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Comparing the impact of different exercise interventions on fatigue in individuals with COPD: A systematic review and meta-analysis

Lok Sze Katrina Li[1,2], Stacey Butler[2], Roger Goldstein[2,3] and Dina Brooks[2,4,5]

Abstract

To systematically review randomized controlled trials that compared the effectiveness of different types of exercise on the symptom of fatigue in individuals with chronic obstructive pulmonary disease (COPD). MEDLINE, EMBASE, EMcare, PsychINFO, and Cochrane library were searched from inception to October 2018. Studies were included if individuals with COPD were randomized into two or more physical exercise interventions that reported fatigue. Of the 395 full-texts reviewed, 17 studies were included. Fifteen studies reported the impact of exercise on health-related quality of life with fatigue as a subdomain. Reduction in fatigue was observed following endurance, resistance, or a combination of both exercises. There was no significant difference between continuous and interval training ($n = 3$ studies, pooled standardized mean difference (SMD) $= -0.17$, 95% CI $= -0.47$, 0.12, $p = 0.25$) or between endurance and resistance training ($n = 3$ studies, SMD $= -0.35$, 95% CI $= -0.72$, 0.01, $p = 0.07$) on fatigue in people with COPD. Fatigue reduction is not usually a primary outcome of exercise interventions, but it is frequently a secondary domain. The type of exercise did not influence the impact of exercise on fatigue, which was reduced in endurance, resistance, or a combination of both exercises, enabling clinicians to personalize training to match targeted outcomes.

Keywords

COPD, chronic obstructive pulmonary disease, exercise, fatigue, systematic review

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Introduction

Chronic obstructive pulmonary disease (COPD) is a progressive condition characterized by chronic airflow limitation.[1] In addition to respiratory symptoms such as dyspnea and coughing, fatigue is very highly prevalent.[2,3] Fatigue is a subjective experience and may be described as tiredness, lethargy, or exhaustion.[3,4] Interviews with individuals with COPD have noted the negative effects of fatigue on their daily and social activities which impacts their overall quality of life.[5]

Fatigue has been measured through different scales and questionnaires,[6] either by asking a single question regarding a rating of fatigue on numeric or visual

[1] School of Health Sciences, Division of Health Sciences, University of South Australia, Australia
[2] Department of Respiratory Medicine, West Park Healthcare Centre, Ontario, Canada
[3] Department of Medicine, University of Toronto, Ontario, Canada
[4] Department of Physical Therapy, University of Toronto, Ontario, Canada
[5] School of Rehabilitation Science, McMaster University, Ontario, Canada

Corresponding author:
Lok Sze Katrina Li, Division of Health Sciences, School of Health Sciences, University of South Australia, City East Campus, GPO Box 2471, Adelaide, South Australia 5001, Australia.
Email: katrina.li@unisa.edu.au

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scale (0–10)[6] or by using a scale such as the Fatigue Severity Scale (FSS) which has nine items specifically querying the severity of fatigue in different situations.[7] Multidimensional instruments such as the Fatigue Impact Scale (FIS)[8] and the Multidimensional Fatigue Inventory (MFI-20)[9] are comprised of several questions related to various aspects of fatigue, such as physical functioning and overall impact on daily activities. Fatigue may also be measured as part of a patient self-reported quality of life questionnaire such as the Chronic Respiratory disease Questionnaire (CRQ) which has a fatigue domain consisting of four questions on the severity and frequency of fatigue.[10]

The effectiveness of exercise in the management of fatigue has been demonstrated in various conditions such as multiple sclerosis and cancer.[11,12] In COPD specifically, a recent Cochrane Systematic Review has confirmed that pulmonary rehabilitation (PR) is superior to usual care for improvements in the domain of fatigue.[13] However, the treatment effect between the exercise-only subgroup and the comprehensive PR subgroup was not significant.[13] As exercise as part of a PR program is usually a combination of endurance and resistance training, it is unknown whether either modality is superior for fatigue reduction. Thus, the aim of this systematic review was to determine if a specific type of exercise intervention is superior to another in the management of fatigue in individuals with COPD.

Methods

The review complied with the Preferred Reporting Items for Systematic Reviews and Meta-analysis guidelines and the protocol was registered (PROSPERO no: CRD42018110357). Since the original registration, the protocol was updated to reflect inclusion of only randomized controlled trials that compared between at least two physical exercise interventions. The more specific inclusion criteria narrowed the scope of the review to focus specifically on exercise interventions.

