Original research

Efficacy of unsupervised exercise in adults with obstructive lung disease: a systematic review and meta-analysis

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ABSTRACT

Introduction The benefits of unsupervised exercise programmes in obstructive lung disease are unclear. The aim of this systematic review was to synthesise evidence regarding the efficacy of unsupervised exercise versus non-exercise-based usual care in patients with obstructive lung disease.

Methods Electronic databases (MEDLINE, CINAHL, Embase, Allied and Complementary Medicine Database, Web of Science, Cochrane Central Register of Controlled Trials and Physiotherapy Evidence Database) and trial registers (ClinicalTrials.gov, Current Controlled Trials, UK Clinical Trials Gateway and WHO International Clinical Trials Registry Platform) were searched from inception to April 2020 for randomised trials comparing unsupervised exercise programmes with non-exercise-based usual care in adults with chronic obstructive pulmonary disease (COPD), non-cystic fibrosis bronchiectasis or asthma. Primary outcomes were exercise capacity, quality of life, mortality, exacerbations and respiratory cause hospitalisations.

Results Sixteen trials (13 COPD, 2 asthma, 1 chronic bronchitis: 1184 patients) met the inclusion criteria. Only data on COPD populations were available for meta-analysis. Unsupervised exercise resulted in a statistically but not clinically significant improvement in the 6-Minute Walk Test (n=5, MD=22.0 m, 95% CI 4.4 to 39.6 m, p=0.01). However, unsupervised exercise did lead to statistically significant and clinically meaningful improvements in St. George's Respiratory Questionnaire (n=4, MD=−11.8 points, 95% CI −21.2 to −2.3 points, p=0.01) and Chronic Respiratory Disease Questionnaire domains (dyspnoea: n=4, MD=0.5 points, 95% CI 0.1 to 0.8 points, p<0.01; fatigue: n=4, MD=0.7 points, 95% CI 0.4 to 1.0 points, p<0.01; emotion: n=4, MD=0.5 points, 95% CI 0.2 to 0.7 points, p<0.01; mastery: unable to perform meta-analysis) compared with non-exercise-based usual care.

Discussion This review demonstrates clinical benefits of unsupervised exercise interventions on health-related quality of life in patients with COPD. High-quality randomised trials are needed to examine the effectiveness of prescription methods.

Key messages

What is the key question?

- Are unsupervised exercise interventions effective for inducing improvements in exercise capacity, quality of life and healthcare use outcomes?

What is the bottom line?

- Unsupervised exercise interventions are effective at improving St. George's Respiratory Questionnaire and Chronic Respiratory Disease Questionnaire domain scores, but do not result in clinically meaningful improvements in the 6-Minute Walk Test.

Why read on?

- This systematic review provides a wealth of information on interventions used to date, as well as synthesised data on commonly used clinical outcomes in relation to unsupervised exercise.

INTRODUCTION

There is a strong evidence base showing the effectiveness of supervised exercise interventions, such as traditional centre-based pulmonary rehabilitation, for the management of obstructive lung disease as demonstrated by improvements in symptoms, exercise capacity and quality of life outcomes.[1–3] When delivered following acute exacerbations of chronic obstructive pulmonary disease (COPD), such supervised interventions also reduce hospitalisations.[4] Despite these points, relatively few people with obstructive lung disease have access to such programmes or may find it difficult to engage with, or adhere to, face-to-face exercise programmes delivered in a supervised setting.[5 6] Barriers to access and long-term adherence include time requirements, travel constraints and the use of specialist equipment, which may not be available in the home setting.[7 8]

With the clear benefits of exercise interventions and the issues surrounding compliance, it is important to adapt programmes to various patient needs. One approach to addressing common barriers with supervised exercise programmes, such as time requirements and travel constraints (for both the healthcare professionals and patients), is to tailor programmes to be delivered in the patient's home in an unsupervised manner. Some studies have compared supervised exercise programmes to unsupervised programmes[9 10] and suggest unsupervised interventions might be able to offer time, space and/

► Additional material is published online only. To view, please visit the journal online (http://dx.doi.org/10.1136/thoraxjnl-2020-216007).

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Received 17 August 2020
Revised 18 January 2021
Accepted 9 February 2021

To cite: Taylor D, Jenkins AR, Parrott K, *et al*. *Thorax* Epub ahead of print: [*please include* Day Month Year]. doi:10.1136/thoraxjnl-2020-216007

or cost-effective ways to improve exercise adherence, fitness and symptoms. While there have been systematic reviews examining the efficacy of exercise interventions for patients with COPD across different settings, they have not specifically examined the efficacy of unsupervised exercise versus usual care.[11] There is a lack of clarity in the way unsupervised exercise interventions are defined (eg, home rehabilitation, telerehabilitation or self-management programmes), and to the best of our knowledge, there are no reviews to date which have compiled all of the available evidence on unsupervised exercise interventions across multiple obstructive lung diseases. Such evidence would provide valuable information to healthcare providers in the management of obstructive lung disease, particularly in settings where resources are limited for delivering supervised exercise interventions.

The objectives of this systematic review were to establish an up-to-date synthesis of available evidence from randomised controlled trials and to derive estimates of effect for unsupervised exercise interventions on functional exercise capacity, quality of life and healthcare use outcomes for people with obstructive lung disease.

METHODS

The protocol for this study (CRD42018092273) was registered in advance on PROSPERO (International Prospective Register of Systematic Reviews, www.crd.york. ac.uk/PROSPERO/).

Participants/population

Adults (ie, >18 years) with a clinical diagnosis of COPD, non-cystic fibrosis bronchiectasis or asthma, as defined by the authors of included studies, were included.

Intervention

Studies were included if patients were randomised to an unsupervised exercise training intervention. For the purposes of this review, exercise was defined as 'physical activity consisting of planned, structured and repetitive bodily movement done to improve and/or maintain one or more components of physical fitness'.[12] The following criteria were applied for an unsupervised exercise intervention to be considered for inclusion: includes aerobic and/or resistance-based exercises; evidence of prescription to participants (ie, frequency, intensity, time and type of exercise (FITT) principles); a baseline assessment of exercise performance (if assessing exercise capacity as an outcome); can run alongside a supervised or unsupervised education programme; can include an introductory supervised 'run in' period of up to 2 weeks, which is for the purposes of demonstration, instruction or familiarisation, but not a formal supervised programme (eg, pulmonary rehabilitation); and can include remote contact with healthcare professionals using technologies such as telephones or tablet/smart devices, as long as this does not take place during exercise (ie, real-time instruction/coaching).

Comparator

The comparator was any concurrent control group that did not receive an exercise intervention (including referral to pulmonary rehabilitation in the study period). Any study that had a control arm/usual care of non-exercise-based interventions (eg, education, counselling and breathing/relaxation/airway clearance therapy) was still included if the intervention arm also received these treatments.

Outcomes

Primary outcomes were exercise performance/capacity (eg, 6-Minute Walk Test (6MWT), Incremental Shuttle Walk Test (ISWT) and Endurance Shuttle Walk Test (ESWT)), health-related quality of life (HRQoL) (eg, St. George's Respiratory Questionnaire (SGRQ), Chronic Respiratory Disease Questionnaire (CRQ), Hospital Anxiety and Depression Score and Asthma Control Questionnaire), disease impact (Chronic Obstructive Pulmonary Disease Assessment Tool (CAT)), all-cause mortality, exacerbations and respiratory cause hospitalisations.

Secondary outcome measures were all-cause hospitalisations, length of hospital stay, emergency department visits, outpatient visits, general practitioner visits, adverse events, aerobic fitness/capacity, peripheral muscle strength, physical activity levels (PALs) and activities of daily living.

Study design

Studies were considered for inclusion if they adopted a randomised controlled trial design with randomisation of participants at an individual or cluster level or quasi-randomised method. Randomised cross-over trials, up to the point of cross-over, were also eligible.

Search strategy

To identify any relevant ongoing or published systematic reviews, searches were conducted using Database of Abstracts of Reviews of Effects, PROSPERO and the Cochrane Database of Systematic Reviews.

The following bibliographic databases, platforms and trial registers were searched: MEDLINE, CINAHL, Embase, Web of Science Core Collection, Cochrane Central Register of Controlled Trials, Physiotherapy Evidence Database, Allied and Complementary Medicine Database, ClinicalTrials.gov, Current Controlled Trials, UK Clinical Trials Gateway and WHO International Clinical Trials Registry Platform. Searches were completed within each source from inception to April 2020 with no limits set on language. Attempts were made to translate any relevant non-English language texts. These searches were supplemented with internet searches (ie, Google Scholar), Conference Proceedings Index (Web of Science), forward and backward citation tracking from included studies, review articles and contact with study authors.

Search terms were structured around the population (eg, "Lung Diseases, Obstructive"), intervention (eg, "Exercise") and study type (eg, "randomised"). An example of a full search strategy is presented in online supplemental table S1.

Search results were compiled using EndNote referencing software (Clarivate Analytics, Philadelphia, Pennsylvania, USA). Following removal of duplicate citations, two reviewers screened titles and abstracts independently. For studies that were not excluded based on title/abstract, full-text papers were requested and independently assessed by two reviewers for eligibility. Any discrepancies in decisions of study eligibility were resolved through discussion, and, if required, a third reviewer.

Data extraction and quality appraisal

Data extraction was completed using an adapted form on Microsoft Excel based on the Cochrane Data Extraction Template. The characteristics and data extracted are listed in online supplemental table S2. One reviewer undertook data extraction for each study, with the accuracy of this extraction cross-checked by a second reviewer.

Risk of bias (quality) assessment

Two reviewers independently assessed the risk of bias within the included studies using the Cochrane Tool for Risk of Bias, in accordance with the Cochrane Handbook. The domains evaluated were selection bias, performance bias, detection bias, attrition bias, reporting bias and other bias.[13] Each of these domains were categorised as having high, low or unclear risk of bias, with the overall risk of bias for each study then determined as high (more than two 'unclear' domains or more than one 'high'-risk domain), moderate (two unclear domains or one high-risk domain) or low (no unclear or high-risk domains). Any disagreements in risk of bias assessments were resolved through further discussion and, if required, the input of a third reviewer.

