Balance training interventions for balance impairment and function in people with multiple sclerosis: a systematic review protocol

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Review question/objective

The aim of this systematic review is to establish whether balance training is an effective intervention for improving balance related outcomes in ambulant people with multiple sclerosis (MS).

The review will seek to answer the following specific questions:

In a population of ambulant people with MS, does a program of balance training exercises:

1. influence outcome measures relating to balance impairment?
2. change outcome measures relating to balance-related activity limitation?
3. impact outcome measures relating to social participation?
4. change the incidence of falls?
5. have any adverse effects?

Background

Multiple sclerosis is a chronic, progressive neurological condition, characterized by autoimmune mediated inflammation and demyelination of the central nervous system. The precise etiology of MS remains unclear but appears to be multifactorial. A clear genetic predisposition for development of MS exists, however this only accounts for part of the susceptibility. The incidence of relapsing-remitting MS is 2.5 times higher in females than males. A number of predominantly viral, infectious agents have been linked with MS, although none conclusively. It is thought that an interaction between an endemic infectious agent and genetic predisposition may explain the increase in incidence of MS associated with extremes of latitude.
In the majority of people (80%), MS follows a relapsing-remitting course of exacerbation and recovery during which disability may accumulate through residual impairments from periods of relapse. Relapsing-remitting MS is typically followed by a secondary progressive stage of slowly progressing disability associated with increasing axonal damage. A minority of patients (15%) experience a primary progressive disease course characterized by gradual deterioration from the time of diagnosis without periods of relapse. Unlike relapsing-remitting MS, this disease pattern has an equal gender distribution and is not responsive to immunomodulatory therapy. Around 5% of people with MS follow a progressive relapsing pattern of both insidiously progressive disability and discrete exacerbations.2

The incidence of MS in the UK is 5.5 new cases per 100,000 people each year.3 The prevalence of MS in the population has varied in epidemiological studies but the average has been estimated at 110 per 100,000 in England and Wales, a total of around 60,000 people.4 Multiple sclerosis carries a high societal cost both from direct health and social care costs and indirect costs such as lost productivity resulting from loss of employment of the person with MS or their family and friends. Annual costs per person with MS in 2010 were estimated to be $41,335 globally and over $48,000 in the UK.5 Increased costs due to MS are significantly correlated with greater disability and reduced quality of life.6 Both disability7 and quality of life8,9 are characterized by mobility limitations. Over 90% of people with MS experience reduced mobility10 and preservation of mobility is viewed as the highest clinical priority for people with MS.11

Multidisciplinary management of people with MS is imperative to achieve optimal outcomes.12 Medical management of MS currently consists of three major components:12

• Immunomodulatory disease-modifying therapies that aim to reduce relapse rates in relapsing-remitting MS but do not prevent progression or affect overall disability
• High-dose steroids to manage acute relapse exacerbations and speed up recovery but do not result in improvements in functional outcomes
• Multidisciplinary management plans to manage symptoms such as spasticity, increased fatigue and bladder and bowel dysfunction.13

Physiotherapy is a key component of multidisciplinary rehabilitation after an acute relapse and an ongoing maintenance programme.12 Interventions are generally based on patient-centred goals and may address difficulties with social participation and functional activities as well as specific impairments, such as weakness, fatigue or spasticity.

Balance is a fundamental motor skill that is a prerequisite for mobility tasks such as walking and transferring.14 It is defined as a person’s ability to maintain their projected centre of mass within the manageable limits of their base of support (static balance) or while in transit to a new base of support (dynamic balance).14 Balance is a complex multifactorial motor skill requiring integration of sensory information from the visual, vestibular, somatosensory and proprioceptive systems, selection of appropriate balance strategies through central processing and the execution of the balance strategy via neuromuscular responses to maintain postural stability.15

The complex nature of balance control means that any combination of motor, sensory, vestibular or cognitive impairments can affect a person’s ability to maintain postural control.16 In people with MS, balance impairment is correlated with impairments such as strength,17 foot sensation18 and
spasticity\textsuperscript{19} and is concomitant with gait impairment.\textsuperscript{20} Balance is commonly affected from early in the disease process,\textsuperscript{16} even in the absence of other functional limitations\textsuperscript{21} Balance impairment is a strong predictor of falls in people with MS.\textsuperscript{22} Falls are experienced by around 50\% of people with MS annually\textsuperscript{22,23} and carry an increased risk of fracture compared to the general population.\textsuperscript{24,25}