Study selection and eligibility criteria

A systematic search was conducted in MEDLINE, EMBASE, EMcare, PsycINFO, and Cochrane library from inception to 4 October 2018. Search terms and Medical Subject Headings used included the population (COPD), intervention (range of exercise interventions), and outcome (fatigue). The main search terms for the range of interventions were exercise, rehabilitation, self-management, and counseling (see the Online Supplementary Table 1). The search strategy was developed with the assistance of an academic librarian in Medline which was then adapted to other databases. At the point of search, there were no restrictions on publication period or language.

Studies were included if individuals with COPD were randomized into two or more physical exercise interventions in which fatigue was subjectively measured. Studies were excluded if: (1) participants did not have a physician or spirometry confirmation of COPD as the main diagnosis; (2) exercise interventions consisting of unsupervised exercise training, only breathing exercises or inspiratory muscle training; (3) comparators consisting of a control (usual care) group that did not receive supervised exercise interventions; (4) where measurements of fatigue were restricted to post exercise, such as leg fatigue assessed prior to and following a field walking test or a laboratory measure of exercise tolerance; (5) the reports were published in languages other than English, French, Italian, Spanish or Chinese; and (6) conference abstracts, study protocols, nonrandomized trials, or reviews.

All search results were imported into Endnote (version x8, Clarivate Analytics, Philadelphia, PA, USA) and then to the Covidence systematic review software[14] to remove duplicates. Titles and abstracts were screened against a priori eligibility criteria by two independent reviewers (KL, SB). Relevant reviews, abstracts or in ambiguous cases, full text of relevant or ambiguous reviews and abstracts were obtained and reviewed. Full text was reviewed by two independent reviewers (KL, SB), and a third reviewer (DB) was consulted for final decision on disagreements. For study protocols and conference abstracts, the reviewers searched for published version of the studies. Reference lists of relevant reviews were search for potential additional records. One reviewer (KL) provided guidance to assist a fluent speaker of each language to review non-English full text against the eligibility criteria.

The revised Cochrane risk-of-bias tool for randomized trials (RoB2) was used to assess risk of bias in five domains including risk arising from randomization process, deviation from intended interventions, missing outcome data, measurement of outcome, and selection of the reported result. A reviewer (KL) completed the risk of bias assessment following signaling questions from the guideline[15] and categorized each study into “low,” “some,” or “high” risk of bias.

Results were checked by a second reviewer (SB); any disagreements were resolved through discussions.

Data extraction

An a priori data extraction template was used to extract data on publication details (author, year, and country), study design, intervention (description, duration, dose, intensity, mode of delivery, adherence, fidelity reporting, etc.), sample size (consented and included in analysis), participant group demographics (e.g. mean age, sex distribution, smoking history, definition, and severity of COPD), and fatigue (measurement tool used, pre- and post-intervention fatigue measure, change scores if reported). Where fatigue measures were only reported in the figures of studies, an online software (WebPlotDigitizer Version 3.9) was used for data extraction.[16] Details on study intervention were extracted using the Template for Intervention Description and Replication checklist.[17]

Data synthesis

Studies that compared between similar interventions (e.g. continuous compared with interval training) were grouped and compared. Participant characteristics, details on exercise interventions, and changes of fatigue measurements pre- and post-intervention were reported descriptively. Changes in fatigue were considered clinically significant based on previously reported minimal important difference scores for individual fatigue measurement tools (CRQ domain score $= 0.5$,[10] FSS score $= 4.4$,[18] FIS score $= 10$,[19] Pulmonary Functional Status and Dyspnea Questionnaire (PFSDQ) score $= -3$,[20] and MFI-20 $= 2$[21]) The Fisher's exact test was used to determine if there are associations between program length and clinically significant fatigue reduction.

Meta-analyses were performed for studies that compared similar exercise interventions using Review Manager (RevMan) Version 5.3 (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014). The mean difference of fatigue measurements pre- and post-intervention was calculated and converted into standardized mean difference (SMD) to allow comparison between studies that used different tools to measure fatigue. Where the standard deviation (SD) of the mean difference was not reported, these were estimated using procedures recommended by the Cochrane handbook.[22] The fixed effects model was used as results of χ^2 and I^2 statistics indicated low level of heterogeneity between studies included in the analyses.

Results

Figure 1 includes a summary of the search outcome, screening results, and reasons for records excluded. Of the 395 full text reviewed, 17 studies were included in this review. Two of the most common reasons for exclusion of intervention studies at the full text stage were the lack of comparison between at least two exercise interventions (75 studies) and lack of subjective fatigue measure (54 studies).

Overall, there were some concerns of risk of bias in most of the studies ($n = 12$).[23–34] Four studies[35–38] had high risk of bias and one study had a low risk of bias[39] (Figure 2). Across all included studies, there was a low risk of bias in the selection of the reported results. Given that the measure of fatigue was patient reported, there were "some concerns" on the risk of bias in measurement of the outcome in 13 of the 17 included studies where participants were not blinded.

