive experience for most participants, who reported that exercising led to feelings of empowerment, confidence and normality. People felt that the positive physical outcomes and the experience had led to an increase in confidence in their general functional level, their understanding of MS, and their confidence to undertake activities outside of the group[301].

Motivating factors included wanting to take control - both of their MS and of the related consequences, including falls[116].

'I don't want to play dead' - Linda[116]

Self-awareness was identified as affecting initial and ongoing engagement. The ability to individually identify ways to overcome setbacks was viewed as important in maintaining engagement, for example being able to assess individual capability on a day to day basis as part of managing falls risk[116].

Anxiety was identified as a strong potential barrier to engagement in exercise programmes in all the studies. Concerns relating to the physical impact of engaging in exercise led some participants to initially avoid over exertion for fear of losing more physical ability. However, in the follow up study of the balance and exercise programme, most participants reported experiencing only short term effects of fatigue, which did not impact significantly on either their usual life or the decision to continue the programme[301].

Programme structure, format and content

The participants of both programmes expressed a strong preference for group based activities. The importance of role models, camaraderie, social contact and support when starting a new activity were all highlighted. Participants suggested that they would not have enough 'will-power' to sustain individual exercise without the input that a group provides[301].

There was a recurrent theme about the need for individuality within the activities undertaken with group sessions. Participants highlighted the need for exercise to be individually challenging with incremental steps to progress according to ability. They emphasised the importance of options to give variety and avoid boredom and the use of novel activities to sustain interest and engagement[301]. Developing an understanding of personal capability and risks and to have individual problem solving opportunities were perceived as important within the group falls management programme[116].

Although a preference for group activities was apparent, there was a consistent theme for the group/activity to be separate from the 'non-disabled' population[301]. Participant quotes suggest that this links both to personal anxieties about looking abnormal, and awareness that access to aids is often necessary to enable exercise (e.g. supports, rest areas, availability of fans etc.).

> *'I wouldn't go to that* [the pool]*, …I'm just being realistic, I wouldn't go to something that was all just able-bodied people and me'* Participant B14[301]

Programme goals were recognised to affect motivation and engagement. Goals and outcomes needed to be meaningful to programme participants. Falls programmes should focus on positive aspects such as maintaining function rather than simply avoiding falls (adjustment not avoidance[116]). Exercise programmes should focus on normalising MS rather than viewing it as an 'illness'. Responsive outcomes, considered meaningful to participants were also considered important to evaluate progress[301].

The data emphasised the importance of exercise sessions being tailored to the needs of participants. For instance facilities to rest (such as chairs next to equipment), accessibility and logistical issues were considered important to promote engagement. Finance was also highlighted as a key issue[301].

Assistive strategies were also identified as important to maintain motivation, engagement and adherence[116,301]. Across studies a range of potential options for achieving this were discussed by the authors, which included email and telephone contacts, exercise guides in a variety of formats, online resources and exercise buddies. However no qualitative data was gathered to provide a participant perspective on these options[116,301].

Leadership and support

The importance of appropriate leadership was a consistent theme. Leaders with specialist skills and knowledge about both MS and exercise prescription, progression and adaptation were considered key to optimise participant engagement and outcomes[301].

A wide range of perspectives were identified concerning the role of the leader and their impact on engagement and adherence. On one hand, themes were developed which centred on programme leaders fulfilling a supportive ‘expert’ role, which included prescribing appropriate exercises, advising on symptom management and encouraging engagement and adherence[301]. Conversely, there was discussion of the importance of leaders acting in a more facilitatory role, acknowledging participant expertise in self-managing symptoms and enabling individuals to problem-solve issues[116]. This dichotomy is also seen in other aspects of the leader’s role. For example, when prescribing and progressing exercises it was felt that leaders should avoid ‘overprotecting’ participants, whilst at the same time avoiding ‘over-pushing’ them[301].

4.5 Discussion

This systematic review incorporated 31 publications, including both grey and peer-reviewed literature. A total of 1036 participants were included; 967 of whom were included in the final data analyses. This represents an overall attrition of 7% (n=69).

4.5.1 Overall completeness and applicability of the evidence

Participants

Of the 967 participants included in the final analyses, demographic data was available for 855, of whom 70% (n=596) were female. Whilst the gender split is representative, the MS characteristics reflect a bias towards mild - moderately affected participants relative to the wider MS population[308]. The majority of studies included relatively young participants; none reported a mean age greater than 60 years. A range of MS types and severities were included, however the majority of studies which used the EDSS reported means between 3 and 4.5. All participants were ambulant for at least some of their day.

Methodology

This review aimed to undertake a comprehensive evaluation of the evidence base, therefore a range of source documents was included. However, the inclusion of data from single group studies has the potential to inflate estimates of effect size[276], and so results from these studies should be interpreted with caution.

The methodological quality of the comparator group studies was variable, with incomplete reporting of procedures and outcomes in several studies. This led to a high risk of bias in approximately 30% of the papers in five of the six Cochrane risk of bias domains (Section 4.4.4). In addition, the generally small sample sizes contribute to the wide confidence intervals within the meta-analyses and make the likelihood of a type II error relatively high. The methodological quality of the qualitative studies as measured by the CASP appraisal tool[268] was very good; however the relatively reductionist approach of such tools has been acknowledged[309].

4.5.2 Review objective 1: To evaluate the existing evidence base for interventions targeting falls in multiple sclerosis.

This review included eight source documents relating to programmes specifically targeting falls risk, or evaluating falls related outcomes. Of these, two documents pertained to education-based approaches, and six were predominantly exercise-based.

Whilst both education-based documents included programme evaluations, only one had been published in a peer-reviewed journal[240]. Neither included comparison groups, and neither programme measured change in falls risk or rate. However, both evaluations reported positive short-term outcomes including improved self-efficacy and better use of falls avoidance/falls management strategies. These outcomes align with the content of the programmes, which primarily focussed on these areas. However, the use of non-standard outcome measures (e.g. adaptation of the FES) makes comparison of the magnitude of effect between these studies and those in other groups problematic.

Of the six exercise-based interventions evaluating falls outcomes, all reported improvements in the intervention arms at study completion. However, there was a wide variation in methodological quality, particularly with the methods of falls reporting, and lack of blinding, leading to a risk of bias. Meta-analysis was only possible for two studies[235,241]; this suggested a modest reduction in risk ratio, with wide confidence intervals crossing one (pooled RR 0.75, 95% CI 0.12-4.80). This is likely to be associated with the relatively small pooled sample size, particularly within the control groups. Importantly, none of the studies included a follow up period, making it impossible to assess the long term reduction in falls risk. Furthermore, only the number of fallers is reported (i.e. falls risk). No data on falls rate (which, based on the older peoples' literature, may be more responsive to intervention[99]) is included.

Of the 'other' papers, Stephens[288] stated that participants in the intervention arm reported fewer falls on average than the control group during the programme. However, there was no statistical analysis of this outcome, and there were no differences between the groups post-intervention. The two remaining studies reported ‘proxy’ measures of falls, limiting the interpretation and generalizability of their findings.

4.5.3 Review objective 2: To develop recommendations for the specific content that should be included in a falls programme targeting balance as a falls risk factor for people with multiple sclerosis

The review included papers from 26 studies which evaluated exercise-based interventions and analysed balance outcomes. The studies included 30 different intervention arms, as some studies compared more than one type of intervention. The interventions were classified into six broad types, with comparison of content and effect broken down accordingly.

Effect

The largest group of interventions were ‘general exercise’ programmes (N=11 separate intervention groups). Their content was wide ranging, including individualised physiotherapy interventions, non-specific ‘exercise’ (both in an individual and group format) and specific exercise approaches such as yoga and core stability training. Meta-analysis suggested a moderate but statistically significant overall effect in balance performance (SMD 0.57, (0.23 – 0.91)) , and despite the wide variety of interventions, analysis of heterogeneity did not suggest a significant issue[115]. The large number of single group studies within this analysis increases the risk of bias, and the wide range of intervention types limits interpretation of the results.

Data relating to the effect of strength (n = 4), endurance (n = 3) and 3D training (n = 1) programmes was available for eight studies. Four studies used active console games (Nintendo Wii and similar) as the intervention. Meta-analysis of three suggested a small positive effect (SMD 0.39 (0.23 – 0.91)), although there was variability of outcomes between studies. It is possible that some of this variability can be accounted for by methodological issues. For example, the control group participants in Nilsagard’s[283] study were far more active (based on self-report diaries) than the intervention group, potentially confounding results. Overall, the small sample sizes, wide range of outcome measures and other methodological issues suggest that results should be interpreted with caution.

Interventions that utilised specific gait, balance and functional training approaches were included in six studies. Meta-analysis was possible for five of the six studies, and suggested a moderate effect size (SMD 0.82 (0.55-1.09)). However the magnitude of effect in absolute terms suggests that these results should be treated with caution. In this meta-analysis, the pooled mean difference across the five studies was 6.67 points on the Berg balance scale (BBS) (95% CI 4.49-8.84). This may not represent a true change since these values are smaller than the minimal detectable change (MDC) of 7 points as determined by previous MS studies[310]. At the very least, this finding suggests that it would be prudent to power studies based on a small effect size, rather than the moderate effect size seen within this meta-analysis.

Furthermore, the results of this review highlight a potential issue with the assumption that improvement in balance measures is likely to equate to a corresponding reduction in falls risk. Cattaneo[241] and Sosnoff[239], both reported modest improvements with BBS (mean difference 5.91(95% CI 1.45-10.17) and 3.90 (95% CI -3.01-10.81) respectively, alongside a reported decrease in falls. In Coote's study[235,284], the mean post intervention difference in BBS between the exercise and control group was 8.8 points (95% CI 3.73-13.87)[284], indicating improved balance performance in the intervention group. However, the falls risk ratio for this same group comparison was 1.72 (95% CI 0.43-6.90)[235], suggesting that participants in the intervention group were, on average, *more* likely to fall than those in the control group. Whilst these seemingly contradictory results may be an artefact of a relatively small control group with a low proportion of fallers in comparison to the intervention group, it is possible that they indicate a more complex interaction such as a change in behaviour. For example participants may have increased confidence to undertake more risky activities as their balance performance improves, leading to an increased risk of falls. At the very least, this finding suggests that future studies must measure falls incidence/rate by prospectively recording falls data.

Content

The complexity of rehabilitation interventions is widely acknowledged, with the recognition that interactions between individual elements of a programme contribute to outcomes and overall effectiveness. The need to clearly describe the elements within this 'black box' of rehabilitation has been emphasised[311]. In this review the reporting of programme content was variable; some studies provided considerable detail whilst others provided little or none. As with many other evaluations of therapy-based interventions[312], the lack of a clear description of 'physiotherapy' and 'rehabilitation' approaches leads to a difficulty in drawing conclusions about their potential utility. Within the specific exercise interventions, content analysis was guided by the existing evidence base (e.g. ACSM guidelines[271], categorisations used in previous reviews[272]), however the relative lack of evidence supporting the validity of these guidelines, particularly within MS, is acknowledged. One of the problems associated with this approach is the reductionist nature of the assessment. However detailed descriptions of content within the results section of the review (section Interventions addressing balance outcomes 4.4.7) aims to address this issue.

The four studies that included active console game interventions were all published in 2013, reflecting the growing interest of this type of intervention in rehabilitation practice. Three of these used similar interventions[283,285,287], although the games selected and methods of determining progression varied. Whilst the small sample sizes and methodological limitations precludes clear inferences being drawn, a point of interest is that the study with the largest overall effect on balance was the only one where game selection was random, rather than led by participant or therapist choice[287].

In general, the exercise programmes using strength and endurance approaches demonstrated relatively modest improvements in balance outcomes. Analysis of their content highlighted that in many instances, exercises were undertaken in a supported position, often in sitting. With the exception of the strength training study by DeBolt [286], all studies used weight machine programmes in association with free weights, although the proportion of each element was not specified. Similarly, all three endurance programmes used interventions which focussed on seated exercises such as static cycling, apart from Sabapathy[292] who also included treadmill training. Using ACSM measures of exercise intensity[271] none of the strength and endurance programmes achieved greater than a moderate intensity of exercise. The relatively modest effect on balance outcomes may be attributed to the lack of specificity to balance in the training programmes, and/or the lack of training intensity. It is therefore not possible to recommend or refute the potential contribution of these types of interventions to balance and/or falls outcomes.

Specific gait, balance and functional training programmes demonstrated the largest pooled effect on balance outcomes of any of the intervention types. The ‘core’ components of these programmes involved exercise in standing, including bilateral and single leg activities. Analysis of content highlighted that, in comparison to studies in older people[272], few programmes included movements around the base of support in three dimensions, suggesting a potential area of development. In addition, there was generally poor documentation on approaches used to minimise upper limb support. Furthermore, only two studies included sensory re-training and only one documented the inclusion of dual-task activities. Retraining both these aspects have been shown to positively impact on balance and falls outcomes in older people[313,314]. Given the high prevalence of sensory impairments in MS[22], and the recent publication of a study highlighting improvements in balance secondary to sensory retraining[315], it could be argued that future programmes should include these elements. It should also be ensured that programmes include challenging task specific balance activities.

Intensity and duration

Of the 27 trials, data relating to treatment intensity and programme duration was available for 17. When compared to the recommended intensity and duration figures from the older people's literature[272], the interventions in this review were generally of relatively short duration and included a low total dose of exercise, even assuming full programme adherence. In contrast to Sherrington[272], there was only a weak, non-significant correlation between total dose and effect size. However, there was a significant moderate correlation between treatment intensity (minutes/week) and effect size thereby supporting the general principle that high intensity of exercise is required to optimise outcome. The significant negative correlation between programme duration and effect size might suggest that short duration programmes of high intensity could be more effective in this group. One potential explanation is that there is a drop off over time with longer duration programmes, which impacts on their effectiveness. A major factor to consider in this respect is the minimal follow-up period of the majority of programmes included in this review. This is an important methodological limitation given that studies have shown decreased participation, with an associated reduction in treatment effect, even relatively soon after the completion of formal MS exercise programmes[316]. Methods to maintain engagement are thus an important consideration in future programme developments.

One option to increase intensity of practice per week and to encourage integration of programmes into daily life could be the use of home-based practice. A major limitation with many of the studies in this review is the incomplete information provided regarding additional home practice that participants were asked to undertake. Where it was mentioned (e.g. Mills[298]), no guidelines on recommended duration and frequency of practice were given. As a consequence this aspect could not be included in dose calculations for most studies. As home practice of exercise has proven cost-effective in achieving recommended treatment dose in other groups[317], consideration of this aspect in the development of future MS falls programmes is recommended.

4.5.4 Review objective 3: To evaluate the evidence relating to the optimal method of delivery of programmes targeting balance and/or falls in multiple sclerosis

Programme leadership

There was wide variation in the structure and format of programmes; this reflects current clinical practice. Most programmes were based on health-centred models, led by healthcare professionals, with a high emphasis on exercise prescription and supervision being provided by the session leaders. The qualitative data highlighted that people with MS had a strong preference for programme leaders to be appropriately qualified, and knowledgeable about the specific aspects of MS which may impact on exercise engagement and performance. Experiences with leaders who lacked this specialist knowledge was cited as a factor contributing to non-adherence and lack of confidence[318], whilst those who '*knew what they were talking about'* (Participant 11/3[319]) were highlighted as an important motivator.

However, whilst the majority of programmes were led by healthcare professionals, there is recognition in other MS studies that this role could be fulfilled by other knowledgeable individuals[318]. There is also recognition of the importance of other sources of support such as social networks, family and friends[319], a finding which is supported by the older people's falls literature[320].

The relationship between participant and programme leader appeared to affect engagement and adherence. There were a range of preferences for leadership styles; some participants advocated a facilitatory approach while others suggested that leaders needed to 'push' participants. In the studies exercise prescription, progression and review was typically carried out *by* leaders *to* participants, which conflicts with the self-management/self-efficacy ethos encouraged within current policy and practice guidance[321]. It is evident within the wider literature that careful consideration is required when recommending a leadership style for falls programmes involving exercise. For example, in a qualitative evaluation of participation in a general exercise programme, participants expressed a strong preference for exercise activities they viewed as 'safe'[322]. The outcome data from this review suggests that the degree of challenge to balance and the level of practice intensity (both associated with a degree of risk) are key factors which are likely to influence outcome. Managing the potential conflict between risk and benefit requires careful facilitation, and it is likely that leadership approach may be pivotal in achieving this.

Within the wider literature, the potential impact of leadership style on programme engagement has been investigated. This has led to the development of a number of supporting theoretical frameworks and facilitation techniques. For example, it is proposed that preferred leadership style may be related to participant self-efficacy and readiness to engage in exercise activities: Bandura's 'stages of change' model[323] suggests that those who are in a pre-contemplative stage may respond more positively to more facilitatory approaches, whilst others may find a more active and challenging approach more stimulating. Similarly, research suggests that the use of specific techniques such as motivational interviewing may increase engagement and improve participant perceptions of general exercise and physical activity programmes[324,325]. However, not all studies have reported positive results[326,327], suggesting that further evaluation is required.

Programme format

Although a range of formats for programme delivery were used, nine of the exercise programmes used a one-to-one approach. Whilst this approach does potentially allow greater opportunities for individualisation of exercise activities, there is limited opportunity for peer information exchange and support. In contrast, both of the education-focussed falls programmes[240,302] had a high emphasis on group interaction and the development of shared knowledge through the exchange of experiences and ideas. From the qualitative data, it would appear that the group format is viewed positively by participants; allowing mutual support, sharing of experiences and learning from and with others. However it should be noted that the participants within the qualitative studies who expressed this view had all participated in group exercise programmes, thus potentially creating a source of bias. It is possible that their initial participation was influenced by a preference for group activities at the outset. Nonetheless, the wider literature suggests that a group programme has value in the opportunities it provides for 'vicarious experiences', such as observing others achieving goals through exercise or problem solving activities[328–330].

The use of group exercise sessions may have both advantages and disadvantages. If participants work on similar exercises simultaneously, a competitive element may be introduced, facilitating progression. However, tailoring exercise to individual ability levels can be difficult when participants undertake the same exercise concurrently. One solution is the use of circuit-training as implemented by two studies in this review[331,332]; this allows a competitive element alongside individualised tailoring of exercises. Sessional attendance (either individual or group) for a balance-focussed falls intervention could also have other disadvantages. There is evidence in other populations, for instance, that programmes primarily run using attended sessions may be less effective in encouraging and maintaining overall physical activity levels than those using integrated lifestyle-based approaches[333–335]. One explanation may be that participants view group attendance and exercise participation as synonymous, making them less likely to engage in practice outside of scheduled sessions. Given that the evidence suggests that relatively high intensity of exercise is required to optimise outcome, interventions are required which promote sustained independent exercise which is integrated into daily life. In older people's falls management, function-based home programmes have demonstrated immediate beneficial outcomes which are at least comparable to attended programmes, whilst also demonstrating long-term maintenance of improvements at 12 month follow-up[336].

Venue of attended sessions

The programmes in the review were predominantly delivered in healthcare settings, although other models of delivery were used. These included home based programmes and group programmes run in community settings (such as leisure centres). The shift in emphasis away from health-centric care to self-management for people with long term conditions means that greater use of community services is generally encouraged[321]. However, the finding that participants preferred to exercise in an environment away from the general population must be considered. This contrasts with the wider literature, where engagement in physical activity within the mainstream environment is viewed positively[337], with participants describing feelings of liberalisation, normalisation and freedom. When developing MS falls programmes, it will be important to consider how this could be achieved whilst at the same time addressing the expressed need for a supportive and 'safe' environment. In other groups, programmes have incorporated 'step up' activities in a mainstream setting following completion of an initial programme of exercise[338]. This may enhance ongoing engagement in exercise in a more financially sustainable manner.

4.5.5 Review objective 4: To identify the key issues that could affect the clinical and cost effectiveness of the programme, including adherence and participant satisfaction/engagement

Eighteen studies included data relating to adherence. Analysis included attrition and adherence data as well as qualitative data.

Attrition rates ranged from 0-33%. There were no significant associations between attrition rate and study methodology, although larger studies tended to have greater rates of attrition. Reasons for attrition varied, and included health and MS specific issues such as relapses, as well as social factors (lack of time, transport and family commitments).

Reported adherence ranged from 65-100%. There were no significant differences in adherence with differing intervention types and supervision methods. However, the data suggests that, in agreement with the wider literature[339], there was a trend towards independent home-based programmes having lower rates of adherence. The validity of the adherence data generated by exercise diaries may be questioned, given the reported weak correlation between diary-recorded and actual levels of activity[340]. In addition, measures of adherence as determined by attendance data do not capture important details such as actual participation in exercise activity and intensity of practice achieved. Whilst three of the four studies using active console game intervention did not report any adherence data, these types of interventions, along with telemedicine-type approaches (e.g. Finkelstein[294]) present an opportunity for direct measurement of both engagement and participation. In addition, a recent study[341] suggests that adherence to 'novel' interventions such as exergaming may attract better adherence than conventional exercise programmes.

The qualitative data highlighted that, having a strong belief that exercise would be beneficial and a wish to take control were two key factors which influenced engagement with exercise programmes. The wider literature suggests that these factors are linked to self-efficacy concepts such as developing an understanding of personal limitations[337], as well as to self-regulation and self-awareness. Studies of engagement in general physical activity in MS[342], demonstrate that participants with relatively low levels of physical activity tend to over-estimate the amount of activity they engage in, both in relationship to their peers and relative to recommended guidelines. In addition, participants who are relatively inactive demonstrate a low threshold of stressors (e.g. lack of time, MS symptoms, family and social problems) which prevent engagement in physical activity. This is in contrast to those with higher levels of activity who tend to prioritise activity despite having similar demands on their time and energy. This suggests that falls programmes should facilitate the development of self-efficacy and support programme engagement on an individual level.

The need to set relevant and achievable goals relating to engagement in exercise was highlighted as important. This resonates with the wider rehabilitation literature[343], however it may prove challenging for MS falls programmes. For example, some people with MS view falls as a 'necessary evil'[344]; this may complicate setting goals which focus on reducing falls risk/rate since they may be of less perceived relevance than goals relating to maintenance of mobility, ADL and independence. It is possible that this may, at least in part, impact on the uptake with falls programmes, as demonstrated by Finlayson[240].

Anxiety was perceived as a significant barrier to engaging in exercise programmes. This included anxiety relating to the impact of exercise on MS related symptoms and anxiety relating to falls and/or injury whilst undertaking exercise. However, whilst the qualitative data suggests that the actual effects were less significant than anticipated[301], the attrition rate for this particular study was high (22%)[280]. Given that all participants interviewed had completed the whole programme, it is possible that the experience of those who stopped attending the exercise group was quite different. Additional research exploring reasons for discontinuation of exercise programmes would be valuable to inform this aspect further.

4.5.6 Strengths and limitations of the review

A strength of this review is its comprehensive nature, including 32 studies with a total of 1105 participants. The review comprised a range of methodologies, including qualitative and quantitative data, controlled trials, feasibility and pilot studies and grey literature. This could also be viewed as a weakness; for example, the potential for non-controlled trials to have larger effect sizes could have inflated the outcomes of data synthesis[276].

Undertaking separate analyses has enabled comparison between differing methodologies, however caution should be exercised if using the findings to inform future studies (e.g. for power calculations).

Owing to limited research on falls management in MS, the review aimed to evaluate the evidence for programmes addressing falls outcomes as well as those exercise interventions addressing balance outcomes (on the basis that impaired balance is a key modifiable risk factor for falls). However, the small number of programmes directly targeting falls is a limitation. Similarly, the heterogeneous outcomes and poor use of best practise standards for measuring and reporting falls interventions limits the generalizability of the findings. Future studies should address these issues as a priority. Whilst the wide range of balance-focussed interventions makes comparison between studies challenging, the use of pre-existing categorisation procedures did enable an initial evaluation of the intervention components.

A further strength is the detailed analysis of data relating to programme content, structure and format, dose, adherence and attrition rates not explored in previous reviews of balance interventions in MS[247]. However, there are limitations with the methods used. For example an assumption of 100% adherence was made when calculating treatment dose; whereas actual adherence rates ranged from 45-100% (4.4.10). Whilst the lack of clear and consistent reporting methods prevented the dose calculations being adjusted to the adherence rate for each study, it is notable that the correlation between treatment intensity and outcome does reflect the findings of similar analyses in other populations, strengthening the credibility of the findings.

4.6 Summary and recommendations

Falls interventions

This review provides some evidence to suggest that an education-based approach is effective in improving knowledge and falls self-efficacy in MS. This conclusion should be viewed with caution since it is based on one peer-reviewed publication[240] and there has been no evaluation to date of the effect of these types of programme on falls risk or rate. Although there is more literature relating to the effect of exercise-based approaches, there are significant methodological issues within several studies, and wide variation in the types of interventions and outcome measures used. Nevertheless, all of the studies reported short-term outcomes in favour of the interventions, suggesting that exercise may be an appropriate intervention to manage falls. Future studies should use best-practice falls recording procedures and undertake appropriate follow-up assessments to more comprehensively evaluate effectiveness.

Exercise-based interventions evaluating balance outcomes

This review demonstrates that a range of exercise interventions improve balance outcomes in MS. Programmes incorporating gait, balance and functional training showed the greatest effect. However, the pooled effect sizes bring into question whether the magnitude of effect represents clinically meaningful change in balance, or is large enough to affect falls outcomes, based on their current format. Therefore it is important to consider the main elements of the intervention driving the effect, and how these may be optimised.

Analysis of the content of the exercise interventions indicates that programmes which achieve a high intensity of challenging balance exercise are likely to lead to the greatest benefit in balance (and therefore potentially falls) outcomes. Whilst the review does suggest that this type of exercise is feasible in people with MS, maintaining long term engagement and integration of exercise into daily life will undoubtedly affect programme outcome. The qualitative review has highlighted a number of issues; however, further exploration is required into methods to best support people with MS to develop the skills, confidence and motivation to successfully engage in such a programme on a long-term basis.

The studies evaluated exercise programmes which were delivered in a range of formats (e.g. group and individual attended programmes, home-based programmes). The qualitative review suggests that people with MS have a preference for group activities, indicating that existing generic falls programmes (which predominantly use this type of structure) could potentially be an appropriate resource for MS falls management. However, the preference for participants to attend MS specific groups and the identification of key barriers to attendance related to MS symptoms (e.g. fatigue, relapses etc.) indicates that generic programmes and traditional weekly-attendance models of delivery are barriers for many potential participants.

This review has identified that education and exercise focussed balance interventions are feasible in MS, and may lead to improvements in key falls-related risk factors. However, the most suitable method of programme format and delivery method has yet to be determined.

5 Study Two: Building stakeholder consensus: Development of a falls management intervention model for people with multiple sclerosis

5.1 Background and purpose

Experience in services for older people shows that a range of factors impact on the utility of fall prevention programmes. Optimising programme utility is important since adherence to rehabilitation packages can be poor[338,345] particularly in interventions which include a preventative component[261]. Consequently, these issues should be carefully considered early in the programme development process. Alongside an evaluation of the evidence, stakeholder input is critical to ensure the programme structure and format is feasible and acceptable to both service users and providers. The benefits of a stakeholder-focussed approach include:

- Ensuring that evidence-based recommendations are incorporated into a feasible, sustainable intervention
- Optimising adherence by addressing the specific needs of service users[262,264]
- Ensuring a fit with existing models of service delivery and key drivers relating to service commissioning to enable implementation within routine practice
- Addressing issues which may adversely affect future research projects, including participant recruitment and retention

5.2 Aims and objectives

The aim of this study was to explore service users' and providers' views of the most suitable methods and formats of delivery for the proposed falls programme, considering:

a. Acceptability for service users
b. Optimizing adherence and user participation
c. Ensuring sustainability

The specific objectives were to:

1. Determine the most appropriate model for the falls programme, including aims, outcomes and approach
2. Recommend programme structure, format and delivery methods
3. Explore factors affecting participant engagement with and adherence to the programme, both over the short term and longer term
4. Highlight factors affecting sustainability and the integration of the programme within existing service provision
5. Evaluate the degree of agreement amongst the study participants at each stage of the process.

5.3 Methodology

The study used a consensus development approach, employing a nominal group method[346]. This approach uses iterative processes to combine expert opinion in order to reach agreement[347]. The primary aim is to optimise reliability and validity by ensuring the output is based on a shared understanding of the key ideas and principles amongst the participants[348]. Evaluations highlight that these methods are unlikely to create new knowledge, rather that they make the best use of existing knowledge by bringing together relevant stakeholders in a process of sharing, reflection and decision-making[349].

Whilst there are a number of different consensus development methods, the method most frequently described is the Delphi technique[350]; a 'structured process which utilises a series of questionnaires or rounds to gather and provide information' [347](page 9). This is usually structured as an anonymous process, with participants contributing independently, remotely from the research base. The procedure has the benefits of limiting the chances of over-dominance of individual panellists, being convenient for participants and enabling input from individuals who are widely geographically dispersed. However, the Delphi technique has been criticised for lack of group interaction[350] which limits the exploration of views and resolution of disagreements by group discussion[348]. In addition, some Delphi studies have demonstrated poor reliability when the output of different panel groups are compared[347].

By contrast, interacting or focus group approaches use a relatively unstructured method to facilitate face-to-face group discussion[351]. There is a lack of empirical evidence comparing focus groups to other consensus development methods. However there is criticism that the relatively free group exchanges may lead to a tendency for group members to conform, with the subsequent loss of minority or opposing points of view[351,352]. In addition, it has been suggested that interacting or focus groups may be likely to 'over focus' on one or two ideas, and therefore fail to thoroughly explore the range of issues around a topic[349].

The nominal group technique (NGT) aims to utilise aspects of both the Delphi and focus group processes, being defined as 'a structured meeting that attempts to provide an orderly procedure for obtaining information from target groups who are most closely associated with the area'[353] p980. The NGT draws on expert input to develop consensus through sequential rating, discussion and debate followed by re-rating of opinions; using both individual and group activities within a structured and facilitated process[352,354]. The procedure aims to stimulate discussion and sharing of ideas whilst ensuring that all participants have equal representation[355].

There is relatively little research assessing the NGT[349], however evaluations suggest that the process is time efficient for participants, and that the output can be highly reliable[353]. A comparison of focus and nominal groups concluded that NGT participants generated a wider range of ideas and had higher satisfaction ratings than focus group members[351]. Criticisms of the NGT include the potential for the process to be relatively 'researcher heavy' in comparison to other processes due to the need for significant preparatory work, high levels of facilitation during the meeting and data collation, interpretation and dissemination activities to complete the process[348,349]. However, given that this project aimed to bring together service users and providers, the ability to facilitate group interaction whilst minimising potential power imbalances was critical in the final decision to use NGT as the selected research method for this study.

5.4 Method

It is essential to clearly describe the specific NGT method used, since several modifications exist[349]. This study used a modification of the classical NGT initially documented by the RAND Corporation in 1992 (Bernstein, cited by Murphy[349]). A comparison of the 'classical' and 'modified' NGT is shown in Figure 5-1.

'Classical' NGT[346]	'Modified' NGT [348]
PRIOR TO MEETING	
	Questionnaire of trigger statements is developed in a systematic manner (e.g. survey of stakeholders, literature review)
	Rating round 1: Recruitment of NG members and individual completion of questionnaire.
PANEL MEETING	
'Problem' is revealed to panel members	Aggregated questionnaire responses returned to panellists for review
Panellists individually brainstorm ideas	Facilitated group discussion of scoring, including rationale for individual scores
Ideas are shared with the group in a round robin	**Rating round 2:** Individual re-rating of questionnaire
Ideas are discussed and grouped together where appropriate	Responses re-analysed
Rating round 1: Each participant individually rates each idea	Aggregated scores are returned again. Further discussion of rationale
The ratings are tabulated and presented to the group	**Rating round 3:** Final individual re-rating of questionnaire
The overall ranking is discussed, including rationale for individual scores	
Rating round 2: Revised ideas are individually re-rated	
FOLLOWING MEETING	
Collation of responses and development of position statement	Collation of responses and development of position statement

Figure 5-1 Comparison of 'Classical' and 'Modified' Nominal Group Techniques (NGT)

5.4.2 Sample

Participants

The key principle of the NGT is the use of experts within the consensus development process. In this context, 'expert' has been defined as 'a group of informed individuals' and 'people considered expert in their field'[347] (page 196). This study aimed to involve people affected by MS (both health professionals and people with MS) in the development process of designing a falls management intervention. Therefore, the potential pool of 'experts' for this study included service users, rehabilitation professionals and service commissioners.

In recruiting NGT panel members, it is recommended that participants should reflect the full range of characteristics of the intended population in order to increase credibility[349]. In addition, inclusion of individuals with related expertise and experience is appropriate to provide alternative viewpoints[346]. Consequently, purposive sampling methods were used aiming to achieve maximum variation with a final group membership of:

- People with MS who had/had not fallen, and who were from across the spectrum of disease type and severity
- A range of rehabilitation professionals from a variety of backgrounds and service delivery settings
- Service commissioners
- Other individuals likely to be able to contribute expertise to the group (for example fitness professionals who run falls groups for older people).

Formation of nominal groups and sample size

The use of more than one panel meeting impacts positively on the reliability and generalizability of the outcome of NGT[349]. Hence, in this study three nominal group panels were convened covering the main geographical localities of the study area. With a recommended group size of no more than 12 members per nominal group[356], this represented a total sample of 36 individuals.

This project was innovative since it included both service users and professionals in the same panel, the intention being to promote the exchange of ideas and development of a shared understanding and true consensus between stakeholders[357]. Within the traditional processes of service development, expert panels tend to be organised within discrete homogenous groupings[358]. To date there has been limited evaluation of the effectiveness or impact of using heterogeneous groups, however there is a general recommendation that a mix of panellists is appropriate when the overall aim is to identify and explore uncertainty[346], as was the case with this study.

Recruitment

Whilst the main aim of the NGT is to ensure all participants have equal representation, there may still be some influence within groups based on status and perceived hierarchical relationships[348,349]. Therefore, to minimise this aspect, every effort was made to ensure at least half of the participants were people with MS.

Three recruitment methods were used for the MS service users. Firstly those who participated in study one, and who expressed an interest in involvement in future research, were invited to take part by letter or email. Secondly, the study was advertised in the SWIMS newsletter; and thirdly this information was distributed via the local MS Society support group network.

Professionals were recruited via advertisement and targeted visits to local networks, professional groups and existing services. This included liaison groups of MS specialist nurses and rehabilitation professionals and a peninsula wide network of professionals with a special interest in falls rehabilitation.

Participants were excluded if they were unable to effectively give informed consent, or had severe communication difficulties which would prevent participation in the nominal group sessions.

5.4.3 Plan

The stages of the nominal group process are summarised on the flowchart in Figure 5-2 and explained overleaf.

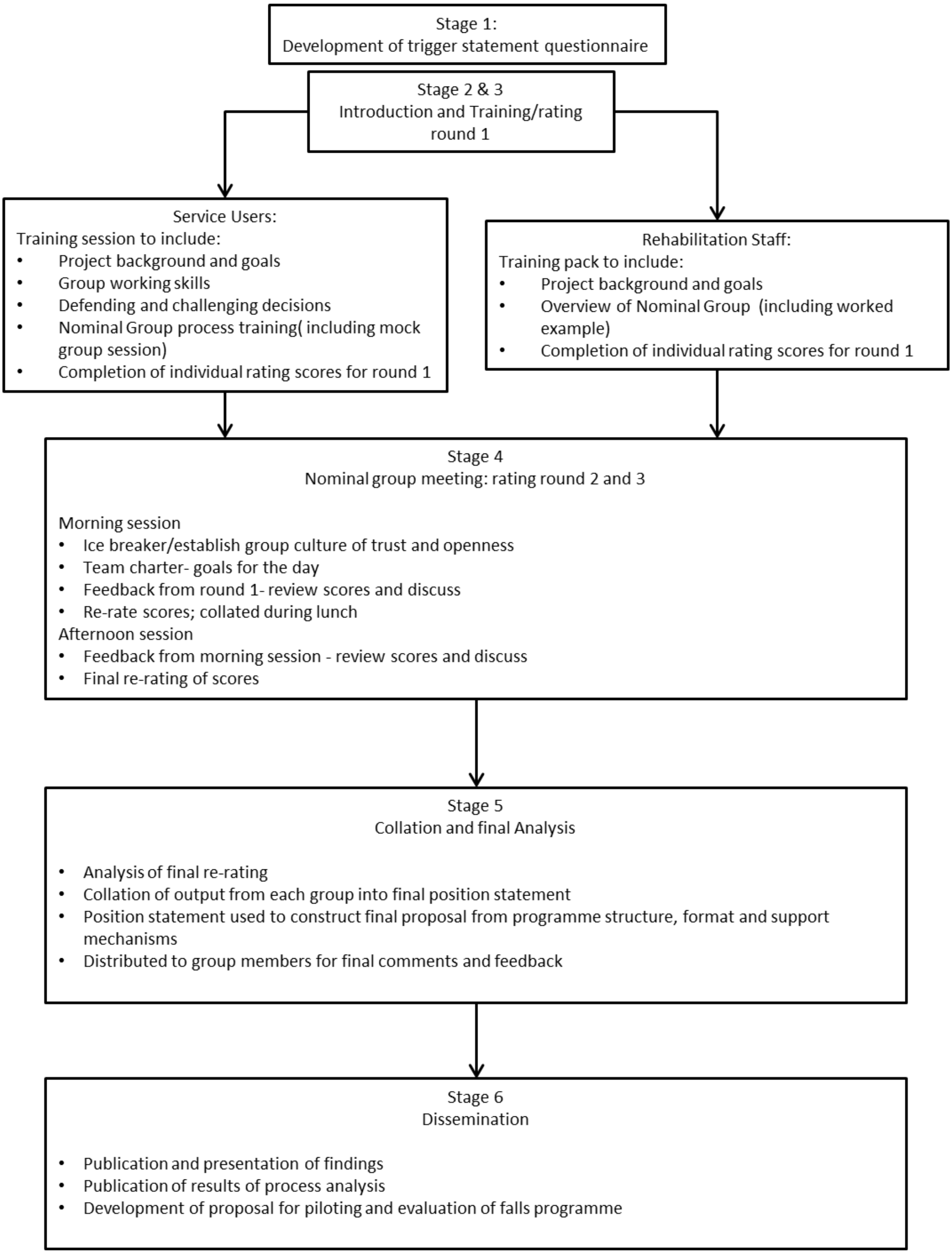


Figure 5-2: Nominal Group stages

NGT stages

1. Development of trigger statement questionnaire

Developing appropriate trigger materials to be used within the NGT is critical to success of the process[358]. Recommendations from the literature suggest that the questions must be perceived as stimulating, relevant and clear to enable participants to make a meaningful contribution[349,359]. Appropriate wording of statements also influences the reliability and validity of NGT outcomes[347]. To achieve this, it is recommended that stakeholders are involved in both the initial selection and development of trigger materials[349].

For this study, the structure and content of the trigger statement questionnaire was initially guided by the results of systematic review two (chapter 2). Statements were grouped into the following key areas which related to the main objectives of the project: Models of falls programme (e.g. group vs. individual format); logistical and service delivery issues (e.g. venue, fit with existing services); programme structure and support methods (e.g. methods to ensure intensity, optimising adherence and ensuring long term engagement). Statements were worded using deliberately challenging language in order to stimulate reflection and debate. Participants were asked to rate their level of agreement with each statement using a Likert scale of 1-9 (1 = strong disagreement, 5= neutral, 9= strong agreement). There was also space for free text comments[360].

Once the initial draft was completed, the material was sent to five individuals who were external to the development process for piloting and comment (people with MS =3, neurology rehabilitation professionals =2). Minor wording changes were suggested which were integrated into the final trigger statement questionnaire.

2. Introduction and training

Ensuring that nominal group participants are appropriately briefed and supported in the process maximises engagement, satisfaction and output[349]. Initially, potential volunteers were sent general explanatory information as part of the informed consent process. On recruitment, participants were given an overview of the project aims and research background and fully briefed regarding the nominal group technique, with on-going support available. For rehabilitation and service commissioner members, this took the form of a mailed briefing paper which included an outline of the key stages of the process and the provision of relevant examples. The MS service users were invited to attend a half-day training session, facilitated by the project researcher with support from the local National Institute for Health Research Collaboration for Leadership in Applied Health Research and Care user involvement group, who have extensive experience in facilitating patient and public involvement. This session was considered vital to facilitate full service user engagement in an unfamiliar process where team dynamics and the ability to challenge, discuss and defend viewpoints was key to developing a truly shared consensus[357].

3. Rating round one

Group members were asked to individually rate their responses to the NGT trigger statement questionnaire (Appendix 7.4.1). For the professionals, the trigger statement pack was included with the introductory briefing, while for MS service users it was distributed and completed within the half-day training session. On receipt of the pack, members were asked to consider the information, respond to the statements and return completed questionnaires to the researcher for collation prior to the meeting.

Once the round one trigger statement questionnaires were returned, the scores were collated for each nominal group meeting, and the individual statements prioritised according to the degree of response variability as represented by the mean deviation around the median (MDM) (see data analysis, section 5.4.5). As it was not feasible to undertake in-depth discussion of all 20 statements in the NGT meeting, prior to each meeting the 10 statements with the largest MDM were initially prioritised, and then discussed with one or two panel members and a member of the research team to confirm and refine the order of discussion[349].

4. Nominal group meeting and rating rounds two and three

Three nominal group meetings were convened. The groups were structured into a series of steps, summarised within the flowchart (

Figure 5-2)[361]. Special attention was paid to ensure that the venues were comfortable and conducive to group work, away from any of the participants' work settings[349]. The meeting involved an iterative consensus-building process, with a mix of individual and group-based activities. Group discussions were facilitated to highlight any ambiguities within the statements and to encourage individuals to share and discuss their scoring rationale[348]. To minimise any potential group pressure for conformity, time was allocated within the session for members to undertake re-rating on an individual basis[352].

Feedback and re-rating

At each stage, participants were provided with written feedback of their own scores and the aggregated scores of the whole group in the form of the group median, interquartile and absolute range of responses for all statements[347]. In addition, participants received a copy of any free text commentary they had included in their questionnaires as an aide memoir. In round two, discussions were focussed around the 10 prioritised statements. In round three, any statements where group IQR was greater than two were discussed, along with any other issues raised by participants.

Facilitation

The importance of appropriate facilitation is consistently highlighted in evaluations of the NGT[348,355,358]. Recommendations include the use of a facilitator experienced in running the NGT process[348] and the need for facilitators to possess expertise relevant to the topic, while remaining objective in their approach[353]. The facilitator role has been summarised as process management[352]; facilitating the timing and focus of discussions;

managing the group to ensure an appropriate dynamic, equal representation and free exchange of ideas[348] and documenting changes as the meeting progresses[355].

In this study, the nominal group meetings were co-facilitated by the project researcher and a research team member with extensive training and experience in running consensus groups. In addition, another team member acted as an observer, to make a non-attributable record of the process and dynamics relating to the consensus discussions, which were used as a reference source during the analysis process.

5. Collation of responses and development of position statement on falls intervention programme

Following completion of the NGT meetings, the final participant responses were summarised into a position statement which aimed to represent the consensus of the participants. Participants were invited to comment on a draft of the position statement as part of the data triangulation process. It is intended that the final position statement forms the basis of the delivery plans for the proposed falls intervention.

5.4.4 Ethical approval

Ethical review

Ethical approval was gained from both the University of Plymouth Faculty of Health Ethics Committee and The South West (2) NHS Research Ethics Committee (Ref 13/SW/0309), taking into account the ethical principles first presented by Beauchamp and Childress[362,363]. Although there were minimal risks to participants, considerations were made to the following aspects related to participant well-being:

Fatigue and mobility issues

As fatigue is common in MS, regular rest breaks were scheduled into each session, and participants were invited to take breaks whenever required. All meetings were undertaken in accessible venues, in order to minimise any risk to participants with mobility limitations.

Potential distress

During the workshop, aspects of living with MS and how it had impacted on the participants' ability to exercise were discussed. The facility to take time out from the session, alongside support from a member of the team was provided at each NGT session if anyone became distressed at any point. Participants were also signposted to other sources of support (e.g. MS Society support service) after the workshop where required.

Professional considerations

As the nominal group session included a detailed discussion of an area of clinical practice, there was a risk that poor or malpractice may be disclosed. To address this, professional participants were reminded at the outset of their requirement to adhere to professional standards and informed that should anything be disclosed during the session to raise concern then this would be necessarily reported to their line manager. MS participants would also have been supported to report any issues relating to their experiences through local patient advice and liaison services (PALS) or via the Patients' Association helpline had any issues arisen.

5.4.5 Data analysis

Quantitative data analysis

Statement rating scores

Data analysis was an on-going process. Summary data of the Likert scale trigger statement data were presented at each stage, with participants receiving individualised score sheets showing group median, interquartile and absolute range alongside their responses for each statement to enable comparison and to act as a trigger for the facilitated discussions (appendix 7.4.2). On completion of the process, the aggregated median, IQR and absolute range for all participants was calculated, both within and across all three nominal groups.

Evaluation of consensus/agreement

A wide variety of methods of evaluating the results of NGT studies have been reported[349], however the two main outputs are assessment of consensus and evaluation of agreement. In the NGT literature, 'consensus' has been described as 'a single statement (or set of statements) that all participants accept (or at least no one disagrees with strongly enough to veto)' [349] (page 20). A range of definitions and measures of consensus have been used, and there are no definitive guidelines as to how this should be assessed[353]. One method recommended is the division of Likert scale responses into three as follows, with all scores for a statement needing to fall within one of the pre-determined bands in order to be classified as achieving 'consensus'[346]:

Scores of 1-3: Disagree

Scores of 4-6: Neutral

Scores of 7-9: Agree

There is however, recognition that a simple yes/no assessment of consensus may be somewhat reductionist, failing to recognise the range of opinion and reasoning informing the decision making process[349].

By contrast, assessment of 'agreement' seeks to identify any 'central tendency' among the group, and to indicate the range and spread of opinion around this point[349]. Methods using simply the median and IQR are criticised as having the potential to significantly impact on results since they exclude scores which represent outlying viewpoints[349]. Therefore a more appropriate assessment is the calculation of the mean deviation from the median (MDM) for each statement[348,364]. The MDM is calculated as:

$$\frac{Sum\ of\ individual\ deviations\ from\ the\ median}{Number\ of\ participants}$$

A further stage in the analysis of agreement is the categorisation of the MDM to indicate strong, moderate or weak agreement[348,364]. This is undertaken by calculating the round one absolute MDM (sum of the MDM for each statement divided by the total number of statements). The resulting absolute MDM is then split into thirds.

Statistical analyses

The ordinal Likert scale data was analysed using non-parametric statistics. Four main analyses were carried out:

1. The individual rating scores for each round for all participants were compared using the Wilcoxon signed-rank test with a Bonferroni correction for multiple analyses[217].
2. The level of agreement for each statement (as represented by the MDM) was compared between rounds using a Wilcoxon signed-rank test as above.
3. Comparison of scoring between the three nominal group meetings was undertaken using the Kruskal-Wallis H test. *Post hoc* analyses was undertaken

for any statements where significant differences between the groups were found, using Bonferroni adjusted Mann-Whitney U tests[217].

4. Analysis of the scoring between professional and service user participants was undertaken using a Mann-Whitney U test.

Qualitative data analysis

The NGT process generated two types of qualitative data; free-text responses from the trigger statement questionnaires and transcriptions from the NGT meetings. It is acknowledged these data represent different forms of communication. However, comparison suggests that whilst written data tends to contain less elaboration and depth of emotion, the content and messages are generally similar[365,366]. In this study, free-text responses were recorded on a spreadsheet at each stage of the NGT process, whilst group meetings were audio recorded and fully transcribed on completion of each session. The content of the two data sources was checked for similarity following transcription and subsequently combined for analytical purposes. Anonymised transcribed data were then entered into NVIVO and analysed thematically using a pragmatic process of data immersion, generation of categories and themes, coding and interpretation[367].

Data integration

The results from the nominal group process included a mix of quantitative (statement ratings scores) and qualitative (free-text comments and nominal group session transcripts) data, providing complementary information. As recommended by Bryman[368], the qualitative and quantitative data was initially analysed separately and subsequently combined as appropriate to meet the study objectives. The results section initially includes an overview of the quantitative data; however the detailed discussion of the quantitative responses to individual statements has been integrated with the qualitative data for clarity.

