Effects of Exercise on Falls, Balance, and Gait Ability in Parkinson's Disease: A Meta-analysis

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Abstract

Postural instability and falls are complex and disabling features of Parkinson's disease (PD) and respond poorly to anti-Parkinsonian medication. There is an imperative need to evaluate the effectiveness of exercise interventions in enhancing postural stability and decreasing falls in the PD population. The objectives of our study were to determine the effects of exercise training on the enhancement of balance and gait ability and reduction in falls for people with PD and to investigate potential factors contributing to the training effects on balance and gait ability of people with PD. We included 25 randomized control trials of a moderate methodological quality in our meta-analysis. The trials examined the effects of exercise training on balance and gait ability and falls against no intervention and placebo intervention. The results showed positive effects of exercise intervention on enhancing balance and gait performance (Hedges' g = 0.303 over the short-term in 24 studies and 0.419 over the long-term in 12 studies; P < .05) and reducing the fall rate (rate ratio = 0.485 over the short-term in 4 studies and 0.413 over the long-term in 5 studies; P < .05). The longest follow-up duration was 12 months. There was no evidence that training decreased the number of fallers over the short- or long-term (P > .05). The results of our metaregression and subgroup analysis showed that facility-based training produced greater training effects on improving PD participants' balance and gait ability (P < .05). The findings support the application of exercise training to improve balance and gait ability and prevent falls in people with PD.

Introduction

Falls are common in people with Parkinson's disease (PD), with a high incidence rate of 40% to 70%.[1,2] Falls are the most problematic feature in people with PD because they can lead to devastating outcomes such as physical injury and negative psychological effects that limit their mobility and ability to perform daily activities.[3] Fall prevention is, therefore, an urgent need for PD patients.

Postural instability is a cardinal symptom of PD and may make it difficult for individuals to perform functional tasks such as transferring and walking,[4,5] resulting in poor self-perceived balance confidence[6] and eventually predisposing individuals to falls.[7] Because postural instability responds poorly to anti-Parkinsonian medication,[8] exercise training, a component of physical therapy, has been an important intervention in conjunction with current medical treatments to improve postural stability and reduce falls in individuals with PD. There is an imperative need to evaluate the effectiveness of exercise interventions in these areas.

An increasing number of studies have explored the effects of exercise training for individuals with PD.[9-47] They have considered various categories of exercise training such as balance training, walking exercises, muscle strengthening, and stretching exercises. No review study hitherto has shown a reduction in falls, but given the small number of studies available, further work was required to determine if exercises could reduce falls in people with PD.[48-51] Furthermore, no meta-analysis has investigated the long-term effects of training, which are more clinically meaningful than its short-term effects because of the progressive nature of PD.

Balance training commonly refers to exercises that challenge one's control of the body's center of mass during destabilizing movements and/or decrease the size of one's base of support.[49] Gait training involves alternating step

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movements that challenge one's dynamic control of the body's center of mass. In our meta-analysis, we focused on exercises with balance and gait training components, with the primary objective being to examine the effects of training on enhancing balance and gait ability and reducing falls over the short- and long-terms. For effects on balance and gait ability, we considered short-term effects as the training effects after treatment completion and long-term effects as the carryover effects of treatment at follow-up intervals (with durations of 4 weeks or greater). Fall data collected during the intervention period and the follow-up period were included, respectively, for the short- and long-term analyses. Our second objective was to explore if the effect sizes in the short- and long-terms were influenced by the features of exercise intervention and the characteristics of individuals with PD.

Methods

Search Criteria

We conducted an extensive search of the literature up to May 8, 2015, using electronic databases, including the CINAHL database, MEDLINE, PubMed, Academic Search Premier via EbscoHost, and Cochrane Library. The keywords used to conduct the literature search were combined with the following English terms: (Physical therapy OR physiotherapy OR rehabilitation OR training OR exercise OR movement) AND Parkin* AND (balance OR postural stability OR gait OR fall). We found other potential studies by examining the reference lists of each identified article.

Study Selection

The studies eligible for this review were randomized controlled trials (including the first phase of crossover trials) for PD individuals, with outcomes related to balance, gait and/or falls. The inclusion criteria for trials were randomized controlled trials that involved experimental group(s) receiving interventions aimed at enhancing balance and gait performance, such as balance, gait, or strengthening exercise, and a control group that did not receive any intervention or just received placebo training that did not include balance, gait, or strengthening exercises (ie, active joint mobility and muscle stretching exercises).

Two investigators (the first and second authors) determined the eligibility of studies by screening the trial titles, abstracts, and full texts. Studies were excluded if they were not randomized controlled trials; if the experimental interventions did not involve any gait, balance, or strengthening exercise; or if the control group had undergone balance, gait, or strengthening exercises for their lower extremities. In addition, studies with low methodological quality, as judged by the Cochrane risk-of-bias tool were excluded

from our meta-analysis.[52] All the discrepancies related to trial eligibility were resolved by discussion with a third party (the corresponding author).

Data Extraction and Quality Assessment

The 2 investigators developed a data extraction sheet. The first author extracted all data, and the second author checked their accuracy. The data included population and intervention characteristics; outcomes related to balance, gait, and/or falls; and the methodological quality of the trials evaluated via the Cochrane risk-of-bias tool. The participants' characteristics included their age, disease severity as measured by the Hoehn and Yahr Staging Scale, medication status during assessment, and fall risk. Participants were classified as having a higher risk of falling if one of the following was indicated in the inclusion criteria: a history of falling in the past 12 months, experiencing freezing of gait in the past month, gait disturbance, postural instability with balance and mobility problems, reduced lower-limb strength, or reduced balance confidence.[53] The gait disturbance included subjective gait disturbance[17] or a score of 1 or 2 on the gait item of the Unified Parkinson's Disease Rating Scale.[17] The postural instability included an instability during postural transfers,[11] functional reach ≤25 cm,[12] or an inability to achieve the criterion on one of the balance tests in the QuickScreen Clinical Falls Risk Assessments.[12]

The intervention characteristics consisted of the percentage of balance and gait training within the total training program, total training hours and duration, training hours per week, amount of supervision given, and training location.[54] The balance training components included exercises that challenged one's control of the body's center of mass with destabilizing movements and/or while standing on an unstable or small base of support. The gait training components involved walking exercises over ground or on a treadmill. We calculated the percentage of balance and gait training within the total training program by dividing the time spent in balance and gait training by the duration of each training session when the information was available. Otherwise, we estimated it by dividing the time equally among balance training, gait training, strength training, and other exercises such as stretching and meditation in each training session. All the discrepancies were resolved by discussion with a third party (the corresponding author). In the case of missing and unpublished data, we attempted to contact the authors and successfully obtained information from 4 studies.[19,23,24,27]

The Cochrane risk-of-bias tool consists of 5 domains, including sequence generation, allocation concealment, blinding, incomplete outcome data, and selective outcome reporting. Each domain comprises 3 outcomes: low, high, and unclear risks of bias. Studies with a low risk of bias in 3 or more domains were suggested as trials of a moderate to high methodological quality and were included in the final

meta-analysis. In contrast, studies with a low risk of bias in fewer than 3 domains were judged as trials of a low methodological quality and were excluded.

