

ABSTRACT

BACKGROUND: A systematic review and meta-analysis was conducted to examine the effect of exercise training on daily physical activity (PA) in people with chronic obstructive pulmonary disease (COPD).

METHODS: MEDLINE, PubMed, EMBASE, CINAHL, Physiotherapy Evidence Database (PEDro) and Cochrane Central Register of Controlled Trials were searched from their inception to week 27 of 2010, using the keywords 'COPD', 'exercise', 'therapy' and 'physical activity'. All studies except case-reports were eligible for inclusion provided they investigated the effects of ≥ 4 weeks of supervised exercise training on PA in patients with COPD. Study quality for the randomised trials (RT) and single-group interventional studies was rated using the PEDro scale and Downs and Black Tool, respectively.

RESULTS: No randomised controlled trials met our study criteria. The two RTs had a mean PEDro score of 5. The five single-group studies had a mean Downs and Black score of 19 ± 3 . When combined, a small effect on PA outcomes was demonstrated (overall mean effect = 0.12; $p = 0.01$).

CONCLUSIONS: There are no randomised controlled trials that examine the effect of ≥ 4 weeks of supervised exercise training on PA. Taken together, the RTs and single-group studies demonstrate that exercise training may confer a significant but small increase in PA.

Keywords: COPD, Exercise training, Physical activity, Systematic review, Meta-analysis

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is characterised by progressive airflow obstruction caused by a loss of elastic recoil and airway narrowing, that is not fully reversible in response to bronchodilators.¹ The prevalence of COPD in people aged ≥ 40 years, measured in 9,425 adults from 12 countries, was estimated to be 10%.² Worldwide, COPD is expected to be the third leading cause of death by 2030.³ It is also a leading cause of hospitalisation, especially in older populations.⁴

Many individuals with COPD are inactive in daily life, most likely as a strategy to minimise dyspnea.⁵ Physical activity (PA) is defined as any bodily movements produced by skeletal muscles that results in energy expenditure beyond resting state.⁶ Lower levels of PA in COPD have been associated with impaired health-related quality of life, increased healthcare utilisation and reduced survival.⁷⁻¹⁰ A recent study that collected data using a portable metabolic monitor demonstrated that the time spent in moderate intensity PA diminishes with worsening disease.¹¹ As the level of habitual PA appears to play an important role in the mortality and healthcare burden associated with COPD,^{7, 12} optimising PA is an important goal in the management of people with this condition.⁷ Several studies have investigated the effect exercise training, undertaken in the context of pulmonary rehabilitation, on daily PA.¹³⁻²⁰ However, there is considerable variability in study findings and therefore the effect of exercise training on PA is unclear.

The aim of this review was to systematically search the literature and undertake a meta-analysis of data from studies that have evaluated the effect of exercise training on PA in people with COPD.

METHODS

Data Sources

Study identification began with electronic searching of computerised databases, namely MEDLINE, PubMed, EMBASE, CINAHL, Physiotherapy Evidence Database (PEDro) and Cochrane Central Register of Controlled Trials from inception to week 27 in 2010 (Box 1). The subject headings used in the search were ‘COPD/chronic obstructive pulmonary disease’, ‘therapy’ and ‘exercise’ with key terms comprising of ‘accelerometer’, ‘pedometer’, ‘physical activity’ and, ‘energy’. Secondary searches included hand searching reference lists of all identified studies and PubMed ‘related articles’ function. Clinical trials registries were also reviewed to identify any randomised controlled trials (RCTs) that may have been ‘in press’.

Study Selection

Studies were eligible for inclusion criteria if they: (i) were written in English, (ii) recruited people with COPD, (iii) investigated the effect of supervised exercise training of at least 4 weeks in duration on PA, (iv) measured PA using activity monitors and, (v) reported PA in absolute values such as steps or activity counts. Studies that utilised any design other than case reports were eligible for inclusion. Where necessary, authors were contacted to obtain PA data in absolute values. If the authors did not respond, the study was excluded from the meta-analysis.

