

## CRITICALLY APPRAISED TOPIC

### FOCUSED CLINICAL QUESTION

For a 35-year-old female with relapsing-remitting multiple sclerosis, does gait training improve dual task performance?

### AUTHOR

<b>Prepared by</b>	Corinne Bohling	<b>Date</b>	11/23/2015
<b>Email address</b>	Corinne_bohling@med.unc.edu		

### CLINICAL SCENARIO

In the clinic, patient AG is a 35-year-old female with relapsing-remitting MS who presented for PT with complaints of decreased gait speed, with gait speed further decreased when she tried to carry a conversation. Because AG has two children aged 7 and 9, it was important for her to be able to walk while focusing on and talking to her children at home and in public with other distractions. Since her primary goal was to increase gait speed, we wanted to provide her with gait training and wondered if the gait training would also affect her ability to dual task.

Many patients with relapsing-remitting MS seek physical therapy treatment for declining gait speed, but these patients may also demonstrate deficits in dual task performance. For a physical therapist who is treating a patient with MS to improve gait speed using gait training techniques, it would be useful to know if the same technique also improves dual tasking to help determine an appropriate treatment plan to optimize both treatment efficiency and patient outcomes.

### SUMMARY OF SEARCH

[Best evidence appraised and key findings]

- A total of 10 separate studies identified by the search strategy met the inclusion criteria, including one randomized controlled trial, one matched controlled trial, seven cross-sectional studies, and one single group pretest-posttest trial. This Critically Appraised Topic paper considers three of these studies, including one randomized controlled trial and two cross-sectional studies.
- A home-based electronic step training intervention had no significant effect on dual task performance, however both cross-sectional studies found a significant negative correlation between walking speed and dual task cost of walking, indicating that increased gait speed corresponds to decreased dual task cost.
- None of the three studies included gait training as an intervention, and the two studies that found an association between gait speed and dual task performance did not provide evidence of causality.

### CLINICAL BOTTOM LINE

There is evidence to suggest that increased gait speed is associated with improved dual task performance, though causality and the effects of gait training on dual task performance have not been established. The relationship of gait speed to dual task performance indicates that it is possible that a gait training intervention may improve dual task performance, but there is no direct evidence of the ability of gait training to impact dual task performance from the included studies.

***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			
Patient/Client Group	Intervention (or Assessment)	Comparison	Outcome(s)
Adult	Gait train*	(not applicable)	Dual task*
Female	Gait rehabilitation		Dual-task*
Woman	Locomotor train*		
Multiple Sclerosis	Locomotor rehabilitation		
Relapsing-remitting	Walking		
Relapsing remitting			

### Final search strategy:

1. Multiple sclerosis
2. Physical therapy OR physiotherapy OR rehabilitation
3. Gait train\* OR gait rehabilitation OR locomotor train\* OR locomotor rehabilitation OR walking
4. Dual task\* OR dual-task\*
5. 1 AND 2 AND 3 AND 4

Databases and Sites Searched	Number of results	Limits applied, revised number of results (if applicable)
PubMed	13	NA
CINAHL	7	NA
PEDro	1	NA

## INCLUSION and EXCLUSION CRITERIA

Inclusion Criteria
<ol style="list-style-type: none"> <li>1. Published in English</li> <li>2. Randomized Controlled Trials, Controlled Trials, Uncontrolled Trials, Systematic Reviews, Meta-Analyses, Cross-Sectional Studies</li> <li>3. Measured dual-task performance as outcome measure</li> <li>4. Intervention or outcome measure included gait training, stepping, or walking component</li> </ol>
Exclusion Criteria
<ol style="list-style-type: none"> <li>1. Case Studies, abstracts, conference proceedings, dissertations, letters to the editor, narrative review articles, article corrections</li> <li>2. Studies that included adults with cognitive or physical disabilities not related to MS</li> </ol>

## RESULTS OF SEARCH

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

Author (Year)	Study quality score	Level of Evidence	Study design
Hoang, P. (2015) <sup>1</sup>	9/11 (PEDro Scale)	1b	RCT
Kramer, A. (2014) <sup>2</sup>	7/11 (PEDro Scale)	2b	Matched Controlled Trial
Sosnoff, J. (2014) <sup>3</sup>	10/11 (NIH Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies (NIHQAT) <sup>A</sup> ; non-applicable items 7, 10, and 13 were excluded from scoring.)	2b	Cross-Sectional Study
Motl, R. (2014) <sup>4</sup>	10/11 (NIHQAT; non-applicable items 7, 10, and 13 were excluded from scoring.)	2b	Cross-Sectional Study
Learmonth, Y. (2014) <sup>5</sup>	10/11 (NIHQAT; non-applicable items 7, 10, and 13 were excluded from scoring.)	2b	Cross-Sectional Study
Kalron, A. (2010) <sup>6</sup>	8/11 (NIHQAT; non-applicable items 7, 10, and 13 were excluded from scoring; item 4 was not reported and was scored as a "no".)	2b	Cross-Sectional Study
Monticone, M. (2014) <sup>7</sup>	9/13 (NIHQAT; non-applicable item 7 was excluded from scoring; items 3 and 4 were not reported and were scored as "no".)	2b	Cross-Sectional Study
Nilsagard, Y. (2014) <sup>8</sup>	11/14 (NIHQAT)	2b	Single Group Pretest-Posttest Trial
Sandroff, B. (2015) <sup>9</sup>	8/11 (NIHQAT; non-applicable items 7, 10, and 13 were excluded from scoring; item 4 was not reported and was scored as a "no".)	2b	Cross-Sectional Study
Prosperini, L. (2015) <sup>10</sup>	8/11 (NIHQAT, non-applicable items 7, 10, and 13 were excluded from scoring.)	2b	Cross-Sectional Study

<sup>A</sup> The NIH Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies (NIHQAT) was accessed at <https://www.nhlbi.nih.gov/health-pro/guidelines/in-develop/cardiovascular-risk-reduction/tools/cohort>.

## BEST EVIDENCE

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

- Hoang, P. (2015): This study provides the highest level of evidence and is most relevant to my clinical question. While it does not exclusively use gait training as an intervention, the effects of step training on dual task performance among other outcome measures are reported.
- Sosnoff, J. (2014): This is one of the three 2b-level studies that scored 91% on the quality assessment measures, which is the highest of all of the 2b-level studies listed above. While the quality assessment measure was not intended to be used as a tally sheet for scoring, the three studies that were assessed to include 10/11 quality criteria also raised the fewest red flags for internal validity. This study examines the effects of mobility and cognition on the dual-task cost of walking, which may provide evidence to support or oppose the use of mobility training to improve dual-task outcomes.
- Motl, R. (2014): Another of the 2b-level studies with a 91% score on quality assessment measures, this study investigates the relationships between mobility, cognition, and various symptoms of MS with the dual-task cost of walking. This may also provide evidence regarding the use of mobility training to improve dual-task outcomes.