Balance strategies may be adaptive or anticipatory mechanisms that vary according to the individual, the task and the environment.\textsuperscript{15} Balance training covers a range of interventions focused on providing patients with the opportunity to practice and develop strategies to maintain balance in a variety of contexts.\textsuperscript{26} Exercises may be static or dynamic and require the individual to select and activate neuromuscular responses in an attempt to maintain their centre of gravity within their base of support or during transit to a new base of support. Balance may be challenged by real or threatened perturbations that are evoked by anticipation of or resulting from the action of external forces, self-generated movement of the individual's body, or movement of the environment. The selection of balance strategies may be challenged further by removing part of the sensory information used to generate the motor response, such as by exercising with closed eyes or standing on an unstable surface. Alternatively, the processing of sensory information may be challenged by requiring another cognitive task to be completed simultaneously. Exercises may be done individually or in a class, and may involve equipment such as wobble boards, virtual reality systems and movable platforms or may consist of choreographed movements such as Tai Chi or dance.

Balance is a learnt motor skill, amenable to training.\textsuperscript{14} Balance training has been shown to be effective in improving balance in healthy adult\textsuperscript{27} and elderly\textsuperscript{28} populations. Although balance impairment in MS may result from intractable impairments to the sensory, cognitive or motor elements of balance control, balance control strategies are highly adaptable. Balance training has the potential to improve the ability to make postural corrective responses through improved intersensory interaction\textsuperscript{29} and neuromuscular coordination and adaptive neural modifications at both spinal and cortical levels.\textsuperscript{30} Balance training may allow people with MS to maximize the unaffected control mechanisms and hone their ability to select and action neuromuscular responses in a timely manner to respond to perturbations. In trials of populations with similarly permanent impairments that impact on their balance, such as Parkinson's Disease,\textsuperscript{31} stroke,\textsuperscript{32} peripheral neuropathy\textsuperscript{33} and vestibular schwannoma surgery,\textsuperscript{34} balance training has resulted in improvements in balance.

A systematic evaluation of the evidence for the effectiveness of balance training for people with MS has not been conducted previously. A systematic review into the effectiveness of all forms of exercise in MS did not draw any conclusions regarding the effectiveness of exercises focused on balance.\textsuperscript{35} However, recent trials of specific balance training interventions for people with MS conducted since the search period of Rietberg et al.'s review\textsuperscript{35} have reported positive results\textsuperscript{36,37} and therefore a systematic review of effectiveness is warranted. A systematic review of balance training as opposed to all exercise interventions provides a more focused review question that allows the question of effectiveness to be predicated only on outcome measures relevant to the intervention, increasing the likelihood of a valid and clinically useful conclusion.

**Keywords**

Multiple Sclerosis; Balance; Exercise; Balance training
Inclusion criteria

Types of participants

This review will consider studies that include adults aged 16 years or older with a confirmed diagnosis of MS according to the McDonald criteria. Participants should be independently ambulatory (equivalent to an Expanded Disability Severity Scale score of less than 6), and are free from acute exacerbation.

Types of interventions

This review will consider studies that evaluate balance training exercise interventions. Balance training is defined as exercises in which participants use voluntary muscle activity to achieve the goal of maintaining their centre of gravity within manageable limits of their base of support or in transition to a new base of support. Exercises may include maintaining balance in response to an external force, to perturbations arising from voluntary movement, or may involve maintaining balance with reduced or altered sensory input. Examples of balance training exercises include static or dynamic standing balance training, balance training with eyes closed, balance training on unpredictable surfaces, virtual reality balance training such as the Nintendo Wii Fit®, Tai Chi, unsupported walking, yoga or unsupported whole body vibration.

Balance training interventions may be based in community, hospital or home settings. They may be individual or group activities and may be supervised by a physiotherapist, physical trainer or peer or may be self-directed (for example following a set programme on a sheet or DVD).

