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, AMED, Web of Science, Cochrane Central Register of Controlled Trials, PEDro) 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 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: 1,184 patients) met the inclusion criteria. Only data on COPD populations was available for meta-analysis. Unsupervised exercise resulted in a statistically but not clinically significant improvement in 6MWT (n=5, MD=22.0 metres, 95% CI 4.4 to 39.6 metres, p=0.01). However, unsupervised exercise did lead to statistically significant and clinically meaningful improvements in SGRQ (n=4, MD=-11.8 points, 95% CI -21.2 to -2.3 points, p=0.01) and CRQ 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 to non-exercise based usual care.

Discussion: This review demonstrates clinical benefits of unsupervised exercise interventions on HRQoL 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 health care utilisation outcomes?
- **What is the bottom line?** – Unsupervised exercise interventions are effective at improving SGRQ and CRQ domain scores, but do not result in clinically meaningful improvements in 6MWT.
- **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 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 health care 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/or cost-effective ways to improve exercise adherence, fitness, and symptoms. Whilst 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 (e.g. home-rehabilitation, tele-rehabilitation 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 health care providers in the management of obstructive lung disease, particularly in settings where resources are limited for delivering supervised exercise interventions.

The purpose of this systematic review was to establish an up-to-date synthesis of available evidence from randomised controlled trials and derive estimates of effect for

unsupervised exercise interventions on functional exercise capacity, quality of life, and health care 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 (i.e. >18 years) with a clinical diagnosis of COPD, non-cystic fibrosis bronchiectasis or asthma as defined by authors of the study 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 (i.e. FITT principles: frequency, intensity, time, and type of exercise); 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 (e.g. pulmonary rehabilitation); 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 (i.e. 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 (e.g.

education, counselling, breathing/relaxation/airway clearance therapy) was still included if the intervention arm also received these treatments.

Outcomes

Primary outcomes were exercise performance/capacity (e.g. 6 minute walk test (6MWT), incremental shuttle walk test (ISWT), and endurance shuttle walk test (ESWT)), health-related quality of life (e.g. St. Georges Respiratory Questionnaire (SGRQ), chronic respiratory disease questionnaire (CRQ), hospital anxiety and depression score (HADS), and asthma control questionnaire (ACQ)), disease impact (COPD 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 (GP) visits, adverse events, aerobic fitness/capacity, peripheral muscle strength, physical activity levels (PAL), 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 crossover, 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 (DARE), PROSPERO, and the Cochrane Database of Systematic Reviews (CDSR).

The following bibliographic databases, platforms and trial registers were searched: MEDLINE, CINAHL, EMBASE, Web of Science Core Collection, Cochrane Central Register of Controlled Trials (CENTRAL), Physiotherapy Evidence Database (PEDro), Allied and Complementary Medicine Database (AMED), ClinicalTrials.gov, Current Controlled Trials, UK Clinical Trials Gateway and World Health Organisation 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 (i.e. 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 (e.g. “Lung Diseases, Obstructive”), intervention (e.g. “Exercise”) and study type (e.g. “randomised”). An example of a full search strategy is presented in Table S1.

Search results were compiled using EndNote referencing software (Clarivate Analytics, Philadelphia, PA, 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 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’ or more than one ‘high’ risk domain), moderate (two ‘unclear’ 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 version 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 standard deviation of changes was not available we calculated using other reported parameters (e.g. 95% confidence intervals), imputed using correlation coefficients derived from other studies in the same meta-analysis or assuming a conservative correlation coefficient of 0.5, or (for unstandardized 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 I^2 statistic was greater than 40% potential sources of the statistical heterogeneity were explored. We pre-specified subgroup analysis to explore heterogeneity in the primary outcomes according to the following clinical and methodological factors: diagnosis (COPD, Bronchiectasis, 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); 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 pre-specified 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 6,240 records for screening, of which 4,362 records were excluded based on title and 1,602 on abstract. Full texts

were obtained for the remaining 276 records of which 16 studies met the inclusion criteria (Figure 1).

Characteristics of included studies

The sixteen included studies were published between 1977 and 2020 (Table S3). Of the included studies, 13 focussed on COPD (14-26), 2 on asthma (27, 28), and 1 on chronic bronchitis (29) as an obstructive lung disease. A total of 1,184 obstructive lung disease patients (1,055 COPD, 105 asthma, 24 chronic bronchitis) were randomised, of which 59% were males. Study sample sizes varied in size between 16 and 191 patients. COPD disease severity varied from mild to very severe and asthma 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 to 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 utilised in the meta-analysis have been summarised in Table 1. A detailed overview of the characteristics of all eligible studies can be found in Table S3.

The risk of bias assessment was hindered by poor study reporting (Table S4).

