



Cochrane
Library

Cochrane Database of Systematic Reviews

Interventions for preventing falls in people with multiple sclerosis (Protocol)

Hayes S, Kennedy C, Galvin R, Finlayson M, McGuigan C, Walsh CD, Coote S

Hayes S, Kennedy C, Galvin R, Finlayson M, McGuigan C, Walsh CD, Coote S.
Interventions for preventing falls in people with multiple sclerosis.
Cochrane Database of Systematic Reviews 2017, Issue 1. Art. No.: CD012475.
DOI: 10.1002/14651858.CD012475.

www.cochranelibrary.com

TABLE OF CONTENTS

| | |
|------------------------------------|---|
| HEADER | 1 |
| ABSTRACT | 1 |
| BACKGROUND | 1 |
| OBJECTIVES | 3 |
| METHODS | 3 |
| ACKNOWLEDGEMENTS | 6 |
| REFERENCES | 7 |
| APPENDICES | 8 |
| CONTRIBUTIONS OF AUTHORS | 9 |
| DECLARATIONS OF INTEREST | 9 |
| SOURCES OF SUPPORT | 9 |

[Intervention Protocol]

Interventions for preventing falls in people with multiple sclerosis

Sara Hayes¹, Catriona Kennedy², Rose Galvin¹, Marcia Finlayson³, Christopher McGuigan⁴, Cathal D Walsh⁵, Susan Coote¹

¹Department of Clinical Therapies, Faculty of Education and Health Sciences, University of Limerick, Limerick, Ireland. ²School of Nursing and Midwifery, Robert Gordon University, Aberdeen, UK. ³School of Rehabilitation Therapy, Queen's University, Kingston, Canada. ⁴Department of Neurology, St. Vincent's University Hospital & University College Dublin, Dublin, Ireland. ⁵Health Research Institute (HRI) and MACSI, Department of Mathematics and Statistics, University of Limerick, Ireland

Contact address: Sara Hayes, Department of Clinical Therapies, Faculty of Education and Health Sciences, University of Limerick, Limerick, Ireland. sara.hayes@ul.ie.

Editorial group: Cochrane Multiple Sclerosis and Rare Diseases of the CNS Group.

Publication status and date: New, published in Issue 1, 2017.

Citation: Hayes S, Kennedy C, Galvin R, Finlayson M, McGuigan C, Walsh CD, Coote S. Interventions for preventing falls in people with multiple sclerosis. *Cochrane Database of Systematic Reviews* 2017, Issue 1. Art. No.: CD012475. DOI: 10.1002/14651858.CD012475.

Copyright © 2017 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

ABSTRACT

This is a protocol for a Cochrane Review (Intervention). The objectives are as follows:

The aim of this review is to evaluate the effectiveness of interventions designed to reduce the rate of falls in people with multiple sclerosis (MS). Specific objectives include comparing the effectiveness of single, multiple and multifactorial interventions designed to reduce the rate of falls in people with MS.

BACKGROUND

Multiple sclerosis (MS) is one of the most prevalent diseases of the central nervous system (CNS) with recent prevalence estimates indicating that MS directly affects 2.3 million people worldwide (Browne 2014). Global annual incidence estimates range from 0.07 to 13.75 per 100,000 people (Browne 2014). Wide variations occur in relation to the prevalence and incidence of MS, according to geographic location, with parts of Northern Europe and Canada being the most commonly affected (Browne 2014). It is the most common disabling neurological disorder among young people.

Traditionally MS has been categorised according to clinical phenotype as primary-progressive, relapsing-remitting, secondary-progressive and progressive-relapsing (Lublin 1996). However, it has been suggested that a classification based on clinical and radio-

logical activity be instigated (Lublin 2014). MS is an immune-mediated disease characterised by inflammatory demyelination and neurodegeneration within the CNS. This damage to the CNS structures in turn leads to impairments in cognition, muscle strength, muscle tone, sensation, coordination and gait, all of which are associated with an increased risk for falls. Despite the recent increased availability of disease-modifying medical treatments and their potential to delay the clinical progression of MS, falls continue to present as a common and serious health concern in people with this disease.