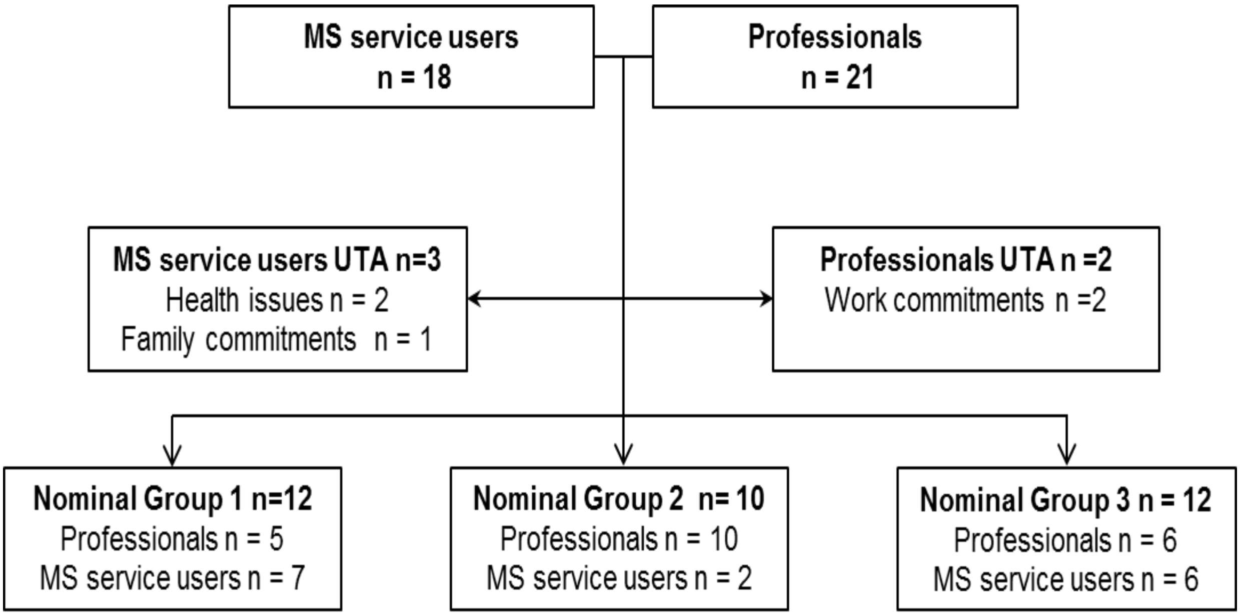
5.4.6 Study quality

The study methods, analyses and reporting were carried out in accordance with best practice guidance for qualitative[369] and mixed-methods research[370].

5.5 Results

5.5.1 Recruitment and participant characteristics

Thirty nine people were recruited, of whom five were unable to attend the meetings, leaving 34 participants (Figure 5-3). Of these, 15 were people with MS and 19 represented a range of professional groupings (Table 5-1).



UTA: unable to attend

Figure 5-3: Participant flow chart

Professionals	Profession	Specialism	Number
	Therapy assistant	Rehabilitation	1
	Service Commissioner	Long term conditions	1
	Specialist Nurse	MS	2
	Occupational Therapist	Community rehabilitation	1
		Neuro rehabilitation	1
		Falls Service lead	2
	Physiotherapist	Community (general)	5
		Community (neurology)	3
		Consultant neurology	1
		Falls specialist	1
		Private (neurology)	1
MS service users	**Self- reported MS Classification**		
		Relapsing remitting	6
		Primary progressive	2
		Secondary progressive	5
		Other/Unknown	2
	Gender		
		Female	11
		Male	4
	Years since diagnosis		
		0 - 5	2
		6 - 10	5
		11 - 15	3
		16+	5
	Mobility		
		Walking unaided	7
		Walking with stick(s)/ crutches	7
		Walking with frame/ wheelchair	1
	Falls status (self-report)		
		≥2 falls in past year	7
		1 fall in the past year	2
		No falls reported	6

Table 5-1: Participant characteristics

5.5.2 Quantitative analysis

All participants completed all three ratings rounds, although the completion rate for individual statements varied between 94% and 100%. Overall completion rate was 98.5% across all three rounds.

Statement rating scores (all participants)

A summary of the results of the rating analysis for all participants is shown in Table 5-2. Overall, there was minimal change in the median and IQR for any of the statements, with no significant difference in the scores between rounds one and three (p>0.05).

Analysis of consensus/agreement (Table 5-2)

Using the Jones definition[346], consensus was reached on only two statements (statements two and three), both concerning programme content. In the overall analysis of agreement, there was a significant difference in the MDM between each of the rounds (p<0.017), with decreasing values for all statements between the rounds indicating an increase in the level of agreement with each round of discussion and re-rating. There was no association between those statements prioritised for discussion and the degree of consensus or agreement achieved (Table 5-3).

In the classification of the *level* of agreement using the Vella categorisation procedure[364], absolute mean deviation for round one was 1.38, resulting in cut-offs for low, medium and high agreement as follows:

- High agreement: MDM ≥0.93
- Moderate agreement: MDM 0.47- 0.92
- Low agreement: MDM ≤0.46

In the final rating round agreement for 16 statements was ranked as low, with four statements ranked as moderate (statements 1, 2, 3 and 19); none of the statements were ranked as having high agreement.

Comparisons between groups

There were significant differences in the scores between the three nominal group meetings in all three rounds (Table 5-3), with four statements rated significantly differently in round one, seven in round two and six in round three. Three statements were consistently scored differently between the groups (statements 5, 14 and 15), two were scored differently in two of the rounds (statements 9 and 13) and five statements were scored significantly differently in one round only (statements 2, 16, 18 and 19). *Post hoc* analyses indicated that the groups where significant differences occurred most frequently were groups two and three, whilst the least differences were between groups one and three.

When professional and MS participant scores were compared, there was a significant difference between the average scoring on individual statements in all three rounds (Table 5-4, Table 5-5). The number of statements where there was a significant difference in scoring decreased across the rounds, with only two statements having a difference in scoring between the two groups in round three. In all instances where there was a difference in scoring between the groups, the MS service user median was higher.

Number	Statement	Median scores (Interquartile range)			Absolute range			Mean deviation from the median (MDM)		
		R1	R2	R3	R1	R2	R3	R1	R2 *p0.001*	R3 *$p<0.001$*
1	Reducing falls should be a primary goal of the programme	8 (2)	8 (2)	8 (1)	5-9	3-9	3-9	1.00	0.97	0.91*
2	People with MS should be given specific exercises to carry out to improve balance	8 (1)	8 (1)	8 (0)	4-9	6-9	6-9	0.85	0.62	0.52*
3	Advice to help people cope with falls should be a key part of any falls programme	9 (1)	9 (1)	9 (1)	6-9	7-9	7-9	0.47	0.50	0.58*
4	Exercise is more effective when carried out in a group	6.5 (3)	6 (2.75)	6 (2)	3-9	3-9	4-9	1.50	1.44	1.12
5	Exercises should be done on a daily basis	7.5 (2.75)	7 (2)	7 (2)	2-9	2-9	2-9	1.53	1.32	1.24
6	Exercising for an hour at a time is unrealistic	6.5 (3)	6 (3)	6 (2)	1-9	2-9	2-9	1.68	1.55	1.33
7	Participants should be able to choose the types of exercise in their falls programme	7 (2)	5 (2)	6 (2)	2-9	3-8	2-9	1.50	1.15	1.24
8	People should be able to access the falls programme without having to be referred	8 (2)	8 (2)	8 (2)	4-9	5-9	3-9	1.19	0.94	1.06
9	Any sessions outside the home should be organised in a hospital setting	2 (2)	2 (2.75)	2 (2)	1-9	1-9	1-9	1.42	1.35	1.36
10	Exercise should always be supervised	5 (3)	5 (3)	5 (3)	1-9	1-9	1-9	1.79	1.79	1.67
11	It is unreasonable to expect people with MS to do balance exercises that are difficult for them	4 (4)	4 (2.75)	4 (2)	1-9	1-8	1-8	1.97	1.56	1.48
12	The role of the programme leader should be to push participants to their limits	5 (3)	5 (1)	6 (2)	1-8	1-7	2-8	1.55	1.38	1.12

Number	Statement	Median scores (Interquartile range)			Absolute range			Mean deviation from the median (MDM)		
		R1	R2	R3	R1	R2	R3	R1	R2 *p0.001*	R3 *p<0.001*
13	Programme leaders must have formal qualifications	7.5 (3)	8 (3)	7 (3)	3-9	3-9	4-9	1.56	1.41	1.21
14	A falls programme should be provided within existing resources	5 (3)	5 (3)	5 (3)	1-9	1-9	1-9	1.88	1.82	1.70
15	It is reasonable to ask participants to pay a contribution to the cost of any attended sessions	5 (1.75)	5 (1)	5 (2)	1-8	1-8	2-8	1.00	0.91	1.00
16	Living in a remote location means that taking part in a programme away from home is impossible	5 (3)	5 (2)	5 (2)	1-8	1-9	2-9	1.56	1.41	1.30
17	Being able to see improvements in function is more important than measures of balance or falls	7 (2)	6 (2)	7 (2)	3-9	3-9	4-9	1.32	1.33	1.06
18	Daily diaries are essential to check that exercises are carried out	6 (2)	5 (2)	5 (2)	2-9	1-9	2-9	1.36	1.64	1.52
19	Programme leaders should regularly discuss progress with individual participants	8 (2)	8.5 (1)	8 (1)	5-9	5-9	5-9	0.94	0.76	0.76*
20	It is unrealistic to expect people to undertake a falls programme for 3-6 months	3 (2)	3 (2)	3 (2)	1-9	1-9	1-9	1.53	1.38	1.30

R1: round 1; R2: round 2; R3: round 3. *P= significance using Wilcoxon signed-rank test; *statements classified as having moderate agreement* [364]; Scoring ranges: Scores of 1-3: Disagree; Scores of 4-6: Neutral; Scores of 7-9: Agree; MDM scoring: lower MDM indicates greater agreement

Table 5-2: Nominal group rating results (all participants)

Statements 1-10

Statement	1	2	3	4	5	6	7	8	9	10
Round 1 median (IQR)										
Group 1	8 (1.25)	8 (0.25)	9 (0.25)	6.5 (2.25)	8 (2.5)[c]	7 (3)	7 (2.25)	7.5 (2)	2 (1.25)	5 (3)
Group 2	8.5 (2.75)	8 (2.5)	8.5 (1)	7 (3)	6 (1.5)	5.5 (2.5)	5 (1.75)	9 (2)	3.5 (3.75)	5 (1.75)
Group 3	9 (1.25)	9 (1)	9 (0.25)	5 (2.5)	8 (1.25)[b]	7 (1.5)	7 (2.25)	8 (2.5)	2 (2)	5 (5.5)
Round 2 median (IQR)										
Group 1	8 (0.5)	8 (1)	9 (0.25)	6.5 (2.25)	7 (1.25) [c]	7 (3)	5 (2.25)	8 (2)	2 (1.25)	5 (1.5)
Group 2	7.5 (1)	8 (1)	8.5 (1.75)	6.5 (1.75)	6 (1)	5.5 (2.5)	5 (1.75)	9 (1.5)	4.5 (2)	5 (1.5)
Group 3	8.5 (2.25)	8.5 (1)	9 (1)	5 (3)	9 (1.25) [b]	5 (1.5)	6 (2.5)	8 (2.25)	2 (2)	4 (6)
Round 3 median (IQR)										
Group 1	8 (1)	8 (1)	9 (1)	6.5 (1.25)	7 (1) [c]	6 (2.25)	6.5 (1.25)	8 (1.25)	1.5 (1) [a]	5 (1.5)
Group 2	7.5 (1)	8 (1)	8.5 (1.75)	6.5 (1)	6 (0.75)	6 (2.25)	5 (1.5)	9 (1.5)	4.5 (2)	5 (1.5)
Group 3	7 (1.5)	8 (1)	8 (1)	5 (2.5)	8 (2) [b]	6 (1.5)	7 (2)	7 (2.5)	2 (1)	4 (4.5)

Statements 11-20

Statement	11	12	13	14	15	16	17	18	19	20
Round 1 median (IQR)										
Group 1	4 (2.25)	4 (2.5)	7 (3.25)	5 (2)	5 (0.25) [c]	5 (2.25)	7 (2.5)	6 (1)	8 (2)	2.5 (1)
Group 2	3.5 (3.75)	4.5 (2.5)	6 (3.5)	3.5 (2.75)	5 (0)	3.5 (1.75)	7 (2.75)	6 (3.25)	7.5 (2)	3 (2.5)
Group 3	5.5 (4)	5.5 (2.25)	8.5 (1.25)	7 (1.75) [b]	7 (1.25) [b]	5.5 (2) [b]	6.5 (2.25)	5 (0.75)	9 (1)	3.5 (4)
Round 2 median (IQR)										
Group 1	4 (1.5)	5.5 (4)	8 (2.25)	5.5 (1.5)	5 (0.25)	5 (1.25)	6 (2.5)	6.5 (2)	8 (1.25)	2.5 (1.25)
Group 2	4 (2.75)	5 (1)	6 (1.75)	3 (1.5) [a]	5 (0.75)	4 (1)	7 (1)	4 (3.75)	8 (1.5)	3 (1.75)
Group 3	4 (4.25)	6 (1)	9 (1) [b]	5.5 (2.75)	7 (1.25) [b]	5.5 (2.5)	6 (3)	5 (2)	9 (0.25)	3 (3)
Round 3 median (IQR)										
Group 1	3.5 (2)	7 (1.5)	8 (2)	5 (2.25)	5 (1)	5 (1.5)	7.5 (2.5)	6.5 (1.25)	8 (2)	2 (1)
Group 2	4 (2.75)	5.5 (1)	6 (2)[a]	3 (1)[a]	5 (0.75)	4 (1)	7 (0.75)	4 (2.75)[a]	8 (1.5)	3 (1.5)
Group 3	4 (4.5)	6 (2)	8 (1.5)[b]	5 (2)[b]	7 (1)[b]	5 (3)	7 (2.5)	5 (1.5)	9 (1)	4 (3)

Scoring ranges: Scores of 1-3: Disagree; Scores of 4-6: Neutral; Scores of 7-9: Agree; [a]=significant difference between Group 2 and Group 1 scoring; [b]=significant difference between Group 2 and Group 3 scoring; [c]= significant difference between Group 1 and Group 3 scoring (all *p<0.017)*; =statements prioritised for discussion round 1; =statements prioritised for discussion round 2

Table 5-3: Comparison of scoring between nominal group meetings

STATEMENT	1	2	3	4	5	6	7	8	9	10
ROUND 1										
All participants median (IQR)	8 (2)	8 (1)	9 (1)	6.5 (3)	7.5 (2.75)	6.5 (3)	7 (2)	8 (2)	2 (2)	5 (3)
Professional Median (IQR)	8 (3)	8 (2.5)	9 (0.5)	6 (2)	6 (2.5)	5 (2.5)	5 (2)	7.5 (2.75)	2 (1.5)	4 (3)
MS service user Median (IQR)	9 (1)	8 (1)	9 (1)	9 (3.75)	8 (2)	7 (3)	7 (1)	8 (2)	3 (3)	6.5 (3)
p	0.10	0.12	0.54	0.87	0.02*	0.02*	0.05	0.44	0.02*	<0.01*
ROUND 2										
All participants median (IQR)	8 (2)	8 (1)	9 (1)	6 (2.75)	7 (2)	6 (3)	5 (2)	8 (2)	2 (2.75)	5 (3)
Professional Median (IQR)	8 (2)	8 (0.5)	9 (1)	5 (2)	6 (2.5)	5 (1.5)	5 (1.5)	9 (2)	2 (2.5)	5 (3)
MS service user Median (IQR)	8 (1.5)	8 (1)	9 (1)	7 (3.5)	7 (1.5)	7 (2.5)	6 (2.75)	8 (2)	2 (2.5)	6 (3)
p	0.89	0.20	0.76	0.08	0.03*	0.13	0.79	0.36	0.57	0.02*
ROUND 3										
All participants median (IQR)	8 (1)	8 (0)	9 (1)	6 (2)	7 (2)	6 (2)	6 (2)	8 (2)	2 (2)	5 (3)
Professional Median (IQR)	7.5 (1)	8 (1)	9 (1)	6 (2)	6 (1.75)	5.5 (2)	6 (2)	9 (2)	2 (2)	4 (2.75)
MS service user Median (IQR)	8 (2)	8 (1)	9 (1)	7 (1.75)	7 (2)	6 (2)	6 (1)	8 (2)	2 (2.5)	6 (3)
p	0.25	0.07	0.97	0.40	0.10	0.38	0.69	0.76	0.37	0.01*

IQR: Inter-quartile range; Scoring ranges: Scores of 1-3: Disagree; Scores of 4-6: Neutral; Scores of 7-9: Agree; p: Significance using Mann-Whitney U test; *: $p < 0.05$

Table 5-4: Comparison of scoring between professional and MS service user participants (statements 1-10)

STATEMENT	11	12	13	14	15	16	17	18	19	20
ROUND 1										
All participants median (IQR)	4 (4)	5 (3)	7.5 (3)	5 (3)	5 (1.75)	5 (3)	7 (2)	6 (2)	8 (2)	3 (2)
Professional Median (IQR)	3 (2.5)	5 (2.75)	8 (3)	5 (4)	5 (1)	4 (2.5)	6 (2.5)	6 (1.75)	8 (2)	3 (3.5)
MS service user Median (IQR)	6 (3.5)	5 (3)	7 (4)	6 (2.5)	5 (2)	6 (2)	7 (1)	6 (2)	9 (1)	3 (1)
p	0.01*	0.79	0.44	0.15	0.76	0.01*	0.01*	0.87	0.18	0.73
ROUND 2										
All participants median (IQR)	4 (2.75)	5 (1)	8 (3)	5 (3)	5 (1)	5 (2)	6 (2)	5 (2)	8.5 (1)	3 (2)
Professional Median (IQR)	4 (3)	5 (1.5)	8 (3)	4 (3)	5 (1)	5 (2)	6 (2)	5 (3.25)	9 (1)	3 (3)
MS service user Median (IQR)	4 (3.5)	5.5 (2)	8 (2)	6 (2)	5 (1.5)	5 (2)	7 (2.75)	7 (2.5)	8 (1)	3 (1.5)
p	0.19	0.26	0.77	0.03*	0.80	0.11	0.39	0.10	1.00	0.91
ROUND 3										
All participants median (IQR)	4 (2)	6 (2)	7 (3)	5 (3)	5 (2)	5 (2)	7 (2)	5 (2)	8 (1)	3 (2)
Professional Median (IQR)	4 (2.5)	6 (1.75)	7.5 (2.75)	3.5 (2.75)	5 (1)	4.5 (2.75)	7 (1.75)	5 (2.5)	8 (1)	3 (1.75)
MS service user Median (IQR)	4 (3.5)	6 (2)	7 (1.5)	5 (2)	5 (2)	5 (2.5)	7 (2)	6 (2.5)	8 (1.5)	3 (2)
p	0.33	0.88	0.56	0.01*	0.83	0.12	0.28	0.11	0.81	0.86

IQR: Inter-quartile range; Scoring ranges: Scores of 1-3: Disagree; Scores of 4-6: Neutral; Scores of 7-9: Agree; p: Significance using Mann-Whitney U test; *: $p < 0.05$

Table 5-5: Comparison of scoring between professional and MS service user participants (statements 11-20)

5.5.3 Thematic analysis

The thematic analysis data are presented according to the five main objectives, with sub-themes for each:

1. Programme outcomes
    - Programme aims
    - Monitoring of progress and outcomes
2. Programme content
    - Education elements
    - Exercise elements
        i. Type of exercise
        ii. Choice
        iii. Difficulty and challenge
3. Programme format
    - Access
    - Structure and setting
    - Frequency, intensity and duration
4. Programme Leadership
    - Role of the leader
    - Leadership approaches
    - Skills and attributes
5. Programme sustainability
    - Resources/funding
    - Participant contribution

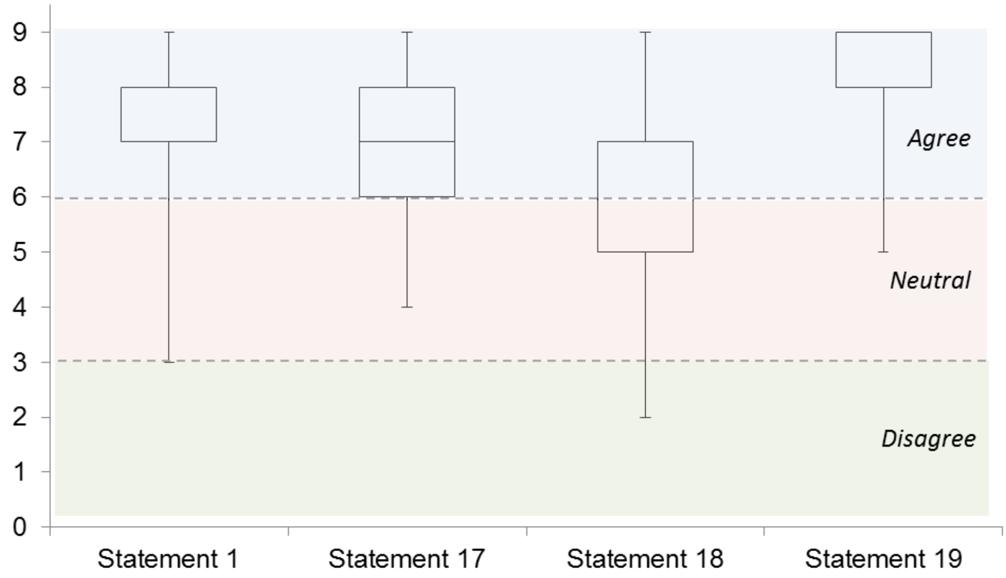
Each theme is discussed below, with a presentation of the relevant round three ratings scores included in each section. Participant quotations are referenced by group meeting and participant classification as follows:

Quotation key:

- NG1P: meeting 1 Professional participant
- NG1MS: meeting 1 MS service user participant
- NG2P: meeting 2 Professional participant
- NG2MS: meeting 2 MS service user participant
- NG3P: meeting 3 Professional participant
- NG3MS: meeting 3 MS service user participant

1. Programme outcomes

Outcome statements



Box refers to median and inter-quartile range, whiskers denote TOTAL range

Figure 5-4: Graphical summary of programme outcome statements

Statement		Median (IQR)	Range	MDM *p<0.001*
1	Reducing falls should be a primary goal of the programme	8 (1)	3-9	0.91
17	Being able to see improvements in function is more important than measures of balance or falls	7 (2)	4-9	1.06
18	Daily diaries are essential to check that exercises are carried out	5 (2)	2-9	1.52
19	Programme leaders should regularly discuss progress with individual participants	8 (1)	5-9	0.76

IQR: inter-quartile range; Scoring: Scores of 1-3: Disagree; Scores of 4-6: Neutral; Scores of 7-9: Agree; MDM: mean deviation from the median- lower MDM indicates greater agreement

Table 5-6: Programme outcome statement scoring (round 3 scores)

Programme aims

The group rating scores demonstrated agreement that reducing falls should be a primary goal of the programme (final combined median score 8, IQR1). However, there was also recognition of the importance of functional outcomes (final median score 7, IQR 2). Group discussions expanded on this, suggesting that reducing falls should not be the sole primary outcome, as there was a need to decrease falls without a compromise to levels of activities and participation.

> *If I was commissioning a group and everyone in the group had fallen 3 times before they joined and no times afterwards, but they had spent 6 weeks being miserable, or living lesser lives because they were taking less risks as a result, then that's not an outcome I would be particularly interested in. NG3P14* (service commissioner) Verbal comment

> *Okay, what we want to do is to stop them falling over, but what are they going to do then? Okay, so they have less falls, and …they might not break a hip; from the NHS point of view that's great and from the patient's point of view it's pretty good too. But we've had patients that suddenly go out and get on a bus and go shopping in town centres: that's what makes the difference. NG2P9* Verbal comment

It was also highlighted that focusing purely on reducing falls would preclude individuals who are yet to fall from accessing the programme. It was highlighted that as a preventative strategy, including those at risk of falls may be cost-effective in the long-term.

> *The discussion has made me think. I don't fall (yet) so reducing falls is a difficult indicator. Maybe the focus is on improving/maintaining balance and coordination of muscular strength/use with a view towards reducing risk of falling. NG3MS16* Written comment

There was recognition that the high frequency of falls in people with MS could mean that aiming to completely prevent falls may not be realistic. It was suggested that other outcomes such as a decrease in injury as a result of falls, increased confidence and decreased fear should also be considered as programme aims.

> *You can never stop someone from falling, but educate and reduce the risk factors attributing to falls NG1P 5* Written comment

> *The psychological aspect of falls is very, very important; I had one severe fall in October 2004 and I still remember that, every time and every step I take. NG3MS15* Verbal comment

> *Falls cause injuries - broken/cracked ribs, back injuries etc. which add to the difficulties of MS. NG1MS5* Written comment

> *Falling causes people to lose confidence, and over time reduce their level of activity leading to reduced participation. NG2P8…*

> *…and we also need to look at reducing harm from falls and increasing ability to manage falls which can't be prevented. NG2P12* Discussion excerpt

Developing self-management strategies was also suggested to be an important aspect of the programme. There was a general agreement that awareness of falls risk factors, knowledge and coping strategies should be included as programme aims.

> *Promoting insight and self-directed risk awareness of falls may be an added benefit, building into the early intervention process. NG3P16* Written comment

Other outcomes that were proposed included the tracking of associated cost, including service usage and also the impact of the programme in a wider context including family and carers.

> *It's not just the effect on you; it's the effect on family as well. When I'm trying to walk, everybody stands around in anticipation… Your friends and family are like that, they are very protective and they don't want you to fall, which is very difficult for me because not only does it make me feel bad but it obviously makes them feel quite concerned as well. NG3MS18* Verbal comment

> *The person walking with you is more on edge than you are as far as that's concerned. It affects the people around you sometimes more than you yourself, because you've learned to get over the embarrassment about falling, it's just one of those things that you do. NG3MS20* Verbal comment

Monitoring of progress and outcomes

The importance of regular monitoring of outcomes was recognised in all groups, with the final ratings score reflecting strong agreement that progress should be discussed regularly (final group median 8, IQR 1). There was recognition that outcomes needed to demonstrate the overall effectiveness of the programme at both a service and an individual level;

> *We have to measure something; we're not going to get any money otherwise! NG2P11* Verbal comment

> *An audit trail of effectiveness needs a balance of both functional* [patient centred] *and* [clinical] *outcome measures to obtain funding. NG1P 5* Written comment

The challenges of selecting outcome measures that were reliable, responsive to change, broad enough to match service needs and specific enough to match individual priorities was highlighted. This was perceived to be a particular issue given the potential for MS specific issues to impact on the ability of outcome measures to accurately reflect effectiveness. Participant narratives were suggested as a valuable supplement to outcome measures which may address this issue.

> *You need to make sure that the outcome measures actually fit with what the people want. NG2P8* Verbal comment

> *The questionnaires and things don't always reflect what people tell you. It's quite depressing sometimes but somebody who's done really well, they are really happy, and they fill in their confidence questionnaire and it's not that different. You know that they've benefited and that they're feeling better and they're going out but it doesn't always get captured by the numbers. NG2P9* Verbal comment

> *Improvements in function should be one of the main indicators* [however] *my balance varies; my MS fluctuates so these measures will. It is important to somehow measure the individual's perception of how they are feeling, and how at risk of falling they perceive themselves to be. NG3MS16* Verbal comment

> *We must not only measure, but use narratives as well. NG2P 7* Written comment

Some panel members suggested that regular measuring of outcomes could be a positive experience for participants, supporting the educational elements of the programme, increasing awareness and as a motivational aid. However, there was recognition of the potential for participants to feel 'over assessed'. Panel members suggested that a collaborative approach which included clear explanations about the importance of outcome measurement and monitoring may help this aspect.

> *We use a balance scale in our groups, and quite a lot of our patients want to know how they got on the other end. They love the fact when they've improved; we don't always even tell them how much by, you can just say your score is better. NG2P11...*

> *…I just think if you’re a patient, you want to see an improvement in yourself and you don’t care the hell what’s going on a piece of paper and just want to make sure that you are doing well, and that’s encouraging. NG2MS10* Discussion excerpt

> *I think we have to be very careful of measurement, I think that sometimes it’s overused and not explained, the thing people kept telling me was that they felt judged, they felt demeaned by measurement and they really didn’t enjoy it. NG2P7* Verbal comment

The use of falls diaries as part of the monitoring process was the subject of considerable debate within the panel meetings, and the final group median score of 5 (IQR 2, absolute range 7) reflected the diversity of opinions. There was general recognition that diaries had the potential to be a useful tool, both for progress monitoring, motivation and as an aide memoir for people with cognitive or memory issues, which are common MS symptoms.

> *Diaries can be motivational and enable you to get into a routine. NG3MS17* Verbal comment

> *Useful to ensure that exercises carried out regularly and consistently. Easier to abandon exercise altogether if you are not documenting everything (a bit like cheating on a diet). NG2P 13* Written comment

> *Diaries may be especially helpful for people with cognitive impairment NG3P19* Written comment

However, there was recognition that the impact of using a diary was personal, with some feeling that daily diary completion could be very burdensome. It was suggested that choice within the diary monitoring process, and different options may be helpful. There was also discussion about who should check the diaries – some considered that checking by programme facilitators could feel intrusive and reduce self-efficacy and independence.

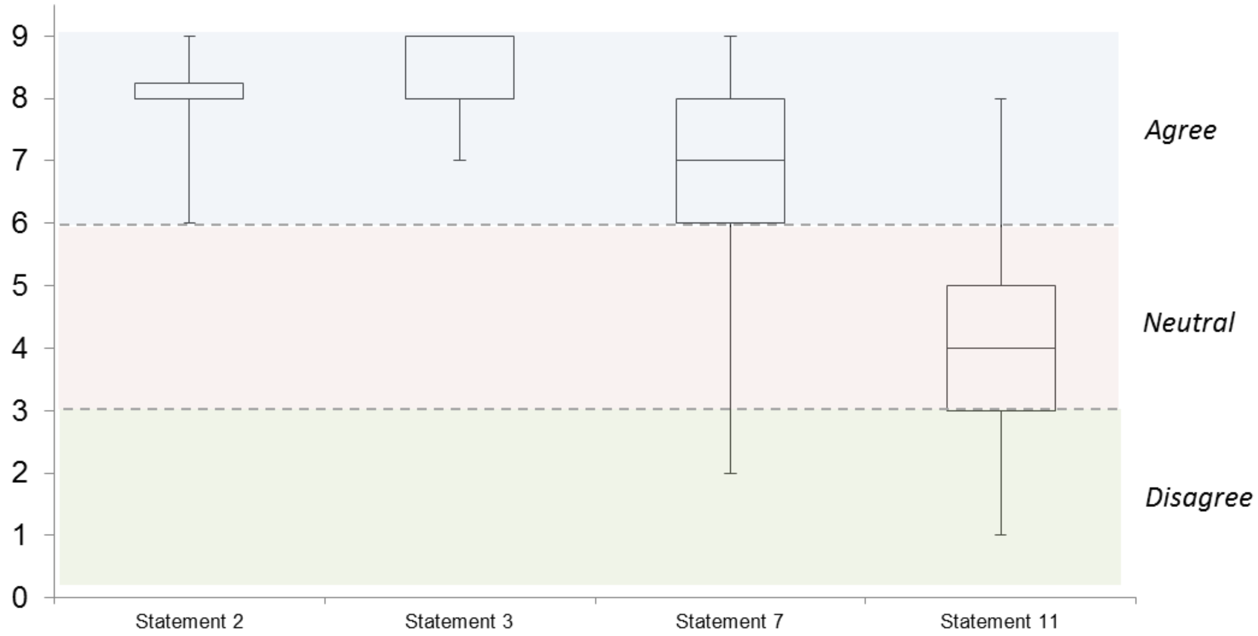
> *The system should be easy to use or it will increase the hassle factor and get abandoned. NG2P 13* Written comment

> *That’s the thing I really hate - I have problems with, but everybody, they hate bits of paper to fill in. You want to be able to talk to them about it. NG2MS10* Verbal comment

If a person wants to do them and it helps, then fine - but it could become a bit 'schooly'. NG3P 14 Verbal comment

2. Programme content

Content statements



Box refers to median and inter-quartile range, whiskers denote TOTAL range

Figure 5-5: Graphical summary of programme content statements

Statement		Median (IQR)	Range	MDM *p<0.001*
2	People with MS should be given specific exercises to carry out to improve balance	8 (0)	6-9	0.52*
3	Advice to help people cope with falls should be a key part of any falls programme	9 (1)	7-9	0.58*
7	Participants should be able to choose the types of exercise in their falls programme	6 (2)	2-9	1.24
11	It is unreasonable to expect people with MS to do balance exercises that are difficult for them	4 (2)	1-8	1.48

IQR: inter-quartile range; Scoring: Scores of 1-3: Disagree; Scores of 4-6: Neutral; Scores of 7-9: Agree; MDM: mean deviation from the median- lower MDM indicates greater agreement

Table 5-7: Programme content statement scoring (round 3 scores)

There was consensus that the falls programme should include both exercise and educational content (educational elements, final median score 9, IQR 1; exercise elements final median score 8, IQR 0). In all three sessions there was recognition that, whilst these elements are part of the majority of existing falls services, the type and format of the content of an MS falls programme would be different.

> *People with MS have very separate needs to 'average' users of falls services (e.g. over 65's) NG3P17* Written comment

Educational elements

The statement relating to the educational content of the programme was not explicitly discussed at the NGT meetings due to the high level of agreement in the ratings scores. However, within the free-text comments it was highlighted that the educational elements of the programme should include general falls prevention/ management content; plus psychological aspects such as fear of falling and MS specific issues, including the impact of fatigue.

> *It* [Education] *should be a standard component, but not just generic advice NG2P13* Written comment

> *Including practical advice on what to do in the event of a fall, in order to minimise injury. Should also include environmental and personal aspects. NG3P14* Written comment

> *Education and practical skills; prevention, confidence building, coping strategies. NG3P15* Written comment

> *Strategies to avoid a 'long lie', getting up and raising the alarm are vital. NG3P20* Written comment

> *Should also include impact of sleep deprivation / fatigue NG2P7* Written comment

The importance of individualised advice and content was emphasised, alongside the need to include family and carers in this process.

> *Advice would be good for both the person with MS and family and friends. NG3MS 18* Written comment

Participants highlighted the need to consider cognition and memory issues when devising and delivering the falls programme, suggesting that supporting materials in a range of formats would be useful to supplement any face-to-face content.

Exercise elements

Amongst the participants there was a strong perception that exercise should be integral to any falls programme. There was considerable discussion in the NGT meetings as to what constituted 'exercise': For some this related to general day-to-day physical activities such as walking when shopping, while others perceived exercise to be a specific and formal exercise programme, typically prescribed by a physiotherapist. Despite extensive debate, there remained a diversity of opinion. Regardless of format, exercises that had a strong functional element were considered most appropriate.

> [Exercise] *is essential to a successful programme. NG2MS12* Written comment
>
> *The key part of an MS-based falls prevention programme should be individualised exercises to work on the key balance, strength and functional difficulties, and taking into consideration factors such as fatigue and cognition. NG2P13* Verbal comment
>
> *'Exercise' means more than just group or formal exercises, and incorporates activity and movement within everyday life. NG1P6* Written comment
>
> [Exercise should be]... *linked to daily functions and activities for maximum benefit and minimum disruption of daily life. NG3P14* Verbal comment

The importance of specificity in any exercise prescription was emphasised, with suggestions that exercises should be individually tailored and formatted to take account of MS specific problems. Participants also advocated that the most effective exercises were simple to perform and targeted to participant goals.

> *We are often trying to get the exercises varied and interesting but also collaborating so they are both individualised and you know chosen from evidence-based things that we know would work. NG3P15* Verbal comment
>
> *It's got to be possible and also suitable; you can't just use ridiculous exercises. I think you can have a really ridiculously complicated exercise that becomes impossible to do, it's got to be quite simple. NG2P11* Verbal comment

Choice

The rating scores relating to choice of exercise type within a falls programme highlighted a range of opinion in this area (final median score 6, IQR 2, absolute range 7). Rehabilitation professionals emphasised the need for exercise prescription to be based on best available evidence, potentially limiting the degree of choice within a programme. However, there was recognition that it was important to consider individual preferences for exercise and to be able to tailor a programme in line with evidence-based guidance. The need for an accurate initial assessment to inform and guide exercise prescription was emphasised.

> *The whole point is to follow an evidence-based programme. However, selection within the programme can be possible. NG3P17* Written comment

> *An exercise program needs to have some core elements to be effective, but within that participants should be able to have some flexibility. Also they should be able to practice activities which are important to them. NG2P12* Verbal comment

> *Giving the participant some scope as to which exercise they carry out may enhance compliance as everyone likes different things. NG2P13* Verbal comment

> *It's about the assessment being done properly in the first place so that you can actually gauge, and not make people feel like they failed to do the difficult exercises or bored them with the easy ones, you've kind of been able to slot them into the right place right from the beginning. NG2P20* Verbal comment

Participants with MS highlighted the collaborative aspects of exercise prescription as a significant factor influencing engagement with and adherence to exercise programs. There was recognition that personal choice was important, however there was widespread agreement that professional input was essential to guide and support engagement with exercise. It was emphasised that education as to why specific exercises were important should be an integral aspect, as this was critical to optimise adherence.

> *I would like my goals to be taken into consideration, but equally I need help to identify the exercises that can help me achieve those goals. It's all very well me saying that my balance sucks, but I need someone to say why my balance sucks and what they can do about it. NG3MS16* Verbal comment

> *I still think we have to have a say in what's done, but I also think there are some exercises that may be we are not keen on but we should still probably be doing. So certainly to me it's got to be a two-way street as opposed to just going one way, either way really. NG3MS17* Verbal comment

> *Participants need to have appropriate insight into the benefit of an exercise to increase adherence to the exercise and programme. NG3P20* Written comment

Difficulty and challenge

This trigger statement generated considerable discussion and a range of opinions (final group median 4, IQR 2, absolute range 7). The need for exercises to be challenging in order to be effective was recognised by both professional group members and people with MS; however striking a balance between challenge and achievability was highlighted as a key consideration.

> *My comment is, difficult is okay, impossible is not. NG2MS12* Verbal comment

> *It's just hard, and if it's not hard it won't work. I think it has to be hard for it to work; hard at some degree at any rate. NG2P8* Verbal comment

> *It's getting the balance between, it's got to be challenging enough to actually progress balance, if it's easy you're not going to progress the balance at all; but at the other end if they're too difficult then people give up. You've got to progress, to start something easy and then move up. NG2P10* Verbal comment

Safety, both for participants and professionals, was raised as an important consideration when prescribing highly challenging balance exercise.

> *There's a difference between difficult and safe. As long as they are safe, they are still hard because they are wobbling about, but they are safe. NG2P11* Verbal comment

> *I would be extremely concerned if somebody was standing either side of me and wanting to catch me if I fell. My concern would be for the person, not for me because I seem to bounce, the person who was trying to catch me might injure themselves and that would prevent me from actually attempting the exercise. NG3MS18* Verbal comment

Similarly, it was highlighted that falls programme participants were likely to need significant encouragement and support to develop the confidence to undertake highly challenging balance exercise. There was recognition that lack of confidence was often more of a barrier to exercise and physical activities than physical ability.

> *Participants will usually move away from more challenging exercises and they are usually the ones that they need to participate in to improve their balance. NG1P5* Verbal comment

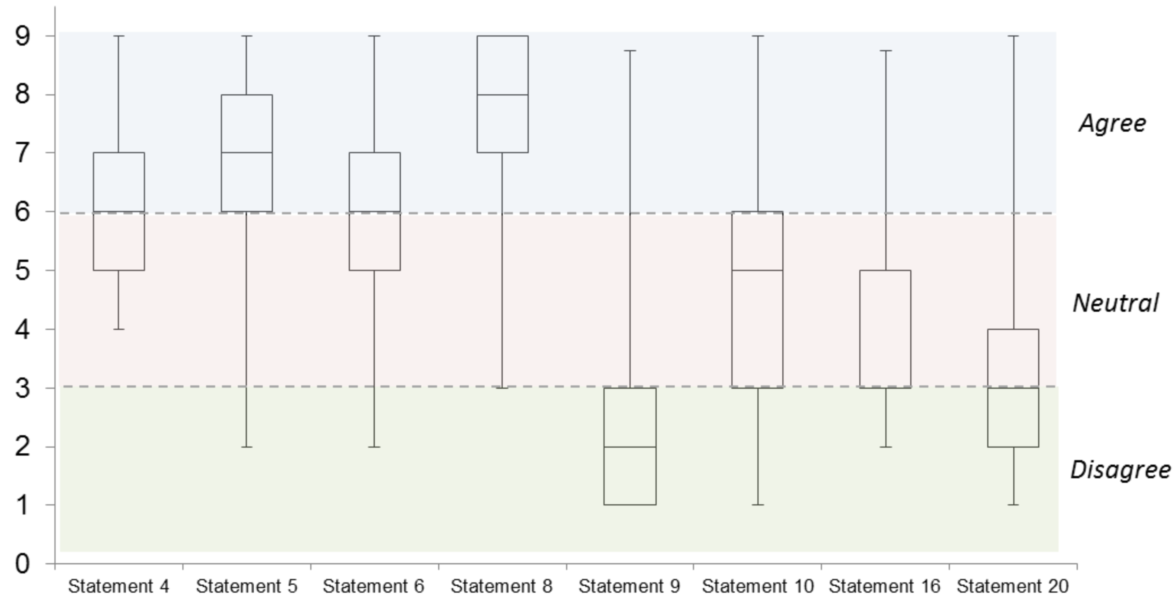
> *I think sometimes you have to push yourself to know what you can and can't do physically and mentally. NG3MS20… You might try those* [difficult] *exercises with a little 'prodding'... NG3MS16. - I think I might need a little bit more than 'prodding'… NG3MS17* Discussion excerpt

The importance of matching level of challenge to level of ability was highlighted as a difficulty, particularly within group exercise settings. Some suggested that the exercises should have a range of potential modifications to vary the level of challenge, thereby enabling progression.

> *I used to do an exercise class, it was 10 core exercises and within each exercise there was a progression, so that everyone can do the same exercise- they're all doing the same thing but the level of difficulty increases, and that worked quite well. NG2P8* Verbal comment

3. Programme format

Format statements



Box refers to median and inter-quartile range, whiskers denote TOTAL range

Figure 5-6: Graphical summary of programme format statements

Statement		Median (IQR)	Range	MDM *p<0.001*
4	Exercise is more effective when carried out in a group	6 (2)	4-9	1.12
5	Exercises should be done on a daily basis	7 (2)	2-9	1.24
6	Exercising for an hour at a time is unrealistic	6 (2)	2-9	1.33
8	People should be able to access the falls programme without having to be referred	8 (2)	3-9	1.06
9	Any sessions outside the home should be organised in a hospital setting	2 (2)	1-9	1.36
10	Exercise should always be supervised	5 (3)	1-9	1.67
16	Living in a remote location means that taking part in a programme away from home is impossible	5 (2)	2-9	1.30
20	It is unrealistic to expect people to undertake a falls programme for 3-6 months	3 (2)	1-9	1.30

IQR: inter-quartile range; Scoring: Scores of 1-3: Disagree; Scores of 4-6: Neutral; Scores of 7-9: Agree; MDM: mean deviation from the median- lower MDM indicates greater agreement

Table 5-8: Programme format statement scoring (round 3 scores)

Access

Panel members identified that barriers to program access should be minimised. There was recognition that barriers varied between people, but a general agreement that referral processes were an obstacle in many situations. This perception was reflected in the scoring for trigger statement 8, suggesting that participants were generally in favour of an open-access system for the falls programme (final group median 8, IQR 2).

> *I suppose there's a variation between some people who will overcome all sorts of barriers to get there because they really want to come, and other people who down the road is too far NG2P7* Verbal comment

> *Referral by a professional can be time-consuming. Self-referral would be best. NG1MS1* Written comment

> *Individual people know what is helpful to them and should be able to refer themselves. NG3MS18* Verbal comment

Self-referral was generally perceived as positive, facilitating personal choice and control, with agreement that those who self-refer may be more motivated to engage.

> *I think people should be encouraged to refer themselves as it is an important 1st step in committing to an exercise programme. People who have self-referred may show greater motivation and/or compliance. NG2P12* Written comment

> *I think it would be nice to be able to refer yourself rather that you relying on going to see your GP or your MS nurse, but they should also be able to mention 'oh this is available', but not necessarily have to do the referral. Because that delays things as well NG3MS17* Verbal comment

There was also recognition that an open access process minimised the 'medicalisation' of the programme, representing a method of access usually associated with lifestyle activities such as yoga and Pilates.

> *Referral makes it sound like it's a patient being referred, you know I don't 'refer' myself to the gym, you choose and you just go. NG3P14* Verbal comment

However, it was identified that self-referral may not suit all individuals, with discussion around the potential for more reticent individuals to be disadvantaged.

> *Self-referral is difficult because you could get a vocal so-and-so like me who is going to go for everything... It could turn into the noisiest get all the input whereas*

> *a person who is suffering more, who needs it who is then either not referred at all or way down the waiting list because there are all these people who are good at making their presence felt but who may not benefit as much. NG3MS16* Verbal comment

Additionally, there was recognition that effective self-referral was dependent upon potential participants and health professionals such as MS Specialist Nurses and Neurologists being aware of resource availability, making signposting and effective communication between providers and service users essential. As in previous studies[371], participants with MS highlighted a general lack of discussion around falls, with a perception that falls were either not recognised as a problem, or were viewed as something to be expected and accepted, almost a 'necessary evil'.

> *Its part and parcel, we tend to, like you say we go down and you don't hurt yourself that much. If my husband falls I tell him to man up! NG3MS17* Verbal comment

> *Equally, we are hearing that even people who say 'I fall over' are not having that discussion* [with medical professionals] *because either the contact is so limited or they don't sense it is important. NG3MS17* Verbal comment

> *One of the things that keeps coming up is the need for information, that people with MS can have information about what is available, because we may be under using it simply by not knowing it's there. NG3MS20* Verbal comment

The need for an assessment process either prior to or on entry to the programme was discussed, with aspects such as medical stability and suitability for the programme being highlighted as important elements.

> *As long as there is an initial assessment* [by a skilled health professional] *to ensure suitability for the individual. NG3P15* Written comment

> *I think it would be reassuring for the leader to have some kind of baseline, to know if one of us has low blood pressure so we are likely to keel over or whatever, its useful information to have. NG3MS16* Verbal comment

> *Within the programme team you need to have someone who can do that initial assessment and medical assessment. NG3P20* Verbal comment

Structure and setting

The scores for the statements relating to programme structure were relatively neutral, with a final group median of 5 for the statement relating to the use of group format (IQR

2). Within the groups, this aspect was explored in some depth. There was recognition that a variety of personal factors may affect peoples' preference for group or individual activities.

> *I've got patients who have MS who will not go to groups, so it's making sure that there is something available for them... and you know I don't want to go to groups either, so everybody's… NG2P9* Verbal comment
>
> *I met a lady last week, she is terrified, she hates seeing people in wheelchairs and people who are struggling. I can sympathise, she's been twice before to different places and she just gets so upset; she says it's not worth it. And I can't argue, what can I say? NG2MS12* Verbal comment
>
> *I know there are also people that, the idea of a group, getting up in front of the group and moving around and looking potentially awkward and uncomfortable and maybe ungainly would be their absolute worst nightmare. So I guess it's about understanding individual's choices and giving the option. NG3P14* Verbal comment

However there was a strong perception that group formats provided important positive aspects. Opportunities to work alongside other people with MS in a group setting offered a strong social element, alongside learning opportunities, problem-solving and motivation from peers.