Quantitative Data Synthesis and Analysis

The outcome measures consisted of balance and gait outcomes and falls. Only one outcome of balance and gait ability in each of those studies was pooled for meta-analysis. We pooled the outcomes that were most frequently used by studies to minimize the heterogeneity and most comprehensive in measuring balance and gait ability.[49,55] The final priority order of outcome measures was score on Berg's Balance Scale, time of Timed Up and Go test, gait velocity of walking test at comfortable or fast speed, score of freezing of gait questionnaire, distance of 2-minyte walk test, time of sit-to-stand, and composite equilibrium score of sensory organization test.

Effect sizes were calculated using Hedges' *g* for the balance and gait outcomes, the fall incidence rate ratio, and the fall risk ratio. For each outcome measure of the participants' balance and gait ability, Hedges' *g* of the short-term training effect was calculated by dividing the difference between the changes of the preintervention and postintervention means in the experimental and control groups through the estimated pooled standard deviation of the changes. The pooled standard deviation of the changes was estimated by standard deviation of the changes in the experimental and control groups, with bias corrected from the sample size in each group. For the long-term training effect in the trials with more than one follow-up evaluation, the value at the longest follow-up assessment replaced that at the postintervention assessment.

Fall incidence rate ratio was calculated according to the fall incidence rate in each group or obtained directly from the trials that presented the data. The fall risk ratio was calculated based on the number of persons who fell (*fallers*) during the study period in each group or obtained directly from the trials that presented the data. In the trials with follow-up periods, the rate and risk ratio values during the trial period after treatment completion were analyzed to explore the long-term fall prevention effects.

To decrease the unit-of-analysis error,[56] if there were multiple intervention groups in one trial, groups with similar intervention characteristics were combined to form a single intervention group to compare with the control group.[35,38] The sample size of the single intervention group was the sum of the individual sample sizes of each intervention group. The means and standard deviations of the single-intervention group were calculated based on the individual group data. Intervention groups with different characteristics were considered as different groups and compared separately with the control group. Within one study, the sample size of the control group was divided equally among different intervention groups for comparison.[20,22,34,37] The group

means and standard deviations remained unchanged. For the crossover studies, only first-phase data were included in the data analysis.[27]

Statistical heterogeneity was assessed with the I^2 statistics. If there was significant heterogeneity between studies, the random-effects model of meta-analysis was used; otherwise, the fixed-effects model was used to analyze the training effects.[57] Publication bias was evaluated using Egger's test to determine whether any association existed between the effect and sample sizes. For the effect sizes with significant heterogeneity across studies, univariate metaregression tests were performed to explore the correlations between the participant and intervention characteristics and effect sizes. The Cochrane handbook recommended a minimum of 10 studies to have the robustness of meta-regression; therefore, univariate metaregression was only performed for gait and balance outcomes.[56,58] When there was significant correlation, subgroup analyses for each contributing factor was conducted.[55,58] For instance, when risk of falling was found to be a significant factor affecting the effect sizes, meta-analyses for studies with participants at higher risk of falling and for those with participants at lower risk of falling were conducted in separate analyses consequently. Regarding the cutoff used for the subgroup analysis, the training location included facility, and community and home-based locations, and these determined the cutoff. The Comprehensive Meta-Analysis software (Version 2, Biostat, Englewood, NJ) was used to perform the meta-analyses, with the level of significance set at $P < .05$.

Results

Trial Flow and Study Characteristics

A total of 3413 studies were identified by database searches and 7 additional studies were identified by reference checks. Based on the titles and abstracts, 115 studies were selected to determine their eligibility. Finally, 38 articles were included in the qualitative synthesis. A total of 25 studies that had a moderate to high methodological quality were included in the final quantitative synthesis of the meta-analysis (Table 1). Figure 1 shows the flow of information through the review. All eligible studies reported the effects of training on participants' balance and gait ability, and 8 studies examined the effects of training on outcomes related to falls. Table 2 summarizes the characteristics of the 25 studies.

Effects on Balance and Gait Outcomes

For the short-term effects (the immediate effects after treatment completion) on participants' balance and gait ability, 1881 participants from the 24 studies were finally included in the data analysis. The fixed-effects model of the meta-analysis was used because there was a low level of heterogeneity in the effect size

Table 1. Cochrane Risk of Bias of 38 Articles Included Into Qualitative Synthesis.

First Author, Year	Outcomes of Interest for Meta-analysis	Adequate Sequence Generation	Concealed Allocation	Blinding	Incomplete Outcome Data Addressed	Free of Selective Reporting
Allen, 2010	Center of pressure sway in standing Fall efficacy Scale–International Freezing of gait questionnaire Limit of stability (distance) Sit-to-stand test (time of 5 repetitions) Walking test at comfortable speed (gait velocity) Walking test at fast speed (gait velocity)	Y	Y	Y	Y	Y
Almeida, 2012[a]	Timed Up and Go test (time) Walking test at comfortable speed (gait velocity, step length)	UC	UC	Y	N	UC
Amano, 2013[a]	Walking test at comfortable speed (cadence, double-leg-support time, gait velocity, step duration, step length, swing time)	UC	UC	Y	UC	UC
Ashburn, 2007	Berg Balance Scale Functional reach test (distance) Number of fallers	Y	Y	Y	Y	Y
Cakit, 2007[a]	Berg Balance Scale Dynamic gait index Fall Efficacy Scale Tolerated maximum speed on treadmill	UC	UC	Y	N	UC
Canning, 2012	Walking test at comfortable speed (gait velocity under single task, dual tasks, and multiple tasks) 6-Minute walk test (distance)	Y	Y	Y	Y	UC
Canning, 2015	Coordinated stability test of balance Fall Efficacy Scale–International Fall risk score Fall incidence rate ratio Fall relative risk (number of fallers) Freezing of gait questionnaire Short Physical Performance Battery Walking test at fast speed (gait velocity)	Y	Y	Y	Y	Y
Choi, 2013[a]	Reaction time of jump in response to cue Single leg stance test (time) Tandem stance test (time) Timed Up and Go test (time) 2-min walk test (distance)	UC	UC	Y	N	UC
Conradsson, 2015	Falls Efficacy Scale–International Mini balance evaluation systems test Modified figure-of-eight test (time, number of oversteps) Walking test at comfortable speed (cadence, gait velocity, stride length under single task and dual tasks)	Y	Y	Y	Y	Y
De Bruin, 2010	Walking test at comfortable speed (cadence, gait velocity under single task and dual tasks, stride length)	Y	UC	Y	Y	UC

