Treadmill training for patients with Parkinson's disease (Review)

Mehrholz J, Friis R, Kugler J, Twork S, Storch A, Pohl M

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[Intervention Review]

Treadmill training for patients with Parkinson's disease

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ABSTRACT

Background

Treadmill training is used in rehabilitation and is described as improving gait parameters of patients with Parkinson's disease.

Objectives

To assess the effectiveness of treadmill training in improving the gait function of patients with Parkinson's disease and the acceptability and safety of this type of therapy.

Search methods

We searched the Cochrane Movement Disorders Group Specialised Register (see Review Group details for more information) (last searched March 2009), Cochrane Central Register of Controlled Trials (*The Cochrane Library 2009*, Issue 2), MEDLINE (1950 to March 2009), and EMBASE (1980 to March 2009).

We also handsearched relevant conference proceedings, searched trials and research registers, and checked reference lists **(last searched March 2009)**. We contacted trialists, experts and researchers in the field and manufacturers of commercial devices.

Selection criteria

We included randomised controlled trials comparing treadmill training with no treadmill training in patients with Parkinson's disease.

Data collection and analysis

Two review authors independently selected trials for inclusion, assessed trial quality and extracted data. We contacted the trialists for additional information. We analysed the results as standardised mean differences (SMDs) and mean differences (MDs) for continuous variables and relative risk differences (RD) for dichotomous variables.

Main results

We included eight trials (203 participants) in this review. Treadmill training improved gait speed (SMD **0.50; 95% confidence interval (CI) 0.17 to 0.84; P = 0.003**; I^2 = 0%) (fixed-effect model), stride length (SMD 0.42; 95% CI 0.00 to 0.84; P = 0.05; I^2 = 0%), walking distance (MD = 358 metres; 95% CI 289 to 426; P < 0.0001; I^2 = 30%), but cadence did not improve (MD 1.06; 95% CI -4.32 to 6.44; P = 0.70; I^2 = 0%) at the end of study. Treadmill training did not increase the risk of patients dropping out (RD -0.07; 95% CI -0.18 to 0.05; P = 0.26; I^2 = 51%) (random-effects model). Adverse events were not reported.

Authors' conclusions

Patients with Parkinson's disease who receive treadmill training are more likely to improve their impaired gait hypokinesia. However, the results must be interpreted with caution because there were variations between the trials in patient characteristics, the duration and amount of training, and types of treatment. Additionally, it is not known how long these improvements may last.

PLAIN LANGUAGE SUMMARY

Treadmill training for people with Parkinson's disease

The role of treadmill training for people with Parkinson's disease in improving gait parameters is unclear. Gait hypokinesia is typically one of the primary movement disorders associated with Parkinson's disease. It is an important determinant of disability and quality of life for people with mild to moderate Parkinson?s disease. Treadmill training uses specialised machines to facilitate gait rehabilitation. This review identified eight trials including 203 participants which evaluated this type of therapy. Treadmill training did improve gait speed, stride length and walking distance; cadence did not improve. Acceptability of treadmill training for study participants was good and adverse events were rare.

It is not, however, clear if such devices should be applied in routine rehabilitation or when and how often they should be used.

BACKGROUND

Parkinson's disease (PD) is a progressive and disabling degenerative disorder that is characterised clinically by bradykinesia, tremor, rigidity, and postural instability. Disability occurs at all stages of the disease and the severity of disabilities usually increases with disease duration. Patients frequently have gait impairments, difficulty in linking movements together smoothly, and episodes of freezing. These problems together with balance disturbances lead to an increased incidence of falls with the concomitant risk of fractures. In fact one study found that 27% of Parkinson's patients have had a hip fracture within 10 years of their diagnosis (Johnell 1992).

Gait hypokinesia is one of the primary movement disorders associated with PD (Morris 2000). It is an important determinant of disability and quality of life in mild to moderate Parkinson disease (Muslimovic 2008). Kinematic measures have occasionally been found to been altered in individual patients and abnormal slowness of gait is the only symptom that has been consistently reported in group comparisons between control patients and patients with idiopathic PD (Morris 2000). Cadence control remains unaffected throughout its entire range in PD and gait hypokinesia is directly attributable to an inability to internally generate sufficiently large steps. Therefore, improvements of walking speed and stride length are the primary goals of gait therapy in patients with PD (Pohl 2003). An additionally to be mentioned goal is to reduce gait freezing when it is present.

The current management of PD focuses on pharmacological therapy; at present levodopa is regarded as the most effective treatment. However, many patients show abnormal involuntary movements due to levodopa known as dyskinesias (Jankovic 2000). Drugs other than levodopa such as dopamine agonists initially control symptoms for many patients but levodopa and polytherapy are often necessary in the treatment of PD, particularly in the advanced stages (Motto 2003).

Despite new pharmacological resources, treatment becomes unsatisfactory in a large proportion of patients. After five years of levodopa treatment, many patients experience severe motor complications such as motor fluctuations and dyskinesias. Theseare difficult to manage with the available drug strategies. Complications cause functional disability and impact on the person's quality of

life (Motto 2003).

In recent years, interest in functional neurosurgery of basal ganglia has increased. Patients who have developed severe motor complications that are refractory to the available pharmacological interventions could be considered surgical candidates (Motto 2003). Three major targets for functional neurosurgery are the thalamus ventro-intermediate nucleus, internal globus pallidus, or subthalamic nucleus. Two different techniques, radiofrequency lesioning or high frequency stimulation (Limousin 1998) have been proposed. However, there is still a debate concerning risks and benefits of surgery. A Cochrane review team is evaluating theses issues (Motto 2003).

Despite optimal medical and surgical therapies for PD, patients develop progressive disability (Deane 2001). However, the effectiveness of non-pharmacological options such as exercises have recently been demonstrated (Goodwin 2008). A good example for patient-tailored exercises is physiotherapy (Ashburn 2004; Comella 1994; de Goede 2001). The aim of physiotherapists is to enable PD patients to maintain their maximum level of mobility, activity, and independence. This outcome can be attained through monitoring of the patient's condition, implementation of appropriate physical treatments, and incorporating a range of approaches to movement rehabilitation (Deane 2001). However, in spite of established pharmacological and conventional approaches there is still a need for new concepts to improve the gait of people with PD.

Recently, the use of electromechanical devices such as treadmill training has provided a promising investigational therapy in the rehabilitation of patients with hemiparesis and impaired gait (Moseley 2005). Treadmill training as a supplement to conventional therapies may improve the results of other gait training therapies. With seriously afflicted hemiparetic patients who cannot walk under their own power, treadmill training with bodyweight support (BWS) is recommended. As described recently, treadmill training with BWS has also been used with PD patients. Results suggested better improvement in gait parameters when compared with conventional gait therapy (Miyai 2002, Pohl 2003). However, the most effective combination of training parameters (for example, amount and timing of BWS during the gait cycle and belt speed and acceleration) is still unknown. There is, therefore, a need for a systematic evaluation in the form of a systematic review of the available literature. The present review assesses the effectiveness and acceptability of treadmill training in the treatment of gait disorders for patients with PD.

OBJECTIVES

To assess the effectiveness of treadmill training with or without body weight support in improving the walking function of patients with PD.

METHODS

Criteria for considering studies for this review

Types of studies

We included randomised controlled trials (RCTs) and randomised controlled cross-over trials where only the first period was to be analysed as a parallel group trial.

Types of participants

We included studies with participants of either gender and any age who were diagnosed with PD using the UK Parkinson's Disease Brain Bank Criteria (or PD diagnostic criteria as defined by the study authors) regardless of drug therapy, duration of treatment, duration of PD, or level of initial impairment.

Types of interventions

We compared treadmill training versus no treadmill training (main analysis) for improving gait. We assumed that co- interventions such as other rehabilitation interventions and medication or treatment were comparable between groups.

Types of outcome measures

The primary outcomes were walking speed (continuous outcome) and stride length (continuous).
The secondary outcomes were cadence (continuous) and walking distance (continuous).
Another secondary outcome was the acceptability and safety of treadmill training. We investigated the safety of treadmill training using the incidence of adverse outcomes such as cardiovascular events, injuries, and pain, and any other reported adverse events. To measure the acceptance of treadmill training we used drop outs from the study due to any reason.

Search methods for identification of studies

We used the search strategy developed for the Movement Disorders Group and identified relevant trials by searching the following electronic databases:

- Cochrane Movement Disorders Group Specialised Register;
- Cochrane Central Register of Controlled Trials

(CENTRAL) (*The Cochrane Library*; last searched March 2009);

- MEDLINE (1966 to March 2009);
- EMBASE (1966 to March 2009);
- Pedro (last search March 2009).