> *I turn up regularly at the group exercise sessions, partly, probably a third of it is for the camaraderie, the meeting people and seeing everybody is all right, and then you have a laugh. NG2MS12* Verbal comment
>
> *Motivation and adherence to exercise are likely to be enhanced through the peer support achieved through group exercise. Left to your own devices it would be easy for procrastination or fatigue to take over and an exercise regime to be quickly abandoned. NG2P13* Verbal comment
>
> *With regard to exercise groups that I've been a participant in, somehow there is some kind of, um, 'group energy' that comes about. I don't know if its competition or what it is, but there definitely is something there in the group. NG3MS15* Verbal comment

The need to ensure all participants were busy and challenged during exercise elements of a group programme was highlighted, with the suggestion that an exercise circuit might allow for individualisation of exercises. Successful group formats were acknowledged as being reliant on achieving and maintaining a critical mass of participants, both for the positive group elements and also from a finance and sustainability perspective.

> *The only thing I think is that people with MS are individuals and* [an exercise which is] *pushing one person might not be extending another person at all. So it's okay to have a group, but not a large group because if somebody can't do it now just sink into the background and not be part of the group energy. NG3MS20* Verbal comment

The feasibility and choice of setting for program elements held away from home was the subject of significant discussion. The logistical challenges of rurality were recognised, however there was consensus that living in a remote location made access 'difficult' rather than 'impossible' (final group median 5, IQR2).

> *It depends on having enough people to make up a group as well, in our area it's a rural environment, so we run the group in a village hall but people from the next village won't go, it's as simple as that. NG2P9* Verbal comment

> *If you've got people who have problems with their balance, then buses aren't an option-they just won't consider them. Even taxis, not every taxi firm is happy to put walking frames and things in their boot. If they are paying £5 each way that is £10 a week, that's a lot of money so I think it really is, probably up there with the main reasons why people don't access groups. NG2P11* Verbal comment

The need to optimise convenience for participants was emphasised, with discussions highlighting the impact of travelling distance and time on MS specific issues such as fatigue. It was agreed that the number of essential face-to-face sessions in a programme was an important factor to consider.

> *This issue can't really be understated I don't think, I think it's the number one reason why people don't, in my experience, access community groups. Transport is always, or, I would say probably 90% of the time, travel and transport is the reason why people choose not to come to the groups. NG2P11* Verbal comment

> *I've got a person with MS I've been treating at home for a while and really he would be much better off going into the therapy unit but it's just that he lives on a really steep hill. It would have to be an ambulance or wheelchair taxi to get him down and then in and it's a long journey, and he gets fatigued when he comes back. It's just more hassle than it's worth. So I'm still seeing him at home even though I think you'd be better off in a gym based environment now. NG2P13* Verbal comment

> *I think if they're coming for a one-off, that's something that you can work around, but if you're coming week after week I wonder how much convenience and accessibility has a part to play. NG2P12* Verbal comment

Participants strongly disagreed that sessions away from home should be held in a hospital setting (final group median 2, IQR 2), explaining that this would 'medicalise' the programme, and that people with MS were likely to perceive hospitals as focused around 'illness'.

> *My experience with a falls team* [for older people] *being in an acute hospital was that people didn't come, didn't want to come, and having a falls group out in the community, people came.NG2P20* Verbal comment

> *I wouldn't want sessions to be in a hospital. They hold for many people the feeling that you are ill and we aren't, we just happen to be hosts to a disease that we don't want but has chosen to come. We're not ill as in ill, we are finding it difficult to cope but nevertheless not needing hospitals. NG3MS18* Verbal comment

> *It relates to the comment earlier about the group energy and getting to know people as well. I mean, I don't know anyone who would choose to go out and hang out in a hospital for fun! It's about the distinction-am I a patient or am I just living a life? That's a big, big distinction. So I would say absolutely they shouldn't be, they should avoid being in a hospital setting if at all possible. NG3P14* Verbal comment

Additionally, the growing pressure on hospital facilities was highlighted by both professionals and people with MS. However, some commented that a hospital setting added legitimacy to the programme as well as the perception of safety. There was a suggestion that these aspects should be considered if programs were based away from hospitals by ensuring that participants were aware of the 'professional' nature of the programme.

> *In my experience with community hospitals around our patch, we can only dream of the space they have in some sports halls-we could do some proper walking without falling over the parallel bars or other equipment. We talked about safety in a hospital, but as far as I'm concerned to have more space would be better because you can do more with more space. NG2P11* Verbal comment

> *The idea of a hospital setting for me gives it some validity. I've got MS; I don't want to just turn up to a random place not knowing… I'd like to think that*

> *somebody is a professional, and you know, has got a plan in mind. NG2MS12* Verbal comment

It was also recognised that the risk of falls was likely to be similar regardless of setting, however consideration of issues such as access to help and risk management was emphasised as being important.

> *In terms of if someone is wobbly and they are going to fall, they can fall anywhere. I think if you go to a village hall, I think you might want some kind of contact like your mobile in case there is an accident NG2P8* Verbal comment

In general, community-based settings were viewed positively, with panel members suggesting that sessions within community venues tended to be more enjoyable and social, and that participants appeared to be more independent than in a hospital setting.

> *In my experience running two* [Parkinson's] *groups, one in a community setting and one in a hospital, the people that were in the community were more empowered, making their own cups of tea for example whereas in the hospital everyone sat and waited to be waited on. It was different NG3P15* Verbal comment

It was recommended that providers should think creatively when choosing a venue for falls programmes, thinking broadly about opportunities in each specific area. A range of options for community-based settings were proposed, including village halls, gym facilities, schools and private practices.

> *Wherever it is it's got to have that 'it' feeling about it in that it is a place that you want to be, a place that feels light and bright and airy and empowering and motivating. I don't want to feel like I've been put in a naughty corner somewhere! NG3MS16* Verbal comment

Despite the positive perceptions of group-based activities, there was wide recognition that applying learning and undertaking exercise at home is essential to the success of a falls programme, regardless of whether group sessions were included or not. Participants highlighted the challenges associated with undertaking home exercise, and the need for motivational strategies to be included.

I don’t, I don’t, I need to be in a group for things to happen properly. I’ve tried this lots of times to do things properly; I’m thinking this all needs a group. Singly I don’t know if I would bother to do it. NG2MS10….

…. I agree: In our falls and balance group I always say ‘now who’s done the exercises since last week’? And I’ll get about two hands out of eight, and I know that when they come to me for two hours of exercise and when they go home they probably don’t do anything like so much, even having a hand-out with the pictures and words. NG2P12 Discussion excerpt

The input needs to be given in such a way that we enjoy it; we remember it or we have prompts to remember it, and we go away and we do it. So that is, whether it’s a group or individual, those rules must apply because the only way it’s going to work is with the time, motivation and energy that we find to put into it. NG3MS16 Verbal comment

Frequency, intensity and duration

Panel members consistently recognised that achieving appropriate intensity, dose and duration of exercise is important. Reference was often made to the existing evidence base for falls interventions for older people to inform this. Scoring of trigger statements 5 (intensity) and 6 (frequency) was relatively neutral, however whilst median scores remained similar, the mean deviation scores for both statements reflected a building of consensus.

The need for frequency of practice of both behavioural and exercise elements was highlighted. Panel members emphasised the importance of establishing routines and habitual practise for successful long-term engagement with the programme. Professional panel members drew upon evidence-based guidelines recommending regular exercise. However this was balanced with the recognition that rest was also important to ongoing improvements in strength, balance and endurance.

Regular consistent exercise is important, but rest days are needed to allow muscles to recover and to present unnecessary fatigue, and also to prevent starting with great enthusiasm and then abandoning. While stretches can be done daily, more specific high balance exercises may realistically be carried out 3 times a week. The Otago exercise approach with 3 exercise days a week and two walk or general mobility days seems more realistic, and also fits in with more normal adult guidelines of 30 minutes exercise five days a week. NG2P13 Written comment

There was a strong recommendation that frequency of practice should be realistic, balancing energy and time requirements for the programme with other health and lifestyle commitments. The need for a home-based element was strongly emphasised since frequent attendance at sessions was likely to make the programme unsustainable, both financially and logistically.

> *I agree that theoretically exercise should be done daily, and if you can then that's great and will give maximum benefit. But I also recognise that with issues such as fatigue, busy families and life in general this is not always possible. NG1P6* Written comment

There was a recognition that MS specific issues may also impact on participants' ability to achieve frequency of practice. It was identified that regular attendance to sessions outside the home may be challenging for many participants, and that the programme structure needed to be flexible to account for periods of non-engagement as a result of issues such as relapses.

> *If you're an MS person there is no guarantee you can be there one week and the next week, it's a day on day thing; not even a week on week thing or a month on month thing. You would like to be there for that time, but there's no guarantee you will be. NG2MS10* Verbal comment

> *It's not a question of motivation necessarily, it's a question of falling ill in between times or having hospital appointments that clash or just life - I don't think I could do something, guarantee I'd be there every week at the same time for 20 weeks. NG3MS14* Verbal comment

When discussing the duration of exercise within single sessions, there was the perception that exercising for an hour was not impossible, but could be a challenge.

> *Lots of people with MS treated either at home or in rehab units would regularly practise daily exercise in physio for an hour at a time in order to maximise rehab. NG2P13* Written comment

> *Exercising for an hour is impossible for me - 10 minute chunks of exercise at a time are best. NG1MS2* Verbal comment

Participants highlighted that the content and format of sessions was likely to impact tolerance, as well as the fitness and ability level of participants. There was general consensus that non-stop exercise for an hour was probably unrealistic, however building rest breaks into a group programme could make it achievable for most participants and allow for peer discussion and ongoing motivation. The need for sensitive facilitation in a group setting was seen as being important to ensuring that individuals felt empowered to make appropriate decisions about their own limitations, rather than being influenced by perceived group pressure.

> *Our* [patient led] *exercise group is nearly 2 hours, which seems a long time but it isn't really. We have a laugh, we have a joke and do what we can, no more than that. With the little bits of chat, it's, it's a long time, but it isn't really because you're not, it's not continuous with all these breaks in the middle. NG2MS12* Verbal comment

> *In our groups we aim to get everything set so they are actually sitting down at three o'clock and exercising through until four. But we do build in little breathers, but I think it's partly because people have come all that way want to give them value for money, so that's why; I think half an hour feels a bit like short change. NG2P8* Verbal comment

> *They won't stop even if you tell them to stop, the educational part of that before you start the group is going to have to be really clear, because otherwise people will go home absolutely exhausted because they tried to push as hard as perhaps the best person in the group, or the most able person in the group. And that will put them in bed for two days NG2P12* Verbal comment

However, there was the suggestion that exercising 'little and often' may be more feasible overall, and would be a more constructive fit with the use of pacing for the management of MS related fatigue.

> *Personally, if I'm doing stuff at home exercising I do it in short blocks, and have lots of rest and cappuccinos! NG2MS12* Verbal comment

> *Daily, in the form of exercises at home - if you want me to do two hours of exercise you can forget it; I have better things to do even though it may help me self-manage my condition. NG3MS16* Verbal comment

Panel members highlighted the potential to integrate exercise into functional activities as a way of achieving intensity of practice without the associated negative effects on fatigue, time commitments and motivation.

> *I think it might be helpful if the programme incorporated [functional activities] rather than saying 'try and do this certain programme at home for however long'. Saying 'actually, in the tasks you're undertaking at home every day, if you did it*

this way then actually you would be incorporating or helping to progress what you learnt in the class'. NG2P12 Verbal comment

The data relating to programme duration reflects the perception that long term engagement and commitment is required to maintain progress. Being able to see ongoing benefits was viewed as a critical factor in the maintenance of motivation. Similarly, the participants recognised that the educational components would need to be integrated into participants' lifestyles, and that it would take time for these aspects to become habitual.

It's part of a lifestyle change isn't it? The programme hopefully will get people going, but it's about kind of carrying on with that, because the moment you stop exercising, you soon go backwards again! NG2P9 Verbal comment

It should be partly a behaviour changing programme, and so should easily cover three to six months. NG1P6 Written comment

Panel members recognised the challenge of maintaining engagement in a programme over such a long period, and suggested that there needed to be an open and honest discussion at the outset to make this clear. It was proposed that maintaining ongoing engagement is likely to be dependent upon the success of integrating the exercise and educational aspect of the programme into the participant's daily lifestyle.

*From my experience of the things I've put in place, people struggle to do it [*attend on a weekly basis*] for that period of time. That isn't to say they shouldn't have the choice, but maybe we need to just be more flexible. NG3P14* Verbal comment

There was a recommendation that the programme needed to integrate methods to aid adherence, help people get back on track after relapses or other issues, and recognition that the programme structure (e.g. a time limited versus a rolling programme) could impact upon this.

I say if it works, no it's not unrealistic. If I can feel benefit I will keep going NG3MS16 Verbal comment

I think as well as along with the motivation… it's important to help people deal with the fact that some days and weeks they're just not going to be able to exercise, and sometimes they will have setbacks and not just giving up, but being able to come back and keep coming back. Because all of us have times when

> *you aren't able to exercise and don't feel like going to the gym. NG2P7* Verbal comment

The issues related to resourcing a long-term programme were highlighted, with the suggestion that it may be unrealistic to expect services to be commissioned over a long period. Peer support groups and local gym facilities were highlighted by participants as potentially cost-effective options to address this issue:

> *We bring people in for a 12 week period, however I think people may be more likely to continue if there was an ongoing group afterwards as well. NG2P11* Verbal comment

> *Yes we want it and we want it to keep going, however as an intervention, can we expect a commissioning group to fund continual lifelong ever increasing cost?* NG3MS16 Written comment

4. Programme leadership

Leadership statements

Box refers to median and inter-quartile range, whiskers denote TOTAL range

Figure 5-7: Graphical summary of programme leadership statements

Statement		Median (IQR)	Range	MDM *p<0.001*
12	The role of the programme leader should be to push participants to their limits	6 (2)	2-8	1.12
13	Programme leaders must have formal qualifications	7 (3)	4-9	1.21

IQR: inter-quartile range; Scoring: Scores of 1-3: Disagree; Scores of 4-6: Neutral; Scores of 7-9: Agree; MDM: mean deviation from the median- lower MDM indicates greater agreement

Table 5-9: Programme leadership statement scoring (round 3 scores)

Role of the leader

Five main leadership roles were identified during the group discussions:

a) Assessment

Panel members consistently identified that assessment was a key role. Members emphasised that it was critical for the programme leader to be aware of individual capabilities and limitations in order to appropriately structure the programme content, incorporating both education and exercise elements. Whilst the importance of an accurate initial assessment to determine suitability for the programme was recognised, the need for day by day assessment of individual capabilities was deemed critical, particularly due to the variable nature of MS and its wide ranging symptoms.

> *I think that's where the assessment would have to be done properly first because hopefully we could assess that and you know where to gauge it for you. It will be no good somebody coming in and saying, being asked to do something that is unreasonable. NG2P12* Verbal comment

> *On the day you're doing the group, on a weekly basis, people can come in one week and can feel they can do a lot more and perhaps the next week, for a variety of reasons there are some limitations to what they can actually achieve that week. NG2P20* Verbal comment

b) Exercise prescription and progression

The second role identified was in the prescription and progression of exercise elements. Panel members described the need for the leader to inspire participants to undertake exercise and to 'sell the benefits' of this. There appeared to be unanimous agreement from panel members of the need for exercise prescription and progression to be individually tailored, as was regular guidance and feedback. These were considered essential elements of this role.

> *The role of the programme leader is to listen, to devise an adaptive programme which has flexibility and focuses on the specific needs of the person with MS. NG3P20* Verbal comment

> *A skilled facilitator needs to provide effective individually tailored aspects of a common exercise set within the programme. NG3P17* Written comment

c) Safety and risk management

Safety and risk management activities were considered critical parts of the role of the programme leader. Examples included tailoring exercises to ensure optimal safety, assessing and accessing extra support staff when required and being aware of legal and governance issues. Communication and collaboration were identified as important aspects to assist management of this issue.

d) Education

Facilitating the educational aspect of the programme was viewed as another key role; however it was identified that this should involve both the provision of education, and facilitation of learning. Panel members with MS highlighted the importance of enabling people to take responsibility for their own progress, particularly with regard to the home exercise aspect.

> *Giving people the tools to take control of their condition is really important. NG1P6* Written comment
>
> *Patients can and should take responsibility for their own exercise if they can, once the exercises have been individualised and risk assessed. NG1P4* Written comment
>
> *If it is exercise within classes then yes they should be supervised. If it's exercises that I do at home, no thank you. NG3MS16* Verbal comment

e) Encouraging adherence

There was widespread agreement that adherence to any long term programme, be it for people with MS or healthy individuals, is challenging. The programme leader was felt to have an important role in sensitively encouraging participants to (ideally) remain actively engaged, or to re-engage rather than simply walking away. It was recognised that this would be a challenge for many participants.

Leadership approaches

In discussion, the participants explored leadership approaches which could be used to maximise effectiveness of the programme

a) Inspiration and motivation

A central approach to optimise success was the use of inspirational and motivational strategies. Panel members suggested that the leader needed to instil confidence and trust in participants, and to break down psychological barriers to participation. Other key leadership characteristics were the need to be enthusiastic, aspirational and to ensure that sessions were fun and enjoyable.

> *The results are obviously better when people enjoy it. NG3MS20* Written comment

> *I always think if I believe it works that they will pick up all that energy, they will get that, but if I'm just sat there looking bored then they won't get the fact that exercise works. That to me is the skill of the group leader, is to inspire there and then, but inspire for the rest of the week as well. NG3P17* Verbal comment

> *A large part of the balance exercises is that they are psychologically difficult, so there is a barrier stopping you doing more than perhaps you're capable of. So it's the programme leader's responsibility to try to encourage a little bit more than that. NG2P11* Verbal comment

A key aspect included the need to establish a positive rapport with the programme participants.

> *I think the relationship between the therapist, the enabler, whatever we want to call this wonderful being who is leading this group, and the people of the programme is utterly paramount. Because unless that sense of trust, respect, friendliness is there, the opportunity isn't going to be exploited to the full. NG3MS16* Verbal comment

b) Testing the boundaries

This trigger statement (statement 12) stimulated significant and avid discussion at each panel meeting. Whilst the rating scores were relatively neutral throughout, there was some narrowing of opinions, with a final group median of 6 (IQR 2). Much of the discussion centred on the use of the deliberately provocative term 'push'. In discussion, there was consensus that an important leadership approach was to enable participants to test their boundaries in order to achieve the degree of challenge necessary to stimulate improvement. However it was repeatedly emphasised by panel group members that this should focus on encouragement and facilitation, with sensitivity to individual needs rather than 'pushing' people which was interpreted by some as implying 'bullying'.

> *I don't like the word 'push', if you encourage, or somebody says 'well I'm ready to try this' or you suggest that this week you might be able to take this to the next stage and they agree and you do that, then that's great, that is how you get better. But if you push people too hard they just don't come back. So it's a balance isn't it? NG2P9* Verbal comment

> *I don't think that you can push us to the limits without us walking out of the class and never coming back. That's not to say, there's got to be the challenge as we've said before, but not to such an extent that we are struggling afterwards. NG3MS17* Verbal comment

> *You do need to really, really, really challenge people. We quite often to do things which they really don't think they can do, and I think if you didn't get to that point, we wouldn't achieve the results that we do in the groups. NG2P11* Verbal comment

> *Not push, but guide and encourage to reach their potential. NG1P6* Written comment

c) Supervision and feedback

Supervision and feedback was seen as essential to encourage and maintain engagement with the programme. However, members identified that a collaborative, partnership approach was essential. This was considered to be particularly important given the 'expert' knowledge of individual participants in relation to their own MS symptoms and problems.

> *It's a partnership, because the therapist needs to know, or have an idea of your limitations perhaps, then the people with MS also need to have an idea of their own limitations so that they can tell the therapist when they're reaching that point. So it's always a two-way conversation. NG3P19* Verbal comment

It was also identified that supervisory feedback approaches needed to be flexible to both the needs of individual participants and the timeline of the programme. For example, feedback and correction to exercise application might require a more prescriptive approach initially, but then a shared approach as participants gained confidence and experience. The importance of supervision as a mechanism by which participants could learn to tune into their own abilities was emphasised, with a balance of hands on/hands off approaches being advocated.

The thing about having frequent supervision is that you're constantly getting that improvement in self-awareness, which is important. NG3P20 Verbal comment

Support should be more frequent and should taper once a participant is competent and happy to continue alone… but with the option to be reviewed earlier in between if requested for specific problems. NG2P13 Written comment

It's how you are progressing things, it's part of the gaining confidence, it's about being able to do things without somebody standing right next to you. NG2P12 Verbal comment

The need for supervision by leaders who were not overbearing was emphasised. This approach was felt to enhance appropriate peer supervision and feedback within group sessions, thereby encouraging positive group dynamics and stimulating vicarious learning.

It is important to break down the barriers - some people feel real peer pressure, that's not good. NG2P 12 Verbal comment

I've experienced running a group where individuals actually found people within the group.., and then knowledge and of their condition management; that was useful. NG3P15 Verbal comment

Skills and attributes

Panel members readily acknowledged that the role of the programme leader was challenging.

It is a difficult role, and a very responsible role. I think it's a skill that has to be there by people leading any sort of a group. Everybody is an individual, everybody has a goal to get something out of that group and it may not be the same thing. It's about the person who is leading it. NG3P16 Verbal comment

A large number of skills and attributes were considered necessary for successful leadership (Figure 5-8). The key attributes included being professional, knowledgeable, and inspirational. Regardless of professional discipline, qualification or years of experience, it was also seen as essential for the leader to have MS specific knowledge.

I know that some people are very nervous about exercise, and they need it to be quite targeted and they will need to believe that it's been done carefully for them. NG2MS10 Verbal comment

It's not just that somebody is highly qualified that's important, it's that somebody has experience of and understands MS. I have had physio from a non-neuro *physio, and it's much less imaginative, and it felt much more like exercises as rote, that it is not as effective or as enjoyable as having someone specialist looking at the way you're doing your exercises and responding to the what you're doing. NG3MS16* Verbal comment

It depends on whether the physiotherapist actually knows any of the exercises that benefit that part of the balance system. I don't think some of the trainers at the gym, they might be able to make your biceps twice as big, but as far as balance is concerned they are swimming in the fog! NG3MS20 Verbal comment

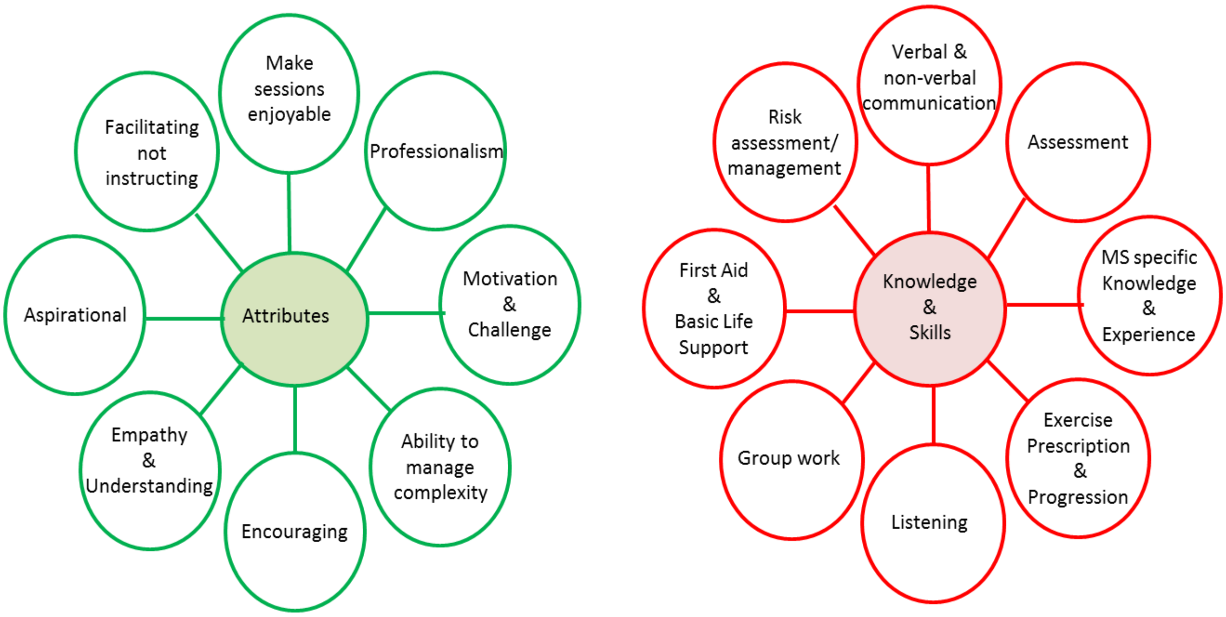


Figure 5-8: Summary of leadership skills and attributes identified within the NGT meetings

Responses to the statement relating to formal qualifications demonstrated general agreement that these were important (Final group median 7, IQR 3); however, there was significant discussion relating to the relative value of formal qualifications as compared to evidence of competence and/or experience (for example by therapy assistants/support staff). The importance of MS-specific postgraduate training and experience in addition to a formal qualification was highlighted by a number of professional panel members.

Somebody who is a qualified physio. Somebody who had done a course on MS I think. That's what I would like. NG2MS10 Verbal comment

Personally I would rather have an experienced support worker over a brand-new band five Physio any day. So for me it's experience and years on the job. Patients with MS who fall are actually quite complex from the therapy point of view, so it's not the sort of thing I would feel confident that I would just start a brand-new band five first day on the job. I just wouldn't, because I think you need

> *a lot more understanding around it and experience, so I think it's about training and breadth and depth of training. NG2P11* Verbal comment

> *When I trained you didn't do anything about falls and balance, then I did a course which was absolutely brilliant and then I feel, that's only training but that's put me in a much better position to be able to run the group. NG2P8* Verbal comment

It was suggested that individuals such as experienced support staff could potentially undertake many of the activities associated with group leadership. Whilst there was only one support staff representative who attended the panel meetings, there was general consensus that this role was more appropriate to supervising an existing programme rather than initial assessment and progression activities.

> *Today, when my balance group is on, my assistant is going to take it, but because it's in the village hall she's got an OT in the background helping out. And the OT is qualified, but the assistant who's been running the groups for about 20 years is in a much better position without a qualification but with training. NG2P8* Verbal comment

> *The actual group, absolutely fine with people you know, but when you get new people you want to know how to challenge them on a really personal level. I do think you need a professional then, I think it's quite limiting without. NG2P10* (support worker) Verbal comment

> *It's interesting, I'm an OT with a postural stability instructor (PSI) qualification as well and I work closely with a fitness instructor who is also a PSI, and she will often defer to me, because although she's done that training she hasn't got the medical understanding. So there really is something about the breadth and depth of experience and training that is vital, absolutely vital NG2P20* Verbal comment

Regardless of the qualifications and experience of the programme leader, the panel members emphasised the need to have an appropriate number of staff present to maintain safety whilst enabling activities to be challenging.

> *On a very practical note you actually need more pairs of hands. I want to be able to challenge everybody and everyone to feel challenged but it's how much backup does that person have to enable that? My worst nightmare is a group being run for the lowest common denominator; 'oh we'll do it all in sitting because actually I'm too scared to get anyone up in standing or I haven't got enough pairs of hands to get everyone up'. So staffing, having enough pairs of hands it's always a tricky one. NG3P17* Verbal comment

A range of other individuals were identified who could potentially make an important contribution to the success of the programme. Examples include the use of volunteers to supplement the input provided by trained staff, both within attended sessions and as mentors within the community. Similarly, the potential benefits of developing a peer support network were highlighted to help shared learning and ongoing motivation.

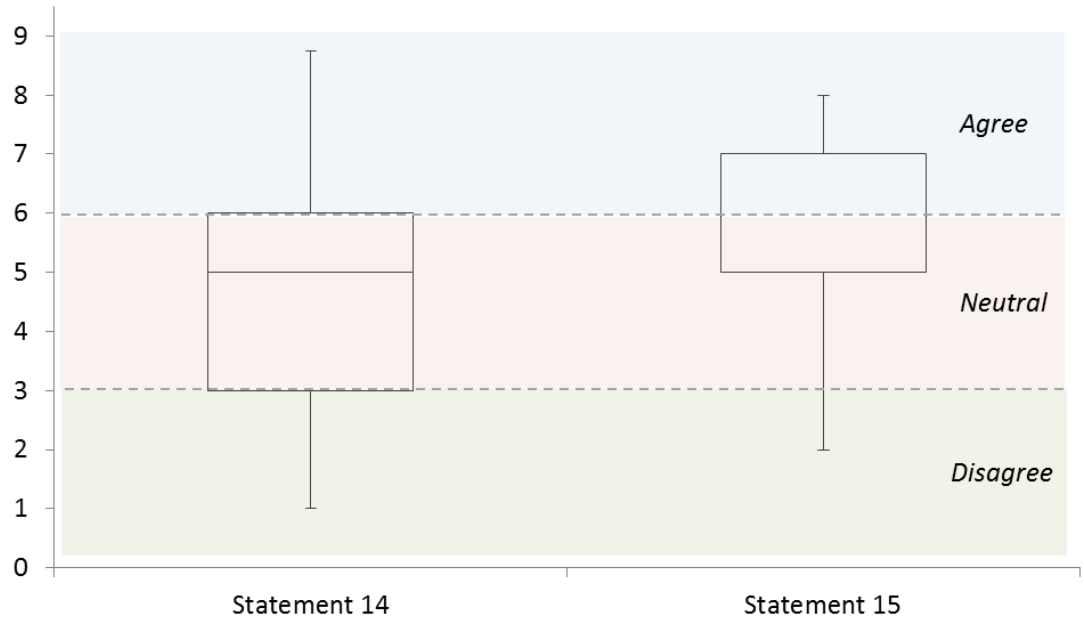
> *We were talking about group sessions and group working because it gave you group energy and now we're talking about machines and not people. What's wrong with people? I mean to say, there are people out there, there are people that want to help. You know, you've got more than enough charity shops locally that rely on volunteers to staff them and they are only working in shops. I'm sure some of these people who volunteer for certain things could be helpful. It's much better to have people than machines. NG3MS20* Verbal comment

> *I thought it would be, somebody qualified, but maybe you could have volunteers who would help because somebody like me, I need somebody there to help but I wouldn't expect a physio to be with me the whole time in a group session, I would only want a physio to be in attendance. NG2MS10* Verbal comment

> *We* [falls service for older people] *have falls buddies, and they are volunteers who support people In their own homes, and there are lots of other services that also use trained volunteers. NG3P14* Verbal comment

5. Sustainability

Sustainability statements



Box refers to median and inter-quartile range, whiskers denote TOTAL range

Figure 5-9: Graphical summary of programme sustainability statements

Statement		Median (IQR)	Range	MDM *p<0.001*
14	A falls programme should be provided within existing resources	5 (3)	1-9	1.70
15	It is reasonable to ask participants to pay a contribution to the cost of any attended sessions	5 (2)	2-8	1.00

IQR: inter-quartile range; Scoring: Scores of 1-3: Disagree; Scores of 4-6: Neutral; Scores of 7-9: Agree; MDM: mean deviation from the median- lower MDM indicates greater agreement

Table 5-10: Programme sustainability statement scoring (round 3 scores)

The scoring for both of these trigger statements was neutral, with little change in median scores and IQR between the rounds (see Table 5-10). The related discussion informs the detail behind these neutral scores.

Resources/funding

Long-term sustainability was considered critical within the context of resources and funding. Participants identified the importance of ‘doing it properly’ in order to optimise effectiveness and satisfaction for both staff and service users.

> *You need the ring fenced time to give something like that so that you are doing your assessment properly and you are really giving people, you know targeting exercise properly at people and not just putting people in the group because it’s easier to treat them in a group than it is to treat them one-to-one. NG2P12* Verbal comment
>
> *It needs to have its own resources because you get fed up trying to run everything on a shoestring and rushing in and doing a group and then rushing off again to the next thing. NG2P8* Verbal comment

Professional participants consistently identified the difficulties associated with current levels of service provision and funding, suggesting that meeting the demands of a new MS falls service within existing resources would be challenging

> *Additional funding should be acquired as resources are extremely stretched as it is. Unless it could be proved that they were taking a vast number of the waiting list/caseload. NG1P5* Written comment
>
> *I think the danger is if it’s not given its own resources is it doesn’t get done properly and it isn’t effective and actually it’s just an extra drain on everybody’s time and resources without actually doing what you set it up to do NG2P7* Verbal comment

It was suggested that an MS falls program would meet the general goal of shifting the focus of health and social care provision towards prevention, and that potential savings in terms of the reduced costs of managing falls and the consequences of falls in MS may present a funding opportunity. However it was recognised that the potential lag between commissioning the service and determining its impact in meaningful terms would present problems.

[One of the other participants] *has said that every time they fall over they have to get a paramedic to pick them up. I don't know what the cost is of an ambulance paramedic called to pick someone up if they fall over, but could there be some sort of cost benefit analysis that could enable money to be diverted to prevention rather than picking up our pieces after we have fallen over? Surely that's cheaper in the long run? NG3MS16* Verbal comment

I know we are talking about MS, but from a generic physio point of view, which services do you take the existing resources away from? NG2P11 Verbal comment

The problem with cost benefit analysis and those things is that you have to get the money first, so you've got to fund both of them at the same time [initially] and that's the bit where we are stuck at the moment - we can't do that, not at the moment, we haven't got any spare. It is committed and then some so we can't. NG3P14 (service commissioner) Verbal comment

Within the funding discussions there was widespread agreement that rehabilitation services for people with MS were limited, with many describing the difficulty they had accessing interventions, particularly when there was a perceived need for longer term input. This was the case even for those who described themselves as falling regularly. This experience was validated by the health professionals who commented that few people with MS were referred to existing falls programs. Amongst service users there was a strong belief that these generic (typically oriented towards older people) services did not meet their needs.

…if you're someone young with say progressive MS, you may be grieving for your former self anyway without having it thrust in your face that you are falling around like your Gran. NG3MS16 Verbal comment

It's true, and if you have a falls clinic referral, the letter at the top says 'Department of the care of the elderly' and the patient comes in and goes 'what's this? Why am I being sent this appointment'? And you have to explain, 'well, actually…' NG3P17 Verbal comment

Potential alternative funding sources were suggested, which included personal health budgets and support from charitable bodies and voluntary sectors; with an emphasis placed on tapping into these sectors to supplement manpower where appropriate.

Lateral thinking with imagination may help e.g. volunteers. NG3P 19 Written comment

> *I've broadened it because we are looking at wider resources, I've put down charities - there are all sorts of funding streams and there will be personal health budgets to come. NG3P16* Written comment
>
> *There are grants out there-there are ways and means to find money and things to do this sort of programme. It isn't all about it being on the NHS or the council. NG3MS17* Verbal comment

Participant (monetary) contribution

Participant payment was discussed as a means of contributing towards the cost of falls group interventions; however it was acknowledged that this would depend on the setting and focus of the programme. For example, contribution to attend a group run within an NHS context was considered inappropriate, while this was not viewed in the same way if a group was implemented within the voluntary sector.

> *If it is run as a hospital group I don't think you can ask a fee. If run independently by qualified volunteers in a church hall, then a contribution to cover the hire of the hall, tea/coffee would be reasonable. NG2P8* Written comment

In general there was recognition that while participant contribution could add value to a programme, it might also be a potential barrier. Participants recommended that the overall burden on participants in terms of travel and other associated costs should be considered when making any decisions related to participant contribution.

> *It is reasonable to ask, but cost limits participation in our experience! NG2P9* Written comment
>
> *Attending appointments will already cost money, so any charge should be minimal. NG2P12* Written comment
>
> *Payment should be on a sliding scale so no one misses out because of their inability to pay. NG3MS18* Written comment
>
> *There is evidence that retention levels are higher in a group session for which people pay a small fee rather than those that are free. NG3P14* Written comment
>
> *I think if you pay for it, you value it more than something you're getting free to a certain extent. NG3MS20* Verbal comment

5.5.4 Development of position statement

Following data analyses results were synthesised into a final position statement summarising the key recommendations. This statement was circulated to all NGT participants. All of the 13 who provided feedback (7 service users, 6 professionals) felt their views and the discussions from their NGT sessions were appropriately represented. Three participants suggested minor amendments which were all incorporated into the final position statement which is presented on page 275.

5.6 Discussion

This study aimed to inform the structure, content and delivery method of an MS specific falls programme. It utilised a novel application of the nominal group technique, with every effort made to engage professional and service users as equal participants. The discussion includes an evaluation of both the nominal group process and the study outcomes.

5.6.1 Nominal group process

Participants

The purposive sampling strategy aimed to recruit professional participants with varied expertise relevant to the topic area. The final sample included individuals with MS specific knowledge, experience of running generic falls programmes and professionals from a variety of different healthcare professions. However, only one service commissioner and one therapy assistant were recruited, and no representatives from the private or voluntary sectors were available to attend the NGT meetings. The challenge of recruiting a wide range of participants to consensus studies has been highlighted previously. Keeney[347] found that the experts most willing to engage in Delphi studies were typically those with a direct interest in the topic, and who therefore may not be truly representative of the wider population. Allen[348] argues that, due to the level of commitment required to participate fully within a NGT study, a balance should be struck between including a wide range of viewpoints and ensuring that all participants are willing and able to commit fully to the process. In this study, all the participants made valuable contributions to the NGT sessions; however, future research should aim to explore the perspectives of staff groups which were less widely represented. It may be that the use of research methodologies which are less time intensive for participants (e.g. telephone interviews) may allow more successful recruitment from these groups.

In contrast to other studies, this study aimed to recruit people with MS to attend the NGT sessions alongside professional participants. This sample included individuals with a variety of MS types, mobility levels and falls history. Although the initial aim was for people with MS to make up at least half of each NGT session, this was not achieved in meeting two, where only two people with MS attended alongside 10 professional participants. Although the MS participants contributed fully to this session, the nominal group scoring within this group differed most frequently from the scores of the other groups which both had more equal representation from service users. The effect of group composition on NGT scoring within heterogeneous groups has not yet been evaluated. However, studies comparing differing homogenous nominal groups (e.g. separate groups of physicians and patients) have demonstrated differences in scoring between the groups[358].

Structure and organisation

The structure and organisation of the sessions appeared to work well; participants reported that they felt well-prepared and had a clear understanding of the aim and purpose of the sessions. The service-user training was also well received, with a number of participants reporting that they would not have felt confident to contribute during the meetings prior to attending the training sessions.

The NGT statements were generally perceived as clear, and were successful in stimulating discussion. However, the wording of the statements could have impacted on the outcome of the process. For example, eight of the 20 statements included the word 'exercise', which may have led the participants to make assumptions about the inclusion of exercise within the programme. Alternative methodologies such as focus groups may have presented a more open forum for discussion.

As recommended, this study utilised a number of ratings rounds within the NGT process with the aim of facilitating convergence of opinion[349]. It is recognised that there may be a number of reasons contributing to the trend for participants' opinions to converge during successive ratings rounds, including the influence of peer/group pressure and the tendency for individuals to use others' perspectives to influence their own interpretations[346]. Whilst these processes are a normal part of group interaction, one of the major considerations in this context is the lack of evidence relating to whether increased convergence of opinion can necessarily be assumed to reflect an increased level of accuracy relating to the final decision[349].

Data presentation and analyses

This study utilised a range of methods for presenting and analysing the rating scores in successive rounds. The use of median and interquartile range for participant feedback was valuable and, based on participant feedback, was clear and straightforward to interpret. However, there was minimal change in the scores between rounds, possibly representing a lack of sensitivity of this method of analysis due to lack of representation of extreme scores. In contrast, analysis of the level of agreement using the MDM appeared to be more responsive to change, possibly representing a more appropriate method of analysis in this context.

Categorisation methods to classify levels of agreement and consensus have been used in a number of previous studies[346,348,364]. In this study, the level of consensus and agreement achieved was comparatively low. Low-moderate consensus has been considered acceptable in some studies involving ‘non-clinical’ decisions[348], however it is possible that the deliberately provocative wording of the trigger questions may have influenced the results. In some nominal group studies, rewording of statements is integrated into the process in order to facilitate development of consensus[358]. However, this was not undertaken in this study as the intended outcomes were more exploratory in nature. In addition, the overall facilitation style and structure of the group did not emphasise the development of agreement as a goal in order to avoid participants feeling under any pressure to conform to group opinion.

The inclusion of qualitative data significantly contributed to meeting the study aims, which was to enhance our understanding of the structure, content and delivery of a future falls programme. For example, in half of the statements, the final rating scores were neutral: Had only quantitative data been collected (e.g. quantitative questionnaire), the wide ranging perspectives presented within the nominal group meetings would not have been reflected.

5.6.2 Study outcomes

Programme aims

The results indicate that a reduction in falls should be a primary aim of the programme. The recognition that complete prevention of falls may be unrealistic in people with MS echoes findings of clinical trials in other conditions (both neurological and non-neurological), where falls prevention programs generally lead to a greater reduction in falls rate than falls risk[99]. Less widely discussed is the importance of reducing falls whilst maintaining or improving activity and participation in daily life. Work by Laybourne[372] highlighted the risk to activity and independence outcomes that a pure focus on falls reduction may present; nevertheless, the majority of falls prevention studies continue to include falls as the primary outcome measure[99]. The findings of this NGT study suggest that activity and participation measure should be included alongside a measurement of falls rate as key outcomes of any falls programme.

Programme content

There was consensus in all three nominal groups that the falls programme content should include both balance-focussed exercise activities and falls management education and advice. This approach contrasts with existing research on falls management in MS, where programmes have tended to focus on one of the two aspects in isolation[239,240]. Whilst discussing the education focused aspects it is notable that the majority of the recommendations for specific content came from professional participants. Although those people with MS recognised the wider consequences of falls (such as loss of confidence, limitations to function and impact on family and carers), they did not provide suggestions as to how these issues should be addressed. It is possible that this reflects a lack of experience to draw from which may, at least in part be attributable to the current lack of provision of services of this nature.

When discussing the exercise component, there were a range of opinions as to what this would entail. For some the term exercise referred to ‘general physical activity’, for others is was interpreted as being ‘function-based exercise’, while for others the definition was narrower in scope, referring more specifically to exercises designed to improve impairments such as balance or strength (such as those typically provided by a physiotherapist). Despite the range of personal interpretations of ‘exercise’, it was widely acknowledged that there were three key features of this component, namely that it should be evidence-based, specifically tailored to an individual’s problems and abilities, and that the exercises should be ‘realistically challenging’. The heavy emphasis placed on these features by the participants endorses the importance of skilled exercise prescription and regular reviews to ensure appropriate progression.

Programme approach

The overall programme approach was not a specific trigger question in this NGT. However, within the group discussions, data emerged indicating the need to establish an appropriate programme ethos. The importance of the participant voice as a central aspect was a recurring theme; there was a strong perception that self-management and individual responsibility were critical factors impacting on the success of all elements of the programme. This included the need for both education and exercise elements to be individualised to optimise engagement and effectiveness. This aspect has not been studied in MS falls research to date. However, results of generic falls education program evaluations suggest that the provision of nonspecific falls prevention advice is less effective than individualised education programmes[246]. In addition, externally generated risk identification and modification advice has been viewed as intrusive and an unnecessary imposition by participants in some studies[373].

Alongside the need for participants to take individual responsibility, there was recognition of the importance of providing targeted support to participants. This was considered particularly relevant when encouraging participants to undertake balance exercises that were personally challenging, due to both safety concerns and lack of confidence amongst participants and their relatives. As with other studies[301], there was widespread acknowledgement that input from programme leaders was crucial for a number of key aspects including assessment, exercise prescription and support to build confidence.

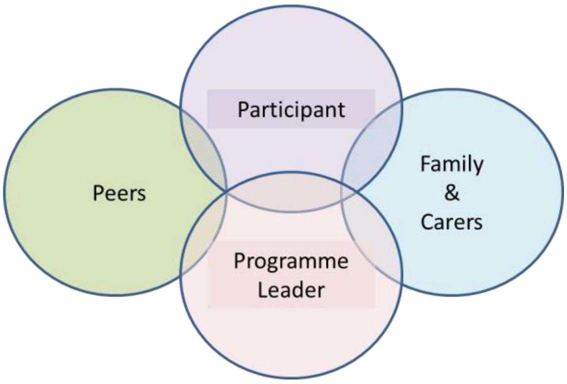


Figure 5-10: Key relationships within the falls programme

The nature of the relationship between the programme leader and participant was felt to be critical to achieving the balance between 'expert' and 'participant'. The data also highlights the importance of other relationships impacting on the programme, such as family, carers and peers (see Figure 5-10). The overall recommendation for the programme is for an approach which develops a 'collaborative partnership'.

As well as ensuring the programme content and delivery methods support active participant engagement, it was suggested that program models which move away from a 'health' focus towards a 'lifestyle' or 'education' focus may be beneficial. The finding that self-funding (as would be usual in non-national health funded programmes) could increase participants' perceptions of the value of the programme was interesting, although this requires further exploration and may not be supported by wider evidence. For example, qualitative evaluations of general physical activity programmes in the USA and UK suggest that payment reductions and low overall cost appear to be incentives to participation[374,375]. However these studies generally involved participants who were involved in programmes with a pre-existing cost which was subsequently reduced, rather than those where a small initial charge was being levied.

An important aspect which has not been previously highlighted in the literature is the potential for seemingly small issues to impact on participants' perceptions of, and engagement with, the programme: Examples included the use of inappropriately headed notepaper (Elderly Care) leading to a perception that the programme is unsuitable. Within the nominal group discussions there were also a number of occasions where participants highlighted that they felt individuals were less likely to engage in programs that were not perceived as being 'professional', 'legitimate' and/or MS specific. This emphasises the need to achieve a balance between developing a programme which is open, welcoming and accessible, but also perceived as being led by skilled and knowledgeable professionals. The involvement of service users in programme developments can effectively highlight and address issues such as these[376].

Programme format

Access

Accessing services is a significant issue for people with MS, with research indicating significantly lower referral rates to preventative services for mobility impaired people with MS when compared to the general population[377]. This NGT study highlights the need for the falls programme to be widely publicised and easily accessible, ideally via self-referral. Existing referral systems were perceived as limiting access, although some form of suitability and general health screening prior to entry onto the programme was recognised as being important. In the wider literature, direct access to health services has been associated with greater participant satisfaction, higher programme completion rates and improved health outcomes, alongside lower service costs[378–380]. However, some studies suggest that the characteristics of self-referrers differs in comparison to the wider population; those using direct access systems tend to be younger, more highly educated and with more acute problems[381,382]. Whilst none of these studies specifically included people with neurological conditions, it seems reasonable to suggest that some people may need support and encouragement to engage with the falls programme were self-referral to be utilised. A study by Warriner[383] suggests that support in the form of a simple invitation may be as effective as more comprehensive education and awareness raising programmes; the associated costs of this approach would be unlikely to be prohibitive.

Programme structure

Choice of home or group-based activities

These findings agree with the qualitative findings from literature review two (section 4.4.10), suggesting positive perceptions of group-based activities. In the wider literature, evaluations consistently highlight the advantages of group interaction as a factor motivating attendance, ongoing engagement in exercise and commitment to maintaining behaviour change[384]. Moreover, an opportunity for shared experiences within a group may encourage participants to challenge themselves through vicarious experience of others' achievements [240,342]. Programmes delivered in a group setting may also offer 'economies of scale' to a provider, enabling more individuals to access the programme at a time.

Challenges with regard to the delivery of group programmes are also apparent. For instance, NGT participants highlighted that group programmes are unlikely to be frequent enough to provide a sufficient intensity of exercise to reduce falls, thereby requiring group sessions to be supplemented by a significant amount of home-based practice. Whilst this was viewed positively as supporting the 'self-directed' ethos of the programme, there was an acknowledgement that, based on current evidence, participants often report lacking the confidence to exercise away from the perceived safety of a supervised environment[337,385]. Providing opportunities for participants to learn how to follow through and apply programme content at home are likely to be key in addressing this issue.

Whilst there is no published assessment of participant experiences of home-based MS falls programmes, evaluation of home-based falls programmes for older people has suggested that major advantages include the convenience for participants and the 'real-life' nature of the setting[386], allowing programme content to be integrated into daily activities from the outset[387] . Individually tailored home-based programmes may lead to improved perceptions of control and ownership amongst participants, which could improve self-efficacy. Greater self-efficacy may positively impact decisions relating to the adoption of home and lifestyle modifications, and home-based programmes may allow greater choice over type, planning and progression of exercise activities[336,373]. A concern however, highlighted in both this study and literature review two (section 4.4.10) is the potential for risk of injury with unsupervised exercise. There is however minimal evidence supporting this claim; the investigations that have included home-based exercise programs in persons with MS have reported few adverse events[239,286,388].