Description of the condition

Interventions for preventing falls in people with multiple sclerosis (Protocol)

Copyright © 2017 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

1

Fall rates of 56% have been reported among people with MS (measured using prospective measures) in a recent meta-analysis of 537 individuals, with 37% of the study population falling recurrently (Nilsagard 2015). This study demonstrated that most falls occurred indoors (65%) between 6 a.m. and 6 p.m. (75%). In addition, primary progressive MS and Expanded Disability Severity Scale (EDSS) (Kurtzke 1983) levels of 4.0 and 6.0 were associated with significantly increased odds of falls ($P < 0.05$). The falls rate was also lower in women than men (relative risk (RR) 0.80; 95% confidence interval (CI) 0.67 to 0.94) and decreased with increasing age (RR 0.97 for each year, CI 0.95 to 0.98). In a study by Matsuda 2011, 28% of people with MS who had reported to have fallen (265 of a total of 455 respondents) suffered a fracture. A population-based European study reported that the incidence rate of fracture was significantly higher among people with MS than age- and gender-matched peers without MS (Bazelier 2011). People with MS with a history of falls report significantly poorer physical and psychological health status compared with non-fallers with MS (Coote 2013). Falls can further have an adverse impact on fear of falling and falls self-efficacy, and can contribute to activity curtailment, physiological deconditioning, loss of independence, and institutionalisation (Finlayson 2010; Matsuda 2012). A recent systematic review with meta-analysis identified four factors significantly associated with falls in people with MS: balance dysfunction, the use of a mobility aid, cognitive dysfunction, and progressive MS subtype (Gunn 2013). Given the high prevalence of falls among people with MS and the associated serious and wide-ranging consequences, an increased number of randomised controlled trials have evaluated the effect of falls prevention interventions among people with MS.

Description of the intervention

To our knowledge there currently is no classification of falls prevention interventions in the MS literature. The effectiveness of several categories of falls prevention interventions has been reviewed systematically among older adults (Gillespie 2003; Gillespie 2012) and people post-stroke (Verheyden 2013) by Cochrane. These categories are also used by the few researchers that have examined fall prevention or management in MS. However the Prevention of Falls Network Europe (ProFaNE) (Lamb 2005; Lamb 2011) proposes the following categories for older adults: exercises, medication, surgery, management of urinary incontinence, fluid or nutrition therapy, psychological intervention, environment/assistive technology, environment (social environment), knowledge interventions and other interventions. In the ProFaNE taxonomy, interventions are also classified as single interventions, multiple interventions or multifactorial interventions. A single intervention consists of only one intervention component which is delivered to all participants in the intervention group, (e.g. exercise). Multiple interventions consist of a combination of two or more intervention components, delivered to all of the participants in the in-

tervention group, (e.g. exercise plus psychological interventions). Multifactorial interventions consist of more than one intervention component, but participants receive different combinations of interventions based on an individual assessment to identify potential risk factors for falls.

For the purpose of this review, we will include all potential falls prevention interventions and these interventions will be categorised according to the ProFaNE taxonomy (Lamb 2005; Lamb 2011).

How the intervention might work

Falls prevention interventions are designed to minimise known modifiable personal, task and environmental risk factors for falling, and thereby prevent falls and associated injuries. Interventions are designed to reduce the falls rate by targeting improvement in personal risk factors, e.g. reduced balance function, and incorporate exercises to improve joint flexibility, muscle strength, reaction times and coordination. Other interventions are aimed at improving non-physical personal risk factors, e.g. the presence of cognitive impairment, and include strategies to promote risk awareness, planning and attention. Interventions are also designed to reduce falls by promoting improved task performance, e.g. safe mobility aid use, and include participant education regarding task analysis and planning. Interventions are additionally designed to ameliorate the falls rate by addressing environmental risk factors, e.g. home environmental modifications, and include the provision of aids for personal care.

Single component interventions are designed to address and ameliorate specific risk factors for falling. For example, in Cochrane Reviews focusing on falls prevention interventions among older adults, vitamin D prescription interventions have been shown to be effective in reducing falls rates among older adults in care facilities (Cameron 2012) and exercise interventions have been shown to be effective in reducing falls rates among older adults living in the community (Gillespie 2012). There is potential for this improvement to be mediated indirectly through the effect of exercise on balance function and mobility functions. To date in the MS literature, of the few falls interventions that have been evaluated, most have predominantly used combinations of education and exercise, targeting mobility, balance, and falls self-efficacy outcomes. The association between balance, mobility impairments, and falls in MS is complex. Programmes focused on balance and stability in older adult populations have been shown to decrease falls in other populations (Gillespie 2012) whereas those that target mobility alone have tended to be either ineffective or to increase falls in older adult populations (Gillespie 2012).

