

## Balance and Falls in Parkinson's Disease: A Meta-analysis of the Effect of Exercise and Motor Training

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**ABSTRACT:** This systematic review with meta-analysis aimed to determine the effects of exercise and motor training on the performance of balance-related activities and falls in people with Parkinson's disease. Sixteen randomized and quasi-randomized controlled trials that assessed the efficacy of exercise and/or motor training against no intervention or placebo intervention were included. The primary outcome measures were balance-related activity performance (15 trials) and falls (2 trials). The pooled estimate of the effect of exercise and motor training indicated significantly improved balance-related activity performance (Hedges'  $g$ , 0.33; 95% confidence interval, 0.11–0.55;  $P = .003$ ), but there was no evidence

of an effect on the proportion of fallers (risk ratio, 1.02; 95% confidence interval, 0.66–1.58,  $P = .94$ ). Balance-related activity performance improved to a greater extent in the trials of programs involving highly challenging balance training, but the difference in effect sizes was not statistically significant ( $P = .166$ ). Exercise and motor training can improve the performance of balance-related activities in people with Parkinson's disease. However, further research is required to determine if falls can be prevented in this population. © 2011 Movement Disorder Society

**Key Words:** Parkinson's disease; exercise; motor training; balance

Falls are a major problem for many people with Parkinson's disease (PD).<sup>1</sup> Reduced balance is known to be an important risk factor for falls in this population.<sup>2–4</sup> Balance requires maintenance of the body's center of mass within the limits of the base of support while sitting or standing, and control of the center of mass while moving to a new base of support during walking or running.<sup>5</sup> Balance is often assessed with tasks

designed to make controlling the center of mass over the base of support difficult.<sup>6</sup> However, many daily activities, such as walking or standing up from a chair, are also balance-related, as they require control of the center of mass while moving to a new base of support. Therefore, balance can be measured indirectly by tests of the individual's ability to perform balance-related activities, particularly in individuals with impaired mobility.<sup>7</sup>

Most people with PD will ultimately develop reduced balance,<sup>8</sup> which worsens with disease progression.<sup>9,10</sup> Reduced balance is associated with falls, poor mobility, disability, and reduced quality of life in people with PD.<sup>2,11–13</sup> There is therefore a pressing need to explore interventions that may improve balance in this population.

The effect of exercise and motor training on balance in people with PD is unclear. Research to date has used a range of interventions and outcome measures designed to target and reflect balance.<sup>14–23</sup> Nonetheless, meta-analysis is able to combine studies with broadly similar interventions and outcomes and therefore provide a comprehensive summary of the available evidence.<sup>24</sup> Two published meta-analyses have addressed the effect of exercise on PD but did not

Additional Supporting Information may be found in the online version of this article.

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focus on balance outcomes.<sup>25,26</sup> One published review article specifically addressed the effects of exercise on balance<sup>27</sup> but did not include a meta-analysis.<sup>28</sup>

Therefore, to examine whether exercise and motor training improves balance-related activity performance and falls in people with PD, we conducted meta-analyses of randomized and quasi-randomized controlled trials that assessed the efficacy of these interventions against no or placebo intervention. Meta-regression was used to investigate if the total dose of exercise and the presence of highly challenging balance training were associated with the size of estimates of the effect of intervention on balance-related activity performance.

## Materials and Methods

### Data Sources and Searches

A literature search was conducted on September 24, 2009, to identify studies of the effects of exercise and motor training in people with PD. Databases searched were MEDLINE, EMBASE, AMED, PsycINFO, the Cochrane Central Register of Controlled Trials, and CINAHL. The electronic search strategies are available as Supporting Information on the Web site. The search was supplemented with searches of the Physiotherapy Evidence Database (PEDro; <http://www.pedro.org.au>) and examination of trials included in previously published systematic reviews.<sup>25–27,29–41</sup>

### Study Selection

Included trials were published randomized (or quasi-randomized, ie, not truly random but intended to produce similar groups) controlled trials of interventions for people with PD. The intervention was required to be exercise or motor training or a multifaceted intervention where most of the intervention was exercise or motor training and there was an aim (explicit or implicit) to improve performance of balance-related activities for at least 50% of the intervention (including cueing, strength, and fitness training). The effects of the intervention were required to be compared with a no-intervention or placebo control group (including social support or “interest” talks), and the ongoing effects of the intervention were evaluated with a measure of balance or a balance-related activity. Trials evaluating the effect of whole-body vibration were excluded as this was not considered exercise or motor training.

To determine eligibility, trial titles and abstracts were screened independently by 2 investigators (N.E.A. and C.G.C.). If it was clear that the trial did not meet the inclusion criteria, it was excluded. The full article was obtained for the remaining trials. Further eligibility assessment was then independently conducted for these trials by 2 investigators (N.E.A. and S.S.P.), using a standardized form containing the details of the inclusion criteria. Differences of opinion

regarding trial eligibility were resolved by discussion with the remaining 2 investigators (C.G.C. and C.S.).

### Data Extraction and Quality Assessment

A data extraction sheet was developed, pilot-tested on 5 randomly selected included trials, and modified accordingly. For each trial, 1 investigator (N.E.A.) extracted all data, and a second investigator (C.S.) checked the extracted data. Discrepancies were resolved by discussion. Care was taken to identify duplicate reports of trials. Published data only were used.

Information extracted from each trial comprised a description of participants, details of the exercise and motor training program, and details of outcome measures. The risk of bias from reported methodology for each trial was evaluated by 1 investigator (N.E.A.) in consultation with the other investigators using the Cochrane risk-of-bias tool.<sup>24</sup> This tool was used to assess and report the quality of the included trials, but trials were not excluded on the basis of this assessment.

### Data Synthesis and Analysis

The primary outcome measures were determined a priori; these were balance-related activity performance and proportion of fallers. The balance-related activities analysis involved the pooling of the most comprehensive balance measure from each trial.<sup>24</sup> The measure from each trial was chosen prior to analysis according to the following order of priority: the Berg Balance Scale,<sup>42</sup> the Timed Up and Go,<sup>43</sup> gait velocity/time, turning time, sit to stand time, Functional Reach,<sup>44</sup> and single leg stand time. Where a trial reported results for more than 1 of these outcomes, only the outcome of the highest priority was used.

Secondary outcome measures included individual balance-related activity performance measures. These were the Berg Balance Scale, the Timed Up and Go, turning time, sit to stand time, Functional Reach, single leg stand time, gait velocity/time, step/stride length, and gait cadence.