Strategy for data synthesis

All meta-analyses were performed using Review Manager V.5.4 and in accordance with Cochrane guidance.[13] We contacted study authors to obtain any missing numerical outcome data. In very few cases, where all methods to obtain data had been exhausted, estimates of effect for individual studies were extracted from previous systematic reviews and guideline documents. Measures of effect were mean differences for all continuous outcomes. We focused on changes from baseline to end of intervention period for continuous outcomes as this was the method of reporting that was most common across studies and to help remove between-person variability from the analysis. For individual studies where SD of changes was not available, we calculated using other reported parameters (eg, 95% CIs), imputed using correlation coefficients derived from other studies in the same meta-analysis or assuming a conservative correlation coefficient of 0.5, or (for unstandardised mean difference estimates only) opted to use post-intervention values only in the analysis. Risk ratios were used for dichotomous outcomes. Individual study data for continuous and dichotomous outcomes were combined statistically using an inverse random-effects method. Statistical heterogeneity in all meta-analyses was interpreted by the I^2 value. In meta-analyses where the I^2 statistic was greater than 40%, potential sources of the statistical heterogeneity were explored. We prespecified subgroup analysis to explore heterogeneity in the primary outcomes according to the following clinical and methodological factors: diagnosis (COPD, bronchiectasis and asthma) and severity of disease; exercise intervention characteristics (FITT principles, methods of delivery or support, including run-in period); comparator (no intervention or non-exercise-based intervention); outcome measures (generic or disease-specific, objective or self-reported); and study design (allocation method/duration of follow-up). There was only one primary outcome where the I^2 statistic was greater than 40% and could be resolved by our prespecified subgroups. For this meta-analysis (SGRQ), heterogeneity was best explained by exercise intervention characteristics. We did not perform subgroup analyses on any other primary outcomes. We also planned to perform sensitivity analysis by excluding studies with a moderate or high risk of bias, but this was not possible due to a lack of studies with a low risk of bias.

RESULTS

After duplicates were removed, searches identified 6240 records for screening, of which 4362 records were excluded based on title and 1602 on abstract. Full texts were obtained for the remaining 276 records, of which 16 studies met the inclusion criteria (figure 1).

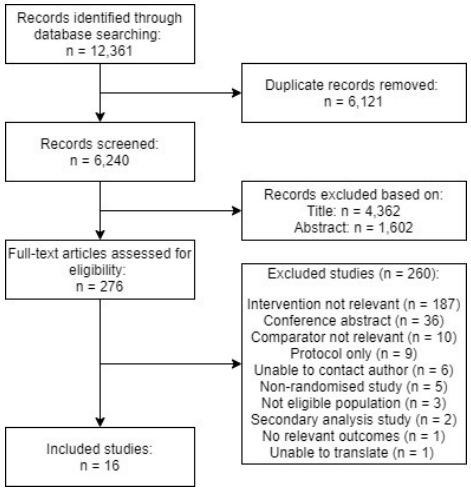

Figure 1 Flow diagram of the study selection.

Characteristics of included studies

The 16 included studies were published between 1977 and 2020 (online supplemental table S3). Of the included studies, 13 focused on COPD[14–26]; 2 focused on asthma[27 28]; and 1 focused on chronic bronchitis[29] as an obstructive lung disease. A total of 1184 patients with obstructive lung disease (1055 COPD, 105 asthma and 24 chronic bronchitis) were randomised, of which 59% were men. Study sample sizes varied in size between 16 and 191 patients. COPD disease severity varied from mild to very severe, and asthma varied from mild to moderate.

All studies were randomised controlled trials, which allocated patients to either a control group (usual care) or to an intervention, including unsupervised exercise. The control group in some studies received educational support,[22 24 25] telephone calls[22 25 26] and clinic follow-ups,[19 29] in addition to usual care. The unsupervised exercise interventions lasted between 6 weeks and 1 year. Exercise sessions varied in session frequency, from 2 days a week to daily exercise. Desired exercise intensity was not reported in all studies, but of those which reported set exercise intensity, there was variation with exercise programmes ranging from moderate to high intensity.[16 18–22 24 26] The designed exercise programmes covered aerobic, resistance and strength training. The characteristics of included studies which were used in the meta-analysis are summarised in table 1. A detailed overview of the characteristics of all eligible studies is shown in online supplemental table S3.

The risk of bias assessment was hindered by poor study reporting (online supplemental table S4).

Primary outcomes

Exercise capacity

6-Minute Walk Test

Meta-analysis of five trials[17 18 22 25 26] in patients with COPD demonstrated a statistically significant improvement in 6MWT performed with unsupervised exercise (MD=22.0 m, 95% CI 4.4 to 39.6 m, p=0.01) (figure 2A). Statistical heterogeneity was not apparent (I^2=0%). However, the magnitude of effect did not meet the threshold of 30 m for clinically important improvement.[30] Four further trials reported 6MWT as an outcome[14–16 20] in a COPD population, but data could not be obtained from one study,[16] and in three other studies,[14 15 20] data could only be retrieved from previous systematic reviews.[1 30 31] Extraction of trial data from previous reviews is not a widely accepted approach, but analysis with the three additional studies is

Table 1 Characteristics of included studies in the meta-analysis

	Bourbeau *et al* 2003[15] (Canada)	Chen *et al* 2018[17] (China)	Elçi *et al* 2008[18] (Turkey)	Hernández *et al* 2000[19] (Spain)	Ho *et al* 2012[21] (Taiwan)	Lahham *et al* 2020[22] (Australia)	Mitchell *et al* 2014[23] (UK)	Moore *et al* 2009[24] (UK)	Nguyen *et al* 2013[25] (USA)	Pradella *et al* 2015[26] (Brazil)
Respiratory diagnosis and disease severity	COPD Stable, moderate–severe	COPD Stable, moderate–very severe	COPD GOLD stages I–IV	COPD Stable, moderate	COPD Stable, mild–very severe	COPD Stable, mild	COPD Stable, mild–very severe	COPD Stable, moderate–severe	COPD Stable, mild–very severe	COPD Stable, mild–very severe
Intervention description and duration	Home-based exercise intervention for 1 year	Home-based lower-limb exercise intervention for 12 weeks	Home-based PR programme targeting lower (walking) and upper limbs (weights) with 24 sessions over 3 months	Home/outdoor-based walking exercise programme for 12 weeks	Home-based walking exercise programme paced to music for 12 weeks	Home-based aerobic (walking) and resistance (upper and lower limb) exercise training for 8 weeks	Home-based manual incorporating education and exercise programme (walking, upper and lower limb resistance training using weights) for 6 weeks	Home-based high intensity interval exercise video/DVD for 6 weeks	Self-management programme incorporating exercise intervention (online or face-to-face) for 12 months	Home-based walking PR programme for 24 sessions
Exercise frequency	3 days/week	3 days/week	2 days/week	6 days/week	5 days/week	5 days/week	Daily (walking), 3 days/week (upper and lower limb training)	4 days/week	4 days/week	3 days/week
Exercise intensity	Guided by Borg score	Best effort, not exceeding Borg score of 5	75% of 6MWT speed (walking)	≥70% of max speed of ISWT	80% VO_2peak initially, increased gradually each month based on ISWT	80% of walking speed from 6MWT Intensity gauged by Borg scale	Not reported	High intensity	Gauged by Borg score	60%–70% HRmax
Exercise time (min)	30–45	20–30	90	60	30	30	30 min (walking), not reported (resistance)	30	30	40
Exercise type	Aerobic and resistance	Resistance	Aerobic and resistance	Aerobic	Aerobic	Aerobic and resistance	Aerobic and resistance	Aerobic and resistance	Aerobic and resistance	Aerobic
Intervention run-in period	Supervised session at home	One study visit	One supervised session	Home visit	One research visit	Home visit	One study visit	One study visit	Home visit	1 week run-in at rehab centre
Additional support	Living well with COPD booklet (supervised education component) Monthly telephone calls	Exercise supervised by family member	Exercise supervised by family member and weekly telephone calls	2-week reviews at hospital	Monthly reviews and progression	Weekly motivational interviewing Better living with COPD booklet	Biweekly phone calls using motivational interviewing	Education material	Biweekly reinforcement and feedback with motivational interviewing	Educational booklet and weekly phone call
Comparator	Same level of care without add-on management programme	Usual care	Usual care	Usual care and 2-week reviews at hospital	Usual care	Usual care and weekly phone calls. Better living with COPD booklet	Usual care	Usual care and education booklet	Usual care, biweekly phone calls and education	Usual care and weekly phone call

COPD, chronic obstructive pulmonary disease; GOLD, Global Initiative for Chronic Obstructive Lung Disease; HRmax, maximum heart rate; ISWT, Incremental Shuttle Walk Test; 6MWT, 6-Minute Walk Test; PR, pulmonary rehabilitation; VO_2peak, peak oxygen consumption.

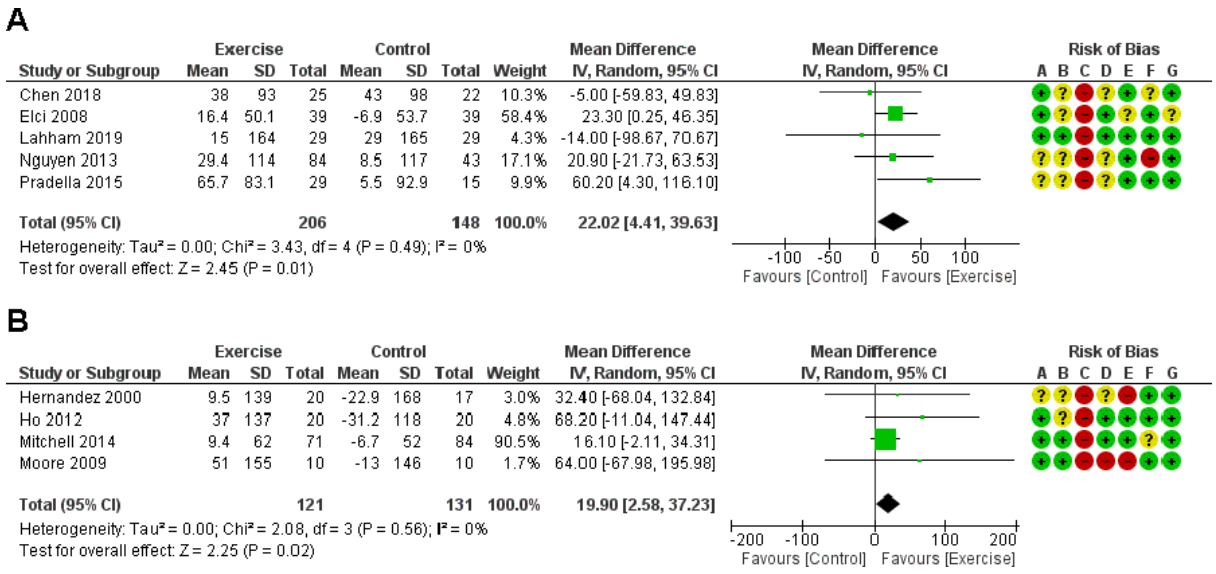

Figure 2 Trial-level data, effect estimates and forest plot of comparison for change in 6MWT distance following an unsupervised exercise intervention versus usual care in studies reporting 6MWT for which data were able to be obtained (A), and for change in ISWT following an unsupervised exercise intervention versus usual care (B). Risk of bias legend: A, random sequence generation (selection bias); B, allocation concealment (selection bias); C, blinding of participants and personnel (performance bias); D, blinding of outcome assessment (detection bias); E, incomplete outcome data (attrition bias); F, selective reporting (reporting bias); G, other bias. 6MWT, 6-Minute Walk Test; ISWT, Incremental Shuttle Walk Test; IV, inverse variance.

provided in online supplemental figure S1. Data from the three studies had a minimal effect on the overall magnitude of effect of unsupervised exercise interventions (MD=25.3 m, 95% CI −1.0 to 51.5 m, p=0.06), but their inclusion led to substantial heterogeneity (I^2=71%).