Quality Assessment

Two members of the review team (CN and JM) independently extracted data using a standardised assessment form. Quality assessment for the RCTs and randomised trials (RTs) was rated using the 10-point PEDro scale.²¹ Quality assessment for the single-group studies

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was rated using a modified Downs and Black tool.²² This tool consists of 27 questions, that relate to study description, external validity, internal validity and statistical power.²² To minimise ambiguities, the question pertaining to statistical power was assigned one point if prospective sample size calculations were provided (and 0 points if these details were absent), which resulted in a maximum score of 28. This modification to the Downs and Black tool has been used previously.²³

Data Extraction and Analysis

Consistency between reviewers for both quality assessment methods was calculated using Kappa statistics. Due to the heterogeneity in PA outcome measures, the random-effects approach was used in the meta-analysis. Effect sizes were calculated by dividing the differences in PA, (before and after the intervention) by the pooled standard deviation. Regarding interpretation, ≤ 0.2 was considered small, 0.5 was considered moderate and ≥ 0.8 was considered large.²⁴ The I^2 test was used to quantify statistical heterogeneity of the studies.²⁵ A value of $\leq 25\%$ reflects low heterogeneity, 50% is moderate and 75% represents high heterogeneity. A p value of < 0.1 was used to indicate that the heterogeneity was not due to chance alone and it would be inappropriate to combine the results in a summary. A funnel plot was assessed visually to detect publication bias where a symmetric inverted funnel shape indicates that bias is unlikely. Comprehensive Meta Analysis version 2.2.050 (BiostatTM, New Jersey, USA) was used for meta-analysis.

RESULTS

The search strategy yielded 1,840 records of which 128 (7%) were duplicates and thus excluded (Figure 1). Of the remaining 1,712 records, 1,686 (98%) were excluded based on title or abstract and 19 (1%) were excluded after reviewing the full text. There were no RCTs

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that met our study criteria. A total of seven studies met the criteria for inclusion; two (29%) were RTs in which two groups of participants received different interventions, both of which were designed to optimise PA and five (71%) were single-group interventional studies in which all participants received the same intervention. Authors of two of the studies were contacted for PA data in absolute values.

Quality Assessment

Table 1a and 1b presents the quality assessment score for each of the RTs and single-group studies, respectively. Reviewers agreed on 100% of all PEDro items (Kappa statistic = 1). The mean (SD) PEDro score for the RTs was 5 ± 0 points. Reviewers agreed on 96% of all Downs and Black items with a Kappa statistic of 0.92. The mean Downs and Black score was 19 ± 3 points.

Subject Characteristics

Table 1a and 1b also summarise the subject characteristics of the RTs and single-group interventional studies, respectively. The sample sizes ranged from 8¹³ to 116.¹⁸ Considering all studies together, the participants were predominantly male ($n = 419$, 72%). Based on the forced expiratory volume in one second (FEV₁) expressed as a percentage of the predicted normal value, participants in most studies had severe airflow obstruction.²⁶

Interventions and Methods for Measuring Physical Activity

The duration of supervised exercise training ranged between 6 weeks and 6 months.^{13-16, 18, 20,}

²⁷ The monitors used to measure PA comprised the NL-2000 pedometer,¹⁴ the Yamax Digi-Walker SW-200 pedometer,¹³ the DynaPort Activity Monitor,¹⁵ the Z80-32K Activity Monitor,¹⁶ the Actiwatch,²⁰ the TriTrac-R3D[®] accelerometer²⁷ and the RT-3 accelerometer.¹⁸

Effects on Physical Activity

Table 2a and 2b summarise the findings of the RTs and single-group studies, respectively. In the RTs, both groups received exercise training. One study compared an individualised targeted exercise program (ITEP) based on daily activities with a general exercise program (GEP),¹⁶ and the other investigated the effect of using a pedometer to provide feedback regarding walking targets, over and above a program of supervised exercise training.¹³ As both groups in these two studies examined the effect of exercise training on PA, we entered the data from each arm into the meta-analyses. The intervention for all five single group studies comprised supervised exercise training at least twice a week. Asymmetry was observed in the funnel plot for PA in the RTs and single-group interventional studies (Figure 2), suggesting that we could not exclude publication bias. Taken together, PA data entered into the meta-analysis from the RTs and the single-group studies was homogeneous ($I^2 = 0\%$, $p = 0.60$). The effect size for PA though significant was small (0.12; $p = 0.01$) (Figure 3).

