

Exercise training alone or with the addition of activity counseling improves physical activity levels in COPD: a systematic review and meta-analysis of randomized controlled trials

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Background: Physical inactivity is associated with poor outcomes in COPD, and as a result, interventions to improve physical activity (PA) are a current research focus. However, many trials have been small and inconclusive.

Objective: The aim of this systematic review and meta-analysis was to study the effects of randomized controlled trials (RCTs) targeting PA in COPD.

Methods: Databases (Physiotherapy Evidence Database [PEDro], Embase, MEDLINE, CINAHL and the Cochrane Central Register for Controlled Trials) were searched using the following keywords: “COPD”, “intervention” and “physical activity” from inception to May 20, 2016; published RCTs that aimed to increase PA in individuals with COPD were included. The PEDro scale was used to rate study quality. Standardized mean differences (effect sizes, ESs) with 95% confidence intervals (CIs) were determined. Effects of included interventions were also measured according to the minimal important difference (MID) in daily steps for COPD (599 daily steps).

Results: A total of 37 RCTs with 4,314 participants (mean forced expiratory volume in one second (FEV₁) % predicted 50.5 [SD=10.4]) were identified. Interventions including exercise training (ET; n=3 studies, 103 participants) significantly increased PA levels in COPD compared to standard care (ES [95% CI]; 0.84 [0.44–1.25]). The addition of activity counseling to pulmonary rehabilitation (PR; n=4 studies, 140 participants) showed important effects on PA levels compared to PR alone (0.47 [0.02–0.92]), achieving significant increases that exceeded the MID for daily steps in COPD (mean difference [95% CI], 1,452 daily steps [549–2,356]). Reporting of methodological quality was poor in most included RCTs.

Conclusion: Interventions that included ET and PA counseling during PR were effective strategies to improve PA in COPD.

Keywords: pulmonary disease, chronic obstructive, physical activity, interventions

Introduction

Physical inactivity is a key predictor of increased hospitalization and all-cause mortality in COPD.^{1,2} A systematic review comparing activity levels in COPD patients with age-matched controls showed a marked reduction in activity duration, intensity and daily step counts, regardless of disease severity.³ Physical activity (PA) levels are strongly correlated with functional exercise capacity.⁴ In addition, a large 5-year follow-up study showed important associations between levels of PA and health-related quality of life (HRQL) in COPD.⁵

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In light of the strong relationship between PA and health outcomes in COPD, the past decade has witnessed the development of several strategies aiming to improve PA levels in COPD. The number of randomized controlled trials (RCTs) designed to test the efficacy of these interventions is growing rapidly. A recent review that studied the effects of RCTs, non-RCTs and experimental studies of PA interventions concluded that although exercise training (ET) is the most commonly used approach, its effects on PA levels are uncertain.⁶ The inclusion of non-RCTs in this review is a potential source of bias that might overestimate the true effects of PA interventions.⁷ To date, attempts to compare effects of interventions on PA levels using meta-analysis of published RCTs exclusively have not been reported. In this systematic review, we aimed to analyze and compare the effects of various PA interventions reported through RCTs in COPD.

Methods

The systematic review protocol is registered in PROSPERO (CRD42013004460, <http://www.crd.york.ac.uk/PROSPERO>).

Inclusion criteria

Studies that recruited participants diagnosed with COPD according to the Global Initiative for Chronic Obstructive Lung Diseases (GOLD) guidelines were included.⁸ In the case of mixed populations, studies were included if 80% or more of individuals had COPD. RCTs published in peer-reviewed journals that aimed to evaluate the efficacy of interventions to improve PA levels were included. These comprised, but were not limited to, pulmonary rehabilitation (PR), ET, pharmaceutical treatment, self-management or written advice. Studies were included if PA was either a primary or a secondary outcome.

The primary outcome of the review was PA measured either objectively (eg, time spent in PA measured by activity monitors) or subjectively (eg, scores of questionnaires). Secondary outcomes of the review were functional and maximal exercise capacity, HRQL, dyspnea and lung function variables.

Search methods

Databases searched were the Cochrane library, Physiotherapy Evidence Database (PEDro), Embase, MEDLINE and CINAHL. The subject headings were “COPD”, “interventions” and “physical activities” ([Supplementary materials](#)). Databases were searched through two separate

periods: from their inception to the end of January 2015 and from February 2015 to May 20, 2016. In addition, we searched major trial registries including ClinicalTrials.gov, European Union Clinical Trial Register, Australian New Zealand Clinical Trials Registry and WHO International Clinical Trials Registry Platform for relevant projects.

One author (AL) reviewed the title and abstract of trials and two authors (AL and AEH) independently assessed the full text of articles to decide on inclusion. Any disagreement was resolved by discussion. Data were extracted independently by two authors (AL and AEH) using a standardized data extraction sheet ([Supplementary materials](#)). Online software was used to extract data from plots and graphs where necessary (www.arohatgi.info/WebPlotDigitizer).

Quality assessment was performed using the PEDro quality scale, which is an 11-item scale that assesses internal and external validity of clinical trials.⁹ The higher the given score, the better the quality. Cut points of the scale were excellent (9–10), good (6–8), fair (4–5) and poor (≤ 3).

Data interpretation and synthesis

Comparisons of interest were interventions aimed to improve PA versus usual care (or placebo), interventions aimed to improve PA added to PR versus PR alone, and PA intervention versus another active PA intervention. Effects of interventions on continuous outcome measures were assessed using standardized mean differences (SMDs) and 95% confidence intervals (CIs), to allow comparison of effect size (ES) across interventions. Trials reporting effects of interventions using comparable outcome measures at comparable time points were combined in a meta-analysis. Software used to conduct meta-analysis and compute ESs was Review Manager 5.3 manufactured by the Nordic Cochrane Centre. Based on Cohen’s classifications, an SMD of 0.2 is small, 0.5 is moderate and 0.8 or higher is a large effect.

Meta-analysis was conducted where trials were statistically and clinically homogeneous. Statistical homogeneity was defined as $I^2 \leq 40\%$.⁷ Clinical homogeneity was defined as similarity of study population, intervention components and their comparators and selected outcome measures. In the case of PA levels in an included RCT being measured using more than one variable, the variable that best reflects PA levels was selected for meta-analysis (eg, objectively measured time spent in walking was selected over self-reported PA time,¹⁰ and overall PA time was selected over PA time spent in 1 day).¹¹ Objectively and subjectively measured PA variables were not pooled together in a meta-analysis.

When available, change scores were extracted to measure the effects of interventions. In the case of a change score not being directly provided, baseline and final scores were used to measure mean differences, and available variables of the change (eg, correlation coefficient of the change) were used to compute standard deviation of the change.⁷ When necessary, study investigators were contacted for additional information to compute change scores. Final scores at available time points were extracted when change score was unable to be computed.

We intended to perform sensitivity analyses to examine the effects of trial quality by excluding trials without concealed allocation and assessor blinding; however, insufficient data prevented these analyses.