Trials with 2 similar intervention groups had the groups combined to create a single pair-wise comparison with the control group.<sup>24</sup> Where a trial included 2 different intervention groups (4 trials), each intervention was included in a separate comparison, with the number of participants in the control group divided equally between the comparisons and the control group mean and standard deviation left unchanged.<sup>24</sup> Repeating the primary meta-analysis with these different interventions combined into a single pair-wise comparison for each trial did not affect the overall result. For crossover studies, first-phase data only were used.<sup>24</sup> All data used were those collected immediately postintervention. Where the median and interquartile range were reported and the study sample size exceeded 70, the median was used as an approximation of the

mean, and the interquartile range was assumed to equal 1.35 standard deviations.<sup>24,45</sup>

Random-effects meta-analyses were conducted using Comprehensive Meta-Analysis software (Version 2, Biostat, Englewood NJ). The standardized mean difference (Hedges' *g*) was calculated for all meta-analyses except for the proportion of fallers, which was calculated as a risk ratio. Hedges' *g* was calculated using the pre- and post mean and standard deviation (14 trials) or change score data (2 trials) and was standardized using the posttest score standard deviation where available (14 trials). Two trials did not report posttest score standard deviations. For these trials, the posttest score standard deviation was estimated using the standard deviation of the change score and an estimated pretest-to-posttest correlation of 0.6 based on the pretest-to-posttest correlation of walking speed measures in reported trials of people with PD.<sup>23,46</sup> When analyses were repeated using a correlation of 0.5 or 0.7, the results were essentially unchanged. For secondary outcomes, an estimate of the difference in mean outcome scores in the original unit of measurement was calculated by multiplying Hedges' *g* by the largest included trial's standard deviation at baseline.<sup>24</sup> Statistical heterogeneity was quantified with the  $I^2$  and  $Q$  statistics. Publication bias for the primary outcome measures was assessed using Egger's test to determine if there was any evidence of a relationship between sample size and effect size.<sup>47</sup>

Two separate prespecified univariate random-effects meta-regressions were conducted to assess the associations between the total number of hours of intervention in the trials and the presence of highly challenging balance training (yes or no/unclear), and estimates of the effect of intervention on balance-related activity performance. Highly challenging balance training was defined as involving all of: movement of the center of mass, narrowing of the base of support, and minimizing upper limb support.<sup>48</sup> Sensitivity analysis was conducted to determine the effect of omitting studies for which the content of the balance training was unclear. All meta-regression analysis was conducted using the "metareg" command in Stata (Version 10, College Station, TX).

## Results

### Trial Flow and Study Characteristics

Searching identified 2798 records, of which 19 were potentially appropriate for inclusion in a meta-analysis (Fig. 1).<sup>49</sup> Three trials were excluded from the meta-analyses<sup>50–52</sup> because the balance measures they reported were not able to be pooled with any others. The characteristics of the included trials<sup>14,15,18,19,21,22,46,53–62</sup> are summarized in Table 1. The risk of bias assessment<sup>24</sup> for each included study is summarized in Table 2 and shows that 7 of the 16 trials were judged to fulfill the

criteria for at least 3 of the 5 domains, suggesting they were of moderate to high quality. The quality of an additional 8 trials was unclear, as there was insufficient information in the publication to permit judgment regarding adherence to each domain.

### Balance-Related Activity Performance

Fifteen trials<sup>14,15,18,19,21,22,46,53–58,60–62</sup> with outcomes associated with the performance of balance-related activities reported a total of 19 comparisons, involving 747 participants. The pooled estimate of the effect size was statistically significant in favor of intervention (Fig. 2). There was evidence of small sample bias (Egger's test of the intercept  $B_0$ , 1.69; 95% CI, 0.21–3.17;  $t = 2.41$ ; degrees of freedom ( $df$ ) = 17;  $P = .03$ ). The funnel plot of precision and Hedges' *g* showed a disproportionate number of smaller studies with a larger positive effect, suggesting some publication bias (available as Supporting Information on the Web site).

There was a moderate level of heterogeneity in the estimates ( $I^2 = 47\%$ ,  $Q = 33.8$ ,  $df = 18$ ,  $P = .013$ ). Meta-regression was used to investigate if differences in the total number of intervention hours and the presence of highly challenging balance exercises contributed to this heterogeneity. Results showed that there was no association between the total number of intervention hours and the effect of intervention on performance of balance-related activities (effect of dose on Hedges' *g*, 0.0002; 95% CI, –0.018 to 0.018;  $P = .998$ ). There was a larger effect on balance-related activity performance in the 5 comparisons where interventions included highly challenging balance exercises (Hedges' *g*, 0.62; 95% CI, 0.13–1.10,  $P = .015$ ) than in the 14 comparisons that did not, or where the content of the balance exercises was unclear (Hedges' *g*, 0.24; 95% CI, –0.02 to 0.50;  $P = .066$ ). However, the difference between the effects in these 2 groups of comparisons did not reach statistical significance (effect of highly challenging balance training on Hedges' *g*, 0.38; 95% CI, –0.17 to 0.93;  $P = .166$ ). Sensitivity analysis showed that removing the comparisons in which the content of the balance training was unclear (Table 1) had minimal effect on this result (difference in Hedges' *g*, 0.39; 95% CI, –0.24 to 1.02;  $P = .205$ ).

### Falls

The proportion of fallers was reported in 2 trials,<sup>14,22</sup> involving a total of 250 participants. There was no evidence of an effect from intervention (Fig. 3), and there was a moderate level of heterogeneity in the estimates ( $I^2 = 49\%$ ,  $Q = 2.0$ ,  $df = 1$ ,  $P = .16$ ).

### Secondary Outcome Measures

Forest plots and approximate mean differences for the Berg Balance Scale,<sup>14,18,19,21</sup> Timed Up and