Study characteristics

Table 1 presents an overview of included studies. The average age of study participants was 65.6 ± 7.2 years, and study sample size ranged from 24[25,38] to 110.[24] COPD severity according to the Global Initiative of Chronic Obstructive Lung Disease classification system was used as part of the inclusion criteria in eight studies (moderate or severe COPD $n = 2$, severe COPD $n = 1$, moderate to very severe COPD $n = 1$, severe to very severe COPD $n = 4$).[23,24,29,30,32,35,37,39]

Twelve studies compared two intervention groups,[24–26,28,29,32,33,35–39] four studies compared two intervention groups and one control group (no exercise intervention),[23,27,30,31] and one study compared three intervention groups and one control group.[34] Baseline participant characteristics and fatigue measurement for the control group was not reported in one study.[34] The length of the exercise intervention programs ranged between 3 weeks[32] and 24 weeks.[37] The length of the exercise program was not significantly associated with change in fatigue within group ($p = 0.24$) or between groups ($p = 0.45$). One study did not have a standardized length of program as the study recruited participants with acute exacerbation of COPD and provided daily intervention during their stay in hospital which varied in each patient (mean length of stay in electrostimulation with calisthenic exercise group $= 10.5 \pm 4.3$ days; functional

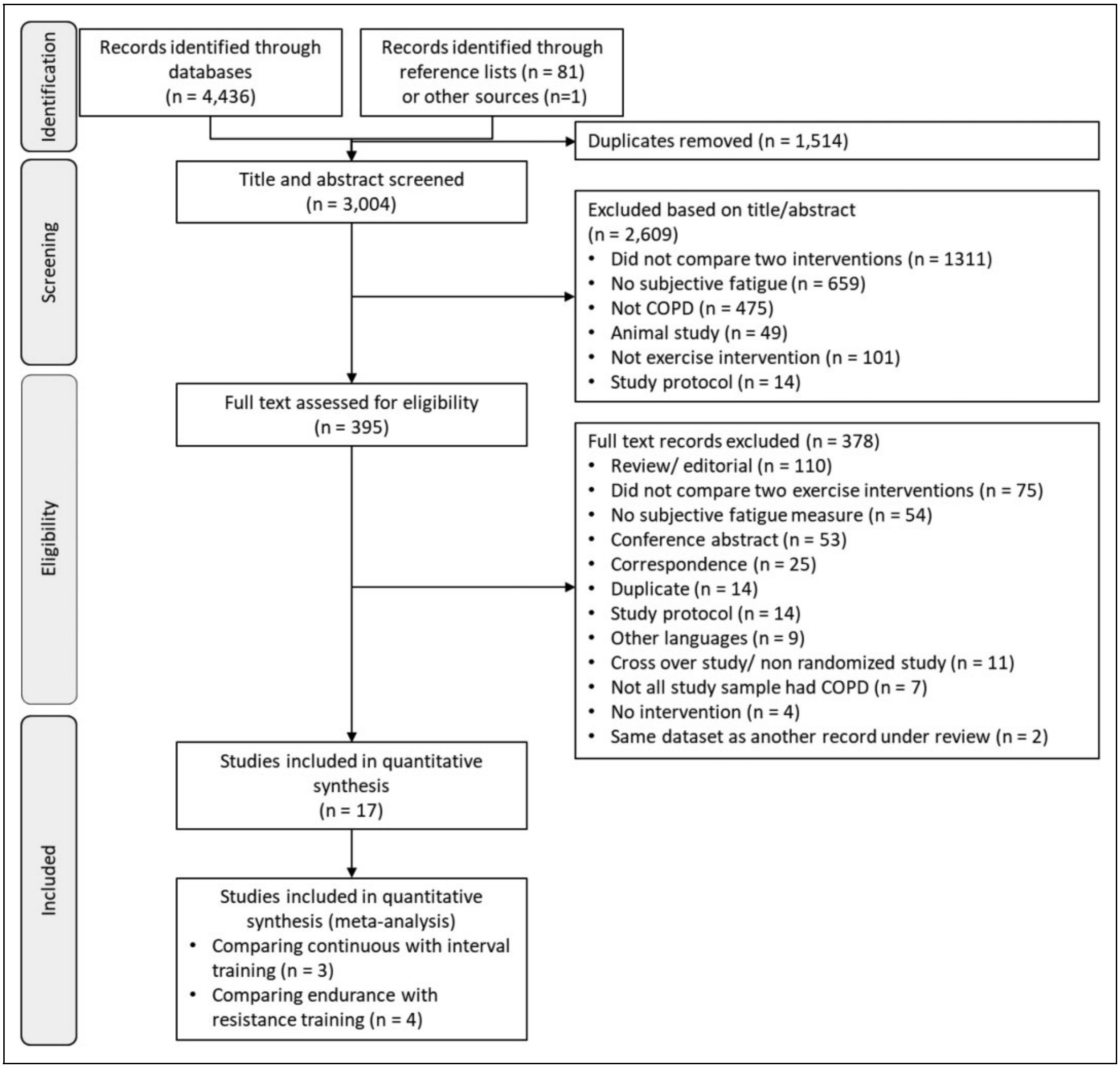

Figure 1. Summary of study flow from identification of studies to final inclusion.