In trials where PA was measured in daily steps, weighted mean differences in steps achieved by interventions were compared. Changes in the number of steps from baseline produced by different interventions were compared to the minimal important difference (MID), which has been estimated to be a change of 599 daily steps.¹² MID is defined as a meaningful change or effect that might be

considered important to produce sizeable change in vital outcomes.¹³

Results

The search yielded a total of 4,178 records identified throughout the two separate periods, with 81 full texts reviewed for eligibility. A Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram (Figure 1) depicts the search process. A total of 37 RCTs identified in 40 separate reports met our selected criteria and were included in the systematic review.

Quality assessment

The quality of included studies ranged from fair to good (median PEDro score, interquartile range [IQR]=6 [5–7]; Table 1), with only one study scoring poorly.¹⁴ A total of 18 studies (48% of included RCTs) failed to conceal allocation, 27 studies (73% of included RCTs) failed to blind subjects and 23 studies (62% of included RCTs) failed to blind outcome assessors. Another common limitation was the inability to report outcomes for >85% of randomized subjects (n=20, 54%; Table 1).

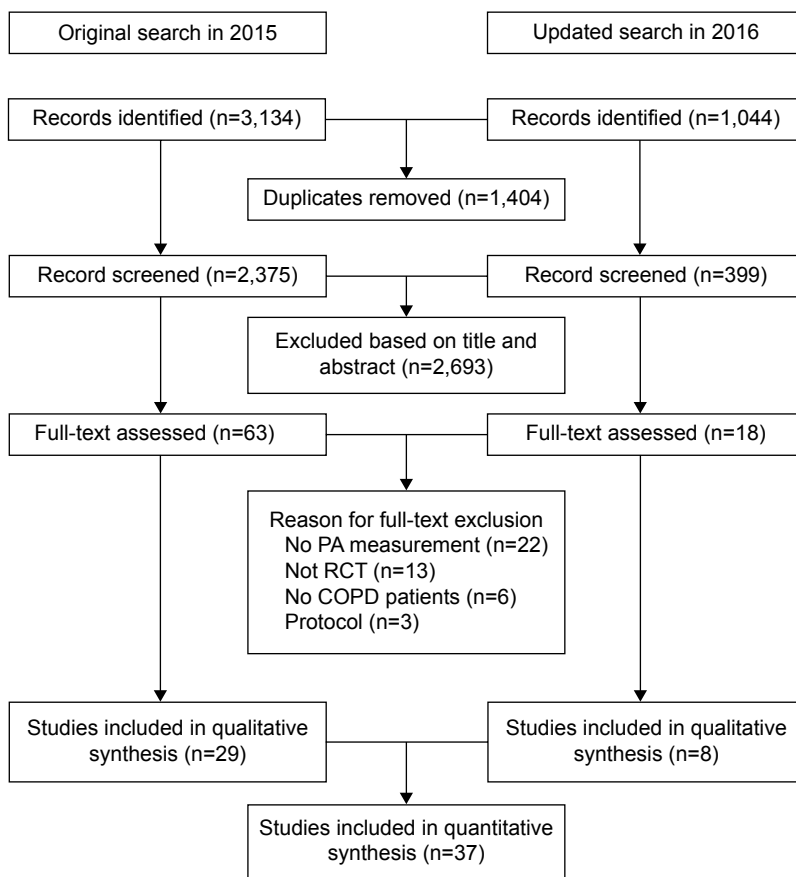


Figure 1 PRISMA flow diagram for database search and study selection process.

Abbreviations: PA, physical activity; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; RCT, randomized controlled trial.

Table 1 Qualitative synthesis of included studies using PEDro scale for the quality of RCTs

Study name	Eligibility criteria ^a	Random allocation	Concealed allocation	Baseline similarity	Blinding (subject)	Blinding (therapist)	Blinding (assessor)	Measure for >85%	ITT	Group comparison	Point measure	Quality score
Studies comparing PA interventions versus usual care (or placebo; n=16)												
Berry et al ¹⁵	*	*	*	*			*		*	*	*	6
Borges and Carvalho ¹⁶	*	*	*	*			*	*	*	*	*	8
Breyer et al ¹⁷	*	*	*	*			*	*	*	*	*	5
Dal Negro et al ^{16,47}	*	*	*	*	*		*	*	*	*	*	10
Faulkner et al ¹⁹	*	*	*	*			*	*	*	*	*	5
Goris et al ⁴⁸	*	*	*	*			*	*	*	*	*	6
Hornikx et al ³¹	*	*	*	*			*	*	*	*	*	6
Hospes et al ³²	*	*	*	*			*	*	*	*	*	5
Jonsdottir et al ³⁹	*	*	*	*			*	*	*	*	*	6
Kruis et al ⁵³	*	*	*	*			*	*	*	*	*	8
Larson et al ²⁰	*	*	*	*	*		*	*	*	*	*	9
Sandland et al ⁵¹	*	*	*	*	*		*	*	*	*	*	6
Schuz et al ⁴¹ ; Walters et al ⁴²	*	*	*	*	*		*	*	*	*	*	8
Steele et al ³⁷	*	*	*	*			*	*	*	*	*	5
Watz et al ⁴⁵	*	*	*	*	*		*	*	*	*	*	9
Wilson et al ²⁴	*	*	*	*			*	*	*	*	*	6
Studies comparing PA interventions added to PR versus PR alone (n=8)												
Altenburg et al ²⁵	*	*	*	*			*		*	*	*	5
Burtin et al ²⁷	*	*	*	*	*		*		*	*	*	7
Cruz et al ²⁹	*	*	*	*	*		*		*	*	*	7
de Blok et al ³⁰	*	*	*	*			*		*	*	*	4
Duiverman et al ⁵⁰	*	*	*	*			*		*	*	*	4
Kawagoshi et al ³³	*	*	*	*			*		*	*	*	5
Kesten et al ⁴³	*	*	*	*	*		*		*	*	*	6
Pleguezuelos et al ⁵²	*	*	*	*	*		*	*	*	*	*	6
Studies comparing PA interventions versus another PA intervention (n=13)												
Berry et al ²⁶	*	*	*	*			*		*	*	*	6
Casaburi et al ⁴⁹	*	*	*	*			*		*	*	*	5
Effing et al ¹⁸	*	*	*	*			*	*	*	*	*	6
Mendoza et al ³⁴	*	*	*	*			*	*	*	*	*	7
Moy et al ³⁵	*	*	*	*			*	*	*	*	*	6
Nguyen et al ³⁶	*	*	*	*			*	*	*	*	*	7
Nguyen et al ⁴⁰	*	*	*	*			*	*	*	*	*	7
Pomidorri et al ²¹	*	*	*	*			*	*	*	*	*	5
Probst et al ²²	*	*	*	*			*	*	*	*	*	5
Sewell et al ²³	*	*	*	*			*	*	*	*	*	6
Tabak et al ³⁸	*	*	*	*	*		*	*	*	*	*	7
Troosters et al ⁴⁴	*	*	*	*	*		*	*	*	*	*	10
Vergeret et al ⁴	*	*	*	*	*		*	*	*	*	*	3

Notes: *Yes, score = 1. ^aItem does not contribute to total quality score. The higher the given score, the better the quality. Cut points of the scale were excellent (9–10), good (6–8), fair (4–5) and poor (3).
Abbreviations: ITT, intention to treat; PA, physical activity; PEDro, Physiotherapy Evidence Database; PR, pulmonary rehabilitation; RCTs, randomized controlled trials.