Multiple component interventions aim to reduce several components of falls risk rather than dealing with single risk factors. Commonly, multiple component interventions focus on two or more common risk factors and provide these to all participants, regardless of their exact risk status. However, there is no assessment and individual tailoring of the intervention to risk factors. There is

some evidence that multiple component interventions may reduce the rate of falls and the risk of falling in older people living in the community (Gillespie 2012).

The rationale underlying multifactorial interventions is that participants undergo an assessment for risk of falling, and a tailored intervention is provided based on their modifiable risk factors. Gillespie 2012 found some evidence that multifactorial interventions may reduce the rate of falls (i.e. the total number of falls per unit of person time that falls were monitored), but not the risk of falling (i.e. the number of people who fell once or more among older people living in the community).

Why it is important to do this review

The incidence of falls in people with MS is three times higher than that in older people, yet recently published clinical guidelines (NGC 2014) do not outline an evidence-based approach to falls interventions among people with MS. This topic has been examined and reviewed systematically among older adults (Gillespie 2003; Cameron 2012; Gillespie 2012) and people post-stroke (Verheyden 2013) by Cochrane. Therefore there is a clear clinical need for synthesised information regarding the effectiveness of falls prevention interventions among people with MS. This clinical need is relevant across multiple disciplines and multiple settings (home, community, clinical setting). A Cochrane systematic review of this topic has the potential to guide clinical decisions regarding care pathways for people with MS who are at risk of falling, and ultimately to improve quality of life of people with MS.

OBJECTIVES

The aim of this review is to evaluate the effectiveness of interventions designed to reduce the rate of falls in people with multiple sclerosis (MS). Specific objectives include comparing the effectiveness of single, multiple and multifactorial interventions designed to reduce the rate of falls in people with MS.

METHODS

Criteria for considering studies for this review

Types of studies

We will include randomised controlled trials (RCTs) and quasi-randomised trials, including randomised and quasi-randomised cluster and cross-over trials. We will include all trials regardless of methodological quality.

Types of participants

We will include adults 18 years of age or older, male and female, with clinically definite MS. People with the clinical diagnosis of MS according to the ICD-8 (code 340) (ICD-8 1965), and the McDonald criteria and subsequent revisions (Schumacher 1965; Poser 1983; McDonald 2001; Polman 2005; Polman 2011) will be included. All subgroups of MS such as relapsing remitting, primary progressive and secondary progressive MS, and people at any time since diagnosis will be included. People with neurological and non-neurological comorbidities that may affect falls, e.g. dementia, Parkinson's disease, and recent orthopaedic surgery, will be excluded.

Types of interventions

Falls prevention interventions will be considered to be any programme in which the primary or secondary aim is to reduce the rate of falls. Some anticipated falls prevention interventions may include: exercise (e.g. aerobic, strengthening, balance), medical intervention (e.g. supplementation with vitamin D), psychological (e.g. cognitive behavioural therapy interventions), environment modifications (e.g. the provision of hip protectors, adaptations to homes), assistive technology interventions (e.g. provision of aids for personal care and protection and personal mobility, eyeglasses, hearing aids, personal alarm systems), surgical interventions (e.g. surgery to address a comorbidity such as hip or knee replacement for osteoarthritis) or other interventions (e.g. educational interventions designed to increase knowledge relating to falls prevention). Acceptable control interventions will include: no treatment, wait-list control, usual care control and interventions that are not intended to reduce falls rate or the number of fallers, (e.g. educational interventions to promote physical activity engagement).

Types of outcome measures

Outcome measures will be examined prior to and at the end of the intervention and at the end of follow-up (e.g. 3-, 6- or 12-month follow-up periods).

Primary outcomes

- The rate of falls (the number of falls per person year), measured using both retrospective and prospective measures, recommended by the International MS Falls Prevention Research Network (IMSFPRN) as the primary outcome for falls prevention trials.
- The number of falls per person.
- The number of recurrent or frequent fallers.
- The number of adverse events resulting from the intervention, e.g. incidence of fall-related injuries.

