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| **CRITICALLY APPRAISED TOPIC** |

**FOCUSED CLINICAL QUESTION**

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| “For a 42 year old female with relapsing remitting multiple sclerosis and moderate disability on the EDSS scale, does dalfampridine extended-release improve gait speed more than gait training with a physical therapist?” |

**AUTHOR**

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**CLINICAL SCENARIO**

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| The patient is a 42 year old female with relapsing-remitting multiple sclerosis with a decrease in gait speed. She is in need of an intervention to assist in increasing her gait speed to improve her overall quality of life.Multiple sclerosis (MS) is a neurological condition, typically progressive that affects the transmission of neuronal signals due to damage of the sheaths of nerve cells in the brain and spinal cord11. 87% of individuals who have been diagnosed with MS are affected by gait related limitations11. Dalfampridine is a medication designed to target and improve walking related symptoms. Unfortunately, without insurance, this medication can cost upwards of $13,00012. The aim of this investigation is to determine the best treatment options, between medication and gait training with a physical therapist, to improve gait speed in individuals who have MS.  |

**SUMMARY OF SEARCH**

[Best evidence appraised and key findings]

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| * Ten studies were identified that met the inclusion/exclusion criteria. Three of the ten studies were identified as providing the best evidence and chosen for further analysis.
* No studies were identified that directly compare gait training with dalfampridine
* Dalfampridine can improve gait speed, however, not all individuals are responders to this drug. Additionally, data presented a return to baseline gait speed after the cessation of the drug.
* There are numerous forms of gait training including conventional gait training, treadmill training with and without body weight support and , robotic-assisted treadmill training. No one method was proven to be more superior than another. Additionally, data lacked maintenance of long term results after the conclusion of therapy.
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**CLINICAL BOTTOM LINE**

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| Based on current research available, it is difficult to determine which intervention, dalfampridine or gait training, is more beneficial in improving gait speed in individuals who have Multiple Sclerosis. However, promising data does imply that both interventions can be successful in improving overall gait speed. Future high level research should focus on direct comparison of outcomes of the two intervention in order to best recommend appropriate treatment for this condition. |

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| ***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*** |

*The above information should fit onto the first page of your CAT*

**SEARCH STRATEGY**

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| **Terms used to guide the search strategy** |
| **P**atient/Client Group | **I**ntervention (or Assessment) | **C**omparison | **O**utcome(s) |
| Middle AgeAgingAdultFemaleMultiple SclerosisMS | Dalfampridine ERDalfampridine Extended ReleaseD-ERAmpyra4-aminopyridinefampridine | Gait TrainingLocomotive TrainingPhysical TherapyPhysiotherapy | Gait SpeedStep CadenceStep RateGait PaceWalking Speed |

**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.*

Search #1 PubMED

#1 Dalfampridine ER or Dalfampridine Extended Release or D-ER or Ampyra or 4-aminopyridine or fampridine

#2 Multiple Sclerosis or MS [MeSH Term]

#3 Gait Speed or Step Cadence or Step rate or Gait pace or Walking speed

#1 and #2 and #3 (46 results)

Search #2 PubMED

#2 Multiple Sclerosis or MS [MeSH Term]

#5 Gait Training

#6 Physical Therapy or Physiotherapy

#4 and #5 and #6 (79 results)

No results found based on PICO question. Therefore, search question was revised (separated question and removed specific gender, disability level and MS type to broaden available data).

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| **Databases and Sites Searched** | **Number of results** | **Limits applied, revised number of results (if applicable)** |
| **PubMed****CINHAL****Cochrane** | **D-ER & Gait Speed=46 results; Gait Train and Gait Speed=79 results****D-ER & Gait Speed=11 results; Gait Train and Gait Speed=16 results****D-ER & Gait Speed=26 results; Gait Train and Gait Speed=0 results** |  |

## INCLUSION and EXCLUSION CRITERIA

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| **Inclusion Criteria** |
| Published in EnglishConfirmed Diagnosis of MSRandomized Controlled Trials, controlled clinical trials, non-randomized controlled clinical trials Cohort Studies, Case Control StudiesStudies involving ambulatory adults |
| **Exclusion Criteria** |
| EDSS level above 7Abstracts, dissertations, unpublished data, alternative diagnosis group (CVA)Studies that include diagnosis other than Multiple Sclerosis |