## SUMMARY OF BEST EVIDENCE

### (1) Description and appraisal of *Effects of a home-based step training programme on balance, stepping, cognition and functional performance in people with multiple sclerosis - a randomized controlled trial* by Hoang P, Schoene D, Gandevia S, Smith S, and Lord SR, 2015.

<b>Aim/Objective of the Study/Systematic Review:</b>
The objective of this study was to determine whether a 12-week home stepping program can reduce risk of falling in people with MS as indicated by performance on multiple functional outcome measures.
<b>Study Design</b> [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 single-blinded, randomized controlled trial with two arms: an intervention group and a control group. Participants were randomized into one of the two groups after completing a baseline assessment. The randomization was performed by an investigator who had neither recruited nor assessed the participants, via computer-generated randomized numbers.  Outcome measures were recorded at baseline prior to randomization into groups, and again within 7 days of completion of the 12-week intervention period. The re-assessments were performed by a physical therapist who was blinded to the participants' group assignments. All participants also recorded any falls on monthly fall calendars; follow-up by telephone was used to retrieve this information if monthly calendar data was not reported by a participant.
<b>Setting</b> [e.g., locations such as hospital, community; rural; metropolitan; country]
This study was registered with the Australian and New Zealand Clinical Trials Registry and was funded by Multiple Sclerosis Research Australia and National Health and Medical Research Council Australia, and therefore is assumed to have taken place in Australia, though the authors do not disclose the specific location of the study. Participants were recruited from either an MS clinic or an MS-specific outpatient rehabilitation gym, and interventions were conducted in the participants' homes, with testing conducted in a gym setting.
<b>Participants</b> [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.
Participants were recruited from an MS clinic and an outpatient rehabilitation gym for people with MS between March of 2013 and February of 2014. The authors do not state how the patients were recruited from these locations. Criteria for inclusion in the study were age between 18 and 65 years, diagnosis of MS according to modified McDonald criteria, no apparent cognitive deficits as demonstrated by completion of written informed consent and ability to understand directions, an EDSS score between 2 and 6, and no evidence of an MS exacerbation within the 3 months prior to study participation. Exclusion criteria included inability to safely perform stepping activities, excessive fatigue, and exercise intolerance as identified by a physical therapist at baseline testing. Sixty people initially showed interest in participating in the study and were assessed for eligibility, but 10 declined to participate after assessment. The remaining 50 people were randomized into a control group with n=22 and an intervention group with n=28. From the control group, 1 person was lost to follow-up due to health. From the intervention group, 5 people were lost to follow-up: 4 stopped the intervention due to personal circumstances and 1 experienced an MS exacerbation. Twenty-three participants in the intervention group and 21 participants in the control group completed the study.  Information regarding participant characteristics between groups includes the initial 50 participants before losses due to follow-up. While the authors report that the groups were similar at baseline, no statistical comparison is provided in the article. The intervention group was 75% female with a mean age of 53.4 years (SD= 10.4 years), an average 11.6-year duration of MS (SD= 9.1 years), and a mean EDSS score of 4.1 (SD= 1.4). The control group was 77% female with a mean age of 51.4 years (SD= 12.8 years), an average 13.4-year duration of MS (SD= 6.9 years), and a mean EDSS score of 4.2 (SD= 1.2). The types of MS, level of disease step, and type of disease modifying drugs appear to be more varied between groups. For example, 18% of the intervention group had secondary progressive MS while 32% of the control group had

secondary progressive MS, 28.6% of the intervention group was in disease step 4 while only 9.1% of the control group was in that step, and 3.6% of the intervention group received Natalizumab while 22.7% of the control group received this drug.

### **Intervention Investigated**

[Provide details of methods, who provided treatment, when and where, how many hours of treatment provided]

#### *Control*

Participants randomized to the control group were allowed to continue their usual physical activity with no study-related intervention.

#### *Experimental*

Those in the intervention group received a home visit by a physical therapist who performed a risk assessment, set up the step training system, and provided training for the participants to use the step training system independently. If deemed appropriate by the physical therapist, participants were instructed to use a frame or walking stick during the step training for safety. The step training system includes a rhythm stepping game, in which participants must follow visual cues on a television screen to step in the indicated directions with the indicated timing to achieve the best accuracy possible. The step training system includes one additional game, which incorporates choice stepping reaction time (CSRT) into the game. This CSRT game involves quick, bilateral stepping. Intervention group participants were instructed to train with the step training system games for a duration of 30 minutes at least twice a week for 12 weeks, and each member of this group received written instructions complete with contact information for questions, and each received a phone call within the first two weeks of the intervention to check for appropriate and safe use of the step training system.

### **Outcome Measures (Primary and Secondary)**

[Give details of each measure, maximum possible score and range for each measure, administered by whom, where]

Self-reported monthly falls calendars were completed by participants and returned to researchers. The method and timing of return for this measure is not described in the article, but researchers did follow up with participants by telephone to retrieve this information if necessary. No other information about this measure is provided.

The remaining outcome measures were completed at baseline before randomization into groups, then again within 7 days of completion of the 12-week intervention period. Participants returned to a gym with an allocation-blinded physical therapist to complete the reassessment.

Choice Stepping Reaction Time (CSRT) was one of two primary outcome measures, and required use of the step training system mat and game system. The mat contains 6 panels: one for each foot in neutral stance, one for each foot forward of neutral stance, and one panel lateral to each of the neutral stance panels. Participants were to follow randomly sequenced directional stimuli on the screen to step onto the corresponding panel. Decision time from stimulus presentation to initiation of movement was measured, as well as movement time from initiation of movement to foot placement. Overall response time was recorded as the sum of the decision time and movement time. The authors do not report how many attempts were included in this measure and it is unclear how the final score after multiple attempts was calculated.

The Stroop Stepping Test (SST) is the second primary outcome measure, also using the step training system mat and game system. The task was similar to that of the CSRT, however, this time each arrow contained a contradictory directional word. In this test, the participants were instructed to step according to the word while trying not to respond to the direction indicated by the arrow. The time required to complete 20 trials was recorded.

Secondary measures included postural sway, which was measured at the waist as displacements of the body in millimetres using a swaymeter on level ground in both eyes open and eyes closed conditions, the Timed Up and Go (TUG), which measures mobility by timing a participant as she stands up from a chair, walks 3 meters, returns to the chair and sits down, and 10-meter walk test, which was timed on a 14-meter track to allow 2 meters at both ends for acceleration and deceleration. A 6-minute Walk Test (6MWT) was also performed as a measure of mobility, performed by measuring the distance that a participant could walk in 6 minutes on a walkway that was 15 meters long.