Characteristics of included RCTs

Included RCTs measured the effects of ET (n=10),^{15–24} activity counseling (n=15),^{25–40} health monitoring (n=1),^{41,42} pharmacological treatment (n=3),^{43–45} nutritional interventions (n=2),^{46–48} oxygen therapy (n=4),^{14,49–51} urban walking circuits (n=1)⁵² and integrated disease management (n=1)⁵³ on PA levels in COPD. PA counseling was delivered either in a center-based setting (n=9),^{25–27,29,30,32–34,39} through phone calls (n=3)^{31,36,37} or by internet-mediated approaches (n=3).^{35,38,40} Studies compared interventions to usual care (n=16),^{15–17,19,20,24,31,32,37,39,41,42,45–48,51,53} PR programs (n=8)^{25,27–30,33,43,50,52} or another active intervention (n=13).^{14,18,21–23,26,34–36,38,40,44,49} Characteristics of included studies are summarized in Table 2.

Characteristics of included subjects

This review included a total of 4,314 participants (males = 58%). Mean age of included participants was 66.2 (SD 4.3) years with a mean forced expiratory volume in one second (FEV₁) % predicted of 50.5 (10.4). All participants had a confirmed diagnosis of COPD according to the GOLD guidelines.⁸

Characteristics of PA measurement tools

RCTs assessed PA using several outcome measures. Objective measures included accelerometers (n=18, 50%),^{16,17,20–23,27,29,33,36,37,41,44–49,51} pedometers (n=8, 22%)^{18,25,30,32,34,35,38,50} and an activity monitor (n=1).³¹ PA was also measured subjectively using validated tools such as Seven-Day PA Recall Questionnaire (n=1),¹⁹ PA Scale for the Elderly (PASE) questionnaire (n=1),¹⁵ Community Healthy Activities Model Program for Seniors (CHAMPS) questionnaire (n=1)²⁶ and the International PA Questionnaire (IPAQ; n=3).^{24,39,53} Nonvalidated tools to measure PA included exercise diary cards (n=1)⁵² and trial-designed activity questionnaires (n=3).^{14,40,43}

Analysis of included interventions

Effects of PA interventions on PA levels

Studies comparing PA interventions versus usual care or placebo

When comparing PA counseling alone to usual care, there were small and nonsignificant effects of counseling on PA for both objective measures (n=2 studies, SMD [95% CI] 0.23 [–0.26 to 0.72], time point 1–3 months; Figure 2)^{31,32} and subjective measures (n=2 studies, –0.27 [–0.04 to 0.58], 12 months; Figure 2).^{37,39} Four months of ET produced moderate to large statistically significant effects on PA (n=3

studies, 0.84 [0.44–1.25]; Figure 2),^{17,19,20} whereas long-term maintenance exercise programs showed small nonsignificant effects on PA at 12 and 15 months post-intervention (n=2 studies, 0.15 [–0.17 to 0.47]; Figure 2).^{15,24} None of the studies included in the meta-analyses had blinded the assessors or the therapists from study groups. One study of essential amino acid (EAA) supplementation^{46,47} reported an increase in steps favoring the intervention arm at 3 months (577.6 steps, *P*=0.02); however, insufficient sample size details prevented ES calculations (Table S1). Important increases in daily steps were also reported in a crossover RCT in favor of the once-daily long-acting beta agonist, indacaterol 150 µg,⁴⁵ compared to placebo at 3 weeks (0.32 [0.02–0.63]; Table S1).

Studies comparing PA interventions added to PR versus PR alone

Adding activity counseling to PR produced short-term improvements in PA at 3 months compared to PR alone (n=4 studies, 0.47 [0.02–0.92]; Figures 3 and 4).^{25,27–30} Two of the four studies included in this meta-analysis had assessor blinding and concealed allocation.^{27,29} When analyzing sustainability of results, pooled meta-analysis showed small to moderate long-term effects of PA counseling added to PR that trended to statistical significance versus PR alone (n=4, 0.28 [–0.08 to 0.31]; *I*², 60%; Figure 4).^{25,27,29,33} Of the included studies pooled in this analysis, the only study with assessor blinding did not report similar long-term effects on steps at 6 months post-intervention (n=1 study, 0.25 [–0.81 to 0.31]; Figure 4).²⁷ Introducing an urban walking circuit promotion program for 12 months after a 3-month course of PR improved baseline walking time when compared to usual care after PR (1.36 [0.84–1.88]; Table S2).⁵²

Studies comparing PA interventions versus another intervention

ET: Although 3 months of high-intensity ET had similar effects to light-intensity training on daily steps and walking time (–0.13 [–0.76 to 0.49] and 0.26 [–0.36 to 0.89], respectively; Table 3), effects on time spent in moderate to vigorous physical activity (MVPA) favored the high-intensity training group at 3 months (1.16 [0.49–1.84]; Table 3).²² When comparing 6 months of home-based walking with fixed speed program to home-based walking with fixed distance,²¹ significant increases in daily metabolic equivalent tasks (0.94 [0.25–1.63]; Table 3) and daily MVPA time (0.72 [0.04–1.39]; Table 3) were achieved by fixed speed walking

Table 2 Characteristics of included studies

Author	Year	Country	n (I/C)	Age, years; mean (SD)	FEV ₁ % predicted L; mean (SD)	Gender (male/female)
Studies comparing PA interventions versus usual care (or placebo; n=16)						
Berry et al ¹⁵	2003	USA	70/70	67.7 (5.8)	58.4 (18.1)	78/62
Borges and Carvalho ¹⁶	2014	Brazil	15/14	65.9 (10.9)	40.4 (14.3)	18/11
Breyer et al ¹⁷	2010	Austria	30/30	60.3 (8.5)	46.3 (17.6)	27/33
Dal Negro et al ^{16,47}	2012 and 2010	Italy	44/44	74 (6.7)	FEV ₁ =0.8 (0.3)	61/27
Faulkner et al ¹⁹	2010	UK	6/8	–	–	–
Goris et al ⁴⁸	2003	the Netherlands	11/9	62 (11)	40 (16)	11/9
Hornikx et al ³¹	2009	Belgium	15/15	67 (6.5)	43 (18)	17/12
Hospes et al ³²	2009	the Netherlands	18/17	62.2 (8.6)	64.7 (16.1)	21/14
Jonsdottir et al ³⁹	2015	Iceland	48/52	59 (4.5)	57.6 (17.7)	46/54
Kruis et al ⁵³ (clustered RCT)	2014	the Netherlands	554/532	68.3 (11.2)	67.8 (20.4)	585/501
Larson et al ²⁰	2014	USA	15/14	71 (7.8)	58.5 (18.5)	–
Sandland et al ⁵¹	2008	UK	10/10	73.4 (6.8)	43.6 (22.5)	14/6
Schuz et al ⁴¹ (Walters et al ⁴²)	2015 (2013)	Australia	90/92	67.7 (7.8)	55.2 (13.4)	96/86
Steele et al ³⁷	2008	USA	52/54	–	40.4 (17.8)	–
Watz et al ⁴⁵ (crossover RCT)	2014	Germany	129	61.4 (8.9)	64.02 (9.38)	87/42
Wilson et al ²⁴	2015	UK	73/75	68.3 (12.4)	41 (16)	91/57
Studies comparing PA interventions added to PR versus PR alone (n=8)						
Altenburg et al ²⁵	2014	the Netherlands	31/30	54 (9.6)	43 (25.9)	32/25
Burtin et al ²⁷	2015	Belgium	40/40	66.5 (7.5)	45.5 (16.03)	66/14
Cruz et al ²⁹	2016	Portugal	16/16	66.5 (8.4)	66.9 (20.1)	27/5
de Blok et al ³⁰	2006	the Netherlands	10/11	64.0 (11.3)	47.3 (17.9)	9/12