**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).*

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| **Author (Year)** | **Study quality score** | **Level of Evidence** | **Study design** |
| **Allart (2015)**1 | **Downs and Black=19/32** | **Level 2a** | **Non-randomized Controlled Study Trial** |
| **Hupperts (2015)** 2 | **PEDro=9/11** | **Level 1b** | **Randomized Control Trial** |
| **Goodman (2007)** 3 | **PEDro=9/11** | **Level 1b**  | **Randomized Control Trial** |
| **Goodman (2009)** 4 | **PEDro=10/11** | **Level 1b** | **Randomized Control Trial** |
| **Schwartz (2012)** 5 | **PEDro=9/11** | **Level 1b** | **Randomized Control Trial** |
| **Hoang (2015)** 6 | **PEDro=7/11** | **Level 1b** | **Randomized Control Trial** |
| **Swinnen (2012)** 7 | **AMSTAR=7/11** | **Level 1a** | **Systematic Review** |
| **Vaney (2012)** 8 | **PEDro=6/11** | **Level 1b** | **Randomized Control Trial** |
| **Van den Berg (2006)** 9 | **PEDro=6/11** | **Level 1b** | **Randomized Control Trial (Pilot)** |
| **Jensen (2014)** 10 | **AMSTAR=7/11** | **Level 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:

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| * **Swinnen (2012)7-**This study is a systematic review the reviewed various types of treadmill training and its effect on gait speed. This study included a synthesis of a number of other studies included in the list of articles that matched my inclusion criteria. Though this study was not able to determine which form of treadmill training has the most significant impact on gait speed, it did identify that all methods of gait training included can improve gait speed short-term. It included eight studies with a total of 161 participants improving the overall effect size of the outcomes. This study provides information on parameters of each protocol to allow therapist to reproduce training methods.
* **Schwartz (2012)5-**This study is a randomized control trial that analysis the effects of robot-assisted gait training in patients with multiple sclerosis compared to those who received conventional walking training. This study received a score of 7/11 for methodological quality on the PEDro scale. Though the outcome of this study was promoting use of robot-assisted gait training, it was determined that conventional gait training control group improved significantly in the 6MWT and 10MWT which measured gait velocity.
* **Goodman (2009)4-** This study is a randomized control trial that analysed the effects of sustained-release frampridine with a placebo. It was one of my higher rated RCT receiving a score of 9/11 on the PEDro scale. I chose this article because it looked at the effect of the drug compared to a control group that did not receive other treatment. In the experimental group who were responders to the drug, walking speed was greater at every visit compared to the placebo group.
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**SUMMARY OF BEST EVIDENCE**

**(1) Description and appraisal of Sustained-release oral fampridine in multiple sclerosis: a randomised, double-blind, controlled trial by Goodman AD, Brown TR, Krupp LB, et al (2009)4**

