|  |
| --- |
| **CRITICALLY APPRAISED TOPIC** |

**FOCUSED CLINICAL QUESTION**

|  |
| --- |
| In an adult with Multiple Sclerosis (MS) and moderate-high risk of falling, is therapeutic yoga more effective than dalfampridine extended-release for improving balance or reducing falls risk?  |

**AUTHOR**

|  |  |  |  |
| --- | --- | --- | --- |
| **Prepared by** | Ellese Nickles | **Date** | November 15, 2015 |
| **Email address** | Ellese\_nickles@med.unc.edu |

**CLINICAL SCENARIO**

|  |
| --- |
| According to the National Multiple Sclerosis Society, patients with Multiple Sclerosis often have impaired mobility due to symptoms affecting gait including weakness, spasticity, poor balance, and fatigue. Therapeutic yoga has been demonstrated to improve balance in healthy populations and older adults and may represent a beneficial form of physical activity for those with MS. 1–3Dalfampridine extended release (Ampyra) is a drug that has been shown to improve gait speed in people with multiple sclerosis. It is currently being prescribed for patients with gait difficulties. I am interested to know if research exists showing dalfampridine is effective for decreasing falls risk. Thus, physical therapists and other clinicians treating patients with MS who demonstrate balance and mobility impairments would benefit from the ability to compare the effects of dalfampridine extended-release to yoga training in reducing falls risk or improving balance in individuals with MS.  |

**SUMMARY OF SEARCH**

[Best evidence appraised and key findings]

|  |
| --- |
| * 3 electronic databases were searched yielding a total of 8 studies selected that met the inclusion and exclusion criteria including 5 randomized controlled trials (RCT), and 3 prospective cohort/quasi experimental research studies. Although they did not meet the criteria for this search, two additional research articles were evaluated in order to complete 10 reviews relevant to the clinical question. The two articles were systematic reviews of available research regarding exercise therapy for fatigue in multiple sclerosis and nonpharmacological interventions for spasticity.
* There were no studies that directly compared the effects of dalfampridine extended-release and yoga interventions. Thus, the best evidence for each of the two interventions was reviewed separately.
* Three studies, including two RCTs evaluating the effects of yoga training and one RCT evaluating the effects of dalfampridine extended release were chosen as “best evidence”. Evidence from these three highest quality studies shows that:
* Use of oral dalfampridine extended-release results in improved balance and mobility. Additionally, evidence shows the drug is safe for patients with MS.
* For individuals with MS who have significant mobility impairments and require use of walking-aids, yoga training interventions delivered in the community improves balance.
* There is significant heterogeneity of research protocols. Overall future needs of research include RCTs of large sample size and high methodological rigor to compare the impact of dalfampridine extended-release with that of yoga training.

Very good summary |

**CLINICAL BOTTOM LINE**

|  |
| --- |
| Current best evidence suggests that both the use of dalfampridine extended-release and yoga training protocols result in improvements in balance, however the two interventions have not been directly compared in the literature. Both administration of dalfampridine as directed by a physician or therapeutic yoga interventions delivered through specially trained yoga teachers are appropriate alternatives to traditional physical therapy interventions focused on treating balance impairments in the MS population. A PT could use this evidence to justify and develop a group yoga class or ongoing yoga training program in the clinic for the MS population and initiate the program utilizing the techniques discussed in the research presented by Ahmadi and Hogan.4,5  |

|  |
| --- |
| ***This critically appraised topic has been individually prepared as part of a course requirement and has been peer-reviewed by one other independent course instructor*** |

**SEARCH STRATEGY**

|  |
| --- |
| **Terms used to guide the search strategy** |
| **P**atient/Client Group | **I**ntervention (or Assessment) | **C**omparison | **O**utcome(s) |
| “Multiple Sclerosis” OR MS“Balance deficits”“Falls risk”“demyelinating disorder” | Ampyra OR “Dalfampridine Extended release”“Potassium channel blockers” Fampridine 4-aminopyridine | “Therapeutic Yoga”Yoga“group exercise” | BalanceFall WalkAmbulat\*Gait |

**Final search strategy:**

*Show your final search strategy from one of the databases you searched. In the table below, show how many results you got from your search from each database you searched.*

**PubMed:**

#1 Search Multiple Sclerosis OR MS OR demyelinating disorder

#2 Search Ampyra OR Dalfampridine OR potassium channel blocker\* OR Fampridine OR 4-aminopyridine

#3 Search Yoga

#4 Search Balance OR Fall\*

#5 Search #1 AND #2 AND #4

#6 Search #1 AND #3 AND #4

# 7 Search #5 AND #6

|  |  |  |
| --- | --- | --- |
| **Databases and Sites Searched** | **Number of results** | **Limits applied, revised number of results (if applicable)** |
| **PubMed** | # 5: 33 results# 6: 16 results# 7: 0 results | Revised search #5: added limits to Humans and articles published within last 10 years. Yielded 2 results. Neither met criteria. Revised search #6: added limits to Humans and articles published within last 10 years. Yielded 3 results. |
| **CINAHL** | #5: 1 result#6: 5 results#7: 0 results | #5 I modified and searched for similar articles using “smartText searching” + the following limiters: Full Text, Published Date (2000-2015), Source Types (academic journals), Subject Major Heading (multiple sclerosis, balance, postural), and Language (English). This yielded 26 articles. However, none of which included either yoga or the drug intervention.  |
| **Cochrane Library** | #5: 6 results# 6: 16 results#7: 0 results | For #5, 5/6 of the results were from the same study and were published conference abstract. |

## INCLUSION and EXCLUSION CRITERIA

|  |
| --- |
| **Inclusion Criteria** |
| * Randomized controlled trials, controlled trials, systematic reviews
* A study which included MS patients either taking Ampyra or participating in a yoga exercise program
* Measured balance and/or falls risk before and after intervention
 |
| **Exclusion Criteria** |
| * Abstracts, guidelines, narrative review articles, dissertations.
 |

**RESULTS OF SEARCH**

**Summary of articles retrieved that met inclusion and exclusion criteria**

*For each article that meets your inclusion and exclusion criteria, score for methodological quality on an appropriate scale, categorize the level of evidence, and note the study design (e.g., RCT, systematic review, case study).*

|  |  |  |  |
| --- | --- | --- | --- |
| **Author (Year)** | **Study quality score** | **Level of Evidence** | **Study design** |
| Ahmadi A, Arastoo AA, Nikbakht M, Zahednejad S. 20134 | PEDRO: 7 | 1b | RCT |
| Coote S, Garrett M, Hogan N, Larkin A, Saunders J. 20096 | PEDRO: 3 | 1b | RCT – Multi center, single blind, block randomized controlled trial |
| Coote S, Hogan N Franklin S. 20145 | PEDRO: 6 | 1b | RCT |
| Coote S, Hogan N Franklin S. 2013 7 | PEDRO: 4 | 1b | RCT |
| Hupperts R, Lycke J, Short C, et al. 20158 | PEDRO: 10 | 1b | RCT- multi site, double blind, randomized. |
| Prosperini L, Gianni C, Fortuna D, Marchetti MR, Pozzilli C. 20149 | Downs and Black: 16/29 | 2b | Observational, nonrandomized design, small sample size |
| Salgado BC, Jones M, Ilgun S, McCord G, Loper-Powers M, van Houten P. 2013 10 | Downs and Black: 19/29 | 2b | Nonrandomized cohort study |
| Senem Guner, Fatima Inanici. 201411 | Downs and Black: 15/29 | 2b | Cohort study: 2 groups, 1 group MS and another group healthy volunteers.  |
| Heine M, van de Port I, Rietberg MB, van Wegen EEH, Kwakkel G. 201512 | AMSTAR 11/11 | 1a | Systematic Review |
| Amatya B, La Mantia L, Demetrios M, Wade DT. 201313 | AMSTAR 11/11 | 1a | Systematic Review |