Intervention arm	Control arm	Time points/outcomes
Exercise maintenance (1 h ×3 times/W supervised ET sessions after 3M of ET program pre-randomization – 15M)	UC (PA advice after 3M of ET program pre-randomization – 15M)	15M: subjective activity score, FEV ₁ , FVC and FER.
Whole-body ET (≥3 ET sessions starting at day 3 of admission, mean sessions =5.6)	UC (daily chest physiotherapy and O ₂ therapy)	6M, 12M, 15M: 6MWD 1M post-discharge: daily walking, standing, sitting and lying time, FEV ₁ % predicted. 1M post-discharge: 6MWD, SGRQ
Nordic walking (3 times/W walking with power poles ET sessions and 1 time/W EDU sessions – 3M)	UC (1 time/W EDU sessions – 3M)	3M, 6M, 9M: movement intensity, 6MWD, SF36
Daily EAA dietetics (4 g ×2 times/day – 12W)	Placebo dietetics (4 g ×2 times/day – 12W)	1M, 3M: daily steps and energy expenditure, FEV ₁ (l/sec). 3M: SGRQ
Health-enhancing PA program (3 times/W supervised ET and EDU sessions with exercise diary – 8W)	UC (8W)	9W: subjective 7-day total PA, ISWT, CRQ, MRC, FEV ₁ % predicted
Respifor® (Nutricia Advanced Medical Nutrition, Schiphol, The Netherlands) nutritional supplement (375 mL ×3 times/day with nutritional consultation sessions – 3M)	UC (3M)	1M, 3M post-discharge: daily PA levels and energy expenditure
PA counseling and GS (3 times/W phone calls – 1M)	UC (1M)	1M: daily steps, walking time and movement intensity during walking, 6MWD, MRC
Individualized exercise counseling (30 min × 5 sessions using MI – 12W)	UC (12W)	12W: daily steps, 6MWD, SGRQ, CCQ, SF36
Partnership with families' self-management (≥30 min ×4 RN/patient/family consultations, 6M of SC treatment and one interdisciplinary team/patient/family meeting – 6M)	UC (6M)	12M: weekly IPAQ subscales: total, vigorous, moderate and walking, SGRQ
Primary care practitioners training for integrated disease management: spirometry use, MI, SC and exercise advice (24M)	UC (24M)	12M: daily IPAQ, SGRQ, CCQ, SF36, MRC
Self-efficacy and UBRT (15 min ×4 times/M EDU sessions – 4M)	UC (gentle chair exercise – 4M)	4M: daily MVPA, LPA, and sedentary time
Ambulatory O ₂ (3.1 kg cylinder O ₂ with a backpack – 8W)	Ambulatory air (3.1 kg cylinder placebo with a backpack – 8W)	8W: daily activity counts, ISWT, ESWT, CRQ
Health monitoring (16×30 min phone calls by trained community nurses – 12M)	UC (12 times/M social phone calls)	6M, 12M: daily steps, SGRQ, SF36
Exercise adherence counseling (12 phone calls, 1 home visit and ≥20 min ×4 times/W maintenance home ET sessions after 8W of PR pre-randomization – 20W)	UC (after 8W of PR pre-randomization – 20W)	20W, 12M: daily PA activity, SR daily exercise time, 6MWD, SOLDQ, SF36, SOB levels, FEV ₁ % predicted
Indacaterol (Onbrez®; Novartis Pharmaceuticals, Basel, Switzerland) 150 µg (1 time/day – 21 days)	Placebo (1 time/day – 21 days)	3W: daily steps, MVPA time and PA levels, adverse events
PR maintenance (1 h ×3 personalized ET sessions and 1 h ×3 EDU sessions – 12M)	UC (PA advice – 12M)	12M: weekly IPAQ, VAS, ISWT, ESWT, CRQ
PA counseling (30 min ×5 sessions using MI – 12W) added to PR (2 h ×3 times/W – 9W)	PR (2 h ×3 times/W – 9W)	3M, 15M: daily steps and steps equivalent*, 6MWD, CRQ, CCQ
Individualized PA counseling (30 min ×8 sessions using MI – 6M) added to multidisciplinary PR (average 1.5 h ×2.5 times/W – 6M)	Multidisciplinary PR (average 1.5 h ×Δ2.5 times/W – 6M)	3M, 6M: daily steps, walking and MVPA time, 6MWD, CRQ
PA-focused behavioral counseling (average 25 min ×8 sessions using SCT: SE, MI and pedometer and diary feedback – 6M) added to PR (1 h ×3 times/W ET and 1.5 h ×1 time/W EDU sessions – 3M)	PR (1 h ×3 times/W ET and 1.5 h ×1 time/W EDU sessions – 3M)	3M, 6M: daily steps and MVPA, PA and sedentary time, 6MWD, SGRQ
Lifestyle PA counseling (30 min ×4 sessions using MI – 9W) added to PR (9W)	PR (9W)	9W: daily steps, SGRQ, SF36

(Continued)

Table 2 (Continued)

Author	Year	Country	n (I/C)	Age; mean (SD)	FEV _{1%} pred; mean (SD)	Gender (male/female)
Duiverman et al ⁵⁰	2008	the Netherlands	31/35	62 (8.6)	–	35/31
Kawagoshi et al ³³	2015	Japan	12/15	74.5 (8.4)	59.4 (21.5)	24/3
Kesten et al ⁴³	2008	USA	25/21	67.4 (7.2)	33.4 (12.4)	20/26
Pleguezuelos et al ⁵²	2013	Spain	34/37	70.4 (2.5)	53.4 (2.9)	–
Studies comparing PA interventions versus another PA intervention (n=13)						
Berry et al ²⁶	2010	USA	89/87	66 (10)	51.5 (19.3)	95/81
Casaburi et al ⁴⁹	2012	USA	11/11	66.9 (9.2)	31.3 (10)	–
Effing et al ¹⁸ (2×2 factorial RCT)	2011	the Netherlands	77/76	63.4 (7.9)	50 (15.6)	89/64
Mendoza et al ³⁴	2015	Chile	52/50	68.7 (8.5)	66.1 (19.4)	62/40
Moy et al ³⁵	2015	USA	154/84	67 (9)	–	223/15
Nguyen et al ³⁶	2009	USA	8/9	68.2 (11)	40.9 (17.7)	6/11
Nguyen et al ⁴⁰	2013	USA	43/41	68.5 (9.6)	51.6 (20.1)	49/35
Pomidori et al ²¹	2012	Italy	18/18	72 (8.2)	48 (12.4)	27/9
Probst et al ²²	2011	Brazil	20/20	66 (8.6)	39.5 (13.3)	21/19
Sewell et al ²³	2005	UK	90/90	68.3 (8.6)	–	99/81
Tabak et al ³⁸	2014	the Netherlands	14/16	66.6 (7.4)	52.8 (14.1)	19/11