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| **Aim/Objective of the Study/Systematic Review:** |
| The aim of this study was to provide detailed evidence on the safety and efficacy of sustained-released fampridine in people with multiple sclerosis for ambulation and leg strength. This study was a randomised, double blind, placebo controlled trial.  |
| **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 study was a 20 week trial that included a total of 8 visits. In the first two weeks of the study, all participants underwent a single-blind placebo period prior to randomization. During this time period all participants were instructed to take one pill every two hours. In the third week of the study (2nd visit), patients were then randomly assigned by a computer generated schedule into two groups (fampridine-10mg twice daily or placebo-tablets twice daily) at a ratio of 3:1. Both groups were instructed to take their pills every 12 hours during the treatment phase which was 14 weeks long. At the end of the treatment phase, participants began a 4-week period of no treatment and returned every 2 weeks for follow up assessments (visits 7 and 8). All participants and personnel were blinded throughout treatment and follow up phase of the study. |
| **Setting**[e.g., locations such as hospital, community; rural; metropolitan; country] |
| 33 centres in the USA and Canada were included in this study. Specific setting location was no described in the article.  |
| **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. |
| This study included 301 participants; 72 participants randomly assigned to the placebo group and 229 assigned to the experimental (fampridine) group. This article did not specify where participants were recruited from. The mean age was 50.9(+/-8.9) years for the control group with 29 males and 43 females. The experimental group had a mean age of 51.5 (+/-8.7) years with 66 males and 162 females. Relapsing remitting (21 in the control group and 62 in the experimental group), primary progressive (14 in the control group, 31 in the experimental group), secondary progressive (35 in the control group, 125 in the experimental group), and progressive relapsing (2 in the control group, 10 in the experimental group) MS courses were included with a majority of participants having secondary progressive MS. The average duration of disease was 12.7 (+/-8.21) years in the control group and 13.4 (8.29) years in the experimental group. Both treatment groups were comparable at baseline on key demographic variables and baseline measures.This study had a dropout rate of 5 participants during the single blind phase of this study; 1 did not receive intervention, 3 dropped out due to adverse events and 1 for withdrawal of consent. During the double-blind phase of the study, 16 participants dropped out (1 in placebo group due to lost to follow-up, 16 in the experimental group due to adverse events (11), withdrawal of consent (4), and for unspecified reasons (2)). 11 patients in the experimental group had one or more serious adverse reaction during the double blind period including UTI, exacerbation, anxiety, seizures, and sepsis. |
| **Intervention Investigated**[Provide details of methods, who provided treatment, when and where, how many hours of treatment provided] |
| *Control* |
| The experimental group received a placebo drug. During the treatment phase, the placebo drug was taken every 12 hours. |
| *Experimental* |
| The experimental group received 10mg of sustained-released fampridine twice per day (total 20 mg per day). During the treatment phase, the drug was taken every 12 hours. |
| **Outcome Measures** (Primary and Secondary)[Give details of each measure, maximum possible score and range for each measure, administered by whom, where] |
| Timed 25 foot walk test: This test was used to measure lower extremity function. A walkway of 25 feet is measured out and participants are instructed to walk the path as quickly as possible, but safely. Patients were allowed to use an assistive device if needed. A time limit of 3 minutes is set for each trial. This measure was done twice at each visit. The average of the two trials were used in the analysis.This study further divided the experimental group into responders and non-responders for analysis of data. Responders were defined as a participants who obtained faster walking speed for at least 3 of the 4 visits during the treatment phase of the study than the maximum gait speed obtained while off the drug (during placebo period in the first two weeks or final four weeks of the study). Analysis of fampridine responders and the placebo group were used in the analysis. Secondary outcomes include Ashworth score for spasticity, the 12-item multiple sclerosis walking scale, and a lower extremity manual muscle test which was completed at each visit. A trained evaluator, usually a physical therapist administered all outcome measures. Evaluators were blinded and the same evaluator administered the measures for the same participant throughout the study. |
| **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] |
| 78 of 224 participants (35%) were identified as responders to the dalfampridine. For the experimental group of responders, the average change in walking speed from baseline was 25.2% (0.16 m/s) (95% CI 21.5%; (0.12 m/s to 28.8%;0.19 m/s). This changed was maintained throughout the 14 week trial. For the experimental group of non-responders, the average change during treatment was 7.5% (0.05 m/s)\_ (95% CI= 5.0%;0.03 m/s to 10.0%;0.06 m/s). This change was small, yet statistically significant. For the control group receiving the placebo drug, the average change was 4.7% (0.03 m/s) (95% CI 1.0%;0.009 feet/s to 8.4%; 0.05 feet/s). The experimental responders group demonstrated statistically significant different speeds during the 14-week treatment period compared to the non-responders and placebo group, however, did not maintain this difference during the follow-up period.­­ \*Note: feet/s was the measurement utilized in this study; numbers presented above reflect conversion to m/s). |
| **Original Authors’ Conclusions**[Paraphrase as required. If providing a direct quote, add page number] |
| The authors of this study determined that the use of sustained-released fampridine demonstrated improvement in walking seed in some people with multiple sclerosis (i.e., responders). Further studies are required to confirm results. Additional, authors were unable to conclude why some individuals responded to famprdine while others did not. |
| **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.] |
| This study received a very high methodological score of 10/11 on the PEDro scale. Due to the blinding of both participants and researchers, this minimized the risk of bias. This study did not include how participants were recruited to be included in this study which may impact selection bias. Authors did not report on concurrent treatment during the treatment period of this intervention which may increase confounding. The consistency amongst assessors and participants also assisted in minimizing bias. this study was a randomised, double blinded controlled trial. The higher level of evidence improves the overall validity of this study. Overall, this study had a low risk of bias. However, results of this study should be analysed with caution due to the division of the experimental group after randomization occurred.  |
| **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 produced favourable results of the use of fampridine to improve walking speed, self-reported walking ability, and lower extremity strength in those that were responders to the drug. Those that were identified as non-responders experienced results similar to the control group. The between group difference of spasticity was not statistically significant. Throughout the 14 week period, responders to the drug maintained an increase in walking speed. Though the change in the non-responder group during treatment was small, it was significant when compared to the placebo group at the first assessment. No significant difference was found between these group during the remaining weeks. At the 2 week and 4 week follow up visit after the 14 week treatment period, responders to the drug saw an immediate return to baseline following the cessation of the drug. This indicates the need to maintain continuous use of the drug for treatment results to remain. Between group treatment effect size on walking speed is 0.13 m/s (Change from baseline in experimental responders group 0.16m/s minus change from baseline in control group .03m/s).  |