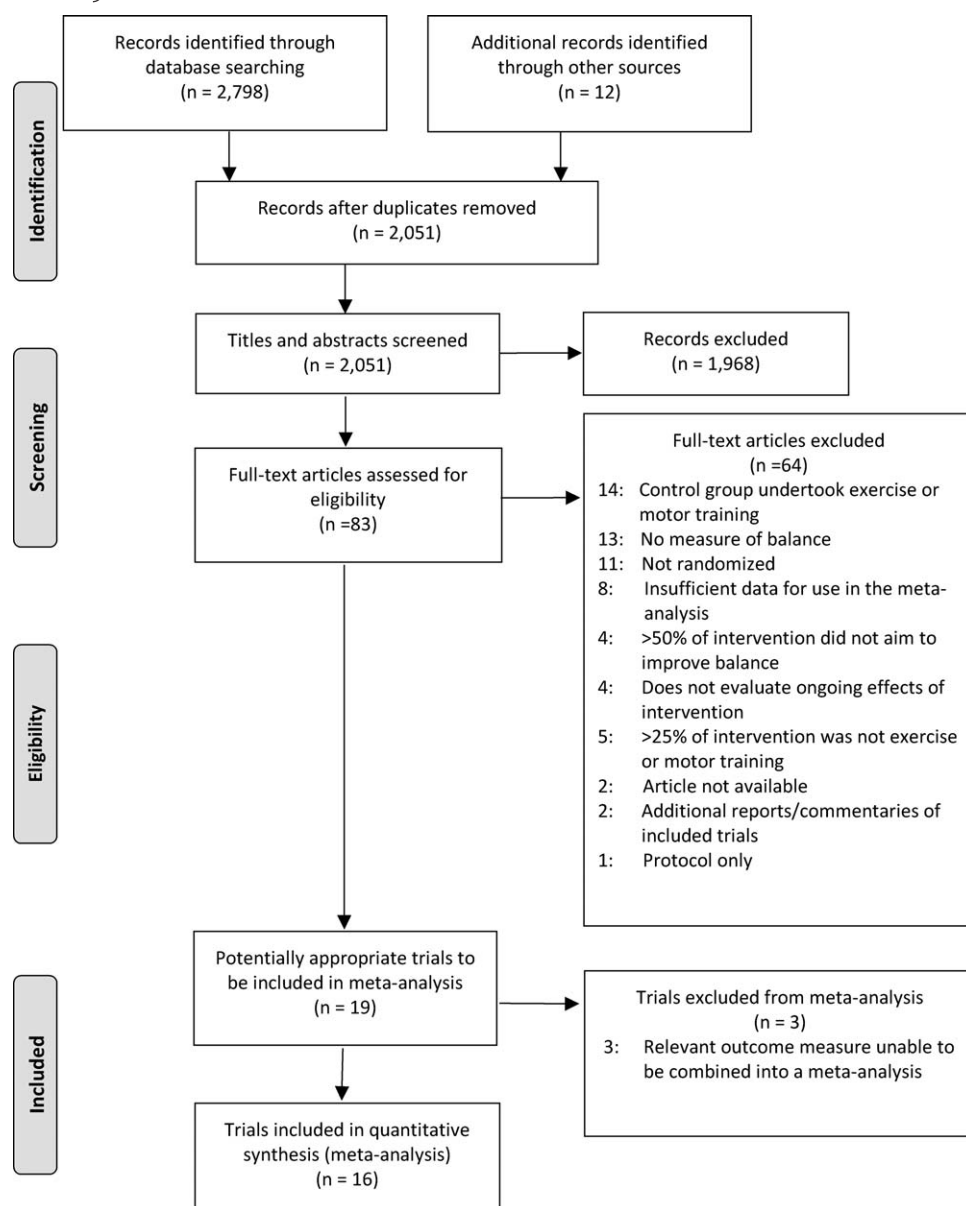


FIG. 1. PRISMA flow diagram<sup>49</sup> showing flow of information through the review.

Go,<sup>18,19,22,53,61</sup> turning time,<sup>53,54,58,62</sup> sit to stand time,<sup>58,60</sup> Functional Reach,<sup>14,22,53,62</sup> and single leg stand time<sup>19,22,53,58</sup> are presented in Figure 4. The pooled estimates (Hedges' *g*) of effect size were all in the direction of showing favorable effects of intervention; however, this favorable result only reached statistical significance for turning time (Fig. 4C), representing a mean difference of approximately 1.2 seconds when turning 360 degrees.

Variation in the estimates was minimal for turning time ( $I^2 = 0\%$ ,  $Q = 0.84$ ,  $df = 3$ ,  $P = .84$ ), Functional Reach ( $I^2 = 0\%$ ,  $Q = 2.67$ ,  $df = 3$ ,  $P = .44$ ), and single leg stand time ( $I^2 = 0\%$ ,  $Q = 2.576$ ,  $df = 3$ ,  $P = .46$ ). There were low to moderate levels of heterogeneity in the estimates of the effect of intervention on sit to stand time ( $I^2 = 37\%$ ,  $Q = 3.16$ ,  $df = 2$ ,  $P = .21$ ) and Timed Up and Go ( $I^2 = 34\%$ ,  $Q = 7.5$ ,

$df = 5$ ,  $P = .18$ ). The Berg Balance Scale estimates showed a high level of heterogeneity ( $I^2 = 72\%$ ,  $Q = 10.6$ ,  $df = 3$ ,  $P = .014$ ).

Forest plots and approximate mean differences for the variables relating to gait are presented in Figure 5. The pooled estimates of the effect size for gait velocity/time<sup>15,18,19,21,22,46,53–58,61,62</sup> and step/stride length<sup>15,18,19,22,46,54,57,59,61</sup> were statistically significant in favor of intervention (Fig. 5A,B). For gait velocity, this represented an improvement with intervention of approximately 0.05 m/s at the preferred pace, which translates to a 0.7-second improvement over 10 m (based on a preferred walk velocity of 0.845 m/s). For step/stride length, this represented an improvement in step length at the preferred pace of approximately 3 cm. Similarly, there was a favorable trend toward a reduction in cadence<sup>15,22,46,57,61</sup> after intervention

**TABLE 1. Characteristics of the 16 included trials**

First author, year, experimental intervention type	Control intervention	Data extracted	Initial sample size	Age (y), mean $\pm$ SD	Disease severity	Assessed ON or OFF	Location and delivery of experimental intervention	Duration of Intervention (wk)	Hours of intervention (approximate)	Highly challenging balance training	Task training (cueing)	Fitness training	Task training (movement strategy)	Strength training	Stretching/ROM exercise	Walking over ground/exercises treadmill
Ashburn, 2007, exercise and strategy	Usual care	Falls—number of fallers Other—pre- and post mean and SD	142	72.1 $\pm$ 9.2	Moderate	ON	Home, individual	6	33	U	N	N	Y	U	Y	N
Blackinton, 2002, exercise	Support group meetings	Pre- and post mean and SD	15	66.5 $\pm$ 12.8	Mild to moderate	ON	Facility, group + home individual	6	15	Y	Y	N	N	U	Y	N
Caglar, 2005, exercise	No intervention	Pre- and post mean and SD	30	65.9 $\pm$ 9.4	Mild to moderate	ON	Facility group + home individual	9	63	U	N	N	Y	N	Y	N
Cakit, 2007, treadmill walking	Not reported	Pre- and post mean and SD	54	71.8 $\pm$ 6.4	Mild to moderate	ON	Facility, delivery not reported	8	8	N	N	N	N	N	Y	Y
Ellis, 2005 (duplicated as de Goede 2004), physiotherapy	No intervention	Pre- and post mean and SD	68	64 $\pm$ 8.6	Mild to moderate	ON	Facility, group	6	18	U	Y	N	Y	U	Y	Y
Fisher, 2008, treadmill walking OR physiotherapy	Education classes	Pre- and post mean and SD	30	62.9 $\pm$ 11.9	Mild	ON	Facility, delivery not reported	8	18	N	N	Y	N	N	N	Y
Hackney, 2008, Tai Chi	No intervention	Mean change, SD difference	33	63.8 $\pm$ 9.2	Mild to moderate	ON	Not reported	10–13	18 20	U Y	N N	N N	Y N	U N	Y N	N N
Hackney, 2009, partnered dance	No intervention	Pre- and post mean and SD	58	67.1 $\pm$ 9.3	Mild to moderate	ON	Facility, group	10–13	20	Y	N	N	N	N	N	N
Kurtais, 2008, treadmill walking	Taught ROM and flexibility exercises but no ongoing intervention	Pre- and post mean and SD	30	64.8 $\pm$ 8.3	Mild to moderate	ON	Facility, delivery not reported	6	12	N	N	Y	N	N	Y	Y
Lehman, 2005, <sup>a</sup> walk with verbal cues	No intervention	Pre- and post mean and SD	11	75.8 $\pm$ 4.2	Mild	ON	Not reported	2	5	N	Y	N	N	N	N	N
Mak, 2008, cued sit to stand OR exercise	No intervention	Pre- and post mean and SD	60	64.1 $\pm$ 7.9	Mild to moderate	ON	Not reported	4	4	N	Y	N	Y	N	N	N
Nieuwboer, 2007, cueing training	No intervention	Falls—number of fallers Other—pre- and post mean and SD	153	68.3 $\pm$ 7.8	Mild to moderate	ON	Home, individual	3	6 4.5	N N	N Y	N N	Y Y	Y N	Y N	N Y
Protas, 2005, treadmill walking and step training	No intervention	Pre- and post mean and SD	18	72.5 $\pm$ 7.8	Mild to moderate	ON	Facility, individual	8	24	Y	N	N	N	N	N	Y
Sage, 2009, aerobic exercise OR SAFEx	No intervention	Pre- and post mean and SD	53	65.9 $\pm$ 9.5	Mild to moderate	ON	Facility, group	12	18	N	N	Y	N	N	N	N
Schenkman, 1998, exercise	No intervention	Mean change, SD difference	51	70.9 $\pm$ 6.7	Mild to moderate	ON	Location not reported, individual	10	20–34 22.5–30	Y N	N N	N N	N Y	N N	Y Y	N N
Thaut, 1996, walk with auditory cues OR walk without cues	No intervention	Pre- and post mean and SD	37	71.1 $\pm$ 7.0	Mild to moderate	ON	Home/community, individual	3	10.5 10.5	N N	Y N	N N	N N	N N	N Y	N N