DISCUSSION

This is the first systematic review and meta-analysis to evaluate the effect of exercise training on measures of PA. The important findings of our review are that; (i) there are no published RCTs that examine the effects of at least 4 weeks of supervised exercise training on PA and, (ii) data from the RTs and single-group interventional studies indicate that, in people with COPD, supervised exercise training confers a significant, but small effect on PA.

Regarding the RTs included in this review, the two groups in both RTs demonstrated a similar magnitude of change in PA following the intervention period. This is perhaps not surprising as both groups in these studies received an intervention that aimed to increase PA

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and it was the effectiveness of an additional strategy (such as feedback using pedometer data or individualisation of exercises) that was being examined. Thus, any difference between the two groups was likely to be small. When the results of the five single-group studies included in this review were considered individually, two (40%) reported a significant increase in PA on completion of the intervention period.^{15, 20} Relative to baseline measures, one reported an improvement of 20% ($p = 0.008$)¹⁵ while the other reported a difference of 36 ± 49 ($\times 10^3$ counts/hour) or approximately 40% ($p = 0.002$).²⁰ When these results of the RTs and single-group studies were combined the effect size for PA was small, but significant (0.14; $p = 0.04$). Exclusion of the data from the RTs from the meta-analysis produced a trivial change in the magnitude of the overall effect size (i.e. from 0.14 to 0.12). To appreciate this change in real terms, using the study by Pitta et al¹⁵ as a reference, an overall pooled effect size of 0.12 or 0.14 is equivalent to an increase of approximately 4.6 or 5.4 minutes of walking per day, following the intervention. In addition to this small effect, the wide 95% confidence intervals for data pertaining to five of the seven studies in Figure 3 indicates that there was considerable variability in PA between individuals. Our data revealing a modest effect size together with substantial variability suggests that future RCTs that aim to demonstrate an effect of supervised exercise training on PA will require very large sample sizes.

We considered that the capacity of individual studies to demonstrate a significant increase in PA may be influenced not only by the nature of the intervention, but by other factors such as; (i) the method used to measure PA, (ii) the frequency of supervised exercise training and, (iii) the clinical stability of participants over the duration of the study period. Regarding the outcome measures, earlier work has demonstrated that in people with COPD, questionnaires do not yield an accurate measure of PA⁵ and pedometers lack the sensitivity to detect steps at the slow walking cadence characteristic of this clinical population.^{28, 29} In contrast,

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accelerometers yield accurate measures of PA in people with COPD and have emerged as a popular choice.⁹ Given their superior accuracy, we considered the possibility that those studies that utilised an accelerometer to measure PA may have been more likely to demonstrate improvements in PA. Examination of Figure 3 revealed, that of the five studies which measured PA using an accelerometer, three (60%) demonstrated a significant effect.^{15, 16, 20} Differences in the nature and potentially the effectiveness of the interventions used in each of the studies preclude us from drawing conclusions regarding the superiority of an accelerometer as an outcome measure. However, future studies may have a greater likelihood of demonstrating change if reliable, valid and responsive accelerometers are used in preference to pedometers or self-report methods.