Incremental Shuttle Walk Test

Meta-analysis of four trials[19 21 23 24] in patients with COPD demonstrated a statistically significant improvement in ISWT performance with unsupervised exercise (MD=19.9 m, 95% CI 2.6 to 37.2 m, p=0.02) (figure 2B). Statistical heterogeneity was not apparent (I^2=0%). However, the intervention effect was heavily weighted towards one trial.[26]

Other reported outcomes

Single trials reported ESWT,[23] Endurance Treadmill Test[26] and 12-Minute Walking Distance [29] as outcome measures in COPD populations; therefore, meta-analyses could not be performed.

HRQoL and disease impact

St. George's Respiratory Questionnaire

Meta-analysis of four trials[15 18 21 26] in patients with COPD showed a statistically significant effect on SGRQ-Total (MD=−11.8 points, 95% CI −21.2 to −2.3 points, p=0.01) and SGRQ-Impact (MD=−12.0 points, 95% CI −19.7 to −4.2 points, p<0.01) scores with unsupervised exercise and favoured intervention effects which were not statistically significant for SGRQ-Symptoms (MD=−6.2 points, 95% CI −14.5 to −2.1 points, p=0.14) and SGRQ-Activity (MD=−12.8 points, 95% CI −25.9 to −0.3 points, p=0.06) scores. However, there was substantial heterogeneity within each domain analysis (SGRQ-Total, I^2=85%, p<0.01; SGRQ-Impact, I^2=74%, p<0.01; SGRQ-Symptoms, I^2=67%, p=0.03; SGRQ-Activity, I^2=89%, p<0.01).

SGRQ (subgroup analysis)

Prespecified subgroup analysis according to intervention period (short term ≤12 weeks vs long term >12 weeks) demonstrated a greater magnitude of effect with short-term intervention for SGRQ (SGRQ-Total, MD=−15.5 points, 95% CI −21.9 to −9.2 points, p<0.01; SGRQ-Impact, MD=−15.4 points, −21.6 to −9.1 points, p<0.01; SGRQ-Symptoms, MD=−9.7 points, 95% CI −18.4 to −0.9 points, p=0.03; SGRQ-Activity, MD=−18.8 points, 95% CI −24.9 to −12.7 points, p<0.01). Heterogeneity was reduced to levels deemed to be unimportant for SGRQ-Total (I^2=33%), SGRQ-Impact (I^2=25%) and SGRQ-Activity (I^2=4%). Heterogeneity was only reduced to moderate levels with SGRQ-Symptoms (I^2=44%) (figure 3A–D). One further trial reported SGRQ as an outcome[28] in asthma patients, but data could not be obtained for meta-analysis.

Chronic Respiratory Disease Questionnaire

Meta-analysis of four trials[19 22–24] in patients with COPD showed a statistically significant improvement on CRQ-Dyspnoea (MD=0.5 points, 95% CI 0.1 to 0.8 points, p<0.01), CRQ-Fatigue (MD=0.7 points, 95% CI 0.4 to 1.0 points, p<0.01) and CRQ-Emotion (MD=0.5 points, 95% CI 0.2 to 0.7 points, p<0.01) scores with unsupervised exercise. Levels of heterogeneity were considered to be unimportant (CRQ-Dyspnoea, I^2=36%; CRQ-Fatigue, I^2=37%; CRQ-Emotion, I^2=0%) (figure 4A–C). There was substantial heterogeneity for CRQ-Mastery scores (I^2=93%, p<0.01). This could not be explained by any prespecified clinical or methodological factors; hence, meta-analysis was deemed inappropriate. One further trial reported CRQ as an outcome[25] in a COPD population, but domain data could not be obtained for meta-analysis.

Medical Research Council (MRC) Dyspnoea Scale

Meta-analysis of three trials[18 19 22] in patients with COPD showed a statistically significant improvement in MRC breathlessness

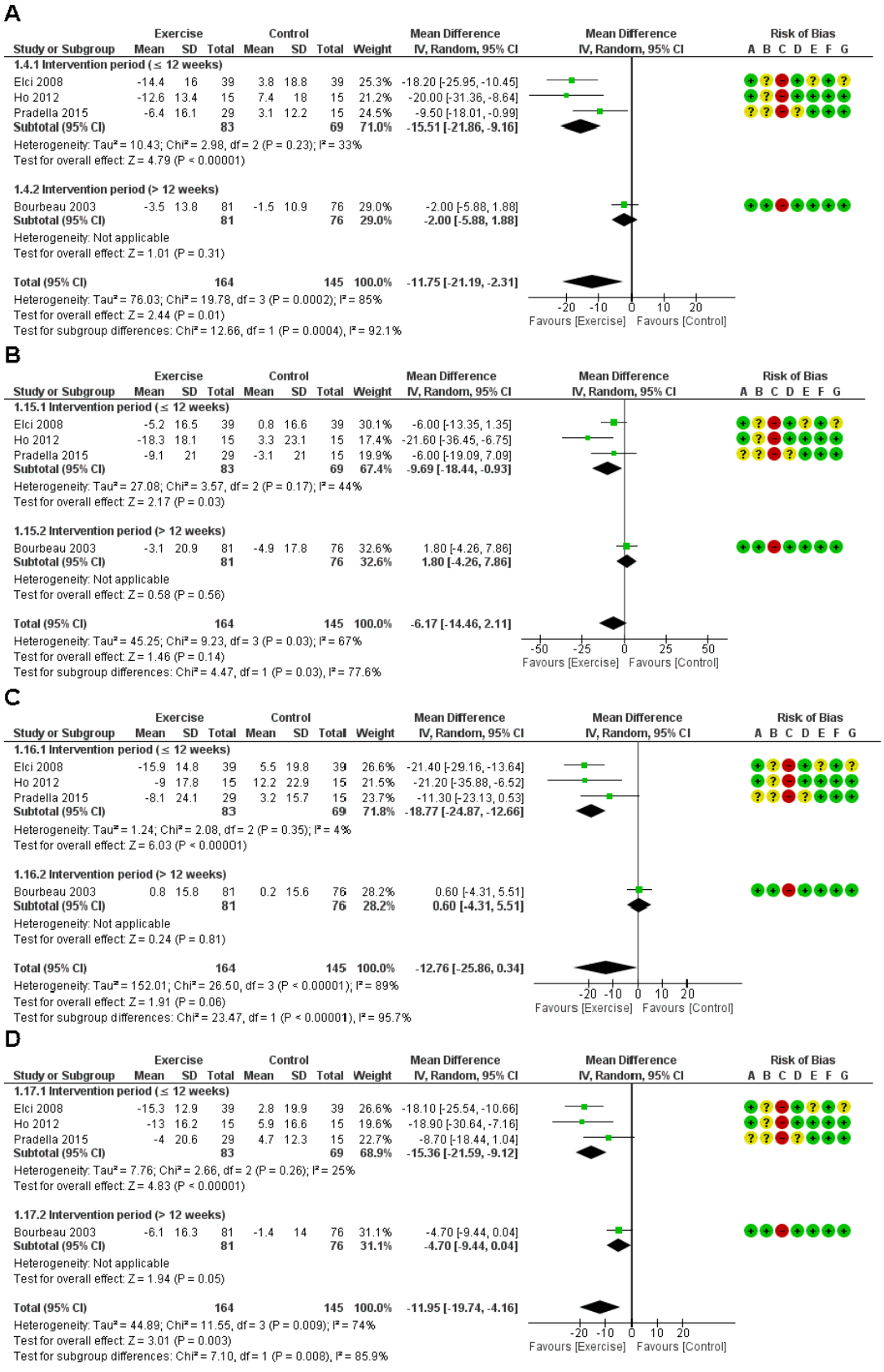

Figure 3 Trial-level data, effect estimates and forest plot of comparison for change in SGRQ-Total (A), SGRQ-Symptoms (B), SGRQ-Activity (C) and SGRQ-Impact (D) scores following an unsupervised exercise intervention versus usual care in all studies reporting SGRQ-Total and domain scores with prespecified subgroup analysis according to duration of interventions. Risk of bias legend: A, random sequence generation (selection bias); B, allocation concealment (selection bias); C, blinding of participants and personnel (performance bias); D, blinding of outcome assessment (detection bias); E, incomplete outcome data (attrition bias); F, selective reporting (reporting bias); G, other bias. IV, inverse variance; SGRQ, St. George's Respiratory Questionnaire.