(continued)

Table 1. (continued)

First Author, Year	Outcomes of Interest for Meta-analysis	Adequate Sequence Generation	Concealed Allocation	Blinding	Incomplete Outcome Data Addressed	Free of Selective Reporting
Duncan, 2012	Backward walking test (gait velocity) Mini balance evaluation systems test Walking test at comfortable speed (gait velocity under single task and dual tasks) Walking test at fast speed (gait velocity) 6-Minute walk test (distance)	Y	UC	Y	Y	UC
Duncan, 2014[a]	Backward walking test (gait velocity) Freezing of gait questionnaire Mini balance evaluation systems test Timed Up and Go test (time under single task and dual tasks) 6-Minute walk test (distance)	UC	UC	Y	Y	UC
Ebersbach, 2010	Walking test at comfortable speed (gait velocity) Timed Up and Go test (time)	Y	UC	Y	Y	UC
Ellis, 2005	Walking test at comfortable speed (gait velocity)	Y	Y	Y	Y	UC
Fietzek, 2014	Freezing of gait questionnaire Freezing of gait score (0-36)	Y	Y	Y	Y	UC
Fisher, 2008	Walking test at comfortable speed (cadence, gait velocity, step length, stride length) Walking test at fast speed (cadence, gait velocity, step length, stride length)	Y	UC	Y	Y	Y
Frazzitta, 2015	Timed Up and Go test (time) 6-Minute walk test (distance)	Y	Y	Y	N	UC
Ganesan, 2014[a]	Berg Balance Scale Tinetti Balance and Gait Scale	UC	UC	UC	Y	UC
Gao, 2014	Berg Balance Scale Timed Up and Go test (time) Number of fallers Number of falls	Y	UC	Y	Y	UC
Goodwin, 2011	Berg Balance Scale Fall Efficacy Scale Number of falls Timed Up and Go test (time)	Y	Y	Y	Y	UC
Hackney, 2008	Backward walking test (gait velocity, stride length) Berg Balance Scale Single leg stance test (time) Tandem stance test (time) Timed Up and Go test (time) Walking test at comfortable speed (gait velocity, stride length) 6-Minute walk test (distance)	Y	UC	Y	Y	UC
Kurtais, 2008[a]	Single leg stance test (time) Sit-to-stand test (time)	UC	UC	Y	Y	UC

(continued)

Table 1. (continued)

First Author, Year	Outcomes of Interest for Meta-analysis	Adequate Sequence Generation	Concealed Allocation	Blinding	Incomplete Outcome Data Addressed	Free of Selective Reporting
	Stair up and down one flight test (time)					
	U-shaped turn test (time)					
	Walking test at comfortable speed (gait velocity)					
Lee, 2015[a]	Berg Balance Scale	UC	UC	UC	UC	UC
Li, 2012	Limit of stability (amplitude, directional control)	Y	UC	Y	Y	UC
	Fall incidence rate ratio					
	Number of fallers					
	Timed Up and Go test (time)					
	Walking test at comfortable speed (gait velocity, stride length)					
Liao, 2014	Fall Efficacy Scale	Y	Y	Y	Y	UC
	Limit of stability (amplitude, velocity, directional control)					
	Obstacle crossing performance (velocity, stride length, and vertical toe obstacle clearance)					
	Sensory organization test (composite equilibrium score)					
	Timed Up and Go test (time)					
Mak, 2008	Sit-to-stand test (time, peak velocity in horizontal and vertical directions)	Y	UC	Y	Y	UC
Morris 2015	Fall incidence rate	Y	Y	Y	Y	Y
	Number of fallers					
	Timed Up and Go test (time)					
	6-m Walk test (velocity)					
Nieuwboer 2007	Fall Efficacy Scale	Y	Y	Y	Y	UC
	Freezing of gait questionnaire					
	Functional reach test (distance)					
	Number of fallers					
	Postural and gait items of the United Parkinson's Disease Rating Scale					
	Single leg stance test (time)					
	Tandem stance test (time)					
	Timed Up and Go test (time)					
	Walking test at comfortable speed (cadence, gait velocity, stride length)					
Park, 2014[a]	Fear of falling questionnaire	UC	UC	UC	UC	UC
	Korean Falls Efficacy Scale					
	Walking test at comfortable speed (cadence, gait velocity)					
Picelli, 2012	Activities-Specific Balance Confidence Scale	Y	Y	Y	Y	UC
	Berg Balance Scale					
	Pull test (rating scale)					
	Timed Up and Go test (time)					
	Walking test at comfortable speed (gait velocity)					

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Table 1. (continued)

First Author, Year	Outcomes of Interest for Meta-analysis	Adequate Sequence Generation	Concealed Allocation	Blinding	Incomplete Outcome Data Addressed	Free of Selective Reporting
Protas, 2005[a]	Walking test at comfortable speed (cadence, gait velocity, stride length) 8-Step test (time) Number of falls	UC	UC	Y	Y	UC
Sage, 2009[a]	Postural and gait items of the United Parkinson's Disease Rating Scale Timed Up and Go test (time) Walking test at comfortable speed (cadence, gait velocity, step length variability, stride length)	N	UC	Y	Y	UC
Smania, 2010	Activities-Specific Balance Confidence Scale Berg Balance Scale Center of foot pressure self-destabilization test (the number of targets reached) Fall incidence rate	Y	Y	Y	Y	UC
Thaut, 1996[a]	Walking test at comfortable speed (cadence, gait velocity, stride length)	UC	UC	UC	Y	UC
Toole, 2000[a]	Sensory organization test (composite equilibrium score)	UC	UC	Y	N	UC
White, 2009	2-Minute walk test (distance)	Y	UC	Y	Y	UC
Wong-Yu, 2015	Activities-specific balance confidence scale Dual-task time up and go test (time) Walking test at comfortable speed (gait velocity)	Y	Y	Y	Y	UC
Yen, 2011	Sensory organization test (composite equilibrium score)	Y	UC	Y	Y	UC