Regarding the frequency of supervised exercise training, both studies that utilised exercise training three times a week, for at least eight weeks demonstrated a significant improvement in PA.^{15, 20} In contrast, of the five studies that offered exercise training only twice a week, only one demonstrated a significant improvement in PA.¹⁶ This suggests that more frequent training may be necessary to show a significant increase in PA. Similarly, the data from Pitta's study¹⁵ suggests that the duration over which exercise training is offered is important. Specifically, the participants in his study demonstrated a small non-significant increase in PA after three months of supervised exercise training, with an additional three months of training required to confer a significant increase. These results are in line with a recent review which concluded that pulmonary rehabilitation programs that exceed 12 weeks in duration were more likely to promote long-term maintenance of training effects.³⁰ Earlier work suggests that at least three months is required for most individuals to change a habit³¹ and therefore, studies that investigate interventions offered over an extended period that comprises frequent supervised exercise training are perhaps the most likely to be successful.

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Regarding the clinical stability of study participants, only Steele et al¹⁸ separated those who experienced an acute exacerbation during the follow-up period from those who did not. Of all the studies included in this meta-analysis, the participants who experienced an acute exacerbation in the study by Steele et al¹⁸ were the only subgroup to demonstrate an effect suggestive of deterioration in PA. This is consistent with earlier work that reported a dramatic decline in PA among individuals with COPD following an exacerbation.³² Notably, this deterioration in PA has been shown to persist for several weeks.³²

LIMITATIONS

The main limitation of this systematic review relates to the lack of RCTs. Further, although all studies included in this review investigated the effect of supervised exercise training on PA, there was disparity in the nature of the individual exercise training programs. Publication bias might have influenced the effect size. Both the RTs and single group interventional studies were of fair methodological quality. These considerations limit the extent to which we draw conclusions about the effect of supervised exercise training in PA in people with COPD.

CONCLUSION

Current data suggests that any effect of exercise training on PA in people with COPD is small. Randomised controlled trials are needed in this area. Future studies may increase their likelihood of demonstrating a positive effect by; (i) measuring PA with an accelerometer, (ii) offering supervised exercise training at least three times a week over a minimum of 8 weeks and, (iii) extending the intervention period for those who experience an acute exacerbation of

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their disease. Large sample sizes are likely to be necessary to demonstrate a statistically significant effect.

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All authors have read and approved of the manuscript.