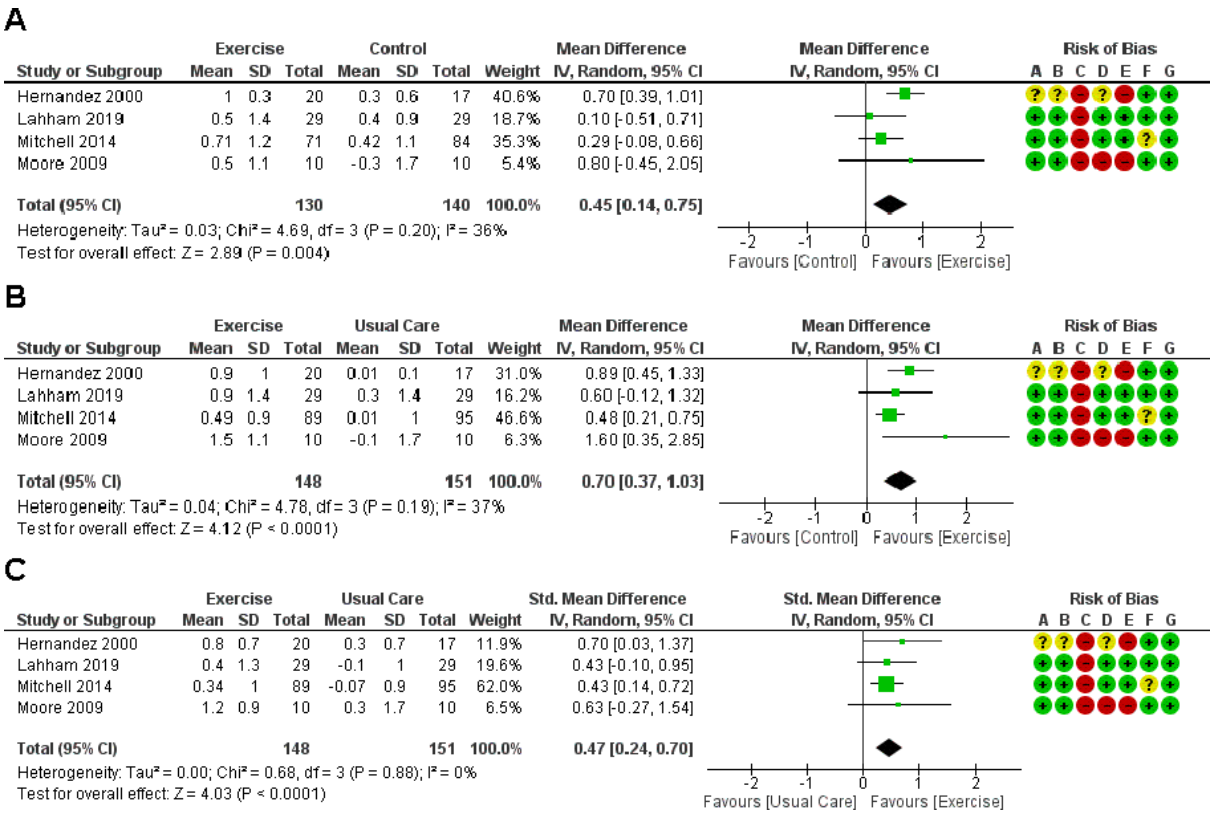

Figure 4 Trial-level data, effect estimates and forest plot of comparison for change in CRQ-Dyspnoea (A), CRQ-Fatigue (B) and CRQ-Emotion (C) scores following an unsupervised exercise intervention versus usual care in all studies reporting CRQ domain scores. CRQ-Mastery scores were not meta-analysed due to substantial unexplained heterogeneity. Risk of bias legend: A, random sequence generation (selection bias); B, allocation concealment (selection bias); C, blinding of participants and personnel (performance bias); D, blinding of outcome assessment (detection bias); E, incomplete outcome data (attrition bias); F, selective reporting (reporting bias), (G) other bias. CRQ, Chronic Respiratory Disease Questionnaire; IV, inverse variance.

score with unsupervised exercise (MD=−0.3 points, 95% CI −0.5 to −0.1 points, p<0.01) (figure 5). Statistical heterogeneity was not apparent (I^2=0%). One further trial[19] reported on dyspnoea using Baseline Dyspnoea Index (BDI) / Transition Dyspnoea Index (TDI) in patients with COPD and therefore was not included in the meta-analysis.

Other reported outcomes

Anxiety and depression in patients with COPD,[14 18 23] asthma control,[27 28] CAT[16 17] and 36-Item Short Form Health Survey in patients with COPD[18 25] were reported as outcomes, but the use of a mixture of different measurement tools and/or being unable to obtain suitable data deemed meta-analysis inappropriate.

Healthcare use

Hospitalisations (respiratory cause), mortality and exacerbations

One trial presented data on respiratory cause hospital admissions, mortality and exacerbations[15]; therefore, a meta-analysis could not be performed for these outcomes. A further trial presented data on respiratory cause hospitalisations,[21] but data could not be obtained for meta-analysis.

Secondary outcomes

Hospitalisations (all cause)

One trial presented data on all-cause hospitalisations[21]; therefore, a meta-analysis could not be performed for these outcomes.

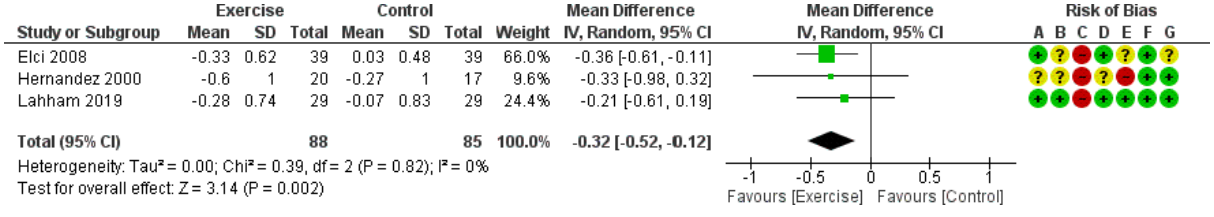

Figure 5 Trial-level data, effect estimates and forest plot of comparison for change in MRC score following an unsupervised exercise intervention versus usual care. Risk of bias legend: A, random sequence generation (selection bias); B, allocation concealment (selection bias); C, blinding of participants and personnel (performance bias); D, blinding of outcome assessment (detection bias); E, incomplete outcome data (attrition bias); F, selective reporting (reporting bias); G, other bias. IV, inverse variance; MRC, Medical Research Council.

Other reported outcomes

Hospital length of stay in patients with COPD,[21] emergency department visits in patients with COPD,[15 21] outpatient visits in patients with COPD,[15] aerobic fitness in either COPD or asthma populations,[19 25 27–29] muscle strength in either COPD or asthma populations,[17 25 28] and PALs in patients with COPD[16 22] were reported as outcomes, but the use of different measurement tools and outcome measurements, or not being able to obtain data across studies meant these outcomes could not be meta-analysed. All trials reporting relevant outcomes which could not be included in meta-analyses are narratively summarised in online supplemental table S5.

DISCUSSION

Summary of main findings

To our knowledge, this is the first review to have synthesised data from randomised trials assessing the effect of unsupervised exercise interventions on functional exercise capacity, quality of life and healthcare use of people with obstructive lung disease in comparison to non-exercise based usual care. This systematic review provides evidence that unsupervised exercise interventions, in addition to non-exercise usual care, can improve the disease-specific quality of life of people with COPD by clinically meaningful amounts, but this is not seen with exercise capacity outcomes. Unfortunately, data were unavailable for meta-analyses from included studies of other obstructive lung diseases such as asthma, so the findings presented are only applicable to that of COPD. No studies of patients with bronchiectasis met the inclusion criteria for this review.

Interpretation of the results

6MWT was the most commonly reported measure of exercise capacity.[14 15 17 18 20 22 25 26] Based on a minimal clinically important difference (MCID) of 30 m,[32] the 22 m 6MWT improvement with unsupervised exercise cannot be considered clinically meaningful for people with COPD. This is in contrast to established literature demonstrating that supervised exercise interventions are effective at increasing exercise capacity,[1] which may indicate the importance of a supervision element.

While data synthesis from four trials[19 21 23 24] suggests that unsupervised exercise may improve ISWT performance by a statistically significant amount, this effect fell below the MCID for COPD (47.5 m),[33] echoing the findings observed with 6MWT. The meta-analysis for ISWT performance was heavily weighted by one large study which incorporated unsupervised exercise as part of a self-management programme,[23] with a 'light touch' approach for prescribing exercise and ensuring adherence, which may limit intervention effects. The larger estimate of effect seen in other included studies, which included a more formalised prescription, perhaps suggests that the lack of clinically meaningful improvement in ISWT with unsupervised exercise should be viewed with some caution.

In terms of quality of life outcomes, synthesised data suggest that unsupervised exercise leads to statistical and clinically meaningful improvements in total scoring of SGRQ[15 18 21 26] and domain scoring of CRQ.[19 22–24] Unsupervised exercise also improved MRC breathlessness score by −0.3 points,[18 19 22] but this fell short of the MCID of −1 point.[34] These findings are in keeping with those of a previous review which included supervised exercise training in people with COPD.[35] It is important to note, however, that due to unexplained heterogeneity, the effects of unsupervised exercise on the mastery domain of the CRQ are still unclear. Furthermore, there was evidence of heterogeneity in estimates of intervention effect on SGRQ. It would appear that the study of Bourbeau *et al*[15] may have been a key contributor to the significant heterogeneity, whereby a 12-month intervention was implemented. Despite reporting significant treatment effects at 4 months, this was not apparent at 12 months, casting doubt on the longer-term impact of unsupervised interventions.[15] It could be that the lack of formal prescription and adherence monitoring may have contributed to this lack of observed effect at the end of the intervention.[15] Given the relative lack of eligible studies over 12 weeks long, further high-quality research is needed to establish the longer-term benefits of unsupervised exercise.

There was a paucity of evidence reporting outcomes related to healthcare use, meaning meta-analysis was not possible. Considering the importance of healthcare use to the future health outcomes of all patients with obstructive lung disease,[36] it is imperative that more trials are conducted which examine the potential benefit of unsupervised exercise interventions on these outcomes.

A key strength of this review is that it is the first to have comprehensively searched for and synthesised data from randomised controlled trials of unsupervised exercise interventions across all obstructive lung diseases. This is the first systematic review to report significant and clinically meaningful improvements in disease-specific quality of life in these patients. In doing so, this review followed a preplanned and publicly available protocol. It is important to highlight that raw study data were obtained to increase the amount of studies in our analyses.

A limitation of our review is that, when writing the protocol, we did not expect such disparity between included trials in terms of how unsupervised exercise was defined, prescribed, monitored and reported. It is clear that the levels of heterogeneity seen across a number of reported outcomes may well be due to the diversity in methods of exercise prescription and support. Despite having success in requesting data for analyses, there were studies presenting relevant outcomes, which could not be obtained for meta-analysis, two of which were asthma focused,[27 28] meaning the findings of our meta-analysis are purely COPD focused. However, a narrative summary of the reported effects within individual studies for which data could not be obtained has been tabulated to supplement the meta-analyses presented. Similarly, our searches were current as of April 2020, and there are ongoing studies which may have been eligible for inclusion had they been completed prior to this date. For example, Zanaboni *et al*[37] are conducting a large multicentre randomised controlled trial with patients with COPD to examine the effects of a longer-term unsupervised exercise intervention on healthcare use, quality of life and exercise capacity. This study will be an important contribution to the area.