Balance of home and group-based activities within the programme

Research has emphasised that there are a number of challenges associated with rehabilitation programmes in which sessions are based away from home[389–391]. The NGT results align with this, highlighting attendance at sessions away from home as difficult (although not impossible), with many similar challenges identified as those in the wider literature. MS specific considerations such as the very high prevalence of fatigue, unpredictability of symptoms, and demographics of this group (many being of working age and with young families) are further barriers to engagement. Panel group members viewed frequency of attendance as especially challenging, particularly when programme structures required regular attendance over a long period in areas with a widely dispersed population. It was argued that a programme with a relatively low number of group sessions, or where sessions are spread over time would be more attractive and feasible to people, thereby taking advantage of the benefits of a group programme whilst minimising some of the logistical barriers. This is yet to be explored empirically.

Setting for sessions away from home

The limited number of MS studies specifically assessing falls outcomes makes evaluation of the effect of setting on programme outcome problematic. Within the older adult literature, meta-analysis suggests that comparisons of falls programmes in home or community settings lead to improvements of a similar magnitude[99]. Similarly, in evaluations of pulmonary and cardiac rehabilitation programmes, no differences were found in falls rate whether the programme was delivered in hospital or community settings[392,393]. To date, direct comparison of the effects of programmes delivered in differing settings has been limited by the significant degree of heterogeneity between interventions.

In this NGT study, there was a strong preference away from 'medically focussed' settings. In the wider literature, community-based settings which are not health-focussed are frequently cited as being attractive to participants as they are perceived as being more socially acceptable, 'normal', and more convenient to access[386,394]. However, the findings of literature review two (section 4.4.10) and this study suggest that choices over the type of setting are not straightforward, as a balance needs to be achieved between accessible, 'user-friendly' venues and those which are perceived as being professional and legitimate. Research suggests that healthcare-facility based programmes are perceived as 'safe', and the staff as 'knowledgeable' by participants[395]; and that the availability of support and backup if required may give confidence to programme facilitators[393]. Conversely, some types of community facility (e.g. sports centre gyms) have been associated with poor engagement and adherence with rehabilitation programmes, with participants reporting them to be ‘unfriendly’ and non-inclusive[396]. However, the findings of both this study and other evidence appears to suggests that, on balance, community venues are preferential to healthcare based settings. Furthermore, this is in line with the current healthcare commissioning and service delivery models, which is an important consideration in ensuring the sustainability of a falls programme[397].

Maintaining engagement

Maintaining engagement to falls programmes has been cited as a key factor influencing outcome, both in the short and long-term[246]. To date no studies have been undertaken exploring adherence to falls programmes in MS, however, as discussed in review two, longer-term adoption of exercise regimes can be poor[316]. In addition to the factors affecting adherence in the general population, people with MS may also experience relapses and/or deterioration in their symptoms which are additional barriers to engagement. Whilst this was not explicitly discussed by the NGT study participants, the findings of study 1 (chapter 3) and subsequent pooled data analysis[250] which suggest that transition phases tend to be associated with increased falls risk, indicate that maintaining engagement is likely to be a significant challenge.

However, there is promising evidence from home-based falls programmes for older people that long term adherence can be achievable in some instances[336,398]. In a systematic review of falls home exercise programmes for older people, factors influencing adherence included type of exercise and type and amount of facilitator support[260]. In this NGT study, the importance of using methods to facilitate adherence and ongoing engagement was consistently stressed. For example, the need to structure activities so that they became habitual and integrated into daily life was emphasised, as was the importance of building elements into the programme that would help participants get back on track after interruptions (for example due to health issues).

Nominal group participants also highlighted the role of adjuncts to support programme engagement. The use of falls diaries was included as a trigger statement; however other suggestions by panel members included use of tele-rehabilitation, mobile telephone apps and online resources. Individual preference was seen to play a strong role in the decision to use any of these adjuncts, it was agreed that choice was important and that ideally a range of options should be available. There was a general acknowledgement that any monitoring or adjunct to facilitate adherence should be quick, simple to use and unobtrusive.

Although the use of adherence aids within MS falls programmes has not been investigated, a range of strategies aiming to improve or maintain engagement with general physical activity and specific exercise programmes have been evaluated in people with MS. This includes motivational interviewing[325,326], the use of interactive online or tele-rehabilitation programmes[294,399–402], efficacy enhancement sessions[327], and customised pamphlets[324]. Trials of telephone and interactive online delivery methods for educational programmes have also been undertaken, predominantly within fatigue management[403,404]. In general, participant satisfaction with the value and utility of these interventions has been high[319,324]. Whilst the majority of trials to date have only included short-term follow up, several studies have demonstrated increased physical activity levels in the intervention groups, as measured using self-report questionnaires[324,400]. However, other trials did not demonstrate significant between-group differences in activity levels or exercise adherence in comparison to control groups[325,327,399]. Given the international shift towards shorter episodes of care, and increasing emphasis on self-management in healthcare delivery[405,406], it could be argued that even if such interventions do not offer superior outcomes when compared to conventional face-to-face delivery methods, they may offer a significant benefit by supporting ongoing programme engagement and potentially offering cost benefits, although this aspect has yet to be explored fully[399,407].

Role of the programme leader

The results of this study emphasise the pivotal role of the group leader to the outcomes and success of the programme. Whilst the majority of the NGT statements relating to programme leadership were rated with neutral responses, the qualitative data emphasised that the reasons for this related to the complexity of the leadership role. For instance it was felt that leaders need to challenge participants to undertake demanding balance exercises, while balancing this with empathy and understanding. The complexity of their role was also reflected in the discussions relating to the leader's qualifications. There was widespread agreement that the role required a range of high-level skills and attributes and that programme leaders should be 'qualified'; however, there were a range of opinions about what type and level of 'qualification' would be most appropriate. This included recognition of the importance of experience, and the need for highly developed interpersonal skills alongside a range and depth of programme and condition-specific knowledge and expertise. Such high levels of expertise may impact on the overall cost of the programme, which needs to be considered when evaluating funding and sustainability issues.

The results suggest that aspects of 'leadership' and 'support' could be provided by a range of individuals, including family and carers, peers and programme staff. Another dimension was the suggestion that volunteers could support the delivery of the programme. The involvement of lay-people in the delivery of self-management programmes was first proposed and evaluated in the 1970's in the USA[408], however in the UK the most widespread introduction of lay-led programmes has been within the NHS 'Expert Patient Programme'. Whilst initial evaluations of the programme were positive, large-scale reviews suggest that its effectiveness may be relatively modest[409], particularly when compared to more comprehensive professional-led programmes[408]. It has been proposed that these differences may be attributed to the complexity of many long-term conditions, which necessitates a flexible and individualised approach. This approach is unlikely to be suited to the relatively prescriptive methods utilised by many lay-led programmes[410]. Within the MS falls programme, the use of volunteers may therefore be better suited to supporting roles rather than overall leadership. In other parts of the world, most notably in developing countries, the use of volunteers to support (rather than lead) programme delivery is widespread. Evaluations of these programmes suggest that high turnover of volunteers can be a challenge, and that effective preparation, training and ongoing support are essential[411]. This aspect would need to be carefully considered when evaluating the cost and benefits of this model of delivery.

Programme sustainability

These results emphasise the importance of developing an MS specific falls programme which is appropriately funded and yet sustainable within current models of service delivery. The qualitative findings highlight the lack of utilisation of existing (typically generic) falls services by the MS participants in this study, despite over half of them reporting having fallen in the past year. Participants described a general ‘normalisation’ of falling and a lack of focus on falls during healthcare interactions, despite recommendations that falls and balance issues should be assessed as part of the regular MS review process[7,412]. This, coupled with the perception that existing falls services are not suitable to their needs, is highly likely to influence uptake of existing falls services. In order to make the case for funding of MS specific falls services, evidence is required to demonstrate the need for, and added value of an MS specific intervention. This has yet to be determined.

5.7 Summary and recommendations

This NGT study aimed to determine the most appropriate format, structure and delivery methods for an MS falls programme, taking into account issues of feasibility, sustainability and fit with existing services. Importantly, the study builds on the findings of study one and review two which concluded that an MS specific programme would be required (sections 3.5.3 and 1.1). The results of the NGT study support this argument by providing evidence that both professional staff and service users perceive the content, design and approach of generic falls services as unsuitable for the needs of people with MS. Based on the outcomes of this study, a final position statement was developed which summarises the key findings related to each specific goal (Figure 5-11).

Position statement summarising Nominal Group study findings

Objective 1: To define the programme aims, outcome and approach

- The programme should aim to decrease falls frequency whilst maintaining (or ideally increasing) functional activity/participation
- The programme format should be tailored to the needs of people with MS and the content should address MS specific issues
- The overall approach of the programme should emphasise professionalism and legitimacy in order to inspire confidence and trust
- The aims of the falls programme should be achieved through an active partnership between participants, programme staff, relatives and carers
- Progress should be reviewed regularly in a collaborative process, using both clinician-rated and patient self-reported outcomes which cover the breadth from impairment to participation

Objective 2: To recommend programme structure, format and delivery methods

- The falls programme should be widely publicised and easy to access
- The programme should include balance-focused exercise AND falls prevention advice, both of which should be individually tailored and consider MS specific issues
- Exercise prescription and progression should be a collaborative process between participants and the group leader. Wherever possible exercise programmes should be evidence-based, tailored to be achievable but challenging and include specific explanation of the intended aims and outcomes.
- Participants need support to develop the confidence to undertake exercises they perceive as being challenging to their balance and stability
- Exercise needs to be undertaken regularly, with strategies built into the programme to support participants to achieve an appropriate frequency and intensity of exercise, in line with the evidence base
- The falls programme should utilise both group and individual activities. Group numbers should be tailored to the available staffing and support to ensure safety
- The falls programme should be facilitated by skilled and qualified professional staff. This includes neurology-specific expertise alongside knowledge of balance-focussed exercise prescription and falls prevention strategies.

Position statement summarising Nominal Group study findings
Objective 3: To explore factors affecting participant engagement with and adherence to the programme, both over the short-term and longer term • The scheduling of group sessions should consider the challenges associated with attendance that are particularly prevalent for people with MS. Occasional group sessions interspersed over the course of the falls programme, rather than weekly sessions, are proposed. • The location for sessions held away from home is very important. Venues should be accessible, inspiring and motivational, while at the same time being risk assessed as safe. • The programme must actively support participants to engage, particularly during home-based activities. Adjuncts to support engagement such as the use of telephone support, online or tele-rehabilitation resources should be considered • Diaries and progress charts should be considered as an *aide memoire*, and/or to assess progress and maintain motivation, but should be simple and non-intrusive. • The programme structure, format and content must be flexible to account for personal issues which may affect short-term engagement. Support and strategies to help participants re-engage with the programme should be included. • The programme must facilitate long-term adoption of exercise and falls prevention strategies; this could include links to follow-on groups and other behaviour change strategies **Objective 4: To highlight the factors affecting sustainability and integration of the programme within existing service provision** • The falls programme must be adequately resourced. This includes provision of appropriate venues, programme resources and staffing. • A range of potential sources of support for the programme should be considered, including health, voluntary and charitable bodies as well as reasonable participant monetary contribution.

Figure 5-11: Nominal group study position statement

6 General discussion and conclusions

6.1 The problem revisited

The work within this thesis was initiated in 2010 after local people with MS highlighted falls as an issue which significantly impacted their lives. In addition, local clinicians identified that they were unsure of the most appropriate strategies to reduce or prevent falls in MS. A review of the MS literature identified falls as an important clinical issue, but with a weak empirical evidence base, both with regard to volume and methodological rigour

The aim of this project was to provide the necessary evidence to inform the development of a model for an evidence-based MS falls management intervention. The specific objectives of the project were to develop an MS falls intervention model by:

1. Evaluating the prevalence, characteristics and consequences of falls in MS
2. Identifying the risk factors associated with falling in people with MS
3. Recommending programme content on the basis of an evaluation of the existing evidence, to ensure the best chance of reducing falls rates.
4. Proposing the format and delivery of the intervention model based on users' and service providers' input, considering:
    a. acceptability for service users
    b. optimizing adherence and user participation
    c. ensuring sustainability

6.2 Summary and interpretation of findings

In keeping with the use of the MRC framework for the development and evaluation of complex interventions to guide the work undertaken throughout this thesis, this section has been structured according to Campbell's tasks for the development phase of the process (see introduction to part 2 Figure 1 (page 114)).

6.2.1 Significance of falls in MS

The results of both study one (observational study, chapter 3 (page 51)) and study two (nominal group technique (NGT) study (chapter 5 (page 195)) confirm the significance of falls as an issue for people with MS. Study one confirmed the high incidence of falls in MS, with more than 70% (n=104) of the participants recording at least one fall. This proportion of fallers is greater than in other studies, possibly due to the greater level of mobility impairment of the sample in comparison to others[250]. A high number of *near* falls were also recorded, with 3785 near fall events being recorded by 128 participants (86% of the total sample). Whilst it is possible that these volunteer participants did so because of a personal experience of falls and near falls, the findings emphasise the relevance of this project for many people with MS. This was further supported by the findings of study two, where both MS service users and professionals identified significant physical and emotional costs associated with falling for both the person with MS and their family.

6.2.2 Potential target group for a falls intervention

Identification of a target group is valuable to ensure efficient use of resources as well as to optimise the outcomes of an intervention. The studies in this thesis inform a number of aspects pertinent to the identification of a target group for an MS falls management programme. The prevalence of falls in study one suggests that a large proportion of people who are experiencing mobility issues would be appropriate for inclusion, as more than half of the participants reported two or more falls in the three month prospective reporting period (52.7% n=78). Systematic review one (chapter 2 (page 33)) identified that those with a progressive MS sub-type were more likely to fall, with a pooled odds ratio of 1.98 (95% CI 1.39-2.80). Whilst there was no statistically significant association between MS classification and falls status in study one, subsequent pooling of this data with three other similar data sets (resulting in a larger sample size (n=537)), demonstrated that people with primary progressive MS are, on average, more than twice as likely to fall than those with relapsing-remitting MS (adjusted OR 2.21, 95% CI 1.20-4.08)[250] (Appendix 7.5.5 (page 365)). Similarly, the non-linear relationship of the EDSS with falls classification (first identified in study one) was supported by the analysis of pooled data, with peaks in falls risk seen in those classified as EDSS 4.0 (n=30) and 6.0 (n=73) (OR 6.33 (95% CI 1.55-25.86) and OR 7.86 (95% CI 1.87-33.07) respectively)[250] (Appendix 7.5.5 (page 365)). Although the outcomes of observational study methodologies do not imply causality, this finding is of clinical relevance since these points of the EDSS are associated with key transition points in mobility status. It is possible that falls could be used as an early marker of mobility deterioration. Additionally it could be argued that interventions which decrease falls could help to maintain mobility and physical activity levels, thus slowing the progression of mobility deterioration.

Whilst general indicators of falls risk such as MS classification are valuable at a population level, they are relatively unhelpful to inform the evaluation of falls risk for individual patients. The results of study one demonstrated that a regression model including the Physiological Profile Assessment, Ashworth Score and EDSS was able to discriminate between people classified as fallers and non-fallers with a sensitivity of 69% and specificity of 70% (AUC C statistic 0.73, 95% CI 0.65-0.81). This has the potential to inform the development of an MS specific falls risk assessment tool for use in clinical practice, thus enabling the identification of individuals who are most likely to benefit from a falls intervention. In papers published since the completion of study one, other potential falls risk assessment tools have also been proposed. Hoang's study identified that a model including measures of postural sway (with eyes closed), co-ordinated stability and fine motor control demonstrated an AUC C statistic of 0.71 (95% CI 0.64-0.79)[231], whilst

Cameron showed that falls history was able to discriminate between fallers and non-fallers with a sensitivity of 89%[413]. However, whilst falls history has the attraction of being quick and simple, the moderate specificity (56%) means that the measure has a limited ability to rule out falls in individuals from a similar population. Furthermore, falls history only identifies people who *have* fallen, rather than those at risk of falls. The position statement developed in study two (chapter 5, section 5.5.3 (page 222)) recommends that both would be candidates for a falls intervention. However, given the current lack of evidence of the effectiveness of interventions in this area, the added complexity of evaluating preventative healthcare interventions, and the resource restrictions in health service provision; it would seem reasonable to initially target those who have already fallen in preference to those at risk of falling.

6.2.3 Identification of mechanisms by which the intervention will lead to the outcome: Falls risk factors

As discussed in the introduction to part two of this thesis (page113), systematic review one and study one identified a number of potential risk factors which could, if addressed effectively, lead to a reduction in falls. The main focus for part two of the thesis was balance, as highlighted by the contribution of postural sway measures and increased reaction time to increased falls risk (study one, section 3.4.4.2 (page 90)). However, other important factors not previously evaluated in MS were also identified. Specifically, study one demonstrated an association between medication usage and falls risk. People classified as fallers reported taking significantly more prescribed medications ($p<0.05$) and significantly fewer over-the-counter medications ($p<0.05$) than non-fallers (Table 3-10). Whilst the use of self-report of medication prescription, and lack of prospective monitoring of medication usage in study one requires these findings to be viewed with caution, they are supported by recently published findings from Cameron[257]. It is possible that increased prescription medication usage is an indicator of more active disease processes, as self-reported deteriorating MS has been previously highlighted as a risk factor for falls[121,252]. However, given the known association between poly-pharmacy and falls in older people[414], further evaluation is warranted.

Other risk factors that were identified in study one have been highlighted in previous research, however, this study has enabled the development of a more detailed understanding of the nature of their contribution to falls in MS. For example, increased spasticity was identified as a risk factor in systematic review one (chapter 2 (page 33)), the findings of study one suggest that the association between spasticity and falls risk is non-linear. In this study, the odds of people with a relatively low level of spasticity (grade one) being classified as a faller was significantly higher than those graded as zero or ≥ two on the Ashworth scale (Table 3-14 (page 93)). This is in line with clinical experience which supports the notion that a person with a consistently 'stiffer' leg may be more stable than someone with lower levels of spasticity. However, the limitations of the Ashworth score as an outcome measure and the use of a single measurement site in this study is recognised. Further research should be undertaken to confirm the findings of study one and to investigate this aspect in more depth.

Study one investigated risk factors which had not been previously evaluated in MS; being the first to include measures of cerebellar, vestibular or autonomic function. The findings suggested that none of these aspects were individually associated with increased odds of being classified as a faller. It is possible that the measures were not sufficiently sophisticated to effectively evaluate the potential contribution of these systems to falls risk. For example, the Brief Ataxia Rating Scale is a relatively crude measure with only two of the five elements directly related to gait and balance. A more sensitive scale such as the SARA (Scale for the Assessment and Rating of Ataxia)[415] may have produced different results; although even in a cohort of individuals with pure cerebellar disease, the presence of extra-pyramidal signs, rather than cerebellar dysfunction, was the factor most closely related to falls[234]. However, given the recent findings that cerebellar dysfunction is associated with measures of sway in MS[416], this aspect should be investigated further.

For some risk factors, the findings of study one differ from those of other research. For example, in other recent studies, fear of falling as measured by the FESi was associated with falls classification[179,256]; which contrasts with our findings. Sample characteristics of the three studies could have affected the results: The mean EDSS in Kalron's study was 3.0 (SD 1.8)[256] and van Vliet's study included participants from across the spectrum of MS disease steps, including 90 (53%) with a disease step classification ≤2 (indicating relatively mild disability)[179]. In contrast, the median EDSS in study one was 6.0 (range 3.5-6.5). Given the link between falls and increasing disability, one possible explanation is that over time participants' fear of falling reduced. The exploratory analysis based on falls frequency in study one showed significantly higher FESi scores in those who reported ≥6 falls in the three month period, underlining that fear of falling remains an important issue for some people. Whether this fear in itself affects risk of falling, as yet remains uncertain.

6.2.4 Identification of intervention components and intensities

The majority of the findings related to this aspect of the development of the falls programme were informed by systematic review two (chapter 4 (page 121)). This review is the first to evaluate the content and the effect of existing interventions targeting falls in MS. The findings suggest that both exercise and education-focussed interventions have the potential to affect falls-related outcomes. Whilst the two exercise interventions included in the meta-analysis demonstrated significant reductions in the number of fallers *and* rate of falls, meta-analysis yielded a modest pooled reduction in risk ratio, with confidence intervals crossing one. However, the fact that the two other exercise studies which reported falls data (as against surrogate measures) both also demonstrated a reduction in falls is promising. This is further supported by a recently published study which showed a significant reduction in the number of fallers and recorded falls with an exercise intervention focussed on core stability, dual task and sensory training[417]. Importantly, this study is the first to utilise prospective falls diary recording methods both before and after the intervention, strengthening the reliability and validity of the findings.

The main outcomes of the education-focussed studies included in review two relate to improvements in confidence, knowledge and self-efficacy (section 4.4.6 (page 135)). Whilst these types of interventions have been shown to also reduce falls in other groups[418], improvements in knowledge and self-efficacy alone may be valuable. In a range of studies, increased knowledge and self-efficacy have been associated with increased programme adherence[419,420], an issue which was recognised as a potential challenge to implementation of the MS falls programme in study two (section 5.5.3 (page 222)). In addition, study two highlighted that entirely preventing falls may be an unrealistic goal, and that improving participants' ability to assess risk, utilise coping strategies and manage falls was therefore essential (section 5.5.3 (page 222)). Given that 20% (n=29) of the participants in study one recorded over six falls in the three month recording period, this seems to be a reasonable recommendation (Table 3-4 (page 78)).

Review two included a detailed evaluation of the content and outcomes of exercise programmes which measured balance. This aimed to inform decisions relating to the type, format and models of exercise intervention which should be utilised in a future MS falls programme. Whilst a review of the effects of physiotherapy interventions on balance in MS has been published previously[247], it included only eleven studies. By contrast, review two included 27 papers in the quantitative analysis of balance outcomes, 17 of which could be included in the meta-analyses. Eight of these papers had been published since 2012, reflecting the increasing focus of research in this area. The meta-analyses of the different exercise categories in review two demonstrated small to moderate effect sizes, with programmes involving gait, balance and functional training yielding the greatest magnitude of effect (SMD 0.82 (0.55-1.09)). Whilst this review highlights the potential value of these interventions to improve balance (and therefore possibly decrease falls), one should be cautious in assuming an effect simply by association.

However, this aspect of the review suggests that specific gait, balance and functional training activities are likely to be the most appropriate exercise types to include in a falls programme. Systematic review two highlighted a number of strategies in addition to 'traditional' balance activities, which may be of importance in targeting key balance mechanisms affected in MS. For instance, given a median reduction in walking velocity of 30% (IQR 57- 12) with the addition of a cognitive task in study one (Table 3-13 (page 92)), the inclusion of dual task training could have a significant effect on functional mobility (and possibly falls), as demonstrated recently in MS[417]. Similarly, the potential value of additional multisensory training has been recognised in falls programmes for older people[421]. This type of training was included in one of the studies in review two which evaluated falls outcomes[241], and also the more recent programme evaluation published by Nilsagard[417]; with both programmes demonstrating significant reductions in falls amongst intervention group participants.

Review two also undertook a detailed evaluation of the effect of differing levels of challenge, intensity, duration and overall dose of exercise on outcome, aspects which have not been explored in MS to date. In agreement with findings in older people[272], activities which present a high degree of challenge to balance appear to be associated with a larger effect than those providing a moderate level of challenge. Similarly, there was a moderate correlation between programme intensity (minutes/week) and effect size (r= 0.58 p= 0.02). Given the variable study methodologies and outcome measures in review two, these results should be incorporated with caution. However, they suggest that undertaking at least 120 minutes of highly challenging balance exercise each week should be a priority. In contrast, in this review, there was a significant moderate negative correlation between effect size and programme duration in weeks (r= -0.49, p= 0.05), and there was no significant association between total dose and effect. As adherence was not measured in detail within these studies, it is impossible to assess whether these outcomes were related to decreased engagement over time in longer duration studies, given the positive association between high intensity practice and effect size. This lack of detail with regard to adherence, along with limited long-term follow-up are major methodological limitations to these studies; these aspects should be a priority for future research. Given the evidence in other groups that sustained engagement with high intensity high challenge exercise is associated with improved falls outcomes[249], it is recommended that the MS falls programme is structured to facilitate long term engagement in exercise, with the recognition that participants may need significant support to achieve this, as indicated by study two (section 5.5.3 (page 222)).

6.2.5 Key intervention processes and outcomes

Outcomes

The possible outcomes of the MS falls programme were discussed in some depth within study two. Importantly this study highlighted that falls reduction should not be at the expense of quality of life. To put it starkly, an effective way of reducing falls is to prevent people from moving about; clearly this would not be the intention of a falls programme. Quality of life has not yet been measured in any of the MS falls research studies, and the potential challenges in choosing an outcome measure within this domain has recently been recognised[422]. Addressing this issue is likely to be a priority in future research to ensure that implementation studies evaluate the impact of the falls programme in this area in a meaningful way.

A range of falls outcomes and reporting methods were used in the studies in review two, including prospective and retrospective falls monitoring, use of proxy measures for falls and measurement of other characteristics such as fear of falling (section 4.4.6 (page 135)). The issues associated with retrospective recall of falls and the need to adopt prospective falls monitoring as the gold-standard measure is recognised both in the general[108] and MS specific literature[255]. Despite this; prospective falls monitoring only occurred in two of the eight papers included in this review. The high return rate of falls diaries in study one (823 / 888= 93%) indicates that this method of data collection is feasible and acceptable to participants with MS; therefore future studies should incorporate this method.

The findings of study one suggest that other outcomes that are considered valuable in the wider falls literature may be less relevant in MS. For example, reduction in injuries associated with falls (particularly a reduction in fracture rates) is a key goal of falls management for older people due to associated morbidity and financial costs[98]. In study one of this thesis, 11% (n= 62) of the 555 falls where participants returned data on causes and consequences were associated with some type of documented injury. However, only 6 of these (1% of the 555 recorded falls) were documented as requiring medical intervention. Other MS studies have reported higher[222] (3%) and lower[423] (0.8%) rates of falls requiring medical intervention; however, these are still significantly lower than those seen in older people (10-20%)[424], or in people who have had a stroke (15%[425] and 30%[426]). Therefore, whilst monitoring of injurious falls is important due to their likely impact on quality of life and fear of falling, it is essential to recognise that selection of injurious falls as a primary outcome for a research evaluation will have a significant impact in terms of study power and sample size.

Processes

The findings of both review two and study two indicate that the falls programme needs to be designed to support participants to undertake regular high intensity, high challenge gait, balance and functional training; and to integrate falls risk management strategies into their daily lives. A range of challenges and opportunities were identified in this area, resulting in a number of recommendations which are summarised in the position statement which forms the conclusion of study two (section 5.7 (page 275)). The use of a theoretical framework to inform programme design has been recommended to support the bringing together of potentially disparate elements into a holistic programme[427]. As in other MS programmes[327,428], aspects of cognitive-behavioural theory are likely to be relevant to the MS falls programme; these will be highlighted within the following discussion.

The overall approach of the MS falls programme was highlighted as a significant factor within study two, and within the qualitative papers included in review two (section 4.4.10 (page 170)). A key recommendation is the need for the programme to utilise a collaborative approach, emphasising the role of the programme leader as a facilitator, working in partnership with the participants. Bandura's social-cognitive theory (SCT) emphasises the importance of this type of approach to maximise self-efficacy through provision of supportive feedback, identification of potential barriers and the development of effective strategies[323]. An additional recommendation from study two was the need to ensure the falls programme moved away from a medical model in its approach. Participants identified that the programme should be 'professional' to increase confidence and emphasise the legitimacy of the advice and guidance, but not 'medical'. This finding has resonance with falls prevention programmes for older people, where it is recommended that programmes should emphasise social and participation benefits rather than health risks in order to optimise engagement and adherence[261,385].

The value of including both group and individual elements within the programme was highlighted in both review two and study two. Group programmes were highlighted as offering social and motivational benefits in study two (section 5.5.3 (page 222)) and review two suggests they may also be associated with better adherence than home-based programmes (section 4.4.10 (page 170))[329]. In addition, SCT suggests that opportunities for vicarious experience and the modelling of behaviours provided by peer group sessions are key factors to optimise ongoing engagement[429]. However, the transfer of behaviour change from the group setting into real-life is challenging[419], and difficulties with regular group attendance as highlighted within study two suggest that a pure group format is unlikely to be successful.

The recommendation from study two for individual, home-based activities to be an integral part of the programme is supported by the findings of review two (chapter 4 (page 121)) and related theoretical frameworks. The health beliefs model suggests that individuals will tend to adopt behaviours if they believe they will address a perceived threat[225]. Self-identification of 'threats' (e.g. self-assessment of environmental and behavioural factors associated with falls) is recognised as a core strategy to support behaviour change in this context[323]. The findings of study one identified that the majority (62% n= 345) of falls occurred indoors, and/or were associated with typical day to day activities (74% n= 412). Therefore, undertaking hazard assessment and modification activities at home, in the environment where the majority of falls actually occur, presents a valuable opportunity to support participants to identify their personal risks and to contextualise strategies from the outset.

Recommendations relating to the format of the programme include the need for a flexible and yet clearly defined programme, and the need to support engagement on an ongoing basis (section 5.7 (page 275)). Study two highlighted the importance of ensuring that the programme was structured to enable some degree of participant choice (section 5.5.3 (page 222)). This is supported by SCT, which highlights the value of self-monitoring and progression to support self-efficacy[419]. However, a number of potential conflicts are presented within this thesis. For example, review two suggests that high challenge, high intensity balance exercise may yield the greatest effect; however, participants in study two identified that they may lack the confidence to undertake activities they perceived as 'hard' without significant amounts of 'supportive encouragement'. Whilst the importance of externally generated feedback and instruction is also recognised within SCT[323], there may still be issues associated with achieving a sufficient degree of challenge: In the review of active console games interventions (section 4.4.7(page 146)), the study with the most significant change in balance was the only programme where the activities were chosen at random[285], rather than being selected by participants or therapists[283,287].

This supports the premise that choice tends to be associated with selecting activities which are well within, rather than towards the boundaries of participants' capabilities. The development of a programme manual, with clearly defined selection parameters and progression options for exercises has been recommended as a strategy to address these issues, as well as to ensure treatment fidelity[428,430].

Supporting participant engagement is a key issue in many types of rehabilitation programme[395,431]. However, some consider that the physical, cognitive and social issues associated with MS present a unique challenge[342]. Study two highlighted the need for the programme to include strategies to enable participants to monitor their progress, to re-engage with the programme (e.g. after relapses) and to support long-term behaviour change (section 5.5.3 (page 222)). Within cognitive-behavioural theory such strategies are identified as being beneficial to facilitate self-motivation, to highlight performance mastery and to support the setting and monitoring of individual goals[419]. A range of strategies have been utilised in other MS rehabilitation programmes, including motivational interviewing[319], customised pamphlets[324] and the use of telephone support[432]. Another method which could be particularly useful for the MS falls intervention would be the inclusion of an online package. This would enable programme leaders to remotely monitor, review and progress exercise prescriptions within pre-defined protocols[399,400]. It would also allow participants to record their progress, to access educational materials in an interactive format and to access peer support through social networking with fellow participants[338]. The online package could be supported by periodic group sessions to maintain motivation, develop group cohesion and problem-solve specific issues.

6.2.6 Potential barriers to the application of the intervention

The in-depth discussions undertaken within study two enabled key issues to be identified which could affect the translation of an MS falls programme into practice. In particular, the inclusion of service users highlighted factors that may not have been considered were an alternative method used. Whilst the need to minimise barriers to access and engagement has been highlighted widely in the literature[384,433], this study identified specific issues related to MS: For example, a strong recommendation was that an MS falls programme should be discrete from 'generic' (older peoples') falls services. Reasons for this included the differing risk factors, and the differing demographics, perceptions and attitudes of service users. Additionally, service users highlighted the significant impact that seemingly small issues could have on their perceptions of, and ultimately their willingness to engage with the programme. This has not been discussed in other studies, and emphasises the importance of maintaining stakeholder engagement throughout the development, application and evaluation of the programme.

Study two identified that a major potential barrier to the successful application of the falls programme was provision of adequate resourcing. This included appropriate facilities (environmental and equipment), availability of professional, user-friendly supporting materials and adequate staffing. High level of skills, knowledge and experience were deemed essential for the programme leadership role. Whilst the importance of ensuring financial support for the programme was recognised, the involvement of non-statutory and third sector agencies were recognised as opportunities to support the application of the programme in practice.

The work undertaken within this thesis has also identified a number of challenges to research evaluation of the MS falls programme. A key issue is the selection of relevant, psychometrically sound outcomes which include participation and quality of life measures. Prospective monitoring of falls before, during *and* after the intervention period is considered essential.

Other important issues to consider for future research are the potential recruitment and randomisation issues highlighted in review two (section 4.4.6 (page 135)). Additionally, the high level of attrition seen in a number of the larger-scale MS studies is of concern, given the relatively short intervention and follow-up periods. By comparison, in a review of 44 falls prevention trials for older people, the median one year attrition rate (including mortality) was 10.9% (IQR 9.1-16%)[246]. Given the nature of MS it is likely that higher attrition rates may occur due to relapses or other health issues; this should be factored into the determination of sample sizes in future studies.

6.3 Contribution to knowledge

Systematic review one was the first to synthesise data relating to MS falls risk factors[220]. At the time, there were relatively few published studies; however the review was able to undertake some meta-analyses, identifying general factors that were associated with increased risk of falling in MS. This analysis, along with the narrative review also highlighted key methodological issues and the limited use of robust measures to evaluate the mechanisms contributing to falls.

Study one (n=150) was able to address some of the issues raised in the systematic review by undertaking an observational analysis of falls risk using validated impairment-focussed measures and prospective collection of falls data. This study also undertook an evaluation of the characteristics and consequences of falls in MS, aspects which had not previously been investigated in depth.

Systematic review two is the first to undertake a comprehensive evaluation of falls and balance-focussed interventions in MS with the specific aim of informing the content, format and delivery method of a falls rehabilitation programme. Whilst previous reviews[247] have evaluated the general outcomes of balance interventions, this review provides a detailed analysis of both outcomes and factors which may contribute to the effectiveness of an intervention. Importantly, the review suggests that existing MS specific interventions may not achieve the level of intensity of highly challenging balance activities that are likely to impact falls outcomes, and that simply utilising existing generic falls interventions is unlikely to meet the specific needs of people with MS.

The Nominal Group study (study two) was innovative in two key ways. Firstly it was unique in its approach to integrally involving service users, health professionals and commissioners in the process of developing a falls management programme. Secondly it breaks new ground in this area in the way in which the nominal group panels comprised both service users and professionals within the same panel. Within the traditional processes of service development, these panels are organised within discrete groupings, which may limit the exchange of ideas and development of a shared understanding between stakeholders.

The outcomes of study two are significant in that they build on the findings of review two by confirming the programme outcomes and content with key stakeholders, and by identifying optimal programme formats and delivery methods. The findings suggest that the traditional model of a falls programme based around weekly attendance to sessions delivered using approaches based predominantly on the medical model are unlikely to be effective or sustainable for participants with MS. The findings will be of value, both from a service commissioning perspective, but also to guide the development of further research projects in this area

6.4 Strengths and limitations of methods

Each of the investigations within this thesis has individual strengths and limitations, which have been discussed within the pertinent chapters (sections 2.4.2 (page 48), 3.5.4 (page 109), 4.5.6 (page 191) and 5.6.1 (page 262)). A general strength is the strong clinical focus of the studies. This includes the involvement of service users and professional staff in the steering group for study one. Furthermore, a key criteria for the selection of outcomes for this study was their feasibility for use within clinical practice; the intention being to enhance future translation to practice. In study two, service user and professional staff involvement was integral throughout the study process, including protocol development, identification and prioritisation of trigger statements and development of the final position statement.

A limitation to the methods is the use of professional and service user participants from one geographical location (the South West peninsula of the UK). Logistical issues made collecting data from participants over a wider area impractical in study one; however, use of an alternative methodology (such as a Delphi study) would have allowed involvement from more geographically diverse participants. The goal to integrate service users fully and collaboratively alongside professional participants led to the decision to utilise a nominal group methodology. Based on feedback from a number of participants in study two, the group training session prior to the NGT study was important to help them to develop the confidence to contribute fully, and the structured nature of the group sessions allowed them space to consider their opinions individually as well as to discuss issues as a group. It is unlikely that this would have been achieved were an alternative methodology used.

The number of available studies and methodological variability is recognised as a limitation in both systematic reviews. Although eight studies were included in review one, interpretation of the results was limited by the variety of data collection and reporting methods. This meant that meta-analysis could only be undertaken for four risk factors, with only four studies being included in each analysis. In contrast, a more recent systematic review[251] was able to include 15 studies, the majority of which could be incorporated into the meta-analyses. Similarly, a number of the exercise categories in review two included very few studies (e.g. education-focussed falls programmes n= 2, 3D training n= 1, endurance training n= 3).

6.5 Further research

Having undertaken a number of studies which inform the development of a model for an MS falls intervention, the next priority is to move towards the feasibility and piloting phase. However, although the studies within this thesis provide a clear outline of programme content, structure and format, there remain a number of unanswered questions. For example, there are areas related to falls risk which require further exploration such as the contradictory findings relating to fear of falling[3,92,121,179,253]. Further research in this area is indicated as fear of falling may have direct implications for the delivery and evaluation of falls programmes. Kasser, for instance, recently identified that fear of falling was an independent predictor of future physical activity levels[434]. If this is the case, fear of falling could significantly affect engagement with the exercise component of the falls.

The feasibility, utility and acceptability of the falls programme needs to be evaluated when implemented in routine practice; this has not yet been determined. Research is also required to inform selection of primary outcome(s). These may include measures of participation and quality of life, activity levels, motor function and balance, alongside the obvious measurement of falls. Evaluation of potential issues which could affect the successful implementation of a fully powered intervention trial is also required, including recruitment rate, willingness of clinicians to recruit and the willingness of participants to be randomized.

6.6 Overall conclusion

This thesis has provided evidence which underlines the significance of falls in MS. It has identified the need to develop a programme which is specifically tailored to the needs of people with MS. A significant proportion of people with MS who have some level of mobility impairment experience falls and near falls; however, the circumstances and risk factors for falling in MS are different from those of other groups[98,426,435]. MS characteristics associated with increased falls risk include progressive MS and key mobility transition points as measured by the EDSS. Clinical factors associated with increased risk of falling included spasticity, continence issues and medication use. However, balance impairment, related to increased sway and increased reaction time was identified as a key (potentially modifiable) risk factor.

A comprehensive systematic review of the literature identified that an MS falls programme which has an education component will enable participants to develop falls self-efficacy and coping strategies, whilst the addition of an exercise intervention which specifically targets balance may reduce overall falls risk. Evaluation of the content and format of the exercise interventions identified that the programme needs to support participants to undertake intensive, highly challenging balance exercise, and to sustain their engagement in the programme. The NGT study supported the findings of this systematic review, and in addition, further advanced our understanding of the key issues likely to impact programme delivery, sustainability and acceptability. This has enabled the development of a proposed programme model which is summarised in Figure 6-1.

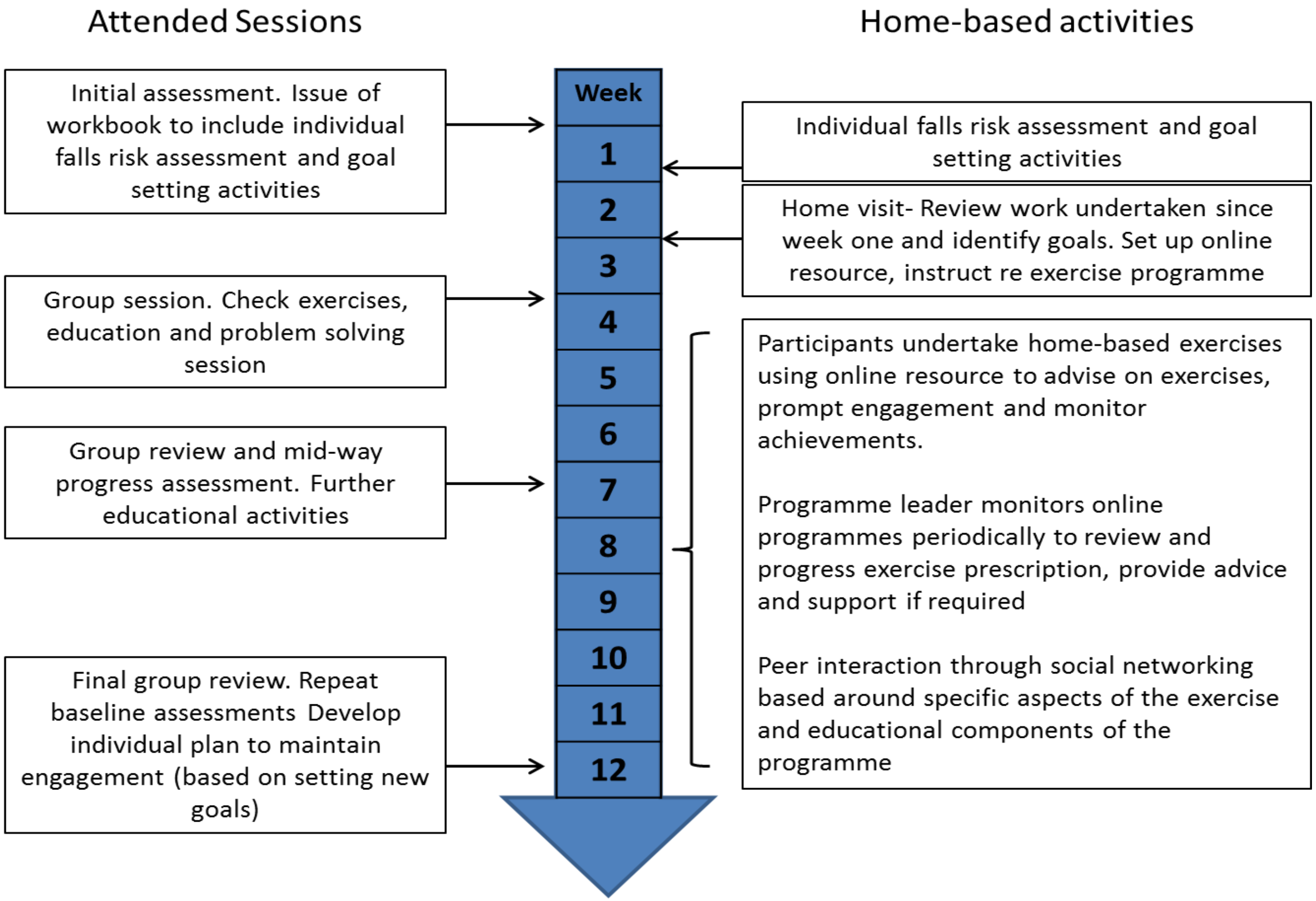


Figure 6-1: Proposed MS falls programme model

The results of study two suggest that the programme should aim to decrease falls frequency whilst maintaining (or ideally increasing) functional activity/participation. The programme should develop a collaborative partnership approach between participants and staff, be easy to access and widely publicised. The location for sessions held away from home is very important. Venues should be accessible, inspiring and motivational, while at the same time being risk assessed as safe.

The format of the programme should have a strong individual element to facilitate the integration of education and exercise activities into daily life, but should also include some group sessions to facilitate peer learning and support opportunities. The scheduling of group sessions should consider the challenges associated with attendance that are particularly prevalent for people with MS. Occasional group sessions interspersed over the course of the falls programme may be more feasible than regular weekly sessions.

The programme structure, format and content must be flexible to account for personal issues which may affect short-term engagement. Adjuncts to support engagement such as the use of online or tele-rehabilitation resources should be considered. Importantly, the programme must be facilitated by skilled and qualified professional staff. This includes neurology-specific expertise alongside knowledge of balance-focussed exercise prescription and falls prevention strategies. Appropriate levels of support must also be provided to enable the program to run safely and effectively. Fundamental to all these aspects is the provision of adequate resourcing and funding to enable the programme to run safely and effectively, and to be sustainable.

This thesis has covered the initial developmental stages of a longer-term project, in a topic of crucial importance to the lives of people with multiple sclerosis. It is now the intention to advance this work by manualising, operationalising and then evaluating the intervention, continuing to maintain the ethos of using rigorous, systematic and user-focussed approaches.

7 Appendices

7.1 Systematic Review One appendices

7.1.1 Adapted Newcastle Ottawa Scale for quality assessment.

Selection (maximum 1 star per section)			Comparability	Outcome (maximum 1 star per section)		
Representativeness of the exposed subjects	Selection of the non-exposed subjects	Method of evaluation of risk factor	Comparability of subjects	Assessment of outcome	Follow up period (was follow up long enough?)	**Adequacy of follow up (losses to follow up etc.)**
Truly Representative (includes all types of MS and range of EDSS levels)	Same community *	Validated Objective Measure *	Study controls for EDSS *	External Observation/ Validated Proxy Measure *	Yes- at least 3 months *	Complete follow up- all subjects accounted for *
Somewhat Representative (limited to specific MS classifications OR disability level)	Different Source (e.g. healthy controls) *	Non-Validated Objective Measure *	Study controls for Age *	Prospective Diary *	No	Subjects lost to follow up unlikely to introduce bias, or description provided of those lost *
Selected Group (limited to specific group AND disability level)	No description	Self-Report *	No controls	Retrospective Self-report		Follow up rate <80% and no description of those lost
No description		No description		Unclear/No description		No statement

7.1.2 Complete data sets for risk factors included in meta-analysis

Balance

Study	N[1]=	Fallers (N=)	Non-fallers (N=)	Mean Difference	Mean Difference SD[2]	OR	Odds Ratio SE[3]	Effect size
Cattaneo	50	17	33	4.8	2.5			1.92
Finlayson	1089	569	520			2.22	0.119097	
Nilsagard	76	48	28	4	7.82	0.94	0.015915	0.51
Soyuer PP[4]	28	14	14	0				
Soyuer SP[5]	34	17	17	0.5				
Soyuer RR[6]	62	16	46	1.5				
Kasser	92	48	44			1.58	0.094469	
Matsuda	155	115	40			1.48	0.028085	

Walking Aid Use

Study	N=	Fallers (N=)	Non-fallers (N=)	Odds Ratio	Odds Ratio SE
Cattaneo	50	17	33	0.35	0.267444923
Finlayson	1089	569	520	2.14	0.101931594
Nilsagard	76	48	28	2.27	0.145130398
Matsuda	361	201	160	4.06	0.101189794

[1] N Number
[2] SD Standard Deviation
[3] SE Standard Error
[4] PP Primary Progressive
[5] SP Secondary Progressive
[6] RR Relapsing Remitting

Cognition

Study	N[1]=	Fallers (N=)	Non-fallers (N=)	Mean Difference	Mean Difference SD[2]	OR	Odds Ratio SE[3]	Effect size
Cattaneo	50	17	33	0.2	2.5			0.08
Finlayson	1089	569	520			1.81	0.093485	
Nilsagard	76	48	28			0.99	0.08608	
Soyuer. PP[4]	28	14	14	2				
Soyuer SP[5]	34	17	17	1				
Soyuer RR[6]	62	16	46	-0.5				
Matsuda	74	51	23			1.27	0.036881	

MS Classification

Study	N=	Fallers (N=)	Non-fallers (N=)	Odds Ratio	Odds Ratio SE
Nilsagard	76	48	28	1.68	0.723233
Soyuer	124	47	77	1.81	0.385688
Matsuda	396	234	162	2.88	0.220073

[1] N Number
[2] SD Standard Deviation
[3] SE Standard Error
[4] PP Primary Progressive
[5] SP Secondary Progressive
[6] RR Relapsing Remitting

7.2 Study one appendices

7.2.1 Assessment schedule: order of testing

1.	Sitting	Demographic/background data	15’
2.	Lying	BARS - knee tibia test Ashworth - ankle FESi (completed orally) BARS- dysarthria (observational) Blood Pressure 1	15’
3.	Standing	Blood Pressure 2	5’
Rest (if required)			5’
4.	Sitting	PPA : sensation, power BARS finger-nose BARS oculomotor PPA edge contrast DVA Test (static)	15’
5.	Standing	PPA balance BARS gait Dual task interference	15’
Rest (if required)			5’
6.	Sitting	SDMT PPA reaction time DVA (dynamic)	10’

7.2.2 Falls Diary

Participant Number:

Each day we would like you to record any fall including a slip or trip in which you lost your balance and landed on the floor or ground or lower level. Please fill in the diary each day detailing any falls, giving as much information as possible. See below for an example of how to fill the diaries in. In your pack you will find 3 months worth of diary pages separated into 2 week batches. Attached to each batch you will find an envelope- please use this to return the completed diary pages to us every 2 weeks. Please send back every page, regardless of whether you have fallen or not.