Intervention arm	Control arm	Time points/outcomes
Nocturnal noninvasive positive pressure ventilation during multidisciplinary PR (1 h ×3 times/W ET sessions – 12W) Pedometer feedback (1 time/M sessions – 12M) added to multidisciplinary home-based PR (1 time/day home ET, 45 min ×1 time/M EDU and 2 h ×2 times/M supervised ET sessions – 12M) Tiotropium (18 µg ×1 time/day – 25W) added to PR (0.5 h ×3 times/W – 8W) Urban walking circuit promotion (leaflets distributed and reviewed 2 times/M – 9M) following PR (1 h ×3 times/W ET sessions – 12W)	Multidisciplinary PR (1 h ×3 times/W ET sessions – 12W) Multidisciplinary home-based PR (1 time/day home ET, 45 min ×1 time/M EDU and 2 h ×2 times/M supervised ET sessions – 12M) Placebo (18 µg ×1 time/day – 25W) added to PR (0.5 h ×3 times/W – 8W) UC (generic PA advice reviewed 2 times/M – 9M) following PR (1 h ×3 times/W ET sessions – 12W)	3M: daily steps, 6MWD, ESWT, FEV ₁ (l/sec) 12M: daily walking, standing, sitting and lying down time, 6MWD, CRQ, MRC 13W, 17W, 21W, 25W: subjective activity time in 2W, endurance time (min) 12M: subjective daily walking time, weekly number of days walked, 6MWD
Lifestyle activity program (1 h ×3 times/W ET sessions, group discussions, individualized counseling and 15 min follow-up phone calls – 3M) Lightweight ambulatory O ₂ (1.6 kg aluminum cylinders – 6M) COPE active (average 2.5 times/W supervised ET and 1 time/W home-based ET sessions – 11M) added to self-management (1 h ×6 individualized SC counseling, 2 h ×4 behavioral change group discussions and 1 EDU session – 3M) PA counseling (30 min ×1 time/M individualized pedometer and exercise diary feedback sessions – 3M)	ET (1 h ×3 times/W ET sessions – 3M) E-cylinder ambulatory O ₂ (10 kg towed on a cart cylinders – 6M) Self-management (1 h ×6 individualized SC counseling, 2 h ×4 behavioral change group discussions and 1 EDU session – 3M) Standardized counseling (30 min ×1 time/M individualized exercise diary feedback sessions – 3M)	3M, 6M, 12M: subjective weekly MVPA levels, 6MWD, SF36, CRQ. 12M: adverse events 3M, 6M: midday PA time 7M, 12M: daily steps, ISWT, ESWT, CRQ, CCQ 3M: daily steps, 6MWD, SGRQ, mMRC
Internet-mediated pedometer-based program (1 time/W GS and pedometer feedback and online social support – 4M) Cell phone-mediated exercise persistence program (individualized PA advice followed by 1 time/W reinforcement, GS and activity feedback – 6M)	Pedometer reporting (1 time/M pedometer and adverse events outcomes reporting to HCP) – 4M Cell phone-mediated self-monitoring program (individualized PA advice followed by 1 time/day activity recording – 6M)	4M: daily steps, SGRQ 3M, 6M: daily steps and % of sedentary and MVPA time, 6MWD, incremental cycle endurance, SGRQ, SF36
Internet-mediated dyspnea self-management program (1.5-2 h dyspnea management face-to-face consultation, 30 min ×4 times/W individualized home ET sessions, 1 time/W in MOI followed by 2 times/M from M2 to M11 exercise GS feedback and structured EDU sessions – 12M) Home-based walking (20–30 min ×4 times/W walking at a fixed speed paced by metronome, 4 times/W supervised sessions in M1 and 2 times/M phone calls support in M2 to M6 – 6M)	General EDU (initial home visit, 2 times/M phone calls and 1 time/M EDU sessions – 12M) Home-based walking (20–30 min ×4 times/W walking a fixed distance, 4 times/W supervised sessions in M1 and 2 times/M phone calls support in M2 to M6 – 6M)	3M, 6M, 12M: subjective weekly exercise duration, 6MWD, CRQ, SF36 6M, 12M: daily METs, METs peak and MVPA time, SGRQ. 12M: 6MWD
ET (1 h ×3 times/W high-intensity and whole-body ET sessions – 12W)	ET (1 h ×3 times/W light-intensity and breathing ET sessions – 12W)	12W: daily steps, walking, sitting, standing, lying and activities cost >3 METs time. Total and activities cost >3 MET energy expenditure, 6MWD, maximum work load, endurance time, SGRQ, MRC
Individually targeted ET (2 h ×2 times/W individualized ET and EDU sessions – 7W) Tele-rehabilitation program (1 time/W internet-mediated pedometer feedback and 90 min ×2 self-management sessions – 4W) added to ET (1 time/W ET sessions – 4W)	General ET (2 h ×2 times/W standardized ET and EDU sessions – 7W) ET (1 time/W ET sessions – 4W)	7W: daily activity counts, ISWT, ESWT, CRQ 3W: daily steps, CCQ, MRC

(Continued)

Table 2 (Continued)

Author	Year	Country	n (I/C)	Age; mean (SD)	FEV ₁ %pred; mean (SD)	Gender (male/female)
Troosters et al ⁴⁴	2014	Belgium	238/219	61.7 (8.4)	65.7 (8.2)	312/145
Vergeret et al ⁴	1989	France	84/75	61.9 (7.8)	–	139/20

Note: *steps equivalent=steps + metabolic equivalent.

Abbreviations: C, control arm; CCQ, Clinical COPD Questionnaire; COPE, community based physiotherapeutic exercise; CRQ, Chronic Respiratory Questionnaire; EAA, essential amino acid; EDU, education; ESWT, endurance shuttle walk test; ET, exercise training; FER, forced expiratory ratio; FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity; GS, goal setting; HCP, health care professionals; I, intervention arm; IPAQ, International PA Questionnaire; ISWT, incremental shuttle walk test; LPA, light PA; LTOT, long-term oxygen therapy; M, month(s); MET, metabolic equivalent task; MI, motivational interviewing; mMRC, Modified Medical Research Council; MRC, Medical Research Council; MVP, moderate to vigorous PA; 6MWD, 6-minute walk distance; PA, physical activity; PR, pulmonary rehabilitation; RCT, randomized controlled trial; RN, registered nurse; SC, smoking cessation; SCT, social cognitive therapy; SE, self-efficacy; SF36, 36-Item Short Form Survey; SGRQ, Saint George Respiratory Questionnaire; SOB, shortness of breath; SOLDQ, Seattle Obstructive Lung Disease Questionnaire; SR, self-reported; UBRT, upper-body resistance training; UC, usual care; VAS, Visual Activity Scale; W, week(s).

at 12 months. Moreover, adding community-based ET to a self-management program showed moderate and significant effects on activity levels at 12 months when compared to self-management alone (0.48 [0.10–0.86]; Table 3).¹⁸