Implications to practice

Given the likely lower cost and time requirements with unsupervised exercise interventions, our review supports their potential use as part of the COPD treatment pathway. Supervised elements may need to be considered if the intervention is intended to maximise changes in exercise capacity, but further head-to-head evidence of supervised versus unsupervised programmes (as done in Holland *et al*[9] and Horton *et al*[10]) would be required to investigate this.

While substantial diversity among the specific interventions existed, the current data would suggest that

incorporating formal prescription relating to basic programming principles (ie, frequency, intensity, time and type) and facilitating compliance should be key considerations for practitioners. However, given the lack of consistency in how these factors have been included in research to date, it is not possible to provide further clarity on how to best integrate these aspects of unsupervised exercise prescription for patients with obstructive lung disease.

Implications to research

The quality of evidence presented within this review and meta-analysis is generally low. The poor reporting that was generally observed across the included studies in this review suggests future randomised controlled trials should work according to Consolidated Standards of Reporting Trials guidelines.

Despite the apparent benefits of unsupervised exercise for people with COPD, higher-quality large-scale randomised controlled trials are needed to examine the relative effectiveness of different approaches to prescription. The impact of further research on the existing evidence base can be highlighted by the CIs of our point estimates. Although we report the overall magnitude of effects in some outcome measures to be clinically meaningful, the majority of the CIs for these point estimates include between-group differences, which would not meet MCIDs. At the same time, the available evidence does not currently favour a clinically meaningful effect of unsupervised exercise on 6MWT, but the CI does contain a change that would surpass the MCID. To build on the existing evidence and for comparison against supervised exercise, it would be advantageous for future studies to incorporate the most common assessments of functional exercise capacity (6MWT and ISWT) and disease-specific quality of life (ie, SGRQ and CRQ), in addition to hospitalisation and exacerbation data.

In order to maximise the translation of findings to applied practice, more studies should examine unsupervised exercise interventions for obstructive lung diseases beyond COPD, across a wider range of disease severity, and should follow up patients over longer periods of time (ie, >12 weeks).

CONCLUSION

In conclusion, our systematic review and meta-analysis provides evidence that unsupervised exercise interventions result in improvements in HRQoL, but not necessarily exercise capacity. However, further higher-quality randomised trials are likely to have an important impact on our confidence in the estimates of effect, particularly to what extent these improvements are clinically meaningful. Despite our intentions to review the evidence in asthma and bronchiectasis, there remains a lack of trials to quantify the benefit of unsupervised exercise in these populations.

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Contributors DT: contribution to conception and design of the project, participation in acquisition: preparing and validation of search strategy, searching bibliographic databases, title and abstract screening, full-text screening and drafting of the manuscript. ARJ: participation in acquisition: preparing and validation of search strategy, searching bibliographic databases, title and abstract screening, full-text screening, data extraction, data analysis, drafting of the manuscript, verification and supervision over the project. KP: contribution to conception and design of the project, participation in acquisition: searching bibliographic databases, title and abstract screening, full-text screening, data extraction and drafting of the manuscript. AB: contribution to conception and design of the project, participation in acquisition: searching bibliographic databases, title and abstract screening, full-text screening, data extraction and drafting of manuscript. ST: contribution to conception and design of the project, participation in acquisition: searching bibliographic databases, title and abstract screening and drafting of manuscript. AWJ: contribution to conception and design of the project, participation in acquisition: preparing and validation of search strategy, searching bibliographic databases, title and abstract screening, full-text screening, data analysis, drafting of the manuscript, verification and supervision over the project.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement All data relevant to the study are included in the article or uploaded as supplementary information.

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Efficacy of unsupervised exercise in adults with obstructive lung disease: a systematic review and meta-analysis

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Supplementary material

Table S1. Example search strategy of a bibliographic database (CINAHL)

No.	Search Term	Field
1	Lung Diseases, Obstructive	MH
2	Bronchiectasis	MH
3	bronchiect*	TX
4	bronchoect*	TX
5	non$cystic fibrosis	TX
6	non$CF	TX
7	Asthma	MH, TX
8	Bronchoconstriction	MH
9	Bronchial Spasm	MH
10	Respiratory Hypersensitivity	MH
11	Bronchitis, Chronic	MH
12	Emphysema	MH, TX
13	chronic N3 bronchi*	TX
14	COPD	TX
15	COAD	TX
16	COBD	TX
17	AECB	TX
18	AECOPD	TX
19	1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18	
20	Exercise	MH
21	Therapeutic Exercise	MH
22	Exertion	MH
23	Physical Fitness	MH
24	Activities of Daily Living	MH
25	Telerehabilitation	MH
26	Exerc* N4 (train* OR fitness OR physi* OR condition* OR strength* OR resist* OR aerobic* OR intervent* OR therap* OR unsupervi* OR program*)	TI, AB
27	Self$manage*	TI, AB
28	physical activit*	TI, AB
29	Rehabilitat*	TI, AB
30	Home$rehab*	TI, AB
31	Home$based	TI, AB
32	Home N4 based	TI, AB
33	20 OR 21 OR 22 OR 23 OR 24 OR 25 OR 26 OR 27 OR 28 OR 29 OR 30 OR 31 OR 32	
34	Clinical trials	MH
35	Randomised Controlled Trials	MH
36	Random assignment	MH
37	Randomised OR randomized	TI, AB
38	Randomly	TI, AB
39	Trial	TI, AB
40	allocated N2 random*	TI, AB
41	34 OR 35 OR 36 OR 37 OR 38 OR 39 OR 40	
42	19 AND 33 AND 41	

Notes: *Truncation operator.

Table S2. List of extracted data and study characteristics

Data extraction	
Study details	- Date of study - Title - Author - Study aim(s) - Total study duration
Methods	- Study design - Intervention - Primary outcome(s) - Secondary outcome(s)
Participants	- Population demographics (age, gender, diagnosis/condition, disease severity, comorbidities) - Inclusion/Exclusion criteria - Total number randomised and randomisation ratio
Intervention/Comparators	- Number randomised to groups - Description of intervention and comparator (setting, method of delivery/support, content, frequency, intensity, time, type, duration) - Details of any 'run-in' session
Outcomes	- Outcome name and definition - Outcome type - Method of outcome measurement and reporting - Missing data and reasoning

Table S3. Characteristics of all included studies

Study (Country)	Sample size, Gender, Age	Inclusion/ Exclusion criteria	Respiratory diagnosis & disease characteristics	Study aim, Design, Unit of allocation	Exercise intervention (setting, components, duration, frequency)	Primary outcome (1) Other outcomes & follow up (2)
Booker, 1984 (1) (UK)	103 participants* Ex: n=32 Con: n=37 Phys: n=34 Age & Gender data not available	Not reported	COPD Disease characteristics not reported	To investigate the effects of progressive exercise training and physiotherapy on patients which Chronic Airflow limitation and to see if these effects were maintained once hospital visits had ceased. RCT, individual	Daily stair climbing intervention with progressive targets for 9-weeks. Study included 3-, 6- & 12-month follow-ups. F: 1-2 times daily I: Not reported T: 2-15 mins T: Aerobic & Strength Run-in: N/A Support: Teaching of breathing control. Con: Usual care	(1) Lung function, blood gases, 6MWT (2) Anxiety & Depression, ADL
Bourbeau et al., 2003 (2) (Canada)	191 participants Int: n=96 Con: n=95 Males: n=106 Females: n=85 Age, mean ± SD Int: 70±7 Con: 69±7	Inclusion: Stable COPD, ≥ 50 years of age, current or previous smoker (≥10 pack-years), FEV_1 between 25%-70% of predicted & FEV_1/FVC < 70%, no previous diagnosis of asthma, left congestive heart failure, terminal disease, dementia, or uncontrolled psychiatric illness, no participation in a respiratory rehabilitation program in the past year, no long-term-care facility stays.	COPD Stable, moderate-severe	To evaluate the impact of a self-management program on the use of hospital services and health status. RCT, individual	Home-based exercise intervention for 1 year. Study included 4-month follow-up. F: 3 days/week I: Guided by Borg score T: 30-45 min T: Aerobic & Strength Run-in: Supervised session at home Support: Living Well with COPD booklet (supervised education component). Monthly telephone calls. Con: Same level of care without add-on management program	(1) Hospital admission (2) Exacerbations, healthcare utilisation, mortality, SGRQ, lung function, 6MWT
Boyd et al., 2012 (3) (USA)	16 participants Int: n=8 Con: n=8 Males: n=1 Females: n=15 Age, mean (range) Int: 53 (38-62) Con: 54 (33-78)	Inclusion: Asthma diagnosis, patients undertaking aerobic exercise ≥3 times a week 6-months prior to study enrolment. Exclusion: Reversible airflow obstruction was utilized to exclude patients with other causes of dyspnoea, current smokers (within 6-months) or with >10 pack-year smoking history, coronary artery disease, congestive heart failure, stroke, severe hypertension, immunodeficiency states, or other conditions that would have interfered with participation, unable or unwilling to provide consent, unable to	Asthma Mild-moderate	To determine feasibility for a larger, future study that will define the effect of moderate intensity aerobic exercise on cellular, molecular, and functional measures in adults with mild-moderate severity asthma. RCT, individual	Community centre walking program for 12-weeks. F: 3 days/week I: Steady state intensity that achieved 60-75% HRmax T: 40 min T: Aerobic Run-in: N/A Support: 3-month gym membership. Education component included. Con: Education only	(1) Serum ECP (2) ACQ, inflammatory markers, lung function, VO_2 peak