The MeEDLINE and EMBASE searches can be found in the Appendices

In addition, we also:

- searched the reference lists of identified trials and review articles;
- handsearched and screened reference lists of potentially relevant conference proceedings **(1998 to March 2009)**(Appendix 2) searched ongoing trials and research registers; contacted trialists, other researchers, and manufacturers of commercial devices in our field of study to identify published, unpublished, and ongoing trials not available in the major databases; contacted trialists and other researchers to obtain additional information on trials published elsewhere and unpublished trials.

Publication status or language did not influence our decisions on inclusion.

Data collection and analysis

Selection and identification of relevant trials

Two authors (JM and MP) independently read titles and, when available, abstracts of identified references and eliminated obviously irrelevant studies. Two review authors (MP and ST) independently examined potentially relevant studies using the predetermined criteria for including studies. We obtained the full text for the remaining studies. Based on our inclusion criteria (types of studies, participants, aims of interventions, outcome measures) two review authors (ST and MP) independently ranked these studies as relevant, irrelevant, or possibly relevant. We excluded all trials ranked initially as irrelevant, but included all other trials at this stage. We resolved disagreement among authors through discussion. If further information was needed to reach consensus we contacted trialists in an effort to obtain missing information.

Assessment of methodological quality

All review authors independently assessed the methodological quality of included trials using the PEDro scale (Maher 2003). The results of quality ratings are presented in Table 1. The items of the PEDro scale are: specification of eligibility criteria; random allocation to groups; concealed allocation; groups similar at baseline; blinding of participants, therapists and assessors; outcome measurements obtained from more than 85% of participants; presence of an intention-to-treat (ITT) analysis; reporting of results of between-group statistical comparisons; reporting of point measures and measures of variability (Herbert 1998). The maximum achievable PEDro sum score is 10 points.

We checked all methodological quality assessments for agreement among the review authors and resolved disagreements by discussion among authors. Two review authors (MP and JM) were co-authors of one included trial (Pohl 2003); two other review authors (ST and JK) did the quality assessment for this trial. We contacted study authors for clarification and to request missing information. However, due to the small number of studies we did not test the robustness of the main results in a sensitivity analysis (Differences between protocol and review).

Data extraction

Two review authors (JM and MP) independently extracted trial and outcome data from the selected trials. If any review author was involved in any of the selected studies another member of our author group who was not involved in the study was requested to handle the study information.

We established the characteristics of unpublished trials through correspondence with the trial co-ordinator or principal investigator. We used checklists to independently record details of the:

- methods of generating randomisation schedule;
- methods of concealment of allocation;
- blinding of assessors;
- use of an intention-to-treat analysis (all participants initially randomised were included in the analyses as allocated to groups);
- adverse events and drop outs for all reasons;
- important imbalance in prognostic factors;
- participants (country, number of participants, age, gender, stage of PD as assessed by Hoehn Yahr for entry to the study, inclusion and exclusion criteria);
- comparison (details of the intervention in treatment and control groups; details of co-intervention(s) in both groups; duration of treatment);
- outcomes and time points of measures (number of participants in each group and outcome, regardless of compliance).

We checked all of the extracted data for agreement among review authors, with another review author (ST, AS or JK) arbitrating any items where consensus was not reached. If necessary, we contacted trialists to request more information, clarification, or missing data.

Statistical analysis

The primary outcome variables of interest were continuous data, entered as means and standard deviations. We calculated a pooled estimate of the mean differences (MD) with 95% confidence intervals (CI). If studies did not use the same outcome, we use the standardised mean difference (SMD) with 95% CI.

For all binary outcomes (such as the secondary outcome 'drop out, from all causes') we calculated relative risks (RR) with 95% CI. Because some trials (or groups within a trial) did not report any adverse events or drop outs, we calculated risk differences (RD) instead of RRs in these specific situations, again with 95% CI. To quantify for heterogeneity we used the I^2 statistic (alpha level 50%) for all comparisons. If we found statistically significant heterogeneity, we calculated the overall effects using a random-effects model instead of a fixed-effect model.

We described variability in participants, interventions, and outcomes studied (clinical diversity) in an additional table (Table 2) and in the Description of studies. The variability did not influence the intention to pool trials.

For all statistical analyses we used the latest version of The Cochrane Collaboration's software Review Manager (RevMan).

RESULTS

Description of studies

See: Characteristics of included studies; Characteristics of excluded studies; Characteristics of ongoing studies.
See:Characteristics of included studies; Characteristics of excluded studies; Characteristics of ongoing studies.

Results of the search

We identified 12 potentially eligible trials (March 2009).
The search strategy retrieved 85 references to studies (8 CENTRAL, 47 MEDLINE, 29 EMBASE). After examination of the titles and abstracts of these references we eliminated 73, excluding them from further review. We obtained full-text copies of the remaining studies and subjected them to further evaluation. We examined the bibliographical references of these studies and, as with our searches of the CENTRAL, MEDLINE, and EMBASE databases, they did not provide any further citations to potentially eligible studies. Two authors (JM and MP) independently assessed all of the full-text papers and resolved any disagreements on their eligibility for this review through discussion and consensus.

Included studies

Eight trials including a total of 203 participants met our inclusion criteria and were included in the analysis (Cakit 2007; Canning 2008; Fisher 2008; Kurtais 2008; Miyai 2000; Miyai 2002; Pohl 2003; Protas 2005) (see Characteristics of included studies and Table 2).

Design

Two trials (Miyai 2000; Pohl 2003) used a cross-over design with random allocation to the order of treatment sequences. Weobtained outcome data from the trialists of this study. The data from the first period was analysed as a parallel group trial for all our analyses. All other studies used a parallel group design with true randomisation-to-group allocation (Cakit 2007; Canning 2008; Fisher 2008; Kurtais 2008; Miyai 2002; Protas 2005).

Sample sizes

The sample sizes in the trials ranged from 10 participants (Miyai 2000) to 54 participants (Cakit 2007). A more detailed description of trial characteristics can be found in Characteristics of included studies and Table 2.

Participants

The mean age of participants in the included studies ranged from 61 years (Pohl 2003) to 74 years (Protas 2005). The mean duration of PD in the included studies ranged from one year (Fisher 2008) to eight years (Protas 2005). The mean Hoehn and Yahr stages ranged from one (Cakit 2007; Fisher 2008; Pohl 2003) to three (Miyai 2000; Miyai 2002). A detailed description of participant characteristics can be found in Table 2. A detailed description of exclusion criteria used in the included studies can found in Characteristics of included studies.

Interventions

The duration of the studies (time frame where treadmill training was applied) was heterogeneous, ranging from one session of about 30 minutes (Pohl 2003) to eight weeks (Cakit 2007; Fisher 2008; Protas 2005).
Most studies (seven) used a four-week, six-week or eight-week study period (Cakit 2007; Canning 2008; Fisher 2008; Kurtais 2008; Miyai 2000; Miyai 2002; Protas 2005). Some trialists used body-weight supported treadmill training (Miyai 2000; Miyai 2002). Others used a speed-dependent treadmill training paradigm (Cakit 2007; Pohl 2003).
The frequency of treatment ranged from a single session to four times a week (Table 2).One study did not describe the applied frequency of training in detail (Cakit 2007). The duration of the treadmill training provided ranged from approximately 30 minutes (Cakit 2007; Pohl 2003; Protas 2005) to 45 minutes each session (Fisher 2008; Miyai 2000; Miyai 2002).
The included trials compared treadmill training with a variety of other interventions. We did a formal meta-analysis of studies that measured the same treatment effect.**Thus we combined treadmill training versus all other approaches as an estimate of the effect of treadmill training compared with a different treatment.** However, we did not compared treadmill training A with treadmill training B as these are measuring entirely different treatment effects.

Outcomes

The primary outcomes differed between the included studies. A detailed description of the primary outcomes for each trial can be found in Characteristics of included studies.
Because reporting of the data for follow-up measures was limited, for our primary outcome we did not do separate analyses for immediately after study end and sustained data from follow up after the end of the study.

Excluded studies

Two of the identified 12 trials were excluded (,Bello 2008; Gianfrancesco 2009). These trials were excluded for various reasons and the details are described in Characteristics of excluded studies. If there was any doubt whether the study should be excluded or not, we retrieved the full text of the article. In cases of disagreement between the review authors, another member of the author group reviewed the information to decide on inclusion or exclusion of a study.

Ongoing studies

One ongoing study **was** identified and described in Characteristics of ongoing studies.

Risk of bias in included studies

All details about the methodological quality are provided for each included study in Table 1.

We wrote to the trialists of all the included studies (Cakit 2007; Canning 2008; Fisher 2008; Kurtais 2008; Miyai 2000; Miyai 2002; Pohl 2003; Protas 2005) requesting clarification of some design features or missing information in order to complete the quality ratings. The correspondence was via email and letter, and we wrote reminders every two weeks if we did not receive an answer.