ROM, range of movement; Y, yes; N, no; U, unclear—insufficient information to categorize.

<sup>a</sup>Part 2 of trial only; SAFEx, sensory attention focused exercise; highly challenging balance training, intervention described as involving all of: movement of the center of mass, narrowing of base of support, and minimizing upper limb support; task training (cueing), the use of cues specifically mentioned; fitness training, aimed to maintain heart rate at 60% or more of maximum heart rate; task training (movement strategy), the practice of strategies to facilitate functional movement specifically mentioned; strength training, intervention described as involving added resistance to exercise; stretching/ROM exercises, short- or long-duration stretches and/or range of movement exercises were specifically mentioned; walking over ground/exercises, a walking program or walking exercises specifically mentioned; walking treadmill, walking on a treadmill specifically mentioned.



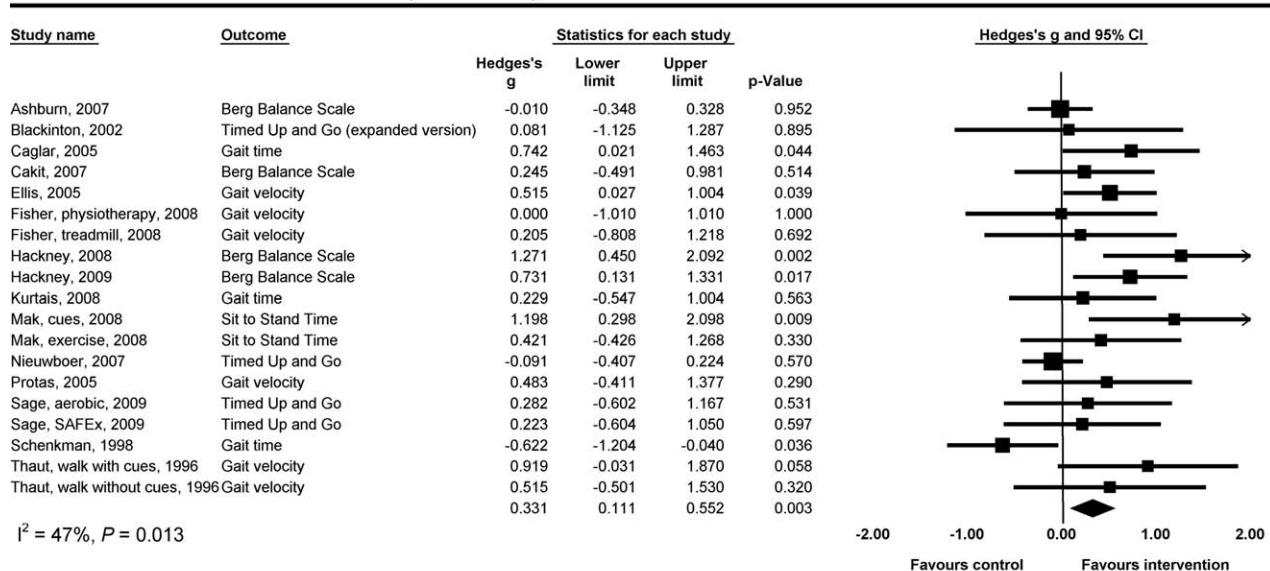
**TABLE 2.** Review authors' judgments for the Cochrane risk-of-bias checklist<sup>24</sup> for the 16 trials included in the review

First author, year	Outcomes of interest for meta-analysis	Adequate sequence generation?	Allocation concealment?	Blinding?	Incomplete outcome data addressed?	Free of selective reporting?
Ashburn, 2007	Berg Balance Score	Y	Y	Y	Y	Y
	Falls			Y		
	Functional Reach			Y		
	Sit to stand time <sup>a</sup>			Y		
	Timed Up and Go <sup>a</sup>			Y		
Blackinton, 2002	Functional Reach	U	U	Y	U	U
	Gait velocity (preferred pace)			Y		
	Single leg stand time			Y		
	Timed Up and Go (expanded)			Y		
	Sit to stand time*			Y		
Caglar, 2005	Gait velocity (preferred pace)	N	U	Y	Y	U
	Number of steps (preferred pace)			Y		
	Turn time			Y		
Cakit, 2007	Berg Balance Score	U	U	U	U	U
	Gait velocity (maximal pace on treadmill)			U		
Ellis, 2005 (duplicated in de Goede 2004)	Gait velocity (preferred pace on treadmill)	Y	N	Y	Y	U
Fisher, 2008	Cadence (preferred pace)	Y	Y	Y	Y	U
	Gait velocity (preferred pace)			Y		
	Stride length (preferred pace)			Y		
	Sit to stand time <sup>a</sup>			Y		
Hackney, 2008	Berg Balance Score	Y	U	Y	Y	U
	Gait velocity (preferred pace)			Y		
	Single leg stand time			Y		
	Stride length (preferred pace)			Y		
	Timed Up and Go			Y		
Hackney, 2009	Berg Balance Score	Y	U	Y	Y	U
	Gait velocity (pace not reported)			Y		
	Stride length (pace not reported)			Y		
	Timed Up and Go			Y		
Kurtais, 2008	Gait velocity (preferred pace)	U	U	Y	Y	U
	Single leg stand time			Y		
	Sit to stand time			Y		
	Turn time			Y		
Lehman, 2005 <sup>b</sup>	Step length (preferred pace)	U	U	U	Y	U
Mak, 2008	Sit to stand time	Y	U	Y	Y	U
Nieuwboer, 2007	Cadence (preferred pace)	Y	Y	Y	Y	U
	Falls			U		
	Functional Reach			Y		
	Gait velocity (preferred pace)			Y		
	Step length (preferred pace)			Y		
	Single leg stand time			Y		
	Timed Up and Go			Y		
Protas, 2005	Cadence (fast pace)	U	U	Y	Y	U
	Gait velocity (fast pace)			N		
	Stride length (fast pace)			Y		
	Falls <sup>a</sup>			Y		
Sage, 2009	Cadence (preferred pace)	U	U	N	U	U
	Gait velocity (preferred pace)			N		
	Step length (preferred pace)			N		
	Timed Up and Go			N		
Schenkman, 1998	Functional Reach	U	U	N	U	N
	Gait velocity (preferred pace)			N		
	Turn time			N		
Thaut, 1996	Cadence (preferred pace)	U	U	U	Y	U
	Gait velocity (preferred pace)			U		
	Stride length (preferred pace)			U		