*(All 10 articles should appear in the reference list at the end)*

**BEST EVIDENCE**

The following 3 studies were identified as the ‘best’ evidence and selected for critical appraisal. Reasons for selecting these studies were:

|  |
| --- |
| * Hupperts R, Lycke J, Short C, et al. 20158: This was the best available evidence for the effects of dalfampridine on balance in individuals with multiple sclerosis given the larger sample size, multi-site testing, and randomized controlled research design.
* Hogan N, Kehoe M, Larkin A, Coote S. 20145: Larger sample size, clearly defined inclusion and exclusion criteria and evaluates the effectiveness of yoga intervention in more severely disabled patients (those who require use of bilateral
* Ahmadi A, Arastoo AA, Nikbakht M, Zahednejad S. 20134. This study was chosen to include a second RCT for yoga intervention effect on balance in individuals with multiple sclerosis, from a different group of researchers. Additionally, the outcomes measures used to assess were appropriate and the Pedro score was higher than other available evidence.
 |

**SUMMARY OF BEST EVIDENCE**

**(1) Description and appraisal of “Prolonged-Release Fampridine and Walking Balance in MS: Randomised Controlled MOBILE Trial” by Hupperts R, Lycke J, Short C, Gasperini C, McNeill M, Medori R, Tofil-Kaluza A, Hovenden M, Mehta LR and Elkins J (2015)**8

|  |
| --- |
| **Aim/Objective of the Study/Systematic Review:** |
| The purpose of this study was to determine the effects of prolonged-release dalfampridine on participants taking prolonged-release dalfampridine compared with a placebo group in terms of self-assessed walking disability, dynamic and static balance, subjective well-being and participants’ global impression of change in walking. Additionally, this study aimed to evaluate safety and tolerability of prolonged-release dalfampridine. |
| **Study Design**[e.g., systematic review, cohort, randomised controlled trial, qualitative study, grounded theory. Includes information about study characteristics such as blinding and allocation concealment. When were outcomes measured, if relevant]Note: For systematic review, use headings ‘search strategy’, ‘selection criteria’, ‘methods’ etc. For qualitative studies, identify data collection/analyses methods. |
| * This was a multicentre randomized controlled trial.
* Randomized allocation: Subjects were randomly assigned using a centralized “Interactive Web Response System” to be in either a dalfampridine group (intervention/experimental group) or a matched placebo group (control group).
* Double blind: Both the subjects and investigators/assessors were blinded to group allocation.
* Outcomes measured were collected on the initial screening day and at weeks 2,4,8,16,20, 24, and 26 (2 weeks after patients had ceased treatment).
* Sample consisted of 132 participants screened over a 14 day period
* Intention to treat was accounted for and all 132 participants involved in the study received at least one treatment (one dose), and one post-baseline assessment.
* The study was performed over the time period from August 30, 2012 (when the first patient was treated) and August 8, 2013 (when the trial ended).
 |
| **Setting**[e.g., locations such as hospital, community; rural; metropolitan; country] |
| This was a multisite study, which included 24 sites in six countries. Sites for clinical trial locations included the following cities: * Belgium: Arth, Brugge, Brussels, Leuven, and Yvoir
* Canada: Halifax (Nova Scotia), London (Ontario), Gatineau (Quebec), Greenfield Park (Quebec), and Montreal (Quebec).
* Italy: Ancona, Brescia, Empoli, Palmero, and Roma
* The Netherlands: Breda, and Sittard-Geleen
* Sweden: Goteborg, and Stockholm
* United Kingdom: London
 |
| **Participants**[N, diagnosis, eligibility criteria, how recruited, type of sample (e.g., purposive, random), key demographics such as mean age, gender, duration of illness/disease, and if groups in an RCT were comparable at baseline on key demographic variables; number of dropouts if relevant, number available for follow-up]Note: This is not a list of the inclusion and exclusion criteria. This is a description of the actual sample that participated in the study. You can find this descriptive information in the text and tables in the article. |
| * 132 people were recruited to participate in this study. 132 participants were included in the intention to treat analysis
* Inclusion criteria: individuals aged 18-70 years old, with diagnoses of all four types of MS >/= 3 months duration (Researchers used revised McDonald criteria for diagnosis) and Expanded Disability Status Scale score: between 4.0-7.0.
* Exclusion criteria: Treatment with 4-aminopyridine or 3,4-diaminopyridine </= 30 days prior to screening, known allergy to pyridine-containing substances, any history of seizure, epilepsy or other convulsive disorder; renal impairment (creatine clearance < 80 ml/min); onset of MS exacerbation </= 60 days before screening and body mass index >/= 40 kg/m2. (p. 2)
* Key demographics:
* Mean age: 49.8 (age ranged from 18 to 70 years old)
* Gender: 54% female
* Mean BMI: 26.6
* Mean duration of illness/disease (since first diagnosis): 11.6 years
* Type of MS: RRMS (33%), SPMS (52%), PPMS (18%), PRMS (2%)
* Baseline information:
* Mean EDSS (5.7)
* Median TUG speed placebo group (0.32 m/s); dalfampridine group (0.38 m/s)
* Median BBS placebo group (41 points); dalfampridine group (43.8 points)
* Median MSIS-29 PHYS score placebo groups (57.5 points); dalfampridine group (50 points)
* Participants were comparable between treatment groups in terms of key demographics as well as baseline outcome measures including MSWS-12 score, TUG speed, Berg Balance Scale score, MSIS-29 PHYS score, EQ-5D-5L utility score and EQ-5D-5L VAS.
* The authors reported similar attrition rates in each group (approximately 81% completed treatment). The authors also described reason for dropouts or discontinuation, which were similar in between groups.
 |
| **Intervention Investigated**[Provide details of methods, who provided treatment, when and where, how many hours of treatment provided] |
| *Control* |
| * 64 Patients were allocated to the control group and received placebo treatment.
* No information was provided regarding administration of the placebo medication or how the researchers ensured that participants were compliant. However, they did report that treatment kits were assembled and labelled with participant identification numbers in order to maintain blinding of both investigators and the participants when kits were provided.
* Of the 64, 52 completed treatment. Of the 12 who discontinued treatment 5 did so due to adverse effects, 1 due to lack of efficacy, 4 because “CrCl out of range, and 2 because another medication which was unacceptable for the study was required.
* 81% of those allocated to the control group followed up.
 |
| *Experimental* |
| * 68 participants were randomized to the experimental group, assigned to receive extended release dalfampridine (10 mg tablets, twice daily).
* No information was provided regarding administration of the medication or how the researchers ensured that participants in the experimental group were compliant. The same protocol for kit assembly and distribution was performed for the experimental group as for the control group to ensure double blind experimental set up.
* Of the 68 participants analysed (intention to treat), 55 completed treatment. Of those who discontinued treatment, 7 did so due to adverse effects, 1 due to lack of efficacy, 2 due to consent withdrawal, 1 because CrCl was out of range and 2 because they were required to taken an unacceptable concomitant mediation.
* 80.9% completed follow-up.
 |
| **Outcome Measures** (Primary and Secondary)[Give details of each measure, maximum possible score and range for each measure, administered by whom, where] |
| Outcomes measures were assessed at screening, day 1 and weeks 2,4,8,12,16, 20, 24, and 26. The authors do not explicitly report who performed clinical assessments but do state in their trial design that “all patients and trial staff, including the principal investigator, were blinded to patient treatment assignments” (p. 2)**Berg Balance Score (BBS):** 14* Purpose of the test: BBS is used to measure static balance.
* The test involves 14 tasks and the assessor is to rate performance on a scale from 0 points (unable to perform) to 4 points (able to perform independently). All points are summed for a total score, where a higher score indicates better balance. If two or more questions were missing for an assessment, the score was set to missing. If less than 2 questions were missing, the “respondent specific mean score” was used.
* Minimum score: 0 points
* Maximum score: 56 points

**TUG test** * Purpose of the test: assess functional mobility and dynamic balance.
* The test measures the time required for a patient to stand from a standard arm chair, walk 3 meters (at a comfortable and safe pace), turn around, return to the chair and sit down. Subjects are allowed use of walking aides that they use in their daily lives. The test is quick (can be performed in less than 5 minutes), and requires minimal equipment (a standard armchair and a stopwatch).
* Score recorded as time in seconds.