Most trialists provided at least some or all requested and required data. We did not receive all requested data for one trial (Protas 2005).

Using the PEDro scale, two authors (JM and MP) independently assessed the methodological quality of all the included trials except one (Pohl 2003), which was rated by the two other review authors (ST and JK). The assessors disagreed only in the use of an intention-to-treat analysis (Miyai 2002) and the concealment process for allocation (Cakit 2007; Kurtais 2008; Miyai 2000; Miyai 2002; Protas 2005). However, all disagreements were discussed and finally arbitrated by another author.

The ratings for each of the PEDro items and the total PEDro score (that is, the score derived from adding all PEDro scale items) are listed in Table 1.

Three included studies used concealed allocation of participants to groups (Canning 2008; Kurtais 2008; Pohl 2003). The allocation concealment classification is described in more detail in Characteristics of included studies. Four included studies described outcome assessors who were blinded to group allocation (Cakit 2007; Canning 2008; Kurtais 2008; Pohl 2003). One study (Pohl 2003) had four arms and used three treatment groups (two treadmill training groups and one physiotherapy group) and one control group (Characteristics of included studies). Since the results of the treadmill training groups did not differ significantly, we combined the results of both treadmill groups in one (collapsed, treadmill) group

and compared this with the combined results of the control group and the physiotherapy group.

Another study (Fisher 2008) had three arms and used two treatment groups (one treadmill training group and one 'low -intensity' training group) and one ('zero-intensity') control group (see Characteristics of included studies). Since the results of the low-intensity training group and the (zero-intensity) control group did not differ significantly, we combined the results of both groups in one (collapsed control) group and compared this with the treadmill training group.

Effects of interventions

Treadmill training versus all other interventions (no treadmill training)

Comparison 1.1 Gait speed at the end of intervention phase

Seven studies with a total of 153 participants compared treadmill training versus no treadmill training on gait speed. Treadmill training improved gait speed. The pooled standardised mean difference (SMD, fixed-effect model) for gait speed was **0.50 (95% CI 0.17 to 0.84; P = 0.003;** level of heterogeneity I^2 = 0%) at the end of the study(Analysis 1.1).

Comparison 1.2 Stride length at the end of intervention phase

Five studies with a total of 95 participants compared treadmill training versus no treadmill training on stride length. Treadmill training improved stride length. The SMD (fixed-effect model) for stride length was 0.42 (95% CI 0.00 to 0.84; P = 0.05; I^2 = 0%) at the end of the study (Analysis 1.2).

Comparison 1.3 Walking distance at the end of intervention phase

Two studies with a total of 41 participants compared treadmill training versus no treadmill training on walking distance. Treadmill training improved walking distance. The MD (fixed-effect model) for walking distance was 358 metres (95% CI 289 to 426; P < 0.0001; I^2 = 30%) at the end of the study(Analysis 1.3).

Comparison 1.4 Cadence at the end of intervention phase

Four studies with a total of 78 participants compared treadmill training versus no treadmill training on cadence. Treadmill training did not improve cadence. The MD (fixed-effect model) for cadence was 1.06 (95% CI -4.32 to 6.44; P = 0.70; I^2 = 0%) at the end of the study (Analysis 1.4).

Comparison 1.5 Acceptability and safety at the end of intervention phase

All eight trials, with a total of 197 participants, reported rates of participants who dropped out. We pooled the reported drop outs from all causes during the trial period. The use of treadmill training in patients with PD did not increase the risk of participants dropping out (risk difference (RD) (random-effects model) **-0.07; 95% CI -0.18 to 0.05; P = 0.26**; I^2 = 51%). Adverse events were not reported (Analysis 1.5).

The reported drop-out rates for all reasons at the end of the treatment phase varied. Four trialists reported no drop outs at the end of the study (Fisher 2008; Miyai 2000; Pohl 2003; Protas 2005), five trialists reported a drop-out rate of less than 15% (Canning 2008; Fisher 2008; Miyai 2000; Pohl 2003; Protas 2005). The highest drop-out rate was found with 48% (23 drop outs out from 54 included participants)(Cakit 2007)and the main reason for drop out was that they withdrew from the study.

Reported reasons for drop outs were in the control group:

- 9 withdrew (Cakit 2007)
- 4 were medically unfit (Cakit 2007);
- 4 showed unwillingness (Cakit 2007);
- 2 discontinued assessment (Kurtais 2008)
- 3 had modification of medication (Miyai 2002)

Reported reasons for drop outs were in the treadmill training group:

- 2 had ill health (Cakit 2007)
- 4 withdrew (Cakit 2007)
- 1 showed noncompliance, discontinuing treatment (Kurtais 2008)
- 1 had modification of medication (Miyai 2002)

Sensitivity analysis

To test the robustness of the main results we used for our planned sensitivity analysis subgroups of the methodological features of concealment of allocation, ITT analysis, and blinding of assessors and also for best PEDro scoring results trials (Analysis 2.1).

Comparison 2.1: Sensitivity analysis by trial methodology

To examine the robustness of results, we specified variables in a sensitivity analysis that we believed could influence the size of effect observed (concealed allocation, blinding of assessors, intention-to-treat analysis, and a PEDro total score below six points; Analysis 2.1).

- Including only studies with adequate concealed allocation for the primary outcome gait speed

Three trials with a total of 74 patients with adequate concealment of allocation were included. Treadmill training did not improve gait speed. The pooled standardised mean difference (SMD, fixed effects model) for gait speed was 0.41 95% confidence interval (CI) -0.06 to 0.88; P = 0.09; level of heterogeneity I^2 = 0%) at the end of study (Analysis 2.1).

- Including only studies with intention-to-treat analysis

Six trials with a total of 122 patients described an intention-to-treat analysis. Treadmill training did improve gait speed. The pooled standardised mean difference (SMD, fixed effects model) for gait speed was 0.43; 95% confidence interval (CI) 0.07 to 0.80; P = 0.02; level of heterogeneity I^2 = 0%) at the end of study (Analysis 2.1).

- Including only studies with blinded assessors for the primary outcome gait speed

Three trials with a total of 75 patients described a blinded assessors for the primary outcome gait speed. Treadmill training did improve gait speed. The pooled standardised mean difference (SMD, fixed effects model) for gait speed was 0.57; 95% confidence interval (CI) 0.09 to 1.05; P = 0.02; level of heterogeneity I^2 = 18%) at the end of study (Analysis 2.1).

- Including only studies with a PEDRO Score of six points or above for the primary outcome gait speed

Five trials with a total of 102 patients had a PEDRO Score of six points or above for the primary outcome gait speed. Treadmill training did improve gait speed. The pooled standardised mean difference (SMD, fixed effects model) for gait speed was 0.43; 95% confidence interval (CI) 0.03 to 0.83; P = 0.04; level of heterogeneity I^2 = 0%) at the end of study (Analysis 2.1).

Subgroup analysis

Although initially planned, we decided against a formal subgroup analysis, due to limited number of studies (Differences between protocol and review).

DISCUSSION

Summary of main results

The aim of this review was to evaluate the effects of treadmill training to improve gait in patients with PD.

We included eight trials with a total of 203 participants in this review. We found at least some evidence that the use of treadmill training may improve gait parameters, such as gait speed and stride length, of patients with PD at Hoehn Yahr stages one to three. However, this description of evidence is based on only eight small studies. It is not known how long gait improvements after treadmill training may last.

Potential biases in the review process

A risk of publication bias is present in all systematic reviews. However, we searched extensively for relevant literature in databases and trial registers and handsearched reference lists and conference abstracts. Additionally, we contacted and asked authors, trialists and experts in the field for information on other unpublished and ongoing trials. No statistical or graphical evidence for publication bias has been found (Figure 1; Figure 2).

Figure 1. Funnel plot of comparison: 1 treadmill training versus no treadmill training, outcome: 1.1 Gait speed.