Y, yes; N, no; U, unclear.

<sup>a</sup>Outcome unable to be included in a meta-analysis as no or insufficient data given.<sup>b</sup>Part 2 of trial only.

## Balance-related activities (n = 747)



**FIG. 2.** Forest plot from the meta-analysis of exercise and motor training on measures of balance-related activity performance showing estimates of effect size with 95% confidence intervals. Relative weight for each trial is indicated by the size of the corresponding square.

compared with control (Fig. 5C). There was very little heterogeneity in the estimates of the effect of intervention on gait (gait velocity/time,  $I^2 = 6\%$ ,  $Q = 16.04$ ,  $df = 15$ ,  $P = .38$ ; step/stride length,  $I^2 = 0\%$ ,  $Q = 6.07$ ,  $df = 11$ ,  $P = .87$ ; cadence,  $I^2 = 0\%$ ,  $Q = 3.499$ ,  $df = 7$ ,  $P = .84$ ).

## Discussion

This systematic review provides evidence that exercise and motor training can improve performance of balance-related activities in people with PD. However, it remains unclear whether exercise and motor training can reduce falls in this population. Exercise and motor training were found to have a small positive effect on balance-related activity performance, gait velocity, and step/stride length, as well as a moderate effect on turning time. The meta-regression results suggest that the inclusion of highly challenging balance training may improve the efficacy of intervention on balance-related activity performance, but this requires further investigation.

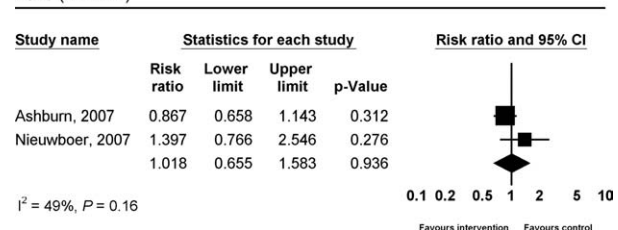
This is the first systematic review to conduct meta-analyses of the effect of exercise and motor training on the performance of balance-related activities. The results of this review uphold and quantify the results of the recent narrative review suggesting positive effects from exercise on balance in PD.<sup>27</sup> In the current review, the measure of balance-related activity performance included 15 trials with a total of 747 participants. Although the overall quality of 8 of the included trials was unclear, the remaining 7 trials were of moderate to good quality (Table 2). However, the included trials did show some evidence of publica-

tion bias, with some small studies having a relatively large positive effect size. Therefore, these results should be interpreted cautiously and generalized only to people with mild to moderate PD. In the future, larger meta-analyses may be able to investigate relationships between trial design features and results.

There was no evidence from this review that exercise and motor training can reduce falls in people with PD. However, of the 2 trials included in the meta-analysis on falls, 1 did not include highly challenging balance exercises and did not aim to reduce falls,<sup>22</sup> while the type of balance training used in the other trial was unclear.<sup>14</sup> However, results of this review do suggest that exercise and motor training may improve balance, and balance is known to be an important risk factor for falls in this population.<sup>2-4</sup> Furthermore, exercise has been shown to reduce falls in the general older population.<sup>48,63</sup> For these reasons, further research is required to determine if falls can be prevented in people with PD.

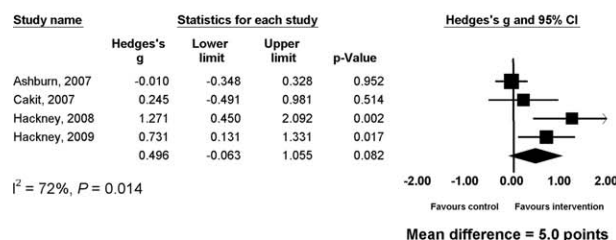
As expected, there was a moderate to high level of heterogeneity in the meta-analyses of this review. We

### Falls (n = 250)

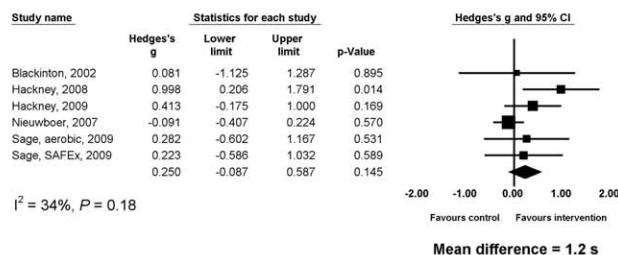


**FIG. 3.** Forest plot from the meta-analysis of exercise and motor training on falls showing estimates of effect size with 95% confidence intervals. Relative weight for each trial is indicated by the size of the corresponding square.

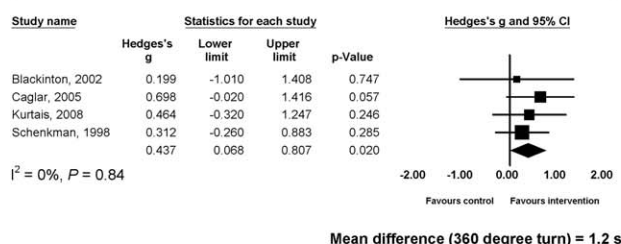
## A. Berg Balance Scale (n = 238)



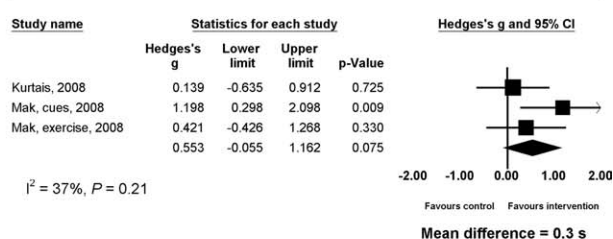
## B. Timed Up and Go (n = 281)



