Optimising Home-Based Rehabilitation for COPD

Submitted by

Angela Therese Burge

Master of Physiotherapy (Cardiothoracic)

Bachelor of Physiotherapy (Honours)

A thesis submitted in total fulfilment of the requirement for the degree of

Doctor of Philosophy

Discipline of Physiotherapy, School of Allied Health, Human Services and Sport

College of Science, Health and Engineering

La Trobe University

Bundoora, Victoria 3086

Australia

May 2020

Acknowledgements

The time, support and commitment from my supervisors Professor Anne Holland and Professor Michael Abramson was beyond what I could have ever imagined. Words cannot express the depth of my admiration and gratitude for their constancy and wisdom.

The generous friendship, counsel and assistance from Narelle, Janet and Natalie.

The unwavering confidence and care from my parents, in every possible way.

The love, inspiration and firm belief in working to make a better future for everyone – thank you Tabby, Henry and Ben.

Dedication

To Pop and Digger, my grandfathers who suffered from this terrible disease, and my grandmothers who cared for them.

Table of Contents

List of Figures

List of Tables

List of Abbreviations

COPD	chronic obstructive pulmonary disease
CRQ	Chronic Respiratory Questionnaire
DALY	disability-adjusted life year
ESWT	endurance shuttle walk test
ISWD	distance walked on incremental shuttle walk test
ISWT	incremental shuttle walk test
LIPA	light intensity physical activity
MID	minimal clinically important difference
MVPA	moderate to vigorous intensity physical activity
MIST	modified incremental step test
NHMRC	National Health and Medical Research Council
SpO_2	oxyhaemoglobin saturation
6MWD	distance walked on six-minute walk test
6MWT	six-minute walk test
SEM	standard error of the mean
SGRQ	St George Respiratory Questionnaire
QALY	quality-adjusted life year
$\dot{V}O_2$	peak oxygen uptake

Summary

Home-based pulmonary rehabilitation delivers equivalent improvements in exercise capacity and health-related quality of life, accompanied by an improved rate of program completion, when compared to traditional centre-based programs for people with chronic obstructive pulmonary disease (COPD). However, the optimal model had not been defined. The body of work in this thesis has addressed gaps in knowledge and provided evidence to underpin clinical implementation of entirely home-based pulmonary rehabilitation. The themes explored were: methods to improve physical activity and analyse physical activity outcomes; facilitation of the home-based assessment of exercise capacity; and cost-effectiveness of home-based pulmonary rehabilitation. These themes were addressed in the following studies:

1. A Cochrane systematic review of interventions to improve physical activity in people with COPD.
2. A comparison of conventional and compositional approaches to analysis of physical activity outcomes.
3. A prospective study of the modified incremental step test (MIST) to assess the feasibility, reliability and responsiveness to pulmonary rehabilitation in the home-based setting.
4. An economic analysis of home and centre-based pulmonary rehabilitation including healthcare costs in the 12 months following completion.

These studies demonstrated that there was limited evidence for improvements in physical activity in people with COPD following pulmonary rehabilitation, regardless of program location. However, the compositional approach did identify some associations between movement behaviours and participant features that may inform development of future interventions. The utility of the MIST for home-based assessment of exercise capacity and prescription of training intensity was demonstrated, along with favourable cost-effectiveness comparisons with a traditional program model. This research provides new evidence to support the clinical implementation of home-based pulmonary rehabilitation as an alternative for people who cannot access centre-based programs.

Statement of Authorship

This thesis includes work by the author that has been published, accepted for or submitted for publication as described in the text.

Except where reference is made in the text of the thesis, this thesis contains no material published elsewhere or extracted in whole or in part from a thesis accepted for the award of any other degree or diploma.

No other person's work has been used without due acknowledgement in the main text of the thesis.

This thesis has not been submitted for the award of any degree or diploma in any other tertiary institution.

All substantive contributions by others to the work presented including jointly authored publications, is clearly acknowledged.

Ethics approval from the Human Research Ethics Committees at Alfred Health (261/11, 207/16), Austin Health (H2011/04364), Wimmera Health Care Group (CRC 19/6) and La Trobe University (FHEC 11/134) in Australia and Universidade Nove de Julho (235/249) in Brazil was gained for research procedures presented in this thesis.

Statement of Authorship: Student

For chapters two, three, four and five, the extent of the candidate's contribution was as follows:

Chapter	Title	Publication status	Extent of contribution
2	Interventions for promoting physical activity in people with COPD	Published	70%
3	The impact of pulmonary rehabilitation on 24-hour movement behaviour in people with chronic obstructive pulmonary disease: new insights from a compositional perspective	Submitted for publication	70%
4	Application of the modified incremental step test for pulmonary rehabilitation	Submitted for publication	70%
5	Home-based pulmonary rehabilitation for COPD using minimal resources: an economic analysis	Published	70%

Signed: 

Date: 28th May 2020

Statement of Authorship: Supervisor

I hereby certify that the declaration above is a correct reflection of the extent of the contributions made by the student candidate towards each chapter in the thesis.

Name of Supervisor	Signature	Date
Prof Anne Holland		28th May 2020

Publications and Presentations

All of the research and manuscripts presented in this thesis were conducted and written during the period of candidature for the specific purpose of obtaining the degree of Doctor of Philosophy. Manuscripts were prepared according to journal requirements.

The contributions of all authors including the candidate towards each study is stated in the prefaces of chapters two through to five.

Published Manuscripts

Burge AT, Holland AE, McDonald CF, Hill CJ, Lee AL, Cox NS, Moore R, Nicolson C, Lahham A, Gillies R, Abramson MJ, Mahal A. Home-based rehabilitation for COPD using minimal resources: an economic evaluation. *Respirology* 2020;25:183-190. doi: 10.1111/resp.13667

Burge AT, Cox NS, Abramson MJ, Holland AE. Interventions for promoting physical activity in people with chronic obstructive pulmonary disease (COPD). *Cochrane Database of Systematic Reviews* 2020;4;CD012626. Doi: 10.1002/14651858.CD012626.pub2.

Submitted Manuscripts

Burge AT, Rodrigues-Junior JC, Abramson MJ, Cox NS, Bondarenko J, Webb E, Marceau T, Handley E, Macdonald H, Askin A, Santos Araújo Calasans GA, Pereira do Amaral D, Dreger J, Dal Corso S, Holland AE. Application of the modified incremental step test for pulmonary rehabilitation. Submitted to *Physical Therapy* on 12th May 2020.

Burge AT, Palarea-Albaladejo J, Holland AE, Abramson MJ, McDonald CF, Mahal A, Hill CJ, Lee AL, Cox NS, Lahham A, Moore R, Nicolson C, O'Halloran P, Gillies R, Chastin SFM. The impact of pulmonary rehabilitation on 24-hour movement behaviour in people with chronic obstructive pulmonary disease: new insights from a compositional perspective. Submitted to *Journal of Physical Activity and Health* on 28th May 2020.

Published Abstracts

Burge A, Dal Corso S, Bondarenko J, Handley E, MacLachlan S, Abramson M, Holland A**.** Feasibility and reproducibility of the modified incremental step test for pulmonary rehabilitation**.** *Respirology* 2019;24:TO082**.**

Burge A, Cox N, Abramson M, Holland A. Interventions for promoting physical activity in people with COPD: a Cochrane systematic review. *Respirology* 2018;23:TO052.

Burge A, Cox N, Abramson M, Holland A. Interventions for promoting physical activity in people with COPD: a Cochrane systematic review. *American Journal of Respiratory and Critical Care Medicine* 2018;197:A7069.

Burge, A, Holland A, McDonald C, Hill C, Lee A, Cox N, Moore R, Nicolson C, Lahham A, Gillies R, Abramson M, Mahal A. Home-based rehabilitation for COPD using minimal resources: an economic evaluation. *Respirology* 2017;22:TO102.

Burge, A, Holland A, McDonald C, Hill C, Lee A, Cox N, Moore R, Nicolson C, Lahham A, Gillies R, Abramson M, Mahal A. Home-based rehabilitation for COPD using minimal resources: an economic evaluation. *Respirology* 2017;22:AO177.