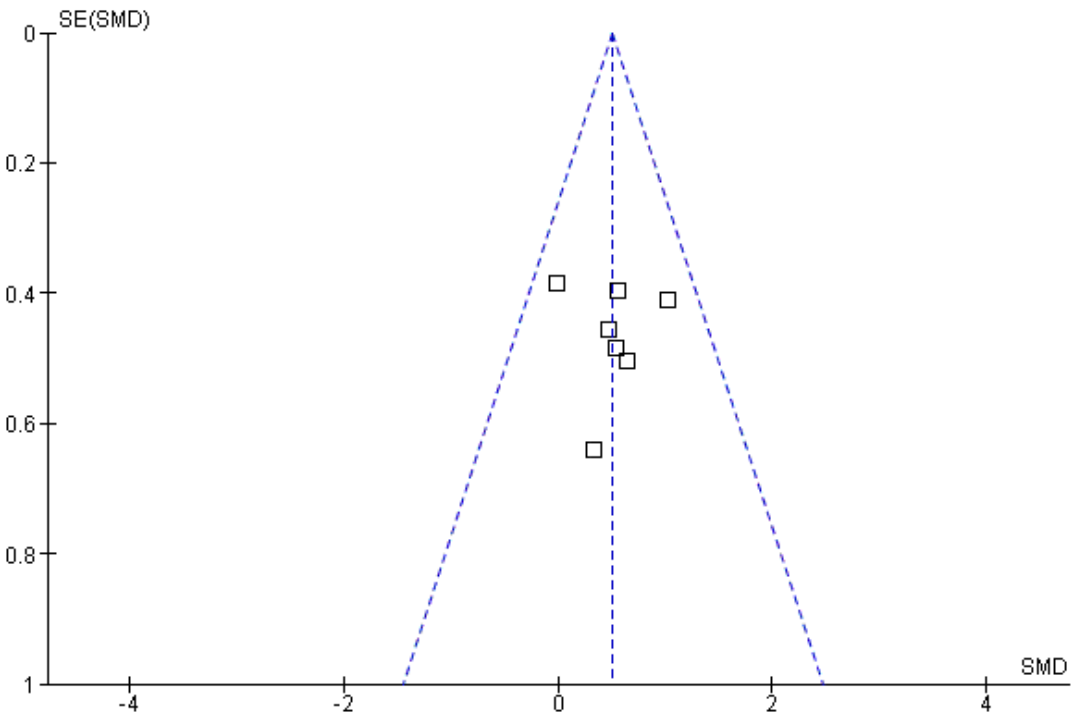
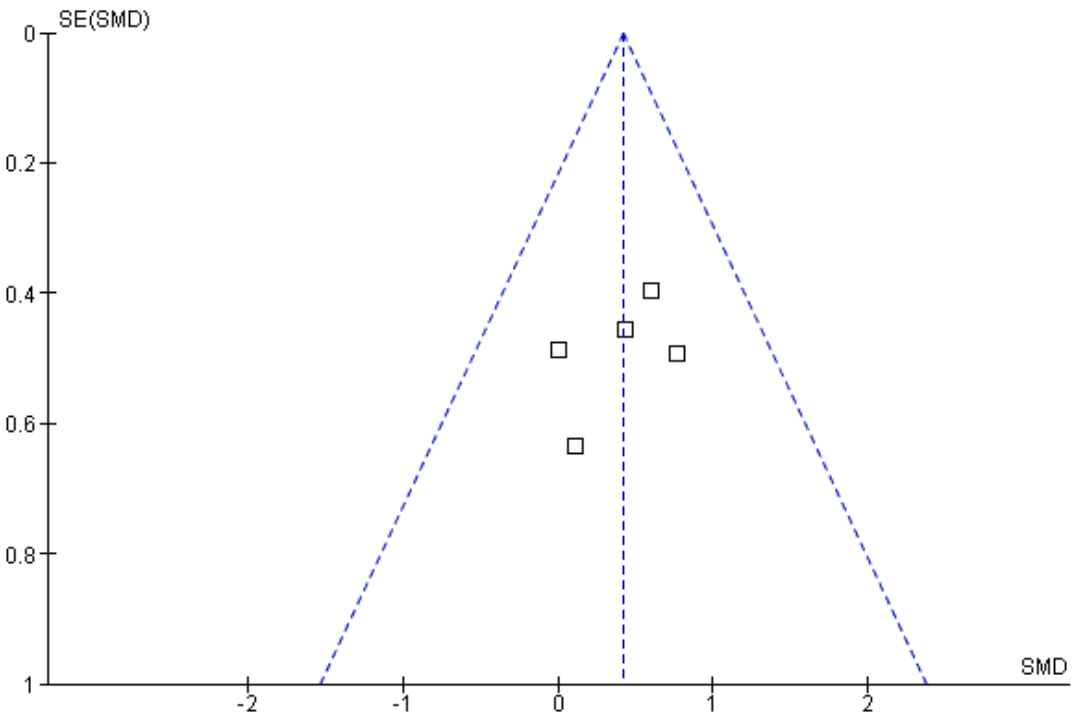


Figure 2. Funnel plot of comparison: 1 treadmill training versus no treadmill training, outcome: 1.2 stride length.



There was heterogeneity between the trials in terms of trial design (two, three, or four arms; parallel group or cross-over trial; duration of follow up; selection criteria for patients), characteristics of the therapy interventions (especially frequency and duration of intervention), and participant characteristics (Hoehn Yahr severity at baseline). There were also methodological differences in the mechanisms of the randomisation and allocation concealment methods used, blinding of primary outcomes, and the use of intention-to-treat analysis.

While the methodological quality of the included trials was generally moderate to very good (the PEDro score ranged from five to eight), trials investigating treadmill training are subject to potential methodological limitations. These limitations include inability to blind the therapist and patients, so-called contamination (provision of the intervention to the control group), and co-intervention (when the same therapist unintentionally provides additional care to either the treatment or comparison group). All these potential methodological limitations introduce the possibility of so-called performance bias.

One could argue that the clinical diversity of included trials with respect to duration and frequency of intervention could compromise a pooled analysis. However, the analyses of the primary outcome did not reveal statistically heterogeneity (Analysis 1.1).

Lastly, our aim was to provide a systematic overview about the current evidence and decided to pool the data of all available trials in a formal meta-analysis.

The exclusion of certain patient groups, such as patients with unstable cardiovascular conditions, patients with cognitive and communication deficits, and patients with a limited range of motion in joints at the start of the intervention may limit any general applicability of the findings.

However, using the results from the primary outcomes it is possible to explore the apparent effectiveness of treadmill training for improving gait in patients with PD. It might be important to consider that treadmill training might be just one way to apply many repetitions of gait cycles. However, one could argue that the gait training provided by a treadmill will lead to better results because people are forced to use higher gait speeds than over ground, as recently shown in one included study. In this study of Pohl and co-workers, patients with PD were able to walk up to three times faster on a treadmill than over ground
(Pohl 2003). Gait training on a treadmill could be seen as a 'forced-use-therapy, because patients are forced to use faster gait cycles and therefore higher velocities as they would self-select over ground.

One could argue, that the study of Pohl et al (Pohl 2003) is some-

what different from all other included trials, in terms of duration of training, that this study should be excluded from the pooled analysis. According to our predefined inclusion and exclusion criteria(Mehrholz 2009), and in an effort to find all randomised controlled trials on treadmill training, we decided to include this study. However, the influence of duration, frequency, and intensity of treadmill training on the gait parameters of patients with PD could be the subject of further evaluation

T readmill training has the potential to increase the number of repetitions of practice. However, it is important to mention that not all of the included studies had an active control group with matched number of repetitions of practice as in the experimental group. . Also the co-interventions were not perfectly comparable between t he included tr ials. In one study it is still unclear what was done i n the control group (Cakit 2007). One could argue that the se variation in t he control intervention s w ould lead to bias a nd may therefore may o verestimate the effect sizes , which seems clinically meaningfu l .

Agreements and disagreements with other studies or reviews

At the time of writing the protocol for this Cochrane review we were not aware of any systematic reviews about the topic. However, recently we have found a review by Herman et al which included randomised controlled and non-controlled studies on treadmill training in PD (Herman 2008). Although Herman et al gave a comprehensive overview of all the randomised studies we found, a pooled analysis for a possible treatment effect was not done. Additionally, descriptions of patient acceptance and side effects of treadmill training in PD were not conveniently provided. According to our protocol(Mehrholz 2009), and with the intention of reducing possible sources of bias, we only included randomised controlled trials. This Cochrane review is therefore to our knowledge the first systematic review with a pooled estimate of treatment effects and patient acceptance for treadmill training in patients with PD.

AUTHORS' CONCLUSIONS

Implications for practice

This systematic review provides evidence that the use of treadmill training in patients with PD may improve gait parameters such as gait speed and stride length. This apparent benefit for patients is, however, not supported by all secondary variables.