Secondary measures of cognitive function included the trail making test (TMT), the symbol digits modalities test (SDMT), and divided attention as calculated by comparing performance on the cognitive TUG to the participant's TUG performance. The TMT is a two-part test involving scanning, visuomotor tracking, and cognitive flexibility. The authors used the difference in execution time between a participant's performances on each part to estimate executive functioning. The SDMT is a written test in which participants are instructed to match 9 symbols with corresponding numbers from the top of the page with symbols listed

across the remainder of the page in order to write the corresponding number below each symbol. The number of correct responses on the SDMT within the allotted time were recorded to represent processing speed, attention, and working memory. The cognitive TUG is performed similarly to the TUG, but adds the dual task of counting backwards by threes while completing the TUG task. The authors then compared the time to complete the cognitive TUG to the time to complete the TUG to assess divided attention.

The 9-hole peg test (9-HPT) was also performed with results reported in seconds, though the authors do not provide a description for how this test was administered. Traditionally, the 9-HPT assesses that amount of time taken to place 9 pegs in a peg board with one hand, with the time measured in seconds.<sup>11</sup> The z-scores from performances on the 9-HPT, SDMT, and 10-meter walk test were averaged for each participant to determine a multiple sclerosis functional composite score (MSFC) to measure impairment and disability.

### 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]

Statistically significant between-group differences were found for both primary outcome measures (re state them), a confidence interval of 95% was used for statistical calculations. The intervention group scored a mean of  $0.99s \pm 0.12$  on the CSRT at baseline and  $0.89s \pm 0.11$  at reassessment, while the control group scored  $0.98s \pm 0.12$  at baseline and  $0.98s \pm 0.18$  at reassessment, for an effect size of  $f = 0.33$  and a P value of 0.041. On the SST, the intervention group mean scores were  $72s \pm 25.8$  at baseline and  $52.6s \pm 16.6$  at reassessment, while the control group scored  $71.1s \pm 25$  and  $69s \pm 22$  at baseline and reassessment, for an effect size of  $f = 0.41$  and a P value of 0.011.

Significant differences were also found in the secondary measures of the CSRT decision and movement time components, postural sway with eyes open, 10-meter walk test, the 9-HPT, and the MSFC, all in favour of the intervention group. The CSRT decision time at baseline and reassessment were  $0.99s \pm 0.12$  and  $0.89s \pm 0.11$  for the intervention group and  $0.98s \pm 0.12$  and  $0.98s \pm 0.18$  for the control group ( $f = 0.33$ ,  $P=0.041$ ). The CSRT movement time at baseline and reassessment were  $1.4s \pm 1.7$  and  $1.26s \pm 1.7$  for the intervention group and  $1.4s \pm 1.6$  and  $1.5 \pm 5.2$  for the control group ( $f = 0.33$ ,  $P=0.039$ ). The mean postural sway with eyes open at baseline and reassessment was  $97mm \pm 46$  and  $62mm \pm 30$  for the intervention group and  $131mm \pm 75$  and  $128mm \pm 101$  for the control group ( $f = 0.33$ ,  $P=0.040$ ). The 10-meter walk test times at baseline and reassessment were  $12.5s \pm 5.0$  and  $10.5s \pm 4$  for the intervention group and  $11.4s \pm 4.3$  and  $11.1s \pm 4.9$  for the control group ( $f = 0.37$ ,  $P=0.023$ ). The mean scores on the 9-HPT at baseline and reassessment were  $30.4s \pm 9.0$  and  $26.8s \pm 5.4$  for the intervention group and  $27.5s \pm 9.2$  and  $29.6s \pm 8.3$  for the control group ( $P=0.001$ ). The mean scores on the MSFC at baseline and reassessment were  $0.42 \pm 2$  and  $-0.61 \pm 1.4$  for the intervention group and  $0.5 \pm 2$  and  $-0.27 \pm 2.3$  for the control group ( $P=0.001$ ). For the 9-HPT, the MSFC, and the dual-task TUG, effect sizes were not published, though the authors note that there was significant group-by-covariate interaction for these measures.

For the TUG dual task, the times at baseline and reassessment were  $15.8s \pm 7.3$  and  $13.8s \pm 4.8$  for the intervention group and  $17.1s \pm 8$  and  $14.5s \pm 5.5$  for the control group, with a P-value of 0.036, indicating statistical significance favouring the control group, though no effect size was reported.

No statistically significant differences were found for the remaining measures, including sway with eyes closed, 6-minute walk test, TUG single task, SDMT, the difference between TMT parts B and A, or number of falls at 6-month follow up.

No adverse events were reported in the intervention group, and 82% of the intervention group completed the full intervention, with an average total practice time of 71 minutes  $\pm$  60 per week. Within the intervention group, 2 participants with an EDSS of 6 used a frame and 2 participants with an ADSS of 5 used a walking stick during step training for safety.

### Original Authors' Conclusions

[Paraphrase as required. If providing a direct quote, add page number]

The authors conclude that, for adults with MS, the step training program that they designed can be used safely in the home without supervision and that the intervention can improve participants' performance in stepping tasks, coordination, standing balance, and functional tasks for this population. However, the authors state that further research is needed with appropriately powered studies to determine whether this intervention significantly reduces a participant's number of falls or significantly affects other outcomes, including fear of falling and fatigue.

### 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 was determined to have a score of 9/11 on the PEDro scale; two points were deducted for lack of blinding of subjects and lack of blinding of the therapist who initiated the intervention with each participant. However, the nature of studies that employ active physical interventions make blinding of subjects and those who administer the therapy difficult if not impossible. Given these limitations, the study has a relatively high PEDro score, which suggests that the study design was of moderately high quality.

The lack of information about recruitment methods, procedure used to collect information about monthly falls, the calculation of total CSRT scores for each participant, the number of attempts allowed or required during CSRT scoring, protocol for use of the swaymeter, and the effect size for TUG dual task, 9-HPT, and MSFC are all potential causes for concern about the study's validity. Without information about the standardized procedures used to collect data for all assessments, there is potential for undocumented bias in the study results due to confounding factors such as practice effect during the testing, biased reporting of falls or CSRT performance, or introduction of error or bias through unstandardized use of the swaymeter. Information about recruitment methods would also be helpful to assess bias. Finally, while the TUG dual task, 9-HPT, and the MSFC were found to have significant group-by-covariate interaction, it would be helpful to see information about effect size, perhaps broken down into effect sizes for different baseline characteristics, to allow better-informed interpretation of the effects that the intervention may have had on these variables.

The two primary outcome measures, the CSRT and the SST, were measured using very similar tasks and the same specific equipment used in the intervention, thereby introducing bias through the increased familiarity of the intervention group with the game system. As a result, the control group may be experiencing learning effects during these outcome measures, thereby confounding the results for these tasks.

The ANCOVA analysis was appropriate for this study given the effects of baseline characteristics on the outcome measures used in the study. Missing data was reported through numbers of participants lost to follow up, however, no information was provided about the baseline characteristics of the participants lost to follow up or of the remaining group members after loss of participants. This information would be helpful to better compare the two groups that are ultimately analysed in the study.

Furthermore, the authors report no conflicts of interest, but if the authors considered marketing their step training program for financial gain or recognition, it may have introduced bias to the study design and analysis.