Conference Presentations

- Thoracic Society of Australia and New Zealand Annual Scientific Meeting March 2017; Canberra, Australia (oral)
- Australian Physiotherapy Association Conference October 2017; Sydney, Australia (oral)
- Asia Pacific Society of Respirology Congress November 2017; Sydney (oral)
- Thoracic Society of Australia and New Zealand Annual Scientific Meeting March 2018; Adelaide, Australia (oral)
- American Thoracic Society International Conference May 2018; San Diego, USA (poster)
- European Respiratory Society International Conference September 2018; Paris, France (poster)
- Hospital in the Home Conference November 2018; Brisbane, Australia (oral)
- Thoracic Society of Australia and New Zealand Annual Scientific Meeting March 2019; Gold Coast, Australia (oral)

Invited Presentations

November 2018	Hospital in the Home Society Annual Conference. Brisbane, Australia
October 2017	'Alternative Models of Pulmonary Rehabilitation for Chronic Lung Disease' seminar. Austin Health (Melbourne, Australia)

Grants and awards

Grants

Grant	Value
National Health and Medical Research Council, Dora Lush Biomedical Scholarship (PhD Stipend) 2015-2018	$107,204
Hospital in the Home Dr Nicholas Collins Fellowship Achievement Award 2017	$10,000
Asia Pacific Society of Respirology Congress Travel Award 2017	$150
Lung Foundation Australia/Cochrane Airways Australia Scholarship 2018	$2500
La Trobe University School of Allied Health Higher Degree Research Support Grants	
February 2016	$1000
January 2018	$730
April 2018	$1425
September 2018	$1700
Thoracic Society of Australia and New Zealand Annual Scientific Meeting	
Travel Award 2016	$590
Travel Award 2017	$500
Travel Award 2018	$350

This work was supported by an Australian Government Research Training Program Scholarship.

Awards

October 2017	Best clinical research presentation (cardio-respiratory) Australian Physiotherapy Association Conference (Sydney, Australia)
January 2020	American Thoracic Society International Trainee Scholarship

Chapter 1.

Introduction

1.1 Overview

(a) Chronic obstructive pulmonary disease (COPD)

Chronic obstructive pulmonary disease (COPD) is a common and disabling disease, commonly due to exposure to noxious particles or gases, leading to lung injury with local and systemic inflammation. The resulting small airways disease and parenchymal destruction varies between individuals, but generally clinical presentation is characterised by persistent respiratory symptoms and airflow limitation which are treatable but not curable.[1]

A major cause of morbidity and mortality, estimates for global prevalence of COPD (11%)[2] are mirrored in the Australian population, where it is estimated that up to 8% of Australians aged 40 and over have features consistent with a diagnosis of COPD.[3] Estimates are considered conservative due to under-diagnosis and anticipated increases due to an aging population.[1, 4, 5]

The burden associated with COPD is also driven by co-existing chronic conditions, which may be related to the disease process, or to ageing and presence of other risk factors including smoking.[1] People with COPD commonly experience arthritis, asthma, back pain, cancer, cardiovascular disease, diabetes and mental health problems, with over 90% of Australians with COPD reporting more than one comorbidity.[6] Globally, around three million deaths are attributable to COPD annually.[7] In Australia, COPD ranks fifth among the leading causes of death (2017 figures).[8]

(b) Magnitude of the social and economic impact of COPD

In terms of overall burden of disease, COPD is the fifth leading cause of disability-adjusted life years (DALYs) lost across the world.[9] For people over 65 years of age, Australian figures show that COPD was the second leading cause of total disease burden for men and the leading cause for women, and that this respiratory burden increased with increasing geographical remoteness based on access to services.[10]

The impact of COPD is associated with substantial costs to society. Spending attributed to COPD accounts for 1.3% of total Australian direct health expenditure, primarily attributable to hospitalisations ($977 million in 2015-16).[10] The disease costs the Australian community an estimated $8.8 billion annually in financial costs, including health and hospital costs, lost productivity, premature death and a low rate of employment.[4] The increasing prevalence of COPD and accompanying costs expected as the population ages provides incentive for efficient

implementation of evidence-based interventions, to reduce the burden of COPD to individuals, families, the health system and society.

(c) Clinical challenges in managing COPD

The primary symptoms of COPD are breathlessness, cough and sputum production. Other symptoms such as chest tightness, wheezing and fatigue are common and contribute to impairment of physical function and quality of life.[1] The natural history of COPD is characterised by progressive deterioration with episodes of acute deterioration in symptoms referred to as an exacerbation.[11] The challenge for individuals to manage symptoms and exacerbations is well acknowledged,[12] providing additional impetus for application of scalable and effective treatment strategies.

1.2 Non-pharmacological interventions for COPD: pulmonary rehabilitation

International evidence-based clinical practice guidelines for the management of COPD unequivocally recommend non-pharmacological strategies (such as pulmonary rehabilitation and regular exercise) for all people with COPD.[11] Pulmonary rehabilitation is a well-established '*comprehensive intervention based on a thorough patient assessment followed by patient-tailored therapies that include, but are not limited to, exercise training, education, and behaviour change, designed to improve the physical and psychological condition of people with chronic respiratory disease and to promote the long-term adherence to health-enhancing behaviours*'.[13] Programs usually involve attendance at an outpatient group program twice a week for 7-8 weeks. Current recommendations state that referral should be considered for all people with COPD who have dyspnoea or other respiratory symptoms, reduced exercise tolerance, disease-imposed activity restriction or impaired health status.[13] Pulmonary rehabilitation is supported by Level 1 evidence for clinically important improvements in exercise capacity and dyspnoea in people with COPD.[14] Benefits attributable to completion of pulmonary rehabilitation include improvements in symptoms and health-related quality of life, as well as reduction in health care utilisation.[15]

(a) Barriers to pulmonary rehabilitation participation for people with COPD

Despite the burden of COPD to individuals and health care systems, and strong evidence for physiological, symptom-reducing and psychosocial benefits of pulmonary rehabilitation,[16] this intervention is widely recognised to be underutilised.[17] It is estimated that only 5-10% of Australians with COPD have access to pulmonary rehabilitation.[18] Up to half of people who are

referred to pulmonary rehabilitation never attend, and up to a third of participants do not complete a program.[19]

Numerous factors contribute to the gap between the knowledge of the benefits of pulmonary rehabilitation and the actual delivery of services to suitable patients.[16] Factors relating to environment, knowledge, attitudes and behaviours interact to influence referral, uptake, attendance and completion of pulmonary rehabilitation.[20] Identified system-level issues include limited availability of services, especially in regional and rural settings. A paucity of awareness of program benefits by both healthcare professionals and patients also contributes to poor referral rates and uptake of existing programs. Patient-related barriers include the burden of travel to hospital-based programs and logistical challenges, especially in the context of distressing dyspnoea and limited mobility or for people in employment.[21]

Overcoming these challenges will be imperative to improving access and uptake of pulmonary rehabilitation. In order to extend the known benefits of pulmonary rehabilitation to those who would benefit, new models that overcome the system- and patient-related barriers have been identified as critical elements for further study.[22] The COVID-19 pandemic has also necessitated a transition away from centre-based models of care.

1.3 Alternative models of delivery: home-based pulmonary rehabilitation

Home-based pulmonary rehabilitation is one strategy that may overcome patient-related barriers to pulmonary rehabilitation, including travel, transport and disability. Home-based models for pulmonary rehabilitation have been compared to usual care[23-33] or hospital-based programs.[34-39]

(a) Evidence for clinical effectiveness of home-based pulmonary rehabilitation

In trials comparing home-based with hospital-based programs, a wide variety of study designs, supervision and contact protocols have been employed (Table 1). Evidence of power calculations was not presented in all studies[34, 37, 38] and sample sizes ranged from 35[38] to 287.[40] Three studies employed non-inferiority designs[35, 39, 40] and two studies reported the number of participants who did not consent due to a preference for centre-based programs.[39,40] In some studies, participants allocated to home-based interventions received up to 24 home visits[38] and were required to make up to ten hospital visits.[35, 37] Additionally, not all home and hospital-

based groups received equivalent exercise prescription[34-36] or incorporated education and self-management program components.[22, 38]

A range of outcome measures have been utilised in these studies (Table 2). Most commonly, health-related quality of life has been assessed by the Chronic Respiratory Questionnaire (CRQ)[34, 35, 37, 39, 40] and exercise capacity using the 6-minute walk test (6MWT). No systematic differences were demonstrated between home- and hospital-based programs. All of the five studies that assessed health-related quality of life demonstrated home and centre-based within-group improvements that met the minimal important difference in CRQ(34,37,39,40) and St George Respiratory Questionnaire.(35) Home and centre-based within-group improvements in exercise capacity met the minimal important difference in all with the exception of two studies (both groups,(35) centre-based group(39)). Current Australian and New Zealand Pulmonary Rehabilitation Guidelines recommended that home-based pulmonary rehabilitation that includes "regular contact to facilitate exercise participation and progression be offered to patients with COPD as an alternative to hospital-based pulmonary rehabilitation (weak recommendation, moderate-to-low quality evidence)".[41]

The only Australian study to date was an NHMRC-funded randomised controlled equivalence trial that compared home-based with hospital-based pulmonary rehabilitation. It demonstrated that a new model of structured home-based pulmonary rehabilitation produced equivalent clinical outcomes and, for the first time, similar intervention costs when compared with a conventional centre-based program.[39, 42] There were key differences between previous work and the development of this 'HomeBase' model. Participants received home-based delivery of all program components, including exercise, education and self-management training. Telephone appointments were conducted by respiratory physiotherapists who were trained in motivational interviewing techniques and specific exercise goal setting was a critical component of every contact. Exercise programs were designed so that the home-based group received a similar 'dose' of exercise to the centre-based group. This was confirmed by diary entries for exercise time in the home-based group, which correlated with objective measures of physical activity.[43] Improved completion rates and acceptability were demonstrated, and participants noted the time-convenience and flexibility in training opportunities as benefits of the model.[44]

Another unique aspect of this study was the capacity to assess the long-term impact on physical activity behaviour following pulmonary rehabilitation. It has been postulated that a home-based program may favourably influence behaviour change[38] and a key difference between this model of home-based pulmonary rehabilitation and the traditional centre-based model is the lack of direct supervision of exercise training. In this context, promotion of physical activity becomes

critically important. In the HomeBase model, this was achieved by specific prescription and progression of intensity and duration with completion of a home diary and revision of specific goals. Staff received specific training and through weekly structured telephone modules, applied the principles of motivational interviewing to promote problem solving and facilitate health behaviour change.[45] Home-based participants demonstrated similar levels of physical activity to those in the centre-based program.[46] However, it was noted that measures of physical activity remained low across both groups. The importance of physical activity for people with COPD, and current knowledge regarding promotion of physical activity, will be explored in the next section.