Abbreviations: Y, low risk of bias; N, high risk of bias; UC, unclear risk of bias.
[a]Studies excluded from the quantitative synthesis for meta-analysis because of low methodological quality, with less than 3 domains having low risk of bias.
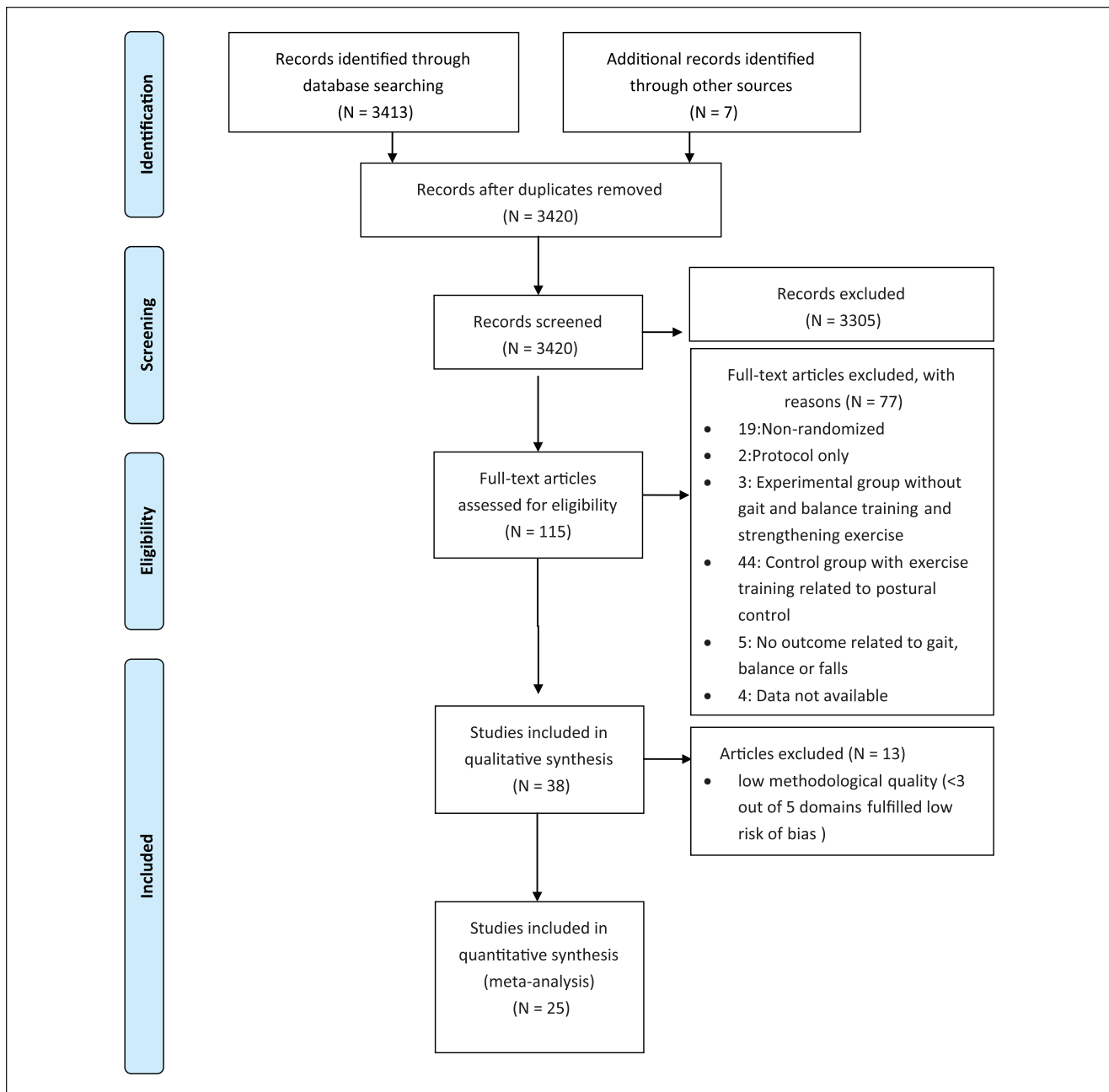
Figure 1. PRISMA flow diagram showing flow of information through the review.

estimates among the 24 studies with 29 comparisons ($I^2 = 22\%$; $P > .05$). The meta-analysis found statistical significance in favor of the intervention group ($P < .001$), with a small overall mean effect size (Hedges' $g = 0.303$; Figure 2A).

For the long-term effects (the carryover effects at follow-up intervals), 941 participants from 12 studies with 13 comparisons were included in the final data analysis. The follow-up period ranged from 4 weeks[31,35,38] to 12 months.[39,40] There was a moderate level of heterogeneity in the effect size estimates ($I^2 = 50\%$; $P < .05$), and the

random-effects model was used in the meta-analysis. The results of the meta-analysis showed statistical significance in favor of the intervention group ($P < .001$), with a mild overall effect size (Hedges' $g = 0.419$; Figure 2B).

Effects on Falls

Among the studies, 8 explored the effects of training on fall prevention along with the outcomes related to the fall rate or number of fallers[15,17,23,26,27,31,36,39]; 6 studies reported the

Table 2. Characteristics of the 30 Comparisons in 25 Included Trials.