### **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.]

It is interesting that the intervention group practiced the stepping games for longer average times each week than they were requested to do by the researches, which suggests that the in-home, game format of this intervention may appeal to participants and potentially increase adherence. Due to no reported adverse events in this study, the step training program appears to be safe for independent home use after patient evaluation, system set up, and instruction by a physical therapist with follow-up during the first 2 weeks.

For ANOVA,  $f$ -values of 0.25 and 0.40 are considered to be medium and large effect sizes, respectively. For outcome measures with a  $P$  value  $\leq 0.05$ , the CSRT total time, sway with eyes open, and 10-m walk test all demonstrate moderately large effect sizes, with the SST showing a large effect size with intervention. The CSRT and SST are very similar to the intervention itself, however, so these high effect sizes may be influenced by learning effects. The improvement in sway with eyes open and the 10-meter walk test are encouraging indicators of improved standing balance and walking speed as a result of the step training program intervention. The MCID for the 10-meter walk test in geriatric and SCI populations is reported to be 0.13m/s, 0.16m/s for people with stroke, and 0.15 for people with TBI,<sup>12</sup> so the 0.2m/s improvement demonstrated in this study is likely to be clinically meaningful. No information is currently available for clinical significance of swaymeter measurements, so it is unclear whether the 3.5 cm reduction in sway displacement with eyes open in the intervention group is clinically meaningful.

It is also interesting that there was significant improvement on the 9-HPT with intervention given that the step training program was not designed to train upper extremity functions. The 3.6s improvement in the 9-HPT performance of the intervention group surpasses the reported MDC of 2.6s for people with Parkinson's disease, though MCID data is currently unavailable. However, it seems reasonable that a 3.6s improvement would translate to noticeable improvements in coordination and speed of upper extremity movements during daily activities. This improvement in upper extremity function despite lack of upper extremity training in the intervention suggests that the intervention may have affected the central nervous system in ways that could improve more generalized motor control and speed of movement in addition to the effects on lower extremities.

The lack of independently significant differences on the cognitive tests suggest that the intervention was not effective at improving cognition. While change in performance on the dual task TUG was reported to be significant, the improvement was greater in the control group (17.1s at baseline – 14.5s at reassessment = 2.6s) than for the intervention group (15.8s at baseline – 13.8s at reassessment = 2.0s), however, because improvements on the dual task TUG were correlated with scores at baseline, and because the control group

performed worse on the dual task TUG at baseline, it is difficult to compare the effect of the intervention on dual task performance with the provided data.

**(2) Description and appraisal of *Mobility and cognitive correlates of dual task cost of walking in persons with multiple sclerosis* by Sosnoff JJ, Socie MJ, Sandroff BM, Balantrapu S, Suh Y, Pula JH, and Motl RW, 2014.**

<p><b>Aim/Objective of the Study/Systematic Review:</b></p>
<p>The objective of this study was to determine whether cognitive function and mobility correlate with dual task cost (DTC) for people with multiple sclerosis (MS).</p>
<p><b>Study Design</b></p> <p>[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]</p> <p>Note: For systematic review, use headings 'search strategy', 'selection criteria', 'methods' etc. For qualitative studies, identify data collection/analyses methods.</p>
<p>This was a cross-sectional study with no control group and no intervention. Those administering the assessments were not blinded to participants' performance on other assessments within the study. Outcomes were measured in a single visit for each participant and were performed in an order that alternated between active and inactive assessments in order to minimize fatigue.</p>
<p><b>Setting</b></p> <p>[e.g., locations such as hospital, community; rural; metropolitan; country]</p>
<p>Participants were recruited from the community in Urbana, Illinois, and assessments were performed at a local neurology clinic.</p>
<p><b>Participants</b></p> <p>[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]</p> <p>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.</p>
<p>Participants came from a convenience sample recruited by referral from local neurologists and met three inclusion criteria, including diagnosis of MS as confirmed by the participant's neurologist, no relapses within the past 30 days, and the ability to ambulate at least 25 feet in 180 seconds with or without aid. The sample included 96 community-dwelling participants with an average age of 52.7 years (SD=11.2 years) with a range of 30 to 78 years, and a median EDSS score of 4.5 with a range of 2.0 to 6.5 and an inter-quartile range of 3.0. Gender of participants was not reported. Because this cross-sectional study did not include an intervention, participants were not assigned to groups and there were no follow-up assessments. No dropouts were reported for this single-visit study.</p>
<p><b>Intervention Investigated</b></p> <p>[Provide details of methods, who provided treatment, when and where, how many hours of treatment provided]</p>
<p><i>Control</i></p>
<p>This non-interventional cross-sectional study did not include a control group.</p>
<p><i>Experimental</i></p>
<p>While there was no intervention or treatment in this study, all participants underwent four assessments during their single study visit at a local neurology clinic. These assessments included a neurological exam to determine an Expanded Disability Status Scale (EDSS), assessment of dual task cost (DTC), cognitive assessment using the Symbol Digit Modalities Test (SDMT), and mobility assessment using the Timed 25-Foot Walk (T25FW) test. Active and inactive tests were administered in alternating order (for example, the</p>



SDMT might be performed between the T25FW test and the DTC testing) to minimize fatigue. The authors do not indicate who administered the assessments.

### **Outcome Measures** (Primary and Secondary)

[Give details of each measure, maximum possible score and range for each measure, administered by whom, where]

Each participant underwent a neurological exam to determine an EDSS score and assessments for three outcome measures: dual task cost (DTC) testing, the Timed 25-Foot Walk (T25FW) test, and the Symbol Digit Modalities Test (SDMT). Because the inclusion criteria required participants to be able to walk at least 25 feet in 180 seconds, the possible range of EDSS scores for participants was 0 to 6.5, with 6.5 indicating the highest level of disability for a participant who was still able to ambulate further than 5 meters without rest with the use of bilateral assistance.

The DTC testing was performed by comparing two trials of the participant walking at a self-selected, "usual" pace on a 26-foot GaitRite pathway to two trials of the participant walking at a self-selected pace while performing the cognitive task of orally listing as many fruits and vegetables or as many words that start with "D" as possible while walking. The GaitRite pathway is embedded with sensors that allow calculation of gait and spatiotemporal parameters from individual footfalls. The DTC was calculated as a percent change in velocity between the two walking conditions, with a positive DTC indicating that the participant decreased gait speed while performing the cognitive task, and a negative DTC indicating that the participant increased gait speed while performing the cognitive task as compared to walking without the cognitive task.

The T25FW test was performed by having participants walk over a straight 25-foot level path with no obstacles as fast and safely as possible. Participants were instructed to keep walking past the end position of the 25 feet to minimize deceleration during the test. The test was performed twice and the two times to complete the T25FW were averaged and recorded in seconds.

The SDMT involved providing participants with a sheet of paper displaying a key of 9 symbols which were paired with 9 corresponding numbers, followed by a series of 110 symbols. Participants were instructed to match each symbol with its corresponding number in order without skipping any symbols, with the goal of matching as many symbols to numbers as possible in 90 seconds. The quantity of correctly provided numbers at the end of 90 seconds was recorded, with a highest possible score of 110 correct numbers.