Notes: Is there anything that has affected you being able to fill in your diary this fortnight? *Form below for example only:*				
Day	**Did you fall?** A fall includes a slip or trip in which you lost your balance and landed on the floor or ground or lower level	**How many times did you fall?**	**Did you nearly fall?** A near fall is an occasion where you felt you were about to fall but did not actually fall	**How many times did you nearly fall?**
	Yes No		Yes No	

Fall 1: **Time of day**		**Where were you?**		**What type of activity were you doing?**		**How fatigued were you?**		**Were you in a hurry?**	
	✓		✓		✓		✓		✓
Morning		Inside	✓	Personal Hygiene		Not at all		Not at all	✓
Afternoon		Outside		Working in the kitchen		As usual		As usual	
Evening	✓			Cleaning Indoors		Somewhat more than usual	✓	Somewhat more than usual	
Night				Working Outdoors		Much more than usual		Much more than usual	
				Other Activities	✓	⇨ Details of Other Activities (if applicable):			
				Physical/ Leisure Activities		*Transferring from bed to chair*			

Day:	**Did you fall?** A fall includes a slip or trip in which you lost your balance and landed on the floor or ground	**How many times did you fall?**	**Did you nearly fall?** A near fall is an occasion where you felt you were about to fall but did not actually fall	**How many times did you nearly fall?**

	or lower level			
	Yes No		Yes No	

Fall 1: Time of day		Where were you?		What type of activity were you doing?		How fatigued were you?		Were you in a hurry?	
	✓		✓		✓		✓		✓
Morning		Inside		Personal Hygiene		Not at all		Not at all	
Afternoon		Outside		Working in the kitchen		As usual		As usual	
Evening				Cleaning Indoors		Somewhat more than usual		Somewhat more than usual	
Night				Working Outdoors		Much more than usual		Much more than usual	
				Other Activities		⇨ Details of Other Activities (if applicable):			
				Physical/ Leisure Activities					

Fall 2: Time of day		Where were you?		What type of activity were you doing?		How fatigued were you?		Were you in a hurry?	
	✓		✓		✓		✓		✓
Morning		Inside		Personal Hygiene		Not at all		Not at all	
Afternoon		Outside		Working in the kitchen		As usual		As usual	
Evening				Cleaning Indoors		Somewhat more than usual		Somewhat more than usual	
Night				Working Outdoors		Much more than usual		Much more than usual	
				Other Activities		⇨ Details of Other Activities (if applicable):			
				Physical/ Leisure Activities					

7.2.3 Falls diary supplementary questions

Consequences of the fall	
Injuries	
Care required	
Number of visits	
Type of specialist	
Days Admission	
Activity associated with fall	
Standing, turning, walking	
On/off chair/ bed/ bath/ toilet	
Standing on chair/ ladder	
Stairs	
Step	
Climbing	
Site of fall (further detail)	
Path	
Lawn/ garden	
Stairs	
Street	
Public building	
Other house	
Vehicle	
Public transport	
Perceived cause of fall	
Trip	
Slip	
Vision	
Distracted	
Dizzy	
Balance	
Legs gave way	
Not sure	
Other details	

7.2.4 Logistic regression: reduced model output and diagnostics

Omnibus Tests of Model Coefficients

		Chi-square	df	Sig.
Step 1	Step	25.105	4	.000
	Block	25.105	4	.000
	Model	25.105	4	.000

Model Summary

Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	179.634[a]	.156	.208

a. Estimation terminated at iteration number 4 because parameter estimates changed by less than .001.

Hosmer and Lemeshow Test

Step	Chi-square	df	Sig.
1	5.892	8	.659

Contingency Table for Hosmer and Lemeshow Test

		Dichotomised Falls = Non Faller		Dichotomised Falls = Faller		Total
		Observed	Expected	Observed	Expected	
Step 1	1	12	11.376	3	3.624	15
	2	9	10.270	6	4.730	15
	3	12	9.604	3	5.396	15
	4	7	8.980	8	6.020	15
	5	9	7.861	6	7.139	15
	6	7	6.668	8	8.332	15
	7	4	5.743	11	9.257	15
	8	4	4.630	11	10.370	15
	9	5	3.398	10	11.602	15
	10	1	1.469	12	11.531	13

Classification Table[a]

	Observed		Predicted		
			Dichotomised Falls		Percentage Correct
			Non Faller	Faller	
Step 1	Dichotomised Falls	Non Faller	47	23	67.1
		Faller	24	54	69.2
	Overall Percentage				68.2

a. The cut value is .500

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I.for EXP(B)	
								Lower	Upper
Step	PPAriskscore	.494	.131	14.308	1	.000	1.639	1.269	2.118

1[a]	EDSS	-.304	.196	2.402	1	.121	.738	.503	1.084
	AshworthGastroc2			7.064	2	.029			
	AshworthGastroc2(1)	1.252	.522	5.754	1	.016	3.496	1.257	9.720
	AshworthGastroc2(2)	.815	.479	2.892	1	.089	2.259	.883	5.780
	Constant	.802	.966	.690	1	.406	2.230		

a. Variable(s) entered on step 1: PPAriskscore, EDSS, AshworthGastroc2.

Casewise List[b]

Case	Selected Status[a]	Observed	Predicted	Predicted Group	Temporary Variable	
		Dichotomised Falls			Resid	ZResid
94	S	N**	.874	F	-.874	-2.636

a. S = Selected, U = Unselected cases, and ** = Misclassified cases.

b. Cases with studentized residuals greater than 2.000 are listed.

Interpretation of residuals

Diagnostic test	Analog of Cook's influence statistics	Leverage value	Standardized residual	DFBETA for constant	DFBETA for PPAriskscore	DFBETA for EDSS	DFBETA for Ashworth 1	DFBETA for Ashworth 2+
Criteria	Number of values >1	Number of values greater than 3x the average leverage[a]	Number of values lying outside ±1.96[b]	Number of values >1				
Result	0	0	1	0	0	0	0	0
Individual values								
1	.01429	.02648	-.72482	-.07867	.00485	.01184	.01504	.00675
2	.01245	.02741	-.66477	-.06817	.00620	.00938	.01385	.00703
3	.10454	.08457	-1.06374	-.18096	.01524	.02008	-.13085	-.01940
4	.03860	.03001	-1.11692	-.14448	-.00924	.02974	.02016	.00160
5	.00964	.02992	-.55919	-.05016	.00777	.00549	.01151	.00708
6	.01279	.02719	-.67637	-.07019	.00597	.00984	.01409	.00699
7	.01079	.02876	-.60370	-.05765	.00725	.00705	.01254	.00714
8	.06204	.03481	-1.31152	-.17275	-.01785	.03856	.02131	-.00213
9	.04575	.02610	1.30665	.14643	-.00645	-.02318	-.02693	-.01102
10	.02414	.03067	.87347	.11349	.00797	-.02368	-.01554	-.00083
11	.02328	.05915	.60856	.09834	.00108	-.01530	.06692	.01431
12	.02296	.02647	-.91886	-.11233	-.00126	.02051	.01811	.00477
13	.00889	.03073	-.52960	-.04531	.00800	.00453	.01080	.00698
14	.05466	.07428	.82537	.18683	.00128	-.03224	.00916	.09395
15	.02659	.02861	.95002	.12128	.00589	-.02414	-.01769	-.00246
16	.11041	.08073	1.12127	.24568	-.01105	-.03669	.00955	.12306
17	.01642	.02599	-.78446	-.08912	.00323	.01441	.01610	.00629
18	.07125	.02800	1.57268	.15621	-.01667	-.02041	-.03275	-.01758
19	.01764	.02592	-.81408	-.09429	.00233	.01573	.01659	.00601
20	.02818	.02757	-.99692	-.12536	-.00426	.02415	.01904	.00363
21	.01591	.02606	-.77101	-.08677	.00362	.01382	.01587	.00641
22	.05823	.02697	1.44954	.15243	-.01193	-.02183	-.03018	-.01457
23	.03704	.06764	.71458	.12006	-.00266	-.01681	.08348	.01587
24	.01316	.04600	.52245	.06518	.01199	-.01687	-.00588	.00393
25	.01808	.02592	-.82420	-.09606	.00201	.01618	.01675	.00591
26	.00685	.04249	.39298	.05209	.00475	-.01006	.03357	.00926

27	.01002	.01887	-.72172	-.04845	.00491	.00605	.01643	.01194
28	.01230	.03854	.55400	.04950	.01203	-.01382	-.00773	.00007
29	.00961	.01939	-.69718	-.04549	.00548	.00528	.01589	.01184
30	.01776	.05368	.55961	.09341	.00749	-.01874	.00579	.05400
31	.01111	.01806	-.77726	-.05521	.00343	.00786	.01757	.01205
32	.01654	.02503	.80256	.07106	.00951	-.01636	-.01522	-.00548
33	.01644	.02538	.79466	.07051	.00967	-.01633	-.01498	-.00527
34	.00833	.04049	.44436	.04829	.00437	-.00872	.04017	.00802
35	.09117	.05895	-1.20640	-.21621	-.00163	.03623	-.01030	-.12566
36	.20216	.04161	-2.15785	-.23886	-.01936	.04205	-.20018	-.03874
37	.01025	.01865	-.73432	-.04998	.00459	.00645	.01670	.01198
38	.01038	.01853	-.74161	-.05086	.00440	.00668	.01685	.01199
39	.00758	.02387	-.55680	-.02927	.00775	.00151	.01247	.01066
40	.02066	.01947	-1.02001	-.08471	-.00512	.01671	.02145	.01101
41	.02919	.01793	1.26452	.09094	-.00485	-.01330	-.02852	-.01927
42	.01598	.02717	.75635	.06770	.01039	-.01617	-.01380	-.00427
43	.19826	.04202	-2.12610	-.23682	-.01839	.04131	-.19900	-.03808
44	.01702	.02338	.84321	.07378	.00862	-.01642	-.01647	-.00660
45	.01303	.03686	.58351	.05249	.01205	-.01433	-.00858	-.00044
46	.01374	.01907	.84058	.03814	.00862	-.00961	-.01821	-.01281
47	.01308	.02650	.69323	.03461	.01125	-.01034	-.01331	-.00770
48	.01744	.01333	1.13631	.03961	-.00023	-.00563	-.02754	-.02382
49	.00774	.01506	-.71157	-.01862	.00515	.00026	.01768	.01696
50	.03243	.01546	1.43695	.03627	-.01137	.00013	-.03570	-.03458
51	.04860	.02477	-1.38318	-.06792	-.02077	.01967	.02735	.01663
52	.01288	.02792	.66966	.03382	.01151	-.01035	-.01253	-.00694
53	.03975	.01673	1.52851	.03468	-.01487	.00202	-.03790	-.03765
54	.05720	.06502	.90693	.07146	-.01153	-.00205	.10487	.00235
55	.00765	.01532	-.70110	-.01791	.00539	.00004	.01742	.01682
56	.00761	.01546	-.69592	-.01757	.00551	-.00006	.01729	.01675
57	.01224	.03143	.61418	.03174	.01191	-.01024	-.01071	-.00525
58	.00981	.03902	.49141	.03861	.00373	-.00617	.04606	.00565
59	.02197	.01364	1.26057	.03866	-.00471	-.00337	-.03109	-.02838
60	.14953	.04136	-1.86175	-.14940	-.00995	.02160	-.18303	-.01990
61	.00804	.01439	-.74210	-.02071	.00439	.00092	.01841	.01734
62	.00882	.01290	-.82175	.00763	.00211	-.00369	.02200	.02420
63	.00670	.03468	.43188	.01897	.00445	-.00327	.03668	.00290
64	.04090	.04188	.96726	.08375	-.00412	-.00959	.00241	.08262
65	.00643	.02018	-.55891	.01106	.00773	-.00620	.01466	.01792

66	.02143	.04637	.66386	.02776	-.00076	-.00053	.06994	.00053
67	.00929	.01279	-.84648	.00702	.00132	-.00328	.02257	.02458
68	.09460	.02300	2.00458	-.04381	-.03250	.02492	-.05103	-.06396
69	.03298	.01529	1.45745	-.02157	-.01218	.01157	-.03929	-.04560
70	.01687	.01279	1.14119	-.00814	-.00042	.00360	-.03024	-.03257
71	.00476	.03277	.37490	.00549	.00472	-.00129	.02843	.00104
72	.05869	.02095	1.65619	-.09237	-.01984	.02859	-.04756	-.06424
73	.00756	.02173	-.58327	.03265	.00750	-.01029	.01664	.02261
74	.00697	.03707	.42559	.02229	.00772	-.00608	.00225	.02862
75	.06991	.04407	1.23146	.04155	-.01569	.00460	-.00238	.08807
76	.10179	.07607	1.11191	-.01955	-.02277	.02177	.12258	-.01959
77	.02411	.04936	-.68138	-.01791	.01234	-.00494	.00224	-.04439
78	.00670	.02448	-.51676	.02901	.00805	-.00969	.01429	.01981
79	.01275	.03488	.59399	-.01404	.01198	-.00154	-.01251	-.01276
80	.02831	.01663	1.29360	-.06759	-.00601	.01757	-.03780	-.04871
81	.03936	.03883	-.98708	-.04083	.00586	.00055	.00025	-.07550
82	.01394	.01639	-.91447	.04375	-.00100	-.00945	.02619	.03250
83	.01490	.02623	.74375	-.02473	.01053	.00143	-.01831	-.02037
84	.01487	.04246	.57913	.00335	.00184	.00222	.05661	-.00215
85	.01806	.04769	.60060	-.02032	.00124	.00723	.05866	-.00683
86	.01364	.02385	-.74724	.07041	.00434	-.01653	.02366	.03405
87	.05143	.03596	-1.17423	-.00502	-.00033	-.00449	.00124	-.08334
88	.11930	.08308	1.14746	-.07321	-.02496	.03328	.12387	-.03031
89	.00288	.03394	.28643	.00661	.00595	-.00308	.00128	.01410
90	.05773	.02516	1.49565	-.14147	-.01383	.03529	-.04701	-.06873
91	.00120	.02462	.21808	-.00011	.00346	-.00081	.01060	.00063
92	.01659	.03756	.65204	-.04393	.01173	.00441	-.01623	-.02037
93	.02909	.02579	-1.04827	.09041	-.00621	-.01641	.03157	.04301
94	.25380	.03523	-2.63638	.03714	-.03280	-.00571	-.19796	.00656
95	.06613	.02596	1.57530	-.14868	-.01690	.03805	-.04917	-.07238
96	.04854	.03636	-1.13431	-.00347	.00108	-.00522	.00154	-.08018
97	.03638	.02762	-1.13172	.09407	-.00973	-.01574	.03318	.04455
98	.01852	.02349	-.87743	.08046	.00033	-.01699	.02750	.03863
99	.02773	.04623	-.75639	.00850	.01139	-.01003	.00361	-.04657
100	.03830	.03924	-.96839	.00256	.00643	-.00792	.00267	-.06617
101	.01422	.02366	-.76593	.07199	.00383	-.01665	.02425	.03478
102	.01130	.02538	-.65877	.06229	.00638	-.01566	.02067	.03028
103	.05559	.03186	-1.29967	.09943	-.01713	-.01383	.03577	.04667
104	.00557	.03569	.38784	-.00577	.00470	.00098	.02957	-.00109

105	.08909	.07687	1.03435	-.06209	-.01853	.02757	.11287	-.02519
106	.01611	.03847	.63455	-.04174	.01186	.00390	-.01549	-.01931
107	.01785	.03509	.70047	-.05005	.01122	.00590	-.01827	-.02333
108	.01459	.02357	-.77737	.07293	.00351	-.01671	.02460	.03521
109	.01677	.02337	-.83719	.07759	.00168	-.01694	.02638	.03734
110	.01142	.02527	-.66367	.06277	.00628	-.01572	.02084	.03050
111	.02481	.02530	.97782	-.08522	.00494	.01584	-.02967	-.04060
112	.02011	.03072	.79651	-.06234	.00962	.00913	-.02231	-.02933
113	.00906	.03678	.48722	.00941	.00779	-.00328	.00146	.03179
114	.01005	.02678	-.60419	.05678	.00728	-.01487	.01869	.02769
115	.01278	.03582	.58642	.00912	.00698	-.00226	.00112	.04052
116	.06701	.04359	1.21255	-.01012	-.01485	.01406	-.00498	.07799
117	.01332	.02399	-.73624	.06945	.00463	-.01644	.02330	.03361
118	.00808	.02949	-.51582	.04713	.00811	-.01318	.01531	.02311
119	.03475	.05788	.75203	-.03400	-.00425	.01365	.07935	-.01265
120	.01887	.03304	.74327	-.05551	.01060	.00730	-.02008	-.02600
121	.15982	.04371	-1.87003	.05279	-.01014	-.01708	-.17295	.01639
122	.00766	.03006	-.49705	.04498	.00817	-.01276	.01456	.02208
123	.04063	.03831	-1.00994	.00113	.00518	-.00731	.00241	-.06980
124	.02984	.03645	.88816	.00248	-.00108	.00424	-.00127	.06272
125	.01301	.02413	-.72541	.06850	.00490	-.01635	.02295	.03317
126	.00541	.03669	.37681	.00841	.00734	-.00354	.00150	.02185
127	.07312	.04456	1.25213	-.01182	-.01667	.01532	-.00546	.07931
128	.02543	.03570	.82879	.00433	.00102	.00266	-.00068	.05897
129	.02336	.02638	.92837	-.07908	.00639	.01396	-.02772	-.03756
130	.12688	.05088	-1.53842	.05816	.00075	-.02175	-.15510	.02037
131	.00195	.03137	.24514	.00557	.00507	-.00268	.00111	.01085
132	.01440	.03545	-.62587	.08387	.00704	-.02001	.02099	.03338
133	.03497	.06368	.71707	-.06115	-.00284	.01796	.07372	-.01674
134	.06111	.03432	1.31120	-.17916	-.00685	.03935	-.04491	-.07003
135	.05759	.03984	-1.17813	.14731	-.01185	-.02511	.03709	.05485
136	.03471	.04063	.90529	-.03717	-.00175	.01222	-.00356	.05697
137	.00644	.04016	.39240	-.01760	.00470	.00330	.02967	-.00326
138	.01249	.03617	-.57686	.07593	.00771	-.01867	.01899	.03043
139	.01982	.04809	.62635	-.06576	.01201	.00843	-.01662	-.02343
140	.03216	.04016	.87668	-.03483	-.00068	.01117	-.00319	.05549
141	.07548	.03869	-1.36952	.04355	-.00755	-.01142	.00269	-.08782
142	.10139	.03864	-1.58838	.04012	-.01592	-.00781	.00109	-.10058
143	.13357	.03896	-1.81511	.03557	-.02441	-.00381	-.00062	-.11179

144	.07135	.03880	-1.32951	.04402	-.00603	-.01203	.00296	-.08527
145	.03977	.04425	-.92688	.04418	.00766	-.01622	.00509	-.05548
146	.02789	.03945	.82416	-.03058	.00116	.00927	-.00253	.05259
147	.07597	.04782	1.22985	-.06355	-.01573	.02476	-.00805	.06943
148	.00143	.02965	.21651	.00095	.00439	-.00163	.00076	.00808
Total N	148	148	148	148	148	148	148	148

[a]: Expected leverage is (k+1)/N, where k is the number of predictors and N is the sample size. In this case it would be (6/148 =0.041). Leverage diagnostics look for the number of values which are greater than three times the average leverage

[b]: Standardized residuals: no more than 5% should lie outside ±1.96, and no more than % outside ±2.58.

7.2.5 Receiver operating characteristic curve cut-off calculation: model 2

Cut-off point	**Sensitivity**	**Specificity**	**C statistic: ((1-Sn)2+(1-Spec)2)**	**Youden index =max((sn+sp)-1)**
0.0000000	1.000	0.000	1.000	0.000
.1986913	1.000	0.014	0.972	0.014
.2047113	.987	0.014	0.972	0.001
.2104549	.987	0.029	0.944	0.016
.2148994	.987	0.043	0.916	0.030
.2278483	.987	0.057	0.889	0.044
.2373389	.987	0.071	0.862	0.059
.2381150	.987	0.086	0.836	0.073
.2439440	.987	0.100	0.810	0.087
.2517618	.987	0.114	0.785	0.101
.2604752	.987	0.129	0.760	0.116
.2671380	.987	0.143	0.735	0.130
.2672961	.974	0.143	0.735	0.117
.2744420	.974	0.157	0.711	0.132
.2843428	.974	0.171	0.687	0.146
.2875670	.962	0.171	0.688	0.133
.2938188	.949	0.171	0.689	0.120
.3011838	.936	0.171	0.691	0.107
.3042069	.936	0.186	0.667	0.122
.3061293	.936	0.200	0.644	0.136
.3077073	.936	0.214	0.621	0.150
.3114080	.923	0.214	0.623	0.137
.3154769	.923	0.229	0.601	0.152
.3185774	.923	0.243	0.579	0.166
.3212727	.910	0.243	0.581	0.153
.3243720	.897	0.243	0.584	0.140
.3266832	.885	0.257	0.565	0.142
.3283168	.885	0.271	0.544	0.156
.3328432	.885	0.286	0.524	0.170
.3393116	.885	0.300	0.503	0.185
.3434546	.885	0.314	0.484	0.199
.3446034	.885	0.329	0.464	0.213
.3475528	.885	0.343	0.445	0.227
.3509172	.885	0.357	0.427	0.242
.3531732	.885	0.371	0.408	0.256

.3549821	.885	0.386	0.391	0.270
.3567175	.885	0.400	0.373	0.285
.3611095	.885	0.414	0.356	0.299
.3658318	.885	0.429	0.340	0.313
.3685570	.872	0.429	0.343	0.300
.3695547	.859	0.429	0.346	0.288
.3712847	.859	0.443	0.330	0.302
.3734402	.859	0.457	0.315	0.316
.3753306	.846	0.457	0.318	0.303
.3766430	.846	0.471	0.303	0.318
.3788144	.846	0.486	0.288	0.332
.3828565	.846	0.500	0.274	0.346
.3855034	.833	0.500	0.278	0.333
.3878395	.821	0.500	0.282	0.321
.3934060	.808	0.500	0.287	0.308
.3976910	.795	0.500	0.292	0.295
.3982919	.782	0.500	0.298	0.282
.4008312	.782	0.514	0.283	0.296
.4038000	.782	0.529	0.270	0.311
.4046653	.782	0.543	0.256	0.325
.4084418	.769	0.543	0.262	0.312
.4147498	.769	0.557	0.249	0.326
.4245437	.769	0.571	0.237	0.341
.4330009	.756	0.571	0.243	0.328
.4346669	.744	0.571	0.249	0.315
.4357206	.744	0.586	0.237	0.329
.4397350	.731	0.586	0.244	0.316
.4450878	.718	0.586	0.251	0.304
.4512850	.705	0.586	0.259	0.291
.4566010	.705	0.600	0.247	0.305
.4599473	.705	0.614	0.236	0.319
.4726133	.705	0.629	0.225	0.334
.4835347	.692	0.629	0.233	0.321
.4887231	.692	0.643	0.222	0.335
.4959784	.692	0.657	0.212	0.349
.5017015	.692	0.671	0.203	0.364
.5074242	.692	0.686	0.193	0.378
.5105590	.692	0.700	0.185	0.392
.5139259	.679	0.700	0.193	0.379
.5200953	.667	0.700	0.201	0.367
.5245843	.667	0.714	0.193	0.381
.5282350	.654	0.714	0.201	0.368
.5339733	.654	0.729	0.193	0.382

.5428914	.641	0.729	0.203	0.370
.5491378	.628	0.729	0.212	0.357
.5523246	.615	0.729	0.222	0.344
.5570459	.615	0.743	0.214	0.358
.5602915	.603	0.743	0.224	0.345
.5621172	.603	0.757	0.217	0.360
.5640554	.603	0.771	0.210	0.374
.5663325	.590	0.771	0.221	0.361
.5734282	.577	0.771	0.231	0.348
.5804304	.577	0.786	0.225	0.363
.5828437	.577	0.800	0.219	0.377
.5852087	.564	0.800	0.230	0.364
.5893512	.551	0.800	0.241	0.351
.5927714	.551	0.814	0.236	0.366
.5938053	.538	0.814	0.248	0.353
.5951550	.526	0.814	0.260	0.340
.6018716	.513	0.814	0.272	0.327
.6100352	.500	0.814	0.284	0.314
.6123852	.487	0.814	0.297	0.301
.6205343	.474	0.814	0.311	0.289
.6302480	.474	0.829	0.306	0.303
.6342348	.474	0.843	0.301	0.317
.6373916	.462	0.843	0.315	0.304
.6387138	.462	0.857	0.310	0.319
.6412976	.449	0.857	0.324	0.306
.6439946	.436	0.857	0.339	0.293
.6481954	.423	0.857	0.353	0.280
.6544893	.423	0.871	0.349	0.295
.6585747	.423	0.886	0.346	0.309
.6611960	.410	0.886	0.361	0.296
.6664094	.397	0.886	0.376	0.283
.6731289	.385	0.886	0.392	0.270
.6829042	.372	0.886	0.408	0.258
.6922466	.359	0.886	0.424	0.245
.6978899	.346	0.886	0.441	0.232
.7023283	.333	0.886	0.458	0.219
.7079547	.333	0.900	0.454	0.233
.7145404	.321	0.900	0.472	0.221
.7171882	.321	0.914	0.469	0.235
.7221642	.308	0.914	0.487	0.222
.7279219	.295	0.914	0.505	0.209
.7323239	.282	0.914	0.523	0.196
.7370494	.269	0.914	0.541	0.184

.7416516	.256	0.914	0.560	0.171
.7450539	.244	0.914	0.580	0.158
.7474223	.231	0.914	0.599	0.145
.7551817	.218	0.914	0.619	0.132
.7633379	.205	0.914	0.639	0.119
.7661536	.192	0.914	0.660	0.107
.7716208	.192	0.929	0.657	0.121
.7768610	.192	0.943	0.656	0.135
.7816027	.192	0.957	0.654	0.149
.7955303	.179	0.957	0.675	0.137
.8068200	.167	0.957	0.696	0.124
.8135025	.154	0.957	0.718	0.111
.8210287	.154	0.971	0.717	0.125
.8291553	.154	0.986	0.716	0.140
.8389524	.141	0.986	0.738	0.127
.8447246	.128	0.986	0.760	0.114
.8564382	.115	0.986	0.783	0.101
.8663977	.103	0.986	0.806	0.088
.8679082	.090	0.986	0.829	0.075
.8717356	.077	0.986	0.852	0.063
.8749435	.077	1.000	0.852	0.077
.8762187	.064	1.000	0.876	0.064
.9004759	.051	1.000	0.900	0.051
.9337469	.038	1.000	0.925	0.038
.9489567	.026	1.000	0.949	0.026
.9549117	.013	1.000	0.975	0.013
1.0000000	0.000	1.000	1.000	0.000

Yellow box indicates optimal cut-off point

7.3 Review two appendices

7.3.1 Cochrane risk of bias tool assessment criteria[265]

Studies will be evaluated as low/ high or unclear risk based on the following criteria:

Random Sequence Generation (selection bias)

- Describe the method used to generate the allocation sequence. Should be described in sufficient detail to allow an assessment of whether it should produce comparable groups

Allocation concealment (selection bias)

- Describe the method used to conceal the allocation sequence in sufficient detail to determine whether intervention allocations could have been foreseen before or during enrolment

Blinding of participants and personnel (performance bias)

- Describe all measures used, if any, to blind trial participants and researchers from knowledge of which intervention a participant received. Provide any information relating to whether the intended blinding was effective

Blinding of outcome assessment (detection bias)

- Describe all measures used, if any, to blind outcome assessment from knowledge of which intervention a participant received. Provide any information relating to whether the intended blinding was effective

Incomplete outcome data (attrition bias)

- Describe the completeness of outcome data for each main outcome, including attrition and exclusions from the analysis. State whether attrition and exclusions were reported, the numbers in each intervention group (compared with total randomised participants), reasons for attrition or exclusions where reported, and any reinclusions in analyses for the review

Selective reporting (reporting bias)

- State how selective outcome reporting was examined and what was found

7.3.2 Downs and Black quality Assessment[266]

Studies using a non-controlled methodology will be assessed according to the following criteria:

Reporting	Scoring
Is the hypothesis / aim / objective clearly described?	1. Yes 0.No
Are the main outcomes to be measured clearly described in the introduction or methods section?	1. Yes 0.No
Are the characteristics of the patients included in the study clearly described?	1. Yes 0.No
Are the interventions of interest clearly described?	1. Yes 0.No
Are the distributions of principle confounders in each group of subjects to be compared clearly described?	1. Yes 0.No
Are the main findings of the study clearly described?	1. Yes 0.No
Does the study provide estimates of the random variability in the data for the main outcomes?	1. Yes 0.No
Have all important adverse events that may be a consequence of the intervention been reported?	1. Yes 0.No
Have the characteristics of patients lost to follow up been described?	1. Yes 0.No
Have actual probability values been reported (e.g. 0.035 rather than <0.05) for the main outcomes except where the probability value is less than 0.001?	1. Yes 0.No
External validity	
Were the subjects asked to participate in the study representative of the entire population from which they were recruited?	1. Yes 0.No
Were those subjects who were prepared to participate representative of the entire population from which they were recruited?	1. Yes 0.No
Were the staff, places and facilities where the patients were treated representative of the treatment the majority of patients receive?	1. Yes 0.No
Internal validity: bias	
Was an attempt made to blind study subjects to the intervention they have received?	1. Yes 0.No
Was an attempt made to blind those measuring the main outcomes of the intervention?	1. Yes 0.No
If any of the results of the study were based on 'data dredging', was this made clear?	1. Yes 0.No

Reporting	Scoring
In trials and cohort studies, do analyses adjust for different lengths of follow up of patients or in case control studies is the time period between the intervention and outcome the same for cases and controls?	1. Yes 0.No
Were the statistical tests used to assess the main outcomes appropriate?	1. Yes 0.No
Was compliance with the interventions(s) reliable?	1. Yes 0.No
Were the main outcomes measure used accurate and reliable?	1. Yes 0.No
Internal validity: confounding (selection bias)	
Were the patients in different intervention groups (trial and cohort studies) or were the cases and controls (case control studies) recruited from the same population?	1. Yes 0.No
Were study subjects in different intervention groups (trial and cohort studies) or were the cases and controls (case control studies) recruited over the same period of time?	1. Yes 0.No
Were study subjects randomised to intervention groups?	1. Yes 0.No
Was the randomised intervention assignment concealed from both patients and health care staff until recruitment was complete and irrevocable?	1. Yes 0.No
Was there adequate adjustment for confounding in the analyses from which the main findings were drawn?	1. Yes 0.No
Were losses of patients to follow-up taken into account?	1. Yes 0.No
Power	
Did the study have sufficient power to detect a clinically important effect where the probability value for a difference being due to chance is less than 5%?	1. Yes 0.No

7.3.3 CASP Qualitative Assessment [268]

Qualitative papers will be assessed according to the following criteria:

Criteria	**Scoring**
Was there a clear statement of the aims of the research?	1. Yes 0.No
Is a qualitative methodology appropriate?	1. Yes 0.No
Was the research design appropriate to address the aims of the research?	1. Yes 0.No
Was the recruitment strategy appropriate to the aims of the research?	1. Yes 0.No
Was the data collected in a way that addressed the research issue?	1. Yes 0.No
Has the relationship between researcher and participants been adequately considered?	1. Yes 0.No
Have ethical issues been taken into consideration?	1. Yes 0.No
Was the data analysis sufficiently rigorous?	1. Yes 0.No
Is there a clear statement of findings?	1. Yes 0.No
How valuable is the research?	1. Yes 0.No

7.3.4 Full details of included studies

1. Quantitative studies

Study ID	Ahmadi 2010[278]	Armutlu 2001[290]	Brichetto 2013[285]	Broekmans 2011[291]	Cakit 2010[281]
Country	Iran	Turkey	Italy	Belgium	Turkey
Aim/Objective	To determine the effects of a yoga intervention	To evaluate the effects of neuro-rehabilitation and pressure splints to treat ataxia	To evaluate Wii versus standard balance exercise	To evaluate the effects of resistance training with +/- ES	To evaluate the effects of cycling training
Inclusion Criteria	EDSS 1-4	SP or PP MS, predominant problems ataxia, EDSS 3-5.5, Muscle power >3	Definite MS diagnosis, fear of falling or at least 1 fall in the past year	MS diagnosis, ambulatory	MS diagnosis, EDSS<6, ability to stand >3 secs
Exclusion criteria	Participation in physical activity <3/12 prior to study, co-morbidities	Corticosteroids<1/12 prior to study	Unstable MS, relapse within 3/12, EDSS <6	>3 relapses in 1 year, EDSS>1	Steroid or immunosuppressive therapy within 4/52
Recruitment	Not stated	Hospital outpatients	Outpatients of MS centre	Local volunteers	N=Not stated
Age (mean(SD))	mean 34 (9.05)	33.61 (range 23-45)	42 (10.7)	47.8 (10.6)	37.9 (10.43)
Gender	21F	10M 16F	14M 22F	13M 23F	13M 20F
MS Status/Classification (SD)	Not specified (all sub types eligible)	EDSS 4.7 (range 3.5-5.5)	mean disease duration 11.5 years	EDSS 4.3 (0.2)	mean time since diagnosis 7.7years (4.1)
Co-morbidities	All excluded	None reported	None reported	None reported	None reported
N eligible	Not stated	26	Not stated	38	60
N recruited/analysed	21	26	36	36	45
N analysed	21	26	36	36	33
Setting	Not stated	Physiotherapy dept.	Rehabilitation unit	Not stated	Not stated
Length of follow up	Length of follow up not stated	Post intervention	Post intervention	2 weeks following the end of the intervention	Post intervention

SD: standard deviation; N: number; M: male; F: female; ES: electrical stimulation

Table 7-1: Peer reviewed publications (part 1)

Study ID	Cattaneo 2007[241]	Coote 2013[235]/ Hogan 2013[284]	DeBolt 2004[286]	Finlayson 2009[240]	Finkelstein 2008[294]
Country	Italy	Ireland	USA	USA	USA
Aim/ Objective	To evaluate the effects of balance retraining	To evaluate the effect of a 10 week physio programme on falls	To evaluate the effect of a home based resistance exercise programme	Evaluation of a group fall risk management program	To assess the feasibility of a telerehabilitation exercise programme
Inclusion Criteria	Ability to stand independently >30 seconds, ability to walk 6M	Confirmed MS diagnosis, resident in Republic of Ireland	Clinically definite MS, ability to walk at least 20M without resting	Self-reported diagnosis of MS, at least one fall in the past year, occasional use of a mobility device	Confirmed diagnosis of MS, MS disease step 2-5
Exclusion criteria	Berg Balance <53, subjects who had already received the prescribed treatment regime	Current exacerbation of symptoms, steroids within 3 months, pregnancy, <18 years of age	None stated	Raw score of 9 or more on a cognitive measure	MSK diagnoses, ≥1 exacerbation within 3/12, steroid within 60 days, MMSE <23
Recruitment	Convenience sample of inpatient MS rehab unit	Self, physio, neurologist, GP or MS nurse referral	Volunteer participants	Flyer distribution and newsletter publicity	12 consecutive patients meeting recruitment criteria
Age (mean(SD))	mean 46 (10.2)	55 (10.75)	50.7 (7.8)	56.7 (7.4)	52 (4)
Gender	13M 31F	40M 70F	8M 29F	5M 25F	2M 10F
MS Status/ Classification (SD)	Not specified (all sub types eligible)	mean time since diagnosis 15.35 (4)	EDSS 1-6	MS diagnosed approx. 16 years on average	9 moderate MS, 2 mild, 1 severe (self-report)
Co-morbidities	None reported	None reported	None reported	mean of 1.7 other health conditions	None reported
N eligible	50	Not stated	Not stated	Not stated	12
N recruited/ analysed	50	111	37	30	12
N analysed	44	111 n.b missing data in several cells (no reason reported)	37 (1 W/D from control) analysis not stated	23 (participants who attended at least 5 of the 6 sessions)	12
Setting	Inpatient rehabilitation unit		Home based	Group setting	home
Length of follow up	Post intervention	2 weeks following the end of the intervention	Post intervention	Post intervention	Post intervention

SD: standard deviation; N: number; M: male; F: female; W/D: withdrawn

Table 7-2: Peer reviewed publications (part 2)

Study ID	Freeman 2010[299]	Freeman 2004[295]	Huisinga 2012[296]	Kasser 1999[300]	Kileff 2005[297]
Country	UK	UK	USA	USA	UK
Aim/Objective	To evaluate the effect of core stability based training on balance and mobility	Pilot study of a group exercise programme	Effect of supervised resistance training on postural control	To evaluate the effects of balance training	To evaluate the effects of a 12 week aerobic training programme
Inclusion Criteria	Definite diagnosis of MS, able to walk independently with or without unilateral assistance	Adults with confirmed diagnosis of MS, independently ambulant	Cognitive competency, age 19-65, no pregnancy, no concurrent neurological disorders	MS diagnosis, must be able to maintain independent weight bearing for 10 mins	EDSS 4-6, mobile with or without an aid
Exclusion criteria	Relapse in the previous 3/12, medical conditions contra indicating participation in core stability exercise	Within 1/2 of relapse, other disorder precluding exercise	None stated	Severe relapse within 6/12, visual impairments	Mild or severe MS, fatigue as main symptom, recent relapse
Recruitment	Multiple centres undertook a single case study; participants were also analysed as a group	Volunteer participants	Recruited through university medical centre	Volunteer participants	Recruited through neurology outpatient clinics
Age (mean(SD))	32-59	50 (11.9)	43.2 (10.1)	52 (5.2)	45 (range 33-61)
Gender	6M 2F	2M 8F	2M 13F	1M 3F	8F
MS Status/ Classification (SD)	5PP, 3RR	EDSS mean 5 (range 3-6.5)	EDSS 3.9 (1.5)	range of sub types	EDSS 4-6
Co-morbidities	None reported	None reported	None reported	None reported	None reported
N eligible	N/a- first eligible patient at each centre recruited	Not stated	Not stated	Not stated	Not stated
N recruited/ analysed	8	10	15 MS and 15 HC	4	8
N analysed	8	10	15	4	6
Setting	outpatient physio	local hospital	gym	laboratory	Physio outpatient dept.
Length of follow up	4 weeks following the end of the intervention	4 weeks following the end of the intervention	Post intervention	12 weeks following the end of the intervention	Post intervention

SD: standard deviation; N: number; M: male; F: female; HC: healthy controls

Table 7-3: Peer reviewed publications (part 3)

Study ID	Learmonth 2012[280]	Lord 1998[282]	Mills 2000[298]	Nilsagard 2013[283]	Prosperini 2010[279]
Country	UK	UK	UK	Sweden	Italy
Aim/Objective	To evaluate the effects of a 12 week group exercise class intervention	A comparison of the outcomes of facilitatory and task orientated treatment interventions	To evaluate the effects of an 8 week tai chi class	To evaluate the use of Nintendo Wii in a rehabilitation setting	Evaluate the effects of a visuo-proprioceptive training programme
Inclusion Criteria	MS diagnosis, EDSS 5-6.5, MMSE>24	Clinically stable MS (chronic progressive or relapsing remitting)	Clinically confirmed MS	Diagnosis of MS, self-report of balance impairment, ability to walk 100M without resting	MS diagnosis with self-reported falls or fear of falling. Objective balance disturbance, walking without aid or rest
Exclusion criteria	Relapse within 3/12	None stated	None stated	Cognitive/linguistic issues, relapse, other disease interfering with balance	Relapse within 2/12, severe visual disturbance, vestibular or otological issues, cardiac disease
Recruitment	MS service register	Hospital outpatients	Not stated	From Swedish MS registry	Not stated
Age (mean(SD))	51 (8)	53 (9.5)	range 42-56	49.7 (11.3)	40.3 (11.7)
Gender	9M 23F	5M 15F	3M 5F	20M 64F	16M 24F
MS Status/ Classification (SD)	EDSS 5.98 (0.43)	mean time since onset 16.15 (range 4-28)	all secondary progressive	range of sub types	variety of classification EDSS median 3.5 (range 1.5-5.5)
Co-morbidities	None reported	None reported	None reported	None reported	None reported
N eligible	159	23	Not stated	179	Not stated
N recruited/ analysed	32	23	8	84	40
N analysed	24	20	8	80	40
Setting	community leisure centres	Not stated	home/ centre	Physio outpatient dept.	lab
Length of follow up	baseline, week 8 and post intervention	Post intervention	Post intervention	1 week following the end of the intervention	Post intervention

SD: standard deviation; N: number; M: male; F: female;

Table 7-4: Peer reviewed publications (part 4)

Study ID	Prosperini 2013[287]	Sabapathy 2011[292]	Sosnoff 2014[239]	Stephens 2001[288]	Tarakci 2013[289]
Country	Italy	Australia	USA	USA	Turkey
Aim/Objective	To evaluate the effects of a home based Nintendo Wii programme	A comparison of endurance and resistance training	To evaluate the effect of a 12 week home based falls exercise intervention	To evaluate the effects of an awareness through movement programme	To evaluate the effects of group exercise training
Inclusion Criteria	Age 18-50, RR or SP MS, EDSS<5.5, walking min 100M, objective balance disturbance	MS diagnosis, independent ambulation with or without use of a walking aid	Confirmed diagnosis of MS, able to walk 25 ft. independently, age 50-75, relapse free 30 days, at least 1 fall in the past 12 months	MS diagnosis, ability to stand independently without assistive device and walk 100ft with or without assistive device	Ambulatory patients with MS, EDSS 2-6.5
Exclusion criteria	Use of assistive device or AFO, relapse 6/12 medication change 3/12, otological or vestibular disease	None stated	Cognitive issues	<18 years old, relapse <1/12, surgery <3/12	Relapse within 30 days, other neuro disorder
Recruitment	Volunteers of those regularly attending the MS centre	Local volunteers recruited by poster	Local MS centre	Local MS support groups and physician practices	Referred by local neurologist
Age (mean(SD))	36.2 (8.7)	55 (7)	60 (6.1)	54 (10.05)	40.57 (10.27)
Gender	11M 25F	4M 12F	6M 21F	4M 8F	35M 64F
MS Status/ Classification (SD)	EDSS median 3.25 (range1.5-5)	variety of MS classification and disease step course	EDSS median 5 (IQR2.5)	EDSS 4.75 (1.1)	EDSS 4.29 (1.40)
Co-morbidities	None reported	None reported	None reported	None reported	None reported
N eligible	45	21	231	Not stated	110
N recruited/ analysed	36	21	27	12	110
N analysed	34	16	22	12	99
Setting	home	Not stated	community setting	University classrooms	Not stated
Length of follow up	Post intervention	Post intervention	Post intervention	Post intervention	Post intervention

SD: standard deviation; N: number; M: male; F: female;

Table 7-5: Peer reviewed publications (part 5)

Study ID	Wiles 2001[293]
Country	UK
Aim/Objective	To evaluate the effects of physiotherapy treatment on mobility
Inclusion Criteria	Definite or probable MS, c/o difficulties in walking. Able to walk >5M with or without aid
Exclusion criteria	No current relapse
Recruitment	Hospital outpatients
Age (mean(SD))	47.2 (range 28.2-68.8)
Gender	15M 27F
MS Status/ Classification (SD)	mean time since onset 5.7 (range 4-6.5)
Co-morbidities	None reported
N eligible	Not stated
N recruited/ analysed	42
N analysed	40
Setting	home/ physio dept.
Length of follow up	Post intervention
SD: standard deviation; N: number; M: male; F: female	

Table 7-6 Peer reviewed publications (part 6)

Frankel 2013[302]	Gutierrez 2005[303]
USA	USA
To evaluate the effects of the free from falls MS programme	Evaluation of an individual strength training programme
Any participants of the free from falls MS programme	Must be able to walk> 1 city block, no coexisting orthopaedic, visual or tremor issues
Not stated	None stated
Local MS chapters	Convenience sample of local population
Not stated	43.3 (12.1)
Not stated	2M 7F
Not stated	EDSS 4.44 (1.67)
None reported	None reported
Not stated	Not stated
143	9
143/111*	9
Group setting	university/ local gym
*Post intervention (n=143) and at 6 months (n=111)	Post intervention

Table 7-7: Grey literature

3. Qualitative studies

Study ID	Learmonth 2013[301]	Peterson 2010[116]
Aim/Objective	To explore the experience of participating in a 12 week group exercise class	To explore changes in falls self-efficacy following participation in an educational programme
Design	Focus groups	Phenomenological study
Inclusion	MS diagnosis, EDSS 5-6.5, MMSE>24	Purposive sample, participants >40, >1fall in the past year, perceived need to manage falls
Exclusion	Relapse within 3/12	None stated
Recruitment	Participants to an exercise study (Learmonth 2012)[280]	Participants in a pilot falls management programme (Finlayson 2009)[240]
Age, mean (SD)	52.6	58-67
Gender	4M 10F	3M 3F
MS Status/Classification	EDSS 6-6.5	All completed ADL independently
Co-morbidities	None reported	None reported
N eligible	Not stated	Not stated
N recruited	14	6
N analysed	14	6
Setting	Community leisure centres	n/a
Length of follow up	n/a	n/a

n/a: not applicable; MSIS: MS impact scale; SD: standard deviation

Table 7-8: Qualitative studies

7.4 Study two appendices

7.4.1 Trigger statement questionnaire

Building stakeholder consensus: Development of a falls management intervention for people with Multiple Sclerosis (MS)

Background information for falls programme workshop participants

Falls in MS

We are aware that falls are a significant issue for people with MS, leading to injury, loss of function and consequences relating to anxiety and quality of life. From recent research we have found that specific aspects of balance and mobility contribute to falls risk in MS. Therefore we now wish to develop a falls programme to address these issues with the aim of reducing the impact of falls for people with MS. There are other issues which may also be important contributors to falls risk (such as continence problems, leg stiffness and medication); however, for now we wish to focus specifically on falls management by improving balance and mobility in order to be able to assess how well the programme works at each stage.

Falls programmes

There are a number of different ways that a falls programme which focuses on balance and mobility could be structured. To date, there have been few falls programmes specifically developed for people with MS. In other groups, falls programmes have been developed in a number of different formats which can be broadly divided into education-based and exercise-based programmes.

Education-based programmes aim to encourage people to understand more about falls, the contributing factors and what they can do to reduce the risks and consequences. These are typically run as a series of education sessions, either in groups or at home using information from leaflets, videos or home visits.

Exercise-based programmes may use a wide range of activities which aim to improve a person's balance, therefore reducing falls risk. How this is structured and formatted is very variable, and may include formal exercise sessions, home exercises, group formats and/or individual sessions. The key factors in other groups which appear to affect how well balance programmes can reduce falls risk include people being willing and able to carry out the exercises regularly, for the programme to include exercises that really challenge people's balance and for people to stick with the programme over a long period.

Aims of the workshop sessions

The aim of this two-stage process is to come to an agreement on the structure and format of a falls programme for people with MS based on the views of experts. In this scenario, the experts will include people with MS, people involved in providing rehabilitation and care to people with MS, people who are involved in other falls programmes and people who develop and fund services.

In stage one (before the workshop), participants will be asked to rate their response to a series of statements on a standard rating scale. There is also space available for comments should participants wish to add them. This will be returned to the session organiser before the session.

At the workshop, the responses of all the participants to the statements will be shared and discussed. Participants will be asked to share their reasons for the marks they gave and to consider how the views of other participants may affect their response to the statement (or not). Participants will then be asked to re-rate the trigger statements taking into account the outcome of the discussion and their own opinion.

Trigger statements (round 1)

Study Pseudonym: (*to be completed by researcher prior to distribution)*

Please read the statements below and circle your response to each. You do not need to give a reason for your answer, but if you would like to add comments, you are welcome to do so. There is no right or wrong answer to any of the questions.