The exercise intervention may include warm up/cool down and some exercises that do not meet the definition of balance training, but at least 70% of the programme contents must meet the definition of balance training for the intervention to meet the inclusion criteria. Where training protocols are included in appendices, these will be used to establish whether a training regime meets this criteria. Where a balance training intervention is described in the intervention methods but no training protocol is included, the authors will be contacted for details. Examples of exercises interventions that do not meet the definition of balance training include exercises in which the subject's body weight is not supported solely on their feet or exercises in which the subject does not need to maintain balance independently (i.e. seated exercise, exercises in water, exercises with hands-on therapist support, cycling, use of gym machines, swimming, hippotherapy).

The balance training interventions will be compared to control interventions that may include no treatment, usual health care, normal activity or other forms of exercise not targeted at training balance responses.

Types of outcomes

This review will consider studies that include outcome measures relating to balance impairment or the impact of balance impairment on function and quality of life.

Primary outcomes include any validated outcomes that measure balance impairment or activity limitation related to balance tasks. This may be a single balance task (e.g. timed unsupported stand) or combination of functional balance tasks (e.g. Berg Balance Scale). Examples include:
Balance impairment outcomes:
- Posturography
- Timed unsupported stand
- Functional Reach.

Balance-related activity limitation outcomes:
- Timed up and go
- Berg Balance Scale
- Tinetti Balance Measure
- Brunel Balance Assessment
- BESTest
- Dynamic Gait Index
- Walking speed i.e. 10-meter walk test (timed walking distance outcomes such as the Six Minute Walk Test will not be included as they are influenced significantly by aerobic capacity and fatigue).

Secondary outcomes include any validated outcomes that measure participation restriction related to balance. This may include balance specific outcome measures (e.g. Activity-specific Balance Confidence Scale) or more generic quality of life rating scales (e.g. SF-36).

Additional outcomes include: number of falls experienced, incidence of falls post-intervention and adverse events associated with the exercise intervention.

To ensure that outcomes were recorded at similar time points, outcomes will be grouped together into the following time points for comparison:
- Baseline
- End of intervention (immediate effect)
- 0-6 weeks following end of intervention (short-term effects)
- 7-26 weeks following end of intervention (medium-term effects)
- 27+ weeks following end of intervention (long-term effects).

**Types of studies**

The review is restricted to randomized controlled trials (RCTs) in which subjects are randomized to a treatment group or control group receiving no treatment, usual health care, normal activity or other forms of exercise not targeted at training balance responses. Trials in which there are more than one treatment group will be included. For crossover RCTs, data for the initial interventions only will be included due to the potential for long term treatment effect.
Search strategy

The search strategy aims to find both published and unpublished studies that address the review question. A three-step search strategy will be utilised in this review. An initial limited search of MEDLINE and CINAHL using the intervention keywords “balance” “balance training” “exercise” and “vestibular rehabilitation” individually combined with the population keyword “multiple sclerosis” will be used to identify relevant studies. Analysis of the title and abstract text, key words and index terms of the studies from the initial search will be undertaken to identify a comprehensive list of population and intervention specific search terms to be used in the second search. These terms will be combined with standardized search strategies for RCTs to construct the final search strategy. Both English and non-English studies will be considered for inclusion in this review as resource exists to identify and where necessary translate the key data.

A second search using all identified keywords and index terms will then be undertaken across the following databases:

- Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library, latest issue)
- MEDLINE (1996 to present)
- EMBASE (1980 to present)
- PEDro - The Physiotherapy Evidence Database (http://www.pedro.fhs.usyd.edu.au/index)
- CINAHL (1982 to present)
- AMED (1985 to present).

Following the electronic searches the reference lists of included papers will be examined for additional relevant studies and a cited reference search completed through Web of Science. Conference proceedings will be searched through the Conference proceedings Citation Index (CPCI-S) and the Science Citation Index (SCI) through ISI Web of Science.

Ongoing and Unpublished trials will be identified through a search of the following online trials registers and grey literature databases.

- Current Controlled Trials (http://www.controlled-trials.com)
- The World health Organisation International Clinical Trials Registry Platform (http://www.who.int/trialsearch)
- System for Information on Grey Literature in Europe (SIGLE) (http://www.opengrey.eu)
- Index to Theses (http://www.theses.com).

Where published data is incomplete the authors of the study will be contacted to provide further information prior to inclusion in the review.
Assessment of methodological quality

Papers selected for retrieval will be assessed by two independent reviewers for methodological validity prior to inclusion in the review using the standardised critical appraisal instrument from the Joanna Briggs Institute Meta Analysis of Statistics Assessment and Review Instrument (JBI-MAStARI) (Appendix I). Any disagreements that arise between the reviewers will be resolved through discussion, or with a third reviewer.