Secondary outcomes

- Falls risk, measured using measures including, but not restricted to, the Physiological Profile Assessment.
- Quality of life (including psychological aspects such as fear of falling), measured using measures including, but not restricted to, the Multiple Sclerosis Impact Scale-29 (Hobart 2001).
- Balance function, measured using measures including, but not restricted to, the Berg Balance Scale (Berg 1989), Mini-BEST test (Franchignoni 2010).
- Psychological aspects such as fear of falling; activity curtailment due to fear of falling.
- Cognition, measured using measures including, but not restricted to, the Symbols Digit Modalities Test (SDMT) (Smith 1982).
- Measures of MS disease progression, including but not restricted to the Expanded Disability Severity Scale (EDSS) (Kurtzke 1983), and Patient Determined Disease Steps (PDDS) (Hohol 1995).
- Measures of mobility including, but not restricted to the Six Minute Walk Test (Fry 2006), and MS Walking Scale-12 (Hobart 2003).
- Measures of functional outcome, including but not restricted to the Functional Independence Measure (Keith 1987).
- Self-reported fatigue, measured using measures including, but not restricted to, the Modified Fatigue Impact Scale (MFIS) (Fischer 1999).
- Measures of participation, including but not restricted to the Community Integration Measure (McColl 2001).
- Outcomes that reflect cost, service utilisation and care burden.

Self-report and objective measures will be included.

Search methods for identification of studies

A systematic search without language or date restrictions will be conducted using the optimally-sensitive strategy developed for Cochrane to identify all relevant published and unpublished RCTs (Lefebvre 2011). We will employ the services of a professional translator if required, for study selection and data extraction.

Electronic searches

The Information Specialist will search the Trials Register of the Cochrane Multiple Sclerosis and Rare Diseases of the CNS Group, which, among other sources, contains trials from:

- Cochrane Central Register of Controlled Trials (CENTRAL) (2016, most recent issue);
- MEDLINE (PubMed) (1966 to date);
- Embase (EMBASE.com) (1974 to date);
- Cumulative Index to Nursing and Allied Health Literature (CINAHL) (EBSCOhost) (1981 to date);

- Latin American and Caribbean Health Science Information Database (LILACS) (Bireme) (1982 to date);
- ClinicalTrials.gov (www.clinicaltrials.gov); and
- World Health Organization (WHO) International Clinical Trials Registry Platform (apps.who.int/trialsearch).

Information on the Trials Register or the Review Group and details of the search strategies used to identify trials can be found in the 'Specialised Register' section within the Cochrane Multiple Sclerosis and Rare Diseases of the CNS Group [module](#).

The keywords that will be used to search for trials for this review are listed in [Appendix 1](#).

We will extend the search to other resources, including:

- PsycINFO (1806 to date); and
- Physiotherapy Evidence Database (PEDro) (1999 to date).

Searching other resources

We will:

- handsearch the reference lists of all retrieved articles, texts and other reviews on the topic;
- contact researchers active in this field for additional data, if necessary; and
- contact principal authors of unpublished manuscripts to ask if they are willing to disclose their unpublished data.

Data collection and analysis

Selection of studies

Titles and abstracts of the citations retrieved by the literature search will be screened independently by two review authors (SH, SC) for inclusion or exclusion, based on predetermined inclusion criteria. The full text of potentially relevant studies will be selected for further assessment and at least two authors will ascertain and agree on eligibility based on the full article. The eligibility (on the basis of the information available in the published data) of these studies will be evaluated independently. Papers assessed in full text that do not meet the inclusion criteria will be listed in the 'Characteristics of excluded studies' table with the reasons for exclusion. Any disagreement regarding inclusion will be resolved by discussion, or by referral to a third assessor (RG) if necessary.

Data extraction and management

For each included study, two review authors (SH, RG) will independently extract data from the selected trials using standardised forms and enter the data into the RevMan software ([Review Manager 2014](#)). We will extract data on the following:

- study design;
- characteristics of participants (number, setting, age, type of MS, EDSS score);

- inclusion and exclusion criteria;
- brief description of experimental intervention;
- brief description of control intervention;
- methodological quality of studies;
- description of setting;
- description of outcomes;
- date of study and location of study.