electrostimulation group = 9.0 ± 2.5 days; control group = 9.2 ± 3.2 days).[30] Two studies followed up on participants at 8 weeks[38] and 12 weeks[34] following the end of the interventions while all other studies did not have a follow-up phase.

Exercise interventions were delivered by physical therapists ($n = 9$),[23,26,29,31,32,34,36,38,39] study investigator ($n = 2$),[30,35] exercise therapist ($n = 1$),[24] and rehabilitation staff ($n = 1$)[33]. It was unclear who provided the exercise intervention in four studies.[25,27,28,37] Only 1 of the 17 studies stated that intervention providers were trained in the study intervention protocol.[38] Another study stated that two of the three weekly exercise-training sessions were supervised by an exercise physiologist to ensure adherence to the exercise protocol.[24]

Fatigue was assessed with the MFI-20,[37] FSS, and FIS[23] in the two studies that had a specific aim to examine the effects of the intervention on fatigue in people with COPD. The FSS was also used in a study that compared effects of the interventions on physical condition in people with COPD.[30] The primary aim of the remaining studies was to assess the effect of the interventions on health-related quality of life, and measures of fatigue were incorporated as part of the CRQ[24–29,31,33–35,38–40] or PFSDQ.[36]

Types of interventions

Three types of exercise interventions (endurance, resistance, and combination of endurance and resistance training) were compared within the studies[23–36,38,39]

Figure 2. Summary of the ROB of included studies. ROB: risk of bias.

(Table 1). There were major variations between training protocols among the studies, and a detailed description of the study interventions in accordance with the TIDIER checklist is provided in the Online Supplementary Table 2. Studies that compared between similar interventions were grouped and described below followed by a synthesis of the intervention effects and meta-analysis of the effect on fatigue when permitted.

Continuous compared with interval endurance training. Three studies compared continuous with interval training that were performed through cycling[29,32] and a combination of cycling and treadmill walking.[28] The training workload and duration for both intervention groups varied significantly across the three studies (see the Online Supplementary Table 2).

No significant between-group differences in change in fatigue following the intervention were reported in all three studies. A meta-analysis of three studies (total 175 participants) indicated no significant difference in reduction of fatigue between the two types of training (pooled standard mean difference $= -0.17$, 95% CI $= -0.47$, 0.12, $p = 0.25$; Figure 3).

Endurance compared with resistance training. Six studies compared endurance with resistance training.[23,30,33–35,38] Endurance training was performed through cycling,[23,30,34] treadmill,[35] combination of treadmill and cycling[33] or a combination of walking and cycling exercise.[38] Resistance training was performed through body weight exercises,[23] use of free weights,[35] gymnastic apparatus,[34] elastic band,[30] or a combination of body weight, free weights, and elastic bands.[33,38]

Only one of the six studies reported a significant between-group difference where the electrostimulation with calisthenic exercise group (with elastic band) resulted in a significant reduction of FSS score compared with the functional (cycling) electrostimulation group,[30] and the remaining five studies that compared endurance with resistance training did not report a significant change in fatigue between groups following the intervention.[23,33–35,38]

Of the six studies that compared between endurance to resistance exercise on fatigue, results of four studies were pooled in meta-analyses.[23,33–35] Two studies were excluded from the meta-analyses as

Table 1. Overview of included studies.