Implications for research

There is still a need for well-designed large-scale studies to evaluate benefits and harms of treadmill training in patients with PD. Further research should address specific questions about duration of effect, frequency and duration of treadmill training.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Cakit 2007

Methods	Randomised controlled trial Method of randomisation: not described
Participants	Country: Turkey Sample size: 54 participants (27 in treatment group, 27 in control group) Inclusion criteria: medically stable; able to walk a 10m distance; able to give informed consent Exclusion criteria: neurological conditions other than PD; scored greater than 3 on the Hoehn and Yahr Disability Scale; scoring less than 20 Mini-Mental State Examination; postural hypotension; cardiovascular or musculoskeletal disorder; visual or vestibular disturbance
Interventions	2 arms (1) training group: 8 weeks exercise programme including stretching, range of motion exercise and treadmill training with incrementally increasing belt speed (2) control group: 8 weeks not described further
Outcomes	Outcomes were recorded at baseline and after 8 weeks of therapy and included • walking distance on treadmill (metres) • tolerated maximum walking speed (km/h) • Falls efficacy scale • Dynamic gait index • Berg balance scale
Notes	

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	Not described

Canning 2008

Methods	Randomised controlled trial Method of randomisation: sealed opaque envelopes
Participants	Country: Australia Sample size: 20 participants (10 in treatment group, 10 in control group) Inclusion criteria: Hoehn and Yahr stages I to II; no freezing 'on' medication; subjective disturbances of gait (UPDRS gait subscore of 1; no history of falls; normal cognitive function
Interventions	2 arms (1) experimental group: 6 weeks home based treadmill walking, 30-40 minutes a day, 4 times a week, 7 of 24 sessions supervised by physiotherapist (2) control group: 6 weeks usual care including maintaining usual physical activity levels

Canning 2008 (*Continued*)

Outcomes	Outcomes were recorded at baseline, after 6 weeks of therapy and after 12 weeks after baseline and included • walking capacity measured with the 6-minute walk test (m/ 6 minutes) • Parkinson's disease quality of life questionnaire (PDQ-39) • fatigue (7-point Likert scale) • safety
Notes	

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Yes	20 sealed opaque envelopes were delivered to the administrative assistant responsible for allocation. 10 contained a piece of paper with the letter "E" written on it, and 10 contained a piece of paper with the letter "C" written on it. An administrative assistant shuffled the envelopes and then picked one at random, each time she was asked to allocate a recruited participant. The administrative assistant played no part in recruitment and allocated all participants

Fisher 2008

Methods	Randomised controlled trial Method of randomisation: patients self selected a card with eyes closed
Participants	Country: USA Sample size: 30 participants (10 in high-intensity exercise group, 10 in low-intensity group, and 10 in zero-intensity group) Inclusion criteria: diagnosis of PD within 3 years of study participation; 18 years of age or older; medical clearance from the primary care physician to participate in an exercise program; and ability to walk Exclusion criteria: a score of less than 24 on the MMSE; physician-determined major medical problems such as cardiac dysfunction; musculoskeletal impairments or excessive pain in any joint that could limit participation in an exercise program; and insufficient endurance and stamina to participate in exercise 3 times a week for a 1-hour session
Interventions	3 arms (1) high-intensity exercise group: body weight supported treadmill walking, up to 45 minutes a day, for 24 supervised sessions in 8 weeks (2) low-intensity group: general or traditional physiotherapy, for 24 sessions in 8 weeks (3) zero-intensity (no-exercise) group: six 1 hour education class over 8 weeks
Outcomes	Outcomes were recorded at baseline, after 8 weeks of therapy and included • walking velocity (m/s) • step length (m) • stride length (m)

Fisher 2008 (*Continued*)

	• step width (m) • cadence • double-limb support time (% of gait cycle) • hip, knee and ankle range of motion (degree) • UPDRS • Hoehn and Yahr staging
Notes	In our analysis the groups **2 and 3 were collapsed to one treatment group (pooled as one control group)**

Risk of bias

Item	**Authors' judgement**	**Description**
Allocation concealment?	Unclear	Patients were allocated to groups by self selecting a card with eyes closed

Kurtais 2008

Methods	Randomised controlled trial Method of randomisation: no further description in publication by the authors
Participants	Country: Turkey Sample size: 30 participants (15 in treadmill training group, and 15 in control group) Inclusion criteria: stable medication, not participated in a rehabilitation programme in the previous 3 months Exclusion criteria: severe cognitive impairment; severe musculoskeletal cardiopulmonary or other systemic disorders
Interventions	2 arms (1) treadmill training group: 6 weeks supervised treadmill walking, 40 minutes a session, 3 times a week (2) control group: not further described by the authors
Outcomes	Outcomes were recorded at baseline, after 7 weeks and included: • 20m walking time (s) • timed U-turn task (s) • turning around a chair • climbing up and down a flight of stairs (s) • arising from an armless chair (s) • standing on one foot (s) • VO_{2peak} ($mL*kg^{-1}*min^{-1}$) • exercise duration (min) • Metabolic Equivalent of Task (MET)
Notes	

Risk of bias

Kurtais 2008 (*Continued*)

Item	Authors' judgement	Description
Allocation concealment?	Yes	Random sequence created by a computer, generated list was used by an independent person to allocate participants

Miyai 2000

Methods	Randomised cross-over trial Method of randomisation: no further description
Participants	Country: Japan Sample size: 10 participants (5 in treadmill training group, and 5 in control group, before first cross over) Inclusion criteria: Hoehn and Yahr stage 2.5 to 3, MMSE greater than 27
Interventions	2 arms (1) treadmill training group: 4 weeks body weight supported treadmill training, 45 minutes a day, 3 days a week (2) control group: 4 weeks conventional physiotherapy, 45 minutes a day, 3 days a week
Outcomes	Outcomes were recorded at baseline, after 4 weeks and included • UPDRS • walking endurance **(m/ 6 minutes)** • gait speed (s/10m) • steps (steps/10m)
Notes	R aw data kindly provided by the authors were used for all analys es

Miyai 2002

Methods	Randomised controlled trial Method of randomisation: not described by the authors
Participants	Country: Japan Sample size: 24 participants (12 in treadmill training group, and 12 in control group) Inclusion criteria: diagnosis of PD, Hoehn and Yahr stage 2.5 to 3, MMSE greater than 27 Exclusion criteria: on-off phenomenon
Interventions	2 arms (1) treadmill training group: 4 weeks body weight supported treadmill training, 45 minutes a day, 3 days a week, with a total of 12 sessions (2) control group: 4 weeks conventional physiotherapy, 45 minutes a day, 3 days a week, with a total of 12 sessions
Outcomes	Outcomes were recorded at baseline, after 1, 2, 3, 4, 5 and 6 months and included • UPDRS • gait speed (s/10m) • steps (steps/10m)

Miyai 2002 (*Continued*)

Notes	R aw data kindly provided by the authors were used for all analys es Because the details of the studies of Miyai 2000 and Mixai 2002 looks similar at a first look, we contacted the lead Author Prof. Miyai . H e clearly s tated that these trials are dissimilar and i nvolve different patients

Pohl 2003

Methods	Randomised cross-over trial Method of randomisation: sealed opaque envelopes
Participants	Country: Germany Sample size: 17 participants Inclusion criteria: early PD, defined as Hoehn and Yahr stages I through III; subjective disturbances in gait; stable drug program, and in stable cardiovascular condition Exclusion criteria: paroxysmal motor fluctuations, such as on-off and wearing-off phenomena, class B, C, or D exercise risk by the ACSM criteria; cognitive deficits (defined as scores of less than 26 on the MMSE; moderate or severe depression (defined as scores of greater than 17 on the Beck Depression Inventory); and orthopedic and other gait-influencing diseases such as arthrosis or total hip joint replacement
Interventions	4 arms (1) treadmill training group with incremental speed increase: 1 session treadmill training, 30 minutes (2) treadmill training group without increases of gait speed: 1 session treadmill training, 30 minutes (3) physiotherapy group: 1 session physiotherapy including gait training, 30 minutes (4) control group: resting in a chair for 30 minutes
Outcomes	Outcomes were recorded at baseline, after 1 session of 30 minutes and included • gait speed (m/s) • steps (steps/10m)
Notes	R aw data of the authors used for all analyse s, data of treadmill groups were collapsed in to one group (n=8) and data of physiotherapy and control group were also collapsed into one group (n=9)

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Yes	Sealed opaque envelopes were used for allocation procedure. They contained one of four sequences: 'A', 'B', 'C' and 'D' An assistant blinded to group assignment and not involved in patient recruitment allocated all participants by opening one sealed envelope

Protas 2005

Methods	Randomised cross-over trial Method of randomisation: not stated by the authors
Participants	Country: USA Sample size: 18 participants (9 in the treadmill and 9 in the control group) Inclusion criteria: postural instability-gait difficulty predominant PD; experiences with freezing episodes, and/or a history of falls; stable regimen of antiparkinsonian medications; ability to stand and walk without assistance; stage 2 or 3 of the Hoehn and Yahr staging; and scores of moderate or higher on all scales of the Neurobehavioral Cognitive StatusExamination (Cognistat) Exclusion criteria: not used/not described
Interventions	2 arms (1) treadmill training group: treadmill training to improve gait and standing abilities for approximately 30 minutes including forward and backward walking and side stepping, 3 times a week for 8 weeks, 24 sessions of treadmill walking and stepping training (2) control group: no training
Outcomes	Outcomes were recorded at baseline and after 8 weeks and included • gait speed (m/s) • cadence (steps/min) • stride length (cm) • step test (steps/s)
Notes	

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	N ot described by the authors