TABLE 1. RANDOMISED CONTROLLED TRIALS OF OUTPATIENT HOSPITAL-BASED VERSUS HOME-BASED PULMONARY REHABILITATION PROGRAMS: PROGRAM FEATURES.

Study Number of participants Country	Program features	
	Hospital-based	**Home-based**
Strijbos 1996[38] n = 35 the Netherlands	Patient education Training (supervised): aerobic and strength Training (unsupervised): walking and stair climbing daily (≥ 15 min) After 3 to 4 weeks, commenced on stationary bicycles • workload increased up to 70% baseline peak workload, then duration increased 12 weeks, 2 sessions/week, 1 hour/session 25 hospital visits	Training (unsupervised): aerobic and strength, exercise days (≥ 30 min), other days (≥ 15 min) After 3 to 4 weeks, commenced on stationary bicycles • workload increased up to 70% baseline peak workload, then duration increased 12 weeks, 2 sessions/week 24 home visits, 3 visits to GP, 3 visits from local home-care nurse, 2 hospital visits
Puente-Maestu 2000[37] n = 41 Spain	Aerobic training: treadmill (60 min) 8 weeks, 4 sessions/week 33 hospital visits	Aerobic training: walking with pedometer (3 to 4 km) 8 weeks, 4 sessions/week 10 hospital visits (weekly during intervention)
Maltais 2008[35] n = 252 Canada	Pre-intervention: 4 weeks of educational intervention, 2 lectures/week Aerobic training: stationary leg cycling (25 to 30 min, 80% baseline peak workload) Strength training (30 min)	Aerobic training: portable ergocycles (40 min, 60% baseline peak workload) Strength training: (30 min)

Study Number of participants Country	Program features	
	Hospital-based	**Home-based**
	8 weeks, 3 sessions/week 34 hospital visits	8 weeks, 3 sessions/week 1 home visit (Week 1), 7 weekly telephone contacts, 10 hospital visits
Güell 2008[34] n = 51 (all male) Spain	Pre-intervention: 1 week (2 education sessions, 4 respiratory physical therapy sessions) Respiratory muscle training Strength training: 30 min (start at 0.5 kg; +1 kg/week as tolerated) Aerobic training: cycle ergometer (30 min) • progression: intensity (start at 60% baseline peak workload, +10 watts as tolerated) 8 weeks, 3 sessions/week, 1.5 hours/session 31 hospital visits	Respiratory muscle training Strength training: 30 min (start at 0.5 kg, +1 kg/week as tolerated) Aerobic training: unsupervised street walking at 4 kph (pedometer) • progression: duration (start at 15 min; Weeks 1-3: 30 min; Weeks 4-8: 45 min) 8 weeks, walk daily, probably 3 sessions/week other exercises 8 hospital visits, number of home visits and contacts not specified
Oliveira 2010[36] n = 88 Brazil	Aerobic training: treadmill walking (30 min) Strength training: ankle and hand weights 3 months, 3 sessions/week 37 hospital visits	Aerobic training: walking 60-80% peak heart rate on baseline 6MWT Strength training: ankle and hand weights 3 months, 3 sessions/week 2 hospital visits, number of telephone contacts not specified

Study Number of participants Country	Program features	
	Hospital-based	**Home-based**
Holland 2017[39] n = 166 Australia	Aerobic training: walking 80% of baseline 6MWT speed or cycling 60% peak workload (30 min) Strength training: functional tasks and free weight training 8 weeks, supervised: 2 sessions/week, unsupervised: 3 sessions/week 17 hospital visits	Aerobic training: walking 80% of baseline 6MWT speed (30 min, pedometer) Strength training: functional tasks and free weight training (equipment available at home) 8 weeks, 5 sessions/week 1 home visit (Week 1), 7 weekly telephone contacts, 2 hospital visits
Horton 2018[40] n = 287 United Kingdom	Aerobic training: walking speed • Intensity: 85% $\dot{V}O_2$peak predicted from ISWT • Duration as per ESWT Strength training: supervised 1 session/week, unsupervised 2 sessions/week 7 weeks, 2 sessions/week 15 hospital visits	Aerobic training: walking speed • Intensity: 85% $\dot{V}O_2$peak predicted from ISWT • Duration as per ESWT Strength training: supervised 1 session/week, unsupervised 2 sessions/week 7 weeks 3 hospital visits, 2 telephone contacts

ESWT, endurance shuttle walk test; GP, general practitioner; ISWT, incremental shuttle walk test; 6MWT, six-minute walk test; $\dot{V}O_2$, peak oxygen uptake. Where not stated, assumed one hospital visit for pre-program assessment for all participants, assumed 1 hospital visit for post-program assessment for home-based participants

TABLE 2. RANDOMISED CONTROLLED TRIALS OF OUTPATIENT HOSPITAL-BASED VERSUS HOME-BASED PULMONARY REHABILITATION PROGRAMS: EXERCISE CAPACITY AND HEALTH-RELATED QUALITY OF LIFE OUTCOMES.

Outcomes		Puente-Maestu 2000[37]	Maltais 2008[35]	Güell 2008[34]	Oliveira 2010[36]	Holland 2017[39]	Horton 2018[40]
Health-related quality of life							
CRQ domain scores	dyspnoea	"no differences between the two groups"	0.1 (-0.2 to 0.3)	0.2 (-0.2 to 0.7)		1.6 (−0.3 to 3.5)[#]	−0.2 (−0.6 to 0.1)
	fatigue		-0.1 (-0.4 to 0.2)	0.2 (-0.2 to 0.6)		0.8 (−0.7 to 2.3)[#]	−0.4 (−0.7 to 0.1)
	emotional function		-0.0 (-0.2 to 0.2)	0.6 (0.1 to 1.0)*		0.8 (−1.5 to 3.1)	−0.5 (−0.8 to 0.2)
	mastery		-0.0 (-0.2 to 0.2)	0.4 (-0.1 to 0.9)		0.4 (−1.0 to 1.8)	−0.4 (−0.7 to 0.1)
SGRQ domain scores	total		-1 (-4 to 2)				
	symptoms		-6 (-11 to -1)^				
	activity		-0.2 (-4 to 4)				
	impacts		-0.2 (-4 to 3)				
Exercise capacity							
6MWD (metres)			-3 (-15 to 10)	9 (-25 to 43)	p = 0.44	[#]19 (−3 to 41)	
Incremental exercise test ($\dot{V}O_2$peak)		p < 0.05*					
Cycle endurance time (seconds)		p < 0.05*	9 (-90 to 109)				
ISWD (metres)							−24 (−45 to −2)†
ESWT (seconds)							−141 (−252 to −31)**

Data are mean difference (95% CI) unless indicated. CRQ, Chronic Respiratory Questionnaire; ESWT, time walked on endurance shuttle walk test; ISWD, distance walked on incremental shuttle walk test; 6MWD, distance walked on six-minute walk test; SGRQ, St George Respiratory Questionnaire; $\dot{V}O_2$, peak oxygen uptake.* hospital>home; [#] CI exceeds the upper equivalence limit of minimal important difference and cannot exclude superiority; ^ home-based > centre-based program; † non-inferior to pulmonary rehabilitation; ** in favour of centre-based program. The non-inferiority margin was breached by the lower CI and therefore the non-inferiority of home-based pulmonary rehabilitation was inconclusive.

(b) Physical activity in people with COPD

Physical activity in people with COPD is reduced compared to healthy peers and to people with other chronic conditions.[1, 47, 48] It has been demonstrated that participation in physical activity is reduced across the disease spectrum, with documented reductions in smokers prior to diagnosis, in people with a recent diagnosis and mild COPD before symptom onset and deterioration with increasing disease severity.[49-54]

A lack of physical activity is one of the main risk factors for development of cardiovascular, metabolic and musculoskeletal comorbid conditions in people with COPD.[55] Low levels of participation in physical activity have been independently associated with poor outcomes, including increased risk for hospitalisation and mortality.[56-59] However, there is a lack of clarity regarding the relationship between physical activity and clinical characteristics including impaired exercise capacity and health-related quality of life in people with COPD.[56, 60-62]

Participation in regular physical activity is endorsed for people with COPD.[1] However, there is meagre evidence for improvements in objectively-assessed physical activity measures following interventions in people with COPD. Pulmonary rehabilitation has been commonly proposed as a potential model for delivery of targeted interventions with variable evidence for improvements to date.[63] No analyses have compared different models of pulmonary rehabilitation to date, and whether a home-based program leads to greater improvements in physical activity than a centre-based program.