Disagreements will be discussed and resolved by consensus among the review authors.

Assessment of risk of bias in included studies

The risk of bias for all included studies will be independently assessed by two review authors (SH, SC) using the 'Risk of bias' tool outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). The domains are: sequence generation, allocation concealment, blinding, incomplete outcome data, selective outcome and other biases. Disagreements among the review authors on the methodological quality of the identified studies will be discussed and resolved by group consensus.

We will use the summary quality assessment at the analysis stage as a means of interpreting the results. For each dimension and for the summary assessment we will assign the 'Risk of bias' categories (Higgins 2011) as:

- low risk of bias, plausible bias unlikely to seriously alter the results;
- unclear risk of bias, plausible bias that raises some doubt about the results; and
- high risk of bias, plausible bias that seriously weakens confidence in the results.

Assessing the quality of the body of evidence using the GRADE approach

We will assess the quality of the evidence using the GRADE approach as outlined in the [GRADE handbook](#) in order to assess the quality of the body of evidence relating to the following outcomes for the main comparisons:

- the rate of falls;
- the number of fallers and frequent fallers;
- the number of adverse events;
- falls risk; and
- quality of life.

We will use the [GRADEpro](#) Guideline Development Tool to import data from Review Manager 5.3 (Review Manager 2014) in order to create a 'Summary of findings' table. As per the *Cochrane Handbook for Systematic Reviews of Interventions* guidelines, the 'Summary of Findings' table will include the following information (Higgins 2011): a list of all important outcomes; a measure of the typical burden of these outcomes; absolute and relative magnitude of effect; numbers of participants and studies addressing

these outcomes; a rating of the overall quality of evidence for each outcome and a space for comments.

A summary of the intervention effect and a measure of quality for each of the above outcomes will be produced using the GRADE approach. The GRADE approach uses five considerations (study limitations, consistency of effect, imprecision, indirectness and publication bias) to assess the quality of the body of evidence for each outcome. The evidence can be downgraded from 'high quality' by one level for serious (or by two levels for very serious) limitations, depending on assessments for risk of bias, indirectness of evidence, serious inconsistency, imprecision of effect estimates or potential publication bias.

Measures of treatment effect

According to the study characteristics, we will determine the treatment effect of:

- falls intervention versus another intervention (not designed to reduce falls);
- falls interventions versus no treatment;
- falls intervention versus another falls intervention, e.g. single exercise intervention versus multiple component exercise plus education intervention.

According to the type of outcomes reported we will use the following effect measures:

- dichotomous data: odds ratio (OR), risk ratio (RR) or risk difference (RD); and
- continuous data: mean difference (MD) or standardised mean difference (SMD) if the studies assess the same outcome but measure it in a variety of ways (for example, SF-36, MSQOL-54).

A rate ratio (RaR) and 95% confidence interval (CI) will be used to compare the rate of falls between intervention and control groups. For risk of falling and number of adverse events we will use a risk ratio (RR) and 95% CI based on the number of people falling and the number of people reporting adverse events in each group.

Unit of analysis issues

Data analysis will take into account the level at which randomisation occurred (e.g. cluster-randomised trials; cross-over trials, and repeated measurements).

Dealing with missing data

If trial data are insufficient or missing, we will attempt to obtain additional information from the authors of included studies by personal communication. Our method of dealing with missing data will depend on the nature of the missing data. If the data are missing at random we will analyse only the available data (ignoring the missing data). If the data are not missing at random we will

consider the following options, in consultation with the statistician on our review team (CW):

1. imputing the missing data with replacement values, and treating these as if they were observed (e.g. last observation carried forward, imputing an assumed outcome such as assuming all were poor outcomes, imputing the mean, imputing based on predicted values from a regression analysis);
2. imputing the missing data and accounting for the fact that these were imputed with uncertainty (e.g. multiple imputation, simple imputation methods (as point 1) with adjustment to the standard error); or
3. using statistical models to allow for missing data, making assumptions about their relationships with the available data.