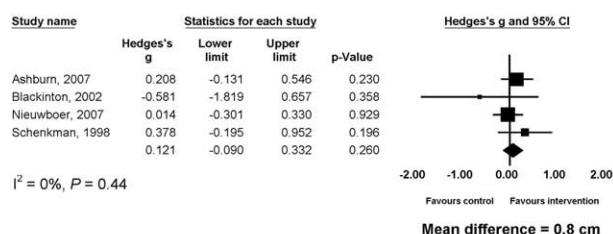
## C. Turning time (n = 108)



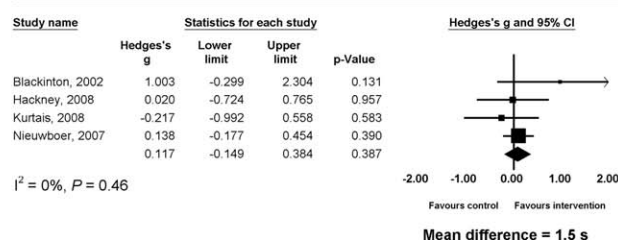
## D. Sit to stand time (n = 76)



## E. Functional Reach (n = 340)



## F. Single leg stand time (n = 211)



**FIG. 4.** Forest plots from the meta-analyses of exercise and motor training on secondary outcomes not relating to gait showing estimates of effect size with 95% confidence intervals and approximate mean differences. **A:** Berg Balance Scale. **B:** Timed Up and Go. **C:** Turning time. **D:** Sit to stand time. **E:** Functional Reach. **F:** Single leg stand time. Relative weight for each trial is indicated by the size of the corresponding square.

suggest that despite this heterogeneity, random-effects meta-analysis is appropriate, as all included studies had broadly similar outcomes and interventions, that is, they targeted balance-related activities.<sup>64</sup> We used meta-regression to investigate whether this heterogeneity could be explained by differences in exercise program design and found an indication of a bigger effect of exercise on balance-related activity performance if highly challenging balance training was included. However, this difference in the effect in trials with and without highly challenging balance training did not reach statistical significance. There were not enough trials to conduct meta-regression analyses on the secondary outcome measures, but the high level of heterogeneity in the Berg Balance Scale analysis may reflect that of the 4 pooled trials, only 2 included highly challenging balance training.<sup>18,19</sup>

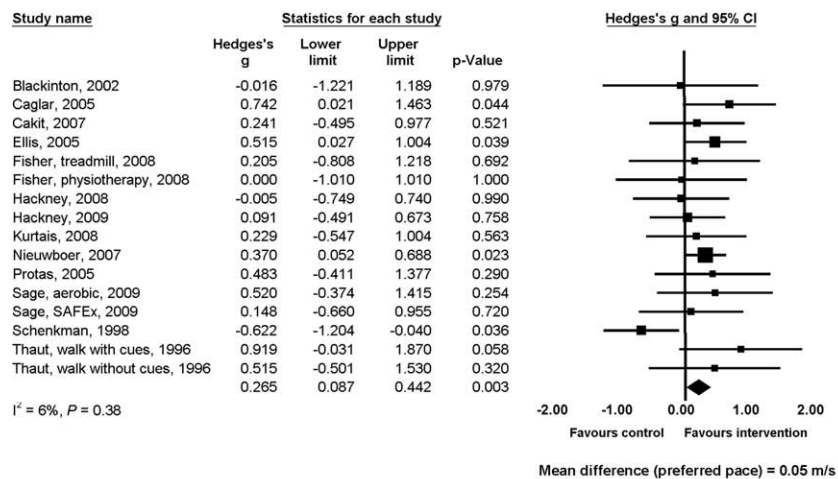
These results suggest that therapists should consider including highly challenging balance training in exercise programs for people with PD. Although many forms of exercise and motor training improve the performance of balance-related activities in this population, exercise that specifically involves movement of the center of mass, narrowing of the base of support, and minimizing upper limb support may produce the

best results. Although this result is encouraging, the longer-term effects of exercise and motor training in this population remain unclear. However, the progressive nature of PD suggests that balance training would be required to be ongoing. Providing highly challenging balance training in a sustainable way for this population is problematic, as it is difficult to achieve the required level of challenge while maintaining safety in group or semisupervised home-based programs. Future research working toward the development of effective programs that are sustainable for the long term would be an important step in solving this problem.

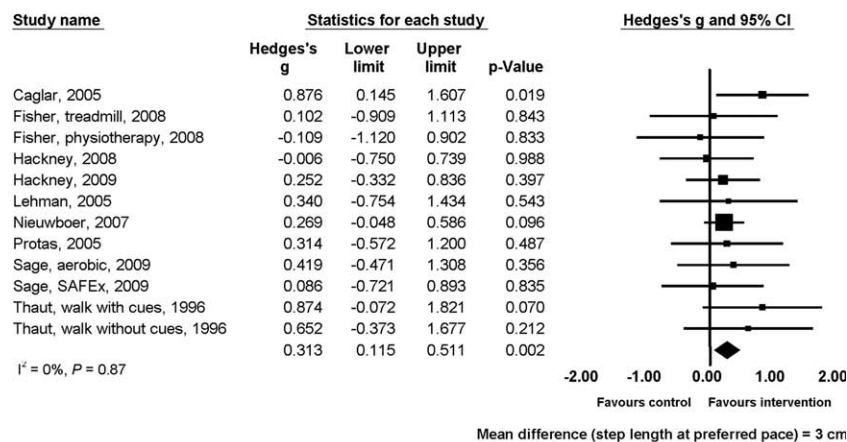
Most of the effect sizes found in these meta-analyses were small to moderate (Hedges'  $g$ , 0.2–0.5) but did represent a meaningful improvement in the outcome measure (eg, a 0.05 m/s improvement in gait velocity has been shown to be meaningful in older adults).<sup>65</sup> Larger effects have been found to occur with more intense interventions following stroke<sup>66</sup> and in the general older population,<sup>48</sup> and this may also be true of people with PD. Trials included in the current review averaged 18 hours of intervention over 7 weeks. This overall low dose of intervention may also explain why the total dose of exercise was not associated with the effect of intervention on performance of



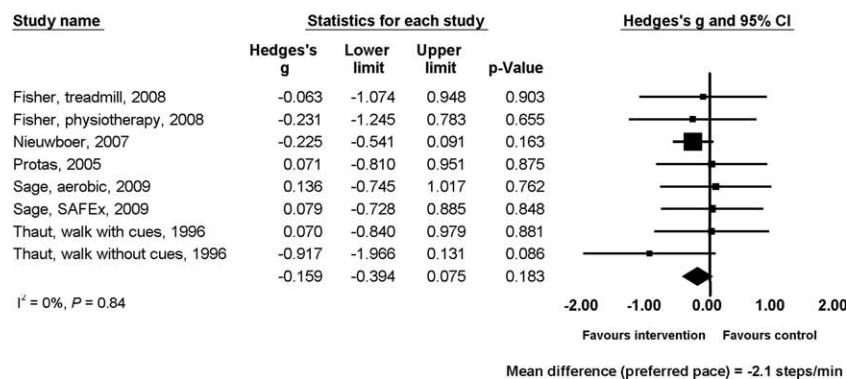
## A. Gait velocity/time (n = 562)



## B. Step/stride length (n = 399)



## C. Cadence (n = 284)



**FIG. 5.** Forest plots from the meta-analyses of exercise and motor training on secondary outcomes relating to gait showing estimates of effect size with 95% confidence intervals and approximate mean differences. **A:** Gait velocity/time. **B:** Step/stride length. **C:** Cadence. Relative weight for each trial is indicated by the size of the corresponding square.

balance-related activities. Future research needs to examine the effect of using a higher dose of intervention on balance outcomes and the performance of balance-related activities.