Author (country)	Study population: Sample size (*n*)	Age (years), mean (SD)	Male (%)	FEV_1% predicted, mean (SD)	FEV_1/FVC%, mean (SD)	Study intervention groups: Name of intervention groups (modality)	Fatigue outcome: Name of fatigue measure	Change in fatigue,[a] mean (SD)
Endurance training: continuous and interval training								
Vogiatzis et al.[29] (Greece)	18	65 (10)	55	44 (4)	47 (14)	INT1:Continuous (cycling)	CRQ	0.67
	18	67 (7)	50	45 (4)	48 (14)	INT2: Interval (cycling)		0.67
Puhan et al.[32] (Switzerland)	50	69 (9)	72	34 (8)	47 (21)	INT1: High-intensity continuous (cycling)	CRQ	0.86 (1.36)
	48	69 (9)	60	35 (9)	49 (19)	INT2: Interval (cycling)		0.94 (1.17)
Mador et al.[28] (United States)	20	72 (8)	NR	42 (13)	49 (11)	INT1: Continuous training (cycle, treadmill)	CRQ	0.70
	21	72 (7)	NR	45 (14)	50 (11)	INT2: Interval training (cycle, treadmill)		0.75
Different types of training: endurance compared with resistance training								
Normandin et al.[33] (United States)	20	69 (7)	55	43 (16)	NR	INT1: High-intensity, lower extremity aerobic endurance conditioning (treadmill, cycle)	CRQ	0.70
	20	67 (9)	50	56 (20)	NR	INT2: Low-intensity peripheral muscle training (body weight, free weight exercise)		0.98
Dodia et al.[35] (India)	20	38 (4)	70	NR	NR	INT1: Lower limb endurance training (treadmill)	CRQ	0.30
	20	42 (4)	70	NR	NR	INT2: Unsupported upper limb endurance training (weights)		0.40
McFarland et al.[38] (United States)	13	72 (11)	46	NR[b]	NR	INT1: Aerobic exercise (walking, cycling)	CRQ	1.5[c]
	11	76 (10)	64	NR[b]	NR	INT2: Functional strengthening (body weight)		2.0[c]
Duruturk et al.[23] (Turkey)	15	61 (5)	73	58 (14)	46 (11)	INT1: Cycling (cycling)	FSS; FIS	−13.2 (8.5); −24.0 (17.6)
	14	61 (5)	93	57 (11)	46 (11)	INT2: Callisthenic exercise (body weight)		−15.8 (11.0); −17.8 (16.2)
	13	64 (6)	85	64 (11)	50 (10)	INT3: Control (education)		1.4 (4.9); 2.1 (4.8)
Lopez et al.[30] (Spain)	13	64 (11)	77	26 (8)	NR	INT1: Functional electrostimulation (cycling)	FSS	4.1
	14	63 (12)	79	34 (6)	NR	INT2: Electrostimulation with calisthenic exercise (elastic band)		2.0
	12	64 (9)	83	30 (7)	NR	INT3: Control (no intervention)		2.0
Different types of training: endurance and/or resistance compared with combined (endurance and resistance) training								
Ortega et al.[34] (Spain)	16	66 (8)	88	41 (11)	45	INT1: Endurance (cycling)	CRQ	0.5
	17	66 (6)	82	40 (14)	44	INT2: Strength (gymnastic apparatus)		0.9
	14	60 (9)	93	33 (12)	39	INT3: Combined (gymnastic apparatus, cycling)		0.4
Mador et al.[25] (United States)	13	68 (2)	NR	40 (4)	52	INT1: Endurance training (cycling, treadmill)	CRQ	0.9
	11	74 (2)	NR	44 (4)	56	INT2: Combined (cycling, treadmill, weights)		0.6
Probst et al.[36] (Brazil)	20	65 (10)	55	39 (14)	47 (14)	INT1: Low intensity (crunches, trunk rotation and flexion)	PFSDQ	−13
	20	67 (7)	50	40 (13)	48 (14)	INT2: High intensity and strength (cycling, treadmill, machine)		−3
Zambom-Ferraresi et al.[27] (Spain)	14	68 (7)	100	48 (12)	46 (7)	INT1: Resistance (resistance machines)	CRQ	0.64 (0.9)
	14	68 (7)	100	44 (12)	45 (10)	INT2: Combined (resistance machine + cycling)		0.75 (0.8)
	8	69 (5)	100	40 (5)	39(6)	INT3: Control (no intervention)		0.00 (0.2)

(continued)

Table 1. (continued)