Chapter 2 presents a Cochrane systematic review of interventions that have sought to improve physical activity in people with COPD using a rigorous methodology and including only randomised controlled trials using objective assessment tools. The two most comprehensive reviews of interventions to promote physical activity in people with COPD were conducted by Mantoani 2016 (60 studies to March 2015)[64] and Lahham 2016 (37 studies to May 2016)[65] and noted poor quality of available evidence. These reviews allowed for inclusion of studies using subjective assessment of physical activity,[64, 65] non-randomised, cohort and experimental designs[65] and combined outcomes for analysis (to express effect sizes) rather than preservation of the original units (e.g. number of steps, time in different intensities of physical activity). Some increases in physical activity were observed following combined interventions (e.g. physical activity counselling and pulmonary rehabilitation/exercise training) and appeared to be related to longer intervention periods. However, the interventions and findings were highly variable and the vast majority studies could not document improvements in physical activity. At this stage, it

is not clear if this is because the interventions themselves are ineffective or if the methods of analysis used to date are inadequate at identifying changes in physical activity. This concept will be explored in the following section.

(c) Difficulties with conventional methods for physical activity data analysis: compositional data analysis

The suitability of standard multivariate statistical approaches to analysis of physical activity data has been brought into question, primarily relating to the violation of fundamental assumptions relating to the constrained nature of time and the relationship between time spent in activity of different intensities.[66] Each day consists of 1,440 minutes and is spent in a sequence of activities or behaviours including sleep, sedentary time (e.g. sitting at a desk or on a couch), light intensity physical activity (LIPA) (usually associated with activities of daily living) and moderate to vigorous intensity physical activity (MVPA). Each individual component has been linked to health outcomes with the approach to physical activity data analysis usually assessing each type of activity or behaviour in isolation. For example, fewer hours of sleep have been associated with increased prevalence of hypertension.[67] However, the amount of time 'available' for each behaviour is inherently limited as a component of a day (Figure 1). As the amount of time in a day is finite,

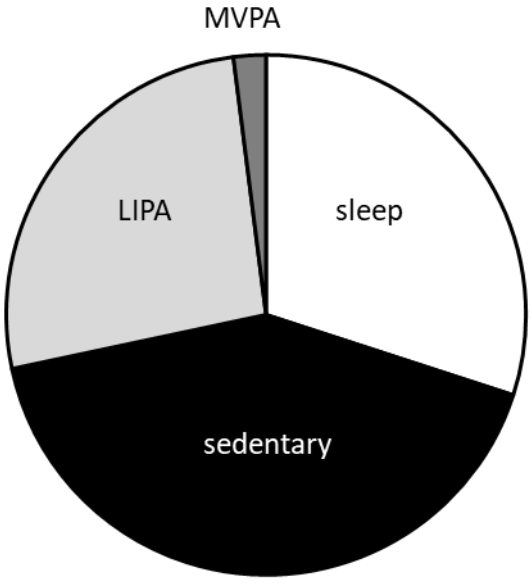


FIGURE 1 TIME IN PHYSICAL ACTIVITY EXPRESSED AS COMPONENTS PARTS OF A DAY.

LIPA, light intensity physical activity; MVPA, moderate to vigorous intensity physical activity.

change in any component must result in concomitant modifications in other components.[68] It may therefore be that the lack/inconsistency of evidence of improvements in physical activity in work to date may relate to the way the data has been analysed, rather than absence of an effect.

Compositional data analysis is well-established in a range of other fields[69] with evolving application within the context of physical activity as researchers strive to understand the impact of – and mechanisms to influence – participation for both general health and disease-specific considerations.[68, 70] This approach has started to be used in studies of physical activity in people with COPD[71, 72] but had not been used to assess change following an intervention.

Chapter 3 presents a comparison of conventional analyses with compositional data analyses for physical activity prior to and following completion of pulmonary rehabilitation in people with COPD.

1.4 The missing links in implementation of home-based pulmonary rehabilitation

Before starting an exercise training program such as pulmonary rehabilitation, an assessment of exercise capacity is needed so as to evaluate the safety of exercise, enable accurate individualised exercise prescription and objectively assess the efficacy of the intervention. Upon referral to pulmonary rehabilitation, routine exercise testing is undertaken prior to program commencement in accordance with international guidelines.[13] Additionally, exercise testing prior to engaging in a physical activity program of at least moderate intensity (as per pulmonary rehabilitation) is recommended for all participants with 'diagnosed or symptomatic pulmonary disease' including COPD.[73]

Exercise training is one of the cornerstones of pulmonary rehabilitation and based on the highest level of scientific evidence.[1] The American College of Sports Medicine guidelines for exercise testing and prescription (frequency, intensity, time and type)[74] are applied to endurance exercise training in individuals with chronic respiratory disease undertaking pulmonary rehabilitation. Accurate prescription of an effective exercise training load is only possible if the results of an exercise test are available. Assessment of exercise capacity following program completion is also routinely employed to determine the efficacy of the intervention and enable recommendations for ongoing care.

Most measures of exercise performance are responsive to pulmonary rehabilitation and are critical tools for outcome assessment. The choice of test is usually determined by time considerations, cost constraints and availability. The most commonly reported tests are field-based walking tests. Such low-cost tests require minimal equipment, are suitable for evaluation in a range of clinical settings and are considered to better reflect daily living than laboratory-based tests.[13]

(a) Home-based assessment of exercise capacity

The most established field-based walking test is the 6MWT; a valid, reliable and responsive measure of exercise capacity in COPD.[75] In addition to assessing the outcomes of pulmonary rehabilitation by quantifying functional exercise capacity (e.g. the distance walked in 6 minutes), it may also be used to quantify the magnitude of a patient's disability, prescribe a walking program and identify the presence of exercise-induced hypoxemia. However, the 6MWT significantly underestimates exercise capacity when conducted at home because there is rarely enough space for the required 30-metre track[76] so participants are still required to attend the hospital for exercise assessments. This is a substantial barrier to delivering an entirely home-based pulmonary rehabilitation program and may exclude some patients from participating. The development of a new assessment that is safe, valid and reliable for use in the home environment, as well as responsive to change with pulmonary rehabilitation, would revolutionise the capacity to deliver effective interventions to a greater number of people with COPD who would benefit.

(b) A new exercise test for pulmonary rehabilitation: modified incremental step test

The Modified Incremental Step Test (MIST) is an incremental externally-paced test suitable for assessing exercise tolerance. It is a modified version of the Chester step test which was developed for use in healthy adults, but found in previous work to be difficult for a large proportion of people with COPD.[77] At a reduced initial cadence and increment rate, the test is performed on a standard commercially available single step (20cm height) and requires the participant to step in time with digitally recorded audio signals. The initial rate of 10 steps per minute increases at a rate of one additional step per 30 seconds. Test completion is determined by the participant (intolerable dyspnoea or leg fatigue) or the physiotherapist (if the participant was unable to follow the rhythm for a period of 15 seconds). The main outcome of the MIST is number of steps. It is a reproducible measure in people with COPD, with intra-class correlation coefficients of over 0.96 for number of steps, maximal oxygen uptake, minute ventilation, heart

rate and oxyhaemoglobin saturation (SpO_2).[78] Direct comparisons of the physiological demands of the MIST and laboratory-based cardiopulmonary exercise testing showed that maximal cardiopulmonary and metabolic responses were elicited.[79] Relationships between the number of steps on MIST have been demonstrated with forced vital capacity, dyspnoea and distance walked on 6MWT in people with acute respiratory conditions admitted to hospital, and no adverse events reported.[79]

This preliminary work indicates that the MIST is safe, well tolerated and reproducible in people with COPD[77-79] and bronchiectasis.[80, 81] However, the proportion of people with chronic lung disease who are unable to undertake the test was not known (e.g. due to knee arthritis or balance deficits). The proportion of people unable to take the test might be higher than for the 6MWT which is conducted on a flat surface. The MIST had not yet been tested in the home environment, a potentially important setting without valid options currently available (Figure 2).

FIGURE 2 PARTICIPANT UNDERTAKING A HOME-BASED MODIFIED INCREMENTAL STEP TEST.

Permission obtained.