Example

Falls are a significant issue in MS								
1 Strongly disagree	2	3	4	5 Neutral	6	7	8	9 Strongly agree
Comments:								
I fall frequently and am worried about injuries								

Trigger statements

Reducing falls should be the primary goal of the programme								
1 Strongly disagree	2	3	4	5 Neutral	6	7	8	9 Strongly agree
Comments:								
Participants should be given specific exercises to carry out to improve balance								
1 Strongly disagree	2	3	4	5 Neutral	6	7	8	9 Strongly agree
Comments:								
Advice to help people avoid and cope with falls should be a key part of the programme								
1 Strongly disagree	2	3	4	5 Neutral	6	7	8	9 Strongly agree
Comments:								
Exercise is more enjoyable (effective) when carried out in a group								
1 Strongly disagree	2	3	4	5 Neutral	6	7	8	9 Strongly agree
Comments:								
Participants should be able to choose the types of exercise in their programme/ there should be a								

range of different exercise formats available 1 Strongly disagree · 2 · 3 · 4 · 5 Neutral · 6 · 7 · 8 · 9 Strongly agree Comments:
Exercise should be supervised 1 Strongly disagree · 2 · 3 · 4 · 5 Neutral · 6 · 7 · 8 · 9 Strongly agree Comments:
It is unreasonable to expect people with MS to do highly challenging exercises 1 Strongly disagree · 2 · 3 · 4 · 5 Neutral · 6 · 7 · 8 · 9 Strongly agree Comments:
The role of the programme leader is to push participants to their limits 1 Strongly disagree · 2 · 3 · 4 · 5 Neutral · 6 · 7 · 8 · 9 Strongly agree Comments:
Programme leaders must have formal qualifications 1 Strongly disagree · 2 · 3 · 4 · 5 Neutral · 6 · 7 · 8 · 9 Strongly agree Comments:
A falls programme should be provided within existing resources 1 Strongly disagree · 2 · 3 · 4 · 5 Neutral · 6 · 7 · 8 · 9 Strongly agree Comments:
Living in a remote location means that taking part in a programme away from home is impossible 1 Strongly disagree · 2 · 3 · 4 · 5 Neutral · 6 · 7 · 8 · 9 Strongly agree
Exercise diaries are essential to encourage participants and monitor progress 1 · 2 · 3 · 4 · 5 · 6 · 7 · 8 · 9

Strongly disagree				Neutral				Strongly agree

Comments:

Having a review of your progress by an outside person is essential

1	2	3	4	5	6	7	8	9
Strongly disagree				Neutral				Strongly agree

Comments:

Reducing falls risk is a long-term commitment

1	2	3	4	5	6	7	8	9
Strongly disagree				Neutral				Strongly agree

Comments:

Please return completed statement sheets in the stamped addressed envelope provided (for service user participants this will be completed and returned during the training workshop)

7.4.2 Example feedback sheet

Building stakeholder consensus:
Development of a falls management intervention for people with Multiple Sclerosis (MS)
Nominal Group rating responses

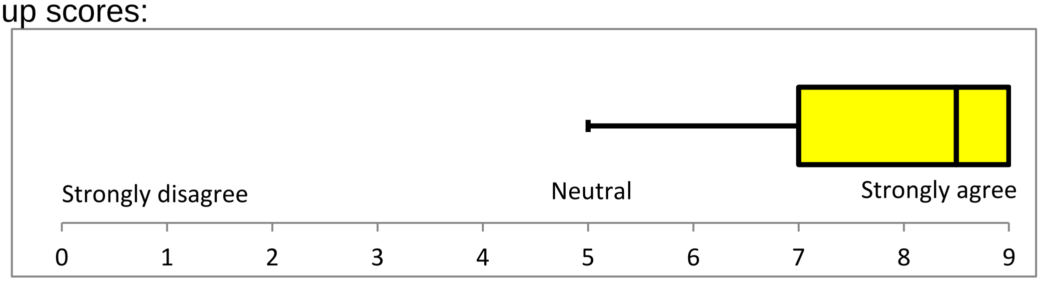
Rating round:

Participant name:

Study ID:

1. Reducing falls should be the primary goal of the programme

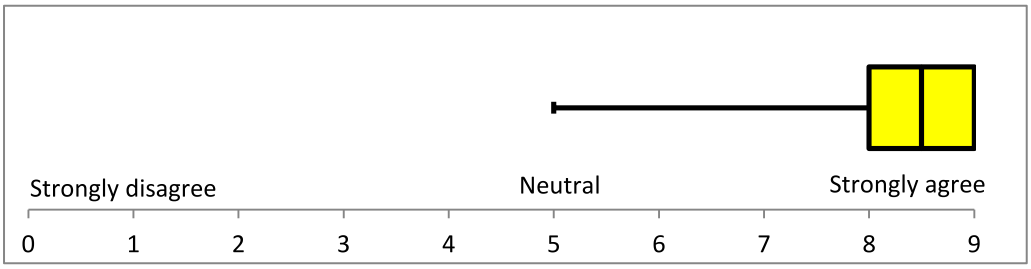
   Group scores:



   Your score: «Q1»
   Your comments: «C1»

2. People with MS should be given specific exercises to carry out to improve balance

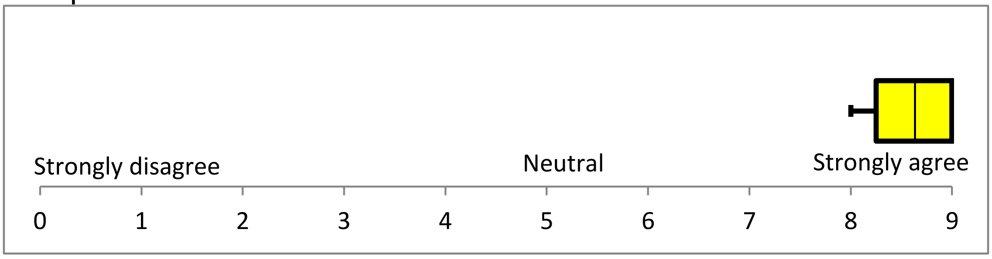
   Group scores:



   Your score: «Q2»
   Your comments: «C2»

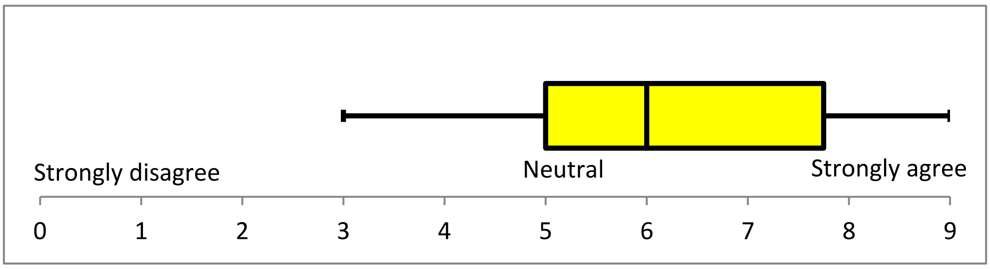
3. Advice to help people avoid and cope with falls should be a key part of any falls programme

Group scores:



Your score: «Q3»
Your comments: «C3»

4. Exercise is more effective when carried out in a group

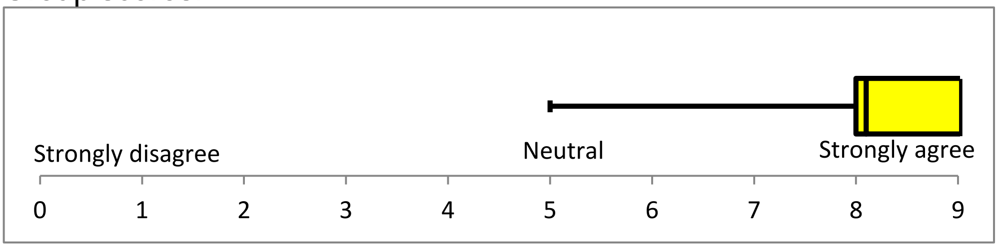


Group scores:

Your score: «Q4»
Your comments: «C4»

5. Exercises should be done on a daily basis

Group scores:

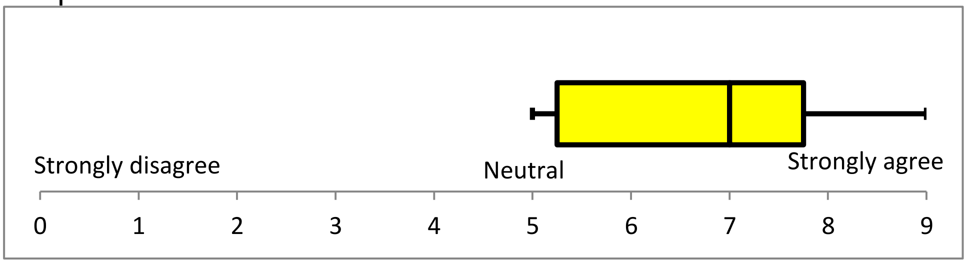


Your score: «Q5»
Your comments:

«C5»

6. Exercising for an hour at a time is unrealistic

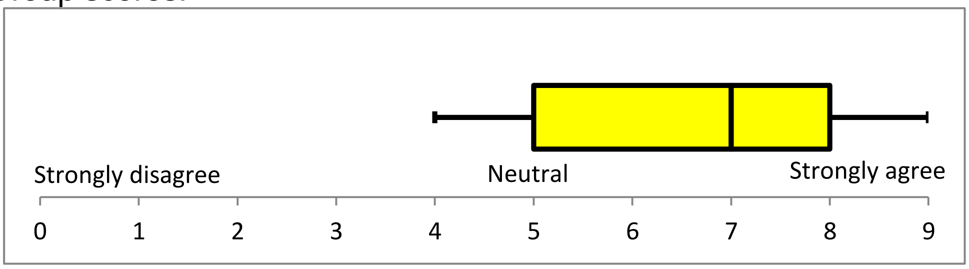
Group scores:



Your score: «Q6»
Your comments: «C6»

7. Participants should be able to choose the types of exercise in their falls programme

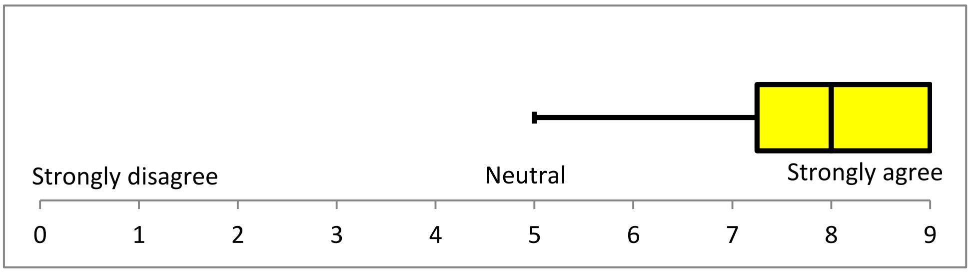
Group scores:



Your score: «Q7»
Your comments «C7»

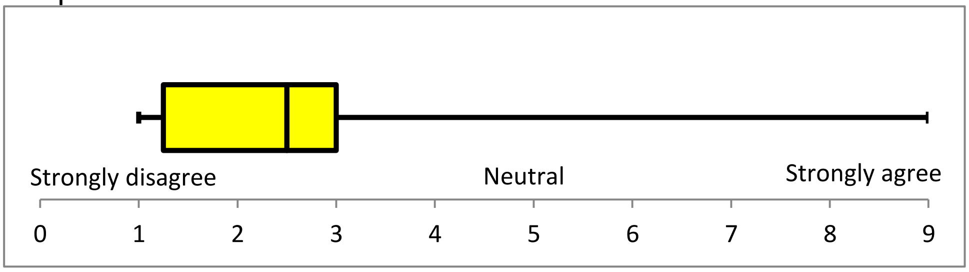
8. People should be able to access the falls programme without having to be referred

Group score:



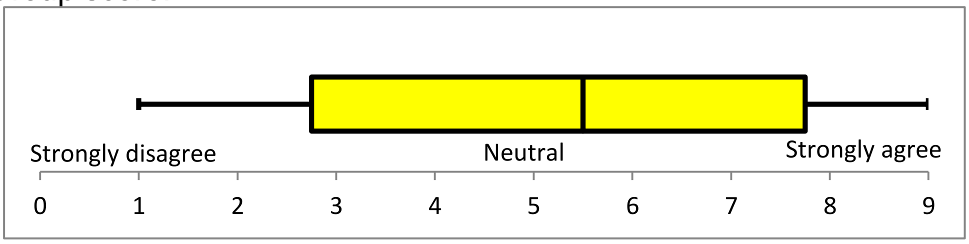
Your score: «Q8»
Your comments: «C8»

9. Any sessions outside the home should be organised in a hospital setting
Group score:



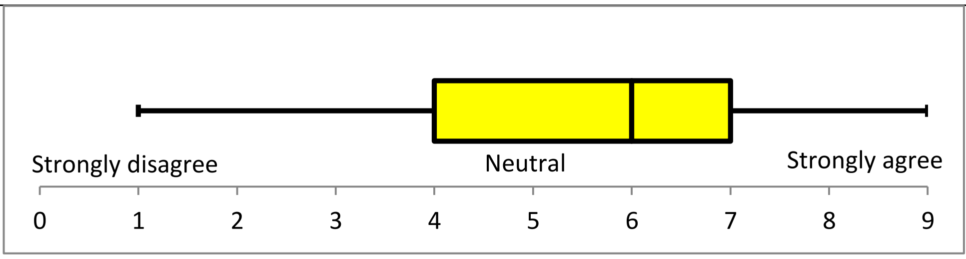
Your score: «Q9»
Your comments: «C9»

10. Exercise should always be supervised
Group score:



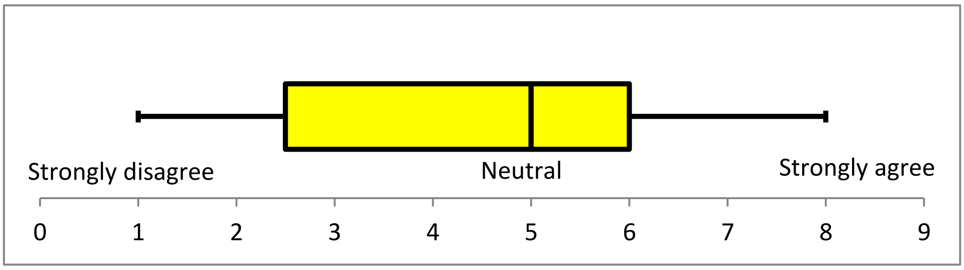
Your score: «Q10»
Your comments «C10»

11. It is unreasonable to expect people with MS to do balance exercises that are difficult for them
Group score:



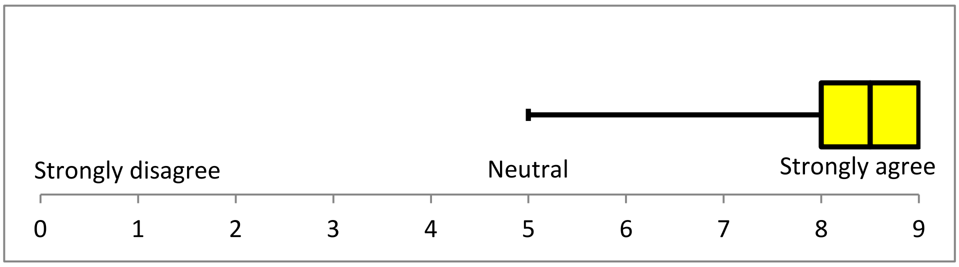
Your score: «Q11»
Your comments: «C11»

12. The role of the programme leader is to push participants to their limits
Group score:



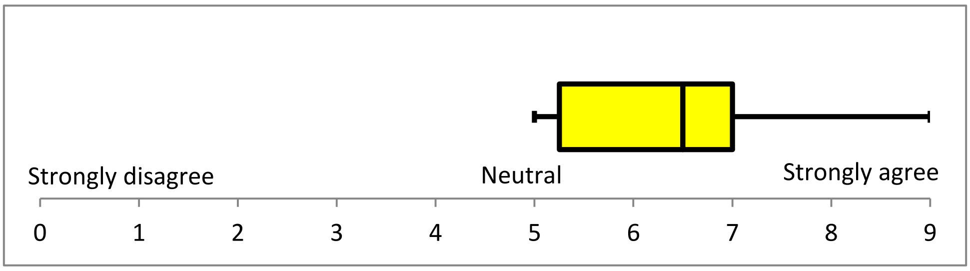
Your score: «Q12»
Your comments: «C12»

13. Programme leaders must have formal qualifications
Group score:



Your score: «Q13»
Your comments: «C13»

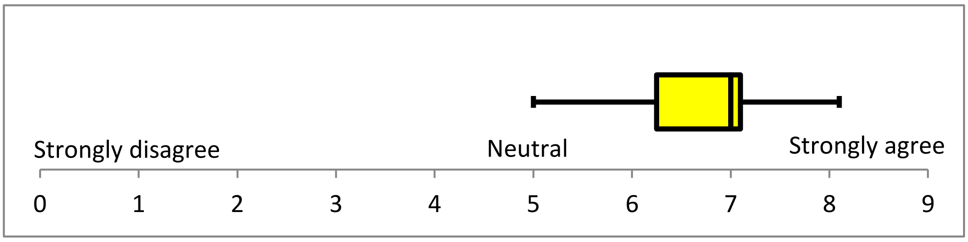
14. A falls programme should be provided within existing resources
Group score:



Your score: «Q14»
Your comments «C14»

15. It is reasonable to ask participants to pay a contribution to the cost of any attended sessions

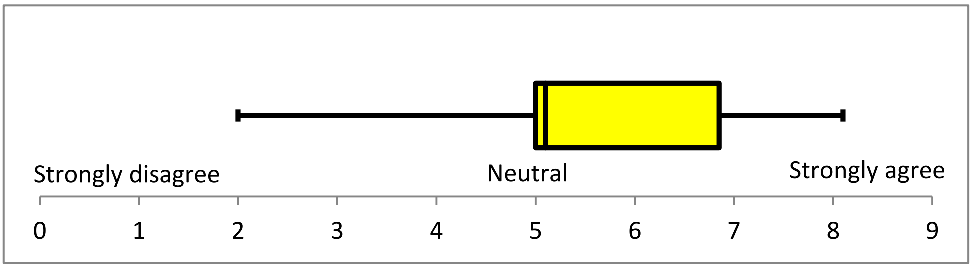
Group score:



Your score: «Q15»
Your comments: «C15»

16. Living in a remote location means that taking part in a programme away from home is impossible

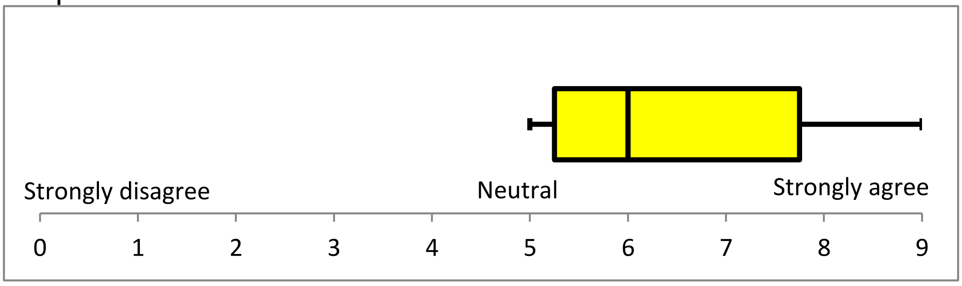
Group score:



Your score: «Q16»
Your comments «C16»

17. Being able to see improvements in function is more important than measures of balance or falls

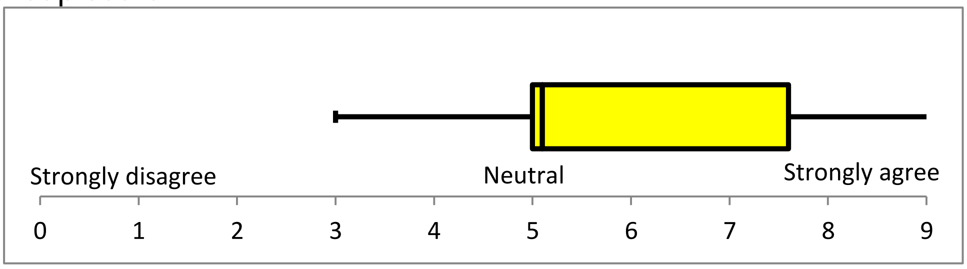
Group score:



Your score: «Q17»
Your comments «C17»

18. Daily diaries are essential to check that exercises are being carried out

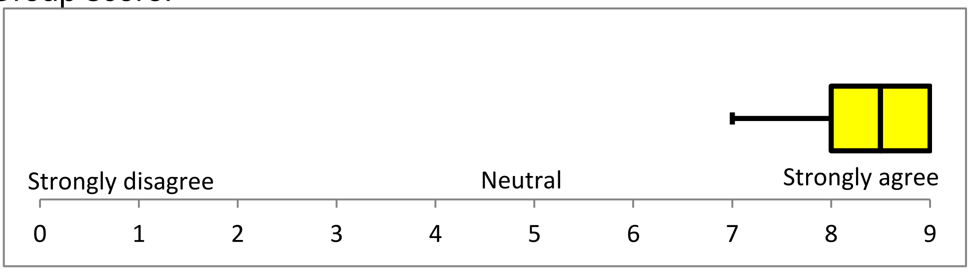
Group score:

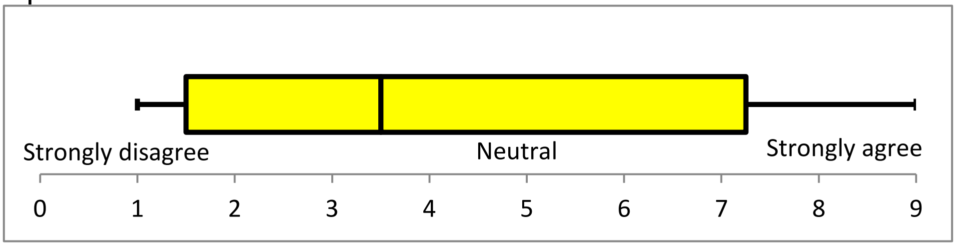


Your score: «Q18»
Your comments: «C18»

19. Programme leaders should regularly discuss progress with individual participants

Group score:



Your score: «Q19» Your comments: «C19»
20. It is unrealistic to expect people to undertake a falls programme for 3-6 months Group score:  Your score: «Q20» Your comments: «C20»

7.5 Published papers relating to this thesis

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7.5.1 Repeated falls: a key outcome or an adverse event?

EDITORIAL

Repeated Falls: a Key Outcome or an Adverse Event?

Published online 23 January 2012 in Wiley Online Library (wileyonlinelibrary.com) DOI: 10.1002/pri.1518

We would like to use this editorial to share with you an ethical dilemma that has arisen recently through our research. As part of our research activities within the field of neurological rehabilitation, we are currently conducting an observational cohort study that investigates the risk factors for falls in people with multiple sclerosis. In order to determine falls risk, the participants are assessed with a range of measures at a single face-to-face session and are then asked to prospectively complete a home diary to record the number of falls they have experienced over the following three-month period. This diary is sent back by the participants, at two weekly intervals, to the researcher who is able to monitor the completion of the forms on an on-going basis. This monitoring of data has the advantage of optimizing response rates (as telephone prompts can be made to those who have not yet returned the forms) but has resulted in us being confronted, quite unexpectedly, by an ethical dilemma: What should we do when we are provided with information that tells us that an individual is falling repeatedly? Indeed, several participants have reported double-digit falls frequencies in a number of bi-weekly diary returns: Is there a time at which our failure to act upon the information we are privy to becomes akin to ignoring what could perhaps be seen as an adverse event?

Protecting the rights and welfare of those who volunteer to participate in research is a fundamental tenet of ethical research (World Medical Association, 2008). Since the declaration of Helsinki in 1964, exploration of many of the potential conflicts associated with ethics in health research has led to clearly established principles relating to protection from harm, informed consent, fair treatment and respect for autonomy. These aspects are discussed in many texts, and an excellent overview of the specific issues relevant to physiotherapy research is supplied by Julius Sim in his 2010 paper addressing conflicts in research ethics (Sim, 2010).

An important aspect relating to the application of ethical principles in research is the need for investigators to consider, monitor and report any adverse events occurring during the research process. An adverse event is defined as 'an untoward occurrence that: (a) results in death,(b) is life-threatening,(c) requires hospitalisation or prolongation of existing hospitalisation, (d) results in persistent or significant disability or incapacity,(e) consists of a congenital anomaly or birth defect, or(f) is otherwise considered medically significant by the investigator' (National Patient Safety Agency, 2011). This includes 'any unfavourable and unintended sign, symptom, or disease temporally associated the research', whether or not it is directly related to it (European Medicines Agency, 2002). Within the field of pharmacology and medicinal product research, there are comprehensive guidelines and systems to ensure appropriate reporting, and response plans are in place should adverse reactions and events occur (European Commission, 2011). However, within other fields of research, including physiotherapy and rehabilitation, there is more limited guidance as to the application of these principles, for instance, where the key outcome being measured might also be considered an adverse event. Such decisions about the classification of and actions required in the event of an adverse event can be challenging. For example, if a research participant reports that they have significant worsening of symptoms after a research intervention, but this is not of sufficient severity to meet the adverse event classifications (listed earlier), should action be taken in the interests of the individual, or should the researcher continue with the intervention in the interests of the wider outcome for the many other individuals who may benefit in the future?

Rehabilitation research can be rife with these types of ethical problems, which are commonly viewed in health-care as the tension between two or more morally defensible alternative health-care actions, including inaction (Beauchamp and Childress, 2001). In the case of our own research, where the aim is to establish the risk factors for falls, best practice research guidance in the field clearly states that prospective reporting of falls over a minimum of a three-month period is the gold standard, both for studies investigating risk factors and those evaluating the effectiveness of interventions (Lamb et al., 2005). In these types of study, participants are usually classified as fallers if they have experienced two or more falls (Masud and Morris, 2001). Thus, the knowledge that the participant has fallen more frequently than twice is not actually required to answer the specific research question being posed.

We are confident that the situation we face in being aware that some of our research participants are experiencing potential adverse events (in this case falls) while they are involved in a period of observational data collection is not unique. In many other populations, researchers have reported that participants have recorded frequent falls during the data collection period (Mackintosh, 2005; Ashburn et al., 2001; Goodwin et al., 2011); and within the wider therapy research arena, it is likely that similar issues will arise related to the specific types of research being conducted.

We feel that our situation raises important ethical and clinical concerns for us as researchers, including when and whether to intervene in those individuals who are reporting frequent and/or injurious falls, and in the case of those patient groups where the evidence base around falls management interventions is limited, what action should be taken. Although we recognize that the very nature of research in the area of falls requires falls to be viewed as a key outcome of interest rather than as an adverse event, we, nevertheless, feel it is important to raise the question as to whether there is a potential for the negative impact to be minimized by the participants if early action is taken.

Unfortunately, we have found no discussion in the literature pertaining to the potential dilemma this holds for the research teams undertaking these studies, nor an exploration of the potential courses of action that may be appropriate in these circumstances. While reflecting on this issue, we have highlighted a number of possibilities that may be appropriate. This includes consideration of potential solutions, such as developing more specific guidance for falls reporting within non-interventional study protocols, in particular relating to when and whether to intervene in subjects who report repeated falls. Other options could be more pragmatic, such as acknowledging the potential for this situation to occur, and making explicit the expectations of 'usual care' to identify and manage the issue appropriately.

Our own opinion is that in this situation, it is questionable as to whether compelling benefits exist, either for the specific research project being undertaken or for the wider evidence base, to justify collecting additional falls data without taking some kind of action to ameliorate the potential negative effects of further fall events. This might, for instance, be in the form of a letter notifying the General Practitioner of the circumstances and frequency of the falls being reported. Although the majority of falls may not lead to an injury of the severity classified as a serious adverse event within current research ethics guidance (National Patient Safety Agency (2011), there is some evidence to demonstrate an increased risk of fall-related injury with greater falls frequency (risk of fracture OR: 3.8; 95%CI: 2.3–6.1 between recurrent fallers and non-fallers) (Pluijm et al., 2006). There is also evidence that identifying those at risk and targeting interventions may reduce fall and injury rates in older people (Rubenstein, 2006; Gillespie et al., 2009), although the types of intervention that may be most effective in the patient group are still open to debate (Gates et al., 2008) and evidence is less conclusive in other populations, such as those with neurological impairments.

As therapists working within the field of rehabilitation, it is less likely that our research will lead to adverse events of the frequency or severity highlighted within ethics guidance as it applies to medicinal and pharmaceutical research. However, as ethical researchers and health-care professionals, there remains a key obligation to first 'do no harm'. Although discussions relating to broad ethical principles are included in research teaching at all levels, it has been our experience that consideration of the specific issues as they relate to the design and conduct of physiotherapy research is somewhat more limited, particularly when considering issues such as adverse events. Take for instance the UK training programme in 'Good Clinical Practice', which has been designed to meet the International Conference on Harmonization good clinical practice, ethical and scientific quality standard for the design, conduct and record of research involving humans (European Medicines Agency, 2002). Despite this certification being required for the wide range of researchers who undertake ethically approved clinically based studies, the focus remains on medical and pharmaceutical interventions. Why might this be the case? Perhaps because there is a perception that ethical questions relating to medical issues are more urgent than rehabilitation issues because of their often 'high-tech', more dramatic and life-and-death nature. Perhaps also because rehabilitation is a relatively new and rather underdeveloped sub-field of bioethics. Regardless of the reason, given the ever-increasing therapy research that is now being undertaken, we believe that it is timely for these issues to be acknowledged, debated and addressed. This will require an open and honest dialogue to take place between researchers, clinicians, service users and ethicists to ensure that the necessary breadth of perspective is gained. Because of the multi-disciplinary nature of the field, we believe that the ethical issues we have raised in relation to falls research could provide a practical impetus to set this discussion in motion.

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7.5.2 Identification of risk factors for falls in multiple sclerosis: a systematic review and meta-analysis

Research Report

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

Hilary J. Gunn, Paul Newell, Bernhard Haas, Jonathan F. Marsden, Jennifer A. Freeman

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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.

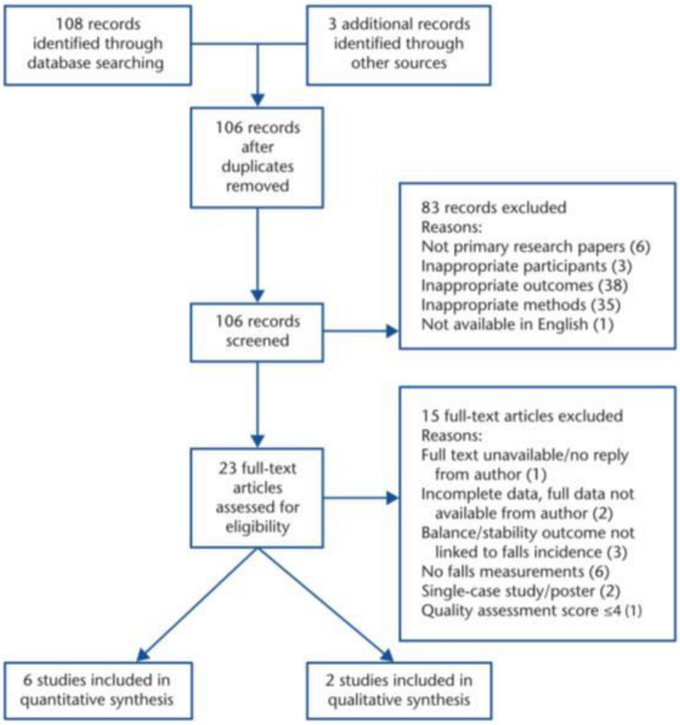

Figure 1.
Flow chart of studies screened for inclusion in the review.

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 (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.

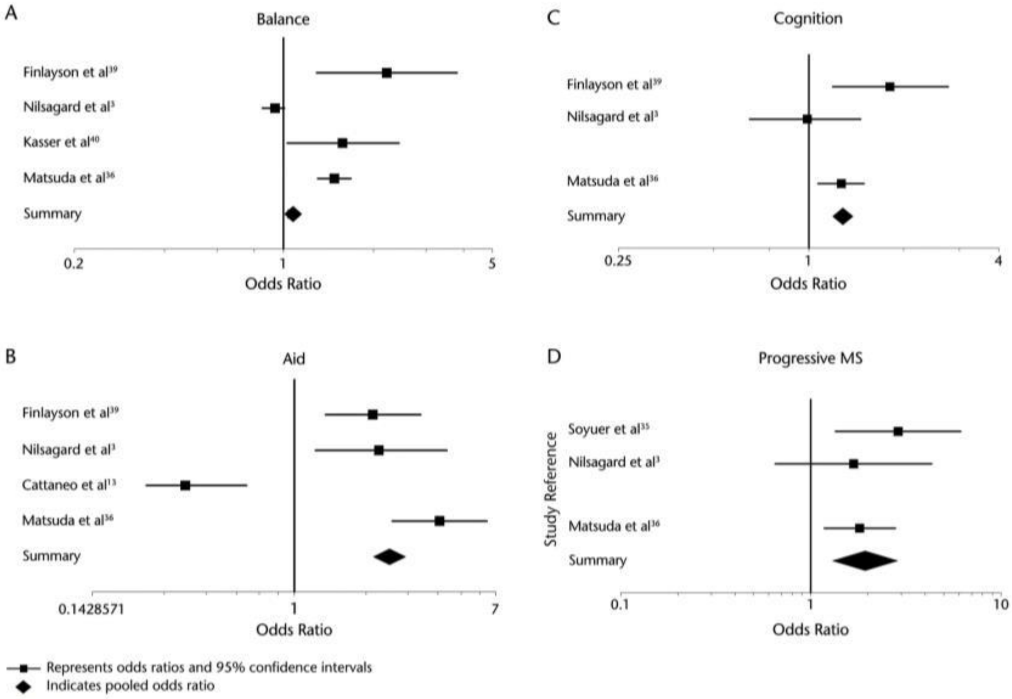

Figure 2.
Forest plots: (A) balance, (B) walking aid use, (C) cognition, and (D) progressive multiple sclerosis (MS) classification.

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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7.5.3 Risk factors for falls in multiple sclerosis: an observational study

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Risk factors for falls in multiple sclerosis: an observational study

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Abstract

Background: People with multiple sclerosis (MS) experience frequent falls, which are associated with impairments and limitations to activities and participations.

Objective: The objective of this paper is to evaluate falls risk factors using robust clinical measures.

Methods: A total of 150 individuals (confirmed MS diagnosis, Expanded Disability Status Scale (EDSS) 3.5–6.5) were recruited, with 148 participants included in the final analysis. Demographic data were collected and performance assessed in eight predictor measures (Physiological Profile Assessment (PPA), Brief Ataxia Rating scale, Ashworth scale (Ashworth), Modified Falls Efficacy scale, Symbol Digit Modalities Test, dual-task interference, lying/standing blood pressure, static/dynamic visual acuity). Participants prospectively recorded falls over three months using a daily diary. People were classified as "fallers" based on reports of ≥ two falls.

Results: A total of 104 participants recorded 672 falls; 78 (52.7%) reported ≥ two falls. Continence issues, previous falls history and use of prescribed medications were each associated with increased risk of being a "faller". Ashworth and PPA risk score contributed significantly to a logistic regression model predicting faller/non-faller classification. The reduced model (Ashworth, PPA, EDSS) showed fair-to-good predictive ability (ROC c-statistic 0.73, sensitivity 70%, specificity 69%).

Conclusion: This study confirms the high prevalence of falls in ambulant people with MS. Important potentially modifiable risk factors are identified, suggesting aspects to target in falls interventions.

Keywords

Multiple sclerosis, accidental falls, risk factors, rehabilitation

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Introduction

Falls are a significant issue in multiple sclerosis (MS), with research demonstrating more than 50% of people falling in any six-month period.[1] People with MS have an increased risk of osteoporotic fractures,[2] and falls are associated with significant limitations to activities and participations.[3] Guidance recommends further research should be carried out with the aim of reducing falls rate in people with MS.[4]

Knowledge of the risk factors for falls in MS is essential to guide the development of an appropriately targeted intervention. Current knowledge relating to specific risk factors for falls in MS is limited. A recent systematic review[5] suggests that use of a walking aid, balance limitations, cognitive impairments and progressive disease sub-type are associated with increased falls risk; however, findings were equivocal for many predictors studied, and other potential risk factors remain under-researched. Issues were also highlighted relating to methodological limitations in many studies, including use of retrospective falls reporting, and lack of a clear definition of a fall in several studies.

We aimed to identify factors associated with increased falls risk in people with MS, using clinically applicable predictor measures. We also aimed to explore which, if any, specific impairments were associated with increased risk of falls, to inform the evidence base for the development of future falls management interventions.

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Materials and methods

This quantitative cohort study involved a one-off assessment of potential falls risk factors, followed by three months of prospective collection of data relating to falls incidence.

Participants

Participants were recruited from a large longitudinal cohort study, the South West Impact of MS study (SWIMS).[6] All potentially eligible participants within the database were identified by the study coordinator and invited to participate by letter ($N = 277$). In addition, 18 individuals made direct contact following local publicity about the project. For pragmatic reasons, to minimise the burden of travel for the assessor, participants were recruited in batches according to geography, with the final sample comprising individuals from across the entire SWIMS catchment area. Inclusion criteria were a confirmed diagnosis of MS as determined by McDonald's criteria[7] and an Expanded Disability Status Scale (EDSS) of between 3.5 and 6.5, scored by telephone interview.[8] Individuals were excluded if they were unable to effectively give informed consent or had co-morbidities likely to significantly impact on balance as determined by the study assessor (HG).

Ethical approval was granted by University and regional National Health Service (NHS) Ethics Committees (10/H0203/66). Participation was voluntary and written informed consent was gained in accordance with the International Declaration of Helsinki.[9]

Predictor variables

Eight potential predictor variables were included. The choice of variables incorporated those aspects previously linked to falls in MS, where the measures used in previous studies lacked specificity.[10,11] Also included were attributes with limited or no evaluation in MS, but which could reasonably be considered as potentially important based on literature in other populations and the prevalence of the attribute in MS (e.g. cerebellar disease, vestibular pathologies, dual-tasking deficits). These were measured using standardised and validated outcome measures which have been shown to have clinical utility. For each variable, higher scores indicate worse performance.

The Physiological Profile Assessment (short form) (PPA) provided a quantitative measure of key physiological risk factors for falls, including strength, sensation, sway, vision and reaction time. Validated in older people,[12] scores can be considered separately, or summed and weighted to give a total risk score, as used in this study.

The Brief Ataxia Rating Scale (BARS) is a quick, clinically applicable test for ataxia, assessing five key aspects of coordination derived from the International Co-operative Ataxia Rating Scale.[13]

The Ashworth scale was used to rate spasticity as measured using the testing guidelines reported in Nuyens et al.[14] Because of reported issues associated with use of multiple muscles and summed scoring of the Ashworth scale,[15] individual measurements were taken of the gastrocnemius and soleus muscles of the ankle reported by the participants as being their "worst" leg.

In line with recommendations, the Modified Falls Efficacy Score (International) (MFESI) was used to assess fear of falling.[16] This produces a single summed score based on the responses to 16 questions.

The Symbol Digit Modalities Test (SDMT) provides a fast, reliable measure which evaluates areas of cognitive function likely to be relevant to falls risk, including working memory and attention.[17] We used the oral version, recording the number of symbols correctly identified during the 90-second test period.

Dual-task interference (DTI) was measured using a 10-metre walk and serial 7 subtraction protocol, as recommended by previous DTI research in older people.[18] While a range of data was recorded, the main statistical analysis used the change in walking time, expressed as a percentage change between the single- and dual-task walks.

Measurement of lying and standing blood pressure assessed autonomic function, in line with previous MS studies.[19] Blood pressure was measured after 15 minutes in supine position and recorded for at least two minutes after standing using a calibrated digital sphygmomanometer (A&D Instruments, Oxford). A drop of > 20/10 mmHg after standing for at least one minute was considered positive.[20]

Vestibular dysfunction, in particular the inability to suppress the vestibular-ocular reflex (VOR) to stabilise gaze during head movements, has been highlighted as a risk factor for falls in older people.[21] In line with Hillman et al.,[22] our test compared visual acuity under seated static and dynamic conditions, where the head was moved passively back and forth through a 400 arc in a horizontal plane at a frequency of approximately 1.5 Hz, equating to a maximum velocity of approximately 1200/sec (Figure 1). Dynamic test movements were guided by the use of audio feedback (audible only to the tester) and a visual range guide. Visual acuity was measured for each eye individually using a Freiburg Visual Acuity Test (FrACT) Landolt C protocol.[23] Visual acuity was recorded using the Visual Acuity Rating (VAR) score.[24]

Outcome variable

In line with best practice guidance, falls were defined as: "a slip or trip in which you lost your balance and landed on the floor or ground or lower level", and people were classified as fallers or non-fallers based on self-reports of two or more falls during the prospective diary return period.[16]

Figure 1. Set-up for dynamic visual acuity test.

Procedures

Data were collected from May 2011 to August 2012. At a single assessment session, demographic and clinical data were collected, followed by the battery of assessments, conducted in a standardised order to minimise fatigue. All assessments were undertaken by one assessor (HG) according to a written protocol.

Participants were asked to prospectively record all falls using a daily diary system for three months immediately following their assessment. Participants received a pack containing 84 daily falls diary sheets, written completion instructions and reply-paid return envelopes. Diaries were returned at two-weekly intervals: Any participant whose diary returns fell behind schedule was followed-up by a reminder telephone call or email.

Data analyses

All data were entered directly onto an Excel spreadsheet which had been developed to minimise potential data input errors; accuracy was checked after each assessment. Any aspect of the assessment for which participants were unable to provide data was recorded, including coding for each reason for non-completion. Individual missing data were excluded from analysis on a case-by-case basis. Participants who failed to return any falls diary reports were excluded from the analyses.

All statistical analyses were run using IBM SPSS Statistics v20. For all analyses, the significance level was set at 5%. Data were summarised using frequencies and percentages, mean and standard deviation or median and interquartile range (IQR) as appropriate. Associations between categorical variables and falls grouping were analysed using Fisher's exact test. For continuous variables, the differences between the two falls groups were compared using independent two-sample *t* tests (for normally distributed data) or Mann Whitney U tests (for non-parametric data). To further explore possible associations between each factor and falls grouping, unadjusted odds ratios (and corresponding 95% confidence intervals (CIs)) were calculated.

For the main statistical analysis, multi-variable logistic regression analysis, adjusting for disease severity as determined by EDSS score, was used to determine which combination of the eight predictor variables best discriminated between the two falls groups. Initially, forced entry was used to include all of the predictor variables plus the EDSS. Subsequently, backwards stepwise elimination was undertaken to develop a reduced model: The order of elimination was determined by evaluation of the Wald statistic for each predictor at each step alongside qualitative evaluation of the variables under consideration. This process is recommended above standard stepwise methods using solely significance-based decision-making to improve the stability and quality of the final model.[25] Further exploratory analyses of the component scores of variables included in the reduced model were undertaken to evaluate the relative contributions of each element to the overall performance of the retained predictor.

Goodness-of-fit of the final reduced model was assessed using the Hosmer and Lemeshow test and model performance was assessed using analysis of the receiver-operating characteristics (ROC) curve as a plot of the sensitivity and 1-specificity for all possible cut-off points. The optimal cut-off point of the model (defined as the point that maximises sensitivity and specificity)[26] was determined using

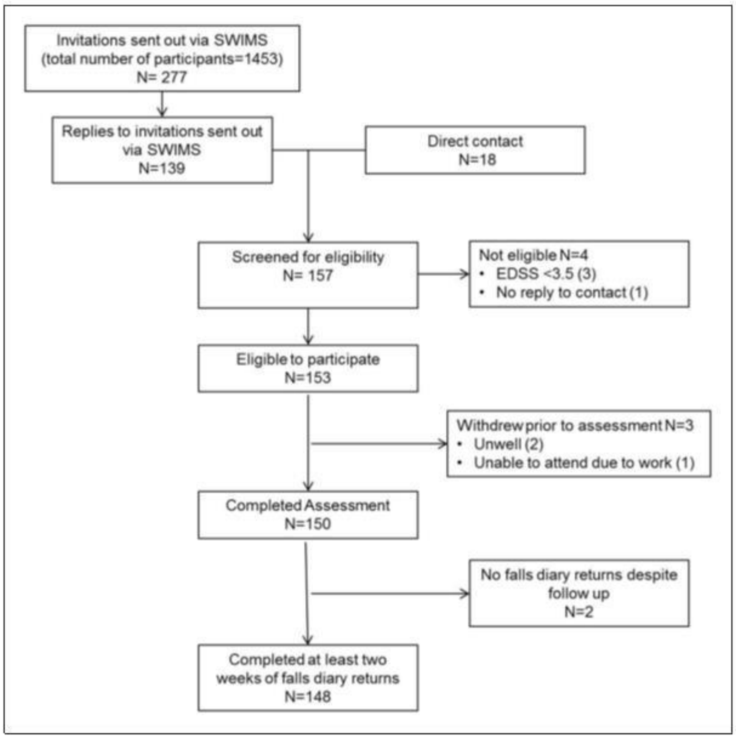

Figure 2. Participant flow diagram.
SWIMS: South West Impact of Multiple Sclerosis database; EDSS: Expanded Disability Status Scale.

least-distance analysis and confirmed by calculating the Youden index.[27] The main assumptions of logistic regression were also investigated[28] using standard diagnostic methods.

Sample size

The aim of the main statistical analysis was to identify the best linear combination of eight possible variables to predict fallers/non-fallers, using multi-variable logistic regression. Based on Peduzzi et al.,[29] a sample size of 145 patients is sufficient for this type of analysis, assuming that the proportion of fallers is no lower than 55%. One hundred and fifty participants were recruited, allowing for a 3% dropout rate.

Results

Figure 2 details the participant flow through the study.

Participant characteristics

Demographic and clinical characteristics of the sample are summarised in Table 1. These characteristics are broadly similar to those reported in the wider MS population.[30]

Falls data

Of the 150 participants recruited, two failed to return any falls diary data despite prompts and were therefore excluded from the subsequent analyses; 148 completed at least two weeks of falls diaries and were included in the analyses. Amongst these 148 participants, a total of 823 of a possible total of 888 falls diaries were returned, a return rate of 92.7%. During the three-month period, 104 participants (70.3%) reported at least one fall, with a total of 672 falls being recorded. Amongst these 104 participants, a median of three falls (IQR 1.25 to 6.75) was reported, with a total range of one to 63 falls. Seventy-eight participants (52.7%) recorded two or more falls, thus meeting the pre-determined criteria to be classified as fallers.

Table 1. Demographic and clinical characteristics.

Characteristic	All participants (n = 148)	Non-fallers (n = 70)	Fallers (n = 78)	p value	Odds ratio (95% CI) (fallers: non-fallers)
Age (years) mean (SD) [range]	57 (10) [33–84]	59 (10) [34–76]	57 (10) [33–84]	0.343[a]	0.98 (0.95 to 1.01)
Gender, n (%)					
Female	114	57 (50)	57 (50)	0.230[b]	Ref
Male	34	13 (38)	21 (62)		1.61 (0.74 to 3.53)
Self-reported MS classification, n (%)					
Relapsing–remitting	42	21 (50)	21 (50)	0.192[b]	Ref
Secondary progressive	66	35 (53)	31 (47)		0.89 (0.41 to 1.92)
Primary progressive	37	13 (35)	24 (65)		1.85 (0.75 to 4.57)
Benign	2	0	2 (100)		[d]
Malignant	1	1 (100)	0		[d]
Bladder issues, n (%)					
None/occasional	87	50 (57)	37 (43)	0.003[b]	Ref
Regular/frequent	61	20 (33)	41 (67)		2.77 (1.4 to 5.48)
Use of any walking aid, n (%)					
No	38	19 (50)	19 (50)	0.710[b]	Ref
Yes	110	51 (46)	59 (54)		1.16 (0.55 to 2.42)
Previous falls (in the past three months), n (%)					
0		46	17	<0.001[b]	Ref
1		11	10		2.46 (0.89 to 6.83)
2 or more		13	51		10.62 (4.65 to 24.22)
EDSS, n (%)					
3.5	26	15 (58)	11 (42)	0.58[c]	Ref
4	19	10 (53)	9 (47)		1.23 (0.37 to 4.03)
4.5	16	6 (38)	10 (62)		2.27 (0.63 to 8.15)
5	9	3 (33)	6 (67)		2.73 (0.56 to 13.37)
5.5	14	5 (36)	9 (64)		2.45 (0.64 to 9.39)
6	46	23 (50)	24 (50)		1.42 (0.54 to 3.74)
6.5	17	8 (47)	9 (53)		1.53 (0.45 to 5.25)
Total number of medications, median (IQR)	5 (2 to 7)	4 (2 to 6)	5 (3,7)	0.278[c]	1.01 (0.92 to 1.12)
Self-reported prescribed medications, median (IQR)	3 (1 to 5)	2 (1 to 4)	4 (2,6)	0.029[c]	1.12 (0.99 to 1.26)
Self-reported OTC medications, median (IQR)	1 (0 to2)	1 (0 to2)	0 (0,1)	0.013[c]	0.79 (0.64 to 0.97)

OTC: over the counter; IQR: interquartile range; CI: confidence interval; MS: multiple sclerosis; EDSS: Expanded Disability Status Scale; SD: standard deviation; [a]p value from two-sample t test, [b]p value from Fisher's exact test, [c]p value from Mann-Whitney test; [d] not calculable as 0 value in one group; Ref: reference category.