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Bello 2008	N ot a randomised controlled trial
Gianfrancesco 2009	N ot a randomised controlled trial

Characteristics of ongoing studies *[ordered by study ID]*

Chulalongkorn 2008

Trial name or title	Treadmill and Music Cueing for Gait Training in Mild to Moderate Parkinson's Disease
Methods	Randomised controlled trial
Participants	30 male participants with idiopathic Parkinson's disease will be recruited Inclusion Criteria: 1. Male PD patients aged 60-80 years with Hoehn and Yahr stage 2-3 diagnosed by attending neurologist 2. Good cognitive function with Thai Mental State Examination >23 3. Stable medication without freezing 4. No prior exercise program within the last 2 months 5. No contraindication for exercise Exclusion Criteria: 1. Medication change during the study program 2. Inability to walk on treadmill (in treadmill groups) 3. Cannot complete 80% of the prescribed program
Interventions	A: Treadmill training with music cueing (3 days/wk, plus home music cueing 3 days/wk x 4 weeks) B: Treadmill training (3 days/wk, plus home walking 3 days/wk x 4 weeks) C: Home walking (6 days/wk x 4 weeks)
Outcomes	Primary Outcome Measures: • Walking performance evaluated with Timed Up and Go test, walking speed, step length, and cadence (within 1 week after training, and at 4 weeks follow up) Secondary Outcome Measures: • Balance (single leg stance time) and fall rate (within 1 week after training, and at 4 weeks follow up) • Aerobic endurance (6 minute walk test; within 1 week after training, and at 4 weeks follow up) • Mentation, mood, behavior, Motor and ADL subscale of UPDRS (within 1 week after training, and at 4 weeks follow up • Patient's satisfaction (within 1 week after training, and at 4 weeks follow up)
Starting date	September 2008
Contact information	• Dootchai Chaiwanichsiri, MD Tel: 662-256-4433 email: dootchai@gmail.com • Wasuwat Kitisomprayoonkul, MD Tel: 662-256-4433 email: wkitisom@yahoo.co.th Department of Rehabilitation Medicine, Faculty of Medicine, Chulalongkorn University Bangkok, Thailand, 10330
Notes	ClinicalTrials.gov Identifier: NCT00750945

DATA AND ANALYSES

Comparison 1. Treadmill training versus no treadmill training

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Gait speed	7	153	Std. Mean Difference (IV, Fixed, 95% CI)	0.50 [0.17, 0.84]
2 stride length	5	95	Std. Mean Difference (IV, Fixed, 95% CI)	0.42 [0.00, 0.84]
3 walking distance	2	41	Mean Difference (IV, Fixed, 95% CI)	357.57 [288.82, 426.31]
4 cadence	4	78	Mean Difference (IV, Fixed, 95% CI)	1.06 [-4.32, 6.44]
5 acceptability and safety of treadmill training	8	203	Risk Difference (M-H, Random, 95% CI)	-0.07 [-0.18, 0.05]

Comparison 2. Sensitivity analysis: Treadmill training versus no treadmill training

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Gait speed	7		Std. Mean Difference (IV, Fixed, 95% CI)	Subtotals only
1.1 All studies	7	153	Std. Mean Difference (IV, Fixed, 95% CI)	0.53 [0.20, 0.87]
1.2 all studies with concealed allocation	3	74	Std. Mean Difference (IV, Fixed, 95% CI)	0.41 [-0.06, 0.88]
1.3 All studies with ITT-Analysis	6	122	Std. Mean Difference (IV, Fixed, 95% CI)	0.43 [0.07, 0.80]
1.4 All studies with blinded assessors	3	75	Std. Mean Difference (IV, Fixed, 95% CI)	0.57 [0.09, 1.05]
1.5 Studies with best PEDro scoring (6 and above points)	5	102	Std. Mean Difference (IV, Fixed, 95% CI)	0.43 [0.03, 0.83]

Analysis 1.1. Comparison 1 Treadmill training versus no treadmill training, Outcome 1 Gait speed.

Review: Treadmill training for patients with Parkinson's disease

Comparison: 1 Treadmill training versus no treadmill training

Outcome: 1 Gait speed

Study or subgroup	Favours control N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Fixed,95% CI	Weight	Std. Mean Difference IV,Fixed,95% CI
Cakit 2007	21	2.61 (0.77)	10	1.86 (0.59)		17.3 %	1.02 [0.22, 1.82]
Fisher 2008	10	1.52 (0.19)	20	1.42 (0.17)		18.5 %	0.55 [-0.22, 1.32]
Kurtais 2008	13	1.13 (3.8)	14	1.16 (2.9)		19.4 %	-0.01 [-0.76, 0.75]
Miyai 2000	5	1.27 (0.3)	5	1.13 (0.44)		7.0 %	0.34 [-0.92, 1.59]
Miyai 2002	10	1.27 (0.36)	10	1.09 (0.37)		13.9 %	0.47 [-0.42, 1.36]
Pohl 2003	8	1.44 (0.18)	9	1.32 (0.18)		11.5 %	0.63 [-0.35, 1.62]
Protas 2005	9	1.45 (0.37)	9	1.27 (0.25)		12.4 %	0.54 [-0.40, 1.49]
Total (95% CI)	**76**		**77**			**100.0 %**	**0.50 [0.17, 0.84]**

Heterogeneity: Chi^2 = 3.50, df = 6 (P = 0.74); I^2 =0.0%

Test for overall effect: Z = 2.97 (P = 0.0029)

Test for subgroup differences: Not applicable

Analysis 1.2. Comparison 1 Treadmill training versus no treadmill training, Outcome 2 stride length.

Review: Treadmill training for patients with Parkinson's disease

Comparison: 1 Treadmill training versus no treadmill training

Outcome: 2 stride length

Study or subgroup	Experimental N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Fixed,95% CI	Weight	Std. Mean Difference IV,Fixed,95% CI
Fisher 2008	10	1.54 (0.16)	20	1.43 (0.19)		28.9 %	0.59 [-0.18, 1.37]
Miyai 2000	5	0.54 (0.15)	5	0.52 (0.19)		11.3 %	0.11 [-1.14, 1.35]
Miyai 2002	10	0.55 (0.17)	10	0.48 (0.14)		22.0 %	0.43 [-0.46, 1.32]
Pohl 2003	8	0.73 (0.11)	9	0.73 (0.09)		19.2 %	0.0 [-0.95, 0.95]
Protas 2005	9	0.72 (0.16)	9	0.61 (0.11)		18.6 %	0.76 [-0.20, 1.73]
Total (95% CI)	**42**		**53**			**100.0 %**	**0.42 [0.00, 0.84]**

Heterogeneity: Chi^2 = 1.67, df = 4 (P = 0.80); I^2 =0.0%

Test for overall effect: Z = 1.97 (P = 0.049)

Test for subgroup differences: Not applicable

Analysis 1.3. Comparison 1 Treadmill training versus no treadmill training, Outcome 3 walking distance.

Review: Treadmill training for patients with Parkinson's disease

Comparison: 1 Treadmill training versus no treadmill training

Outcome: 3 walking distance

Study or subgroup	Experimental N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Cakit 2007	10	726 (93)	21	362 (91)		97.7 %	364.00 [294.45, 433.55]
Miyai 2000	5	438 (349)	5	354 (382)		2.3 %	84.00 [-369.53, 537.53]
Total (95% CI)	**15**		**26**			**100.0 %**	**357.57 [288.82, 426.31]**

Heterogeneity: Chi² = 1.43, df = 1 (P = 0.23); I² =30%

Test for overall effect: Z = 10.19 (P < 0.00001)

Test for subgroup differences: Not applicable

Analysis 1.4. Comparison 1 Treadmill training versus no treadmill training, Outcome 4 cadence.