Assessment of heterogeneity

We will calculate the I^2 statistic for each pooled estimate to assess the impact on statistical heterogeneity. The I^2 statistic may be interpreted as the proportion of total variation among effect estimates that is due to heterogeneity rather than sampling error, and it is intrinsically independent of the number of studies. When the I^2 is $< 30\%$ there is little concern about statistical heterogeneity (Higgins 2011). If there is statistical heterogeneity we will use random-effects models to take account of the between-study variation in our findings (Higgins 2011). Where there is substantial clinical heterogeneity (e.g. in the nature of interventions) then these will be analysed in homogenous subgroups as described at [Subgroup analysis and investigation of heterogeneity](#).

Assessment of reporting biases

To estimate the influence of unpublished papers on the overall effects, and if a sufficient number of studies are identified (at least 10 studies), contour-enhanced funnel plots of effect estimates against their standard errors (on a reversed scale) will be used.

Data synthesis

We will perform separate analyses for trials comparing an active falls prevention intervention with 'treatment as usual', or with a 'placebo' control intervention, and trials comparing two active falls prevention interventions.

We will analyse the data using [Review Manager 2014](#). We will decide whether or not to perform meta-analyses based on the similarity of the included trials. If we cannot carry out meta-analysis because of substantial differences between studies or when there is only one study identified, we will present results in a forest plot (with the pooled summary of outcomes suppressed) and provide a narrative/qualitative review. A power analysis will determine if statistical pooling of data will be appropriate to complete a meta-analysis. In the case of sufficient power, the data of individual trials will be pooled for each outcome using a fixed-effect model (if heterogeneity is not present ($I^2 < 30$)) and using a random-effects model if heterogeneity is present ($I^2 \geq 30$).

Subgroup analysis and investigation of heterogeneity

If we identify a sufficient number of RCTs we will undertake subgroup analyses to establish if the following subgroups affect overall effects:

- participant-related characteristics (e.g. type of impairment at baseline: participants with muscle weakness, participants with ataxia, etc.; age; time since diagnosis of MS; type of MS, level of impairment at baseline; adherence to intervention);
- intervention-related characteristics (e.g. type of falls prevention intervention, duration of intervention; frequency of intervention; intensity of intervention);
- study design characteristics (e.g. type of comparison, type of falls outcome measurement, retrospective falls rate versus prospective falls rate).

Sensitivity analysis

We will perform sensitivity analysis to address the methodological quality of the trial by including or excluding trials with moderate or high risk of bias as described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

ACKNOWLEDGEMENTS

Nil

REFERENCES

Additional references

Bazelier 2011

Bazelier MT, van Staa T, Uitdehaag BM, Cooper C, Leufkens HG, Vestergaard P, et al. The risk of fracture in patients with multiple sclerosis: the UK general practice research database. *Journal of Bone and Mineral Research* 2011;**26**:2271-79.

Berg 1989

Berg K, Wood-Dauphinee S, Williams JI, Gayton D. Measuring balance in the elderly: preliminary development of an instrument. *Physiotherapy Canada* 1989;**41**:304-11.

Browne 2014

Browne P, Chandraratna D, Angood C, Tremlett H, Baker C, Taylor BV, et al. Atlas of Multiple Sclerosis 2013: a growing global problem with widespread inequity. *Neurology* 2014;**83**:1022-4.

Cameron 2012

Cameron ID, Gillespie LD, Robertson MC, Murray GR, Hill KD, Cumming RG, et al. Interventions for preventing falls in older people in care facilities and hospitals. *Cochrane Database of Systematic Reviews* 2012, Issue 12. [DOI: 10.1002/14651858.CD005465]

Coote 2013

Coote SC, Hogan N, Franklin S. Falls in people with multiple sclerosis who use a walking aid: prevalence, factors and effect of balance and strength interventions. *Archives of Physical Medicine and Rehabilitation* 2013;**94**:616-21.

Finlayson 2010

Finlayson M, Peterson E. Falls, aging and disability. *Physical Medicine and Rehabilitation Clinics of North America* 2010;**21**:357-73.

Fischer 1999

Fischer JS, LaRocca NG, Miller DM, Ritvo PG, Andrews H, Paty D. Recent developments in the assessment of quality of life in multiple sclerosis (MS). *Multiple Sclerosis* 1999;**5**:251-9.