Counseling and self-management: Four months of pedometer-based counseling showed important effects on

daily steps when delivered via an internet-mediated program (0.84 [0.59–1.08]; Table 3)³⁵ or through 3 months of individualized sessions (1.08 [0.65–1.15]; Table 3)³⁴ when compared to standard counseling. An internet-mediated dyspnea self-management program also showed important increases in exercise duration assessed by a nonvalidated

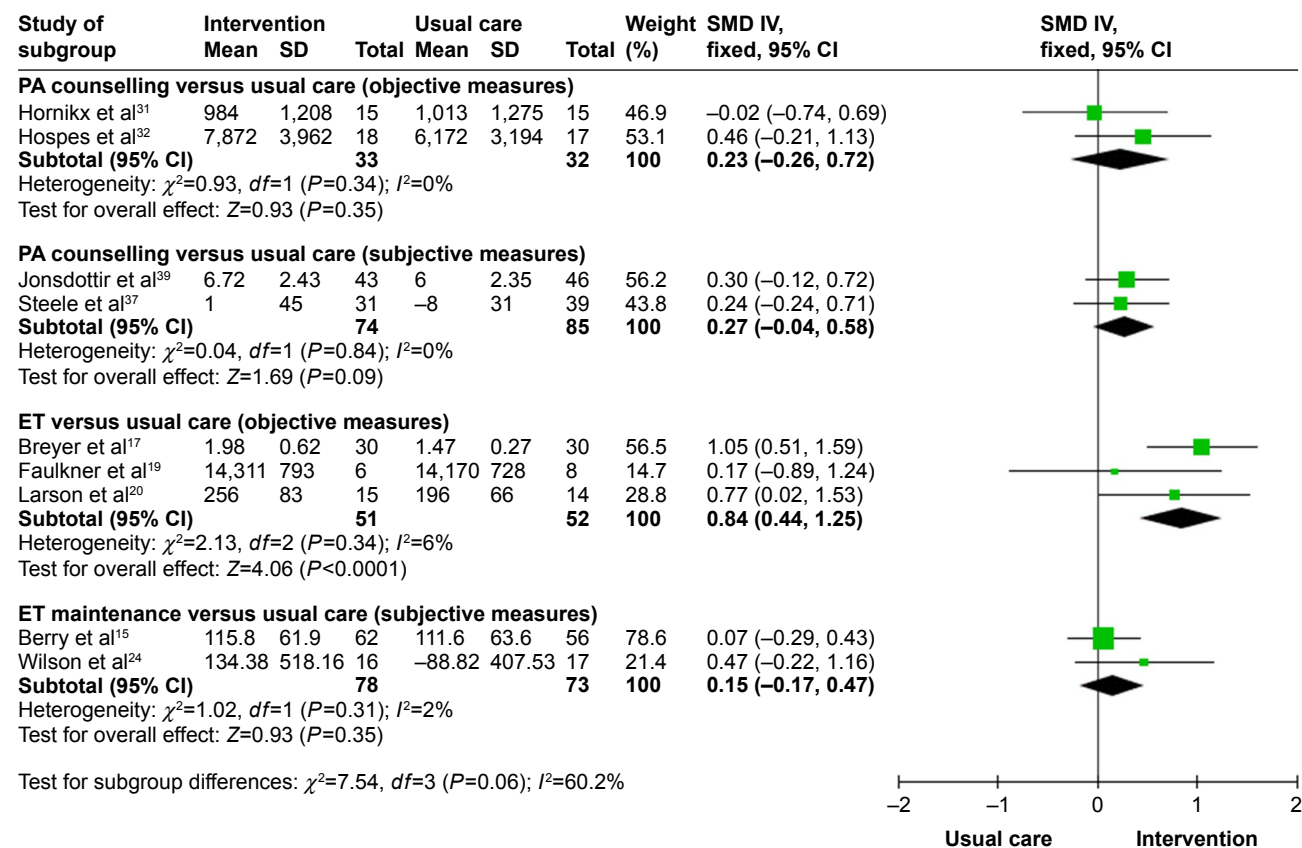


Figure 2 Studies comparing PA interventions versus usual care.

Abbreviations: CI, confidence interval; ET, exercise training; IV, independent variable; PA, physical activity; SMD, standardized mean difference.

Intervention arm	Control arm	Time points/outcomes
Tiotropium HandiHaler 18 µg and salbutamol (1 time/day – 24W) added to individualized activity plan and exercise diary feedback (20 min × 1 time/M sessions using MI – 24W)	Placebo HandiHaler and salbutamol (1 time/day – 24W) added to individualized activity plan and exercise diary feedback (20 min × 1 time/M sessions using MI – 24W)	24W: daily steps and age-appropriate LPA and MVPA time, FEV ₁ (l/sec)
LTOT with portable O ₂ (>15 h/day O ₂ concentrators plus gaseous or liquid O ₂ – 12M)	LTOT with fixed O ₂ (>15 h/day O ₂ concentrators – 12M)	12M: subjective daily indoor and outdoor rest and activities time, subjective daily outdoor distance walked

tool compared to internet-mediated education at 12 months (0.57 [0.13–1.00]; Table 3). None of the other interventions in this group showed important effects on PA when compared to other active interventions (eg, individualized ET versus general ET²³ and the once-daily long-acting muscarinic antagonist, tiotropium added to PA counseling versus placebo added to PA counseling;⁴⁴ Table S3).

MID of PA

Limiting the analysis to 13 trials (456 actively treated subjects) that used daily steps to measure the change in PA from baseline, only the studies that tested the addition of activity counseling to PR (n=4 studies)^{25,27,29,30} showed large effects that exceeded the established MID of 599 daily steps (mean difference [95% CI], 1452 [549–2,356]; Figure 5). While PA counseling alone^{31,32,34–36} and the addition of nocturnal noninvasive ventilation (NNIV)⁵⁰ to PR achieved a mean difference in steps that exceeded MID, the ES was small and did not reach statistical significance (PA counseling [n=5 studies]: 930 [293–1,566], NNIV + PR [n=1 study]:

906 [–655 to 2,467]; Figure 5). ET (n=2 studies)^{18,22} and health monitoring via phone calls (n=1 study)⁴¹ achieved differences in steps that did not exceed the MID for daily steps in COPD (Figure 5).