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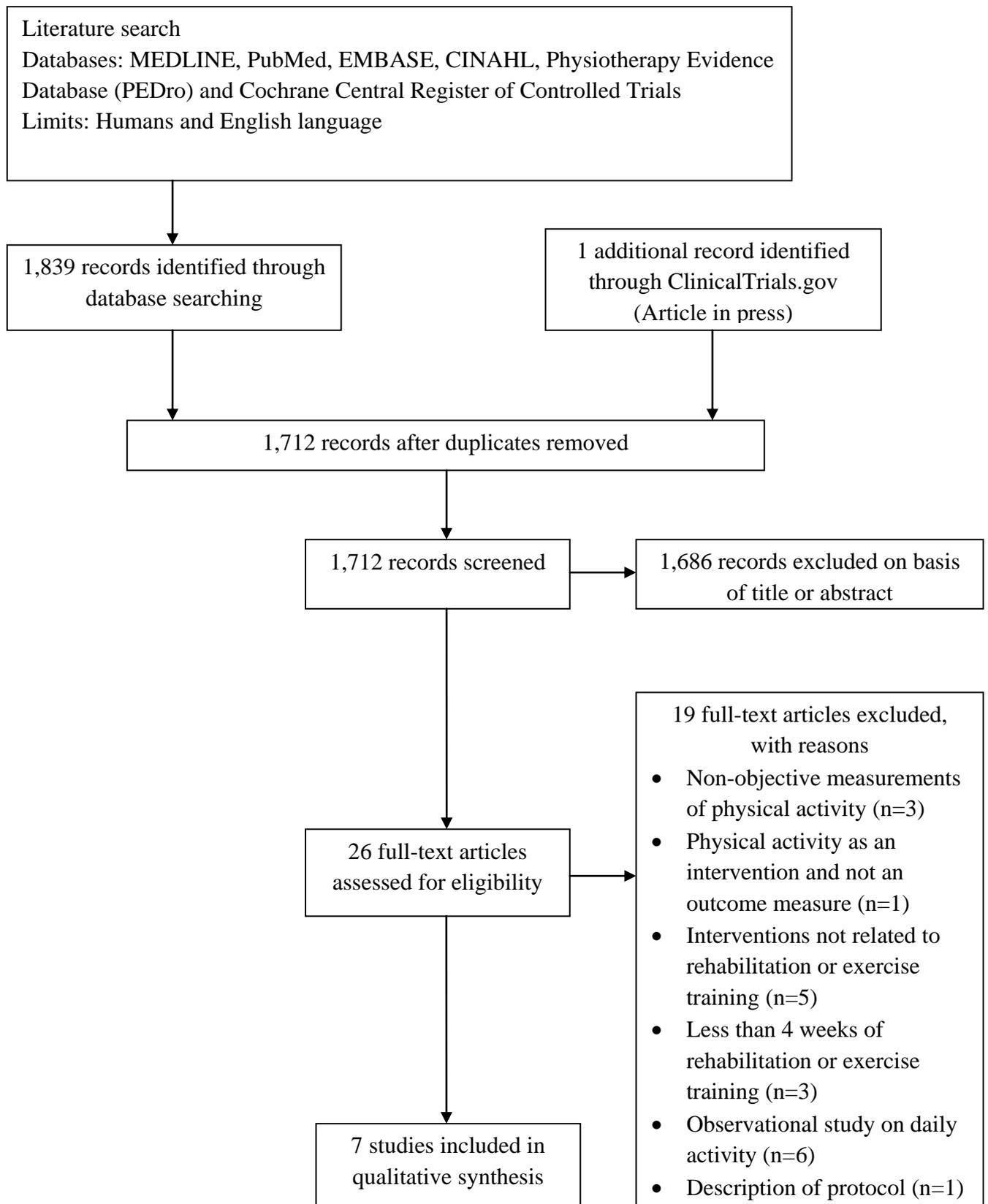
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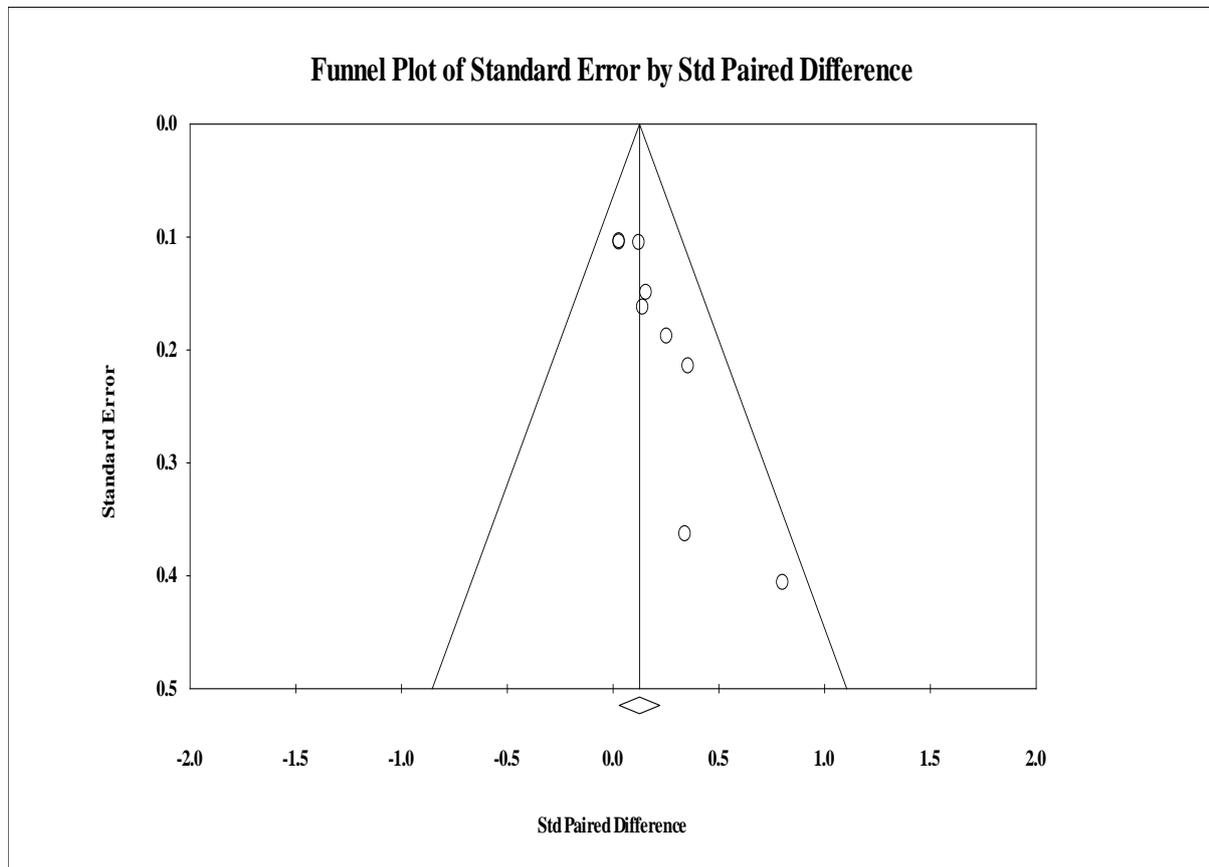
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Figure 1: Flow of information through the different phases of the systematic review.