Franchignoni 2010

Franchignoni FF, Horak M, Godi A, Nardone A, Giordano A. Using psychometric techniques to improve the Balance Evaluation Systems Test: the mini-BESTest. *Journal of Rehabilitation Medicine* 2010;**42**:323-31.

Fry 2006

Fry DK, Pfalzer LA. Reliability of four functional tests and rating of perceived exertion in persons with multiple sclerosis. *Physiotherapy Canada. Physiotherapie Canada* 2006;**58**:212-20.

Gillespie 2003

Gillespie LD, Gillespie WJ, Robertson MC, Lamb SE, Cumming RG, Rowe BH. Interventions for preventing falls in elderly people. *Cochrane Database of Systematic Reviews* 2003, Issue 4. [DOI: 10.1002/14651858.CD000340]

Gillespie 2012

Gillespie LD, Robertson MC, Gillespie WJ, Sherrington C, Gates S, Clemson LM, et al. Interventions for preventing falls in older people living in the community. *Cochrane Database of Systematic Reviews* 2012, Issue 9. [DOI: 10.1002/14651858.CD007146]

Gunn 2013

Gunn HJ, Newell P, Haas B, Marsden JF, Freeman JA. Identification of risk factors for falls in multiple sclerosis: a systematic review and meta-analysis. *Physical Therapy* 2013;**93**:504-13.

Higgins 2011

Higgins JPT, Green S. *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org.

Hobart 2001

Hobart J, Lamping D, Fitzpatrick R, Riazi A, Thompson A. The Multiple Sclerosis Impact Scale (MSIS-29): a new patient-based outcome measure. *Brain* 2001;**124**:962-73.

Hobart 2003

Hobart JC, Riazi A, Lamping DL, Fitzpatrick R, Thompson AJ. Measuring the impact of MS on walking ability: the 12-Item MS Walking Scale (MSWS-12). *Neurology* 2003;**60**:31-6.

Hohol 1995

Hohol MJ, Orav EJ, Weiner HL. Disease steps in multiple sclerosis: a simple approach to evaluate disease progression. *Neurology* 1995;**45**:251-5.

ICD-8 1965

World Health Organization. Report of the International Conference for the Eighth Revision of the International Classification of Diseases. Unpublished document WHO/ICD9/74.4; available on request from Strengthening of Epidemiological and Statistical Services, World Health Organization. Geneva: World Health Organization, 1965.

Keith 1987

Keith RA, Granger CV, Hamilton BB, Sherwin FS. The functional independence measure: a new tool for rehabilitation. *Advances in Clinical Rehabilitation* 1987;**1**:6-18.

Kurtzke 1983

Kurtzke JF. Rating neurologic impairment in multiple sclerosis: an expanded disability status scale (EDSS). *Neurology* 1983;**11**:1444-52.

Lamb 2005

Lamb SE, Jørstad-Stein EC, Hauer K, Becker C. Prevention of Falls Network Europe and Outcomes Consensus Group. Development of a common outcome data set for fall injury prevention trials: the Prevention of Falls Network Europe consensus. *Journal of the American Geriatrics Society* 2005;**53**:618-22.

Lamb 2011

Lamb SE, Becker C, Gillespie LD, Smith JL, Finnegan S, Potter R, et al. Reporting of complex interventions in clinical trials: development of a taxonomy to classify and describe fall-prevention interventions. *Trials* 2011;**12**:125.

Lefebvre 2011

Lefebvre C, Manheimer E, Glanville J. Chapter 6: Searching for studies. In: Higgins JPT, Green S (editors). *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org.

Lublin 1996

Lublin FD, Reingold SC. Defining the clinical course of multiple sclerosis: results of an international survey. National Multiple Sclerosis Society (USA) Advisory Committee on Clinical Trials of New Agents in Multiple Sclerosis. *Neurology* 1996;**46**:907–11.

Lublin 2014

Lublin FD, Reingold SC, Cohen JA, Cutter GR, Sørensen PS, Thompson AJ, et al. Defining the clinical course of multiple sclerosis: the 2013 revisions. *Neurology* 2014;**83**: 278–86.

Matsuda 2011

Matsuda PN, Shumway-Cook A, Bamer AM, Johnson SL, Amtmann D, Kraft GH. Falls in multiple sclerosis. *PM & R: the Journal of Injury, Function, and Rehabilitation* 2011;**3** (7):624–32.