All assessments were performed in a local neurological clinic. The authors do not indicate who conducted the assessments.

### **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]

On average, the percent change in velocity for DTC was 12.5% (SD=9.3%), indicating reduction in gait velocity with performance of the cognitive task, with a range of -14.1% to 42.4% (a negative percentage indicates increased gait speed while performing the cognitive task while a positive percentage indicates decreased gait speed while performing the cognitive task). The number of words listed by the participants during the cognitive tasks ranged from 3 to 12 with an average of 6.9 words. Average performance on the T25FW was 6.8 seconds (SD=3.1 s) with a range of 3.1 to 24.5 seconds. The average score for the SDMT was 45 items (SD=12 items), and ranged between 15 and 79 items.

The authors performed a bivariate correlation analysis that revealed a significant negative correlation between DTC and T25FW ( $r=0.27$ ;  $p<0.05$ ), indicating that improved performance on the T25FW correlated to decreased DTC. The bivariate correlation analysis also revealed that DTC was not related to SDMT performance ( $r=0.01$ ;  $p>0.05$ ). The authors did not report exact p-values for the bivariate correlation analysis or the partial correlation analysis and regression analysis described below.

Interestingly, when the authors conducted a partial correlation analysis, they found that SDMT was significantly correlated with DTC ( $r_p=0.20$ ;  $p<0.05$ ) when they controlled for performance on the T25FW. This correlation between SDMT performance and DTC was positive, indicating that the DTC increased with improved performance on the SDMT. They further found that controlling for SDMT did not affect the correlation between DTC and T25FW ( $r_p=0.29$ ;  $p<0.05$ ).

In a three-step regression analysis, step 1 indicated that DTC was significantly correlated with age and EDSS ( $B=0.23$  and  $0.10$ , respectively;  $p<0.05$ ). In step 2, the authors found that a statistically significant amount of variance in DTC, beyond that explained by age and EDSS, could be explained by performance on the T25FW and the SDMT ( $B=0.31$  and  $0.27$ , respectively;  $R^2$  change =  $0.08$ ;  $p<0.05$ ). The third step revealed that interaction did not explain any further variance in DTC.

### **Original Authors' Conclusions**

[Paraphrase as required. If providing a direct quote, add page number]

The authors conclude that, because their results indicate that cognitive function on the SDMT and walking speed on the T25FW test were independent correlates with DTC, it may be helpful to manipulate patients' mobility or cognition to affect DTC. However, the authors caution that "a substantial amount of variance in DTC" was not explained by either cognitive function or walking speed in this study, indicating that other factors also influence DTC for this population (p.207).

Because the DTC observed in this study is similar to that found in populations with other neurological conditions and diseases, the authors further conclude that the factors influencing DTC may not be disease-specific and therefore a general rehabilitative approach, rather than a disease-specific approach, may be appropriate to address increased DTC across a range of neurological conditions.

In response to the finding that cognitive function was only correlated with DTC when the authors controlled for T25FW performance and that DTC was found to increase with improved cognitive function, the authors discuss the possibility that individuals with higher cognitive functioning place greater priority on cognitive function during the dual task at the expense of walking speed. The authors did not guide prioritization of these tasks during DTC testing in this study, therefore they suggest caution when interpreting their results about the relationship of SDMT performance to DTC. They tentatively conclude that although cognitive functioning has a relatively small independent correlation with DTC, so rehabilitation focused on improving cognitive function may increase DTC rather than the desired decrease in DTC. The authors suggest that rehabilitation geared specifically toward walking function and dual-task performance may be effective at reducing DTC.

## 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 was determined to have a score of 10/11 on the NIH Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies; one point was deducted for the lack of assessor blinding to the participants' performance on separate outcome measures. Criteria #7, #10, and #13 were deemed not to be applicable to the design of this study and were excluded from the total number of points on the assessment tool (for example, the study did not include an intervention or exposure and outcomes were measured at only one point in time). This high score after accounting for the three non-applicable criteria suggests that the study design was of relatively high quality.

The lack of blinding to participants' separate performances on outcome measures, lack of information about who conducted the assessments, lack of information about the specific protocol and scripting for administration of outcome measures, and lack of demographic information such as gender of participants are all potential concerns about the validity of this study. Unblinded assessors may have introduced bias while administering subsequent outcome measures based on a participant's performance on a previously completed outcome measure. Information about the assessors' qualifications, number of assessors, and training provided to the assessors would be helpful to examine potential for decreased reliability or increased bias in the administration and scoring of outcome measures. Further information about any protocol or scripting used for testing would also be helpful to assess validity, since scripting and protocols may introduce bias (for example, a script may subtly promote prioritization of performance on a cognitive task rather than gait speed while undergoing DTC testing). Demographic information about participants such as gender would also be helpful in assessing the generalizability of the study results to patients in clinical practice.

The authors did account for a reasonable number of potential confounding variables, such as age and EDSS, though the authors themselves point out that other variables must exist due to significant variance in DTC that was not explained by the variables examined in the study. No missing data and no dropouts were reported, so the reader is inclined to assume that all participants selected for the study completed all of the outcome measures. The separate analyses, including bivariate correlation analysis, partial correlation analysis, and a three-step regression analysis, are appropriate to the study and are useful in examining the correlations between different factors and DTC while accounting for interactions.

### 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 indicate that increased gait speed on the T25FW test is independently correlated with decreased DTC ( $B=0.31$ , indicating that T25FW test performance explains 31% of the variance in DTC). To a lesser extent ( $B=0.27$ ), cognitive function on the SDMT is also correlated with DTC, with better performance on the SDMT being associated with increased DTC. Age and EDSS were also significantly correlated with DTC ( $B=0.23$  for age and 0.10 for EDSS). The information provided by the authors does not allow conclusions to be drawn about the quantity of change needed in any of the significant factors to correlate with a specific change in DTC, and causation cannot be assumed. The inability of the considered

factors to completely explain the variance in DTC also indicates that other variables may alter DTC. Fatigue, pain, and anxiety, for example, were not considered in this study and may account for some of the remaining unexplained variance in DTC.

The association of age and EDSS with DTC suggests that the increase in DTC that is identified in this adult population with MS corresponds to disability level and the aging process. Since MS is a disease that progresses over time, however, increased age and increased EDSS scores are likely related and the authors did not analyse the data to determine whether both are independently associated with increased DTC. The study results therefore suggest that patients with increased age, increased EDSS, or both may be at greater risk for increased DTC, since the interaction between the two factors cannot be determined from the information provided.

While improved performance on the SDMT is associated with increased DTC in this study, this may not be the case with a different cognitive task or with instructions to prioritize walking speed over SDMT performance during testing. It was appropriate for the authors to caution readers about drawing conclusions about cognitive function's relationship to DTC based on these results.