	Study population					Study intervention groups	Fatigue outcome	
Author (country)	Sample size (*n*)	Age (years), mean (SD)	Male (%)	FEV_1% predicted, mean (SD)	FEV_1/FVC%, mean (SD)	Name of intervention groups (modality)	Name of fatigue measure	Change in fatigue,[a] mean (SD)
Combined endurance and resistance training: different protocols								
McNamara et al.[31] (Australia)	18	72 (10)	28	60 (10)	59 (9)	INT1: Water-based exercise (walking, cycling, weights)	CRQ	NR
	20	73 (7)	50	62 (15)	58 (9)	INT2: Land-based exercise (walking, cycling, weights)		NR
	15	70 (9)	47	55 (20)	53 (13)	INT3: Control (no intervention)		NR
Klijn et al.[24] (Netherlands)	55	61 (7)	35	32 (9)	39 (8)	INT1: Nonlinear periodized exercise program (cycling, resistance machine)	CRQ	1.64
	55	61 (6)	35	32 (9)	39 (9)	INT2: Endurance and progressive resistance training (cycling, treadmill, resistance machines)		0.90
Resistance training: different modalities								
Ramos et al.[26] (Brazil)	17	67[c]	65	NR	50[c]	INT1: Resistance training (elastic tubing)	CRQ	0.70
	17	66[c]	76	NR	54[c]	INT2: Conventional R group (weight machine)		0.30
Endurance training: upper extremity training								
Holland et al.[39] (Australia)	22	67 (8)	64	34 (10)	NR	INT1: Unsupported upper limb endurance training (stick)	CRQ	1.05
	16	69 (7)	63	40 (10)	NR	INT2: Supported upper limb training (Purdue pegboard test)		0.94
Pulmonary rehabilitation: with or without balance training								
Mkacher et al.[37] (Tunisia)	30	64 (3)	100	39 (8)	46 (11)	INT1: Pulmonary rehabilitation (unclear)	MFI-20	GF: −1; PF: −2; RA: −1; RM: 0; MF: 0
	32	61 (4)	100	40 (9)	47 (5)	INT2: Pulmonary rehabilitation and balance (stance, transition, gait, functional strengthening)		GF: −3; PF: −4; RA: −3; RM:0; MF: 0

SD: standard deviation; INT: intervention; CRQ: Chronic Respiratory disease Questionnaire; NR: not reported; FSS: Fatigue Severity Scale; FIS: Fatigue Impact Scale; PFSDQ: Pulmonary Functional Status and Dyspnea Questionnaire; MFI-20: Multidimensional Fatigue Inventory; GF: general fatigue; PF: physical fatigue; RA: reduced activity; RM: reduced motivation; MF: mental fatigue; FEV1: Forced Expiratory Volume in one second; FVC: Forced Vital Capacity.
[a]Change in fatigue calculated by post- and pre-intervention values.
[b]Reported FEV1% predicted in L.
[c]Median value (mean value not reported).

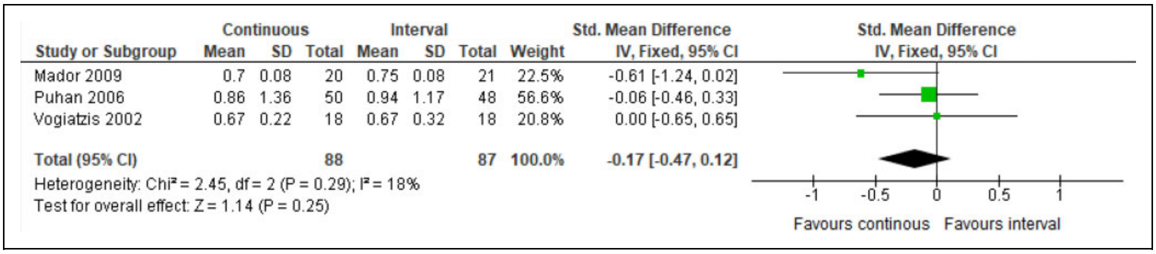

Figure 3. Forest plot comparing effects of continuous and interval training on fatigue.

participants received electrostimulation in addition to exercise training[30] or only reported the median pre- and post-intervention fatigue measures.[38] One study used two fatigue outcome measures (FIS and FSS)[23]; thus, two separate meta-analyses were performed (total 142 participants). Endurance training resulted in a significant reduction in fatigue compared with resistance training when changes in fatigue measures (CRQ[33–35] and FIS[23]) were pooled (pooled standard mean difference $= -0.35$, 95% CI $= -0.68, 0.02$, $p =$ 0.04; Figure 4(a)). However, when CRQ[33–35] and FSS[23] measures were pooled, there was no significant difference on endurance or resistance training on fatigue (pooled standard mean difference $= -0.23$, 95% CI $= -0.56, 0.11$, $p = 0.18$; Figure 4(b)). A sensitivity analysis was performed where results by Duruturk et al.[23] were excluded from the meta-analysis as it was the only study that did not use CRQ as an outcome measurement for fatigue. Results of the sensitivity analysis (total 113 participants) indicated no difference between endurance or resistance exercise on fatigue (pooled standard mean difference $= -0.35$, 95% CI $= -0.72, 0.01$, $p = 0.07$; Figure 4(c)).

Endurance and/or resistance compared with combined endurance and resistance training. One study compared endurance with combined endurance and strength,[25] two studies compared resistance with combined training,[27,36] and one study had three groups and compared between resistance, endurance, and combined training.[34] Resistance training was performed with gymnastic apparatus,[34] resistance machines,[25,27] or a combination of body weight exercises and resistance machines.[36] Endurance training was performed through cycling[27,34] or a combination of cycling and treadmill.[25,36] Exercise modality and prescription of baseline workload were consistent between the endurance or resistance only group compared with the combined (endurance and resistance) group in three studies.[25,27,34] The resistance training component within the combined training group differed in one study,[36] where the low-intensity group did calisthenics exercises (truck rotation and flexion) and abdominal exercises (crunches), while the high-intensity (combined endurance and resistance training) group used resistance machines to train the quadriceps, biceps, and triceps muscle groups.