**MSWS-12*** The purpose of this questionnaire is to assess patients’ perceived limitations of mobility due to MS.
* The patient is asked to rate 12 items based on their experiences during the previous two weeks. The scale ranges from 1, indicating no limitations, to 5 indicating severe limitations/extremely limited.
* Minimum score: 1 points
* Maximum score: 60 points
* For this study the scale was converted to a percentage of 100.

**Seven-item Patient Global Impression of Change (PGIC) scale: (21):** * The Purpose of the PGIC scale is to assess the subjective perception of how the drug has affected walking over the previous seven days.
* The PGIC consists of 7 questions and patients are asked to rate from 1 to 7 where 1 indicates walking is much worse and 7 indicates walking is very much improved).
* Minimum score: 1 points
* Maximum score: 60 points
* The authors transformed the scale to 0-100 where reduction in score was associated with improvement.

**29-item Multiple Sclerosis Impact Scale (MSIS-29) physical subscale:** * The purpose of this self-administered questionnaire is to assess physical and psychological impact of MS on a person’s life.
* The questionnaire consists of two subscales including a physical subscale (with 20 items) and a psychological subscale (with 9 items). Responses are given on a Likert scale from 1 to 5. Scoring involves calculating the total sum for all 29 questions. Higher scores indicate that MS has a greater impact on a person’s life (greater degree of disability) and was considered to indicate poorer health in this study.
* If less than 50% of the items on the physical subset were missing, the mean of non-missing data was used for those missing items. If more than 50% of the items were unanswered, the measure was set to missing.
* Minimum score: 29 points
* Maximum score: 145 points

**EuroQol-5 Dimensions 5-level (EQ-5D-5L):** * The Purpose of this test is to evaluate health based on five dimensions including mobility, self-care, usual activities, pain/discomfort and anxiety/depression.
* The questionnaire contains questions and a visual analogue scale (VAS) in which participants rate each item from 1-5 and the VAS was scored from 0 (being worst health) to 100 (being best health).
* The researchers derived a utility score from 1-5 (no problem-very severe problem) based on responses.

**Safety and Tolerability:** * In order to measure safety of the drug, the researchers performed a physical examination, vital sign measurements and electrocardiograms as well as accounting for adverse events during the trial.
* The authors reported adverse events and serious adverse events starting day 1 up to 26 weeks.
 |
| **Main Findings**[Provide summary of mean scores/mean differences/treatment effect, 95% confidence intervals and p-values etc., where provided; you may calculate your own values if necessary/applicable] |
| * The authors state that they used descriptive statistics to summarize final data instead of a formal statistical hypothesis test. Thus, they calculated changes from baseline at each visit and reported median change from baseline with 95% confidence intervals. Change scores are estimated from graphical presentation of data (actual values not reported)
* **MSWS-12**: The investigators calculated mean change from baseline at thresholds < 1 point improvement, no change, worsening and thresholds including >/= 1 … to >/= 10 points (by 1 point increments). (p. 3)

The authors reported statistically significant differences in the percentages of participants who reached thresholds of >/= 7 (p = 0.0275), >/= 8 (p = 0.0153) and >/= 9 (p=0.0088) (p.5)Median change from baseline for the control group: 0-(~0.5)= ~ -0.5 pointsMedian change for experimental group: 0- (~ - 5) = ~ 5.0 pointsDifference in median change between groups: -.5 – 5.0 = 4.5 points* **MSWS-29:**

Median change from baseline for the control group: 0-(~1)= ~ - 1.0 pointsMedian change for experimental group: 0- (~ - 4) = ~ 4.0 pointsDifference in median change between groups: -1 – 4 = 3 points* **TUG:** Mean percentage changes from baseline were reported for the following thresholds: </= 0% (worsening or no change), > 0% (any improvement), and increasing thresholds from >/= 10% improvement to >/= 40% improvement (by 5% increments)(p.3). The authors reported statistically significant differences in the percentages of participants who reached thresholds of >/= 10% (p = 0.0021) and >/= 15% (p=0.0262) (p.5)

Median change from baseline for the control group: 0-(~ 3)= ~ - 3.0 secondsMedian change for experimental group: 0- (~ 11) = ~ - 11.0 secondsDifference in median change between groups: (-3) – (-11.0) = ~ -8 seconds * **BBS:** Both groups demonstrated improved BBS scores from baseline as early as the 2-week assessment (first assessment following baseline measurements). However, greater improvements (based on median scores between groups) were seen in the experimental group when compared with the control group.

The effect size for control group was 0-1 = 1 pointThe effect size for the experimental groups was 0-3 = 3 pointsDifference between groups was 1-3 = 2 points* **PGIC**: A statistically significant difference in percentage of patients who showed improvement on the PGIC at week 2 assessments was reported (p= 0.023), with greater percentage shown in the treatment group.
* **EQ-5D-5L**: The authors found no difference between control and experimental groups and reported the median treatment difference for the EQ-5D-5L VAS as well as the utility index to be 0.00 (with a 95% confidence interval). (p. 5).
* **Adverse Effects**: The percentage of participants with adverse effects was similar between groups (77% for the control group and 75% for the experimental group) (p.5)