In conclusion, exercise and motor training can improve the performance of balance-related activities in people with PD. We recommend that highly chal-

lenging balance exercises be part of rehabilitation programs for people with PD. It is now important to develop effective, sustainable programs that people with PD can participate in for the long term and to assess the effect of these programs on fall rates. The development of such programs may have a widespread and ongoing impact on improving the quality of life

of people with PD and their families as well as easing demands on health care systems.

## References

- Wood BH, Bilclough JA, Bowron A, Walker RW. Incidence and prediction of falls in Parkinson's disease: a prospective multidisciplinary study. *J Neurol Neurosurg Psychiatry* 2002;72:721–725.
- Latt MD, Lord SR, Morris JG, Fung VS. Clinical and physiological assessments for elucidating falls risk in Parkinson's disease. *Mov Disord* 2009;24:1280–1289.
- Kerr GK, Worringham CJ, Cole M, Lacherez P, Wood J, Silburn P. Predictors of future falls in Parkinson's disease. *Neurology* 2010;75:116–124.
- Robinson K, Dennison A, Roalf D, et al. Falling risk factors in Parkinson's disease. *Neurorehabilitation* 2005;20:169–182.
- Winter DA. A.B.C. (Anatomy, Biomechanics and Control) of Balance during Standing and Walking. Waterloo, Ontario, Canada: Waterloo Biomechanics; 1995.
- Lord SR, Ward J, Williams P. The effect of exercise on dynamic stability in older women: a randomized controlled trial. *Arch Phys Med Rehabil* 1996;77:232–236.
- Howe T, Rochester L, Jackson A, Banks P, Blair V. Exercise for improving balance in older people. *Cochrane Database Syst Rev* 2007;4:CD004963.
- Klawans H, Topel J. Parkinsonism as a falling sickness. *JAMA* 1974;230:1555–1557.
- Bloem BR, Hausdorff JM, Visser JE, Giladi N. Falls and freezing of gait in Parkinson's disease: a review of two interconnected, episodic phenomena. *Mov Disord* 2004;19:871–884.
- Beckley DJ, Bloem BR, Van Dijk J, Roos R, Remler M. Electrophysiological correlates of postural instability in Parkinson's disease. *Electroencephalogr Clin Neurophysiol* 1991;81:263–268.
- Bloem BR, van Vugt JP, Beckley DJ. Postural instability and falls in Parkinson's disease. In: Ruzicka E, Hallett M, Jankovic J, eds. *Advances in Neurology: Gait Disorders*. Philadelphia: Lippincott Williams and Wilkins; 2001:209–223.
- Koller WC, Glatt S, Vetere-Overfield B, Hassanein R. Falls and Parkinson's disease. *Clin Neuropharmacol* 1989;12:98–105.
- Franchignoni F, Martignoni E, Ferriero G, Pasetti C. Balance and fear of falling in Parkinson's disease. *Parkinsonism Relat Disord* 2005;11:427–433.
- Ashburn A, Fazakarley L, Ballinger C, Pickering R, McLellan LD, Fitton C. A randomised controlled trial of a home-based exercise programme to reduce the risk of falling among people with Parkinson's disease. *J Neurol Neurosurg Psychiatry* 2007;78:678–684.
- Protas EJ, Mitchell K, Williams A, Qureshy H, Caroline K, Lai EC. Gait and step training to reduce falls in Parkinson's disease. *Neurorehabilitation* 2005;20:183–190.
- Hirsch MA, Toole T, Maitland CG, Rider RA. The effects of balance training and high-intensity resistance training on persons with idiopathic Parkinson's disease. *Arch Phys Med Rehabil* 2003;84:1109–1117.
- Morris M, Iansek R, Kirkwood B. A randomized controlled trial of movement strategies compared with exercise for people with Parkinson's disease. *Mov Disord* 2009;24:64–71.
- Hackney ME, Earhart GM. Effects of dance on movement control in Parkinson's disease: a comparison of Argentine tango and American ballroom. *J Rehabil Med* 2009;41:475–481.
- Hackney ME, Earhart GM. Tai Chi improves balance and mobility in people with Parkinson's disease. *Gait Posture* 2008;28:456–460.
- Toole T, Maitland CG, Warren E, Hubmann MF, Panton L. The effects of loading and unloading treadmill walking on balance, gait, fall risk, and daily function in Parkinsonism. *Neurorehabilitation* 2005;20:307–322.
- Cakit BD, Saracoglu M, Genc H, Erdem HR, Inan L. The effects of incremental speed-dependent treadmill training on postural instability and fear of falling in Parkinson's disease. *Clin Rehabil* 2007;21:698–705.
- Nieuwboer A, Kwakkel G, Rochester L, et al. Cueing training in the home improves gait-related mobility in Parkinson's disease: the RESCUE trial. *J Neurol Neurosurg Psychiatry* 2007;78:134–140.
- Allen NE, Canning CG, Sherrington C, et al. The effects of an exercise program on fall risk factors in people with Parkinson's disease: a randomized controlled trial. *Mov Disord* 2010;25:1217–1225.
- Higgins JPT, Green S, eds. *Cochrane Handbook for Systematic Reviews of Interventions Version 5.0.2* [updated September 2009]. The Cochrane Collaboration, 2009. Available from: <http://www.cochrane-handbook.org>.
- de Goede CJ, Keus SH, Kwakkel G, Wagenaar RC. The effects of physical therapy in Parkinson's disease: a research synthesis. *Arch Phys Med Rehabil* 2001;82:509–515.
- Goodwin VA, Richards SH, Taylor RS, Taylor AH, Campbell JL. The effectiveness of exercise interventions for people with Parkinson's disease: a systematic review and meta-analysis. *Mov Disord* 2008;23:631–640.
- Dibble LE, Addison O, Papa E. The effects of exercise on balance in persons with Parkinson's disease: a systematic review across the disability spectrum. *J Neurol Phys Ther* 2009;33:14–26.
- Herbert R, Jamtvedt G, Mead J, Birger Hagen K. *Practical Evidence-Based Physiotherapy*. Edinburgh, UK: Elsevier Butterworth Heinemann; 2005.
- Nieuwboer A. Cueing for freezing of gait in patients with Parkinson's disease: a rehabilitation perspective. *Mov Disord* 2008;23(Suppl 2):S475–S481.
- Deane K, Jones D, Ellis-Hill C, Clarke C, Playford E, Ben-Shlomo Y. Physiotherapy for Parkinson's disease: a comparison of techniques. *Cochrane Database Syst Rev* 2001;1:CD002815.
- Deane K, Jones D, Playford E, Ben-Shlomo Y, Clarke C. Physiotherapy versus placebo or no intervention in Parkinson's disease. *Cochrane Database Syst Rev* 2001;3:CD002817.
- Deane KH, Ellis-Hill C, Jones D, et al. Systematic review of paramedical therapies for Parkinson's disease. *Mov Disord* 2002;17:984–991.
- Keus SH, Bloem BR, Hendriks EJ, Bredero-Cohen AB, Munneke M. Evidence-based analysis of physical therapy in Parkinson's disease with recommendations for practice and research. *Mov Disord* 2007;22:451–460.
- Kwakkel G, de Goede C, van Wegen E. Impact of physical therapy for Parkinson's disease: A critical review of the literature. *Parkinsonism Relat Disord* 2007;13:S478–S487.
- Rubinstein TC, Giladi N, Hausdorff JM. The power of cueing to circumvent dopamine deficits: a review of physical therapy treatment of gait disturbances in Parkinson's disease. *Mov Disord* 2002;17:1148–1160.
- Lim I, van Wegen E, de Goede C, et al. Effects of external rhythmic cueing on gait in patients with Parkinson's disease: a systematic review. *Clin Rehabil* 2005;19:695–713.
- Jobges M, Spittler-Schneiders H, Renner CI, Hummelsheim H. Clinical relevance of rehabilitation programs for Parkinson's disease. I: Non-symptom-specific therapeutic approaches. *Parkinsonism Relat Disord* 2007;13:195–202.
- Jobges M, Spittler-Schneiders H, Renner CI, Hummelsheim H. Clinical relevance of rehabilitation programs for patients with idiopathic Parkinson syndrome. II: Symptom-specific therapeutic approaches. *Parkinsonism Relat Disord* 2007;13:203–213.
- Gage H, Storey L. Rehabilitation for Parkinson's disease: a systematic review of available evidence. *Clin Rehabil* 2004;18:463–482.
- Crizzle AM, Newhouse IJ. Is physical exercise beneficial for persons with Parkinson's disease? *Clin Sports Med* 2006;16:422–425.
- Suchowersky O, Gronseth G, Perlmutter J, Reich S, Zesiewicz T, Weiner W. Practice parameter: Neuroprotective strategies and alternative therapies for Parkinson disease (an evidence-based review). *Neurology* 2006;66:976–982.
- Berg K, Wood-Dauphinee S, Williams J, Gayton D. Measuring balance in the elderly: preliminary development of an instrument. *Physiother Can* 1989;41:304–311.
- Podsiadlo D, Richardson S. The timed up and go: a test of basic functional mobility for elderly persons. *J Am Geriatr Soc* 1991;39:141–148.
- Duncan PW, Weiner DK, Chandler J, Studenski S. Functional reach: a new clinical measure of balance. *J Gerontol* 1990;45:M192–M197.
- Hozo SP, Djulbegovic B, Hozo I. Estimating the mean and variance from the median, range, and the size of a sample. *BMC Med Res Methodol* 2005;5:13.