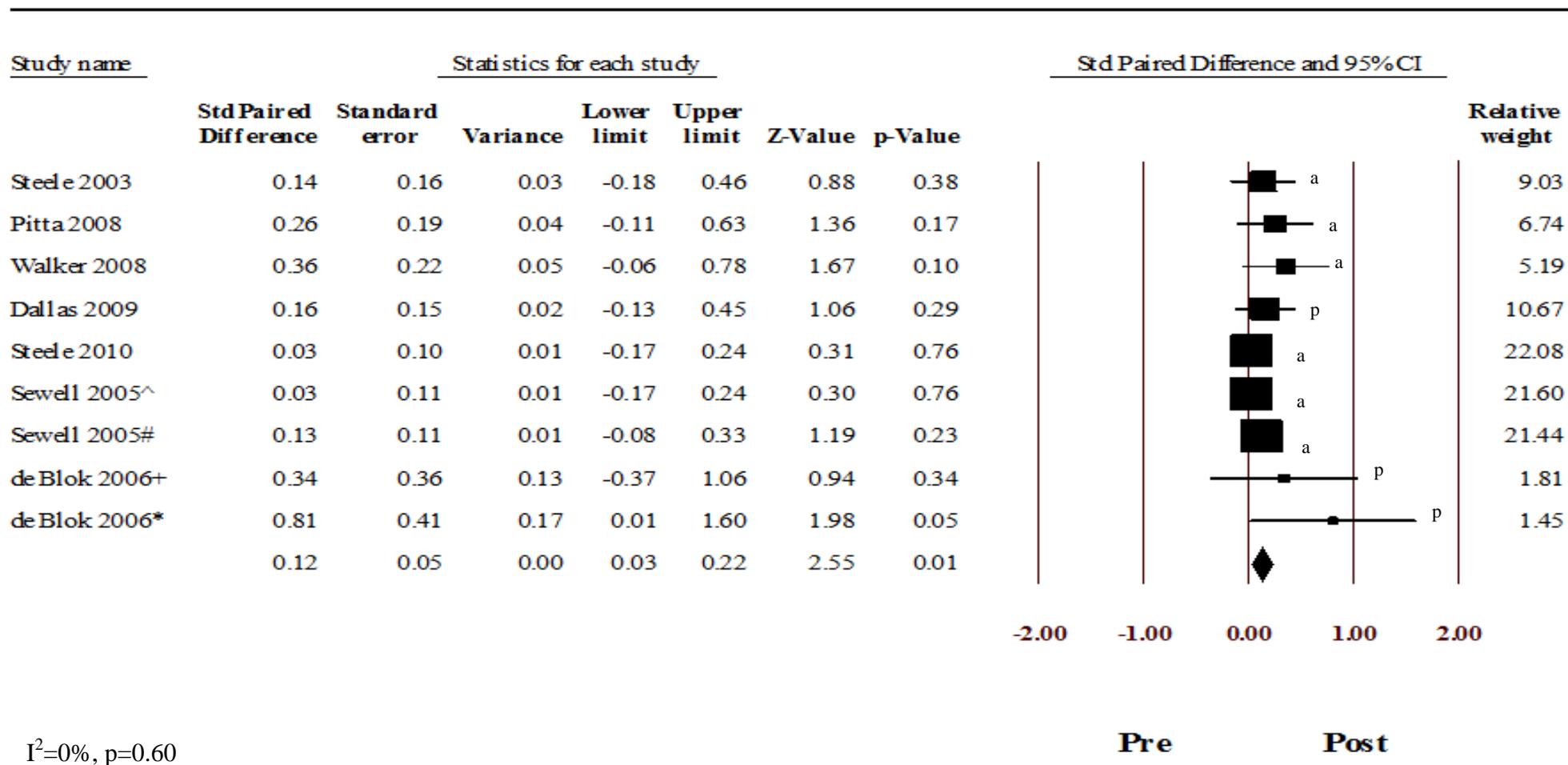
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Figure 2: Funnel plot of physical activity as an outcome measures in the randomised trials and single-group interventional studies. The tendency for data points to fall predominantly on the right of the 0 suggests a publication bias may be present.