**(2) Description and appraisal of Treadmill training in multiple sclerosis: can body weight support or robot assistance provide added value? A systematic review by Swinnen E, Beckwee D, Pinte D, Meeusen R, Baeyens JP, Kerckhofs E (2012)7**

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| **Aim/Objective of the Study/Systematic Review:** |
| The aim of this systematic review is to analyse current research on various methods of treadmill training including traditional treadmill training, body weight support treadmill training, and robot assist treadmill training and its impact on gait-related outcome measures in people who have MS. This study also analysed data to determine if one method of treadmill training is superior to another and what the long term effects of treadmill training on gait are.  |
| **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 study was a systematic review including randomized controlled trials with and without a comparison group and a case report. **Search Strategy**: A search of PubMed, Web of Sciences, Cochrane Library and Pedro electronic databases were used to identify English, French, and Dutch articles published before 2012. The authors also searched the reference list of the articles found on databases for relevant publications.**Selection criteria**: Articles that focused on improving gait function and included gait related outcome measurements with the use of treadmill training with and without body weight support and/or robot assistant in human subjects were included. Articles including adults 19 years and older with a confirmed diagnoses of Multiple Sclerosis. Studies including interventions other than body weight support/robot assist, use of electrostimulation, focus on physical capacity, electomyographic or kinematic data, and/or cardiorespiratory functioning were not included in final review. Authors did not state if the level of evidence was a part of the selection criteria. **Methods**: Two researchers scored the studies and Cohen’s kappa was used to test internal validity. Authors did not provide details on the number of researchers used to select articles. |
| **Setting**[e.g., locations such as hospital, community; rural; metropolitan; country] |
| The settings of the individual studies were not presented in this article.   |
| **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 individuals with MS in a total of 8 studies included in this systematic review. Two studies measured the same subjects with different outcome measures, so 16 participants were accounted for twice. There were 5 randomized controlled trials, one randomized trial without comparison, and two case reports. MS types of relapsing remitting, secondary progressive, and primary progressive were included. Two studies did not report the type of MS diagnosis. A methodology score was used to assist the quality of each study. The average score was 66% with the lowest score being 54% (case report) and highest score being 79% (RCT). The authors did not provide means for age of participants and females vs males included in the 8 studies, but did include descriptive analysis of individual articles. Both males and females were included in all studies with more females than males and ages ranges from 28 years old to 70 years old with a majority of participants in their late 40’s-early 50’s. EDSS scores ranged from 4.9-unable to walk (unreported number). |
| **Intervention Investigated**[Provide details of methods, who provided treatment, when and where, how many hours of treatment provided] |
| *Control* |
| Control groups differed between studies and included gait and dynamic balance exercises, conventional walking therapy overground with and without assistive devices, delayed training, and no training. Frequency of sessions ranged from 12-42 sessions for 30 minutes 2-5 times per week. This article did not specify who provided treatment. |
| *Experimental* |
| Experimental groups differed between studies and included body weight support treadmill training, treadmill training, and robot treadmill training. Frequency of sessions ranged from 12-42 sessions for 30 minutes 2-5 times per week. The percentage of body weight support ranged from 30%-100% with most studies gradually decrease body weight support throughout training period. Treadmill speeds of 0.42m/s-maximum speed tolerated were used in the studies. Two studies reported target heart rate of 55-85% of age-predicted max heart rate. This article did not specify who provided treatment. |
| **Outcome Measures** (Primary and Secondary)[Give details of each measure, maximum possible score and range for each measure, administered by whom, where] |
| The primary outcome measures included improvement in walking speed, walking endurance, EDSS, and gait parameters which includes stride length, cadence, gait cycle time, and foot contact time. This study did not specify who administered these measures and where/what point in the training these measures were taken.Walking Speed: Timed 25 foot walk, twenty meter walk test, and ten-meter walk test were used in the studies to evaluate walking speed. These measures are completed by outlining a walkway of a specified distance and participants are instructed to walk the path as quickly as possible, but safely. This systematic review did not identify the number of trails or maximum possible score.Other outcome measures identified in this systematic review include walking Endurance which including the six minute walk test and two minute walk test, EDSS, and gait parameters which included stride length, cadence, gait cycle time, and food contact time. |