The authors performed *post hoc* statistical testing to compare treatment effects between the experimental and control groups for the MSWS-12 and TUG outcomes measurements. For the MSWS-12, the authors used a previously determined clinically meaningful difference of >/= 4-6 points over three months. The authors determined the percentage of patients in each group reporting improvement in PGIC after two weeks of treatment using a Chi-square test. Additionally, they compared various thresholds of improvement for the outcomes of TUG, BBS, MSWS-12 and MSIS-29. The adjusted for baseline using logistic regression for the MSWS-12 and TUG scores. In order to assess for magnitude of treatment effect over time, the authors also performed a post hoc analysis for the PGIC using a chi-square test at 2 weeks from start of treatment.  |
| **Original Authors’ Conclusions**[Paraphrase as required. If providing a direct quote, add page number] |
| The experimental group showed greater improvements in balance and mobility based on improved TUG speed, BBS total scores, and MSWS-12 score. However, these results did not carry over and score improvements declined almost to baseline at the 26-week follow-up visit once the drug use was discontinued. The authors concluded that based on improvements in measures of mobility and balance, that dalfamptridine extended release is safe and beneficial for patients with MS.  |
| **Critical Appraisal** |
| **Validity**[Identify the strengths and limitations of the study, including potential sources of bias. Comment on the overall methodological quality (including the score) as you determined from your assessment of the article. Comment on anything you believe was missing in the paper.] |
| Pedro scale score: 10/11 based on Eligibility Criteria: Yes; Random Allocation: Yes; Allocation Concealment: Yes; Groups Similar at Baseline: Yes; Subject Blinding: Yes; Therapist Blinding: Yes; Assessor Blinding: Yes; Outcomes for 85% of participants: No; Intention to Treat: Yes; Between-group Statistical Comparisons: Yes; Point and Variability Measures: Yes.This study design demonstrated high internal validity such that the results of this study can be trusted. The authors attempted to avoid bias through blinding of subjects and assessors. They also described randomization and concealment of group allocation and provided evidence that the groups were similar at baseline with key demographic and assessment measures. There was also high external validity of the study, which refers to the generalizability of results or meaningfulness of the study. The authors presented results using appropriate and validated outcomes measures and provided adequate statistical analysis for comparison between experimental and control group. Unfortunately, attrition was an issue in this study. This is in part due to the nature of the relapsing remitting MS. For example, some of the subjects had to discontinue participation in the study due to health issues related to MS, conflicting or contraindicated medications. Importantly, the authors provide excellent details on reasons for discontinuation of participation and these are almost identical between the two groups.  |
| **Interpretation of Results**[This is YOUR interpretation of the results taking into consideration the strengths and limitations as you discussed above. Please comment on clinical significance of effect size / study findings. Describe in your own words what the results mean.] |
| The improvements seen in patients taking dalfampridine were evident as early as two weeks, at the first assessment session. Furthermore, results of this study showed greater improvements in the experimental group, based on reported median change from baseline for TUG, MSIS-29, MSWS-12, and BBS. However, these positive effects did not continue once the use of dalfampridine was discontinued. This is important because it indicates that patients must continue to take the drug in order to experience benefit. This could be problematic if the drug is cost prohibitive or if there is a change in the patient’s medical status in which they must take a contraindicated medication. The authors performed a priori calculation using a bootstrapping statistical assessment from sampled data of a previous study. The researchers estimated that a sample size of 120 patients (60 per group) would result in 84% of samples would be within 8% of true proportion. The authors reported statistically significant differences between groups for a number of outcomes suggesting that dalfampridine will produce improvements in walking ability and balance for people with MS. Because the patient characteristics were comparable at baseline and the numbers of participants who dropped out or had to discontinue were the same, as well as the fact that the reported reasons for discontinuation were similar between groups, we can assume that there are little adverse effects of the drug compared to placebo and therefore that the drug is likely to be tolerable and safe for use in patients with MS. The authors did not provide specific outcome data scores and therefore interpretation of effect size was difficult to perform. This information was only provided in graph form and thus, calculations had to be approximated. Furthermore, the authors did not use a formal statistical hypothesis and therefore it appears the investigators performed data dredging to some extent. |

**(2) Description and appraisal of “The Effect of Community Exercise Interventions for People with MS Who Use Bilateral Support for Gait” by Hogan N, Kehoe M, Larkin A, and Coote S. (2014)**5

|  |
| --- |
| **Aim/Objective of the Study/Systematic Review:** |
| The purpose of this study was to determine the effectiveness of community based yoga and physiotherapy interventions delivered in community settings for individuals with MS who use bilateral support for gait. The study aimed to evaluate balance and mobility outcomes.  |
| **Study Design**[e.g., systematic review, cohort, randomised controlled trial, qualitative study, grounded theory. Includes information about study characteristics such as blinding and allocation concealment. When were outcomes measured, if relevant]Note: For systematic review, use headings ‘search strategy’, ‘selection criteria’, ‘methods’ etc. For qualitative studies, identify data collection/analyses methods. |
| * This was a multicentre, single blind, block randomized controlled trial
* Participants were recruited from 10 regional offices of MS Ireland and screened for eligibility via telephone calls.6
* Randomized allocation: Subjects were block randomized by the national coordinator in MS Ireland to be in one of three intervention groups (individual physiotherapy, group physiotherapy, or yoga training) or a control group. Importantly, participants were not blinded to group allocation and some of the participants allocated to the yoga and control groups demanded to receive physical therapy. These participants were therefore randomized to either group or individual physiotherapy interventions.
* Repeated measure design: Outcomes measured were collected at baseline and at post intervention follow up at 12 weeks.
* Sample consisted of 146 participants.
 |
| **Setting**[e.g., locations such as hospital, community; rural; metropolitan; country] |
| Intervention locations included classes and physiotherapy sessions in 10 regions in Ireland.  |
| **Participants**[N, diagnosis, eligibility criteria, how recruited, type of sample (e.g., purposive, random), key demographics such as mean age, gender, duration of illness/disease, and if groups in an RCT were comparable at baseline on key demographic variables; number of dropouts if relevant, number available for follow-up]Note: This is not a list of the inclusion and exclusion criteria. This is a description of the actual sample that participated in the study. You can find this descriptive information in the text and tables in the article. |
| * 161 subjects were recruited and assessed for eligibility. 15/161 did not meet selection criteria and 146 were included in the study and randomized into one of four groups: group physiotherapy, individual physiotherapy, yoga, and control groups.
* Inclusion criteria: “MS diagnosis confirmed by a consultant physician” (p.2)
* Exclusion criteria: Exacerbation of symptoms due to relapse or initiated steroid treatment within 12 weeks, pregnant at time of referral, or < 18 years old.
* Key demographics:
* Age in semi-interquartile range: Group physiotherapy = 57 years old, individual physiotherapy= 52 years old, Yoga = 58 years old, and control = 49 years old.
* Gender: 36% male, 64% female
* Duration of illness/disease: range of 10-18 years with p value across all groups = 0.002.
* Groups were similar at baseline in terms of gender, Guys Neurological Disability Scale, Type of MS, MSIS, BBS, and 6MWT.
* Groups differed by age at baseline in that the “control group participants were significantly younger and had a shorter time since diagnosis” (10 years vs. 18, 13, and 15). Also, the yoga group reported less impact of fatigue at baseline (30.4 points vs. 40.7, 46.7, and 47 points). (p. 4)
* Number of dropouts: 35/146 participants were lost to follow up at week 12.
* Overall attrition rate was 22.32% and rate of dropouts were similar across groups (72% for group physiotherapy, 77% for individual physiotherapy, 81% for yoga group, and 79% for control group). Reasons for dropouts were similar across groups. (p. 4)
 |
| **Intervention Investigated**[Provide details of methods, who provided treatment, when and where, how many hours of treatment provided] |
| *Control* |
| Control group did not receive any exercise intervention for the 12 weeks. Participants were offered treatment of their choice once the control period ended.  |
| *Experimental* |
| 1. Group Physiotherapy Intervention
* Consisted of 1-hour self-paced circuit style classes. The exercise program was based on previously established falls prevention interventions that have demonstrated positive outcomes in older adults and individuals with MS. The authors provide a protocol of six exercises (sit to stand, squats, heel raises, step ups, side stepping and tandem stance) with recommended progressions for each. Participants were asked to perform sets of 12 repetitions and progressed the exercise when able to complete 3 sets of 12.
* Group physiotherapy frequency was 1 x/ week and duration was 10 weeks.
* Treatment was provided by chartered physiotherapists.
1. Individual Physiotherapy Intervention:
* Consisted of individualized physical therapy treatment sessions. Exercise program and physical therapy plan of care was based on patient problems list and physical therapy goals. ¾ therapists provided strength exercises similar to those given in the group physiotherapy intervention. Additional exercises were also included (lower back exercises, walking, stretching, and bridging exercises)
* Individual physiotherapy frequency was 1 x/ week and duration was 10 weeks.
* Treatment was provided by chartered physiotherapists.
1. Yoga Intervention:
* Consisted of 1-hour yoga classes. The content of yoga classes components included relaxation, meditation, breathing techniques, and stretching. The protocol for classes was not specified in order to represent normal practice, but instructors recorded a log of each session for documentation.
* Yoga intervention frequency was 1 x/ week and duration was 10 weeks.
* Yoga instructors who were members of the Yoga Federation of Ireland provided the intervention.
 |
| **Outcome Measures** (Primary and Secondary)[Give details of each measure, maximum possible score and range for each measure, administered by whom, where] |
| Assessors who performed outcome measurements and clinical assessments were trained in order to standardize measurements and blinded to group allocation to avoid bias. Measurements were performed at baseline (week1), post-intervention (week 12) and follow-up (week 24).6 **29-item Multiple Sclerosis Impact Scale (MSIS-29v2) physical and psychological subscale:** 6* The purpose of this self-administered questionnaire is to assess physical and psychological impact of MS.
* The questionnaire consists of two subscales including a physical subscale (with 20 items) and a psychological subscale (with 9 items). Responses are given on a Likert scale from 1 to 5 points.
* Scoring involves calculating the total sum for all 29 questions. Higher scores indicate that MS has a greater impact on a person’s life (greater degree of disability) and were considered to indicate poorer health in this study.
* Minimum score: 0 points
* Maximum score: 100 points