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Figure 3: Forest plot for physical activity measured in the two randomised trials and the five single-group interventional studies



Physical Activity

p, pedometer; a, accelerometer

The two interventions in both randomised trials have been entered separately into this plot where ^ represents the group that completed a general exercise program, # represents the group that completed an individualised targeted exercise program, + represents the group that completed pulmonary rehabilitation and * represents the group that completed pulmonary rehabilitation with counseling and feedback based on pedometer data

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Table 1a: Characteristics of study participants of randomised trials

Study	PEDro	Sample size (n)	Gender (M/F)	Age (years)	BMI (kg·m ²)	FEV ₁ (L) (%pred)	Protocol
Sewell 2005 ¹⁵	5	90	51/39	67.3±8.4	N/A	0.97±0.45	Individually targeted ex program (ITEP) performed twice a week. One day comprised aerobic exercise and the other day comprised exercises based on daily functional activities identified during the Canadian Occupational Performance Measure + 2 hours of education per week
		90	60/30	69.3±8.7	N/A	0.93±0.39	General ex program (GEP) performed twice a week. One day comprised aerobic exercise and the other day comprised standard exercises including step-ups, sit-to-stand and stationary cycling, wall push-ups, small and large arm circling and shoulder shrugs trunk flexion, trunk rotation and pelvic tilt + 2 hours of education per week
de Blok 2006 ¹²	5	10	5/5	65.7±10.4	29.3±8.4	1.44±0.80 (52±22%)	Pulmonary rehabilitation exercise program + dietary + psychosocial-education modules + lifestyle PA counseling based on pedometer data
		11	4/7	62.5±12.3	28.2±6.6	1.24±0.62 (43±13%)	Pulmonary rehabilitation exercise program + dietary + psychosocial-education modules

Data are mean±SD.

M: male; F: female; BMI: body mass index; FEV₁: forced expiratory volume in one second.