| **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] |
| Out of 966 papers found after a key word search, 8 studies were included in the final systematic review. Due to the variability between studies, mean score findings for each outcome measure were not calculated. Walking Speed: All eight studies reported improvement in walking speed after training. Giesser et al, study reported that subjects who could not walk at the beginning of the trial were able to walker faster over ground at the end of the study. Pilutti et al demonstrated an increase in walking speed from 0.31m/s to 0.44m.s and a mean change of 18% improvement on the T25FW. Lo and Triche demonstrated an improvement of 31% in the T25FW. This study also demonstrated a small effect size for the Lokomat to BWSTT group and a large effect in the BSWTT-lokomat group. Beer et al demonstrated a large effect size for the 20MWT with improvement in both groups (RWTT: 0.21m/s to 0.27 m/s; CWT: 0.24m/s to 0.31 m/s. Newman et al demonstrated improvement in 10MWT from 15.6 (SD: 5.6) seconds to 13.9 seconds (SD: 5.3;P=0.016) after treadmill training. In a 4 week to 6 month follow up, both group’s walking speed returned to baseline in two of the studies (Lo and Triche and Van Den Berg). Schwartz et al demonstrated significant improvement (small effect size) in walking speed only in the CWT group and not the RATT group (mean change from baseline 0.1m/s; SD 0.2). Finally Vaney et al demonstrated improvements in the walking group on the 10MWT (0.09m/s; SD 0.17; 95% CI: 0.01-0.16) and 3MWT: 0.11m/s; SD 0.17, 95% CI 0.04-0.18) and in the RATT group (10MWT: 0.03m/s, SD 0.09, 95% CI:-0.00 to 0.07; 3MWT: 0.03m/s, SD 0.10, 95% CI: -0.01 to 0.07)Effect size (Cohen’s d) of interventions ranged from small to large. This review stated that in two of the studies calculations of cohen’s d was not possible (Beer et al and Glesser et al):**Vaney et al** 10MWT RATT Group: 0.15110MWT CWT Group 0.239 (small effect)Between group differences: 0.0883MWT RATT Group: 0.0763MWT CWT: 0.274 (small effect)Between group differences: 0.198**Schwartz et al**10MWT RATT Group: 0.06710MWT CWT Group: 0.098Between group difference: 0.05**Lo and Triche**T25FW Lokomat-BWSTT: 0.806 (large effect)T25FW BWSST-Lokomat: 0.895 (large effect)Between group difference. 0.089**Van Den Berg et al**10MWS IT Group: 0.10310MWS DT Group: 0.149Between Group difference: 0.0492MWS IT Group: 0.1212MWS DT Group: 0.218 9 (small effect)Between Group Difference: 0.097**Newman et al**10MWT: 0.312 (small effect)2MWT: 0.189Secondary measures of walking endurance, EDSS score and gait parameters showed an overall improvement in most participants throughout the studies |
| **Original Authors’ Conclusions**[Paraphrase as required. If providing a direct quote, add page number] |
| Treadmill training, body weight support treadmill training, and robot assist treadmill training can improve walking speed in individuals with MS. However, due to the limited about of literature, it cannot be determined which form of treadmill training is most effective. |
| **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.] |
| This systematic review received a moderate score of 7/11 on the AMSTAR scale. The author stated that the methodological quality of the individual studies proved to be good, however, each study produced a small amount of subjects. The overall analysis of the studies did not provide necessary detail to compare the interventions. Very little detailed was provided on the search method including the number of readers, however, authors did state that two readers critiqued the level of evidence of the individual studies. The authors reported no evidence on the homogeneity of the studies. The details regarding the individual training protocol were vague and difficult to determine. Only 5 studies included a control and intervention group, however, no details were provided on the protocol for the control 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.] |
| Based on this systematic review, use of treadmill training with and without body weight support and robot assistance did show a favourable effect on the increase in walking speed and endurance of individuals with MS. The results of this study could not determine which method of treadmill training was superior. The effect sizes of the outcomes ranged from small effect to large effect which indicates a wide range of treatment effect. This information does not allow for a strong conclusions that one method of gait training is superior to another. Due to the variability in protocols, it is difficult to compare results of outcome measures. Although, two studies did determine that short term results were not maintained overtime.  |