Data collection

Data will be extracted from papers included in the review independently by two reviewers using the standardised data extraction tool from JBI-MAStARI (Appendix II). The data extracted will include details of the balance training intervention, population, study methods and results from all relevant balance, activity and social participation outcomes that address the review question and objectives. The number of subject dropouts and reasons for dropouts will also be extracted. Where necessary, authors will be contacted to obtain missing data. Reviewers will not be blinded to the study details during data extraction.

Data synthesis

If appropriate, quantitative results of comparable studies will be pooled in a statistical meta-analysis using JBI-MAStARI. For each trial 95% confidence intervals and risk ratios will be calculated for dichotomous outcomes (i.e.: falls post intervention) and 95% confidence intervals and mean differences will be calculated for continuous outcomes (i.e.: activity rating scales such as the Berg balance scale or timed outcomes such as timed unsupported stand). Standardized Mean differences and 95% confidence intervals will be calculated when combining results from studies using different balance measures that measure the same outcome. Where possible, analysis will be based on intention to treat data. To account for any heterogeneity of the time period over which outcomes were recorded, outcome time points will be grouped together into baseline, immediate, short term, medium term and long term effect time periods as described in the inclusion criteria (above). If a trial contains multiple intervention groups, pairwise comparison of intervention groups with the control group will be used for the analysis. The same trial will not be included twice in the same meta-analysis.

Where sufficient homogeneity exists (I^2 < 50%) a meta-analysis will be conducted using a fixed effects model. As a variety of different exercise interventions may meet the intervention inclusion criteria for the review,^36,37,43,44^ where heterogeneity is substantial (I^2 > 50%) the reasons for heterogeneity will initially be explored by examining the clinical heterogeneity of the study designs.

If significant variability in the study interventions exists and there are sufficient numbers of studies using clinically similar interventions then subgroup analysis will be conducted into the different types of intervention (i.e. balance training, Tai Chi, wii, walking). Where there is no significant clinical heterogeneity and I^2 is less than 75% a meta-analysis will be conducted using a random effects model of statistical pooling.Similarly,Subgroup analysis of severity of MS characterised by EDSS score and type of MS (relapsing-remitting, primary progressive, secondary progressive, benign) will be conducted where it is possible from the data in included studies.
Where considerable heterogeneity remains (I² > 75%) and statistical pooling of intervention subgroups is not possible the findings will be presented in narrative form following the guidance in the JBI Review Manual, including tables and figures to aid in data presentation where appropriate.

Conflicts of interest

There are no conflicts of interest
References


11. Heesen C, Bohm J, Reich C, Kasper J, Goebel M, Gold SM. Patient perception of bodily functions in Multiple Sclerosis: Gait and visual function are the most valuable. Mult Scler 2008;14:988-991.


Appendix I: Appraisal instruments MASTARI Appraisal instrument

**JBI Critical Appraisal Checklist for Randomised Control / Pseudo-randomised Trial**

<table>
<thead>
<tr>
<th>Question</th>
<th>Yes</th>
<th>No</th>
<th>Unclear</th>
<th>Not Applicable</th>
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<td>1. Was the assignment to treatment groups truly random?</td>
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<td>2. Were participants blinded to treatment allocation?</td>
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<td>3. Was allocation to treatment groups concealed from the allocator?</td>
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<td>4. Were the outcomes of people who withdrew described and included in the analysis?</td>
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<td>5. Were those assessing outcomes blind to the treatment allocation?</td>
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<td>6. Were the control and treatment groups comparable at entry?</td>
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<td>7. Were groups treated identically other than for the named interventions</td>
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<td>8. Were outcomes measured in the same way for all groups?</td>
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<td>9. Were outcomes measured in a reliable way?</td>
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<td>10. Was appropriate statistical analysis used?</td>
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Overall appraisal: Include □ Exclude □ Seek further info. □

Comments (Including reason for exclusion)

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Appendix II: Data extraction instruments

MAStARI data extraction instrument

### JBI Data Extraction Form for Experimental / Observational Studies

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<td>Author</td>
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**Study Method**

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<td>Retrospective</td>
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**Participants**

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<td>Population</td>
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**Sample size**

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**Interventions**

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