Effects of PA interventions on functional exercise capacity

Compared to standard care, ET interventions including maintenance program¹⁵ and Nordic walking¹⁷ significantly improved 6-minute walk distance (6MWD) after 6 months (0.48 [0.11–0.85] and 0.73 [0.20–1.25]; Table S4), respectively. Exercise adherence counseling also produced important effects on 6MWD at 4 months (0.44 [0.01–0.86]; Table S4).³⁷ However, these effects were not sustained at 12 months when compared to usual care (0.29 [–0.18 to 0.76]; Table S4).³⁷

Adding tiotropium to PR produced moderate effects on treadmill endurance time compared to placebo (0.67 [0.01–1.33]; Table S4).⁴³ Moderate effects on exercise capacity

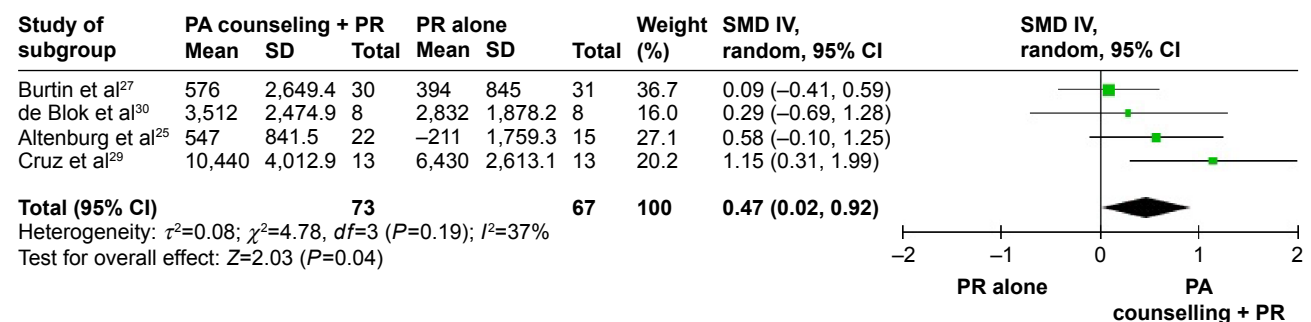


Figure 3 Studies comparing PA counseling added to PR versus PR (short-term effect).

Abbreviations: CI, confidence interval; IV, independent variable; PA, physical activity; PR, pulmonary rehabilitation; SMD, standardized mean difference.

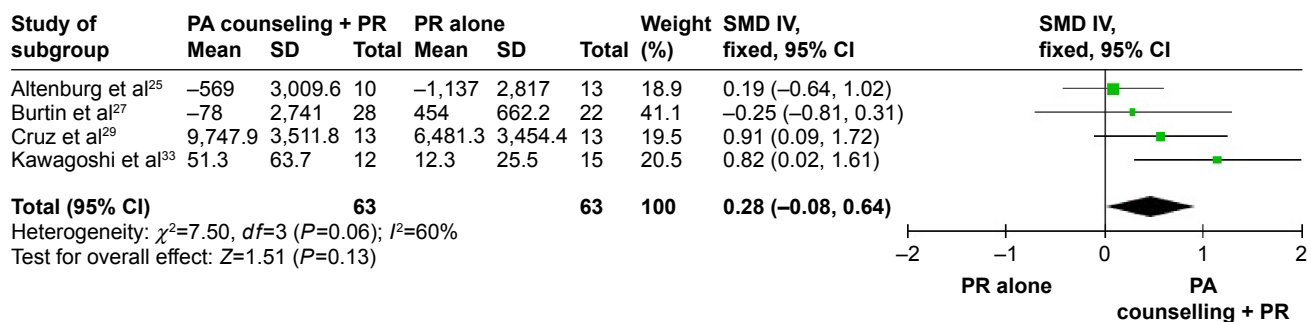


Figure 4 Studies comparing PA counseling added to PR versus PR (long-term effect).

Abbreviations: CI, confidence interval; IV, independent variable; PA, physical activity; PR, pulmonary rehabilitation; SMD, standardized mean difference.

were also achieved after the addition of an urban walking circuit promotion program to usual care 12 months after PR (0.59 [0.12–1.07]; [Table S4](#)).⁵²

The addition of self-management to community-based ET moderately improved incremental shuttle walk distance at 12 months (0.43 [0.09–0.77]; [Table S4](#)).¹⁸ Improvements in endurance shuttle walk time were present after individualized ET compared to general ET at 2 months (0.72 [0.35–1.09]; [Table S4](#)).²³

Effects of PA interventions on HRQL

Compared to usual care, only Nordic walking enhanced HRQL using the 36-Item Short Form Survey (SF36) physical performance domain at 3 months (1.17 [0.58–1.76]; [Table S5](#)).¹⁷ Effects were sustained when reassessed 9 months post-intervention (1.61 [0.98–2.24]; [Table S5](#)).¹⁷

Pedometer-based counseling produced moderate to large effects on HRQL measured using SGRQ at 3 months when compared to standard counseling in two studies (0.43 [0.03–0.83] and 1.04 [0.00–2.07]; [Table S5](#)).^{34,35} One month of activity counseling via tele-rehabilitation produced moderate effects on Clinical COPD Questionnaire when compared to ET (0.53 [1.17–0.22]; [Table S5](#)).³⁸

None of the included interventions showed important effects on dyspnea or lung function when compared to their comparators at measured time points ([Tables S6](#) and [S7](#)).

Discussion

This systematic review found that when compared to usual care, ET including Nordic walking,¹⁷ supervised exercise¹⁹ and self-efficacy enhancing exercise²⁰ produce large effects on PA levels in COPD. These effects were not sustained after a long-term exercise maintenance program.^{15,24} While PA counseling alone failed to improve PA, the addition of counseling to PR programs succeeded in producing an important increase in activity levels^{25,27,29,30,33} compared to

PR alone. Moreover, nutritional^{46,47} and pharmaceutical⁴⁵ interventions significantly increased PA compared to placebo; however, insufficient data and poor methodological quality restricted pooled ES calculations for these interventions. Of all included interventions, only individualized and pedometer-based counseling added to multidisciplinary PR program produced changes that exceeded the newly established MID in daily steps for COPD.^{25,27,29,30}

While PR alone achieved important increases in activity levels,⁶ compared to usual care at 4 months, our analysis showed that providing persistent and individualized feedback on activity levels using wearable monitors in conjunction with PR achieved significant effects on activity levels that exceeded effects produced by PR alone after 3–6 months.^{25,27,29,30} Moreover, the addition of counseling to PR achieved significant differences in daily steps that exceeded the established MID in daily steps at 3 months while PR alone failed to produce comparable outcomes at similar time points. It is important to mention that, of the included studies that evaluated the addition of counseling to PR, three of four studies failed to blind assessors, which indicates a low methodological quality. While this report shows that effects of the combination of PR and activity counseling significantly increased PA in COPD, high-quality research, ideally using large samples followed up for long periods, would shed light on the true effects of this comprehensive strategy.

Current research concentrates on the importance of lifestyle behavioral change interventions to improve PA.⁵⁴ Examples of strategies that implement behavioral change are pedometer-based activity counseling, motivational interviewing and well-constructed self-management interventions.^{55,56} Failure to report robust effects of these interventions may be linked with the wide heterogeneity of self-management interventions. An international expert group has recently published a consensus definition of the construct of self-management.⁵⁷ Future studies should establish programs