Review: Treadmill training for patients with Parkinson's disease

Comparison: 1 Treadmill training versus no treadmill training

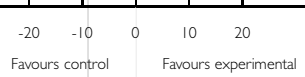
Outcome: 4 cadence

Study or subgroup	Experimental N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Fisher 2008	10	121 (9)	20	120 (9)		62.1 %	1.00 [-5.83, 7.83]
Miyai 2000	5	144 (15)	5	131 (17)		7.3 %	13.00 [-6.87, 32.87]
Miyai 2002	10	141 (21)	10	135 (25)		7.1 %	6.00 [-14.24, 26.24]
Protas 2005	9	120 (8)	9	124 (15)		23.5 %	-4.00 [-15.11, 7.11]
Total (95% CI)	**34**		**44**			**100.0 %**	**1.06 [-4.32, 6.44]**

Heterogeneity: Chi² = 2.41, df = 3 (P = 0.49); I² =0.0%

Test for overall effect: Z = 0.39 (P = 0.70)

Test for subgroup differences: Not applicable

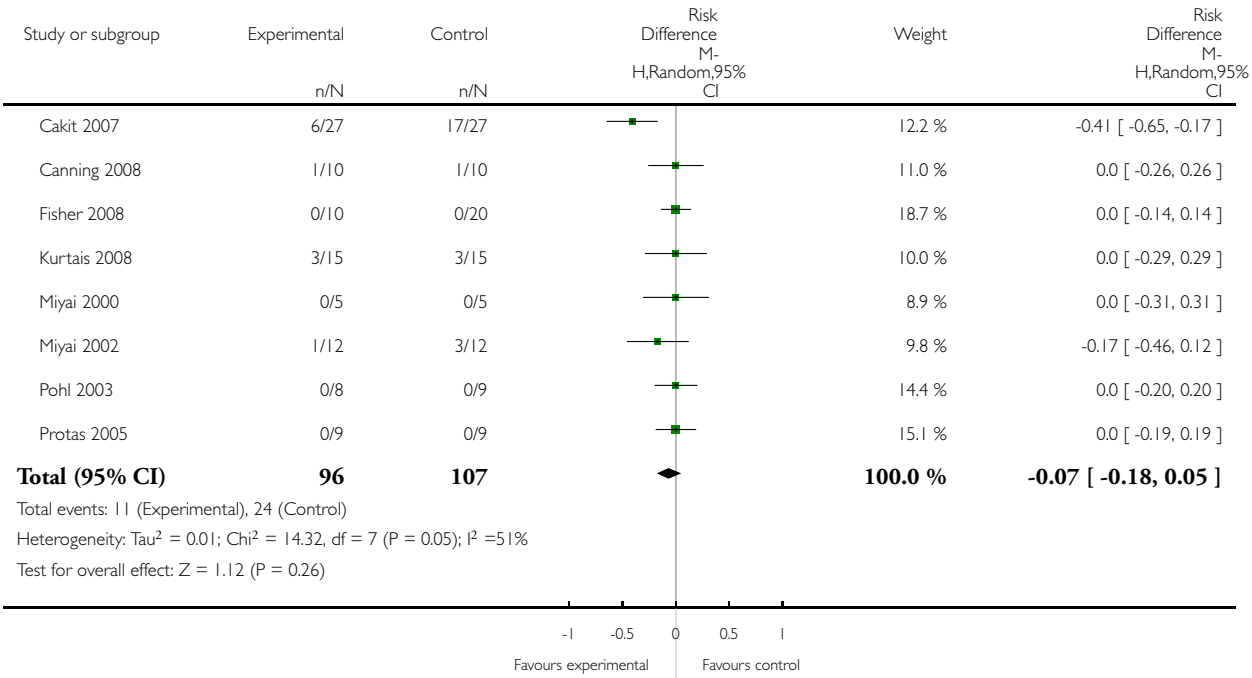


Analysis 1.5. Comparison 1 Treadmill training versus no treadmill training, Outcome 5 acceptability and safety of treadmill training.

Review: Treadmill training for patients with Parkinson's disease

Comparison: 1 Treadmill training versus no treadmill training

Outcome: 5 acceptability and safety of treadmill training



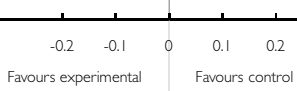
Analysis 2.1. Comparison 2 Sensitivity analysis: Treadmill training versus no treadmill training, Outcome 1 Gait speed.

Review: Treadmill training for patients with Parkinson's disease

Comparison: 2 Sensitivity analysis: Treadmill training versus no treadmill training

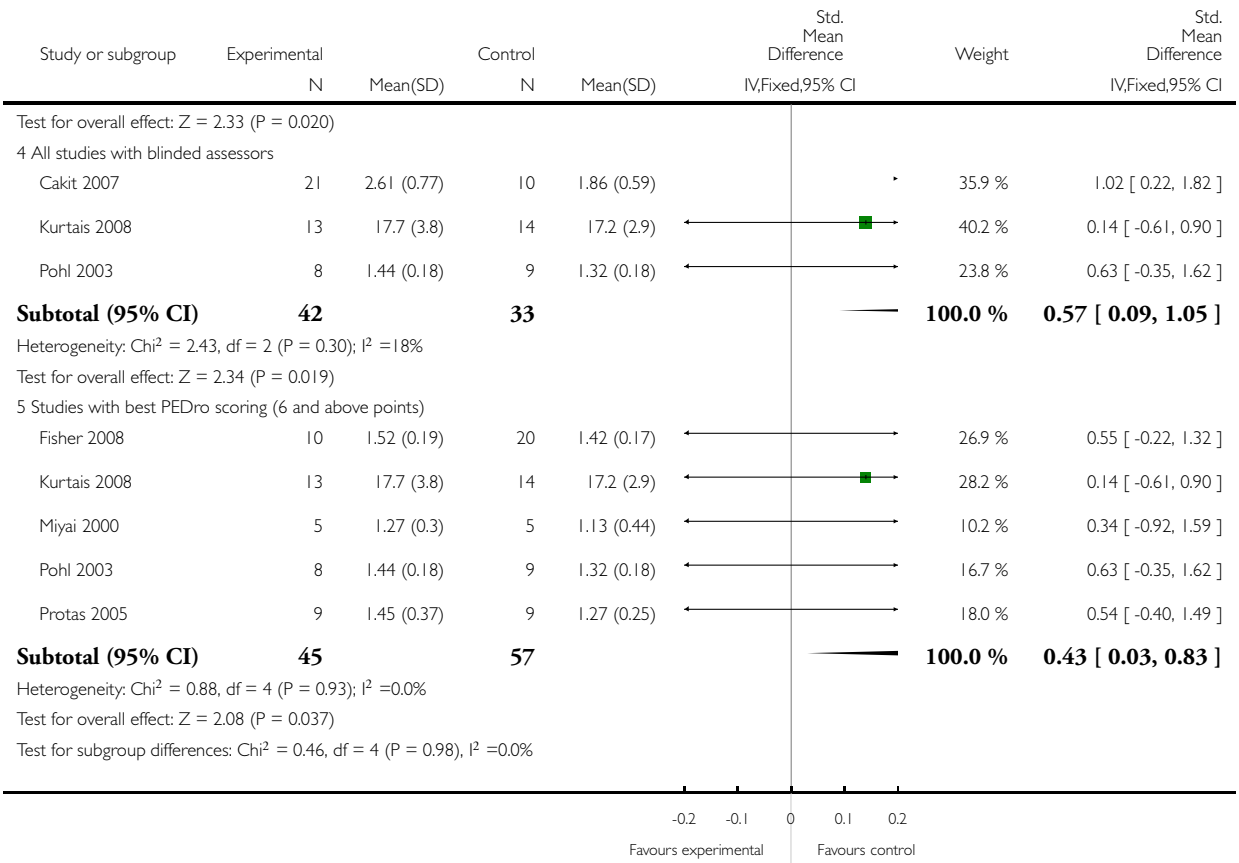
Outcome: 1 Gait speed

Study or subgroup	Experimental N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Fixed,95% CI	Weight	Std. Mean Difference IV,Fixed,95% CI
1 All studies							
Cakit 2007	21	2.61 (0.77)	10	1.86 (0.59)		17.3 %	1.02 [0.22, 1.82]
Fisher 2008	10	1.52 (0.19)	20	1.42 (0.17)		18.5 %	0.55 [-0.22, 1.32]
Kurtais 2008	13	17.7 (3.8)	14	17.2 (2.9)		19.4 %	0.14 [-0.61, 0.90]
Miyai 2000	5	1.27 (0.3)	5	1.13 (0.44)		7.0 %	0.34 [-0.92, 1.59]
Miyai 2002	10	1.27 (0.36)	10	1.09 (0.37)		13.9 %	0.47 [-0.42, 1.36]
Pohl 2003	8	1.44 (0.18)	9	1.32 (0.18)		11.5 %	0.63 [-0.35, 1.62]
Protas 2005	9	1.45 (0.37)	9	1.27 (0.25)		12.4 %	0.54 [-0.40, 1.49]
Subtotal (95% CI)	**76**		**77**			**100.0 %**	**0.53 [0.20, 0.87]**
Heterogeneity: Chi^2 = 2.57, df = 6 (P = 0.86); I^2 =0.0%							
Test for overall effect: Z = 3.15 (P = 0.0016)							
2 all studies with concealed allocation							
Fisher 2008	10	1.52 (0.19)	20	1.42 (0.17)		37.5 %	0.55 [-0.22, 1.32]
Kurtais 2008	13	17.7 (3.8)	14	17.2 (2.9)		39.3 %	0.14 [-0.61, 0.90]
Pohl 2003	8	1.44 (0.18)	9	1.32 (0.18)		23.2 %	0.63 [-0.35, 1.62]
Subtotal (95% CI)	**31**		**43**			**100.0 %**	**0.41 [-0.06, 0.88]**
Heterogeneity: Chi^2 = 0.80, df = 2 (P = 0.67); I^2 =0.0%							
Test for overall effect: Z = 1.70 (P = 0.090)							
3 All studies with ITT-Analysis							
Fisher 2008	10	1.52 (0.19)	20	1.42 (0.17)		22.4 %	0.55 [-0.22, 1.32]
Kurtais 2008	13	17.7 (3.8)	14	17.2 (2.9)		23.4 %	0.14 [-0.61, 0.90]
Miyai 2000	5	1.27 (0.3)	5	1.13 (0.44)		8.5 %	0.34 [-0.92, 1.59]
Miyai 2002	10	1.27 (0.36)	10	1.09 (0.37)		16.8 %	0.47 [-0.42, 1.36]
Pohl 2003	8	1.44 (0.18)	9	1.32 (0.18)		13.9 %	0.63 [-0.35, 1.62]
Protas 2005	9	1.45 (0.37)	9	1.27 (0.25)		15.0 %	0.54 [-0.40, 1.49]
Subtotal (95% CI)	**55**		**67**			**100.0 %**	**0.43 [0.07, 0.80]**
Heterogeneity: Chi^2 = 0.89, df = 5 (P = 0.97); I^2 =0.0%							



(*Continued* . . .)