First Author, Year	Experimental Exercise Type	Control Group	Initial Sample Size	Age (Mean ± SD)	Disease severity (H&Y): Mean ± SD or Range	Fall risks (Higher / Lower)[a]	Medication Status During Assessment (On/Off)	Percentage of Balance and Gait Component in Experimental Exercise	Training Location (Facility, Community, Home)	Training Supervision	Training Duration (Weeks)	Training Hours	Training Hours Per Week	Duration of Follow-up (Weeks)
Allen, 2010	Balance, gait, strength	No training	48	66.0 ± 8.4	2.5 ± Nil[b]	Higher	On	67%	Home	≤Half	24	72	3.0	0
Ashburn, 2007	Balance, gait, strength, other ex[c]	No training	142	72.2 ± 9.2	2-4	Higher	On	50%	Home	≤Half	6	6	1.0	18
Canning, 2012	Gait	No training	20	61.8 ± 8.0	1-2	Higher	On	100%	Home	≤Half	6	12	2.0	6
Canning, 2015	Balance, gait, strength	No training	231	70.6 ± 8.7	2.7 ± 0.6	Higher	On	67%	Home	≤Half	24	72	3.0	0
Conradsson, 2015	Balance	No training	100	73.2 ± 5.7	2.6 ± 0.5	Higher	On	100%	Facility	>Half	10	30	3	0
De Bruin, 2010	Gait	No training	22	66.0 ± 6.6	2.2 ± 0.4	Lower	On	100%	Community	None	13	19.5	1.5	0
Duncan, 2012	Balance	No training	62	69.2 ± 1.7	2.6 ± 0.2	Lower	Off	100%	Community	>Half	48	96	2.0	0
Ebersbach, 2010 (LSVT-BIG therapy)	Balance, gait (LSVT-BIG)	No training	30	67.8 ± 5.5	2.7 ± 0.5	Lower	On	100%	Facility	>Half	4	16	4.0	0
Ebersbach, 2010 (Nordic walking)	Gait (Nordic gait)	No training	30	66.8 ± 8.8	2.6 ± 0.5	Lower	On	100%	Community	>Half	8	16	2.0	0
Ellis, 2005	Balance, gait, strength, other ex[c]	No training	68	63.5 ± 8.5	2.5 ± 0.5	Lower	On	50%[d]	Facility	>Half	6	18	3.0	18
Fietzek, 2014	Gait	No training	22	67.8 ± 6.7	2-3	Higher	On	100%	Facility	>Half	2	3	1.5	0
Fisher, 2008 (treadmill walking)	Gait	No training	15	63.7 ± 13.2	1.9 ± 0.4	Lower	On	100%	Facility	>Half	8	24	3.0	0
Fisher, 2008 (physical therapy)	Balance, gait, strength, other ex[c]	No training	15	62.0 ± 10.0	1.9 ± 0.3	Lower	On	50%	Facility	>Half	8	24	3.0	0
Frazzitta, 2015	Balance, gait, strength, other ex[c]	No training	20	69 ± 7	1.2 ± 0.3	Lower	Off	67%	Facility	>Half	4	60	15	48
Gao, 2014	Balance	No training	80	68.9 ± 7.9	1-4	Higher	On	100%	Facility	>Half	12	36	3.0	26
Goodwin, 2011	Balance, Gait, Strength, Other ex[c]	No training	130	71.0 ± 8.5	2.5 ± 0.9	Higher	On	50%	Facility	>Half	10	30	3.0	10

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Table 2. (continued)

First Author, Year	Experimental Exercise Type	Control Group	Initial Sample Size	Age (Mean ± SD)	Disease severity (H&Y): Mean ± SD or Range	Fall risks (Higher / Lower)[a]	Medication Status During Assessment (On/Off)	Percentage of Balance and Gait Component in Experimental Exercise	Training Location (Facility, Community, Home)	Training Supervision	Training Duration (Weeks)	Training Hours	Training Hours Per Week	Duration of Follow-up (Weeks)
Hackney, 2008	Balance	No training	33	63.8 ± 8.7	2.0 ± 0.4	Lower	On	100%	Facility	>Half	13	20	1.5	0
Li, 2012 (tai chi)	Balance	No training	97	68.3 ± 9.0	1-4	Lower	On	100%	Facility	>Half	24	48	2.0	12
Li, 2012 (resistive ex.)	Balance, strength,	No training	98	69.0 ± 8.3	1-4	Lower	On	50%	Facility	>Half	24	48	2.0	12
Liao, 2014	Balance, gait, strength, other ex[c]	No training	36	65.7 ± 7.3	2 ± 0.7	Lower	On	50%	Facility	>Half	6	12	2	4
Mak, 2008 (balance ex)	Balance	No training	30	65.2 ± 7.4	2.7 ± 0.3	Lower	On	100%	Facility	>Half	4	4	1.0	2
Mak, 2008 (common ex)	Balance, strength, other ex[c]	No training	30	63.0 ± 8.2	2.8 ± 0.3	Lower	On	50%	Facility	>Half	4	6	1.5	2
Morris, 2015	Strength	No training	141	67.2 ± 9.4	2.5 ± 0.8	Lower	On	0%	Facility and home	>Half	8	32	4	52
Nieuwboer, 2007	Balance, gait	No training	153	68.3 ± 7.8	2.8 ± 0.4	Lower	On	100%	Home	>Half	3	4.5	1.5	0
Picelli, 2012	Gait	Other ex[c]	34	68.3 ± nil	3.5 ± nil	Lower	On	100%	Facility	>Half	4	9	2.3	12
Smania, 2010	Balance, gait	Other ex[c]	64	67.5 ± 7.2	3.0 ± 0.2	Lower	On	100%	Facility	>Half	7	17.5	2.5	4
White, 2009 (3 h/wk)	Balance, gait, strength, other ex[c]	No training	53	65.7 ± 8.1	2-3	Lower	On	33%[d]	Facility	>Half	6	18	3.0	0
White, 2009 (4.5 h/wk)	Balance, gait, strength, other ex[c]	No training	55	67.2 ± 9.7	2-3	Lower	On	33%[d]	Facility	>Half	6	27	4.5	0
Wong-Yu, 2015	Balance, gait, strength	Other ex[c]	84	61.0 ± 9.0	2.5 ± 0.3	Lower	On	80%[d]	Community	>Half	8	16	2	52
Yen, 2011	Balance	No training	42	70.7 ± 6.3	2.5 ± 0.5	Lower	On	100%	Facility	>Half	6	6	1.0	4

Abbreviations: H&Y, Hoehn and Yahr; SD, standard deviation.

[a]Participants were classified as having a higher risk of falling if one of the following was indicated in the inclusion criteria: a history of falling in the past 12 months, experiencing freezing of gait in the past month, gait disturbance, postural instability with balance and mobility problems, reduced lower-limb strength, or fall-related balance confidence (Canning et al[53]).

[b]The mean of H&Y was estimated from the Unified Parkinson's Disease Rating Scale Motor score of 29.5 ± 12.8.

[c]Other exercises: exercises not specifically targeted at enhancing balance and gait performance, such as active joint mobility and muscle stretching exercises.

[d]The percentage of balance and gait training within the total training program was calculated by the time spent in balance and gait training, which was provided in the study.