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Table 1b: Characteristics of study participants of single-group interventional studies

Study	Downs & Black	Sample size (n)	Gender (M/F)	Age (years)	BMI (kg·m ²)	FEV ₁ (L) (%pred)	Protocol
Steele 2003 ²⁵	14	38	37/1	63.7±7.8	-	1.2±0.5 (39±17%)	Twice weekly exercise classes. On completion of the first 2 to 3 weeks of the program a home exercise program was given and encouraged at least 3 days a week
Pitta 2008 ¹⁴	21	29	23/6	67±8	25±6	- (46±16%)	Multi-disciplinary rehabilitation including education, support and/or counseling, circuit exercise training (cycling, walking, strength training for quadriceps, pectoralis and triceps, arm cranking and stair climbing) Months 1 to 3, exercise was performed 3 times a week; months 4 to 6, exercise was performed 2 times a week
Walker 2008 ¹⁹	17	23	12/11	66±9	24.4±4.4	0.93±0.32 (36±12%)	2 supervised + 1 unsupervised exercise sessions per week comprising whole body endurance ex + peripheral muscle strengthening
Dallas 2009 ¹³	21	45	21/24	69±8	27±5	(45±18%)	Exercise classes 2 to 3 times per week. Multi-modality aerobic and strength training of lower and upper extremities + education + psychosocial support
Steele 2010 ¹⁷	20	20* 116 [†]	130/6	67.0±9.0 66.8±10.4	28.6±6.3 30.8±7.5	- (36±15%) - (40±16%)	Twice a week rehab-progressive resistance exercises with hand weights, elastic resistance tubing, and/or weight machines. Cardiovascular/ endurance training included use of treadmills, stationary cycles, NuStep, and upper extremity ergometers.

Data are mean±SD.

* COPD participants who had an exacerbation during the study; †COPD participants who had no exacerbation during the study.

M: male; F: female; BMI: body mass index; FEV₁: forced expiratory volume in one second.

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Table 2a: Summary of findings for randomised trials

Study	Duration of intervention	Days of activity monitoring		PA pre	PA post	Within group findings
Sewell 2005 ¹⁵	7 weeks	2	ITEP	4537±8465 activity counts	5819±5665 activity counts	Improvement of 40.6%, p=0.02
		2	GEP	3587±4357 activity counts	3835±6453 activity counts	Improvement of 29.2%, p=0.03
de Blok 2006 ^{12γ}	9 weeks	4	Added counseling + pedometer	2059±941 steps/day	3594±1657 steps/day	Improvement of 1535 steps/day (75%)
				2312±916 steps/day	2985±1730 steps/day	Improvement of 673 steps/day (29%)
						p=0.24 between groups

Data are mean±SD.

^γData from 8 participants were assessed over 4 days without rehabilitation including 1 weekend day. The 4 days data was used in the meta-analysis as it had a greater effect size than that of the 6 days without rehabilitation (including 2 weekend days) data and 7 days data was excluded as it included rehabilitation.

Activity counts rounded to the nearest whole number

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Table 2b: Summary of findings for single-group interventional studies

Study	Duration of intervention	Days of activity monitoring		PA pre	PA post	Within group findings
Steele 2003 ²⁵	8 weeks	5		82±34 VMU	90±38 VMU	p=0.06
Pitta 2008 ¹⁴	3 months	5		55±26 min/day	59±27 min/day	After 3 months; 7% improvement in walking time, p=0.21
	6 months				65±29 min/day	After 6 months; 20% improvement in walking time, p=0.008
Walker 2008 ¹⁹	8 weeks	3		82±53 (x10 ³ counts/hr)	117±84 (x10 ³ counts/hr)	Improvement of 36±49 (x10 ³ counts/hr), p=0.002
Dallas 2009 ¹³	6-12 weeks	7		207±139 counts/hr	240±153 counts/hr	Improvement of 33±149 counts/hr, p=0.14
Steele 2010 ¹⁷	8 weeks	6	Exacerbation (n=20)	165±143 VMU	143±59 VMU	No within group data. p=0.56 between those that had an exacerbation and those that did not
			Non exacerbation (n=92)	163±89 VMU	167±81 VMU	

Data are mean±SD.

VMU: vector magnitude units; mins: minutes; hr: hour

VMU and activity scores rounded to the nearest whole number