Because increased gait speed on the T25FW test was significantly and independently correlated with decreased DTC, it is possible that interventions to increase gait speed may result in decreased DTC. However, because causation cannot be assumed, it may also be possible that dual task training to reduce DTC may also improve gait speed on the T25FW test.

**(3) Description and appraisal of *Walking and cognition, but not symptoms, correlate with dual task cost of walking in multiple sclerosis* by (Motl RW, Sosnoff JJ, Dlugonski D, Pilutti LA, Klaren R, and Sandroff BM, 2014)**

<b>Aim/Objective of the Study/Systematic Review:</b>
The objective of this study was to determine whether cognitive processing speed, walking performance, or symptoms of fatigue, pain, anxiety, and depression correlate with the dual task cost (DTC) of walking in people with multiple sclerosis (MS).
<b>Study Design</b>
[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 cross-sectional study with no control group and no intervention. Those administering the assessments were not blinded to participants' performance on other assessments within the study. Outcomes were measured in a single visit for each participant. The dual task cost (DTC) assessment was performed before the 6-minute walk test (6MWT), with the non-physical outcome measures administered between the DT paradigm and performance of the 6MWT to minimize effects of fatigue.
<b>Setting</b>
[e.g., locations such as hospital, community; rural; metropolitan; country]
No detailed information is provided about the geographic location of this study. Participants were recruited from the North American Research Committee on Multiple Sclerosis (NARCOMS) registry, indicating that participants were recruited from within North America, or from the researchers' laboratory database, indicating that participants may be more local. More specifically, participants had to be willing and able to travel to the research site, which suggests that all participants were likely relatively local to the research site. The research site is not specified, but the authors are affiliated with the University of Illinois at Urbana-Champaign, which suggests that the research site was in or near Urbana or Champaign geographically.
<b>Participants</b>
[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.
Participants were recruited by a flyer that was distributed to patients registered with NARCOMS or listed in the researchers' laboratory database. Of the 511 people who expressed interest in participation, the project

coordinator was able to contact 230 potential participants to be screened for inclusion in the study. No information is provided about how the study coordinator selected the 230 potential participants from the initial 511 people who expressed interest. To be included, potential participants had to be diagnosed with MS and have no history of relapses within the past 30 days, between 18 and 64 years old, able to walk with or without an assistive device, willing and able to travel to the research site and participate in the walking assessments, and able to obtain physician approval to participate in the study. Of the 230 people screened for inclusion, 145 people did not meet inclusion criteria and 3 additional people chose not to participate, leaving a sample of 82 participants who completed the study.

Because there were no interventions in this cross-sectional study and because all outcome measures were taken during a single visit, participants were not divided into groups and there were no dropouts or loss to follow-up in this study population. Of the participants, 77% were female, 83% were college-educated, and 60% were employed at the time of the study. Participants had an average age of 49.4 years (SD=9.1 years), with a median self-reported Expanded Disability Status Scale (SR-EDSS) score of 3.5 (interquartile range = 3). 80% of the participants had the relapsing-remitting form of MS, while 11% had secondary progressive MS and 9% had primary progressive MS. The average disease duration for all participants was 11.6 years (SD=8.2 years).

### **Intervention Investigated**

[Provide details of methods, who provided treatment, when and where, how many hours of treatment provided]

#### *Control*

This non-interventional cross-sectional study did not include a control group.

#### *Experimental*

While there was no intervention or treatment in this study, all participants underwent seven assessments during their single study visit. These assessments included, in the following order to minimize the effects of physical fatigue, the SR-EDSS to establish EDSS score, assessment of DTC, symptomatic scales to include the Fatigue Severity Scale (FSS), the Hospital Anxiety and Depression Scale (HADS), and the short-form McGill Pain Questionnaire (SF-MPQ) to assess fatigue, anxiety, depression, and pain respectively, the oral version of the Symbol Digit Modalities Test (SDMT) to assess cognitive processing speed, and the 6MWT to assess walking performance. The authors do not indicate who administered the assessments.

### **Outcome Measures (Primary and Secondary)**

[Give details of each measure, maximum possible score and range for each measure, administered by whom, where]

The following outcome measures were used with all participants to ultimately determine each outcome measure's relationship to DTC: the SR-EDSS, the FSS, the HADS, the SF-MPQ, the oral version of the SDMT, and the 6MWT. The SR-EDSS is a self-report measure with 18 items that correspond to varying grades of Expanded Disability Status Scale (EDSS) scores, ranging from a score of 0, or no discernible disability, to a score of 9, in which a patient is bedridden. Because participants must be ambulatory to participate in the study, the possible range of EDSS scores for participants was 0 to 6.5.

The FSS is a self-reported questionnaire that assesses the participant's perceived fatigue over the course of the past week; the score is calculated as an average of the 9 items on the scale and ranges from 0 (no perceived fatigue) to 7 (the most severe fatigue with the greatest impact). The HADS is a 14-item self-reported scale that can be divided into two subscales of 7 items each: one subscale for anxiety, and one for depression. Total scores for each subscale on the HADS range from 0 (very infrequent to no symptoms of anxiety or depression) to 21 (the highest frequency of anxiety or depression symptoms). The SF-MPQ is a 15-item self-reported questionnaire that assesses perceived pain over the last 4 weeks, with a low score of 0 representing no pain and a high score of 45 indicating the greatest pain.

The oral version of the SDMT involves providing participants with a sheet of paper displaying a key of 9 symbols which were paired with 9 corresponding numbers, followed by a series of 110 symbols. For the oral version, participants were instructed to match each symbol with its corresponding number by stating the corresponding numbers verbally, in order, and without skipping any symbols, with the goal of matching as many symbols to numbers as possible in 90 seconds. The quantity of correctly provided numbers at the end of 90 seconds was recorded, with a highest possible score of 110 correct numbers.

The 6MWT is used to measure walking performance by measuring the distance in meters walked by the participant in 6 minutes. In this study, participants were directed to walk as fast and as far as possible, and the track consisted of one corridor with 180-degree turns. The length of the corridor was not stated in the study article.

Finally, dual task cost (DTC) was assessed by comparing two trials of the participant walking at a self-selected, comfortable pace on a 4.6-meter GaitRite pathway to two trials of the participant walking at a self-

selected pace while performing the cognitive task of orally listing as many fruits and vegetables or as many words that start with "D" as possible while walking. The GaitRite pathway is embedded with sensors that allowed calculation of gait velocity, cadence, step length, step time, and percent of the gait cycle spent in double support. The DTC was calculated as a percent change in each of these parameters between the averages of the two walking conditions, with a positive DTC indicating that the participant decreased the measured number of units for a given parameter while performing the cognitive task, and a negative DTC indicating that the participant increased the measured number of units for a given parameter while performing the cognitive task. The number of words uttered during each of the cognitive trials was also recorded.

All outcome measures were conducted at the research site during the single study visit. No information is provided about the assessors who administered the outcome measures.