While combined (endurance and resistance) training formed one of the study arms in four studies, no meta-analysis was performed as the comparison groups consisted of a mixture of endurance training,[25] resistance training,[27,36] or both (i.e. an endurance arm and a resistance arm).[34] All four studies reported no significant between-group differences in change of fatigue following the intervention.

Combined endurance and resistance training: Use of different protocols. Two studies compared between two training protocols of combined endurance and resistance training.[24,31] One study compared land-based with aquatic exercise training, training consisted of lower limb endurance exercise (e.g. walking, cycling) and upper limb resistance exercises with weights.[31] Another study compared tradition progressive resistance and endurance training (fixed workload and progression) with nonlinear periodized exercise training (varied workload, duration, and set of interval exercise).[24]

No meta-analysis was performed due to the differences between study comparators. Both studies reported a significant between-group difference where nonlinear periodized exercise training and water-based exercise training resulted in significantly greater improvements in fatigue than endurance and progressive resistance training[24] and land-based exercise group.[31]

Resistance training: Use of different modalities. One study compared between resistance training where both groups of participants performed the same upper and lower limb movements against resistance either through elastic tubing or conventional weight

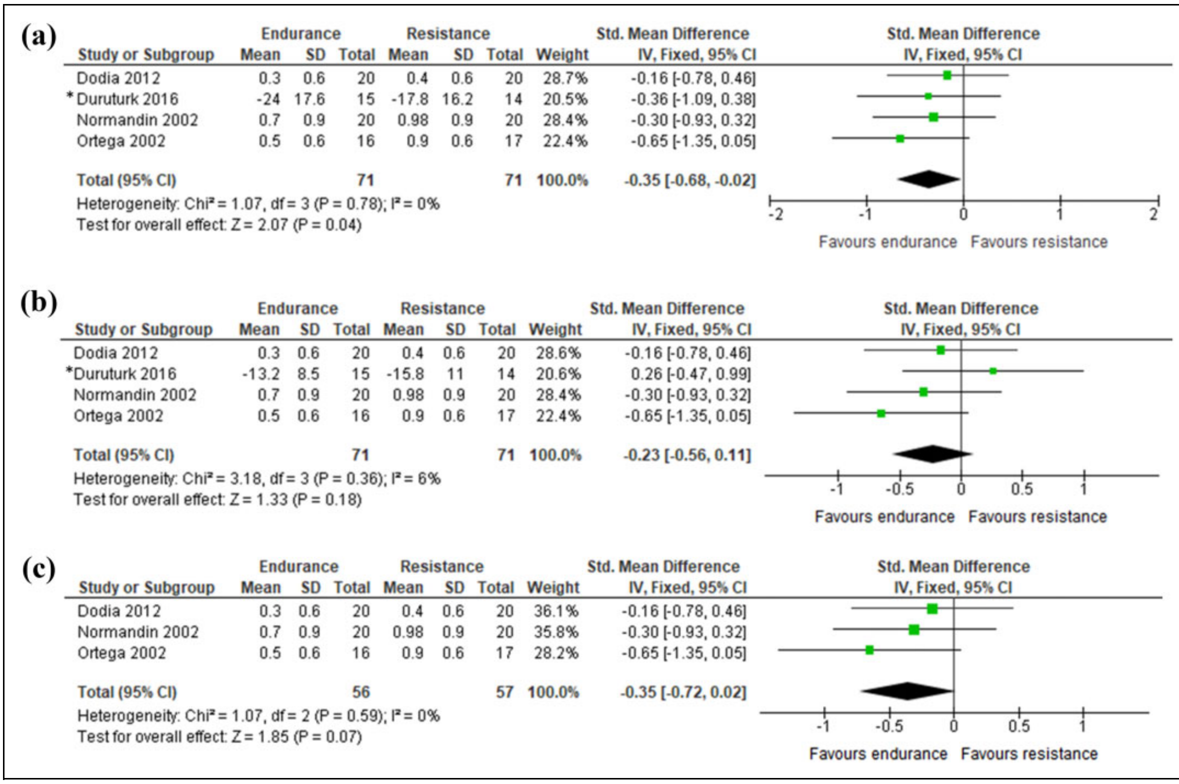

Figure 4. (a) Forest plots comparing endurance with resistance exercise on change in fatigue post-intervention (*results of Fatigue Impact Scale reported in study by Duruturk et al.[23]). (b) Forest plots comparing endurance with resistance exercise on change in fatigue post-intervention (*results of Fatigue Severity Scale reported in study by Duruturk et al.[23]). (c) Sensitivity analysis of studies that compared between endurance and resistance exercise training.

machines.[26] There were no significant differences on fatigue following resistance training using different modalities.