Demographic and clinical characteristics and falls status (Table 1)

There was evidence of significant associations between self-reports of previous falls, medication use and urinary continence issues and whether or not individuals were classified as fallers or non-fallers (all $p < 0.05$). The odds of being classified as a faller for participants reporting two or more falls in the previous three months were more than 10 times the odds for participants who did not report a fall in the previous three months (odds ratio (OR) 10.62, 95% CI 4.65–24.22). Similarly, the odds of being classified as a faller were significantly greater for participants who reported regular/frequent urinary continence issues, compared to those reporting none/occasional issues (OR 2.77, 95% CI 1.40–5.48). There was also an increase in the odds of being classified as a faller with increasing numbers of prescribed medications (OR 1.12, 95% CI 0.99–1.26); and a reduction in odds with increasing numbers of over-the-counter (OTC) medications (OR 0.79, 95% CI 0.64–0.97).

Whilst ORs were greater than one for many of the other characteristics, there was insufficient evidence of significant associations with falls status. Of interest is the non-linear variation in the OR for faller/non-faller seen with EDSS level, with the OR steadily increasing for EDSS 4.0 to 5.0, compared with EDSS 3.5, followed by a decrease in the ORs at each step from 5.5 to 6.5.

Predictor variables and falls status

The summary statistics for the objective assessments indicate worse performance by fallers in all eight predictors (Table 2). However, within the multi-variable logistic regression analysis (which included EDSS as per the study protocol) only two predictor variables are seen to make significant independent contributions to the model: Ashworth scale and PPA. Within the categorical variable of the Ashworth scale, the ORs are non-linear, with a higher OR for those scoring one (OR 7.88, 95% CI 2.16–28.80) compared to those scoring two or more (OR 2.51, 95% CI 0.91–6.95). Increasing PPA score was associated with increased risk of being classified as a faller (OR 1.9, 95% CI 1.34–2.69). Exploratory analysis of the individual aspects of the PPA demonstrates that the key contributing factors are postural sway and reaction time (all $p <$ 0.006, after adjustment for EDSS) (Table 3). It is noted that whilst the p values for these elements indicate statistically significant differences between fallers and non-fallers, the ORs for each individual element are extremely close to one.

From the initial full logistic regression model, a reduced model was developed retaining only the significant predictor variables (Ashworth scale and PPA summed score) (Table 4). The EDSS was retained in the final model in accordance with the initial study protocol. The goodness-of-fit of this model was reasonable (Hosmer-Lemeshow test, $p = 0.659$). Model performance was further assessed using analysis of the ROC curve (Figure 3).[26] The area-under-the-curve c-statistic was 0.73 (95% CI 0.65–0.81), indicating fair-to-good overall predictive ability.[31] Using least distance and Youden index methods, the optimal cut-off point of the model was determined to be 0.51, with sensitivity and specificity at this point being 69% and 70%, respectively. Similar analysis for the best performing single predictor (PPA) yielded a c-statistic of 0.67 (95% CI 0.58–0.76) and sensitivity and specificity values of 56% and 74%, respectively.

Further diagnostics were run on the reduced model to check that the assumptions for logistic regression were satisfied,[28] with no major violations of the assumptions detected.

Discussion

This study demonstrated a prevalence of accidental falls of 70.3% for people with MS, with 52.7% of the cohort reporting two or more falls in the three-month period. This rate of falling is high relative to other studies, with reported rates of 50%–60% for single falls over a similar time period.[5] This may in part be due to the characteristics of our sample, which included individuals with a higher level of disability than other studies.[1,32] However, variations in definitions of falls and falls reporting measures may also, at least in part, account for this discrepancy. Many previous studies used retrospective falls recall,[10,11,32] a method known to be associated with significant under-reporting of falls.[33] Our study has been conducted according to best-practice guidelines in order to ensure our data will be as accurate a reflection of the actual frequency of falls as is possible.[16]

In our study, there was evidence of significant associations between each of urinary continence issues, previous falls history, prescription medication usage and increased risk of being classified as a faller; however, use of OTC medications (predominantly dietary supplements) was associated with a significant reduction in falls risk. This aspect has not been investigated in previous studies and would merit further evaluation – it is possible that other factors may be contributing to this association.

In contrast to others,[1,10,32] our results did not show that either use of a walking aid or EDSS score was significantly associated with falls risk. However, we did observe a pattern of increasing falls risk with EDSS progression from 3.5 to 5.5; the point on the scale just prior to transition from not using a walking aid to using a walking aid. This finding may reflect the clinical characteristics of the different study samples; compared to others our participants tended to have higher EDSS scores[1,34] and more people were in the progressive phase of the disease.[1] If confirmed in future

Table 2. Regression analysis, full model.

Predictor	Non-fallers (n = 70)	Fallers (n = 78)	B	SE	Wald	df	p value	Odds ratio (95% CI) (fallers: non-fallers)
Ashworth score 0 (n (%))	50 (56)	39 (44)	Ref	—	—	—	—	Ref
Ashworth score 1 (n (%))	7 (27)	19 (73)	2.064	0.661	9.74	1	0.002[a]	7.88 (2.16 to 28.8)
Ashworth score 2+ (n (%))	13 (40)	20 (60)	0.921	0.519	3.148	1	0.076	2.51 (0.91 to 6.95)
BP drop greater than 20/10 on standing (n (%))	7 (44)	9 (56)	0.216	0.619	0.122	1	0.727	1.24 (0.37 to 4.17)
FESI (mean (SD))	35.77 (10.08)	38.22 (9.54)	0.009	0.024	0.155	1	0.693	1.01 (0.96 to 1.06)
SDMT number correct (mean (SD))	45 (12.2)	42 (13.7)	0.005	0.02	0.053	1	0.819	1.00 (0.97 to 1.05)
BARS (median (IQR)	6 (3 to 11)	8.5 (4 to 13)	−0.06	0.063	0.824	1	0.364	0.944 (0.83 to 1.07)
PPA (median (IQR))	1.68 (0.93 to 2.69)	2.85 (1.31 to 4.44)	0.641	0.178	12.998	1	<0.001[a]	1.9 (1.34 to 2.69)
Dual task % change[b] (median (IQR))	−26.7 (−53.5 to −11.9)	−34.4 (−71 to −10)	−0.003	0.003	1.238	1	0.266	1.00 (0.99 to 1.0)
DVA change in visual acuity ratio[c] (median (IQR))	−8.5 (5 to 15.5)	−10 (4.5 to 16.25)	0.007	0.025	0.072	1	0.789	1.00 (0.96 to 1.06)
EDSS (median (IQR))	5.5 (4 to 6)	5.5 (4 to 6)	−0.207	0.258	0.649	1	0.421	0.81 (0.49 to 1.35)
Constant			−1.172	1.525	0.591	1	0.442	0.31

EDSS: Expanded Disability Status Scale; BARS: Brief Ataxia Rating Scale; BP: blood pressure; FESI: Falls Efficacy Score (international); PPA: Physiological Profile Assessment; SDMT: Symbol Digit Modalities Test; DVA: Dynamic Visual Acuity; IQR: interquartile range; CI: confidence interval; SD: standard deviation; df: degrees of freedom; B: regression coefficient; SE: standard error; [a]p < 0.05; [b]: n = 70/75; [c]: n = 67/73.

Table 3. Analysis of the Physiological Profile Assessment (PPA) individual elements.

PPA element	Non-fallers (n = 70)	Fallers (n = 78)	p value	Univariate regression[a]					
				B	SE	Wald	df	p value	Odds ratio (95% CI) (fallers: non-fallers)
Strength (mean (SD))	22.6 (9.05)	23.22 (10.17)	0.972[c]	0.01	0.02	0.153	1	0.696	1.01 (0.97 to 1.04)
Sensation (median (IQR))	2.2 (1.2 to 4.4)	2.8 (1.4 to 5.5)	0.160[b]	0.09	0.06	2.4	1	0.121	1.09 (0.98 to 1.22)
Vision (median (IQR))	21 (20 to 21)	21 (18.75 to 21)	0.069[b]	−0.08	0.05	2.23	1	0.135	0.92 (0.83 to 1.03)
P-A sway (max excursion, foam, eyes open, mm) (median (IQR)	38 (31 to 51.25)	51 (37 to 80.5)	0.001[b]	0.02	0.01	7.46	1	0.006	1.02 (1.01 to 1.03)
M-L sway (max excursion, foam, eyes open, mm) (median (IQR))	44 (29 to 76)	64 (39 to 105.5)	0.006[b]	0.01	0.004	8.47	1	0.004	1.01 (1.00 to 1.02)
Total sway area, mm (median (IQR))	1584 (922.5 to 4008.25)	2906 (1522.5 to 8142.75)	0.001[b]	0.00	0.00	8.73	1	0.003	1.00 (1.00 to 1.00)
Reaction time, milliseconds (median (IQR))	268 (238 to 301)	286 (257 to 381)	0.029[b]	0.01	0.002	7.74	1	0.005	1.01 (1.00 to 1.01)
PPA risk score (median (IQR))	1.68 (0.93 to 2.69)	2.85 (1.31 to 4.44)	<0.001[b]	0.43	0.12	13.82	1	<0.001	1.54 (1.23 to 1.93)

P-A: antero-posterior; M-L: medio-lateral; B: regression coefficient; SE: standard error; df: degrees of freedom; OR: odds ratio; CI: confidence interval; IQR: interquartile range; [a]: Adjusting for Expanded Disability Status Scale (EDSS); [b]: p value from Mann Whitney U test; [c]: p value from two-sample t test.

Table 4. Regression analysis, reduced model.

Predictor	B	SE	Wald	df	*p* value	Odds ratio (95% CI) (fallers: non-fallers)
EDSS	–0.304	0.196	2.402	1	0.121	0.74 (0.50 to 1.08)
Ashworth score 0	Ref	—	—	—	—	Ref
Ashworth score 1	1.252	0.522	5.754	1	0.016	3.50 (1.26 to 9.72)
Ashworth score 2+	0.815	0.479	2.892	1	0.089	2.26 (0.88 to 5.78)
PPA	0.494	0.131	14.308	1	<0.001	1.64 (1.27 to 2.12)
Constant	0.113	0.894	0.016	1	0.899	1.12

EDSS: Expanded Disability Status Scale; PPA: Physiological Profile Assessment; B: regression coefficient; SE: standard error; df: degrees of freedom; OR: odds ratio; CI: confidence interval.

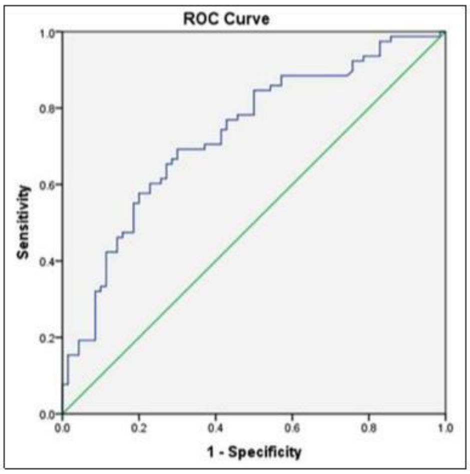

Figure 3. Receiver-operating characteristics curve (ROC) for reduced regression model.

work, our results suggest that a key time for falls interventions programmes may be when people first start to consider using a walking aid.

Our finding that fear of falling as measured by the FESI is not related to falls risk is broadly in agreement with existing MS research in which fear of falling was measured using a simple four-point scale.[1] Our study utilises a robust measure which has recently been validated in a sample of people with MS.[35] This finding may reflect different attitudes towards falls risk when compared to other groups such as older people, in whom falls are known to be associated with perceptions of disability and loss of independence.[36] Whilst previous research in MS has highlighted activity curtailment associated with fear of falling,[3] our results suggest that this strategy may not be directly associated with fear of falling, as measured by the FESI. Fear of falling is acknowledged as a multi-dimensional concept.[37] Factors such as age, role and social expectations may all make significant contributions to the perception of and response to falls, and may account for the differences seen in people with MS compared to other populations. These issues require further exploration as it is likely to be an important consideration in the development of MS falls interventions.

In contrast to other MS studies, cognitive function was not significantly associated with falls risk in our study. This may be related to the aspects of cognitive function measured: Previous studies used global measures of cognitive function such as the mini-mental status examination[32] or self-report[10] whereas we used the SDMT as a specific measure of attention and working memory. Similarly, the only previous study to measure dual-task performance[1] used the timed-up-and-go (cognitive) test which is a sit-to-stand, walk and turn task, rather than a straight walking task; this may account for the differing results.

New attributes that have not previously been objectively evaluated include ataxia, postural hypotension and vestibular dysfunction, all of which have been associated with falls in other non-MS samples.[21,38] In contrast, our study did not demonstrate evidence that any of these attributes are significantly associated with falls risk, although fallers did perform worse than non-fallers in each aspect.

After adjusting for EDSS, the final model for predicting falls risk included only two of the potential predictor measures, the Ashworth scale and the PPA. Spasticity, as measured by a lower limb total Ashworth score, has been shown to be associated with falls in previous MS studies;[1] however, the association was thought to be linear in nature, with falls risk increasing with each step on the Ashworth scale. In contrast, our findings have shown a non-linear relationship, with a score of one being associated with a much higher OR than a score of two or more. Whilst we recognise the limitations of the Ashworth scale as a measurement instrument,[39] it may be that lower grades of spasticity are more associated with falls risk: One possibility is that less muscle stiffness results in less stability in weak lower limbs.

The PPA has not previously been used in MS studies. Exploratory analysis of the individual dimensions of the PPA assessment suggests that changes to postural sway and delayed reaction time were key attributes, whilst sensory changes, strength and vision did not (individually) predict falls classification. However, whilst the differences in scores between fallers and non-fallers were statistically significant for three of the individual elements, the ORs for each element were much lower than the OR associated with the total PPA risk score. The PPA risk score alone was able to predict falls with a 'fair' level of accuracy; however, addition of the EDSS and Ashworth scale to the model improved the accuracy to 'good'.[31] The sensitivity and specificity of this final model were higher than for previously reported models in MS studies;[1,40] confirmation of this is required in future research as this has the potential to form the basis of work to develop an MS-specific falls risk assessment tool.

This study confirms the high prevalence of falls in people with MS and highlights attributes linked to risk of falls. We have also demonstrated that other impairments not investigated previously, such as ataxia, vestibular dysfunction and postural hypotension, may not be significant predictors of falls risk in this group. Strengths of this study are the standardised measures used, which are clinically applicable. Use of specific falls definitions and prospective falls recording using recommended data collection methods also contribute to the methodological strengths of the study. EDSS was measured using the telephone interview method, which has been shown to have good agreement with the original face-to face version (intra-class correlation coefficient: 94.8%),[8] although it is recognised that face-to-face assessment of the EDSS is the gold standard. Limitations to the study include the recognised concerns regarding the validity of the Ashworth scale as a measure of spasticity and potential inaccuracies associated with use of self-report diaries for falls data collection.[16] The use of participant self-report to collect data such as medication use may also have led to some inaccuracies; similarly, detailed information regarding medication dosages and participant adherence was not collected, hence these findings should be interpreted with caution.

A logistic regression model including the PPA and Ashworth scale predicted fallers with a higher degree of accuracy than previously published models. Several of the risk factors identified are modifiable, including postural sway, delayed reaction time, spasticity and urinary continence and are potentially amenable to intervention. Future work will include the development of an intervention targeted to address the modifiable risk factors highlighted by this study.

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Conflict of interest

The authors declare that there are no conflicts of interest.

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7.5.4 Frequency, characteristics and consequences of falls in multiple sclerosis: Findings from a cohort study

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ORIGINAL ARTICLE

Frequency, Characteristics, and Consequences of Falls in Multiple Sclerosis: Findings From a Cohort Study

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Abstract

Objective: To evaluate falls rate and the characteristics of falls (including fall-related injuries) in a multiple sclerosis (MS) cohort.

Design: As part of a study evaluating falls risk, a cohort of 150 participants prospectively recorded actual and near fall events using a daily diary over 3 months, as well as the circumstances of each fall including related injuries.

Setting: Community setting.

Participants: A population-based sample of people (NZ150) with a confirmed diagnosis of MS (Expanded Disability Status Scale, 3.5e6.5) was recruited via a patient-centered longitudinal study database of disease course in people with MS.

Interventions: Not applicable.

Main Outcome Measures: Rate of actual and near falls, circumstances and consequences of falls (including rates and type of injury plus follow-up care).

Results: The response rate for the falls diary was 92.7%. A total of 672 actual falls and 3785 near falls were recorded, with a moderate correlation between the numbers of actual and near falls per person (rZ.474; 95% confidence interval, .34e.59). Men recorded significantly more falls than women. Falls were associated with a range of activities, although 27.6% occurred during general mobility activities such as walking, turning, and moving between positions. Injuries occurred in 11.1% of falls, with 6 individuals requiring medical attention.

Conclusions: People with MS experience high numbers of falls, with associated injuries. Falls occur during a wide range of activities, reflecting their potential impact on daily life. Evaluating the characteristics of individuals who experience frequent near falls but few actual falls may be valuable for research and clinical practice.

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People with multiple sclerosis (MS) have a high prevalence of falls, with research reporting more than 50% of people falling in any 6-month period.[1] Falls in MS are associated with activity curtailment, loss of independence,[2] and increased risk of fracture relative to age-matched populations.[3] A United Kingdom national audit has highlighted the lack of robust studies in this area, specifically studies that evaluate the risk factors and characteristics of falls in MS.[4]

Previous research into falls in older people has demonstrated that falls rates and injury rates are significant predictors of morbidity, and it is recommended that both should be measured alongside the more common evaluation of falls risk.[5] This is particularly relevant given the finding that falls interventions that are shown to affect falls risk may not necessarily affect rates of falls and injuries, and vice versa.[6] Previous MS research on falls has focused predominantly on the factors affecting falls risk,[7-10] with limited published data relating to falls rates or the characteristics of falls. The studies available have highlighted varying falls and injury rates,[11,12] as well as a range of activities that have been associated with falls events.[1,13,14]

This article reports on data collected as part of a prospective cohort study evaluating falls risk in ambulant people with MS; the data pertaining to the assessment of falls risk has been reported elsewhere.[15] The aim of this part of the study was to

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provide data on falls rate and the characteristics of falls. This included an evaluation of the circumstances, perceived causes, and consequences of falls, including fall-related injuries. Data relating to the relationship between actual and near falls were also evaluated.

Methods

Participants

A total of 150 participants were recruited from the South West Impact of MS (SWIMS) database, a patient-centered longitudinal study of disease course in people with MS. This database recruits participants from neurology clinics across the southwest of England and includes individuals with a range of disease subtypes and severity who are broadly representative of the wider MS population.[16,17] Eligibility criteria included a confirmed diagnosis of MS as determined by McDonald et al's criteria,[18] and an Expanded Disability Status Scale (EDSS)[19] score between 3.5 and 6.5. Individuals were excluded if they were unable to effectively give informed consent to participate in the study or had comorbidities affecting mobility, balance, or both. Only 1 potential participant was excluded because of mobility/balance issues, as a hip fracture was sustained the week before the assessment was due.

Potential participants were selected from the database according to responses on the MS Walking Scale-12 (MSWS-12) version 2[20] ("unable to walk at all" box not ticked, MSWS-12 score 15) and/or the physician-recorded EDSS score, and sent an invitation by the SWIMS coordinator. Participants who responded to the invitation were screened by telephone by the assessor (H.G.) using the telephone version of the EDSS[21] and a simple checklist to ensure they met the study inclusion and exclusion criteria.

Permissions for the study were obtained after ethical review by both the university and regional National Health Service ethics committees. Participation was voluntary, and written informed consent was gained in accordance with the International Declaration of Helsinki.[22]

Procedures

After an assessment of potential falls risk factors,[15] participants were asked to prospectively record details of actual falls and near falls in a preformatted paper diary, on a daily basis over a 3-month period. In line with best practice guidelines, falls were defined as "a slip or trip in which you lost your balance and landed on the floor or ground or lower level," and near falls as "an occasion where you felt you were about to fall but did not actually fall."[5(p1619)]

List of abbreviations:	
A&E	accident and emergency
CI	confidence interval
EDSS	Expanded Disability Status Scale
MS	multiple sclerosis
MSWS-12	Multiple Sclerosis Walking Scale-12
PPY	per person-year
SWIMS	South West Impact of Multiple Sclerosis

For each actual fall, participants were asked to use a standardized form based on previously published work in this area,[1] recording detail about the time of day, activities being undertaken at the time of the fall, and any injuries sustained. Perceived rates of fatigue and hurrying were recorded using a 4-point ordinal scale (appendix 1). For near falls, participants were simply asked to record the frequency of such events on a daily basis.

Diaries were returned every 2 weeks; any participant whose diary returns fell behind schedule was followed up by a reminder telephone call or e-mail. Diaries were reviewed immediately on return, and participants were contacted to confirm all falls data and to clarify any entries that were unclear. In an attempt to gather further exploratory data, where participants had recorded the activity associated with their fall as "other," more detail was elicited during the follow-up contact. Participants were also asked a further general question about the perceived cause of the fall (appendix 2).

Data analyses

For the analysis of falls frequency and related circumstances, all actual falls were included. All statistical analyses were undertaken using IBM SPSS for Windows, version 20,[a] using 2-sided tests and 95% confidence intervals (CIs), with the significance level set at 5%. Where computational power allowed, exact significance levels were calculated, otherwise the Monte Carlo approximation method was used. Individual missing data were excluded from analysis on a case-by-case basis. Participants who failed to return any falls diary reports were excluded from the analyses.

Since the data relating to the number of actual falls did not demonstrate a normal distribution, comparisons of the differences between the numbers of falls recorded by demographic and clinical characteristics were summarized using medians and interquartile ranges, and statistical analysis was undertaken using the Mann-Whitney U test (for binomial variables such as sex) or Kruskal-Wallis tests for multiple category characteristics (such as MS classification and EDSS). The relationships between the number of actual falls and continuous characteristics (such as age and number of near falls) were analyzed using the Spearman rho correlation (r).

The falls rate (actual falls) per person-year (PPY) was calculated in Excel[b] using the following formula[23]:

$$\text{Falls rate (PPY)} = (\text{Total no. of actual falls} / \text{Total no. of person days [all participants]}) \times 365$$

The injury rate PPY was similarly calculated.

Data relating to the circumstances associated with all actual falls where detail was recorded were summarized by calculating the frequency and percentage of the total number of falls recorded per categorical grouping (time of day, activities associated with the fall, perceived fatigue and hurrying).

Results

Participants

Of the 150 participants recruited to the study, 148 completed at least 2 weeks of falls diary data returns. Two participants failed to

Table 1 Characteristics of participants

Characteristic	Total (nZ148)	Nonfallers (nZ44)	Fallers (nZ104)	Recorded Falls per Person (Whole Sample) Over 3mo (nZ148)		Recorded Falls per Person (Fallers Only) Over 3mo (nZ104)		
				Median	IQR	Median	IQR	P
Age (y)	57.9 10.01	59 9.65	57 10.14					
Sex								
Women	114 (77)	34 (30)	80 (70)	1.5	0e6	2	1e5	$.02^{*y}$
Men	34 (23)	10 (30)	24 (70)	2.5	0e4	4	2e16	
EDSS								
3.5	26 (17.6)	9 (35)	17 (65)	1	0e2	2	1e4	$.41^{zx}$
4	19 (12.8)	5 (17)	14 (73)	1	0e4	2	1e6.5	
4.5	19 (12.8)	8 (42)	11 (58)	2	0e5	3	2e25	
5	9 (4.0)	2 (22)	7 (78)	3	0.5e8.5	4	2e10	
5.5	14 (9.4)	4 (29)	10 (71)	2.5	0e7	4	2e12	
6	47 (31.7)	14 (30)	33 (70)	2	0e4	3	1.5e7.5	
6.5	17 (11.5)	5 (29)	12 (71)	2	0e5.5	3.5	1e10	
MS classification								
Relapsing remitting	42 (28.4)	12 (29)	30 (71)	1.5	0e4	2.5	1e4	$.27^{zx}$
Secondary progressive	66 (44.6)	20 (30)	46 (70)	1	0e4	2	1e7	
Primary progressive	37 (25.0)	11 (30)	26 (70)	2	0e6	4	2e8	
Other	3 (2.1)	1 (33)	2 (67)	6	3e6	6	3e6	
Mobility aids								
None	38 (25.7)	12 (32)	26 (68)	1	0e4	2.5	1e5	$.17^{zx}$
Walking sticks	76 (51.4)	23 (30)	53 (70)	2	0e5	4	2e9.5	
Elbow crutch	13 (8.8)	4 (31)	9 (69)	2	0e7.5	7	1.5e9.5	
Walking frame	21 (14.2)	5 (24)	16 (76)	2	0.5e3	2	1e3	

NOTE. Values are mean SD, n (%), or as otherwise indicated.
Abbreviation: IQR, interquartile range.
* Mann-Whitney U test.
y Exact P value.
z Kruskal-Wallis test.
x Monte Carloebased P value.

return any falls diary data despite prompts, and were therefore excluded from subsequent analyses. Characteristics of the 148 participants are summarized in table 1.

Falls diary returns

A total of 823 of a possible 888 falls diaries were returned, representing a return rate of 92.7%. Most participants (79%) recorded and returned falls data for the whole 12-week period, with about 10% of participants recording activity for 6 weeks. Of the 4 participants who returned only 2 weeks of falls diaries (despite prompts and reminders), 3 recorded at least 2 falls during the 2-week period. The fourth participant did not record any falls.

Reporting of actual falls and near falls

During the diary data collection period, 104 of the 148 participants recorded actual falls. A total of 672 actual falls were recorded, which equates to a falls rate of 18.41 falls PPY when calculated

Table 2 Number of recorded actual falls and near falls

No. of Recorded Actual Falls n (%)		No. of Recorded Near Falls n (%)				
	(NZ148)	0 nZ20 (13.5)	1 nZ12 (8.1)	2e5 nZ22 (14.9)	6e10 nZ25 (16.9)	11 nZ69 (46.6)
0	44 (29.7)	13 (29.5)	7 (15.9)	4 (0.9)	7 (15.9)	13 (29.5)
1	26 (17.6)	4 (15.4)	3 (11.5)	6 (23.0)	8 (30.7)	5 (19.2)
2e5	49 (33.1)	2 (4.0)	2 (4.0)	11 (22.4)	8 (16.3)	26 (53.0)
6e10	13 (8.7)	1 (7.6)	0	0	0	12 (92.3)
11	16 (10.8)	0	0	1 (6.2)	2 (12.5)	13 (81.3)

including all 148 participants. Of the 104 participants (70% of the total sample) who reported falling at least once, the median fall rate was 3 falls (25th and 75th percentiles: 1.25 and 6.75, respectively), with a range of 1 to 63 falls over the 12-week period. One third of the total sample (49/148, 33%) reported between 2 and 5 actual falls, with 13 (8.7%) of 148 participants reporting between 6 and 10 falls, and 16 participants (10.8%) reporting 11 falls (table 2).

With respect to reported near falls, a total of 3785 events were recorded by 128 participants (86% of the total sample). There was a moderate correlation between the number of actual and near falls recorded (rZ.47; 95% CI, .34e.59). Table 2 details the number of reported near falls relative to the number of reported actual falls. Sixty-nine participants (46.6% of the total sample) recorded 11 near falls, with 13 of these (8.7% of the total sample) also reporting 11 actual falls. Of particular interest is the group of individuals who reported relatively high numbers of near falls but relatively few actual falls, with 18 individuals (12% of the total sample) reporting 11 near falls but 1 actual fall.

Analysis of the relationships between the number of actual falls and demographic and MS disease characteristics is summarized in table 1. There was no evidence of a statistically significant correlation between age and number of falls (all participants correlationZ .14; 95% CI, .30 to .02). Among fallers, men fell significantly more frequently than women, and people with an EDSS of 4.5 to 5.5 reported, on average, higher numbers of actual falls than people with other (lower or higher) EDSS scores, although there was insufficient evidence to support any statistically significant differences in number of falls between the 7 EDSS score groups. Similarly, while there were no statistically significant differences, individuals who used a walking stick or elbow crutch reported more actual falls, on average, than those who used no aid.

Table 3 Circumstances of falls

Circumstance	No. of Recorded Actual Falls (nZ555)	% of Recorded Actual Falls
Time of day		
Morning	207	37.3
Afternoon	197	35.5
Evening	111	20.0
Night	27	4.9
Missing or unclear	13	2.3
Location		
Inside	345	62.2
Outside	196	35.3
Missing or unclear	14	2.5
Reported activities		
Cleaning indoors	43	7.7
Working in the kitchen	48	8.7
Personal hygiene	91	16.4
Physical/leisure	43	7.7
Working outdoors	81	14.6
Other (based on free text details and telephone follow-up):		
Standing, turning, walking (not linked to specific activity)	153	27.7
Transfers	38	6.8
Climbing stairs	39	7
Missing or unclear	19	3.4

Circumstances of actual falls

Complete data about the circumstances and consequences of the fall were available for 555 of the 672 actual falls that were recorded (table 3). Of these 555 falls, most occurred during the day (nZ404, 72.8%), with most falls (nZ345, 62.2%) happening inside. Fifty-five percent of falls were linked to the 5 specific activities described on the questionnaire, with the highest proportions linked to "personal hygiene" activities (nZ91, 16.4%). "Working outdoors" activities were associated with 14.6% of falls (nZ81). However, the largest proportion of falls (nZ230, 41.5%) was associated with "other" activities. Analysis of the free text details and responses to the telephone follow-up (data available for 115 [50%] of "other" entries in total) indicates that these falls were associated with general mobility functions such as standing, turning, or walking (nZ153, 27.7%), stair climbing (nZ39, 7%), or transfers (nZ38, 6.8%).

Perceived causes of falling

Almost one third of actual falls (nZ154, 27.8%) were associated with the participants' feeling "somewhat more" fatigued than usual at the time of their falls, with a further 13.3% occurring when fatigue was reported to be "much more" than usual (nZ74) (table 4). Analysis of self-reported hurrying at the time of falling showed that most falls occurred when participants perceived that they either were not hurrying at all (nZ250, 45% of falls) or were hurrying as usual (nZ153, 27.6% of falls).

In response to the general "cause of falling" question asked during the telephone follow-up of falls diary returns, most falls where a specific cause was identified were associated with loss of balance (nZ107, 19.4% of falls), with tripping, legs giving way, and being distracted being associated with approximately 10% of falls each (see table 4). There were, however, a large number of nonresponses to this question, predominantly as participants tended to identify that they felt that the falls were probably due to a combination of several factors, or to external circumstances that they felt were beyond their control (eg, being knocked off balance by other people, or problems with assistive devices).

Consequences of falls

Of the 555 falls with complete data, 62 falls (11.2%) were associated with reports of injuries. Table 5 details the frequency and types of injury. Most of the injuries were bruising, cuts/lacerations, or sprains/strains. Six individuals required input from health care professionals as a consequence of falling: 3 participants attended a hospital accident and emergency (A&E) unit, and 3 sought input from their general practitioner. All participants who attended A&E were treated as day cases: 2 for checks after a head injury and 1 for assessment and treatment of a fractured finger.

Table 4 Perceived causes of falling

Perceived Cause	No. of Recorded Falls (nZ555)	% of Recorded Falls
Fatigue		
As usual	207	37.3
Much more	74	13.3
Not at all	72	13.0
Somewhat more	154	27.8
Missing or unclear	48	8.6
Hurrying		
As usual	153	27.6
Much more	18	3.2
Not at all	250	45.0
Somewhat more	78	14.1
Missing or unclear	56	10.1
Attribution (based on telephone follow-up)		
Trip	61	11.0
Slip	8	1.4
Vision	2	0.4
Distracted	46	8.3
Dizzy/giddy/faint	10	1.8
Balance	107	19.4
Legs gave way	48	8.7
Not sure	3	0.5
Missing, unsure, or unclear	269	48.5

Three other participants were unable to get up from the floor after falling, despite not having sustained injuries. Of these, 1 individual reported being on the floor for more than an hour before being able to summon help, meeting the criteria for a "long lie."[24(p10)]

Discussion

The analysis of falls risk, falls rates, and injury rates is important to enhance our understanding of the impact of falls, as well as aid the development and evaluation of interventions.[6,25] This study demonstrates that in this cohort, individuals with MS experienced a high rate of falls, calculated at 18.41 falls PPY. This rate is higher than that described in 2 previous MS falls studies, where falls rates of 15.4[1] and 1.6[26] falls PPY were reported. The high rate observed in our study may be explained in part by our sample, which includes individuals from an EDSS range between 3.5 and 6.5, with more than 50% of the sample being classified as EDSS 5.5 and the mean age SD of our sample being 57 10.14 years. In contrast, the study by Kasser et al[26] recruited individuals with a mean age SD of 53 6 years and an EDSS ranging from 0 to 5.5, while Nilsagard et al[1] recruited individuals with a mean age of 50 years (range, 25e75y) and an EDSS of between 3 and 6. This aspect may also be related to the proportion of participants with progressive types of MS, although these data are not reported in Kasser's article.[26]

A comparison of the numbers of falls reported by individuals by differing demographic and MS characteristics has not been documented in previous research. In our study, men reported a higher average number of actual falls than women, and the average number of actual falls increased with increasing EDSS score. While no statistically significant differences were seen between the EDSS groups, interpretation is limited by the small numbers of participants at each EDSS level. Further research, using larger data sets of participants from across the EDSS spectrum, is required to clarify these findings. This is necessary to inform clinical practice with regard to the best time to target falls interventions.

The evidence presented in this article supports recent guidance that highlights the urgent need to develop and evaluate falls interventions in MS.[4] The overall rate of reported injuries requiring medical attention in our study was .18 injuries per PPY. In contrast, previous studies have reported person per year injury rates of .23[11] and .03.[12] This variation could in part be explained by differing study methodologies. The injury rates reported by Cameron et al[12] were ascertained through reviews of a centralized database reporting actual contact episodes with health professionals, whereas our study, and that of Peterson et al,[11] used self-reported data, a method that may be associated with overreporting of injurious falls.[27] Our use of prospective recording of falls and a daily diary recording system aimed to minimize any potential inaccuracies; however, it is acknowledged that a lack of corroboration of injurious falls events is a limitation.

As well as injuries sustained as a result of falling, there is also evidence of falls being associated with a "long lie" in this study. In research into the consequences of falls for older people, a long lie has been associated with a significant increase in morbidity.[28] At present, this type of study has not been undertaken in MS, and the younger age of many of the study participants could suggest they were less vulnerable to the consequences of a long lie than older, potentially frailer individuals. However, this aspect warrants further investigation.

While this study provides data relating to the physical consequences of falls, other potential issues such as the emotional and psychological impact of falling were not evaluated. Fear of falling is a commonly reported issue that has been evaluated as a potential predictor of falls in a number of studies[1,9,15] of people with MS. However, further work is required to investigate the impact and ongoing consequences of fear of falling over time in both fallers

Table 5 Consequences of falls

Type of Injury	No. Reported	Associated Care Required
Head injuries	3	2 Hospital A&E attendances
Confirmed fracture	1	1 Hospital A&E attendance
Cuts and lacerations	18	3 GP attendances
Sprains and strains	13	None
Bruising	20	None
General (nonspecific) injuries	7	None

Abbreviation: GP, general practitioner.

and nonfallers, as the evidence base in this area is much more limited.[2]

In this cohort, a range of activities was associated with falls, suggesting, as previously described, that falls are an "ever present reality"[29(p151)] for this group. The profile of activities associated with falls in our study highlights that many falls events were related to basic activities of daily living such as personal hygiene (16.4% of falls), and domestic activities such as cleaning (7.7%) and working in the kitchen (8.7%). In contrast, the study by Nilsagard et al[1] found that physical or leisure activities were more frequently associated with falling. Participants were not given a specific definition of physical/leisure activities in either Nilsagard's study[1] or ours; therefore, it is possible that differing perceptions between the 2 groups of participants contributed to this variance. However, other factors, such as the geographic location of the studies, may also be significant.

Our study suggests that a relatively high percentage of falls (27.7%) are associated with general mobility tasks such as standing, turning, and walking rather than during specific tasks or activities traditionally associated with perceptions of risk, such as working outdoors or physical or leisure activities. In the analysis of perceived cause of fall, there was variability in the causes that participants ascribed to their falls, although "loss of balance" was most frequently mentioned. However, in many of the falls, participants were unable to identify any particular cause for why they fell, or attributed the fall to external influences. It is recognized that the validity of this aspect of our study could be impacted by these data predominantly being gathered during the telephone follow-up calls rather than through the prospectively completed falls diaries (which could have influenced the high rate of missing data). However, the findings are broadly in agreement with those of Peterson et al,[14] whose study also highlights the potentially complex interactions of environment, activity, and impairments in MS. We agree with Peterson[14] that an educational component in any future falls interventions is likely to be important in order to maximize falls self-efficacy through awareness of the likely causes of falls.

One area that may present an opportunity for future research is to evaluate the characteristics of individuals who experience frequent near falls but who do not actually fall. In our study, this group was relatively small (18% of the total sample). However, further evaluation has the potential to highlight characteristics or attributes that may be associated with successful fall avoidance, which may be valuable to inform the development of future falls management interventions.

Study limitations

Use of specific falls definitions and prospective falls recording using recommended data collection methods contribute to the methodological strengths of this study. However, the use of falls diaries and unconfirmed reports of circumstances and consequences of falls may have led to some inaccuracies. Similarly, detailed information regarding exact symptoms at the time of any falls was not collected. Hence, these findings should be interpreted with caution.

Conclusions

This study confirms the significance of falls as an issue for people affected by MS. Our findings demonstrate that many people with MS experience frequent falls, which are often associated with routine daily activities rather than the more "dangerous" situations commonly associated with falls risk. Our study adds detail about the physical consequences of falls for people with MS, including injuries requiring medical attention with associated resource implications. While most of the reported injuries did not require formal intervention, it is likely that they will still be associated with negative consequences for the individual, in terms of both discomfort and the associated subsequent effects on activities and participation. All these aspects should be considered in the development of targeted interventions to address falls in this group.

Suppliers

a. SPSS Inc, 233 S Wacker Dr, 11th Fl, Chicago, IL 60606.
b. Microsoft Corp, One Microsoft Way, Redmond, WA 98052-6399.

Keywords

Accidental falls; Multiple sclerosis; Rehabilitation; Risk factors

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Appendix 1 Falls Diary

Participant Number:

Each day we would like you to record any fall including a slip or trip in which you lost your balance and landed on the floor or ground or lower level.

Please fill in the diary each day detailing any falls, giving as much information as possible. See below for an example of how to fill the diaries in. In your pack you will find 3 months worth of diary pages separated into 2-week batches. Attached to each batch you will find an envelope—please use this to return the completed diary pages to us every 2 weeks. Please send back every page, regardless of whether you have fallen or not.

Notes: Is there anything that has affected you being able to fill in your diary this fortnight?

Form below for example only:

Day	**Did you fall?** A fall includes a slip or trip in which you lost your balance and landed on the floor or ground or lower level — Yes No	**How many times did you fall?**	**Did you nearly fall?** A near fall is an occasion where you felt you were about to fall but did not actually fall — Yes No	1	**How many times did you nearly fall?**

Fall 1: Time of day	✓	**Where were you?**	✓	**What type of activity were you doing?**	✓	**How fatigued were you?**	✓	**Were you in a hurry?**	✓
Morning		Inside	✓	Personal Hygiene		Not at all		Not at all	✓
Afternoon		Outside		Working in the kitchen		As usual		As usual	
Evening	✓			Cleaning Indoors		Somewhat more than usual	✓	Somewhat more than usual	
Night				Working Outdoors		Much more than usual		Much more than usual	
				Other Activities	✓	1.1 Details of Other Activities (if applicable):			
				Physical/ Leisure Activities		*Transferring from bed to chair*			

Day:	**Did you fall?** A fall includes a slip or trip in which you lost your balance and landed on the floor or ground or lower level — Yes No	**How many times did you fall?**	**Did you nearly fall?** A near fall is an occasion where you felt you were about to fall but did not actually fall — Yes No	**How many times did you nearly fall?**

Fall 1: Time of day	✓	**Where were you?**	✓	**What type of activity were you doing?**	✓	**How fatigued were you?**	✓	**Were you in a hurry?**	✓
Morning		Inside		Personal Hygiene		Not at all		Not at all	
Afternoon		Outside		Working in the kitchen		As usual		As usual	
Evening				Cleaning Indoors		Somewhat more than usual		Somewhat more than usual	
Night				Working Outdoors		Much more than usual		Much more than usual	
				Other Activities		1.1.1 Details of Other Activities (if applicable):			
				Physical/ Leisure Activities					

Fall 2: Time of day	✓	**Where were you?**	✓	**What type of activity were you doing?**	✓	**How fatigued were you?**	✓	**Were you in a hurry?**	✓
Morning		Inside		Personal Hygiene		Not at all		Not at all	
Afternoon		Outside		Working in the kitchen		As usual		As usual	
Evening				Cleaning Indoors		Somewhat more than usual		Somewhat more than usual	
Night				Working Outdoors		Much more than usual		Much more than usual	
				Other Activities		1.1.1.1 Details of Other Activities (if applicable):			
				Physical/ Leisure Activities					

Remember, if you have fallen more than twice today then there are spare sheets at the back of the pack for you to use. Please send these back with each 2-week batch.

Appendix 2 Falls Diary Supplementary Questions

Consequences of the fall
- Injuries
- Care required
- No. of visits
- Type of specialist
- Days admission

Activity associated with fall
- Standing, turning, walking
- On/off chair/bed/bath/toilet
- Standing on chair/ladder
- Stairs
- Step
- Climbing

Site of fall (further detail)
- Path
- Lawn/garden
- Stairs
- Street
- Public building
- Other house
- Vehicle
- Public transport

Perceived cause of fall
- Trip
- Slip
- Vision
- Distracted
- Dizzy
- Balance
- Legs gave way
- Not sure

Other details

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7.5.5 Falls in people with multiple sclerosis- an individual data meta-analysis from studies in Australia, Sweden, United Kingdom and the United States

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Research Paper

Falls in people with MS—an individual data meta-analysis from studies from Australia, Sweden, United Kingdom and the United States

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Abstract

Background: Falls are common in people with multiple sclerosis (PwMS). Previous studies have generally included small samples and had varied methods.

Objectives: The objectives of this paper are to compile fall rates across a broad range of ages and disease severity and to definitively assess the extent to which MS-associated and demographic factors influence fall rates.

Methods: Individual data from studies in four countries that prospectively measured falls for three months were analyzed. We determined fall rates, prevalence of fallers (□1 falls) and frequent fallers (□2 falls), location and timing of falls, and fall-related demographic factors.

Results: A total of 537 participants reported 1721 falls: 56% were fallers and 37% frequent fallers. Most falls occurred indoors (65%) between 6 a.m. and 6 p.m. (75%). Primary progressive MS was associated with significantly increased odds of being a faller (odds ratio (OR) 2.02; CI 1.08–3.78). Fall risk peaked at EDSS levels of 4.0 and 6.0 with significant ORs between 5.30 (2.23–12.64) and 5.10 (2.08–12.47). The fall rate was lower in women than men (relative risk (RR) 0.80; CI 0.67–0.94) and decreased with increasing age (RR 0.97 for each year, CI 0.95–0.98).

Conclusion: PwMS are at high risk of falls and there are important associations between falls and MS-associated disability, gender and age.

Keywords: Accidental falls, multiple sclerosis, risk factors, cohort studies, meta-analysis

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Introduction

Interest in falls in people with multiple sclerosis (PwMS) has increased significantly in the last decade. Studies have reported that at least 50% of PwMS suffer falls within periods of three to six months, with falls in this group being associated with injury,[1–3] fear of falling[4–6] and reduced activity and social participation.[5]

Several studies have identified a diverse range of factors associated with falls among PwMS,[3,7–16] and a recent systematic review identified four factors with major association with falls in PwMS: the use of a mobility aid, imbalance, cognitive dysfunction, and progressive MS subtype.[17] However, past studies have differed significantly with respect to their designs, limiting their generalizability and interpretation of their findings. For example, while most studies of falls in PwMS have included adults over age 18, some have focused on older samples aged at least 45[10] or 55 years of age.[18,19] Among older adults with MS, impairments related to MS and age may contribute to the risk of falling.

Disease severity and gender mix also vary among the published studies. While some investigators have included people with an Expanded Disability Status Scale (EDSS) score of zero,[20–22] others have set a higher EDSS minimum for inclusion.[11,13] Although most studies are representative of the gender distribution of MS, one sample included only women[21] and one mostly men.[2] In addition, most have collected falls data retrospectively, asking participants how many times they have fallen in a specified period of the recent past. However, retrospective data collection likely underestimates fall frequency[13] and hence prospective fall recording, although more time consuming and labor intensive, is recommended.[23] Thus, more recent studies of factors associated with falls in PwMS have collected data prospectively.[11,13,20–22,24]

In order to more accurately assess the relative importance of commonly measured predisposing factors for falls in PwMS, this study combined individual data from studies recently conducted in Australia (AUS), Sweden (SE), the United Kingdom (UK) and the United States (US) to provide the largest sample of PwMS to date with prospectively recorded falls data. This individual level meta-analysis tested the hypothesis that, in PwMS, sustaining a fall or multiple falls is associated with age, gender, mobility aid use, disease severity (EDSS), and disease subtype; we also undertook descriptive analyses to document the frequency of falls by location (indoors vs outdoors) and time of day.

Methods

Standard protocol approvals, registrations and patient consents

Data collected by four centers from 2005 to 2012 were merged. Some of these data have previously been published.[11–13] In addition, unpublished data from Sweden and the US were used. All data were collected in accordance with the International Declaration of Helsinki; institutional review boards or ethics committees at the institutions in each country approved the separate protocols (AUS HC09253; SE 2005:119 and 2012:077; UK 10/H0203/66 and US E7244W). Written informed consent was obtained from all participants.

Participants

Data from 537 PwMS were included in this analysis. The sample included 210 participants from AUS, 125 from SE, 148 from the UK and 54 from the US. All samples used standardized criteria for MS diagnosis.[25,26] Participants were aged 18 years and older. There were no restrictions for MS subtypes. Disease severity was measured by the EDSS[27] in all samples except in AUS, where the Disease Steps scale[28] was used and converted to EDSS by mobility criteria. Common exclusion criteria were inability to understand and sign an informed consent or record falls for linguistic, cognitive or other reasons, and self-reported health conditions that would interfere with testing procedures. Differences among samples are described below.

Additional inclusion criteria for the Australian sample were ability to stand unsupported for 30 seconds and ability to walk 10 meters with or without aid. Participants in the Swedish sample were restricted to an EDSS score between 1.5 and 7.0, an upper age limit of 75 years, and being relapse free for at least 30 days prior to baseline examination. The UK participants were restricted to an EDSS score between 3.5 and 6.5, and full recovery from the most recent relapse was required for inclusion. EDSS was assessed by self-report using a telephone interview.[29] Additional inclusion criteria for the US sample included an EDSS score of 6.0 or less, an upper age limit of 50 years, being relapse free for 30 days prior to baseline examination, and ability to walk at least 100 meters.