**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 mean scores for the 6MWT, SDMT, FSS, HADS depression subscale, HADS anxiety subscale, and SF-MPQ were, respectively, 428.7 m (SD=146.6 m), 47.0 correct responses (SD=10.7), 5.1 (SD=1.4), 7.8 (SD=2.7), 7.3 (SD=2.5), and 10.1 (SD=7.7). For the DTC assessment, the mean uttered words were 7.0 (SD=4.3) for the fruits and vegetables task and 5.8 (SD=3.4) for the words beginning with "D" task. Results from a repeated measures ANOVA revealed that, within the DTC assessment, there were statistically significant main effects of cognitive task performance on velocity (13.5% reduction in velocity,  $p < 0.001$ ), cadence (8.8% reduction in cadence,  $p < 0.001$ ), step length (5.1% reduction in step length,  $p < 0.001$ ). The cognitive task was found not to produce significant effects on step time ( $p = 0.69$ ) or double support time ( $p = 0.99$ ).

Bivariate correlation analysis revealed that the 6MWT was significantly and negatively associated with DTC for velocity and step length ( $r = -0.41$ ,  $p < 0.001$  and  $r = -0.45$ ,  $p < 0.001$ , respectively). The negative correlation indicates that better performance on the 6MWT was associated with a decreased DTC of walking. Performance on the SDMT was also significantly and negatively associated with DTC, with velocity and step length  $r$ -values of  $-0.32$  and  $-0.37$ ,  $p < 0.001$ , respectively. SR-EDSS scores were also significantly and positively associated with DTC (velocity  $r = 0.25$ ,  $p < 0.05$  and step length  $r = 0.28$ ,  $p < 0.01$ ), and was also significantly associated with the 6MWT, SDMT, FSS, SF-MPQ, and the HADS depression subscale ( $r = -0.74$ ,  $r = -0.39$ ,  $r = 0.59$ ,  $r = 0.41$ , and  $r = 0.29$ , respectively, with all  $p < 0.001$ ), but was not significantly associated with HADS anxiety subscale.

None of the symptomatic scores (FSS, HADS, and SF-MPQ) were found to have a significant association with DTC of walking.

In a linear regression of the DTC of walking for velocity and step length on SDMT and the 6MWT, only the 6MWT explained additional variance after controlling for SR-EDSS scores. In this analysis, the 6MWT explained an additional 11% of the variance in DTC of velocity ( $p < 0.001$ ) and an additional 13% of the variance in DTC of step length ( $p < 0.001$ ).

**Original Authors' Conclusions**  
 [Paraphrase as required. If providing a direct quote, add page number]

Because the study results indicate that improved walking performance is significantly associated with decreased DTC of walking both before and after controlling for SR-EDSS, and because cognitive processing speed on the oral SDMT was found not to be associated with DTC of walking after controlling for SR-EDSS and symptoms such as fatigue, pain, depression and anxiety were found not to be associated with DTC, the authors conclude that walking performance may be an effective focus of intervention to decrease the DTC of walking in people with MS.

The authors further suggest that the gait parameters of velocity, cadence, and step length are likely to be modifiable aspects of gait that can contribute to decreased DTC. The authors also posit that these three gait parameters should be included in dual task paradigms in future research to test the possibility that interventions to improve walking performance will reduce the DTC of walking for people with MS.

Limitations identified by the authors include the possibility that different methods of measurement for DTC and testing of populations with different demographics, such as inclusion of more males or increased mean duration of disease, may yield different results. Because the cognitive tasks in this study required verbal fluency, the authors also felt that controlling for scores of verbal fluency or use of alternate cognitive assessment methods may have produced different results.

**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 was determined to have a score of 10/11 on the NIH Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies; one point was deducted for the lack of assessor blinding to the participants' performance on separate outcome measures. Criteria #7, #10, and #13 were deemed not to be applicable to the design of this study and were excluded from the total number of points on the assessment tool (for example, the study did not include an intervention or exposure and outcomes were measured at only one point in time). This high score after accounting for the three non-applicable criteria suggests that the study design was of relatively high quality.

Potential concerns about the validity of this study include the lack of blinding of assessors to participants' performance and scores on each of the measures, lack of information about the assessors, and lack of information about the scripting used by the test administrators. The lack of assessor blinding may introduce bias as researchers may consciously or subconsciously alter their interaction with participants and administration of subsequent tests according to performance on earlier tests. More information about the assessors, such as how many assessors were used, their qualifications, and how they were trained, would help to identify potential problems with reliability and bias. Information about scripting would also be helpful to assess the potential for bias in the instructions given to participants, such as an emphasis on walking speed during the DTC assessment that may lead participants to prioritize walking speed over performance of the cognitive task.

The authors report that all participants completed all of the included outcome measures and no missing data was reported. This study also considered a respectable number of variables, though the authors suggest that verbal fluency may have been a confounding variable that was not accounted for in the study design. The use of bivariate correlation and stepwise linear regression analyses was appropriate to this study to determine relationships between study variables to DTC as well as interactions between variables.

### **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.]

These results indicate that improved walking performance on the 6MWT is independently associated with decreased DTC of walking, regardless of SR-EDSS score. Performance on the 6MWT explained 11% of the variance in the velocity component of DTC and 13% of the variance in the step length component of DTC. This suggests that gait speed is negatively related to DTC of walking though causation cannot be inferred from this study. It is unclear whether a change in gait speed for an individual, perhaps through gait training, would cause a reduction in DTC of walking. Furthermore, this study does not provide information about the effect size of a change in gait speed on DTC, and the minimal clinically important difference for the DTC of walking has not been established, though the authors do cite additional research establishing a link between DTC of walking and falls.

Symptoms of MS, including fatigue, pain, anxiety, and depression were found not to be significantly correlated with the DTC of walking in this study. Self-reported EDSS was significantly correlated with DTC, however, indicating that increased disability is related to the increased DTC of walking, though causation again cannot be inferred about this relationship.

Cognitive processing speed on the oral SDMT was not significantly associated with DTC of walking after controlling for SR-EDSS, but this finding should be interpreted with caution. The cognitive processing speed in this task represents only one form of cognition and relies on verbal fluency, which was not controlled for in the study. It is possible that a different cognitive task or inclusion of controls for verbal fluency may produce different results regarding the relationship between cognitive processing speed and DTC of walking.

## **EVIDENCE SYNTHESIS AND IMPLICATIONS**

The Hoang et al. study used a step training intervention as opposed to a gait training intervention as specified in the PICO question at hand. The step training intervention is similar to gait training in the standing position of the participant, the shifting of weight from one foot to another, and the continuous stepping nature of the intervention task. The effects of step training on dual task performance in this study were unclear due to the interaction of baseline factors with dual task TUG performance. While the step training program did not hinder dual task performance in this study, whether or not this step training program had a significant or clinically meaningful positive effect on dual task performance cannot be determined from the provided data. In light of this study, it appears that step training in clinical practice may or may not improve dual task performance. Based on this evidence, it is advisable to select other evidence-based approaches to affect dual task performance rather than the home-based electronic stepping program used in this study's intervention. While the intervention used in this study involved a specific

electronic game without supervision, the participants did adhere to the recommended 2 sessions of at least 30 minutes of step training per week for 12 weeks and did not see significant effects on dual task performance. This suggests that step training interventions may not be effective to improve dual task performance. However, because step training lacks specificity to the walking required in assessments of dual task performance, this finding may not be relevant to the clinical question about the effects of gait training on dual task performance.