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A. Effects on postural stability in short-term (n=1881)

Study name	Outcome	Hedges's g	Lower limit	Upper limit	p-Value	Hedges's g and 95% CI
Allen 2010	comfortable walking velocity (cm/s)	0.000	-0.575	0.575	1.000	
Ashburn 2007	berg balance scale (0-56)	0.011	-0.327	0.349	0.948	
Canning 2012	comfortable walking velocity (cm/s)	0.124	-0.757	1.004	0.783	
Canning 2015	freezing of gait questionnaire	0.142	-0.116	0.399	0.281	
Conradsson 2015	comfortable walking velocity (cm/s)	0.443	0.029	0.858	0.036	
De Bruin 2010	comfortable walking velocity (cm/s)	0.276	-0.532	1.085	0.503	
Duncan 2012	comfortable walking velocity (cm/s)	0.422	-0.120	0.963	0.127	
Ebersbach 2010 (LSVT-BIG)	time_up and go test (s)	0.786	0.021	1.551	0.044	
Ebersbach 2010 (Nordic walk)	time_up and go test (s)	0.101	-0.669	0.872	0.796	
Ellis 2005	comfortable walking velocity (cm/s)	0.574	0.068	1.080	0.026	
Fietzek 2014	freezing of gait questionnaire	0.395	-0.449	1.238	0.359	
Fisher 2008 (Physiotherapy)	comfortable walking velocity (cm/s)	0.000	-1.010	1.010	1.000	
Fisher 2008 (treadmill walk)	comfortable walking velocity (cm/s)	0.224	-0.789	1.238	0.665	
Gao 2014	berg balance scale (0-56)	0.443	-0.007	0.894	0.054	
Goodwin 2011	berg balance scale (0-56)	0.381	0.028	0.734	0.034	
Hackney 2008	berg balance scale (0-56)	1.071	0.271	1.870	0.009	
Li 2012 (balance ex)	time_up and go test (s)	0.383	-0.040	0.806	0.076	
Li 2012 (strength ex)	time_up and go test (s)	0.375	-0.044	0.794	0.080	
Liao 2014	time_up and go test (s)	0.037	-0.640	0.715	0.914	
Mak 2008 (balance ex)	time_sit-to-stand (s)	1.188	0.289	2.087	0.010	
Mak 2008 (common ex)	time_sit-to-stand (s)	0.435	-0.412	1.283	0.314	
Morris 2015 (strength ex)	time_up and go test (s)	0.207	-0.122	0.536	0.218	
Nieuwboer 2007	time_up and go test (s)	0.049	-0.266	0.364	0.760	
Picelli 2012	berg balance scale (0-56)	1.445	0.670	2.220	0.000	
Smania 2010	berg balance scale (0-56)	0.913	0.365	1.462	0.001	
White 2009 (3h per wk)	2-min walking test (m)	0.132	-0.428	0.693	0.644	
White 2009 (4.5h per wk)	2-min walking test (m)	0.167	-0.389	0.724	0.555	
Wong-Yu 2015	comfortable walking velocity (cm/s)	0.414	-0.024	0.853	0.064	
Yen 2011	sensory organization test_compoisite score	0.103	-0.527	0.733	0.748	
		0.303	0.211	0.395	0.000	

-2.00 -1.00 0.00 1.00 2.00

Favours CON   Favours EXP

Fixed-effects model of meta-analysis: I^2=22%, df=28, P>0.05

B. Effects on postural stability in long-term (n=941)

Study name (follow-up period)	Outcome	Hedges's g	Lower limit	Upper limit	p-Value	Hedges's g and 95% CI
Ashburn 2007 (18 wk)	berg balance scale (0-56)	0.022	-0.322	0.367	0.900	
Canning 2012 (6 wk)	comfortable walking velocity (cm/s)	0.124	-0.757	1.004	0.783	
Ellis 2005 (18 wk)	comfortable walking velocity (cm/s)	0.076	-0.420	0.571	0.765	
Frazzitta 2015 (48 wk)	time_up and go test (s)	0.491	-0.206	1.188	0.167	
Goodwin 2011 (10 wk)	berg balance scale (0-56)	0.434	0.078	0.789	0.017	
Li 2012 (balance ex, 12 wk)	time_up and go test (s)	0.432	0.012	0.852	0.044	
Li 2012 (strength ex, 12 wk)	time_up and go test (s)	0.511	0.085	0.937	0.019	
Liao 2014 (4 wk)	time_up and go test (s)	1.371	0.623	2.118	0.000	
Morris 2015 (strength ex, 12m)	time_up and go test (s)	0.166	-0.163	0.495	0.323	
Picelli 2012 (12 wk)	berg balance scale (0-56)	1.162	0.417	1.906	0.002	
Smania 2010 (4 wk)	berg balance scale (0-56)	0.951	0.401	1.502	0.001	
Wong-Yu 2015 (12 m)	comfortable walking velocity (cm/s)	0.179	-0.256	0.614	0.421	
Yen 2011 (4 wk)	sensory organization test_compoisite score	0.373	-0.262	1.007	0.249	
		0.419	0.224	0.613	0.000	

-2.00 -1.00 0.00 1.00 2.00

Favours CON   Favours EXP

Random-effects model of meta-analysis: I^2=50%, df=12, P<0.05

C. Effects on fall rate in short-term (n=605)

Study name (Intervention period)	Outcome	Rate ratio	Lower limit	Upper limit	p-Value	Rate ratio and 95% CI
Canning 2015 (24 wk)	fall rate	0.730	0.453	1.177	0.197	
Goodwin 2011 (10 wk)	fall rate	0.680	0.431	1.073	0.097	
Li 2012 (balance ex, 24 wk)	fall rate	0.330	0.157	0.695	0.004	
Li 2012 (strength ex, 24 wk)	fall rate	0.470	0.215	1.026	0.058	
Smania 2010 (7 wk)	fall rate	0.321	0.222	0.466	0.000	
		0.485	0.329	0.715	0.000	

0.1 0.2 0.5 1 2 5 10

Favours EXP   Favours CON

Random-effects model of meta-analysis: I^2=62%, df=4, P<0.05

(continued)

Figure 2. (continued)

D. Effects on fall rate in long-term (n=451)

Study name (follow-up period)	Outcome	Rate ratio	Lower limit	Upper limit	p-Value	Rate ratio and 95% CI
Gao 2014 (26 wk)	fall rate	0.469	0.231	0.951	0.036	
Goodwin 2011 (10 wk)	fall rate	0.740	0.411	1.333	0.316	
Li 2012 (balance ex, 12 wk)	fall rate	0.310	0.142	0.678	0.003	
Li 2012 (strength ex, 12 wk)	fall rate	0.400	0.181	0.884	0.024	
Morris 2015 (strength ex, 12 m)	fall rate	0.151	0.071	0.322	0.000	
Smania 2010 (4 wk)	fall rate	0.559	0.371	0.842	0.005	
		0.413	0.270	0.630	0.000	