Table 1. Characteristics of included studies in the meta-analysis

	Bourbeau 2003 (15) **(Canada)**	**Chen 2018 (17)** **(China)**	**Elci 2008 (18)** **(Turkey)**	**Hernandez 2000 (19)** **(Spain)**	**Ho 2012 (21)** **(Taiwan)**	**Lahham 2020 (22)** **(Australia)**	**Mitchell 2014 (23)** **(UK)**	**Moore 2009 (24)** **(UK)**	**Nguyen 2013 (25)** **(USA)**	**Pradella 2015 (26)** **(Brazil)**
Respiratory diagnosis & disease severity	COPD Stable, moderate-severe	COPD Stable, moderate-very severe	COPD GOLD stage 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 program incorporating exercise intervention (online or face-to-face) for 12 months	Home-based walking PR program 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	30-45 min	20-30 min	90 min	60 min	30 min	30 min	30 min (walking), not reported (resistance)	30 min	30 min	40 min
Exercise Type	Aerobic & Resistance	Resistance	Aerobic & Resistance	Aerobic	Aerobic	Aerobic & Resistance	Aerobic & Resistance	Aerobic & Resistance	Aerobic & Resistance	Aerobic
Intervention run-in period	Supervised session at home	1 study visit	1 supervised session	Home visit	1 research visit	Home visit	1 study visit	1 study visit	Home visit	1-week run-in at rehab center
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	Bi-weekly phone calls using motivational interviewing	Education material	Bi-weekly reinforcement and feedback with motivational interviewing	Educational booklet & weekly phone call
Comparator	Same level of care without add-on management program	Usual care	Usual care	Usual care & 2-week reviews at hospital	Usual care	Usual care & weekly phone calls. Better Living with COPD booklet	Usual care	Usual care & education booklet	Usual care, bi-weekly phone calls & education	Usual care & weekly phone call

COPD = Chronic obstructive pulmonary disease, GOLD = Global initiative for chronic obstructive lung disease, 6MWT = 6 minute walk test, HRmax = Maximum heart rate, PR = Pulmonary rehabilitation, ISWT = Incremental shuttle walk test.

Primary Outcomes

Exercise capacity

6MWT: Meta-analysis of five trials (17, 18, 22, 25, 26) in COPD patients demonstrated a statistically significant improvement in 6MWT performed with unsupervised exercise (MD = 22.0 metres, 95% CI 4.4 to 39.6 metres, p = 0.01) (Figure 2A). Statistical heterogeneity was not apparent (I^2= 0%). However, the magnitude of effect did not meet the threshold of 30m 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 another three 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 additional three studies is provided in the supplementary material (Figure S1). Data from the three studies had minimal effect on the overall magnitude of effect of unsupervised exercise interventions (MD = 25.3 metres, 95% CI -1.0 to 51.5 metres, p = 0.06) but their inclusion led to substantial heterogeneity (I^2= 71%).

ISWT: Meta-analysis of four trials (19, 21, 23, 24) in COPD patients demonstrated a statistically significant improvement in ISWT performance with unsupervised exercise (MD = 19.9 metres, 95% CI 2.6 to 37.2 metres, 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 12MWD (29) as outcome measures in COPD populations, therefore meta-analyses could not be performed.

Health-related quality of life and disease impact

SGRQ: Meta-analysis of four trials (15, 18, 21, 26) in COPD patients 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 an intervention effects which was 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): Pre-specified 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%) (Figures 3A-D). One further trial reported SGRQ as an outcome (28) in asthma patients but data could not be obtained for meta-analysis.

CRQ: Meta-analysis of four trials (19, 22-24) in COPD patients 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%) (Figures 4A-C). There was substantial heterogeneity for CRQ-Mastery scores (I^2 = 93%, p < 0.01). This could not be explained by any pre-specified clinical and 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.

MRC Dyspnoea Scale: Meta-analysis of three trials (18, 19, 22) in COPD patients showed a statistically significant improvement in MRC breathlessness 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 BDI/TDI in COPD patients, and therefore was not included in the meta-analysis.

Other reported outcomes: Anxiety and depression in COPD patients (14, 18, 23), asthma control (27, 28), CAT (16, 17), and SF-36 in COPD patients (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 utilisation

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.

Other reported outcomes: Hospital length of stay in COPD patients (21), emergency department visits in COPD patients (15, 21), outpatient visits in COPD patients (15), aerobic fitness in either COPD or asthma populations (19, 25, 27-29), muscle strength in either COPD or asthma populations (17, 25, 28), physical activity levels in COPD patients (16, 22) were reported as outcomes but the use of different measurement tools, utilisation of differing 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 have been narratively summarised in 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 health care 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 bronchiectasis patients 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 metres (32) the 22 metre 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.

Whilst 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 effectiveness. 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 suggests 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 utilisation meaning meta-analysis was not possible. Considering the importance of healthcare utilisation to the future health outcomes of all chronic respiratory disease patients (36), it is imperative that more trials are conducted which examine the potential benefit of unsupervised exercise interventions on these outcomes.

Strengths and limitations

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 pre-planned and publicly available protocol. It is important to highlight that raw study data were obtained to increase the amount of studies in our analysis.

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 focussed (27, 28) meaning the findings of our meta-analysis are purely COPD focussed. 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 COPD patients to examine the effects of a longer-term unsupervised exercise intervention on health care utilisation, 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 the 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 (9, 10)) would be required to investigate this.

Whilst substantial diversity among the specific interventions existed, the current data would suggest that incorporating formal prescription relating to basic programming principles (i.e. frequency, intensity, time, 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 obstructive lung disease patients.

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 to Consolidated Standards of Reporting Trials (CONSORT) 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 confidence intervals of our point estimates. Although we report the overall magnitude of effects in some outcome measures to be clinically meaningful, the majority of the confidence intervals for these point estimates include between-group differences, which would not meet MCID's. At the same time, the available evidence does not currently favour a clinically meaningful

effect of unsupervised exercise on 6MWT, but the confidence interval 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, ISWT) and disease-specific quality of life (i.e. SGRQ, 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 chronic lung diseases beyond COPD, across a wider range of disease severity, and should follow patients over longer periods of time (i.e. >12 weeks).

Conclusion

In conclusion our systematic review and meta-analysis provides evidence that unsupervised exercise interventions result in improvements in health-related quality of life, 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.

Author contributions

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

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Competing interests

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Figure Legends

Figure 1. Flow diagram of study selection.

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.

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 pre-specified 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.

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.

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.