		perform the exercise protocol or provide pre- and post-study measurements or be contacted via telephone or who intended to move out of the area within 6-months.				
Cameron-Tucker et al., 2016 (4) (Australia)	65 participants Int: n=35 Con: n=30 Males: n=29 Females: n=36 Age, mean ± SD Int: 68±9.9 Con: 70±6.8	Inclusion: >18 years of age, COPD diagnosis, >2 months post exacerbation. Exclusion: Cognitive impairment, unable to consent, could not complete questionnaires, did not meet safety to exercise criteria, had attended PR in the previous 2 years.	COPD Stable, mild-very severe	To evaluate the effectiveness of tele-rehab followed by PR versus usual care, that is, a waiting period followed by the same PR. RCT, individual	Tele-rehab walking program for 8-weeks before supervised PR F: Daily I: Moderate T: 30min T: Aerobic Run-in: N/A Support: Weekly telephone calls. Con: Usual care	(1) 6MWT (2) CAT, SNAPPS
Chen et al., 2018 (5) (China)	47 participants Int: n=25 Con: n=22 Males: n=37 Females: n=10 Age, mean ± SD Int: 69±8 Con: 65±12	Inclusion: COPD diagnosis, voluntary participation and signed consent, spouse or child who supports the completion of the intervention and space time for the intervention, never attended PR. Exclusion: MSK or neurologic condition affecting exercise, symptomatic cardiac disease or previous lung surgery, AECOPD requiring change in medication within 2-months, mMRC score of 4.	COPD Stable, moderate-very severe	To evaluate the feasibility of home-based lower limb resistance training in COPD patients and assess the effect of the programme on muscle strength and functional status. RCT, individual	Home-based lower-limb exercise intervention for 12-weeks. Six exercises with 8-12 repetitions. F: 3 days/week I: Best effort, not exceeding Borg score of 5 T: 20-30 min T: Resistance Run-in: 1 study visit Support: Exercise supervised by family member Con: Usual care	(1) Muscle strength (2) FTSST, 6MWT, CAT
De Oliveira et al., 2010 (6) (Brazil)	62 participants Int: n=33 Con: n=29 Males: n=46 Females: n=16 Age, mean ± SD Int: 66±10 Con: 71±9	Inclusion: COPD diagnosis, clinically stable COPD for at least 8 weeks. Exclusion: Hospitalization, clinically unstable COPD, presence of neuromuscular disease, associated respiratory disease, orthopaedic or neurological disease that affected gait; recent impairment due to comorbidities.	COPD Stable, mild-severe	To carry out a comparative analysis of patients with COPD submitted to PR in a clinical setting and at home. RCT, individual	Home-based PR program for 12 weeks. Walking, upper and lower limb weight exercises (10 reps). F: 3 days/week I: 60-80% HRmax based on 6MWT (walking). Initial load of 50% of 1 rep max, increase of 0.5kg every 2-weeks until tolerance reached (weights) T: Not reported T: Aerobic & Strength Run-in: 1 study visit Support: Regular telephone calls to reinforce rehab and set new targets. Education also included. Con: Usual care	(1) 6MWT (2) BODE

Elci et al., 2008 (7) (Turkey)	78 participants Int: n=39 Con: n=39 Males: n=66 Females: n=12 Age, mean ± SD Int: 60±9 Con: 58±11	Inclusion: COPD diagnosis, absence of reversibility in lung function, absence of a diagnosis of any other respiratory disease such as tuberculosis or cancer, ability to understand the PR programme, residence within the Malatya city boundary, signing consent.	COPD GOLD stage I–IV	To assess the effectiveness of a short-term PR programme in stable COPD patients, when implemented by secondary-care community hospital nurses. RCT, individual	Home-based PR programme targeting lower (walking) and upper limbs (weights) with 24 sessions over 3 months. F: 2 days/week I: 75% of 6MWT speed (walking) T: 90 min T: Aerobic & Strength Run-in: 1 supervised session Support: Exercise supervised by family member and weekly telephone calls. Con: Usual care	(1) Lung function (2) SF-36, SGRQ, HADS, mMRC, 6MWT
Hernandez et al., 2000 (8) (Spain)	37 participants Int: n=20 Con: n=17 Gender not reported Age, mean ± SD Int: 64±8 Con: 63±7	Inclusion: Stable disease with optimal drug management, FEV_1 %pred <60%, ex-smoker. Exclusion: AECOPD during study, ischemic heart disease, severe or uncontrolled systemic arterial hypertension, alterations in the thoracic cage, neuromuscular disorders, intermittent claudication, osteoarticular lesions in the lower extremity that could affect normal ambulation.	COPD Stable, moderate	To investigate the effectiveness of a simple home-based program of exercise training of the muscles of ambulation, in which the training intensity was applied in standardized form, using the ISWT. RCT, individual	Home/outdoor-based walking exercise programme for 12 weeks. F: 6 days/week I: ≥70% of max speed of ISWT. T: 1 hour T: Aerobic Run-in: Home visit Support: 2-week reviews at hospital Con: Usual care & 2-week reviews at hospital	(1) Lung function (2) ISWT, VO_2 max, BDI/TDI, MRC, CRQ
Ho et al., 2012 (9) (Taiwan)	41 participants Int: n=20 Con: n=21 Males: n=39 Females: n=2 Age, mean ± SD Int: 73±11 Con: 75±10	Inclusion: COPD diagnosis and currently stable, no AECOPD within last month, do not use oxygen. Exclusion: Previous PR experience, GDS >10, cognitive deficits with SPMSQ <7, unstable heart disease, MSK disease, visual or hearing impairment, any other condition that could affect exercise participation.	COPD Stable FEV_1 %pred, mean ± SD Int: 61±19 Con: 61±26	To investigate the effects of paced walking to music at home with an 80% VO_2 peak for patients with COPD. RCT, individual	Home-based walking exercise programme paced to music for 12-weeks. F: 5 days/week I: 80% VO_2peak initially, increased gradually each month based on ISWT. T: 30 min T: Aerobic Run-in: 1 research visit Support: Monthly reviews and progression Con: Usual care	(1) ISWT (2) Lung function, SGRQ, healthcare utilisation
Jaakkola et al., 2019 (10) (Finland)	89 participants Int: n=44 Con: n=45 Males: n=19 Females: n=70 Age, mean ± SD Int: 40±14 Con: 33±11	Inclusion: 16-65 years of age, mild-moderate asthma diagnosis and/or to have received the reimbursement right for asthma medication in the case of newly diagnosed asthma. Exclusion: Severe asthma diagnosis (FEV_1 %pred <60% & PEF variability >30%), short-acting bronchodilator use >3 times daily and/or permanent daily oral steroid treatment, exercise	Asthma Mild-moderate	To test the hypothesis that regular exercise improves asthma control. RCT, individual	Home/outdoor-based exercise program (variety of exercises including sports) for 24 weeks. Study also included 12-week assessment. F: 3 days/week (aerobic), 2 days/week (strength) I: 70-80% HRmax T: 30 min T: Aerobic & Strength	(1) Asthma control (2) Exercise amount, muscle strength, 6MST, SGRQ

		>3 times a week, diagnosis of serious coronary heart disease, severe hypertension, severe heart failure, severe musculoskeletal disorder, dementia, and/or physician diagnosed chronic obstructive lung disease.			Run-in: 4-week phase to assess suitability and motivation Support: 12-week follow-up and reinforcement Con: Usual care	
Lahham et al., 2020 (11) (Australia)	58 participants Int: n=29 Con: n=29 Males: n=34 Females: n=24 Age, mean ± SD Int: 68±9 Con: 67±10	Inclusion: COPD diagnosis, ≥40 years of age, ≥10 pack-year smoking history, no hospitalizations or exacerbations 1 month prior to enrolment. Exclusion: Asthma diagnosis or co-morbidities that precluded exercise participation.	COPD Stable, mild	To test whether a home-based PR program would achieve significant improvements in exercise capacity in people with mild COPD compared to standard care. A secondary aim was to examine the impact of home-based rehabilitation on dyspnoea, health-related quality of life and physical activity levels. RCT, individual	Home-based aerobic (walking) and resistance (upper and lower limb) exercise training for 8 weeks with a 6-month follow-up. F: 5 days/week I: 80% of walking speed from 6MWT. Intensity gauged by Borg scale T: 30 min T: Aerobic & Resistance Run-in: Home visit Support: Weekly motivational interviewing. Better Living with COPD booklet Con: Usual care & weekly phone calls. Better Living with COPD booklet	(1) 6MWT (2) mMRC, CRQ, PAL
McGavin et al., 1977 (12) (UK)	24 participants Int: n=12 Con: n=12 Males: n=24 Females: n=0 Age, mean ± SD Int: 61±6 Con: 57±8	Inclusion: <70 years of age, male gender, chronic bronchitis diagnosis (MRC working party 1965 definitions), chest condition in a stable state. Exclusion: Reversible airway obstruction (↑30% FEV_1 post-bronchodilator), corticosteroid use, angina, intermittent claudication, disabling MSK conditions.	Chronic bronchitis Stable Disease characteristics not reported	To evaluate a training scheme which was simple to organise and which could be carried out by the patient unsupervised at home without recourse to hospital facilities. RCT, individual	Home-based stair climbing exercise program for 3 months F: 5 days/week I: Not reported T: 2-10 mins T: Aerobic & Strength Run-in: N/A Support: 2-week clinic follow-up and then monthly follow-ups thereafter Con: Usual care & monthly clinic check-up	(1) Lung function, blood gases, 12MWD, submaximal exercise capacity

Mitchell et al., 2014 (13) (UK)	184 participants Int: n=89 Con: n=95 Males: n=101 Females: n=83 Age, mean ± SD Int: 69±8 Con: 69±10	Inclusion: COPD diagnosis, mMRC dyspnoea grade 2-5, clinically stable for 4 weeks. Exclusion: Unable to undertake exercise due to neurological, musculoskeletal or cognitive comorbidities, unable to read English to the reading age of an 8-year-old, had completed PR within 12 months.	COPD Stable FEV_1 %pred, mean ± SD Int: 56±17 Con: 60±17	To establish the short- and medium-term effectiveness of SPACE FOR COPD on patient outcomes, compared with usual care alone. RCT, individual	Home-based manual incorporating education and exercise programme (walking, upper and lower limb resistance training using weights) for 6 weeks. Study also included 6-month follow-up. F: Daily (walking), 3 days/week (upper and lower limb training) I: Not reported T: 30 min/day (walking), not reported (upper and lower limb) T: Aerobic & Resistance Run-in: 1 study visit Support: Bi-weekly phone calls using motivational interviewing Con: Usual care	(1) CRQ (dyspnoea domain) (2) CRQ (fatigue, emotion, mastery domains), BCKQ, HADS, ISWT, ESWT, PRAISE, smoking status.
Moore et al., 2009 (14) (UK)	20 participants Int: n=10 Con: n=10 Males: n=10 Females: n=10 Age, median (IQR) Int: 70 (13) Con: 71 (58-79)	Inclusion: COPD diagnosis with FEV_1 %pred <60%, patients who had not previously attended PR and had access to a video or DVD player at home. Exclusion: Comorbidities that preclude safe exercise training.	COPD FEV_1 %pred, median (IQR) Int: 40 (37-49) Con: 42 (30-55)	To investigate whether a home exercise video programme could improve exercise tolerance and breathlessness in patients with moderate to severe COPD. RCT, individual	Home-based high intensity interval exercise video/DVD for 6 weeks. F: 4 days/week I: High intensity T: 30 min T: Aerobic & Resistance & Strength Run-in: 1 study visit Support: Education material Con: Usual care & education booklet	(1) ISWT (2) CRQ