Another gap in knowledge regarding the MIST was its responsiveness to an intervention e.g. pulmonary rehabilitation. Subsequent to this, it is important to understand whether an observed change over time represents a clinically important effect, so to facilitate treatment decisions based on the results of this test. The minimal clinically important difference (MID) is defined as

'the smallest difference in score in the outcome of interest that informed patients or informed proxies perceive as important and which would lead the patient or clinician to consider a change in the management'.[82] The advantage of defining an MID is that it can be used to determine whether important changes in health status have occurred in individual patients. Methods for determining the MID can be classified as anchor-based or distribution-based. Anchor-based methods involve comparing a patient's change score to another measure of clinically relevant change.[83] Distribution-based methods, such as the standard error of the mean (SEM)[84] and the effect size,[85] are built on the statistical properties of the measure in a population. Concurrent use of both approaches is recommended to evaluate the effects of the methodology on the final value.[86]

An additional consideration in the clinical application of the MIST is the capacity to enable accurate prescription of intensity for exercise training. The recommended exercise training intensity for participants in pulmonary rehabilitation is 60% of peak $\dot{V}O_2$ measured during a laboratory-based cardiopulmonary exercise test with the aim of eliciting physiological training effects.[87, 88] However in clinical practice, exercise prescription is often based on the 6MWT results, with walking training prescribed on the basis of calculated 6MWT speed. This cannot be performed at home and thus accurate exercise prescription in the home environment was not possible. I propose to investigate whether prescription of step training at a cadence that corresponds to 60% of peak $\dot{V}O_2$ (based on best MIST) provides training intensity within the recommended range.

Chapter 4 presents the feasibility, reliability and responsiveness of the MIST, along with prescription of training intensity.

(c) Evidence for cost-effectiveness

Past economic analyses of pulmonary rehabilitation programs have been purely descriptive,[89-92] comparing centre-based models to usual care[93-96] or comparing two different models of centre-based pulmonary rehabilitation (hospital versus community centre).[97] An economic evaluation is a critical determinant of whether this new home-based model is suitable for clinical implementation, including whether program completion results in any reduction in costs following pulmonary rehabilitation. To date, no reliable cost-effectiveness data for a home-based program have been available.[98]

Economic analyses require detailed consideration of both the costs and consequences (or outcomes) associated with the interventions under consideration.

Costs are determined according to the selected perspective. A health system perspective seeks to understand costs to the health system and does not include other costs to society (e.g. lost productivity) or 'out-of-pocket' costs for patients (e.g. co-payments for health services). This data may be sourced at an individual level, but requires investigation through multiple government and administrative sources due to the wide range of funding models. In Australia, these include federal government-funded medical care and investigations (Medicare Benefits Schedule) and prescribed medications (Pharmaceutical Benefits Scheme), as well as state government-funded emergency department presentations, hospital admissions and outpatient appointments. In contrast, the broader societal perspective also incorporates personal expenses relating to health care access (e.g. travel to attend appointments and 'over the counter' medication purchases) as well as implications for society e.g. time off work.[99] With regards to consequences, a multi-outcome approach using clinical measures for both utility and effectiveness is recommended.[100] Utility is commonly assessed using quality-adjusted life years (QALY) which provide an indication of the value attributed to health state. Effectiveness is represented by health gains, or change in important clinical outcomes.[101]

Economic analyses present a comparative analysis of the differences in cost and health outcomes between two treatment alternatives. This is presented on a cost-effectiveness plane (Figure 3a) where health outcomes are presented along the x-axis and costs along the y-axis. This plane is divided into four quadrants according to relative differences in cost and outcome. The 'southeast' quadrant is said to 'dominate' as results in this quadrant indicate that the 'new' intervention has lower costs and greater effect. Uncertainty around the estimates is also represented on this cost-effectiveness plane. Uncertainty around the threshold for cost-effectiveness is presented on a cost-effectiveness acceptability curve (Figure 3b). This graph reflects the probability of a new intervention being considered as a cost-effective alternative using a range of threshold values for the monetary value attributed by the decision-maker.[99, 101] Threshold values vary around the world. Australian regulations do not define an explicit threshold, but AUD$50,000/QALY is considered as the implicit value based on previous decisions.[102]

The lack of information regarding cost-effectiveness and cost-utility for home-based pulmonary rehabilitation, in comparison to the standard centre-based approach, is a gap in the evidence

needed to underpin implementation and funding. Chapter 5 presents an economic analysis comparing home- and centre-based pulmonary rehabilitation.

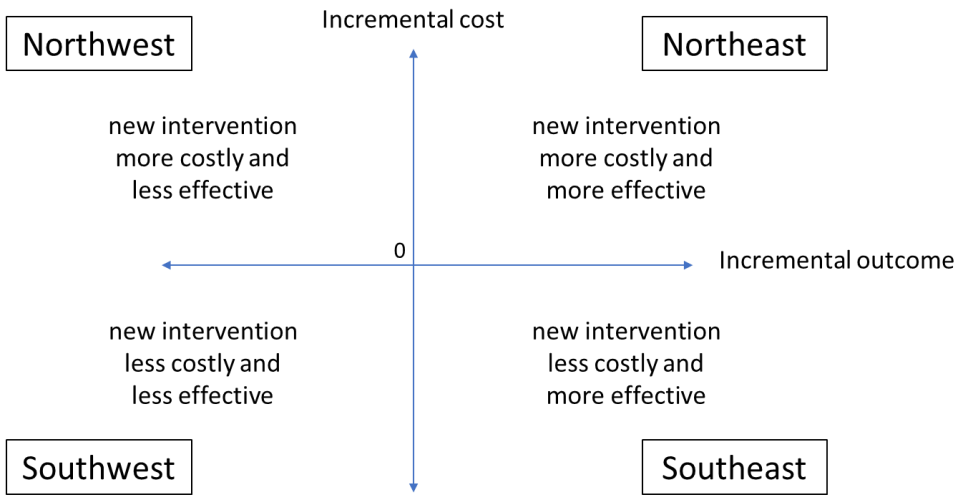


Figure 3a. Cost-effectiveness plane.

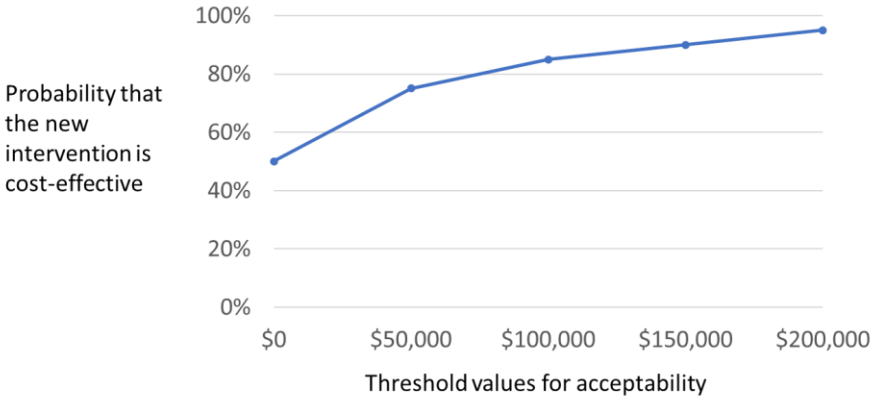


Figure 3b. Cost-effectiveness acceptability curve.

FIGURE 3 COST-EFFECTIVENESS PLANE AND COST-EFFECTIVENESS ACCEPTABILITY CURVE.

1.5 Summary

COPD is a common and disabling disease that poses significant burden to individuals and society. It is not clear if the benefits of pulmonary rehabilitation include improvements in physical activity following program completion or whether this is influenced by the model of intervention delivery or method of data analysis. Equivalent improvements in clinical outcomes have been demonstrated following home-based pulmonary rehabilitation compared to a centre-based model, but program access in the 'real world' has remained limited by a lack of evidence for a home-based exercise test and rigorous economic evaluation.

1.6 Thesis aim and outline

The primary aim of this thesis was to provide evidence to optimise the delivery of home-based pulmonary rehabilitation for people with COPD. To achieve this aim and to address critical gaps in knowledge, four studies were undertaken:

Chapter 2 is a Cochrane Systematic Review completed with the Cochrane Airways Group to investigate the effectiveness of interventions to promote physical activity in people with COPD.

Chapter 3 reports a study comparing a new application of compositional data analysis methods to conventional analysis methods for physical activity data measured before and after pulmonary rehabilitation.

Chapter 4 details the feasibility, reliability and responsiveness of the modified incremental step test to facilitate exercise assessment and prescription in the home environment.

Chapter 5 presents an economic evaluation comparing a new model of home-based pulmonary rehabilitation with conventional centre-based programs.

Chapter 6 summarises the results of chapters 2-5 together with strengths and limitations of the thesis. This chapter also discusses directions for future research, implications for clinical practice and health care policy.

Chapter 2.

Interventions for promoting physical activity in people with COPD

Declaration of Authorship

Student declaration

The nature and extent of contributions to Chapter 2 were as follows:

Name	Nature of contribution	Extent of contribution
Angela Burge	Study concept and design, search strategy, abstract review, data extraction, analysis interpretation, manuscript preparation and review	70%
Narelle Cox	Abstract review, data extraction, manuscript review	10%
Michael Abramson	Study design, data interpretation, manuscript review	10%
Anne Holland	Study concept and design, search strategy, data analysis and interpretation, manuscript review	10%

Supervisor declaration

I hereby certify that the declaration above is a correct reflection of the extent and nature of contributions made toward Chapter 2 of this thesis by the student and all listed co-authors.