**(3) Description and appraisal of Robot-assisted gait training in multiple sclerosis patients: a randomized trial by Schwartz I, Sajin A, Moreh E, et al. (2012)5**

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| **Aim/Objective of the Study/Systematic Review:** |
| The aim of this study was to determine the effectiveness of robotic-assisted gait training on mobility and gait in addition to comparing it to conventional walking treatment on short term and long term results.  |
| **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. |
| Randomized control trial; Participants were randomized via two block randomization into two groups by an independent blinded consultant. The intervention group was trained on the Lokomat for 30 minutes. The control group received conventional gait and dynamic balance exercises for 30 minutes. Both groups trained from 2-3 times per week for 4 weeks. All evaluations and treatments were provided by a physical therapist who was blinded to group allocation. Outcome measures were tested at baseline, after completing intervention, and 3 and 6 months after the end of the intervention. |
| **Setting**[e.g., locations such as hospital, community; rural; metropolitan; country] |
| Intervention setting was not included in the article. |
| **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. |
| 15 participants were randomly assigned to the RAGT group and 17 to CWT group. Participants were recruited from the MS unit at Hadassah medical centre. Individuals with relapsing progression, secondary progressive, and primary progressive were included in this study. For the RAGT group there were 7 males and 8 females, the average age was 46.8 years old, average disease duration was 11.3 years and average EDSS was 6.2. For the CWT group there were 7 males and 10 females, average age was 50.5 years old, average disease duration was 14.9 years and average EDSS was 6. Both groups were comparable at baseline. 4 participants dropped out of the RAGT group and 6 patients dropped out of the CWT group for reasons unrelated to the intervention. |
| **Intervention Investigated**[Provide details of methods, who provided treatment, when and where, how many hours of treatment provided] |
| *Control* |
| The conventional walking treatment group led by a physical therapist completed gait and dynamic exercises, sit to stand treatment and walking with or without assistive devices. This group participated in treatment 2-3 times per week for 4 weeks. Each session lasted 30 minutes.  |
| *Experimental* |
| The experimental group lead by a physical therapist utilized the Lokomat (treadmill, body-weight support systems, and lightweight robotic actuators attached to subject’s legs). This group participated in treatment 2-3 times per week for 4 weeks. Each session lasted about 30 minutes with an additional 15 minutes to get into and out of the device. Speed was determined based off of patient’s maximum tolerance and ranged from 0 km/h to 3 km/h. Initially, each participant had 40% of their body weight supported by the harness system. After 2 week, support was decreased to 30% and after 4 weeks, support was decreased to 20%.  |
| **Outcome Measures** (Primary and Secondary)[Give details of each measure, maximum possible score and range for each measure, administered by whom, where] |
| Primary: All measures were administered by a senior physical therapist who was blinded to the group allocation.10m walk test: Measure for gait velocity. Participants are ask to walk as quickly as possible for 10 meters. Gait velocity is calculated by the distance divided by the seconds it takes to complete the test. Those who are unable to walk receive a score of 0 m/s.6 minute walk test measures exercise tolerance. Participants are instructed to walk as far as they can for 6 minutes. The distance they complete in this time frame is then measured in metersTime up and go test: This measure assess gait efficacy and analyses the ability to transfer from sitting to standing and walking a short distance. Participants begin by sitting in a chair with armrest. They are ask to stand, walk 3 m, turn around, walk back to the chair and sit down. Each participant get 2 trials and the best trial is used for analysis |
| **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] |