Nguyen et al., 2013 (15) (USA)	125 participants* Int(1): n=43 Int(2): n=41 Con: n=41 Males: n=68 Females: n=57 Age, mean ± SD Int(1): 69±11 Int(2): 68±10 Con: 69±8	Inclusion: COPD diagnosis (classic criteria or FEV1/FVC <0.60 with FEV1>80% predicted or CT confirmed emphysema) & clinically stable for at least one month, activities limited by dyspnoea, use of the Internet, oxygen saturation >85% on room air on ≤6L/min of oxygen at the end of a 6MWT. Exclusion: Active symptomatic illness (e.g., cancer, heart failure), participated in PR <6-months ago, or currently participating in >2 days a week of supervised exercise.	COPD Stable, mild-very severe	To test the efficacy of two 12-month dyspnoea self-management programs, Internet-based and face-to-face, compared with a general health education control on the primary outcome of dyspnoea with activities. RCT, individual	Self-management program incorporating exercise intervention (online or face-to-face) for 12 months. Study included 3- & 6-month follow-ups. F: 4 days/week I: Gauged by Borg score T: 30 min T: Aerobic & Strength Run-in: Home visit Support: Bi-weekly reinforcement and feedback with motivational interviewing. Con: Usual care, bi-weekly phone calls & education	(1) CRQ (dyspnoea domain) (2) 6MWT, ITT, muscular endurance, CRQ (other domains), SF-36, self-efficacy
Pradella et al., 2015 (16) (Brazil)	44 participants Int: n=29 Con: n=15 Males: n=36 Females: n=8 Age, mean ± SD Int: 65±8 Con: 62±11	Inclusion: COPD diagnosis, 40-75 years of age, either gender, signed consent. Exclusion: PR participation within 12 months, regular physical activity ≥3 times a week in the past 12 months, other diseases which leads to exercise intolerance, exacerbations within past 4 weeks.	COPD Stable, mild-very severe	To develop an efficient, low-cost, home-based PR program. To evaluate the impact of the program on exercise as measured by the 6MWT and treadmill endurance test. To assess the effect on quality of life in subjects with COPD under partial supervision compared with a control group. RCT, individual	Home-based walking PR program for 24 sessions F: 3 days/week I: 60-70% HRmax T: 40 min T: Aerobic Run-in: 1-week run-in at rehab centre Support: Educational booklet & weekly phone call Con: Usual care & weekly phone call	(1) Lung function (2) 6MWT, SGRQ, lower-limb endurance test

*Contained 2 relevant intervention groups. AECOPD = acute exacerbation of chronic obstructive pulmonary disease, Int = Intervention group, Con = Control group, FEV_1 %pred = Forced expiratory volume in 1 second % of predicted, RCT = Randomised controlled trial, CRQ = Chronic respiratory disease questionnaire, PAL = Physical activity levels, NYHA = New York Heart Association, GOLD = Global initiative for chronic obstructive lung disease, FITT = Frequency, Intensity, Time, Type, N/A = Not applicable, 6MWT = 6 minute walk test, mMRC = Modified medical research council, PASE = Physical activity scale for the elderly, BARTHEL = Barthel index, CAT = COPD assessment tool, ADL = Activities of daily living, Ex = Exercise group, Phys = Exercise + physio group, SGRQ = St Georges respiratory questionnaire, FEV_1/FVC = Forced expiratory volume in 1 / forced vital capacity, ECP = Eosinophil cationic protein, ACQ = Asthma control questionnaire, HRmax = Maximum heart rate, PR = Pulmonary rehabilitation, SNAPPS = Smoking, nutrition, alcohol consumption, physical activity, psychological well-being, symptom management health behaviours, FTSST = 5 times sit to stand test, MSK = Musculoskeletal, BODE = Index for body mass index, airflow obstruction, dyspnoea and exercise, SF-36 = 36 item short form survey, HADS = Hospital anxiety and depression scale, LTOT = Long-term oxygen therapy, GLTEQ = Godin leisure time exercise questionnaire, ISWT = Incremental shuttle walk test, BDI/TDI = Baseline dyspnoea index / transition dyspnoea index, VO2max = maximal oxygen uptake, VO2peak = peak oxygen uptake, GDS = Geriatric depression scale, SPMSQ = Short portable mental status questionnaire, PEF = Peak expiratory flow, 6MST = 6 minute stepper test, 12MWD = 12 minute walk distance, BCKQ = Bristol COPD knowledge questionnaire, PRAISE = Pulmonary rehabilitation adapted index of self-efficacy, SPACE = Self-management programme of activity, coping and education, ESWT = Endurance shuttle walk test, IQR = Interquartile range, ITT = Incremental treadmill test.

Table S4. Risk of Bias Assessment

Study	Random sequence generation	Allocation concealment	Blind participants and personnel	Blind outcome assessment	Incomplete outcome data	Selective reporting (reporting bias)	Other bias	Overall risk
Booker 1984 (1)	Unclear	Unclear	High	Low	Unclear	High	Low	**High**
Bourbeau 2003 (2)	Low	Low	High	Low	Low	Low	Low	**Moderate**
Boyd 2012 (3)	Low	Low	High	Unclear	Low	Low	Low	**Moderate**
Cameron-Tucker 2016 (4)	Low	Low	High	Low	Low	High	Low	**High**
Chen 2018 (5)	Low	Unclear	High	Unclear	Low	Unclear	Low	**High**
De Oliveira 2010 (6)	Low	Unclear	High	Unclear	High	Unclear	Low	**High**
Elci 2008 (7)	Low	Unclear	High	Low	Unclear	Low	Unclear	**High**
Hernandez 2000 (8)	Unclear	Unclear	High	Unclear	High	Low	Low	**High**
Ho 2012 (9)	Low	Unclear	High	Low	Low	Low	Low	**Moderate**
Jaakkola 2019 (10)	Unclear	Unclear	High	Unclear	High	High	Low	**High**
McGavin 1977 (12)	Unclear	Unclear	High	Unclear	High	Low	Low	**High**
Mitchell 2014 (13)	Low	Low	High	Low	Low	Unclear	Low	**Moderate**
Moore 2009 (14)	Low	Low	High	High	High	Low	Low	**High**
Lahham 2020 (11)	Low	Low	High	Low	Low	Low	Low	**Moderate**
Nguyen 2013 (15)	Unclear	Unclear	High	Unclear	Low	High	Low	**High**
Pradella 2015 (16)	Unclear	Unclear	High	Unclear	Low	Low	Low	**High**

Table S5. Narrative summary of findings not included in the meta-analyses

Outcome	Study	Outcome measurement	Diagnosis	Duration of follow-up	Outcome reporting	Findings		
						Intervention	Control	Reported stats
Exercise performance / capacity	Mitchell 2014 (13)	ESWT	COPD	6 weeks	Change from baseline	Mean (95% CI) Time: +210 secs (122 to 297)	Mean (95% CI) Time: +92 secs (33 to 151)	Mean difference (95% CI) Time: 118 secs (17 to 219), p = 0.006
	McGavin 1977 (12)	12MWD	Chronic Bronchitis	3 months	Change from baseline	Mean (range) Distance: ↑64 metres (0 to 165)	Mean (range) Distance: ↓19 metres (-105 to 55)	Intervention: p < 0.001 Control: p > 0.05
	Pradella 2015 (16)	Endurance treadmill test	COPD	8 weeks	Change from baseline	Mean difference ± SD Distance: 317 ± 82 metres	Mean difference ± SD Distance: 31 ± 420 metres	Mean difference (95% CI): 285 metres (-7 to 564)
Health-related Quality of Life	Jaakkola 2019 (10)	SGRQ	Asthma	24 weeks	No data reported	No data reported	No data reported	No data reported
	Nguyen 2013 (15)	CRQ	COPD	12 months	Change from baseline	Mean difference Total: Group 1 (↑8.4 points), Group 2 (↑4.9 points) Dyspnoea: Group 1 (↑2.2 points), Group 2 (↑0.6 points)	Mean difference Total: ↑2.2 points Dyspnoea: ↑0.7 points	Group differences: Total (p = 0.28), Dyspnoea (p = 0.23) Time effect: Total (p < 0.01), Dyspnoea (p = 0.01) Group and time interaction: Total (p = 0.44), Dyspnoea (p = 0.48)
	Elci 2008 (7)	SF-36	COPD	3 months	Baseline data not reported	Baseline data not reported	Baseline data not reported	Baseline data not reported
	Nguyen 2013 (15)	SF-36	COPD	12 months	Change from baseline	Mean difference Physical: Group 1 (↑4.4 points), Group 2 (↑1.6 points) Mental: Group 1 (↓1.1 points), Group 2 (↑1.9 points)	Mean difference Physical: ↑1.5 points Mental: ↓1.0 points	Group differences: Physical (p = 0.68), Mental (p = 0.30) Time effect: Physical (p < 0.01), Mental (p = 0.84) Group and time interaction: Physical (p = 0.63), Mental (p = 0.54)
Subjective symptoms	Hernandez 2000 (8)	BDI/TDI	COPD	12 weeks	Change from baseline	Mean difference BDI: ↑1.6 points MT: ↑0.5 points FI: ↑0.6 points ME: ↑0.6 points	Mean difference BDI: ↓0.3 points MT: ↑0.2 points FI: ↓0.2 points ME: ↑0.2 points	BDI: Intervention (p = 0.03), Control (p > 0.05) MT: Intervention (p = 0.05), Control (p > 0.05) FI: Intervention (p = 0.03), Control (p > 0.05) ME: Intervention (p = 0.01), Control (p > 0.05)
Anxiety & Depression	Booker 1984 (1)	Mood disturbance questionnaire	COPD	9 weeks	Change from baseline	No data reported	No data reported	Significant ↓ in total score in exercise