Name of supervisor	Signature
Prof Anne Holland	

Preface

In Chapter 1, the adverse impact of COPD on physical activity at all stages of disease severity was highlighted. There were a number of studies that have looked at a broad range of types of interventions to improve physical activity in people with COPD but there was a lack of clarity regarding effective models. Pulmonary rehabilitation has been proposed as an intervention package with potential to increase physical activity, but uncertainty remained regarding the necessary components.

The aim of Chapter 2 was to evaluate which interventions are effective at improving objectively-assessed physical activity in people with COPD.

This topic was rated as the highest priority for physiotherapy reviews within the Cochrane Airways Group. The systematic review in this chapter has been published in the *Cochrane Database of Systematic Reviews* which has an impact factor of 6.264.

> Burge AT, Cox NS, Abramson MJ, Holland AE. Interventions for promoting physical activity in people with chronic obstructive pulmonary disease (COPD). *Cochrane Database of Systematic Reviews* 2020;4;CD012626. doi: 10.1002/14651858.CD012626.pub2.

Aspects of this manuscript were presented at the following conferences:

Oral presentation: Thoracic Society of Australia and New Zealand Annual Scientific Meeting, March 2018 (Adelaide, Australia)

> Published abstract: Burge A, Cox N, Abramson M, Holland A. Interventions for promoting physical activity in people with COPD: a Cochrane systematic review. *Respirology* 2018;23:TO052

Poster presentation: American Thoracic Society International Conference, May 2018 (San Diego, USA)

> Published abstract: Burge A, Cox N, Abramson M, Holland A. Interventions for promoting physical activity in people with COPD: a Cochrane systematic review. *American Journal of Respiratory and Critical Care Medicine* 2018;197:A7069

[Intervention Review]

Interventions for promoting physical activity in people with chronic obstructive pulmonary disease (COPD)

Angela T Burge[1,2,3,4], Narelle S Cox[2,4,5], Michael J Abramson[6], Anne E Holland[1,2,3,4]

[1]Department of Physiotherapy, Podiatry and Prosthetics and Orthotics, School of Allied Health, Human Services and Sport, La Trobe University, Melbourne, Australia. [2]Institute for Breathing and Sleep, Melbourne, Australia. [3]Physiotherapy, Alfred Health, Melbourne, Australia. [4]Department of Allergy, Clinical Immunology and Respiratory Medicine, Monash University, Melbourne, Australia. [5]Department of Physiotherapy, Podiatry and Prosthetics and Orthotics, School of Allied Health, Human Services and Sport, La Trobe University, Melbourne, Australia. [6]School of Public Health & Preventive Medicine, Monash University, Melbourne, Australia

Contact address: Angela T Burge, Physiotherapy, Alfred Health, PO Box 315, Melbourne, Prahran VIC 3181, Australia. a.burge@alfred.org.au.

Editorial group: Cochrane Airways Group.
Publication status and date: New, published in Issue 4, 2020.

Citation: Burge AT, Cox NS, Abramson MJ, Holland AE. Interventions for promoting physical activity in people with chronic obstructive pulmonary disease (COPD). *Cochrane Database of Systematic Reviews* 2020, Issue 4. Art. No.: CD012626. DOI: 10.1002/14651858.CD012626.pub2.

ABSTRACT

Background

Escalating awareness of the magnitude of the challenge posed by low levels of physical activity in people with chronic obstructive pulmonary disease (COPD) highlights the need for interventions to increase physical activity participation. The widely-accepted benefits of physical activity, coupled with the increasing availability of wearable monitoring devices to objectively measure participation, has led to a dramatic rise in the number and variety of studies that aimed to improve the physical activity of people with COPD. However, little was known about the relative efficacy of interventions tested so far.

Objectives

In people with COPD, which interventions are effective at improving objectively-assessed physical activity?

Search methods

We identified trials from the Cochrane Airways Trials Register Register, which contains records identified from bibliographic databases including the Cochrane Central Register of Controlled Trials, MEDLINE, Embase, CINAHL, AMED, and PsycINFO. We also searched PEDro, ClinicalTrials.gov, the World Health Organization International Clinical Trials Registry Platform portal and the Australian New Zealand Clinical Trials Registry (from inception to June 2019). We checked reference lists of all primary studies and review articles for additional references, as well as respiratory journals and respiratory meeting abstracts, to identify relevant studies.

Selection criteria

We included randomised controlled trials of interventions that used objective measures for the assessment of physical activity in people with COPD. Trials compared an intervention with no intervention or a sham/placebo intervention, an intervention in addition to another standard intervention common to both groups, or two different interventions.

Data collection and analysis

We used standard methods recommended by Cochrane. Subgroup analyses were possible for supervised compared to unsupervised pulmonary rehabilitation programmes in clinically-stable COPD for a range of physical activity outcomes. Secondary outcomes were health-related quality of life, exercise capacity, adverse events and adherence. Insufficient data were available to perform prespecified

subgroup analyses by duration of intervention or disease severity. We undertook sensitivity analyses by removing studies that were at high or unclear risk of bias for the domains of blinding and incomplete outcome data.

Main results

We included 76 studies with 8018 participants. Most studies were funded by government bodies, although some were sponsored by equipment or drug manufacturers. Only 38 studies had physical activity as a primary outcome. A diverse range of interventions have been assessed, primarily in single studies, but improvements have not been systematically demonstrated following any particular interventions. Where improvements were demonstrated, results were confined to single studies, or data for maintained improvement were not provided. Step count was the most frequently reported outcome, but it was commonly assessed using devices with documented inaccuracy for this variable.

Compared to no intervention, the mean difference (MD) in time in moderate- to vigorous-intensity physical activity (MVPA) following pulmonary rehabilitation was four minutes per day (95% confidence interval (CI) −2 to 9; 3 studies, 190 participants; low-certainty evidence). An improvement was demonstrated following high-intensity interval exercise training (6 minutes per day, 95% CI 4 to 8; 2 studies, 275 participants; moderate-certainty evidence). One study demonstrated an improvement following six months of physical activity counselling (MD 11 minutes per day, 95% CI 7 to 15; 1 study, 280 participants; moderate-certainty evidence), but we found mixed results for the addition of physical activity counselling to pulmonary rehabilitation. There was an improvement following three to four weeks of pharmacological treatment with long-acting muscarinic antagonist and long-acting beta$_2$-agonist (LAMA/LABA) compared to placebo (MD 10 minutes per day, 95% CI 4 to 15; 2 studies, 423 participants; high-certainty evidence). These interventions also demonstrated improvements in other measures of physical activity.

Other interventions included self-management strategies, nutritional supplementation, supplemental oxygen, endobronchial valve surgery, non-invasive ventilation, neuromuscular electrical stimulation and inspiratory muscle training.

Authors' conclusions

A diverse range of interventions have been assessed, primarily in single studies. Improvements in physical activity have not been systematically demonstrated following any particular intervention. There was limited evidence for improvement in physical activity with strategies including exercise training, physical activity counselling and pharmacological management. The optimal timing, components, duration and models for interventions are still unclear. Assessment of quality was limited by a lack of methodological detail. There was scant evidence for a continued effect over time following completion of interventions, a likely requirement for meaningful health benefits for people with COPD.

PLAIN LANGUAGE SUMMARY

What are the most effective ways to encourage people with chronic obstructive pulmonary disease (COPD) to be more physically active?

Background

Being physically active is important for everyone's health. It can be particularly difficult for people with COPD and we do not know the best way to improve physical activity.

Study characteristics

This review includes 76 studies involving 8018 people with COPD (published before 27 June 2019). Most studies were funded by government bodies, although some were sponsored by equipment or drug manufacturers. Many strategies have been developed and different studies have measured physical activity in lots of different ways. This means that it was hard to compare and combine their findings. It was also hard to tell exactly what was involved in some of the interventions, and therefore which components were important for improving physical activity.

Key results

Some studies looked at current interventions for people with COPD, including pulmonary rehabilitation and different types of exercise training as well as self-management and education. Other studies have looked at special types of nutritional supplements, oxygen therapy, surgery, muscle stimulation and singing.

Some strategies that did work involved exercise training, physical activity counselling and COPD medications. Some studies showed that people did an extra 6 to 24 minutes of at least moderate-intensity physical activity, as well as walking for longer or taking more steps each day. However, we are still uncertain about when or how these approaches should be used. Only a few studies followed people up after the intervention finished. It is not clear exactly what needs to be done to improve physical activity in the long term, which is what may be required for health benefits.

Quality of the evidence

The quality of evidence was generally low, due to difficulties working out exactly what people did in the studies, and also because there were lots of single studies (some quite small) looking at different types of interventions. This means that it was difficult to generalise these findings to all people with COPD.