While the study by Sosnoff et al. did not include a gait or walking intervention, the study results do indicate that increased walking speed on the T25FW test is independently correlated with decreased DTC for adults with MS. This suggests that an intervention to improve gait speed may be an effective treatment to decrease DTC of walking, which supports the potential use of gait training to improve dual task performance. The results also indicate, however, that the effect size of increased gait speed on DTC is not reported in this study, so it cannot be determined from this study whether gait training alone could produce clinically meaningful changes in DTC.

The study by Motl et al. also did not include a gait or walking intervention, but the results of this study indicate that increased walking speed during the 6MWT is independently correlated with decreased DTC of walking for adults with MS. This provides further support that an intervention to improve gait speed, such as gait training, may be an effective treatment to improve dual task performance.

The Hoang et al. study has the highest level of evidence of the three included studies: level 1b. However, the findings of this study relate to step training rather than gait training. While this is a high level of evidence, the lack of specificity to a gait training intervention makes generalization of the results to gait training questionable. The remaining cross-sectional studies provide level 2b evidence, however, both studies found significant correlations between gait speed and the DTC of walking, and both studies scored 10 out of 11 on the NIH Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies, which suggests that the studies are of high quality.

While none of the studies included a gait training intervention, the two of the three studies that are most specific to the question at hand suggest that improved gait speed is associated with improved dual task performance. Causality cannot be inferred from the cross-sectional studies, but the evidence overall suggests that interventions designed to improve gait speed may also improve dual task performance. Because difficulty with gait is prevalent among people with MS,<sup>13</sup> the use of gait training in the clinic is appropriate for a majority of physical therapy patients in this population regardless of gait training's effects on dual task cost, and the evidence presented here suggests that gait training may indeed provide the added benefit of improved dual task performance. There is, therefore, slight evidence to support the use of gait training in an attempt to improve dual task performance with minimal risk to the patient.

Future studies investigating the effects of gait speed on dual task performance should include calculations to describe the effect size of a specific increment in increased gait speed on DTC and should focus on the gait parameters of velocity, step length, and cadence as components of the DTC of walking, since these were the components found to be affected during dual task assessment by Motl et al. Additional studies are also needed to determine causality in the relationship between gait speed and dual task performance and to determine the minimal clinically important difference for changes in the DTC of walking. Further research to establish the relationship of various cognitive tasks to DTC of walking would also be helpful to investigate whether increased walking speed is similarly related to DTC when different cognitive functions are required.

Most directly relevant to the question at hand, future studies should include randomized controlled trials that examine the effect of gait training interventions on gait speed and DTC. These studies should include matched control groups, adequately powered sample sizes, scripting and protocol design to clarify any prioritization provided during dual task assessment, and consideration of participants' characteristics and performance at baseline.

## REFERENCES

[List all references cited in the CAT]

1. Hoang P, Schoene D, Gandevia S, Smith S, Lord SR. Effects of a home-based step training programme on balance, stepping, cognition and functional performance in people with multiple sclerosis - a randomized controlled trial. *Mult Scler*. 2015;1-10. doi:10.1177/1352458515579442.
2. Kramer A, Dettmers C, Gruber M. Exergaming With Additional Postural Demands Improves Balance and Gait in Patients With Multiple Sclerosis as Much as Conventional Balance Training and Leads to High Adherence to Home-Based Balance Training. *Arch Phys Med Rehabil*. 2014;95(10):1803-1809. doi:10.1016/j.apmr.2014.04.020.
3. Sosnoff JJ, Socie MJ, Sandroff BM, et al. Mobility and cognitive correlates of dual task cost of walking in persons with multiple sclerosis. *Disabil Rehabil*. 2014;36(3):205-209. doi:10.3109/09638288.2013.782361.
4. Motl RW, Sosnoff JJ, Dlugonski D, Pilutti L a., Klaren R, Sandroff BM. Walking and cognition, but not symptoms, correlate with dual task cost of walking in multiple sclerosis. *Gait Posture*. 2014;39(3):870-874. doi:10.1016/j.gaitpost.2013.11.023.
5. Learmonth YC, Sandroff BM, Pilutti L a., et al. Cognitive Motor Interference During Walking in Multiple Sclerosis Using an Alternate-Letter Alphabet Task. *Arch Phys Med Rehabil*. 2014;95(8):1498-1503. doi:10.1016/j.apmr.2014.03.007.
6. Kalron A, Dvir Z, Achiron A. Walking while talking—Difficulties incurred during the initial stages of multiple sclerosis disease process. *Gait Posture*. 2010;32(3):332-335. doi:10.1016/j.gaitpost.2010.06.002.
7. Monticone M, Ambrosini E, Fiorentini R, et al. Reliability of spatial-temporal gait parameters during dual-task interference in people with multiple sclerosis. A cross-sectional study. *Gait Posture*. 2014;40(4):715-718. doi:10.1016/j.gaitpost.2014.06.015.
8. Nilsagård YE, von Koch LK, Nilsson M, Forsberg AS. Balance Exercise Program Reduced Falls in People With Multiple Sclerosis: A Single-Group, Pretest-Posttest Trial. *Arch Phys Med Rehabil*. 2014;95(12):2428-2434. doi:10.1016/j.apmr.2014.06.016.
9. Sandroff BM, Benedict RH, Motl RW. Nonsignificant Associations Between Measures of Inhibitory Control and Walking While Thinking in Persons With Multiple Sclerosis. *Arch Phys Med Rehabil*. 2015;96(8):1518-1524. doi:10.1016/j.apmr.2015.04.015.
10. Prosperini L, Castelli L, Sellitto G, et al. Investigating the phenomenon of “cognitive-motor interference” in multiple sclerosis by means of dual-task posturography. *Gait Posture*. 2015;41(3):780-785. doi:10.1016/j.gaitpost.2015.02.002.
11. Rehabilitation Measures Team. Rehab Measures: Nine-Hole Peg Test. *Rehabil Meas Database*. 2014. <http://www.rehabmeasures.org/Lists/RehabMeasures/PrintView.aspx?ID=925>. Accessed January 1, 2015.
12. Rehabilitation Measures Team. Rehab Measures: 10 Meter Walk Test. *Rehabil Meas Database*. 2014. <http://www.rehabmeasures.org/Lists/RehabMeasures/DispForm.aspx?ID=901>. Accessed January 1, 2015.
13. Larocca NG. Impact of walking impairment in multiple sclerosis: perspectives of patients and care partners. *Patient*. 2011;4(3):189-201. doi:10.2165/11591150-000000000-00000.