46. Thaut M, McIntosh GC, Rice R, Miller R, Rathbun J, Brault J. Rhythmic auditory stimulation in gait training for Parkinson's disease patients. *Mov Disord* 1996;11:193–200.
47. Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. *BMJ* 1997;315:629–634.
48. Sherrington C, Whitney J, Lord SR, Herbert R, Cumming R, Close J. Effective exercise for the prevention of falls: a systematic review and meta-analysis. *J Am Geriatr Soc* 2008;56:2234–2243.
49. Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *J Clin Epidemiol* 2009;62:e1–e34.
50. Bridgewater K, Sharpe M. Aerobic exercise and early Parkinson's disease. *J Neuro Rehab* 1996;10:233–241.
51. Stallibrass C, Sissons P, Chalmers C. Randomized controlled trial of the Alexander Technique for idiopathic Parkinson's disease. *Clin Rehabil* 2002;16:695–708.
52. Toole T, Hirsch MA, Forkink A, Lehman D, Maitland CG. The effects of a balance and strength training program on equilibrium in Parkinsonism: a preliminary study. *Neurorehabilitation* 2000;14:165–174.
53. Blackinton M, Summerall L, Waguespack K. Tertiary prevention in Parkinson disease: Results from a preliminary study. *Neurol Rep* 2002;26:160–165.
54. Caglar AT, Gurses HN, Mutluay FK, Kiziltan G. Effects of home exercises on motor performance in patients with Parkinson's disease. *Clin Rehabil* 2005;19:870–877.
55. Ellis T, de Goede C, Feldman R, Wolters E, Kwakkel G, Wagenaar R. Efficacy of a physical therapy program in patients with Parkinson's disease: a randomized controlled trial. *Arch Phys Med Rehabil* 2005;86:626–632.
56. de Goede CJT, Ellis T, Wagenaar RC. Effecten van een fysiotherapie-groepbehandeling Parkinson-patienten: een cross-over trial. *Ned Tijdschr Fysiother* 2004;114:78–82.
57. Fisher BE, Wu AD, Salem GJ, et al. The effect of exercise training in improving motor performance and corticomotor excitability in people with early Parkinson's disease. *Arch Phys Med Rehabil* 2008;89:1221–1229.
58. Kurtais Y, Kutlay S, Tur BS, et al. Does treadmill training improve lower-extremity tasks in Parkinson disease? A randomized controlled trial. *Clin J Sport Med* 2008;18:289–291.
59. Lehman D, Toole T, Lofald D, Hirsch MA. Training with verbal instructional cues results in near-term improvement of gait in people with Parkinson's disease. *J Neurol Phys Ther* 2005;29:2–8.
60. Mak MK, Hui-Chan CW, Mak MKY, Hui-Chan CWY. Cued task-specific training is better than exercise in improving sit-to-stand in patients with Parkinson's disease: a randomized controlled trial. *Mov Disord* 2008;23:501–509.
61. Sage M, Almeida Q. Symptom and gait changes after sensory attention focused exercise vs aerobic training in Parkinson's disease. *Mov Disord* 2009;24:1132–1138.
62. Schenkman M, Cutson TM, Kuchibhatla M, et al. Exercise to improve spinal flexibility and function for people with Parkinson's disease: a randomized, controlled trial. *J Am Geriatr Soc* 1998;46:1207–1216.
63. Gillespie L, Robertson M, Gillespie W, et al. Interventions for preventing falls in older people living in the community. *Cochrane Database Syst Rev* 2009;2:CD007146.
64. Higgins JPT. Commentary: Heterogeneity in meta-analysis should be expected and appropriately quantified. *Int J Epidemiol* 2008;37:1158–1160.
65. Perera S, Mody SH, Woodman RC, Studenski SA. Meaningful change and responsiveness in common physical performance measures in older adults. *J Am Geriatr Soc* 2006;54:743–749.
66. Kwakkel G. Impact of intensity of practice after stroke: issues for consideration. *Disabil Rehabil* 2006;28:823–830.