SUMMARY OF FINDINGS

Summary of findings for the main comparison. Pulmonary rehabilitation/exercise training versus no intervention

Population: people with COPD, clinical stability

Intervention: pulmonary rehabilitation/exercise training

Comparisons: intervention versus no intervention

Outcome: time in physical activity (of at least moderate intensity) at end intervention

Interventions	Outcome	Illustrative comparative risks* [mean difference (95% CI) unless indicated]		Number of participants (studies)	Quality of the evidence (GRADE)	Comments
		Assumed risk	Corresponding risk			
		No intervention	Pulmonary rehabilitation/exercise training			
Pulmonary rehabilitation vs. no intervention (8 to 10 weeks)	Time/change in time in MVPA	The mean change in time ranged from −1 to 6 minutes per day, mean time 27 minutes per day	The mean difference was 4 (−2 to 9) minutes per day	190 participants (3 studies; Analysis 1.2)	⊕⊕⊖⊖ **low**[a]	Baseline values: De Roos 2017 no intervention mean 11 (SD 10), pulmonary rehabilitation 12 (11); Wootton 2017 no intervention 46 (39), pulmonary rehabilitation 54 (43)
High-intensity interval training vs. no intervention (8 to 12 weeks)	Time in MVPA	The mean time ranged from 12 to 14 minutes per day	The mean difference was 6 (4 to 8) minutes per day	275 participants (2 studies; Analysis 1.9)	⊕⊕⊕⊖ **moderate**[b]	-
Maintenance (telerehabilitation) following high-intensity interval training vs. no intervention	Time in moderate intensity physical activity	The mean time was 11 minutes per day	The mean difference was 7 (4 to 10) minutes per day	97 participants (1 study; Vasilopoulou 2017; Table 1)	⊕⊕⊕⊖ **moderate**[b]	-

(12 months)			
Maintenance (centre-based) following high intensity interval training vs. no intervention (12 months)		The mean difference was 11 (8 to 14) minutes per day	100 participants (1 study; Vasilopoulou 2017; Table 1)

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; **MVPA**: moderate-to-vigorous physical activity; **SD**: standard deviation

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[a]Downgraded one level for high risk of performance bias. Downgraded one level for imprecision as CI does not exclude possibility of no effect.
[b]Downgraded one level for high risk of performance bias.

Summary of findings 2. Comparison of types of pulmonary rehabilitation/exercise training

Population: people with COPD, clinical stability

Intervention: pulmonary rehabilitation/exercise training

Comparisons: intervention vs. another intervention

Outcome: time in physical activity (of at least moderate intensity) at end intervention

Interventions	Outcome	Illustrative comparative risks* [mean difference (95% CI) unless indicated]		No of participants (studies)	Quality of the evidence (GRADE)	Comments
		Assumed risk	Corresponding risk			
		Comparator	Intervention of interest			
Home-based pulmonary rehabilitation vs. centre-based pulmonary rehabilitation	Change in time in MVPA	The mean change in time in the centre-based group was 5 minutes per day	The mean difference was 6 (−19 to 31) minutes per day	58 participants (1 study; Analysis 4.2)	⊕⊕⊖⊖ **low**[a]	Baseline values: centre-based median 79 (IQR 24 to 136), home-based

(8 weeks)						median 68 (IQR 29 to 121)
Calisthenics vs. exercise training (12 weeks)	Time in MVPA	The mean time in the exercise training group was 75 minutes per day	"no significant inter-group differences in any variable"	40 participants (1 study; Probst 2011; Table 1)	⊕⊕⊖⊖ **low**[b]	-
Physical activity counselling vs. pulmonary rehabilitation (6 to 12 weeks)	Change in time in MVPA	The mean change in time in the pulmonary rehabilitation group was 1 (−3 to 5) minutes per day	The mean difference was 6 (−10 to 22) minutes per day	26 participants (1 study; O'Neill 2018; Table 1)	⊕⊕⊖⊖ **low**[a]	Baseline values: pulmonary rehabilitation mean 15 (SD 5), physical activity counselling mean 14 (SD 15)
Telerehabilitation maintenance programme vs. centre-based maintenance programme (following high-intensity interval training, 12 months)	Time in moderate-intensity physical activity	The mean time in the centre-based group was 22 minutes per day	The mean difference was −4 (−7 to −1) minutes per day	97 participants (1 study; Vasilopoulou 2017; Table 1)	⊕⊕⊕⊖ **moderate**[c]	-

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; **IQR**: interquartile range; **MVPA**: moderate-to-vigorous physical activity; **SD**: standard deviation

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[a]Downgraded one level for high risk of performance bias. Downgraded one level for imprecision as CI does not exclude possibility of no effect.
[b]Downgraded one level for unclear risk of selection, performance, detection, attrition and other potential bias. Downgraded one level for imprecision as CI does not exclude possibility of no effect.
[c]Downgraded one level for high risk of performance bias.

Summary of findings 3. Physical activity counselling

Population: people with COPD, clinical stability

Intervention: physical activity counselling

Comparisons: intervention vs. no intervention, intervention in addition to a standard intervention common to both groups

Outcome: time in physical activity (of at least moderate intensity) at end intervention

Interventions	Outcome	Illustrative comparative risks* [mean difference (95% CI) unless indicated]		Number of participants (studies)	Quality of the evidence (GRADE)	Comments
		Assumed risk	Corresponding risk			
		Comparator	Intervention of interest			
Comparison: intervention vs. no intervention						
Physical activity counselling vs. no intervention (12 weeks)	Change in time in MVPA	The mean change in time was −3 (−0.6 to 0.2) minutes per day	The mean difference was 11 (7 to 15) minutes per day	280 participants (1 study; Demeyer 2017; Table 1)	⊕⊕⊕⊖ **moderate**[a]	Baseline values: no intervention median 15 (IQR 5 to 35), intervention median 14 (IQR 5 to 26)
Physical activity counselling vs. no intervention (following pulmonary rehabilitation, 12 months)	Change in time in moderate intensity physical activity	The mean change was −1 (−13 to 12) minutes per day	The mean difference was 20 (−1 to 41) minutes per day	43 participants (1 study; Wootton 2017; Table 1)	⊕⊕⊖⊖ **low**[b]	Baseline values: no intervention mean 51 (SD 49), intervention mean 59 (SD 52)
Comparison: intervention in addition to a standard intervention common to both groups						
Physical activity counselling with pulmonary rehabilitation vs. pulmonary rehabilitation (6 months)	Time in MVPA	The mean time in the pulmonary rehabilitation group was 28 minutes per day	The mean difference was 24 (2 to 45) minutes per day	26 participants (1 study; Analysis 3.21)	⊕⊕⊕⊖ **moderate**[c]	P = 0.03
	Change in time in MVPA	The median change in time in the pulmonary rehabilitation group was 12 minutes per day	The median change in time was 2 (−12 to 25) minutes per day	113 participants (1 study; Nolan 2017; Table 1)	⊕⊕⊖⊖ **low**[d]	P = 0.16 Baseline values: no intervention median 47 (IQR 18 to 103), intervention median 45 (IQR 20 to 81)
Physical activity counselling with pulmonary rehabilitation vs. sham intervention with pulmonary rehabilitation (6 months)	Change in time in MVPA	The mean change in time in the pulmonary rehabilitation group was 0 minutes per day	The mean difference was −6 (−16 to 3) minutes per day	50 participants (1 study; Analysis 3.25)	⊕⊖⊖⊖ **very low**[e]	Baseline values: no intervention median 29 (IQR 17 to 44), intervention median 33 (IQR 16 to 47)

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **IQR**: interquartile range; **MVPA**: moderate-to-vigorous physical activity; **SD**: standard deviation

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[a]Downgraded one level for high risk of performance bias and detection bias.
[b]Downgraded one level for high risk of performance bias. Downgraded one level for imprecision as CI does not exclude possibility of no effect.
[c]Downgraded one level for high risk of performance, detection and reporting bias.
[d]Downgraded one level for high risk of performance bias. Downgraded one level for imprecision as results do not exclude possibility of no effect.
[e]Downgraded one level for unclear risk of selection, reporting and other bias. Downgraded one level for imprecision as CI does not exclude possibility of no effect.