Recruitment strategies

The Australian sample was recruited by a physiotherapist from the outpatient physiotherapy clinic at the MS Australia (MSA) Center in Lidcombe, Sydney. The Swedish sample was recruited by a physiotherapist inviting PwMS living within the recruitment area of Örebro University Hospital; the Mälarhospital in Eskilstuna; the Primary Health Care of Western and Eastern Östergötland County in Motala and Norrköping, and the Sahlgrenska Hospital in Gothenburg. The US sample was recruited from patients receiving medical care at specialty MS center outpatient clinics at a Department of Veterans Affairs medical center and a university medical center, and from the surrounding area, in the Northwest of the United States. The UK sample was recruited from the South-West Impact of MS database, a patient-centered longitudinal study of disease course in PwMS living in the Southwest of England.

Outcome variables

Prospectively collected falls data were obtained using fall diaries. The participants recorded falls daily for three months following their baseline assessment. The fall diaries were returned using reply-paid return envelopes every two or four weeks with reminders (telephone, letter or email) if the diaries were not received in a timely fashion. All studies used specific definitions of falls based on those recommended in consensus guidelines.[23] Circumstances of the falls, including fall time and location, were either collected for all falls (UK n = 148, SE n = 76) or for the first two (US n = 54, AUS n = 210) or four (SE n = 49) falls each month.

Factors with potential association with falls
Data on walking aid use, demographics and MS subtype were collected at baseline on self-report questionnaires at all study centers.

Data analysis
Following analysis of normality of distribution, the data sets from each country were compared for heterogeneity using a Kruskal-Wallis test, with post hoc analysis using Bonferroni-corrected Mann-Whitney tests for between-group comparisons. Although the data sets were demonstrated to be heterogeneous, sensitivity analysis of the main logistic regression by sequential removal of each country's data set did not significantly affect the outcomes, therefore all data sets were retained in the final analysis. Frequencies were calculated for circumstances of falls with within-variable differences assessed using the one sample test of proportions. Associations between the demographic and MS disease status variables were analyzed using multi-variable logistic regression analysis, including EDSS as a categorical variable. To control for family-wise error rates, adjusted confidence interval (CI) and p values were also calculated using a Bonferroni correction.[30] In these analyses, participants reporting no falls during three months or "non-fallers" were compared with participants reporting one or more falls or "fallers." Additional logistic regression analyses compared factors with potential association with falls between fallers (0 or 1 falls) and frequent (□2) fallers. Fall rates in men and women were compared with an incident rate ratio computed with negative binomial regression.

Results
Demographic and MS disease characteristics for each cohort and for the total sample are presented in Table 1.

Prevalence and rate of falls
Of the total sample, 300 participants (56%) reported falling at least once (defined as fallers) and 197 (37%) participants reported falling at least twice (defined as frequent fallers) in the three-month follow-up periods. Participants reported a total of 1721 falls and the average rate of falls was 1.1 falls/person/month. Within the fallers, the fall rate was 1.9 falls/month. The UK cohort had the highest fall frequency (falls/month), and the US had the lowest. The Australian cohort had the lowest proportion of frequent fallers, but the highest rate of falls within the faller subgroup. The number of falls, fallers and fall rates are summarized in Table 1.

Fall location and time of day
Fall location data were available for 1024 falls and fall time data were available for 1018 falls (Table 2). In all cohorts participants fell more frequently indoors than outdoors (total sample, z = 20.13, p <0.0001—one sample test of proportions), and falls occurred more frequently in the morning and afternoon (total sample = 75%) than in the evening or night.

Factors associated with falls
Logistic regression revealed that being a faller was statistically significantly associated with being classified as having primary progressive MS (unadjusted odds ratio (OR) 2.02; 1.08–3.78) and there was also a trend for association between being a faller and younger age (OR 0.98; 0.97–1.00 for each year). There was a non-linear relationship between being a faller and EDSS classification, with the OR peaking at EDSS levels 4.0 and 6.0 (Figure 1). These peaks were statistically significant both in the unadjusted and adjusted analyses, although the CI were wide in both analyses. The differences found between the fallers and non-fallers were also found when comparing the fallers and frequent fallers, with one exception as the association between being a frequent faller and younger age was statistically significant in this analysis (unadjusted OR 0.97; 0.95–0.99). There were no statistically significant associations between fall status and gender or use of a walking aid (Table 3).

Fall rate (falls/person/month). Interestingly, whereas no significant differences were evident in the proportion of men and women fallers, fall rate was lower in the women than the men (RR = 0.80; CI 0.67–0.94). Similar to the analyses of the odds of being a faller, the rate of falls decreased by 3% with each year of age (Table 4).

Discussion
This is the first meta-analysis of risk factors for falls in PwMS using only prospectively collected fall data. In this large pooled international sample of ambulatory individuals, the average fall rate was approximately one fall/month. Higher odds of being classified as a faller were associated with a primary progressive

Table 1. Demographic and prospective three-month falls data for each cohort and for the total sample.

	Australia (n = 210)	Sweden (n = 125)	United Kingdom (n = 148)	United States (n = 54)	Total sample (n = 537)
Number of falls reported	630	333	672	86	1721
Fallers (□1 fall): frequency (%)	96 (46%)	70 (56%)	104 (70%)	30 (56%)	300 (56%)
Frequent fallers (□2 falls): frequency (%)	56 (27%)	47 (38%)	78 (53%)	16 (30%)	197 (37%)
Falls/person/month (all): mean (SD)	1.0 (3.5)	0.9 (1.6)	1.5 (2.9)	0.5 (0.8)	1.1 (2.8)
Falls/ person/month (fallers): mean (SD)	2.2 (4.9)	1.6 (1.9)	2.2 (3.2)	1.0 (0.9)	1.9 (3.5)
Age (years):					
Mean (SD)	50.3 (11.1)	50.4 (10.7)	57.9 (10)	39.6 (8.25)	51.8 (11.6)
Median	51	53	60	41	53
(Range)	(21–73)	(22–75)	(33–84)	(22–50)	(21–84)
EDSS:	3.83 (2.8)				
Mean (SD)	5.0	4.70 (2.2)	5.0 (2.1)	2.73 (1.8)	4.29 (2.61)
Median	1.0–6.5	4.0	6.0	1.0	5.0
(Range)		1.5–7.0	3.5–6.5	0–6.0	0–6.5
Subtype					
RRMS	160 (76.2%)	61 (48.8%)	42 (28.4%)	51 (94.4%)	314 (58.5%)
SPMS	30 (14.3%)	53 (42.4%)	66 (44.6%)	3 (5.6%)	152 (28.3%)
PPMS	19 (9.0%)	11 (8.8%)	37 (25%)	0	67 (12.5%)
Unknown	1 (0.5%)	0	3 (2.1%)	0	4 (0.7%)
Gender (F:M)	150:60 (71%:29%)	95:30 (76%:24%)	114:34 (77%:23%)	37:17 (68%:32%)	396:141 (74%:26%)
Walk aid (yes)	95 (45.2%)	97 (77.6%)	110 (74.3%)	9 (16.8%)	311 (57.9%)

EDSS: Expanded Disability Status Scale; RRMS: relapsing–remitting multiple sclerosis; SPMS: secondary progressive multiple sclerosis; PPMS: primary progressive multiple sclerosis; F: female; M: male.

Table 2. Fall location and time of day.

Location					
	Australia	Sweden	United Kingdom	United States	Total
Number of falls	121	293	541	69	1024
Indoors	89 (73%)	193 (66%)	345 (64%)	42 (61%)	669 (65%)
Outdoors	32 (27%)	100 (34%)	196 (36%)	27 (39%)	355 (35%)
Time of day					
Number of falls	126	282	542	68	1018
Morning (6 a.m.–noon)	53 (42%)	85 (30%)	207 (38%)	25 (37%)	370 (36%)
Afternoon (noon–6 p.m.)	43 (34%)	128 (45%)	197 (36%)	27 (40%)	395 (39%)
Evening (6 p.m.–midnight)	26 (20%)	61 (22%)	111 (20%)	12 (18%)	210 (21%)
Night (midnight–6 a.m.)	4 (3%)	8 (3%)	27 (5%)	4 (6%)	43 (4%)

MS subtype and higher EDSS scores, consistent with previous studies.[10,28,31] In contrast with previously reported results, use of a walking aid was not significantly associated with higher fall risk.

This meta-analysis provides further detail on the relationship between fall risk in MS and disease severity as measured by the EDSS. It suggests that fall risk peaks at an EDSS score of 4.0 (when quantifiable

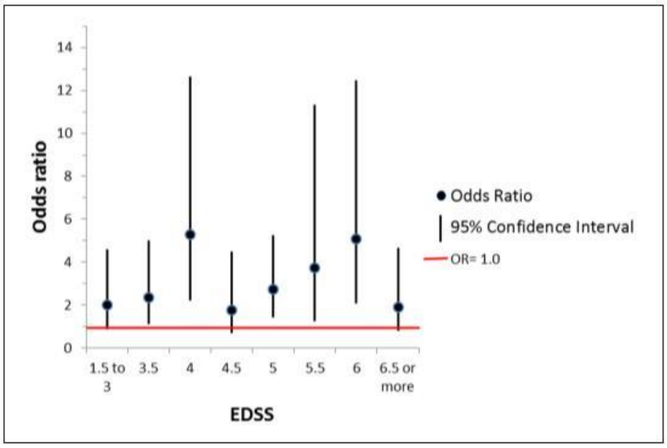

Figure 1. Association between EDSS and risk of being classified as a faller (□1 fall, unadjusted OR).
EDSS: Expanded Disability Status Scale; OR: odds ratio.

mobility limitations are first acknowledged) and 6.0 (when a walking aid is required). While this could be an artifact of the nonlinear nature of the EDSS scale,[32] it may also be that this increase in risk is associated with these important transitions in mobility status. EDSS is primarily a measure of MS-associated impairments, although walking distance and need of walking aids are also included in the scale.[31] In this study we also found an association between falls and primary progressive MS subtype. Since this association was independent of EDSS it does not reflect the higher level of disability in primary progressive MS but may reflect the difficulty of adapting to a constantly, and sometimes fairly rapidly, progressing level of disability.

Interestingly, there were statistically significant associations between more falls and younger age. Sustaining multiple falls was associated with younger age and the relative rate of falls was higher for younger participants. These results are surprising given that previous studies in older adults suggest that older age is a risk factor for more falls.[33] It is possible that in a relatively young sample (mean age 52 years; range 21–84 years), the higher fall rates in the younger participants may reflect differences in activity levels with age, with younger people undertaking more activities that put them at risk for falls. Unfortunately, we did not collect data on exposure, including activities involving standing, walking, and more physically challenging activities, and so are not able to confirm this hypothesis. It is also possible that falls decrease as people with MS become older because they become more aware of their risk for falls and become more cautious and possibly less active.[34]

In our sample the men had a significantly higher fall rate than the women, suggesting that men with MS who fall are at risk for frequent falls. This finding is in line with previous studies.[10,17] We also documented that most falls occurred indoors and during the daytime, guiding fall prevention interventions. Among older adults, risk factors for indoor and outdoor falls differ. Outdoor falls are associated with younger age, being male, and greater physical activity whereas indoor falls are associated with older age, being female, poor health and greater physical disability.[33] Providing information on when and where falls occur may help promote awareness of specific risks in PwMS and caregivers. Personal level interventions, such as use of fall-risk reduction strategies or regular exercise, and environmental level interventions such as reducing hazards and installing safety devices in the home or workplace, could be guided by this information. Strategies on when to use walking aids or scheduling activities and rests could be outlined if a pattern of fall risk is detected.

Strengths of this study

This analysis pooled data from a number of similar studies. This provided a large sample with participants from four different countries covering a major

Table 3. Analysis with adjustments for multiple comparisons.

Factor	□1 Fall					□2 Falls				
	Unadjusted analysis			Adjusted CI and *p* values		Unadjusted analysis			Adjusted CI and *p* values	
	OR	95% CI (L)	*p* (0.05)	99.6% CI	*p* (0.0038)	OR	95% CI (L)	*p* (0.05)	99.6% CI	*p* (0.0038)
EDSS										
□1.0 (*n* = 78)	Ref									
1.5–3.0 (*n* = 53)	2.01	0.88–4.59	0.099	0.59–6.80	0.099	0.95	0.30–3.06	0.934	0.17–5.33	0.934
3.50 (*n* = 55)	**2.35**	**1.10–5.02**	**0.027**	0.77–7.21	0.027	**3.22**	**1.30–7.95**	**0.011**	0.85–12.23	0.011
4.00 (*n* = 46)	**5.30**	**2.23–12.64**	**<0.0001**	**1.47–19.12**	**<0.0001**	**6.33**	**2.44–16.41**	**<0.0001**	**1.55–25.86**	**<0.0001**
4.50 (*n* = 30)	1.76	0.69–4.51	0.239	0.44–7.07	0.239	**4.45**	**1.54–12.79**	**0.006**	0.94–21.16	0.006
5.00 (*n* = 136)	**2.73**	**1.42–5.25**	**0.003**	**1.04–7.17**	**0.003**	**3.50**	**1.56–7.85**	**0.002**	**1.06–11.54**	**0.002**
5.50 (*n* = 24)	**3.75**	**1.24–11.33**	**0.019**	0.73–19.19	0.019	**5.09**	**1.61–16.04**	**0.006**	0.93–27.73	0.006
6.00 (*n* = 73)	**5.10**	**2.08–12.47**	**<0.0001**	**1.36–19.10**	**<0.0001**	**7.86**	**2.97–20.79**	**<0.0001**	**1.87–33.07**	**<0.0001**
6.5–7.0 (*n* = 58)	1.92	0.79–4.66	0.151	0.52–7.13	0.151	**4.08**	**1.49–11.18**	**0.006**	0.92–18.08	0.006
Subtype										
RRMS (*n* = 314)	ref									
PPMS (*n* = 67)	**2.02**	**1.08–3.78**	**0.028**	0.80–5.10	0.028	**2.21**	**1.20–4.08**	**0.011**	0.89–5.46	0.011
SPMS (*n* = 152)	1.50	0.91–2.49	0.111	0.72–3.16	0.111	1.39	0.84–2.30	0.201	0.66–2.91	0.201
Gender										
Male (*n* = 141)	Ref									
Female (*n* = 396)	1.09	0.72–1.64	0.699	0.96–2.00	0.699	0.83	0.54–1.27	0.386	0.44–1.56	0.386
Age										
Per year	0.98	0.97–1.00	0.067	0.96–1.01	0.067	**0.97**	**0.95–0.99**	**0.004**	0.94–1.00	0.004
Walking aid										
No (*n* = 262)	Ref									
Yes (*n* = 311)	1.49	0.93–2.39	0.097	0.74–2.99	0.097	1.34	0.82–2.20	0.240	0.65–2.78	0.240

EDSS: Expanded disability status scale; RRMS: relapsing-remitting multiple sclerosis; SPMS: secondary progressive multiple sclerosis; CI: confidence interval; OR: odds ratio.

Table 4. Relative falls rate.

		RR for fall rate (95% CI)	*p* value
MS subtype	Primary progressive ($n = 67$)	1.42 (0.85; 2.38)	0.18
	Secondary progressive ($n = 152$)	1.36 (0.90; 2.05)	0.15
	Relapsing–remitting ($n = 314$) *reference*	1.00	–
Sex	Female ($n = 396$)	**0.80 (0.67; 0.94)**	**0.01**
	Male ($n = 141$) *Reference*	1.00	–
Age		**0.97 (0.95; 0.98)**	**<0.01**

RR: relative risk; MS: multiple sclerosis; CL: confidence limits.

part of the world where MS is prevalent. The sample size allowed subgroup analyses and the impact of outliers in the separate samples was reduced by merging the data sets. The sample was not restricted by MS subtype, and the participants represent PwMS living both in urban and rural areas. In addition, data were collected during different times of the year and captured different climate conditions. Differences in inclusion criteria across the cohorts also provided a broad spectrum of demographic and diagnostic characteristics for the total sample.

The prospective recording of falls minimized recall bias, enhancing the validity of the results. Using fall diaries returned every two or four weeks combined with reminders resulted in a high return rate. Similar reminder systems are recommended for future studies. Now that many people have cell phones and computers, other approaches to fall counting, such as using telephone text messages, purpose-designed applications, or emailed electronic surveys to capture falls would also be interesting to evaluate.

Limitations of this study

This study has a number of limitations. As this was not a planned multi-site study, data were collected and reported differently at the different sites and participant inclusion and exclusion criteria also differed. The analyses were also limited to data elements collected consistently among the sites, limiting analysis of potentially important variables identified in other studies such as muscle weakness, impaired balance and continence. We were also unable to assess the consequences of falls such as associated injuries, which may have significant personal and financial implications.

The results of this study may also be affected by the limited three-month time period of recording falls. Longer periods may identify additional fallers but have the potential disadvantage of lower reporting compliance. Reporting falls on a regular basis can also increase the awareness of falls risk and thus possibly reduce fall frequency. Moreover, the willingness to participate in a falls study may be higher in those having experienced falls. The risk of over- or underestimating the overall fall prevalence in the present study is albeit considered to be small.

Suggestions for future research

While the evidence base for the factors contributing to falls risk in MS has developed significantly in recent years, the high incidence of falls in PwMS found in this study indicates that there is still a pressing need for research to identify approaches to help PwMS manage falls and reduce fall risk. The International Classification of Functioning, Disability and Health has been suggested as a framework for developing and evaluating multi-disciplinary fall risk consultations to identify individuals at high risk for falls, map their risk factors, and provide accordingly targeted interventions.[35]

This study provides further support to previous evidence indicating that PwMS around the world are at high risk for falls. Those with primary progressive MS are at increased fall risk and fall risk peaks at an EDSS score of 4.0 and 6.0, likely representing transitions in walking ability. Younger patients and men have higher rates of falls. These falls occur most often indoors during the day. As PwMS rarely talk to health care professionals about fall prevention,[20] to help prevent falls, care providers should conduct simple fall risk screening and recommend appropriate interventions to reduce the occurrence of falls in this high-risk group.

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Conflicts of interest
None declared.

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7.5.6 Home or away? Choosing a setting for a falls-prevention programme for people with multiple sclerosis

Home or Away? Choosing a Setting for a Falls-Prevention Program for People with Multiple Sclerosis

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Evidence suggests that choice of setting may be imporehabilitation programs, as well as optimizing participant satisfaction and adherence. This article aims to examine the factors that may inform the choice of setting for a falls-prevention program tailored to the needs of people with multiple sclerosis, including the inuence of setting on program effectiveness, participant engage - ment, cost, and sustainability. Any new program should ensure that the choice of setting is informed by the intended program outcomes as well as an awareness of the opportunities and challenges presented by each type of setting. Evaluations of falls programs for older people suggest that immediate outcomes are similar regardless of setting; however, long-term outcomes may differ by setting, possibly owing to differ- ential effects on adherence. Programs based away frms of maintaining motivation, providing peer-support opportunities, and allowing regular access to facilitator input, while home-based programs offer unique opportunities for context-based practice and the integration of falls-prevention activities into real life. Additionally, home-based programs may address some of the long-term feasibility issues associated with programs away from home. A "mixed" program incorporating elements of home- and community-based activity may be the most sustainable and effective choice to achieve both long- and short-term goals within a falls-prevention program. However, currently there are gaps in knowledge relating to comparative program outcomes, cost, and long-term sustainability. **Int J MS Care. 2014;16:186–191.**

Rehabilitation interventions may be delivered in a wide range of settings and formats. Frequently, the choice of program setting is not an explicit element of the planning and development -

matic, historical, or political factors. However, evidence suggests that program setting may be important in optimizing participant satisfaction and adherence, as well as

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[1] As part of the work of the International MS Falls Prevention Research Network, evidence regarding the role and considerations for program setting were reviewed. This article aims to examine the factors that may inform the choice of setting for a falls program tailored to the needs of people with multiple sclerosis (MS), including the

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pant engagement, cost, and sustainability. As evidence

MS is limited, relevant sources from other areas of the literature have been integrated to highlight some of the potential challenges and opportunities within this aspect of the program design.

In many countries, health rehabilitation programs have historically been based in health-care settings, with individuals attending specic programs, often for relatively long periods of time.[2] Over the past 20 years there has been a global trend toward health-care delivery away from hospitals and closer to patients' homes, with the aim of increasing cost-effectiveness, access, and sustainability. In many countries this trend has included a greater emphasis on the integration of health-focused programs into the wider community. Alongside these changes is the recognition that for people managing long-term conditions, engagement in ongoing hospital-based rehabilitation programs may be incompatible with an increasing emphasis on facilitating self-management, and the aim of providing person-centered (rather than service-based) care.

For individuals who are not inpatients (eg, in acute-care hospitals or rehabilitation hospitals), possible settings for falls interventions can be organized into three broad categories: home-based, within the local community, or health-care facility–based. While home-based programs engage participants on an individual basis, community- and hospital-based programs may include an element of group participation, with varying degrees of individualization within the program.

Effectiveness

Primary Outcomes

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ating falls outcomes makes evaluation of the effect of setting problematic. However, the existing literature suggests that improvements in falls risk, knowledge, and awareness of falls and balance ability can be achieved with home-based,[3] community,[4,5] and health-care facility–based programs.[6] Within the literature on older adults, meta-analysis suggests that falls programs in all three settings lead to a reduction in falls rate and falls risk of a similar magnitude.[7] One of the issues in evalu-

heterogeneity within the various interventions, which limits direct comparison between the effects of different programs delivered in differing settings. Within Gillespie's 2012 review of 159 trials of falls interventions in older people, only two studies were included that compared the outcome of a standardized multifactorial falls intervention across settings. Both these studies compared the outcomes of a falls program when delivered in a community medical practice or specialist hospital setting; thendings of both have suggested no signi - cant differences in rate of falls, risk of falling, or risk of fracture between the settings after 1 year.[7] Similarly, in evaluations of the effectiveness of pulmonary and cardiac rehabilitation programs, no differences were found in primary outcome whether the program was delivered in hospital or community settings.[8,9]

Adherence and Long-Term Engagement

One of the key criticisms of existing falls programs is that while immediate post-intervention evaluation may demonstrate improvements in falls outcomes, these improvements may not be sustained over the longer term. In reviews of falls programs for older people,

of high adherence initially, followed by a drop-off of engagement over time, has been cited as a possible contributory factor.[10] Within cardiac rehabilitation, a systematic review comparing the outcomes of home-based and health-care facility–based programs has suggested that although immediate outcomes were similar, rates

were superior among participants of home-based programs, in both the short and the longer terms.[9]

Setting for an MS Falls Program

Home-Based Programs

Home-based management programs for people with MS have been demonstrated to be both feasible and cost-effective[11]; however, little comparative analysis has been undertaken relating to rehabilitation programs. Home-based models include those that are essentially self-administered and those that include periodic review by external facilitators. Evaluation of home-based falls programs for older people has suggested that major advantages include the convenience for participants and the "real-life" nature of the setting,[12] allowing environ-

the program to be integrated into daily activities from the outset.[13] Home-based programs can also foster skill mastery by allowing the participant to practice skills in the home that have been collaboratively selected with the interventionist to provide "just the right challenge."[14] A concern with home-based programs is the potential for risk of injury with unsupervised exercise. There is, however, minimal evidence supporting this, and the few investigations that have included home-based exercise programs in people with MS have reported few adverse events.[3,15]

Individually tailored home-based programs may lead to improved perceptions of control and ownership among participants, which could improve self-efcacy.

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and home-based programs may allow greater choice over type, planning, and progression of exercise activities.[14,16] Programs based predominantly at home may also facilitate the involvement of family members as sources of support, feedback, and motivation, factors that have been highlighted as important drivers of the maintenance of behavior change and program engagement in falls programs for older people.[17] Conversely, this may lead to an increase in carer burden,[12] potentially negatively affecting the long-term acceptability of the program for some participants and their relatives.

Long-term adherence to home-based falls programs for older people has been demonstrated to be achievable in some instances,[14,18] although long-term facilitator follow-up may be needed to achieve this. Facilitator input

commitment, particularly in geographically dispersed or remote locations. The development of telerehabilitation and e-health interventions presents an opportunity to support engagement in a cost-effective manner[19]; however, use and evaluation of such approaches is currently limited. Another consideration is how and where the preliminary training takes place, as it has been suggested that in-home training delivered by external facilitators may be viewed as intrusive and an unnecessary imposition.[16]

Programs Away from Home

A number of studies suggest that engaging in both exercise- and education-based programs away from home is an attractive option for people with MS. Evaluations of participant experiences of engagement in such programs consistently highlight the advantages of group interaction as a factor motivating attendance, ongoing engagement in exercise, and commitment to maintaining behavior change.[20]
an opportunity for shared experiences within a program may encourage participants to challenge themselves through vicarious experience of others' achievements.[5,21]

Additionally, participants of programs away from home highlight the regular access to "expert" support,

satisfaction with and engagement in rehabilitation programs.[22] Given that both education- and exercise-based aspects of falls management will require participants to

this type of support and feedback may be essential to ensure successful outcomes. In addition, regular contact with a program facilitator may improve the ability

of individual participants, as well as providing valuable feedback cues.[23] However, programs away from home

intensity of exercise to have a positive impact on falls reduction; therefore, participants will probably also need

Some evaluations of community-based programs suggest that this can be problematic, with participants reporting

perceived safety of a supervised environment.[24] Providing opportunities for participants to learn how to follow through and apply program content away from the program setting is likely to be key in addressing this issue.

Research has shown that there are a number of potential challenges associated with programs situated in settings away from home. Many individuals highlight logistic issues (such as availability of transportation and accessibility factors) as being major barriers to engagement, particularly with programs requiring regular attendance over a long period.[17,25] Logistic barriers may be a particular issue with programs based in central hospital facilities, which may be located relatively far from participants' homes,[26] or in areas with a widely dispersed population. An interesting counterargument is that the challenges associated with getting to and from programs away from home may offer a opportunity for
problem-solving and the application of skills learned within the program itself, providing a feeling of achievement for participants, which may in turn encourage further engagement.[27]

Another issue that has been as a barrier to
engagement in programs away from home is the time and energy required for regular attendance, representing an additional burden on people already dealing with the challenges of ongoing health conditions.[17] This may be a particularly important consideration in developing programs for people with MS given the prevalence of
[28] Additionally, given
that many potential participants in a falls program for people with MS may already be balancing work, family, and health commitments, attending a program away

Community Settings

Community-based settings in venues that are not health-focused are frequently cited as being attractive to participants, as they are perceived as being more socially acceptable and "normal," and may be more convenient to access.[12,29] However, the use of community gym facilities has been associated with poor engagement and adherence with programs,[9] with participants perceiving them as "unfriendly" and noninclusive.[30] In people with general physical disabilities, age and gender were found to be predictive of adherence to gym-based programs, with young women being least likely to attend.[31] Conversely, in a program based in church halls and community centers, adherence was greatest in younger women.[32] In MS, studies have suggested that a range of non-hospital-based settings are seen as acceptable, but that there appears to be a preference for settings where exercise can be undertaken away from the general population.[33]

Health-Care Settings

Traditionally, many rehabilitation programs have been delivered in hospital or health-care–facility settings. Research suggests that such programs are perceived as "safe" and the staff as "knowledgeable" by participants[34]; moreover, the availability of support and backup if

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However, some hospital-based falls program trials have experienced high levels of attrition.[35] It has been suggested that contributing factors may be that hospital-based programs may promote an "illness" rather than a "wellness" focus that is unappealing to participants,[12] and that the accessibility and logistics issues associated with attendance may be greater than at other venues.[26]

Discussion

In reviewing the literature relating to the choice of setting for falls rehabilitation programs, it becomes evident that each setting may have strengths and weaknesses and that a "black or white" choice may not be possible. In terms of achievement of primary outcomes, there seems to be little difference in initial effectiveness between the settings; however, maintaining ongoing engagement appears to be a key consideration in achieving a sustained change. In this respect, ensuring ongoing home practice of both the educational and exercise elements of a program is likely to be key to ongoing behavior change and sustained improvements in balance and stability parameters, regardless of whether programs are based within or outside of the home.[36] As such, programs with a strong home emphasis from the outset may have an advantage.

There is evidence, however, that programs delivered

individuals and to organizations. Programs away from home are likely to facilitate peer learning and support opportunities, which have been shown to facilitate ongoing program engagement and the maintenance of behavior change. Additionally, programs delivered in a group setting may offer "economies of scale" to a provider, enabling more individuals to access the program

issues for individuals attending a program away from home mean that "local" venues are likely to be preferred. In areas with a relatively low population density of people with MS, or those with a wide geographic spread, achieving the critical mass necessary to make such programs sustainable may be a challenge. One factor worth considering is the frequency with which participants would be expected to attend. A program with a relatively low number of sessions away from home, or where sessions are spread over time, might be more attractive to people than one requiring attendance once or twice a

group program could be offered while minimizing some of the logistic barriers.

In terms of settings away from home, the evidence appears to indicate that community venues may be preferable to health-care–based settings. This is in line with the current shift in emphasis toward self-management for people with long-term conditions, in which greater use of community settings is being encouraged. A community and/or home-based program is therefore more

service delivery models, which is an important consideration in ensuring the long-term sustainability of a falls program.

The existing evidence base still leaves many questions unanswered. Key weaknesses in current research include a lack of economic evaluation, limited long-term follow-up, and very few evaluations comparing the effect of setting on similar programs. Furthermore, the majority of studies involve individuals who have volunteered to participate in a particular program, which may suggest

program settings. Few studies have included individuals who chose not to participate, or who dropped out of programs following initial recruitment; it could be argued that the evidence presented is therefore relatively unrepresentative of the wider population. Those individuals who are most challenging to engage are likely to be those whose perspectives are relatively underrepresented within the existing evidence base.

Another issue is the relatively limited MS-specific evidence. While learning from the evidence from other groups and programs is essential, simply applying models and programs from one condition to another may be unsuccessful.[7] While this may be due in part to factors related to the content of such programs, preferences for specic program settings and structures may also differ between cohorts. For example, people with MS who

other falls programs, and differences in social, economic, environmental, and personal factors may affect their program setting preference.

Conclusion

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ing to the falls program. The

existing evidence suggests that initial outcomes (such as reduction in falls rates) may be similar regardless of setting. It remains unknown whether this is also the case for outcomes such as participation and dynamic mobility, since these aspects have yet to be evaluated in different settings. This requires further exploration.

Maintaining behavior change over the long term has been idend as a challenge in many falls programs; however, programs that can facilitate ongoing use of falls-prevention strategies may be likely to offer greater long-term benefits. In this respect, programs with a strong home-based focus are typically more convenient for participants, and offer benefits associated with being situated in a real-life context. However, unless home-based programs are developed to include group-interaction opportunities (eg, through telehealth or online facilities), they provide fewer opportunities for participants to learn from and with others, and to access

the facilities typically available in a health-care setting

be possible to achieve a mixed-settings model, which

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ing any associated barriers. For instance, the program could be predominantly home-based from the outset but include a number of community group-based sessions interspersed throughout to support progress, monitor change, and maintain motivation.

The choice of setting must be compatible with the overall aims and content of the program and suited

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cally involving people with MS in the decision-making process would be valuable to explore different options further. □

PracticePoints

- Program setting is an integral aspect of program development and must be compatible with program aims and service user needs.
- Home-based programs offer unique opportunities for context-based practice and the integration of falls-prevention activities into real life.
- Community-based programs may provide greater motivational, peer, and facilitator support opportunities.

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7.5.7 Fall incidence as the primary outcome in multiple sclerosis falls prevention trials

Fall Incidence as the Primary Outcome in Multiple Sclerosis Falls-Prevention Trials

Recommendation from the International MS Falls Prevention Research Network

Susan Coote, PhD, PT; Jacob J. Sosnoff, PhD; Hilary Gunn, MSc, PT

The aim of this article is to provide recommendations on behalf of the International MS Falls Prevention Research Network (IMSFPRN) for the primary outcome measure for multiple sclerosis (MS) falls-prevention interventions. The ar

elements of falls that should be recorded, as well as how these elements should be presented and analyzed. While this information can be used to inform the content of falls-prevention programs, the primary aim of the article is to make recommendations on how the outcome of these programs should be captured. ***Int J MS Care.*** **2014;16:178–184.**

Falls are a common health concern in people with multiple sclerosis (MS), with more than 50% of people with MS suffering a fall in a 3-month period. Resulting injuries may range from mild sprains and strains to fractures and head injuries requiring hospitalization.[1,2] The physical impact of a fall can cause

participation.[3] The longer-term consequences of these fall-related injuries may include time off from work, inability to return to work, increased need for care including institutionalization, and even increased risk of death. Additionally, a fall can lead to concerns about falling[4] that subsequently result in activity curtailment.[5,6] Activity curtailment may lead to a reduction in social interaction or lack of physical activity leading to deconditioning and secondary health problems. Therefore, it is essential to intervene to reduce falls and their adverse consequences.

The International MS Falls Prevention Research Network (IMSFPRN) is a multidisciplinary collaboration between researchers that aims to develop and implement multisite research protocols to advance knowledge on falls and falls prevention among people with MS.[7] The objective of this article is to consider the IMSFPRN's choice and rationale for the primary outcome for MS falls-prevention interventions—reduction in the number of falls—and how this should be measured. We will

fall, the methods of fall recording, the elements of falls that should be recorded, and how these elements are presented and analyzed. The ultimate goal of this article is to make recommendations regarding the primary out-

individuals with MS.

The number of investigations focusing on falls prevention in people with MS is low compared with research on falls prevention in other populations such as older adults (for example, the Cochrane review by Gillespie et al.[8,9] included 159 trials). Therefore, much can be learned from research into falls in older people and other populations. The Prevention of Falls Network Europe (ProFaNE) published a common outcome data set for falls management interventions in older people[10] that served as a starting point for the IMSFPRN discus-

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sion. ProFaNE recommends that prospective falls diaries be used to record falls daily, with monthly returns. The group also recommends that data from the falls diaries be summarized as number of falls, number of fallers/nonfallers and frequent fallers, and annual fall rate per person. Additionally, it suggests that radiologic con-

measure of fall-related injury. However, because the pathology and demographics of people with MS differ from those of elderly fallers, and falls in MS are seemingly distinct from those observed in the elderly,[11] these recommendations may need to be modied to apply them to the investigations of falls prevention among people with MS.

Outcome Measures Used in Existing Falls Research in MS

primary outcome for a falls-prevention program, a range of options should be considered. These include fall risk, the number of people falling, total number of falls in a given period, rate of falls, and injurious falls. In the MS population, where relapses and fatigue are an issue, it may be useful to also capture the number of falls per day and to examine the pattern over a calendar month.

To date, a limited number of falls-prevention and fall risk reduction programs for people with MS have been investigated (Table 1).[12-17] Owing in part to the varied nature of investigations, several different fall-related outcomes have been used. These include balance,

prevention strategies, composite measures of fall risk (ie, retro -
spective recall of falls, and prospective falls diaries. The outcome measures used have a range of strengths and weaknesses. For example, the adoption by people with MS of falls-prevention strategies is a potentially positive outcome, and interventions have been shown to improve relevant knowledge and skills among people with MS.[15] However, people who use fall risk reduction strategies still fall frequently,[18] suggesting that the adoption of fall risk reduction strategies should not be the sole outcome for falls-prevention studies.

Fall Risk as an Outcome Measure

Three meta-analyses[19-21] have focused on risk factors for falls in people with MS, and all have concluded that balance dets, progressive MS, and mobility aid use are associated with and predict falls status. Despite the

Table 1. **Outcomes used in falls-prevention intervention studies to date**

Author, year	Brief study description	Outcomes
Cattaneo et al.,[12] 2007	RCT of balance interventions 1-motor and sensory balance rehab, 2-motor balance strategies rehab, 3-not aimed at balance	Fall frequency (self-report falls in past month) Berg Balance Scale Dynamic Gait Index Dizziness Handicap Inventory
Coote et al.,[13] 2013	RCT of group or individual physiotherapy or yoga, physiotherapy focusing on exercises for strength and balance	Fall prevalence (self-report last 3 months) Berg Balance Scale 6-Minute Walk test Multiple Sclerosis Impact Scale-29 Scale
Esnouf et al.,[14] 2010	RCT of oddstock drop foot stimulator	Canadian Occupational Performance Measure Prospective falls diary during intervention period
Finlayson et al.,[15] 2009	RCT of fall risk management program	Knowledge of fall risk factors Increased knowledge and skills to manage falls and falls risk
Nilsagård et al.,[16] 2014	Single group pre/post exercise intervention focusing on Core Stability, Dual Tasking, and Sensory Conditions	Prospective falls over 7 weeks Berg Balance Scale 4 Square Step Test Sit-to-Stand Test Timed Up and Go (TUG) TUG Cognitive Functional Gait assessment MS Walking Scale-12 MS Impact Scale
Stephens et al.,[17] 2001	RCT of Awareness Through Movement Intervention	Prospective falls diary during intervention Equiscale balance test Sensory Integration of Balance

Abbreviations: MS, multiple sclerosis; RCT, randomized controlled trial.

commonality of conclusions, the ability of balance and mobility measures to predict future falls continues to be unclear. To date, the limited data from prospective studies have been inconsistent, and no studies have presented analyses of individual measures that can be considered excellent in predicting which MS patients will fall. For example, in the largest prospective study to date, the best model to explain falls included the PPA, Expanded Disability Status Scale (EDSS), and Ashworth scale, and had only fair to good predictive ability (sensitivity

limited number of studies as well as lack of consensus in

propose a measure of fall risk for people with MS that can be used as an outcome measure in falls-prevention studies. Additionally, there is evidence from the research on older adults that reducing fall risk does not necessarily lead to a reduction in the number of falls.[8,22] Therefore, the IMSFPRN proposes that the primary outcome should be a reduction in falls rather than fall risk.

In the MS literature to date, a number of definitions of a fall have been used, and these are presented in Table 2.[23-31] In a systematic review of the literature on

Table 2.
sclerosis literature to date

Unexpected event in which participant comes to rest on ground,
Unexpected contact of any part of the body with the ground[23-30]
Landing on the ground or at some other level, such as a chair or bed
Unexpected loss of balance resulting in whole-body contact with the ground
Any event that led to an unexpected contact with a support surface
An event in which the individual unintentionally comes to rest on the ground or a lower surface not as the result of a major intrinsic event (eg, stroke or heart attack) or an overwhelming extrinsic event (such as ice)
Unintentionally coming to the ground or some lower level and other than as a consequence of sustaining a violent blow, loss of consciousness, sudden onset of paralysis as in stroke or an epileptic seizure
A slip or trip in which you lost your balance and landed on the

From Finlayson et al.[31] Reprinted with permission.

falls in older people, Hauer et al.[32] found that the lack

in others precluded comparison between studies. This review led to the definition proposed by ProFaNE,[10]

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pected event in which the participants come to rest on

been used verbatim by several MS studies to date, and

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tion is that it is straightforward and minimizes subjective judgment by the researcher and/or participants. Conse-

Presentation of Data on Falls

One possible successful outcome of a falls-prevention intervention is a reduction in the number of people falling; a second is a reduction in the number of falls that each person has. Therefore, the IMSFPRN is inter-

period, but also in how many times they fell. Within the MS population, an individual's number of falls is very important given the high percentage of recurrent fallers.[21] In analyzing falls data, the absolute numbers for each variable may be recorded, which subsequently may be used to classify each participant's fall status (for example, as a "faller" or "frequent faller"). Lamb et al.[10] recommend that both the number of falls and the number of fallers be presented, as well as the number of frequent fallers. However, they fail to specify the number of falls a person must have in order to be as a "frequent faller." Studies of people with MS to date have

For example, in prospective studies Gunn et al.[33] used

as a faller, Nilsagård et al.[23] considered a faller as anyone having one or more falls, while Hoang et al.[34] used the

Interestingly, overall the results of these investigations highlight similar fall risk factors. As it only takes one fall to cause injury or related consequences, we propose that

falls during the observation period. We also propose that

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ing two or more falls during that period.

The time frame in which falls occur is important and adds to the information on the type and severity of the problem; for example, three falls in 1 month is a potentially different problem than three falls in 1 year. In fallers, the computation of "fall rate" is recommended in the literature on the elderly.[10] This is calculated as the number of falls per person per year and has been used as the primary outcome in a number of Cochrane reviews of the literature on the elderly and stroke-related falls.[9,35,36] Falls per person per year can be computed from any time period of diary recording, allowing comparison across studies with different reporting periods. We therefore propose that MS falls-prevention intervention studies use the number of falls per person per year as the primary outcome, with the number of falls, number of fallers, and frequent fallers as additional outcome variables. The length of time for recording falls will be considered in a later section.

Fall Recording—Retrospective versus Prospective

Several studies of falls in people with MS have highlighted discrepancies between reported/recorded fall prevalence using retrospective recall and fall incidence using prospective falls diaries. In a study of 76 community-dwelling people with MS in Sweden,[23] the reported/recorded retrospective fall prevalence was 36%, while the reported/recorded prospective fall incidence for the same cohort was 63%. Similarly, in a UK sample of 148 people with MS,[33] 57% of the sample retrospectively reported falls, while 70.3% recorded falls prospectively using diaries. These studies are further supported [37] who reported that 63% of their sample underestimated the number of falls they had recorded during a 12-month period. These are not

cognitive dysfunction in people with MS.[38] Therefore, the IMSFPRN recommends that future research with the aim of reducing falls in people with MS should prospectively record falls using falls diaries.

Falls Diaries—Duration and Return Rate

Falls diaries can provide valuable information regarding the occurrence of falls. If designed correctly, they also can provide data on various other aspects of the falls, including the context (time of day, activity at the time, location, etc.), the causes (legs giving way, slip, trip, loss of balance, etc.), and consequences of the fall (injury, activity curtailment, care, etc.). When incorporating a falls diary into a falls intervention, care should be taken to balance the burden on the participant with maximizing data collection.

In order to inform the design of falls diaries, we reviewed those diaries used by four MS research groups to date.[4,33,34,39] All used daily reporting with different formats for recording falls. Three used a 1-month-view calendar with space to write the number of falls beneath each date,[4,34,39] while the other group used a format with one page per day.[33] For all four groups, diaries were presented to the participants in a pack or binder at the start of the trial, and the investigators suggested that these constituted an important visual reminder to record falls. Diaries were generally returned by mail on a monthly basis, although one group used a biweekly time frame for returns.[33] One group using monthly returns used biweekly phone reminders to optimize the accuracy of falls recording,[39] and all followed up by phone or e-mail if the diaries were not returned within 7 to 10 days of the expected date.

The reporting period and frequency of returning diaries is a balance between burden and inconvenience to participants and loss of accuracy of data due to memory problems. For instance, if monthly returns are used, the participants may have forgotten to record for several weeks before it is noticed that a diary is missing, and recall over many weeks to subsequently complete the diary may result in inaccuracies. Biweekly returns may be more accurate in terms of numbers of falls but result in increased postal charges and place extra demands on the participant. Owing to the prevalence of cognitive dysfunction in people with MS, we suggest that biweekly phone reminders be used, and that diaries be returned on a monthly basis, with a further phone reminder if the diary is not received within 7 days of the expected date. A sample falls diary is included in Supplementary Appendix 1, which is published in the online version of this article at ijmsc.org. While this diary is based on the best available information at this time, it does require validation.

Given the young age of people with MS who fall,[21] and their potential familiarity with technology, the use of other forms of reporting and reminders such as text alerts, mobile phone applications, or other fall-sensing devices should be evaluated. To date few studies have been published evaluating these technological approaches in people with MS.

It is not clear for what time frame the falls diaries should be kept, such as 3 months, 6 months, or 12 months. The reporting period needs to be long enough to capture falls before intervention and a change in falls after intervention, but short enough to avoid excessive interruption of everyday life. Fall rates in people with

those observed in older people.[40] For example, in one study,[41] fall rate for the total sample (N = 148) was estimated at 18.4 falls per person per year. When calculated for fallers only (70% of the total sample, n = 104), the fall rate equated to 26.2 falls per person per year (or 2.15 falls per person per month). Based on these data, it is suggested that 3 months is long enough to capture falls frequency before intervention. However, the reporting period should also consider the mechanism of the intervention; for example, interventions targeting behavior change may require a longer time to have an observable impact. Longer-term follow-up after the post-intervention phase should also be considered in order to evaluate the long-term effect of the intervention on fall rate.

Recording the Causes, Context, and Consequences of Falls

The causes, context, and consequences of falls are also frequently included in falls diaries, with researchers either asking about the most recent fall as an example or asking for details of each fall that occurs. The accuracy of self-reports of causes of falls is not known. As some participants have up to 63 falls in a 3-month period,[41] the recording of causes and context for each fall may be overly burdensome. Once again, the balance between the data set and participant burden comes into play. While extensive detailed information on these factors might be important in studies intended to gather a wide range of information to inform intervention development and report predictors of falls, it may be less important in intervention studies where rates of falling are the primary outcome.

Of the falls diaries we reviewed, all but one recorded the context (location, time of day, activity being performed at the time, etc.) and the perceived cause (slip, trip, knee gave way, etc.) of falls. A change in falls context may be a positive outcome for an intervention trial. A person with activity curtailment who rarely left the house and whose pre-intervention falls were all indoors might consider it more positive if their falls happened outside of the home during social or recreational activities, suggesting a possible reduction of their activity curtailment. Therefore, while it is not a priority, the IMSFPRN recommends that the context be considered for recording. The context may allow for individualization of any intervention.

Similarly, a change in the cause of falls might also indicate improvement; for example, a person who falls because of their knees giving way may not experience that after intervention if quadriceps-strengthening exercises are a key component of the intervention. It is probably unreasonable to burden participants with recording these for each fall, but it may be feasible to record the perceived cause of falls for two falls in each month.

The consequences of falls, in terms of injuries or health-care use, are an element of falls that is essential to record. Estimates of injurious falls for people with MS vary. The literature clearly indicates that falls in people with MS are more injurious than those in people without MS. For instance, the ProFaNE group[10] proposes that injurious falls be recorded as the "number of radio-

year." Several studies have suggested that the fracture rate among people with MS is considerably greater than in the general population. A Danish study[42] comparing people with MS to the National Hospital Discharge register found incidence rate ratios of 3.36 (tibia), 6.66 (femur), and 3.20 (hip) for fractures in people with MS. A study of 721 veterans with MS reported that 2.8% of them had an injurious fall coded in their medical

PracticePoints

- The International MS Falls Prevention Research Network (IMSFPRN) proposes that the primary outcome measure of a falls-prevention program should be a reduction in the number of falls, rather than fall risk.
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  should be used. The IMSFPRN proposes to use the Prevention of Falls Network Europe (ProFaNE) "an unexpected event in which
  the participants come to rest on the ground,

- Prospective falls diaries should be used as a measurement tool to record the number of falls each day for a minimum of 3 months. Longer lengths of recording may be required depending on the content of the falls-prevention intervention.
- Falls diaries should also be used to record information on the consequences, circumstances, and perceived causes of a fall.

record, compared with 1.5% of veterans without MS.[1] A British study comparing people with MS to the UK General Practice Register[43] found a threefold increased

are important to record and report. However, falls of a much lesser severity can also result in considerable costs to the person and to the health-care system. It appears that these less injurious falls may be more common than severe injuries. For instance, in a phone survey of the North American Research Committee on Multiple Sclerosis database,[44] 23% reported seeking medical attention for a fall, while another survey of community-dwelling people with MS revealed that 58% of falls were found to be medically injurious.[2] Additionally, given that many falls are not reported to health-care professionals in both the MS[2] and elderly[45] populations, recording medical attention for falls may not be an accurate representation of injurious falls. For that reason, the IMSFPRN proposes that falls diaries contain all self-reported injuries in addition to health-care use information. We also recom-

diary for all study participants be implemented at the start of the trial, with the biweekly phone calls used to verify that information is being recorded accurately.

Conclusions and Recommendations

The IMSFPRN recommends that a reduction in falls should be the primary outcome of falls-prevention programs. Consistent with recommendations from ProFaNE,[10]

event in which the participants come to rest on the

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FPRN recommends using prospective falls diaries to record the number of falls each day. Participants should be reminded by phone every 2 weeks to complete the diaries, which should be returned on a monthly basis with a further reminder if not received within 7 days of the expected date. The length of reporting may depend on the nature of the intervention but should be at least 3 months. Falls data should be presented as the rate of falls per person per unit time, in addition to the total number of falls and the number of fallers. Information on the consequences of each fall—that is, self-reported injury and health-care use—should also be recorded and reported. The IMSFPRN recommends that information on the causes and context of falls should be captured for

□

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