**Modified Fatigue Impact Scale (MFIS):**15* The purpose of this assessment is to evaluate the effects of fatigue in terms of physical, cognitive, and psychosocial functioning.
* The self-report questionnaire consists of 21 questions answered on a 5-point Likert scale.
* Scoring involves calculating the total sum for all items. Higher scores indicate greater impact of fatigue.
* MDC: 16.2
* Cut off score for clinically meaningful fatigue: 38 points
* Minimum score: 0 points
* Maximum score: 84 points

**Berg Balance Score (BBS):** 14* Purpose of the BBS test is to measure static balance.
* The test involves 14 tasks and the assessor is to rate performance on a scale from 0 (unable to perform) to 4 (able to perform independently). All points are summed for a total score, where a higher score indicates better balance. It has been validated for use in people with MS.
* Authors used cut off score of 44/56 points as indicating high risk of falls
* Minimum score: 0 points
* Maximum score: 56 points

Well-presented information in this section**Six Minute Walk Test (6MWT)**:6,16 * Purpose of the test is to assess sub-maximal aerobic capacity/endurance. This assessment has been tested in the MS population
* Participants were instructed to walk as quickly and safely as possible for six minutes and researchers recorded distance. Assistive devices can be used but should be kept consistent from test to test.
* Heart rate of each participant was recorded using a polar monitor during testing.
 |
| **Main Findings**[Provide summary of mean scores/mean differences/treatment effect, 95% confidence intervals and p-values etc., where provided; you may calculate your own values if necessary/applicable] |
| The authors used Predictive Analytic Software (PASW) Statistics 17 to analyse distribution of data. The differences between groups at baseline were analysed using ANOVA (normally distributed data), Kruskal Walllis (nonnormally distributed data), and Chi square test for independence (categorical data) (p. 3). The authors performed a post hoc analysis to compare within-group changes, which revealed that data for the MSIS-29v2 and 6MWT had skewed data that could not be analysed via parametric testing Thus, Wilcoxon Signed Rank Tests, Kruskal Wallis, and Mann Whitney U tests were used. **29-item Multiple Sclerosis Impact Scale (MSIS-29v2) physical and psychological subscale:** * Difference between median scores pre and post intervention reported for each group:
* Group physiotherapy: psychological (-3 points, P= 0.005); physical (-4.54 points, P= 0.004)
* Individual physiotherapy: psychological (-1 point, P= 0.057); physical (-4.52 points, P= 0.012
* Yoga: psychological (1 point, P=0.281); physical (1.3 points, P= 0.645)
* Control: psychological (2 points, P= 0.507); physical (-4.8 points, P= 0.08)
* Significant difference was found from baseline to post intervention measurements for the psychological component in the group physiotherapy group (P=0.005).
* No significant differences were found between groups.

 **Modified Fatigue Impact Scale (MFIS):** * Difference between median scores pre and post intervention reported for each group:
* Group physiotherapy: -5.1 points, P = 0.011
* Individual physiotherapy: -7.4 points, P= 0.001
* Yoga: 2.15 points, P=0.374
* Control: -6.4 points, P=0.062
* The control group showed similar results on MFIS as intervention groups.

 **Berg Balance Score (BBS):** * Difference between mean scores for pre and post intervention for each group:
* Group physiotherapy: 5.7 points, P = <0.0001
* Individual physiotherapy: 3.7 points, P = 0.008
* Yoga: 5.3 points, P < 0.0001
* Control: -3.1 points, P = 0.258
* All interventions showed statistically significant improvement from week 1 to week 12 on BBS as compared to the control group.
* No significant difference was found between intervention groups (p=0.242).

You have presented the key findings very clearly**6MWT**: * Median difference reported for pre and post intervention for each group:
* Group physiotherapy: 20.2 m, P = 0.08
* Individual physiotherapy: 16.2 m, P = 0.002
* Yoga: -25 m, P = 0.553
* Control: 6.5 m, P = 0.363
* Significant differences were found from baseline to post intervention measurements in the individual physiotherapy group (P=0.001)
* Percentage improvements for group physiotherapy group= 20.1% and for individual physiotherapy group = 19.4%. The yoga intervention group worsened by 35%.
 |
| **Original Authors’ Conclusions**[Paraphrase as required. If providing a direct quote, add page number] |
| The author’s findings support group and individual physiotherapy interventions consisting of balance and strengthening exercises to improve balance in individuals with MS. Specifically, the improvements seen in the BBS results demonstrate the effectiveness of all three exercise groups including yoga classes. Their findings support well-designed interventions to be delivered in community settings (home, primary care offices, community care settings). However, the authors recognize the study’s limitations and suggest that findings should be confirmed by studies with “larger, matched control groups” (p.7).  |
| **Critical Appraisal** |
| **Validity**[Identify the strengths and limitations of the study, including potential sources of bias. Comment on the overall methodological quality (including the score) as you determined from your assessment of the article. Comment on anything you believe was missing in the paper.] |
| Pedro scale score: 5/11 based on Eligibility Criteria: Yes; Random Allocation: No; Allocation Concealment: No; Groups Similar at Baseline: Yes; Subject Blinding: No; Therapist Blinding: No; Assessor Blinding: Yes; Outcomes for 85% of participants: No; Intention to Treat: Yes; Between-group Statistical Comparisons: Yes; Point and Variability Measures: Yes.This study design demonstrated poor internal validity based on a Pedro score < 6. Due to the nature of the study, it was impossible to blind subjects to group allocation and some participants who were allocated to the yoga group demanded to be placed in either of the two physiotherapy groups. This introduced selection bias, as the groups were not randomized despite the researchers intention to do so. The authors attempted to avoid bias through a single-blind design in which the assessors did not know group allocation when measuring outcomes. The authors described their methods of randomization and concealment and provided detailed information about participants in each group in terms of demographics and baseline characteristics. The groups were not similar at baseline in terms of number (yoga and control groups were smaller, 13 and 15 participants respectively, than the group and individual physiotherapy groups which had 48 and 35 participants). Also, the control group was younger and reported a shorter time since diagnosis. The groups were similar for all key outcomes measures/clinical assessments except for the MFIS, which was lower in the yoga group at baseline (p.5). There was also high external validity of the study, which refers to the generalizability of results or meaningfulness of the study. The authors presented results using appropriate and validated outcomes measures and provided good statistical analysis for comparison between experimental and control group. Unfortunately, with a dropout rate of 22%, attrition bias was an issue in this study. This is in part due to the variable and progressive nature of the relapsing remitting MS. Fortunately, the authors provide thorough evaluation of the reasons for dropouts in each group and adequate details on reasons for discontinuation of participation. The percentage of subjects analysed at follow up was lowest for the group physiotherapy intervention (72%) and highest for yoga intervention (81%). Excellent |
| **Interpretation of Results**[This is YOUR interpretation of the results taking into consideration the strengths and limitations as you discussed above. Please comment on clinical significance of effect size / study findings. Describe in your own words what the results mean.] |
| This study provides some preliminary evidence to suggest that group exercise interventions, including yoga, can benefit people with MS who require bilateral support for ambulation. The results on the BBS indicate that individual and group physiotherapy as well as yoga classes may reduce falls or falls risk. However, the mean difference was reported to be 5.3 for the yoga intervention. Since the Minimal Detectable Change (MDC) for BBS in people with MS is 6.5 points,14 this limits the clinical significance of the findings. However, based on improvements seen in this study, this information can be used to expand treatment options for this specific population, especially in terms of creating group exercise programs. However, there are significant methodological limitations to the study including selection bias introduced through nonrandomized groups and potential expectation bias based on participants preferring to be in the physiotherapy groups. This created especially an especially small sample for the yoga intervention group. This coupled with high dropout rates across all groups makes it difficult to draw any firm conclusions based on this study. Furthermore, there was high variability within groups at baseline, especially in terms of the 6MWT measure. This could have limited the ability to see significant differences despite large changes seen from baseline to post intervention. Thus, in order for the results to be more trustworthy, controlled trials with larger sample sizes and groups that are similar at baseline should be conducted.  |