| 6MWT: Pre-testing resulted in a mean score of 125.8m in the RAGT group and 151.5 in the CWT group. Post-testing resulting in 133.4 (mean change from baseline=17.6m). in the RAGT group and 175.7m (p<0.01; mean change from baseline=30.2 m) in the CWT group. The RAGT group had an average distance of 120.3m and 121.1m at 3 and 6 months respectively. The CWT group has an average distance of 160.7m (p<0.05) and 140.0m at 3 and 6 months respectively. 10MWT: Pre-testing resulted in a mean velocity of .49m/s in the RAGT group and 0.53m/s in the CWT group. Post-testing resulting in 0.45m/s (mean change from baseline=-0.01m/s). in the RAGT group and .63m/s (p<0.05; mean change from baseline=0.1m/s) in the CWT group. The RAGT group had an average velocity of .46m/s and 0.47m/s at 3 and 6 months respectively. The CWT group has an average distance of 0.6m/s and 0.5m/s at 3 and 6 months respectively. TUG: Pre-testing resulted in a mean velocity of 34.5s in the RAGT group and 33.1s in the CWT group. Post-testing resulting in 28.7s (p<0.05; mean change from baseline=-6.5s). in the RAGT group and 30.9s (mean change from baseline=-3.2s) in the CWT group. The RAGT group had an average score of 28.1s (p<0.05) and 29.6s (p<0.05) at 3 and 6 months respectively. The CWT group has an average distance of 29.4s (p<0.05) and 33.8s at 3 and 6 months respectively. Results indicate that both groups improved in exercise endurance, however, results returned to baseline at follow-up. The CWT demonstrated improvement in gait speed at post-testing, however results returned to baseline at follow-up. Finally, average improvement in gait efficacy was not noted in either the RAGT group or CWT group.There were 3 drop outs in the experimental group and 1 in the conventional walking treatment group, however, none of the drop out were related to the side effects of the interventions. At the 6 month follow up, 4 patients dropped out of the experimental group and 6 dropped out of the control group due to lack of return to follow up. |
| **Original Authors’ Conclusions**[Paraphrase as required. If providing a direct quote, add page number] |
| Though significant within subject gait improvements were noted, there was no significant difference in gait outcome measures between the robotic-assisted gait training and conventional walking treatment groups at any one point in the study. Therefore, RAGT and CWT produced similar outcomes. Though no difference was found between groups, the author believes that due to less effort and personnel required for RAGT, this method may be beneficial in gait improvement for patient who have 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.] |
| The study received a score of 9/11 on the Pedro Scale indicating a moderate methodological score. An exclusion criteria was not identified in the article. Without this information, it cannot be understood if participants had other neurological conditions that may have impacted outcome. Random allocation was utilized for subject group placement and both groups were comparable at baseline. This decreases overall bias and prevents favourable outcomes of one group over the other. While blinding of therapist who completed outcome measures was done, it was not possible to blind therapist who were administering the intervention. Additionally, it was not indicated if participants completed additional maintenance training after the competition of this study. Without intervention and maintenance of improvements during the intervention period, it is obvious that participants will not continue to see gains at 3 and 6 month follow up.  |
| **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.] |
| Overall, this study provided data to support the use of RAGT and CWT in individuals with MS. This study did not produce favourable long term results for either control or experimental group. Participants did demonstrate improvement in the 6MWT and 10MWT in the CWT group at the end of the intervention period. The RAGT saw improvement in the TUG at the end of the intervention period. At the 3 month follow up, the TUG score improved in both groups, the 6MWT had only improved in the CWT and the 10MWT did not improve in either group. The CWT presented with better gait parameter results compared to RAGT group. However, there is not enough evidence in order to determine which intervention is more effective in improving overall gait speed. |