(. . . *Continued*)



ADDITIONAL TABLES

Table 1. Methodological quality of included studies

Study ID	Cakit 2007	Canning 2008	Fisher 2008	Kurtais 2008	Miyai 2000	Miyai 2002	Pohl 2003	Protas 2005
random allocation	yes	yes	yes	yes	yes	yes	yes	yes
concealed allocation	unclear	yes	unclear	yes	unclear	unclear	yes	unclear
baseline comparability	yes	yes	yes	yes	yes	yes	yes	yes

Table 1. Methodological quality of included studies (*Continued*)

blind subjects	no	no	no	no	no	no	no	no
blind therapists	no	no	no	no	no	no	no	no
blind assessors	yes	yes	unclear	yes	no	no	yes	no
adequate follow-up*	no	yes	yes	no	yes	no	yes	yes
intention-to-treat analysis	no	yes	yes	no	yes	yes	yes	yes
between group comparison	yes	yes	yes	yes	yes	yes	yes	yes
point estimates and variability	yes	yes	yes	yes	yes	yes	yes	yes
total PEDro score (out of 10)	**5**	**7**	**6**	**6**	**6**	**5**	**8**	**6**
*defined as drop-out-rate <15%)								

Table 2. Patient characteristics in studies

Study ID	Age, mean (SD) EXP	Age, mean (SD) CON	Hoehn & Yahr stages	mean Duration of disease EXP	mean Duration of disease CON	female/ male EXP	female/ male CON	Duration of therapy	frequency of training
Cakit 2007	72 (6)*		1 to 2	6 years*		15/16*		8 weeks	not described
Canning 2008	61 (6)	63 (10)	1 to 2	6 years	6 years	5/5	4/6	6 weeks	4 times a week
Fisher 2008	64 (15)	62 (10)	1 to 2	1 year	1 year	4/6	13/7	8 weeks	3 times a week

Table 2. Patient characteristics in studies (*Continued*)

Kurtais 2008	64 (11)	66 (5)	mean 2.2 to 2.5	5 years	5 years	7/5	5/7	6 weeks	3 times a week
Miyai 2000	67 (2)*		2.5 to 3	4 years*		5/5*		4 weeks	3 times a week
Miyai 2002	70 (2)	70 (2)	2.5 to 3	4 years	4.5 years	6/5	4/5	4 weeks	3 times a week
Pohl 2003	61 (9)	61 (9)	1 to 2.5	3 years	3 years	3/5	2/7	1 session	N.a.
Protas 2005	71 (7)	74 (9)	2 to 3	7 years	8 years	not described		8 weeks	3 times a week
* information not available by group									

APPENDICES

Appendix 1. Example for MEDLINE search through OVID gateway

Example for Medline search through OVID Gateway:
1.Parkinson$.tw.
2.exp Parkinsonian Disorders/
3.1 or 2
4.Treadmil$.tw.
5.Exercise Test/
6.Exercise Therapy/
7.Physical Therapy Modalities/
8.Motor Activity/
9.Walking/
10.Periodicity/
11.or/4-10
12.randomized controlled trial.pt.
13.controlled clinical trial.pt.
14.randomized controlled trials/
15.random allocation/
16.double?blind method/
17.single?blind method/
18.clinical trial.pt.
19.exp clinical trials/
20.clin$ with trial$.tw.
21.random$.tw.

22.exp research design/
23.or/12-24
24.limit 23 to animal
25.limit 23 to human
26.24 and 25
27.24 not 26
28.23 not 27
29. 3 and 11 and 28
Example for EMBASE through OVID Gateway:
1.Parkinson Disease/
2.Parkinsonism/
3.Parkinson$.tw.
4.1 or 2 or 3
5.Treadmill.tw.
6.Exercise adj5 test.tw.
7.((exercise or physical) adj5 (therapy)).tw.
8.5 or 6 or 7
9.clinical trial/
10.multicenter study/
11.phase 2 clinical trial/
12.phase 3 clinical trial/
13.phase 4 clinical trial/
14.randomized controlled trial/
15.controlled study/
16.meta analysis/
17.double blind procedure/
18.single blind procedure/
19.randomization/
20.major clinical study/
21.placebo/
22.drug comparison/
23.clinical study/
24.(clin$ adj25 trial$).tw.
25.((singl$ or doubl$ or tripl$ or trebl$) adj25 (blind$ or mask$)).tw.
26.random$.tw.
27.control$.tw.
28.or/9-27
29.human/
30.nonhuman/
31.9 and 30
32.30 not 31
33.28 not 32
34.4 and 8 and 33

Appendix 2. List of conference proceedings searched

- World Congress of NeuroRehabilitation;
- World Congress of Physical Medicine and Rehabilitation;
- World Congress of Physical Therapy ;
- World Congress of Neurology;
- World Congress on Parkinson's Disease and Related Disorders;
- Deutsche Gesellschaft für Neurotraumatologie und Klinische Neurorehabilitation;
- Deutsche Gesellschaft für Neurologie;
- Deutsche Gesellschaft für Neurorehabilitation.

HISTORY

Protocol first published: Issue 2, 2009

Review first published: Issue 1, 2010

CONTRIBUTIONS OF AUTHORS

Jan Mehrholz (JM) contributed to the conception and design of the protocol and approved the final manuscript. He searched electronic databases and conference proceedings, screened titles and abstracts of references identified by the search, selected and assessed trials, extracted trial and outcome data, guided the analysis and the interpretation of the data, and contributed to and approved the final manuscript of the review.

Joachim Kugler (JK) and Alexancer Storch (AS)screened titles and abstracts of references identified by the search, located, selected and assessed trials, extracted trial and outcome data, assessed the methodological quality of selected trials, and contributed to and approved the final manuscript of the review.

Sabine Twork (ST) screened titles and abstracts of references identified by the search, located, selected and assessed trials, extracted trial and outcome data, assessed the methodological quality of selected trials, and contributed to and approved the final manuscript of the review.

Robert Friis (RF) drafted the protocol, and assessed the methodological quality of selected trials, and approved the final manuscript of the review.

Marcus Pohl (MP) contributed to the conception and design of the review, drafted the protocol, and assessed the methodological quality of selected trials. Together with JM, he contacted trialists about unpublished data and also entered the data, carried out statistical analysis, helped with the interpretation of the data, drafted the review and approved the final manuscript of the review.

DECLARATIONS OF INTEREST

MP and JM were co-authors of one included trial (Pohl 2003). They did not participate in the quality assessment and data extraction of this study.

SOURCES OF SUPPORT

Internal sources

- Klinik Bavaria Kreischa, Germany.
- Faculty of Medicine, Technical University Dresden, Germany.
- SRH Fachhochschule Gera, Germany.

External sources

- California State University Long Beach, CA, USA.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

There are some differences between the protocol and the review briefly described below. We planned to do a subgroup analysis comparing subgroups of similar interventions in terms of duration and frequency. However, after introducing a sensitivity analysis with incorporating four subgroups, we decided to do not any further subgroup analysis due to the small number of studies and to avoid multiplicity. For primary and secondary outcomes, we did not do, as intended, separate analyses for data immediately after the end of the study and at follow up after the study end to look for any sustained effects. This was due to the small number of studies .

INDEX TERMS

Medical Subject Headings (MeSH)

Exercise Therapy [instrumentation; *methods]; Gait Disorders, Neurologic [etiology; *rehabilitation]; Parkinson Disease [complications; *rehabilitation]; Randomized Controlled Trials as Topic

MeSH check words

Aged; Humans; Middle Aged