**Excellent**

**(3) Description and appraisal of “Comparison of the Effect of 8 Weeks Aerobic and Yoga Training on Ambulatory Function, Fatigue and Mood Status in MS Patients by Ahmadi A, Arastoo AA, Nikbakht M, Zahednejad S, and Rajabpour M. (2013)**4

|  |
| --- |
| **Aim/Objective of the Study/Systematic Review:** |
| The purpose of this study was to compare the effects of aerobic and yoga interventions on participants with MS in terms of balance, mobility, fatigue and mood.  |
| **Study Design**[e.g., systematic review, cohort, randomised controlled trial, qualitative study, grounded theory. Includes information about study characteristics such as blinding and allocation concealment. When were outcomes measured, if relevant]Note: For systematic review, use headings ‘search strategy’, ‘selection criteria’, ‘methods’ etc. For qualitative studies, identify data collection/analyses methods. |
| * This was a randomized controlled trial.
* Randomized allocation: subjects were randomly assigned to one of three groups: 1) treadmill training, 2) yoga practice, or 3) waitlist (control). The authors did not specify the procedure for randomization.
* The subjects and investigators/assessors were not blinded to group allocation.
* Outcomes measured were collected immediately prior to baseline and post intervention at 8-weeks.
* The sample consisted of 31 female participants who were recruited from waiting list for a rehabilitation program in the Physiotherapy Clinic of Jundishapour University of Medical Sciences, Iran.
* Intention to treat was accounted for and all participants involved in the study were offered at least one treatment.
 |
| **Setting**[e.g., locations such as hospital, community; rural; metropolitan; country] |
| The authors do not provide detailed information about the setting of interventions but do report that interventions took place in a physiotherapy clinic. It is assumed that the interventions took place in the physiotherapy clinic of Jundishapour University of Medical Sciences in Iran. The only details provided regarding the intervention environment was that the room temperature was kept between 23-26°C to prevent overheating. |
| **Participants**[N, diagnosis, eligibility criteria, how recruited, type of sample (e.g., purposive, random), key demographics such as mean age, gender, duration of illness/disease, and if groups in an RCT were comparable at baseline on key demographic variables; number of dropouts if relevant, number available for follow-up]Note: This is not a list of the inclusion and exclusion criteria. This is a description of the actual sample that participated in the study. You can find this descriptive information in the text and tables in the article. |
| * 31 female subjects were recruited and screened for eligibility. Recruitment was from a waiting list for a rehabilitation program in the physiotherapy clinic of jundishapour University of Medical Sciences, Iran.
* Inclusion criteria: physician diagnosed MS, Expanded Disability Status Score (EDSS) between 1-4 points, ability to walk on treadmill with/without hand support at a constant speed for 5 minutes.
* Exclusion criteria: pregnancy, addiction, cardiovascular disease, diabetes, thyroid disorders, gout or orthopaedic limitations.
* Key demographics:
* Age range: 19-54 years old, mean: 35.16 +/- 9 years
* Disease duration range: 1-20 years, mean: 5.09 +/- 4.09 years
* EDSS range: 1-4 points, mean: 2.20+/- 1.16 points
* Balance score range: 28-56 points, mean: 46.29 +/- 7.50 points
* Walk time mean: 8.85 +/- 1.82 points
* Walk distance: 117.37 +/- 22.5
* FFS score: 3.85 +/- 1.35 points
* BDI score: 12.74+/- 9.73 points
* BAI score: 9.38 +/- 6.04 points
* Gender: all participants were female
* Groups were similar at baseline on key demographics.
* The authors do not report number of dropouts/attrition rates.
 |
| **Intervention Investigated**[Provide details of methods, who provided treatment, when and where, how many hours of treatment provided] |
| *Control* |
| * 10 participants were randomized to the control group.
* This group was instructed to follow their own routine training program.
* Researchers offered the control group a choice of training or yoga training following intervention period.
 |
| *Experimental* |
| 1. Treadmill training:
* 10 participants were randomized to the treadmill-training group.
* Intervention consisted of 30-minute treadmill sessions with 10 minutes of stretching and range of motion pre and post class.
* Training frequency: 3x/week.
* Intensity: 40-75% age predicted max heart rate (measured using a Polar Electro OY type PE-3000 heart rate monitor). Speed and ratings of perceived exertion using modified Borg were also recorded to monitor intensity.
* Duration: 8 weeks.
* The authors do not specify who delivered the treadmill training.
1. Yoga Intervention:
* 11 participants were randomized to the yoga intervention group.
* Intervention consisted of 60-70 minute yoga classes including postures (held for 10-30 seconds each with rest periods of 30 seconds-1 minute), breathing exercises and meditation.
* Intensity was modified to appropriate level using props such as a chair, swiss ball or a wall for support.
* Frequency: 3x/week
* Duration: 8 weeks
* Yoga classes were taught by yoga instructors and were supervised by a neurologist and a physiotherapist.
 |
| **Outcome Measures** (Primary and Secondary)[Give details of each measure, maximum possible score and range for each measure, administered by whom, where] |
| Outcomes measures were assessed at baseline and at post-intervention follow-up at 8 weeks. The authors do not explicitly report who performed clinical assessments.**Fatigue Severity Scale (FSS):** 17* The purpose of the test is to assess severity of fatigue and its impact on the individual’s activities/lifestyle.
* The assessment is a self-report scale, which consists of 9 items related to how fatigue interferes with daily activities. The subject is asked to rate its severity from 1 (strongly disagree) to 7 (strongly agree)
* The authors reported the mean of all scores with higher scores indicating higher fatigue severity.
* Minimum: 1 points
* Maximum: 7 points
* Cut off score: > 4 points indicates severe fatigue or need for further evaluation.

**Beck Depression Inventory (BDI):** 18* The purpose of this assessment is to quantify severity of depression.
* The self-report questionnaire consists of 21 questions. The subject is asked to rate each item on a four-point scale from 0-3 points.
* Minimum score: 0 points
* Maximum score: 63 points
* Threshold for diagnosis of depression: > 10 points

**Beck Anxiety Inventory (BAI):** 19* The purpose of this test is to assess clinical anxiety in psychiatric populations.
* The self-report measure consists of 21 items which subjects are asked to rate from 0 (not at all) to 3 (severely). The test has items related to anxious mood, specific fears, and autonomic hyperactivity and motor tension of generalized anxiety. Higher scores indicate higher levels of anxiety severity.
* Minimum score: 0 points
* Maximum score: 63 points

**Berg Balance Score (BBS):**14* Purpose of the test: BBS is used to measure static balance.
* The test involves 14 tasks and the assessor is to rate performance on a scale from 0 (unable to perform) to 4 points (able to perform independently). All points are summed for a total score, where a higher score indicates better balance.
* Minimum score: 0 points
* Maximum score: 56 points

**10 Meter Walk Test (10MWT):** 20* The purpose of the test is to assess walking speed in meters per second over a short duration.
* The test measures the time required for a participants to walk 10 meters over a straight path. Three trials are performed and the average of the three trials is recorded.
* Assistive devices may be used but should be consistent from test to test.
* Speed is recorded in meters/second.