0.1 0.2 0.5 1   2   5 10

Favours EXP   Favours CON

Random-effects model of meta-analysis: I^2=61%, df=5, P<0.05

E. Effects on number of fallers in short-term (n=707)

Study name (Intervention period)	Outcome	Risk ratio	Lower limit	Upper limit	p-Value	Risk ratio and 95% CI
Ashburn 2007 (6 wk)	faller no.	0.867	0.658	1.143	0.312	
Canning 2015 (24 wk)	faller no.	0.930	0.776	1.114	0.432	
Li 2012 (balance ex, 24 wk)	faller no.	0.731	0.452	1.183	0.202	
Li 2012 (strength ex, 24 wk)	faller no.	1.192	0.806	1.764	0.379	
Nieuwboer 2007 (3 wk)	faller no.	1.303	0.699	2.427	0.405	
		0.939	0.822	1.072	0.349	

0.1 0.2 0.5 1   2   5 10

Favours EXP   Favours CON

Fixed-effects model of meta-analysis: I^2=0%, df=4, P>0.05

F. Effects on number of fallers in long-term (n=345)

Study name (follow-up period)	Outcome	Risk ratio	Lower limit	Upper limit	p-Value	Risk ratio and 95% CI
Ashburn 2007 (18 wk)	faller no.	1.286	0.510	3.239	0.594	
Gao 2014 (26 wk)	faller no.	0.444	0.222	0.887	0.022	
Morris 2015 (strength ex, 12 m)	faller no.	0.832	0.617	1.122	0.229	
		0.787	0.605	1.024	0.075	

0.1 0.2 0.5 1   2   5 10

Favours EXP   Favours CON

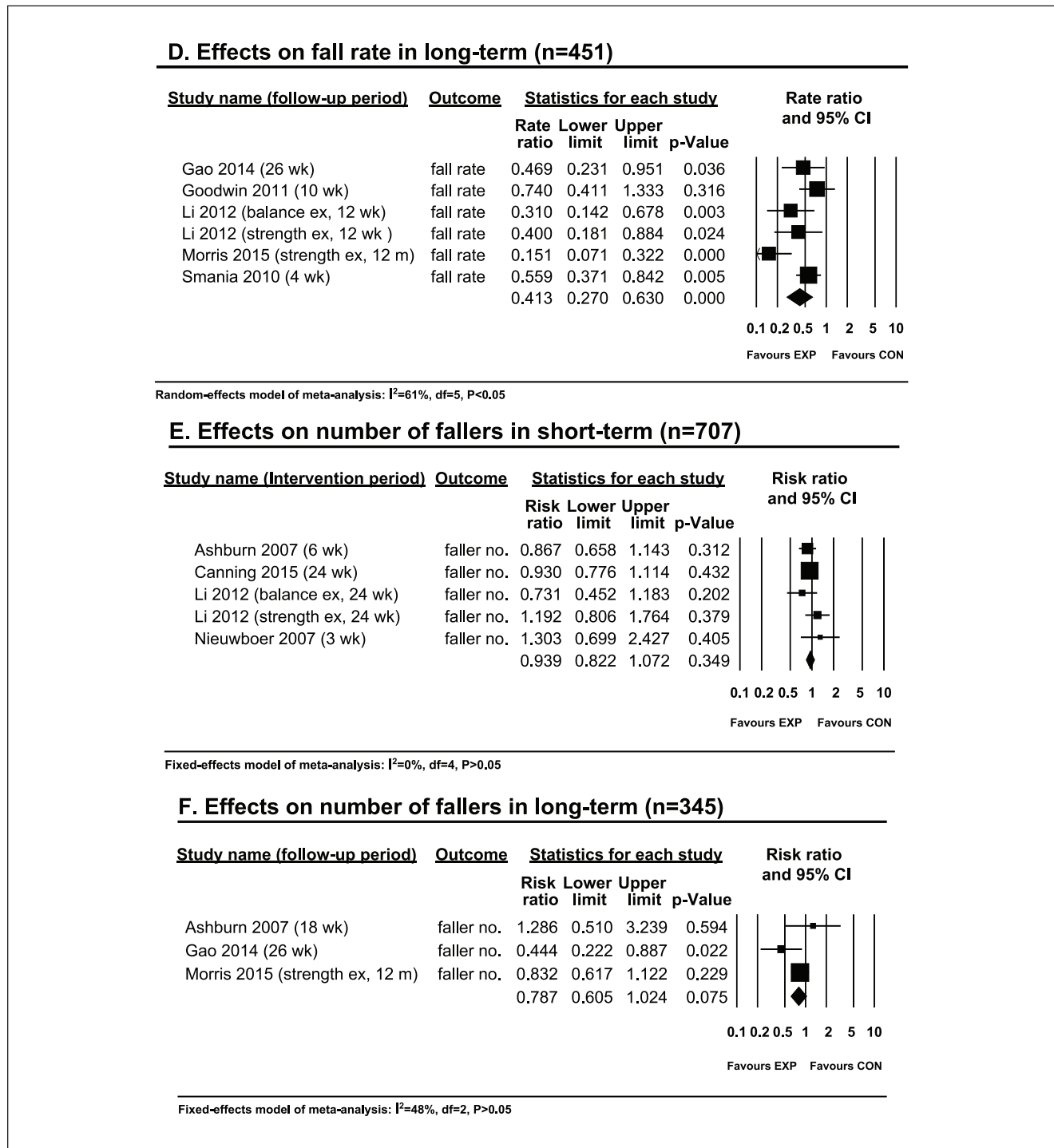Fixed-effects model of meta-analysis: I^2=48%, df=2, P>0.05

Figure 2. Forest plots from the meta-analyses of effects of exercise training demonstrating estimates of effect size with 95% confidence intervals (CIs): A. Short-term effects on balance and gait abilities. B. Long-term effects on balance and gait abilities. C. Short-term effects on fall rate. D. Long-term effects on fall rate. E. Short-term effects on number of fallers. F. Long-term effects on number of fallers.

short-term effects,[15,17,23,26,27,31] and 6 studies reported the long-term effects.[15,17,23,26,31,36,39] The follow-up periods ranged from 4 weeks to 12 months.