Table 3 Studies comparing PA interventions versus another active intervention

Study	Intervention	Control	Outcome (unit)	Intervention arm		Control arm		ES (95% CI)
				n	Mean (SD)	n	Mean (SD)	
Studies that showed effect of ET when compared to another PA intervention (n=3)								
Effing et al ¹⁸	ET and self-management	Self-management	Daily steps (n)	55	815.6 (2,659.4)	55	-374.8 (2,272.3)	0.48 (0.10–0.86)
Pomidorì et al ²¹	Home-based walking with fixed speed	Home-based walking with fixed distance	Daily METs (3.5 mL/kg-min)	18	0.17 (0.14)	18	0.04 (0.13)	0.94 (0.25–1.63)
			Daily METs peak (3.5 mL/kg-min)	18	0.16 (0.20)	18	0.06 (0.13)	0.58 (–0.09 to 1.25)
			Daily highest MVPA (>3 METs) time in 7 days (min)	18	35 (32)	18	13 (28)	0.72 (0.04–1.39)
Probst et al ²²	High-intensity and whole-body ET	Light-intensity and breathing ET	Daily steps (n)	20	4,179 (646.7)	20	4,278.6 (796)	–0.13 (–0.76 to 0.49)
			Daily walking (min)	20	52.7 (40.4)	20	43.5 (26.7)	0.26 (–0.36 to 0.89)
			Daily activities cost >3 METs (min)	20	74 (18.7)	20	53.1 (16.4)	1.16 (0.49–1.84)
			Daily total EE (kcal)	20	1,312.3 (119.4)	20	1,347 (199)	–0.21 (–0.83 to 0.41)
			Daily activity cost >3 METs EE (kcal)	20	408 (118.3)	20	343.8 (442.4)	0.19 (–0.43 to 0.82)
Studies that showed effects of self-management or counseling models when compared to another PA intervention (n=3)								
Mendoza et al ³⁴	Pedometer-based counseling	Standard counseling	Daily steps (n)	50	3,080 (3,254.8)	47	138.3 (1,950.4)	1.08 (0.65–1.51)
Moy et al ³⁵	Internet-mediated pedometer-based program	Pedometer recording only	Daily steps (n)	133	447 (1,817)	68	–346 (1,949)	0.84 (0.59–1.08)
Nguyen et al ⁴⁰	Internet-mediated dyspnea self-management program	General EDU	SR weekly exercise duration (min)	43	221 (184)	41	115 (186)	0.57 (0.13–1.00)

Note: Δ, change from baseline.

Abbreviations: CI, confidence interval; EDU, education; EE, energy expenditure; ET, exercise training; ES, effect size; M, month(s); METs, metabolic equivalent tasks; min, minutes; MVPA, moderate to vigorous PA; PA, physical activity; SR, self-reported; W, week(s).

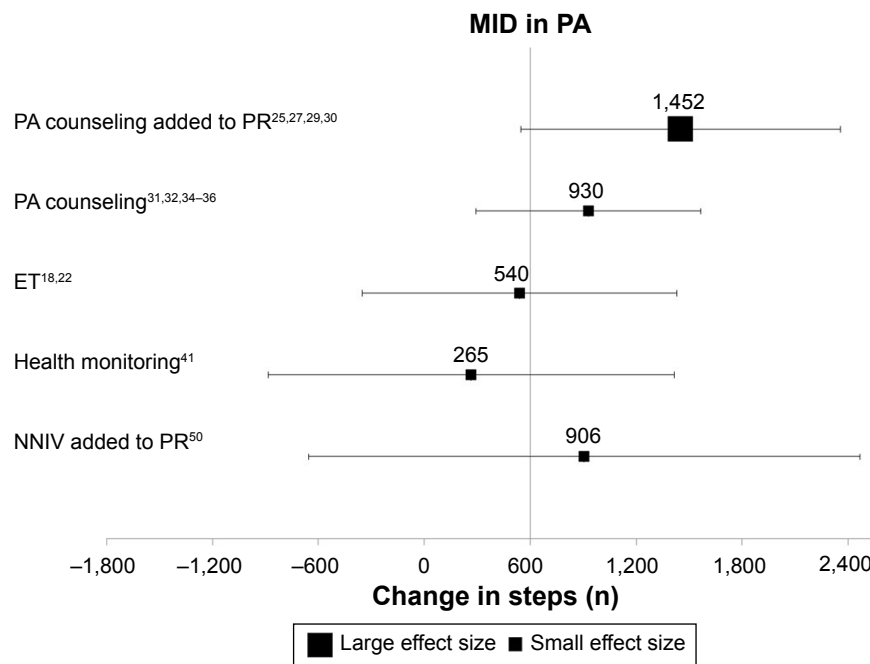


Figure 5 Comparison between differences in daily steps achieved by PA interventions according to the MID of daily steps in COPD.

Abbreviations: ET, exercise training; MID, minimal important difference; NNIV, nocturnal noninvasive ventilation; PA, physical activity; PR, pulmonary rehabilitation.

based on such robust definitions to improve the likelihood of positive outcomes and ensure that interventions are replicable.

Recommendations to improve PA in COPD inspired by other chronic health conditions stressed the importance of developing “stealth interventions”.⁵⁸ These interventions aimed to indirectly improve PA by reducing sedentary behavior time and, as a result, improve light-intensity PA. Reductions in sedentary time are known to reduce cardiovascular risk in other groups.⁵⁹ This is highly relevant to people with COPD, many of whom have cardiovascular comorbidities. Of the studies included in this systematic review, only one studied the effects of PA-focused behavioral counseling using pedometer feedback and motivational interviewing added to 8 months of PR. This study demonstrated significantly reduced sedentary time when compared to PR alone at 3 months (0.96 [0.14–1.78]).²⁹ A recent RCT compared an intervention aimed to increase the time spent in high-intensity activities versus another focused on reducing sedentary time in older adults and suggested that targeting sedentary behavior is more effective in improving physical function.⁶⁰ Future trials should aim to assess the impact of PA interventions on sedentary time in COPD.

While only ET including Nordic walking,¹⁷ community-based¹⁸ training and individualized exercise²³ programs showed large effects on exercise tolerance in people with COPD, these effects do not appear to have a direct relationship with improvements in PA or other important

outcomes such as HRQL or dyspnea. However, PA counseling showed small and insignificant effects on exercise tolerance levels while achieving significant improvements in HRQL.^{34,35,38} These findings suggest that the integration between ET and activity counseling interventions may be imperative in achieving important effects on patient-focused outcomes in people with COPD.

Limitations of the systematic review

Although the overall quality score of the included trials was moderate, 12 included studies demonstrated low quality as assessed by PEDro scale. Low methodological quality was mainly due to lack of concealed allocation and blinding of assessors, which might affect the strength of evidence summarized in this report. A second limitation was the inability to pool all data in a meta-analysis and compute overall effects. The wide heterogeneity of included interventions, assessment time points and frequency of treatment hindered further analysis attempts. The results reported in this systematic review should be interpreted with caution due to these limitations. It is imperative that future trials in this field select high-quality designs and methodology with long-term follow-ups to report sustainability of true effects on PA in COPD.

Much work is under way to address inactivity in COPD. Recently published protocols describe large RCTs designed to test the effects of home-based PR using motivational interviewing,⁶¹ patient-centered home and community-based

PA coaching program,⁶² an integrated pharmacological, ET and self-management program (the PHYSACTO trial)⁶³ and behavioral change self-management program⁶⁴ on activity levels using high-quality methodology. The outcomes of these refined interventions may provide more certainty regarding the most effective interventions to improve PA in COPD.

Conclusion

This review concluded that while ET alone can improve PA in COPD, greater improvements can be made with the addition of PA counseling. Introducing an activity counseling program in conjunction with PR might be essential to enhance PA in people with COPD. Perhaps this sophisticated model will also produce positive effects on other important COPD outcomes such as exercise capacity and HRQL.

Disclosure

The authors report no conflicts of interest in this work.

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