**2 Minute Walk Test (2MWT):** 21* The purpose of this test is to assess endurance with walking.
* This assessment measures the distance that participants are able to walk in two minutes around a shuttle corridor track.
* Assistive devices can be used but should be consistent from test to test.
* Distance is recorded in meters.
* Minimal Detectable Change (MDC) in MS populations: 19.21 meters
 |
| **Main Findings**[Provide summary of mean scores/mean differences/treatment effect, 95% confidence intervals and p-values etc., where provided; you may calculate your own values if necessary/applicable] |
| **Fatigue Severity Scale:** * Authors report that treadmill training and yoga groups showed improvements in fatigue severity. The FFS decreased by 45.08% (p = 0.001) in the treadmill-training group and by 38.69% (p = 0.01) in the yoga practice group.

**Beck Depression Inventory (BDI):** * The authors found a significant improvement in the BDI score for the treadmill training group: BDI score decreased by 34.11% (p = 0.001)
* **The yoga practice group demonstrated significant improvements with BDI score decreasing by 36.11% (p = 0.001).**

**Beck Anxiety Inventory (BAI):** * The authors found a significant improvement in the BAI score for the treadmill training group: BDI score decreased by 78% (p = 0.01)
* The yoga practice group demonstrated significant improvements with BAI score decreasing by 48.56% (p = 0.001).
* A comparison between change in treadmill training group and yoga practice group found that the yoga group had significantly greater improvements in BAI (p = 0.01).
* **The BAI score increased in the control group.**

**Berg Balance Scale (BBS):** * The authors found significant improvements in balance as indicated by BBS scores increasing by 16.45% (p = 0.001 in the treadmill-training group and 12.76% (p = 0.001) in the yoga group.
* Furthermore, the control group demonstrated worse scores on the BBS and decreased by 6.29% (p = 0.07).
* A comparison of treadmill training and yoga group showed no significant differences in change after 8 weeks (p = 0.76)

**10 Meter Walk Test:** * The authors report significant improvements in 10MWT times in the treadmill-training group (decreased walk time by 18.54%, p = 0.001).
* The yoga practice group improved (mean time decreased by 7.40%) while the control group did not (mean time increased by 3.38%). However, the yoga practice and the control groups did not demonstrate significant changes in 10MWT times based on p values of 0.13 and 0.14 respectively.
* The authors compared mean 10MWT times post intervention between groups and found no significant differences between the treadmill-training group and the yoga-training group (p = 0.12) (p. 451).

**2 Minute Walk Test:** * The mean 2MWT distance increased significantly for the treadmill-training group (16.19%, p = 0.001) and the yoga practice group (9.96%, p = 0.001). The mean distance for 2MWT declined 2.01% in the control group, but this change was not significant (p = 0.15).
* No difference was observed between treadmill training group and yoga group for the mean 2 minutes’ walk distance (p=0.26).
 |
| **Original Authors’ Conclusions**[Paraphrase as required. If providing a direct quote, add page number] |
| The authors concluded “these results suggest that treadmill training and yoga practice improved ambulatory function, fatigue and mood status in individuals with mild to moderate MS” (p. 449).  |
| **Critical Appraisal** |
| **Validity**[Identify the strengths and limitations of the study, including potential sources of bias. Comment on the overall methodological quality (including the score) as you determined from your assessment of the article. Comment on anything you believe was missing in the paper.] |
| Pedro scale score: 6/11 based on Eligibility Criteria: Yes; Random Allocation: Yes; Allocation Concealment: No; Groups Similar at Baseline: Yes; Subject Blinding: No; Therapist Blinding: No; Assessor Blinding: No; Outcomes for 85% of participants: Yes; Intention to Treat: Yes; Between-group Statistical Comparisons: Yes; Point and Variability Measures: Yes.This study design demonstrated moderate to high internal validity based on a pedro score >/= 6/11.22 This indicates that the results of this study can be trusted. The authors attempted to avoid bias through blinding of subjects and assessors. They also described randomization and concealment of group allocation. They provided evidence that the groups were similar at baseline with key demographic and assessment measures. The results of the study are meaningful based on high external validity. The authors presented results using appropriate and validated outcomes measures and provided adequate statistical analysis for comparison between experimental and control group.  |
| **Interpretation of Results**[This is YOUR interpretation of the results taking into consideration the strengths and limitations as you discussed above. Please comment on clinical significance of effect size / study findings. Describe in your own words what the results mean.] |
| The results of this study demonstrate the effectiveness of both treadmill training and yoga practice interventions in improving the balance of individuals with mild to moderate MS. Both exercise groups showed statistically significant improvements in balance and mobility scores including the 2 Minute Walk Test and the Berg Balance Scale. They also provide insight into the importance of specificity in training given that the only clinical assessment in which the treadmill training group showed statistically significant improvements but the yoga practice group did not was the 10 Meter Walk Test. On the contrary, the lack of improvements and even worsening of functional mobility in the control group provides excellent support for the importance of exercise and physical activity in this population. The quality of this study could have been improved with greater attention to detail in reporting the interventions, use of a larger sample size, and a more representative sample (including male subjects as well as female subjects). The rigor of this study was lacking in that the subjects and assessors were not blinded to the allocation of groups. Specific strengths of this study include the randomized controlled trial design with randomized allocation of subjects and true experimental design. The authors attempted to reduce bias matching groups such that they were similar at baseline in terms of all key measures. Also, the protocol maintained equal intensity, duration and frequency between the two experimental groups. Thus, this study offers unique insight into comparisons between groups. The authors were able to determine that yoga practice intervention may be more beneficial than treadmill training in terms of treating balance impairments. This is evidenced by the statistically significant changes from pre to post intervention between groups on the BBS. Lastly, statistical analysis was very thorough and clearly presented. |