								physiotherapy + exercise group. No significant changes in exercise alone or control groups.
	Mitchell 2014 (13)	HADS	COPD	6 weeks	Change from baseline	Mean (95% CI) Anxiety: -0.7 points (-1.3 to -1.8) Depression: - 0.5 points (-1.0 to 0.0)	Mean (95% CI) Anxiety: 0.1 points (-0.4 to 0.62) Depression: 0.2 points (-0.3 to 0.8)	Mean difference (95% CI) Anxiety: -0.9 points (-1.6 to -1.0), p = 0.04 Depression: -0.7 points (-1.5 to 0), p = 0.10
	Elci 2008 (7)	HADS	COPD	3 months	Change from baseline	Mean difference Total: ↓4.0 points	Mean difference Total: ↑0.8 points	Intervention: p < 0.01 Control: p = 0.07
Disease impact	Boyd 2012 (3)	ACQ	Asthma	12 weeks	Change from baseline	Mean difference Total: ↓0.22 points	Mean difference Total: ↓0.73 points	p > 0.05
	Jaakkola 2019 (10)	ACT	Asthma	24 weeks	Change from baseline (total number of participants)	Improved: n=26 No change: n=7 Worsened: n=9	Improved: n=17 No change: n=17 Worsened: n=10	Risk difference (95% CI): 0.233 (0.027 to 0.438), p = 0.032
	Cameron-Tucker 2016 (4)	CAT	COPD	8 weeks	Change from baseline	Median difference (IQR) Total: 0 (6)	Median difference (IQR) Total: 0 (6)	p = 0.48
	Chen 2018 (5)	CAT	COPD	12 weeks	Change from baseline	Mean difference Total: ↓3.2 points	Mean difference Total: ↓1.3 points	Intervention: p < 0.01 Control: p = 0.20 Between group: p = 0.98
Hospital admissions (respiratory)	Bourbeau 2003 (2)	Self-report	COPD	1 year	Total number of events during observation period	Total events: 78	Total events: 118	Treatment difference: -39.8% (p = 0.01)
	Ho 2012 (9)	Self-report and healthcare records	COPD	12 weeks	Total number of events during observation period	Data not interpretable	Data not interpretable	No significant differences between groups for hospital admission due to AECOPD
Mortality	Bourbeau 2003 (2)	Healthcare records	COPD	1 year	Total number of events during observation period	Total events: 5	Total events: 9	Statistics not reported
Exacerbations	Bourbeau 2003 (2)	Self-report	COPD	1 year	Total number of events during observation period	Total events: 299	Total events: 362	p = 0.06
Hospital admission (all-cause)	Ho 2012 (9)	Self-report and healthcare records	COPD	12 weeks	Total number of events during observation period	Data not interpretable	Data not interpretable	No data reported
Length of stay	Ho 2012 (9)	Self-report and healthcare records	COPD	12 weeks	Mean duration of stay during observation period	Mean ± SD LOS: 0.2 ± 1.4	Mean ± SD LOS: 0.3 ± 1.3	p = 0.64
Emergency department visits	Bourbeau 2003 (2)	Self-report	COPD	1 year	Total number of events during observation period	Total events AECOPD: 95 Other cause: 57	Total events AECOPD: 161 Other cause: 74	Treatment difference AECOPD: -41.0% (p = 0.02)

								Other cause: -23.0% (p = 0.34)
	Ho 2012 (9)	Self-report and healthcare records	COPD	12 weeks	Mean number of events during observation period	Mean ± SD ED visits: 0.0 ± 0.2	Mean ± SD ED visits: 0.0 ± 0.3	p = 0.52
Outpatient visits	Bourbeau 2003 (2)	Self-report	COPD	1 year	Mean number of events during observation period	Data not interpretable	Data not interpretable	Data not interpretable
Aerobic fitness / capacity	Boyd 2012 (3)	Graded treadmill test	Asthma	12 weeks	Change from baseline	Mean difference $VO_{2\ peak}$: ↑2.64 ml/min/kg Time: ↑1.39 min RER: ↑0.04	Not measured in control group	$VO_{2\ peak}$: p < 0.05 Time: p < 0.05 RER: p > 0.05
	Hernandez 2000 (8)	Incremental cycle ergometer test	COPD	12 weeks	Change from baseline	Mean difference Workload: ↓2.8 watts $VO_{2\ max}$: ↑0.1 $l.min^{-1}$ VO_2: ↑0.5 $l.min^{-1}$ VCO_2: ↓0.1 $l.min^{-1}$ V_E: ↓0.5 $l.min^{-1}$ Dyspnoea: ↓0.7 points Leg discomfort: ↓1.0 points	Mean difference Workload: ↑2.9 watts $VO_{2\ max}$: ↑0.1 $l.min^{-1}$ VO_2: ↑1.5 $l.min^{-1}$ VCO_2: 0 $l.min^{-1}$ V_E: ↑1.4 $l.min^{-1}$ Dyspnoea: ↓1.1 points Leg discomfort: ↑1.1 points	All, p > 0.05
	Jaakkola 2019 (10)	Spiroergometry	Asthma	24 weeks	No data reported	No data reported	No data reported	No data reported
	McGavin 1977 (12)	Incremental cycle ergometer test	Chronic Bronchitis	3 months	Change from baseline	Mean Workload: ↑14.4 watts VO_2: ↑1.3 $l.min^{-1}$ V_E: ↑4 $l.min^{-1}$	Mean Workload: ↓2.6 watts VO_2: ↓121 $ml.min^{-1}$ V_E: ↓2 $l.min^{-1}$	Workload: Intervention (p < 0.05), control (p > 0.05) VO_2: Intervention (p > 0.05), control (p < 0.05) V_E: Intervention (p > 0.05), control (p > 0.05)
	Nguyen 2013 (15)	Incremental treadmill test	COPD	12 months	Change from baseline	No data reported	No data reported	No differences among groups
Peripheral muscle strength	Chen 2018 (5)	CON-TREX leg extensor	COPD	12 weeks	Change from baseline	Mean difference Isometric: ↑17.1 Nm Isokinetic: ↑14.3 Nm	Mean difference Isometric: ↑11.8 Nm Isokinetic: ↑4.6 Nm	Isometric: Intervention (p < 0.01), Control (p = 0.02) Isokinetic: Intervention (p < 0.01), Control (p = 0.06) Between groups: Isometric (p = 0.78), Isokinetic (p = 0.87)
	Jaakkola 2019 (10)	Unclear	Asthma	24 weeks	No data reported	No data reported	No data reported	No data reported
	Nguyen 2013 (15)	Arm endurance	COPD	12 months	Change from baseline	Mean (pre vs post) Lifts per min: Group 1 (↑11.9 reps), Group 2 (↑11.1 reps)	Mean (pre vs post) Lifts per min: ↑1.7 reps	Group differences: p = 0.33 Time effect: p <0.01

								Group and time interaction: p = 0.04
Physical activity levels	Cameron-Tucker 2016 (4)	SNAPPS questionnaire and self-report diary	COPD	8 weeks	Change from baseline	Median difference (IQR) SNAPPS: 0 (4) Mins per day of walking: 14 (26)	Median difference (IQR) SNAPPS: 0 (4) Mins per day of walking: 16 (40)	SNAPPS: p = 0.40 Mins per day of walking: p = 0.10
	Lahham 2020 (11)	Accelerometer	COPD	8 weeks	Change from baseline	Mean difference (95% CI) Total EE: -4 (-1425 to 1418) Steps: 303 (-1607 to 2215) METs/day: 0.1 (-0.1 to 0.2) Sedentary time: 32 min/day (-63 to 128) MVPA time: -5 min/day (-301 to 290)	Mean difference (95% CI) Total EE: 82 (-1299 to 1463) Steps: -106 (-1962 to 1749) METs/day: 0.0 (-0.2 to 0.2) Sedentary time: 8 min/day (-84 to 101) MVPA time: -211 min/day (-497 to 76)	Between group mean differences (95% CI), Home-Standard Care Total EE: -678 (-2190 to 839) Steps: 1089 (-946 to 3125) METs/day: 0.1 (-0.1 to 0.2) Sedentary time: 15 min/day (-86 to 116) MVPA time: -8 min/day (-330 to 314)

ESWT = endurance shuttle walk test, CI = confidence interval, Secs = seconds, 12MWD = Twelve-minute walk distance, SGRQ = St. Georges respiratory questionnaire, CRQ = Chronic respiratory disease questionnaire, BDI/TDI = Baseline and transition dyspnoea index, HADS = Hospital anxiety and depression scale, ACQ = Asthma control questionnaire, ACT = Asthma control test, CAT = COPD assessment tool, IQR = Interquartile range, SF-36 = Short form-36 questionnaire, AECOPD = Acute exacerbation of COPD, LOS = Length of stay, ED = Emergency department, $VO_{2\,peak}$ = Peak oxygen uptake, RER = Respiratory exchange ratio, $VO_{2\,max}$ = Maximal oxygen uptake, V_E = Minute ventilation, SD = Standard deviation, Nm = Newton metres, Reps = Repetitions, Min = minute, EE = Energy expenditure, MVPA = Moderate to vigorous physical activity.

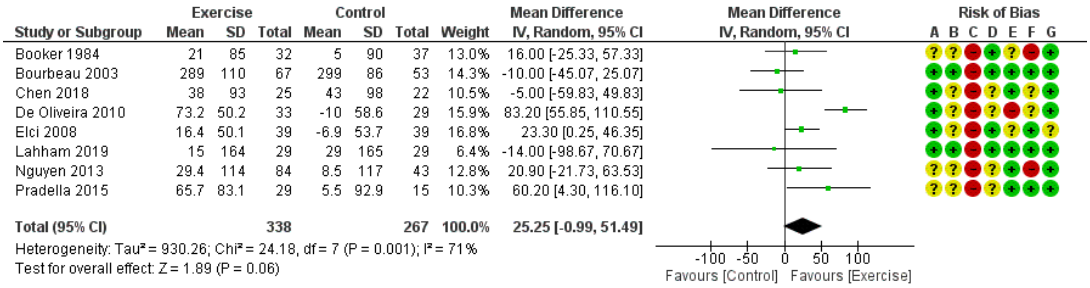

Figure S1. Trial-level data, effect estimates, and forest plot of comparison for change in 6MWT distance following an unsupervised exercise intervention versus usual care for all studies reporting 6MWT, including studies for which data were unclear or not available in published reports (1, 2, 6) and were retrieved from previous systematic reviews (17-19). Risk of bias legend: A) Random sequence generation (selection bias), B) Allocation concealment (selection bias), C) Blinding of participants and personnel (performance bias), D) Blinding of outcome assessment (detection bias), E) Incomplete outcome data (attrition bias), F) Selective reporting (reporting bias), G) Other bias.

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