Endurance training: Use of different protocols in upper extremity training. One study compared unsupported and supported endurance training in the upper limb.[39] The unsupported group completed five upper limb exercises with a stick (0.5 kg) with their arms unsupported, while the other group performed four timed task placing pins on a pegboard with their upper limb supported on a table. There were no significant differences on fatigue between the two upper extremity training protocols.

PR: With or without balance training. One study compared a PR program with and without balance training.[37] There were no details on the specific training protocol of the PR program except for supervised exercise training twice per day, three times per week. For the balance-training group, exercise training was replaced with balance training three times per week. Balance training included stances exercises (e.g. one-legged stance), transition exercise (e.g. sit to stand), gait exercise (e.g. tandem walk), and functional strength exercises (e.g. walking on toes). There were no significant between-group differences in fatigue.

Discussion

This systematic review identified 17 studies that compared exercise interventions and reported their effects on fatigue in people with COPD. Only two of the included studies had a specific aim of assessing the effects of the intervention on fatigue; the remaining 15 studies aim to assess the effects of the interventions on exercise capacity or health-related quality of life. Endurance and/or resistance exercises were the most common exercise interventions. When similar exercise interventions were compared, no specific exercise intervention was more effective than others in the management of fatigue.

Despite at least half of the people with COPD experiencing fatigue on a daily basis,[41] only a small number of studies specifically assessed the effects of different exercise interventions on fatigue. For the current study, 2 of the 17 studies that met the eligibility criteria of the study had a specific aim of investigating fatigue.[23,37] Most studies assessed fatigue as part of a health-related quality of life measurement tool (CRQ), and only three studies used fatigue specific questionnaires (FSS, FIS, and MFI-20).[23,30,37] While the standardized mean differences were used to compare across studies that used different tools to measure fatigue, meta-analysis of studies that compared between endurance and resistance exercise training yielded different results when different measurement tools results were pooled (Figure 4). Comparison between the heterogeneity levels with uni and multidimensional scale results was pooled (Figure 4(a) and (b)), together with the results of the sensitivity analysis (Figure 4(c)) may be indication that there are more similarities between a multidimensional tool and health-related quality of life measurement tool. Future studies should consider the use of a multidimensional fatigue assessment tool, in addition to the quality of life measures, which would provide a more comprehensive description of the impact of exercise interventions on fatigue.

It should be highlighted that clinically significant improvement in fatigue was observed following resistance,[23,26,27,33,34,36,38] endurance,[23,25,33,34,36,38] combined endurance and resistance,[24] continuous,[28,29,32] and interval[28,29,39] training in the included studies. One non-inferiority trial demonstrated that continuous training was not more superior to interval training in people with COPD in terms of improvements in health-related quality of life and exercise capacity.[32] Findings of this review were similar to a previous systematic review that specifically compared resistance with endurance training in people with COPD and reported no difference in their health-related quality of life.[42] While there are recommendations on exercise prescription in relation to muscle fatigue in people with COPD,[43] there is no consensus on the optimal exercise mode or frequency that best manages fatigue. Furthermore, the long-term impact of the interventions on fatigue is not known as only two studies completed follow-up at different time frames.

A limitation of this review is that the specific type of outcome measures used to assess fatigue was not part of the eligibility criteria, with outcome measures that were fatigue-specific or general health-related quality of life measures were included. While CRQ is a commonly used health-related quality of life measure that contains a fatigue domain, it is possible that other studies that compared the impact of exercise interventions in individuals with COPD used the CRQ. It should be emphasized that the aim of this review was to determine if a specific exercise intervention is more effective than others in the management of fatigue in individuals with COPD and is not a systematic review of studies that have used the CRQ. Presence of fatigue in participants was not part of the inclusion criteria for the included studies. Given the small number of studies that compared similar interventions, studies with different levels of risk of bias were included in this review. Language bias was possible as nine studies were excluded at the full text stage.

Conclusion

There are limited studies investigating the impact of exercise in which fatigue is the primary outcome measure. Care is needed with the interpretation of results as the presence of fatigue was not part of the inclusion criteria in the small number of studies included. Meta-analysis results did not identify a specific exercise intervention that was more effective than others in the management of fatigue. Clinicians and patients may personalize exercise to target functional exercise, activities, or quality of life, without concern for a differential impact of the training program on fatigue.

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ORCID iD

Lok Sze Katrina Li https://orcid.org/0000-0001-5931-9567

Supplemental material

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