In terms of the fall rate, the estimated effect sizes showed medium heterogeneity over the short- and long-terms (I^2 = 62% and 61%, respectively; $P < .05$). The fall rate showed a

Table 3. Subgroup Analyses of Effect Sizes Related to Each Contributing Factor.

Contributing Factors to Heterogeneity of Effect Sizes	Long-term Effects on Balance and Gait Abilities	
	Coefficient of Correlation (95% CI)	Effect Sizes in Subgroup Analysis (Hedges' *g*, 95% CI)
Participant's characteristics		
Age (years)	NS	
Risk of falling	NS	
Intervention's characteristics		
Exercise type (percentage of balance and gait training components within exercise program)	NS	
Supervision during training	NS	
Training location	0.218 (0.046, 0.390)[a]	
Facility		0.518 (0.296, 0.741)[b]
Community		0.179 (−0.256, 0.614)
Home-based		0.036 (−0.285, 0.356)
Training duration/hours	NS	

[a]$P < .05$ (or NS: $P > .05$) for the association between contributing factors and effect sizes, using metaregression.
[b]$P < .05$ for effect size of balance and gait abilities or falls in the short-term or long-term in subgroups with specific characteristics of participants or interventions.

significant overall reduction over the short-term (rate ratio = 0.485, $P < .05$; Figure 2C) and long-term (rate ratio = 0.413, $P < .05$; Figure 2D). For the number of fallers, the effect sizes demonstrated insignificant heterogeneity over short-and long-terms. The number of fallers did not decrease significantly over the short-term (risk ratio = 0.939, $P > .05$; Figure 2E) or long-term (risk ratio = 0.787, $P > .05$; Figure 2F).

The statistical significance in all the outcomes over both the short- and long-terms remained when any 1 trial was removed. There was significant publication bias for the effect sizes of balance and gait outcomes over the short- and long-terms among the included studies (Egger's tests: $P < .05$).

Heterogeneity Across Studies and Potential Contributing Factors

The statistical heterogeneity of effects on balance and gait ability showed significance over the long-term ($I^2 = 50\%$; $P < .05$). The effect sizes significantly correlated with the training location during training ($P < .05$). The subgroup analyses showed that greater long-term training effects on balance and gait outcomes was achieved in participants who received facility-based training (Table 3).

Discussion

This is the first review study to report that exercise intervention can improve balance and gait performance over the short- and long-terms in people with PD. For the short-term effects on participants' balance and gait ability, the overall effect size was positive but small, a finding comparable to 2 meta-analyses in people with PD.[48,49] Tomlinson et al[48]

reviewed 29 randomized controlled trials and suggested that physiotherapy has short-term benefits in gait speed and balance outcomes. Allen et al[49] analyzed the effects of exercises in 15 randomized and quasirandomized trials and concluded that exercise training improves the performance of balance-related activities in the short-term. Yet our findings provide more convincing evidence for several reasons. First, all the studies we included had a moderate to high methodological quality according to the Cochrane risk-of-bias tool, whereas most studies had low methodological quality in the review by Tomlinson et al,[48] and only fewer than half of the included studies had a moderate to high quality in the study by Allen et al.[49] Second, the short-term effect size heterogeneity among the studies considered in this review was insignificant and much lower than that reported by the previous studies.[48,49] Third, we extended previous reviews by reporting positive and moderate long-term treatment effects for balance and gait ability. Despite the variation in follow-up periods (ie, 4 weeks to 12 months), this is the first study to demonstrate the benefits of exercise interventions in the longer term.

In addition to the positive balance and gait outcomes, our meta-analysis is the first to report that exercise training could decrease the fall rates of PD participants by about 60% over both the short- and long-terms. In contrast to fall rate, we found training to have an insignificant effect on the number of fallers, a finding that agrees with that of Allen et al.[49] Our review and that of Allen et al[49] included a small number of studies and with exercise as the only intervention. Previous meta-analyses in older people reporting significant reduction in the number of fallers included a large number of studies,[51,59] with exercise intervention alone[59] or

with exercise intervention combined with medicine, psychological treatment, education, and so on.[51] It is possible that the small number of included studies or the type of intervention contributed to our insignificant effects on reducing the number of fallers. More studies are needed to investigate the effects of exercise intervention on fall reduction in people with PD.

We further explored factors that contributed to the effect sizes of balance and gait improvement in an attempt to suggest an efficacious exercise training protocol. The subgroup meta-analysis results showed that training at facilities led to more improvement in balance and gait ability over the long-term than the community- and home-based training. Facility-based training, mostly supervised by physical therapists, could have enabled participants to practice the training tasks at their optimal capacity.[49] Therapists in these studies applied motor learning principles such as progression from simple to difficult tasks,[23,26,28,31,38] attentional strategies,[31,38] and augmented feedback[38] to enhance learning and practice, leading to better retention of the learned balance strategies and reduced fall risk. With respect to the exercise type, there were no significant correlations between the percentage of balance and gait training components and effect sizes of balance and gait ability over the long-term. Strength training was another component and could have a role in enhancing balance and gait performance.[39] Regarding exercise dosage, the training duration of the included trials ranged from 4 to 48 weeks and with a total of 4 to 96 hours. However, there were no significant correlations between the training duration and effect sizes in the long-term balance ability. A few studies instructed participants to perform home exercises during the follow-up period,[15,40,44] but only 2 studies reported participants' compliance with the home exercises.[40,44] Thus, the impact of exercise dose and continuous exercises on balance ability and fall reduction is unclear, and more studies are needed in these areas.

Notwithstanding its significant findings, this study has several limitations. First, similar to a previous review,[49] the included trials showed some publication bias for the effect sizes of balance and gait outcomes over the short- and long-terms, probably because a few studies showed a relatively large positive effect size. Second, some of the included studies did not indicate information such as the training durations of the balance and gait components, and we thus had to estimate such information. Standardization of the estimation method was used to minimize its influence on the sources of effect size heterogeneity in the studies we examined. Third, the differences in key participant and intervention characteristics between studies and the heterogeneity in outcome measures could contribute to the effect size heterogeneity. Finally, few of our included studies examined the effects of training on fall outcomes, and the studies that explored long-term effects had different follow-up durations; therefore, the results should be interpreted with caution.

In conclusion, exercise training can improve balance and gait ability in individuals with PD and decrease their fall rates over both the short- and long-terms, which may provide guidance for treatment or for future trials in the PD population. The correlations between effect sizes and the exercise training program characteristics suggest that greater training effects might be contributed by balance and gait training conducted within facilities. These associations should be examined in further studies to determine the optimal fall prevention protocol for individuals with PD.

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