**Again, very well written and a good description and critique of the study**

**EVIDENCE SYNTHESIS AND IMPLICATIONS**

|  |
| --- |
| Balance deficits are common in individuals with Multiple Sclerosis and can affect an individual’s quality of life and health significantly. Balance impairments increase fall risk and often lead to decreased physical activity and functional decline as well as poor health. The evidence reviewed in this paper provides some support for the use of dafampridine extended release as well as yoga practice as potential balance training interventions for adults with MS. However, to date there have been no research studies conducted that directly compare the effects of dalfampridine extended release and yoga. Thus the findings from studies that looked at each intervention separately were reviewed and analysed. Authors investigating dalfampridine reported findings that suggest that the drug results in favourable outcomes for patients with MS with problems with mobility and balance. As far as safety goes, the study demonstrates that there is very little risk involved for patients in this study. Specifically, the study reviewed pertaining to dalfampridine intervention was the only study found with a sample size large enough to provide sufficient power as well as the multi site (and multi country) design adds to the generalizability of results for patients with MS. It is important to note the inclusion criteria required participants to score between 4 to 7 points on the expanded disability status scale at baseline. Therefore, this study included individuals who were moderately to severely disabled and it is possible that the results would have showed increased differences between groups for individuals with higher baseline mobility. As for yoga interventions, researchers reported support for the use of yoga as a treatment option in this population as patients who participated in yoga training interventions demonstrated improved static and dynamic balance and reduced falls risk. Additionally, researchers reported secondary outcomes benefitting these patients including improved ambulatory function, decreased fatigue severity, and improved mood status.4 Overall, the study by Hupperts and colleagues provides preliminary evidence that dalfampridine is potentially beneficial to individuals with MS, but the results do not show conclusive evidence to strongly recommend this as a treatment. 8 They elaborate that their findings must be confirmed by future prospective studies, but that there is evidence that the drug may result in “clinically meaningful improvements in walking quality/ambulatory function in patients with MS with walking disability.” (p. 7) Additionally, it is important to investigate the efficacy of the drug in combination with physical therapy. It seems plausible that with the combined physiological effects of the dalfampridine along with expert guidance in gait training, strength, balance and coordination exercises, that participants may experience greater improvements and reduced falls risk.Very goodNext, although exercise is recommended for individuals with Multiple Sclerosis, there is a paucity of evidence around the effects of therapeutic yoga interventions on balance. Currently, no systematic reviews or Meta-Analyses exist to provide insight into current research on this specific topic and although there is some evidence for the use of yoga interventions in patients with multiple sclerosis, many of these studies do not include outcomes measurements for balance. Additionally, the overall quality of evidence for my clinical question is generally poor. Because of the nature of the intervention, allocation of concealment, blinding of subjects and blinding of assessors is generally impossible. Furthermore, there is high risk of expectation bias from both researchers and patients. Additionally, the sample sizes in the studies available are generally small, making generalizability difficult. The internal validity and scientific quality of most of the available research is not very good. In considering the effects of yoga on balance in people with MS researchers provide preliminary evidence that the yoga training may infer positive outcomes in terms of balance improvements and falls risk reduction. Further investigation in the topic of exercise interventions revealed a similar gap in knowledge on the effects of various types of exercise on people with MS. The majority of studies available in current research had major study limitations including small sample sizes, and moderate risk of bias due to poor methodological design (under reporting of sample characteristics such as disease-modifying therapies, adverse events, attrition rates, and lack of detailed intervention protocol).12 Because these major study limitations, the effects of yoga on balance and falls risk in this population is still unclear.In conclusion, the current available evidence suggests that both dalfampridine and yoga interventions may be effective and safe for treating people with MS with balance impairments. The limited available studies found through this search demonstrate that there are obvious gaps in our current knowledge relating to the treatment of balance impairments for individuals with MS. First, there is very little high quality research to demonstrate conclusively the effects of dalfampridine and yoga training. Furthermore, there were no studies found in the current search that compared these two intervention options. The overall evidence on the topic of exercise interventions and treatment of balance impairments in individuals with MS is moderate and future research should focus on comparing the use of yoga to other exercise interventions as well as dalfampridine in terms of efficacy for balance training. Additionally, research investigating the long-term effects of these interventions is needed. Finally, in order to be more clinically applicable, future research should investigate optimal frequency, duration and intensity of yoga training. This would help guide the clinical recommendations and interventions offered by clinicians treating patients with MS to provide better evidence based care for these individuals and improve functional outcomes. |
| Very nicely written and summarized |

*Notes*

* *This section synthesizes your appraisal of your articles; you may mention other related research that you have read or that supports your interpretation and discussion of this evidence. Please be sure to address the quality of the evidence available to guide clinical practice related to your PICO question. Discuss the implications for clinical practice and research.*
* *Students may wish/need to discuss implications with clinicians or peers for suggestions*
* *This section should be ¾-1 page*
* *Be sure to address both implications for clinical practice and future research (separately)*

**REFERENCES**

[List all references cited in the CAT]

|  |
| --- |
| 1. Nick N, Petramfar P, Ghodsbin F, Keshavarzi S, Jahanbin I. The Effect of yoga on balance and fear of falling in the older adults. *Pm&R*. 2015:1-7. doi:10.1016/j.pmrj.2015.06.442.2. Gillespie L, Robertson M, Gillespie W, et al. Interventions for preventing falls in older people living in the community. *Cochrane Database Syst Rev*. 2012;9(9):CD007146. doi:10.1002/14651858.CD007146.pub3.Copyright.3. Gothe NP, McAuley E. Yoga Is as Good as Stretching–Strengthening Exercises in Improving Functional Fitness Outcomes: Results From a Randomized Controlled Trial. *Journals Gerontol Ser A Biol Sci Med Sci*. 2015;00(00):glv127. doi:10.1093/gerona/glv127.4. Ahmadi A, Arastoo AA, Nikbakht M, Zahednejad S. Comparison of the E ff ect of 8 weeks Aerobic and Yoga Training on Ambulatory Function , Fatigue and Mood Status in MS Patients. 2013;15(6):449-454. doi:10.5812/ircmj.3597.5. Hogan N, Kehoe M, Larkin A, Coote S. Clinical Study The Effect of Community Exercise Interventions for People with MS Who Use Bilateral Support for Gait. 2014;2014.6. Coote S, Garrett M, Hogan N, Larkin A, Saunders J. with multiple sclerosis. 2009;8:1-8. doi:10.1186/1471-2377-9-34.7. Coote S, Hogan N, Franklin S. Falls in People With Multiple Sclerosis Who Use a Walking Aid : Prevalence , Factors , and Effect of Strength and Balance Interventions. *Arch Phys Med Rehabil*. 2013;94(4):616-621. doi:10.1016/j.apmr.2012.10.020.8. Hupperts R, Lycke J, Short C, et al. Prolonged-release fampridine and walking and balance in MS: randomised controlled MOBILE trial. *Mult Scler J*. 2015:1-10. doi:10.1177/1352458515581436.9. Prosperini L, Giannì C, Fortuna D, Marchetti MR, Pozzilli C. Oral Dalfampridine Improves Standing Balance Detected at Static Posturography in Multiple Sclerosis. 2014;2014.10. Salgado BC, Jones M, Ilgun S, McCord G, Loper-Powers M, van Houten P. Effects of a 4-month Ananda Yoga Program on Physical and Mental Health Outcomes for Persons With Multiple Sclerosis. *Int J Yoga Therap*. 2013;23(2):27-38. http://www.ncbi.nlm.nih.gov/pubmed/24165521.11. Guner S, Inanici F. ScienceDirect Yoga therapy and ambulatory multiple sclerosis Assessment of gait analysis parameters , fatigue and balance. *J Bodyw Mov Ther*. 2015;19(1):72-81. doi:10.1016/j.jbmt.2014.04.004.12. Heine M, I VDP, Mb R, Eeh VW, Kwakkel G. Exercise therapy for fatigue in multiple sclerosis ( Review ). 2015;(9).13. Bhasker A, Fary K, Loredana LM, Marina D, Wade DT. Non pharmacological interventions for spasticity in multiple sclerosis. *Cochrane Database Syst Rev*. 2013;CD009974(2):CD009974. doi:10.1002/14651858.CD009974.pub2.14. Rehab Measures: Berg Balance Scale. *Rehabilitation Measures Database*. 2013.Accessed November 24, 201515. Johnson T. Modified Fatigue Impact Scale (MFIS). *Rehabilitation Measures Database*. 2012. Accessed November 24, 2015.16. 6 Minute Walk Test. *Rehabilitation Measures Database*. 2013.Accessed November 24, 2015.17. Rehab Measures: Fatigue Severity Scale. *Rehabilitation Measures Database*. 2013. Accessed November 24, 2015.18. Rehab Measures: Beck Depression Inventory. *Rehab Meas Database*. 2012.Accessed November 24, 2015.19. Ulusoy, M., Sahin N. EH. Turkish Version of the Beck Anxiety Inventory: Psychometric Properties. *J Cogn Psychother An Int Q*. 1998;12(2).20. Team RM. Rehab Measures: 10 Meter Walk Test. *Rehabil Meas Database*. 2013. Accessed November 24, 2015.21. Rehab Measures: 2 Minute Walk Test. *Rehabilitation Measures Database*. 2013. Accessed November 24, 2015.22. PEDro Statistics. *Physiother Evid Database*. 2015. http://www.pedro.org.au/english/downloads/pedro-statistics/. Accessed November 23, 2015. |