**EVIDENCE SYNTHESIS AND IMPLICATIONS**

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| Overall, current evidence supports the use of gait training or use of dalfampridine to improve gait speed of individuals with multiple sclerosis. Goodman et al (2012)4 determined that 10mg of sustained-released dalfampridine was able to improve gait speed by .16m/s for those who were responders to the drug. While a physical therapist cannot prescribe or recommend this drug to patients, we are able to communicate treatment options with physicians. Presenting the results of this study may support communication efforts to promote the use of this drug. However, one must also take into account the potential of adverse reactions that may occur due to medication use like was seen in this study including seziures, urinary tract infections, exacerbations, and sepsis. Finally, based off interpretation from this study, individuals who are on this drug must continue to take the drug for maintenance of walking ability improvements because gait speed return to baseline after participants were taken off the medication. Swinnen et al (2012)7 and Schwartz (2012)5 both analysed the use of physical therapy gait training and its effect on improving gait speed with interventions such as conventional gait training, treadmill training with and without body weight support and robot assist training. Swinnen et al7 determined that treadmill training (with and without body weight support and robot assist) can improve the overall walking speed and endurance individuals with MS. The use of body weight support can assist a therapist in gait training for those who do not have access to additional assistance or other therapist to provide guarding and support. While the quality of the evidence reviewed was moderate to strong, all studies lacked key information to strongly support a specific method to use in clinical practice. Current data provides inconclusive evidence on identification of the most effective treatment. There is no evidence that provides comparison of both interventions to identify the best intervention to improve gait speed in individuals with MS. One limitation of the use of dalfampridine is that all individuals will be responders to this medication and therefore will not see results of improved gait speed. While Goodman et al4 identified promising results for the responders group, this study did not present efficacy of the entire experimental group which may skew data results. Additional research is required to identify what some individuals are responders and some are not. This information will assist in identifying the most effective intervention for improving gait speed. While it was determine that various forms of gait training can improve gait speed, current data lacked support and evidence as to which method was superior. However, studies with larger numbers and control groups are needed to determine the effectiveness of these methods and to determine which method of treadmill training is best. Though only two studies measured long-term outcomes, they both produce unfavourable results stating the return to baseline after the conclusion of training. Therefore, treadmill training may not be an effective treatment option for individuals who are not able to continue training or maintenance therapy. Schwartz et al5 also determined that RAGT training was not superior to conventional gait training. The mean EDSS score of participants in this study was 2.0-2.5. Therefore, it is difficult to apply these results to individuals who have more severe disability. Additionally, this study is lacking long term follow up. Additionally cost implications and comparisons of both studies would also assist in comparing both interventions. In regards to gait speed, the conventional training group saw improvement in the 10MWT after 4 weeks of the intervention, however, statistical significance was not found at 3 and 6 month follow up.Multiple Sclerosis commonly affects walking and gait speed in individuals with this condition. Research has identified several methods to improve overall gait speed, however, there is no current data that has identified the best method to do so. Future studies should focus on the direct comparison of interventions in order to directly answer the clinical question as to which intervention is superior. Ideally, a controlled study with a group just taking dalfampridine, a group just receiving gait training, and a group receiving both interventions will assist in applying this information into clinical practice.  |

*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)*

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[List all references cited in the CAT]

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