Matsuda 2012

Matsuda PN, Shumway-Cook A, Ciol MA, Bombardier CH, Kartin DA. Understanding falls in multiple sclerosis: association of mobility status, concerns about falling, and accumulated impairments. *Physical Therapy* 2012;**92**: 407–15.

McColl 2001

McColl MA, Davies D, Carlson P, Johnston J, Minnes P. The community integration measure: development and preliminary validation. *Archives of Physical Medicine and Rehabilitation* 2001;**82**:429–34.

McDonald 2001

McDonald WI, Compston A, Edan G, Goodkin D, Hartung HP, Lublin FD, et al. Recommended diagnostic criteria for multiple sclerosis: guidelines from the International Panel on the diagnosis of multiple sclerosis. *Annals of Neurology* 2001;**50**:121–7.

NGC 2014

National Guideline Clearinghouse (NGC). Guideline summary: Multiple sclerosis: management of multiple

sclerosis in primary and secondary care. www.guideline.gov/summaries/summary/48753/multiple-sclerosis-management-of-multiple-sclerosis-in-primary-and-secondary-care (accessed 31 August 2016).

Nilsagard 2015

Nilsagård 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. *Multiple Sclerosis (Houndmills, Basingstoke, England)* 2015;**21**:92–100.

Polman 2005

Polman CH, Reingold SC, Edan G, Filippi M, Hartung HP, Kappos L, et al. Diagnostic criteria for multiple sclerosis: 2005 revisions to the “McDonald Criteria”. *Annals of Neurology* 2005;**58**:840–6.

Polman 2011

Polman CH, Reingold SC, Banwell B, Clanet M, Cohen JA, Filippi M, et al. Diagnostic criteria for multiple sclerosis: 2010 revisions to the McDonald criteria. *Annals of Neurology* 2011;**69**:292–302.

Poser 1983

Poser CM, Paty DW, Scheinberg L, McDonald WI, Davis FA, Ebers GC, et al. New diagnostic criteria for multiple sclerosis: guidelines for research protocols. *Annals of Neurology* 1983;**13**:227–31.

Review Manager 2014 [Computer program]

Copenhagen: Nordic Cochrane Centre, The Cochrane Collaboration. Review Manager (RevMan). Version 5.3. Copenhagen: Nordic Cochrane Centre, The Cochrane Collaboration, 2014.

Schumacher 1965

Schumacher GA, Beebe G, Kibler RF, Kurland LT, Kurtzke JF, McDowell F, et al. Problems of experimental trials of therapy in multiple sclerosis: report by the panel on the evaluation of experimental trials in multiple sclerosis. *Annals of the New York Academy of Sciences* 1965;**122**:552–68.

Smith 1982

Smith A. *Symbol Digits Modalities Test*. Los Angeles: Western Psychological Services, 1982.

Verheyden 2013

Verheyden GSAF, Weerdesteijn V, Pickering RM, Kunkel D, Lennon S, Geurts ACH, et al. Interventions for preventing falls in people after stroke. *Cochrane Database of Systematic Reviews* 2013, Issue 5. [DOI: 10.1002/14651858.CD008728]

* Indicates the major publication for the study

APPENDICES

Appendix I. Keywords for searching the MS Group Register

(((((“falls”[Title/Abstract]) OR “recurrent falls”[Title/Abstract]) OR “reduced falls”[Title/Abstract]) OR “falls prevention”[Title/Abstract])) AND (((“Tertiary Prevention”[Mesh]) OR “intervention”[Title/Abstract]) OR “prevention”[Title/Abstract]))

CONTRIBUTIONS OF AUTHORS

SH drafted the protocol. All authors participated in reviewing and editing as necessary the manuscript. All authors read and approved the final manuscript.

DECLARATIONS OF INTEREST

SH - none.

CK - none.

RG - none.

MF - none.

CM - none.

CDW - none.

SC - none.

SOURCES OF SUPPORT

Internal sources

- No sources of support supplied

External sources

- Health Research Board, Ireland.

Dr. Hayes has been awarded a two-year part-time Fellowship from the Irish Health Research Board to complete this Cochrane Review protocol and subsequent review.