Summary of findings 4. Self-management

Population: people with COPD, clinical stability

Intervention: self-management

Comparisons: intervention vs. no intervention, intervention in addition to a standard intervention common to both groups, intervention vs. another intervention

Outcome: time in physical activity (of at least moderate intensity) at end intervention

Interventions	Outcome	Illustrative comparative risks* [mean difference (95% CI) unless indicated]		Number of participants (studies)	Quality of the evidence (GRADE)	Comments
		Assumed risk	Corresponding risk			
		Comparator	Intervention of interest			
Comparison: intervention vs. no intervention						
Self-management vs. no intervention (12 months)	Time in MVPA	The mean time was 316 minutes a week	The mean difference was 12 (−21 to 45) minutes a week	411 participants (1 study; Jolly 2018; Table 1)	⊕⊕⊖⊖ **low**[a]	P = 0.48
Comparison: intervention in addition to a standard intervention common to both groups						
Self-efficacy training with upper limb exercise vs. education with upper limb exercise	Time in moderate-intensity physical activity	The mean time in the education and upper-limb exercise group was 4 minutes per day	The mean difference was 2 (−1 to 5) minutes per day	35 participants (1 study; Larson 2014; Table 1)	⊕⊕⊖⊖ **low**[a]	-

(16 weeks)						
Comparison: intervention vs. another intervention						
Self-management vs. education and symptom monitoring (16 weeks)	Time in moderate-intensity physical activity	The mean time in the self-management group was 6 minutes per day	The mean difference was 1 (−1 to 2) minutes per day	326 participants (1 study; Blumenthal 2014; Table 1)	⊕⊕⊖⊖ **low**[a]	-

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; **MVPA**: moderate-to-vigorous physical activity

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[a]Downgraded one level for high risk of performance bias. Downgraded one level for imprecision as CI does not exclude possibility of no effect.

Summary of findings 5. Pharmacological interventions

Population: people with COPD, clinical stability

Intervention: pharmacological interventions

Comparisons: intervention vs. placebo, intervention in addition to a standard intervention common to both groups

Outcome: time in physical activity (of at least moderate intensity) at end intervention

Interventions	**Outcome**	**Illustrative comparative risks* [mean difference (95% CI) unless indicated]**		**Number of participants (studies)**	**Quality of the evidence (GRADE)**	**Comments**
		Assumed risk	**Corresponding risk**			
		Comparator	**Intervention of interest**			
Comparison: intervention vs. sham/placebo intervention						
LAMA vs. placebo (3 weeks)	Change in time in MVPA	The median change in time was −6 minutes per day	The median change in time was −1 (IQR −17 to 24) minutes per day	131 participants (2 studies; Beeh 2014; Magnussen 2017; Table 1)	⊕⊕⊕⊖ **moderate**[a]	P = 0.07 Baseline values:

						Beeh 2014 placebo median 73 (IQR 38 to 135), LAMA median 74 (IQR 32 to 132) Magnussen 2017 placebo mean 88 (SD 65), intervention mean 57 (SD 32)
LAMA/LABA vs. placebo (3 to 4 weeks)	Change in time in MVPA	The mean change in time ranged from −16 to −1 minutes per day	The mean difference was 10 (4 to 15) minutes per day	423 participants (2 studies; Analysis 2.3)	⊕⊕⊕⊕ **high**	Baseline values: Watz 2016 placebo mean 130, LAMA/LABA mean 125
Comparison: intervention in addition to a standard intervention common to both groups						
LAMA with behaviour modification vs. placebo with behaviour modification (12 weeks to 6 months)	Time in MVPA	The mean time was 64 minutes per day	The mean difference was 8 minutes per day	426 participants (1 study; Troosters 2014; Table 1)	⊕⊕⊕⊖ **moderate**[b]	P = "not statistically significantly different"

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; **IQR**: interquartile range; **LABA:** long-acting beta$_2$ agonist; **LAMA:** long-acting muscarinic antagonist; **MVPA**: moderate-to-vigorous physical activity; **SD**: standard deviation

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[a]Downgraded one level for imprecision as results do not exclude possibility of no effect.
[b]Downgraded one level for imprecision as no formal analysis of difference presented.

BACKGROUND

Description of the condition

Chronic obstructive pulmonary disease (COPD) is a common, treatable but incurable obstructive lung disease defined by persistent airflow limitation. Diagnosis is confirmed by spirometry in the clinical context of a person presenting with dyspnoea, chronic cough or sputum production, and a history of risk factor exposure (GOLD 2019). Development of COPD is primarily attributable to an enhanced chronic inflammatory airway response to noxious particles or gases, and is strongly linked to a history of smoking. However, there are a number of other risk factors including exposure to air pollution, occupational exposures, genetics, chronic asthma, history of severe childhood respiratory infections and low socioeconomic status (GOLD 2019). Systemic effects, including systemic inflammation and muscle dysfunction, and comorbid conditions, including cardiovascular disease, anxiety and depression, are commonly associated with COPD (Choudhury 2014). Prevalence studies suggest that COPD affects upwards of 384 million people (Adeloye 2015) and is the third leading cause of death worldwide (WHO 2017). Associated with advancing age (Anton 2016), and in the context of the fastest rate of population growth occurring in people over 65 years of age (UN 2015), COPD poses a substantial and growing economic and social burden globally (GOLD 2019).

Description of the intervention

We define the term 'physical activity' as any bodily movement produced by skeletal muscles that results in energy expenditure (Casperson 1985). It is a complex behaviour traditionally described according to type, intensity and duration, and incorporates a subset of undertakings including exercise, occupational and household activities. Public health promotion for regular participation in physical activity typically recommends a minimum of 150 minutes a week of at least moderate-intensity activity as 'sufficient' for health benefits across the adult population (U.S. Department of Health and Human Services 2018). These benefits include reduced risk of all-cause mortality, coronary heart disease, hypertension, stroke, metabolic syndrome, type 2 diabetes and depression (Lee 2012).

Participation in regular physical activity is also endorsed for people with COPD (GOLD 2019). Low levels of physical activity are one of the main risk factors for development of cardiovascular, metabolic and musculoskeletal comorbid conditions in people with COPD, and is observed across the disease spectrum (Van Remoortel 2014). Recent studies show that physical activity is reduced in smokers prior to diagnosis (Furlanetto 2014) and in people with a recent diagnosis and mild COPD before symptom onset (Johnson-Warrington 2014). Physical activity participation is not clearly related to other clinical characteristics including impaired exercise capacity (Fastenau 2013; Gagnon 2015; Van Remoortel 2013; Watz 2009), but is reduced compared to healthy peers (Pitta 2005; Vorrink 2011) and to people with other chronic conditions (Arne 2009). It is further compromised during and after hospitalisation for an acute exacerbation (Pitta 2006a) and with increasing disease severity (Shrikrishna 2012; Troosters 2010; Waschki 2015). In people with COPD, low levels of participation in physical activity have been independently associated with poor outcomes, including increased risks of hospitalisation and mortality (Garcia-Aymerich 2006; Garcia-Rio 2012; Vaes 2014; Waschki 2011).

Much attention has been given to the development of physical activity interventions that incorporate strategies specifically designed to promote the adoption and maintenance of active lifestyles in the general population (Marcus 2006). Such interventions may be provided by a broad range of healthcare professionals and be delivered in a variety of ways (for example, in person, by internet or telephone).

How the intervention might work

Evidence suggests that people with COPD avoid participation in physical activity due to the perception of breathlessness, resulting from inefficiencies related to gas trapping and lung hyperinflation. A vicious circle is perpetuated, where muscle deconditioning results from avoiding activities that involve physical exertion and exacerbate symptoms, further compromising physical capacity to engage in activity (O'Donnell 2014). It is theorised that targeted interventions may be able to interrupt this cycle and increase participation in physical activity at a range of intensities that are associated with health benefits. The dual role of low physical activity levels as both a cause and consequence in chronic disease identifies physical activity as a potentially modifiable target that could affect health-related quality of life and disease trajectory (Esteban 2010; Vaes 2014; Watz 2014a). Whether improvements in physical activity can ameliorate these effects in COPD is unknown.

Many physical and physiological disease features also appear to influence participation in physical activity by people with COPD. However, the quality of association between such features, including lung function, systemic inflammation, body composition, comorbidities and psychosocial factors, and physical activity participation is variable (Gimeno-Santos 2011). Additional considerations, including fatigue (Andersson 2015), balance (Iwakura 2016), and seasonal and environmental factors (Alahmari 2015; Sewell 2010) may also impact on physical activity participation in this group. The broad range of strategies considered to date to address low levels of physical activity in people with COPD (for instance, exercise training, nutritional interventions and behavioural strategies) reflect the complexity of this issue.

There is evidence for a relationship between physical activity and rate of acute exacerbations (Esteban 2014) and therefore targeting improvements in physical activity in people with COPD may be an important therapeutic goal (Langer 2016; Singh 2016). However, achieving consistent improvements in participation and convincing evidence for the positive impact on health outcomes remain elusive.

Why it is important to do this review

Escalating awareness of the magnitude of the challenge posed by low levels of physical activity in people with COPD at all points in the disease course highlights the need for interventions to increase physical activity participation by people with COPD. The widely-accepted benefits of physical activity, coupled with the increasing availability of wearable monitoring devices to objectively measure participation, has led to a dramatic rise in the number and variety of studies that aim to improve physical activity levels in people with COPD. However, little is known about the range of interventions tested so far, partly attributable to the complexities of data analysis and the challenge of rapidly evolving technology, and the relationship between effects on physical activity and other

outcomes including exercise capacity and health-related quality of life. This Cochrane Review aims to evaluate the efficacy of existing interventions to increase physical activity in people with COPD, and to signpost directions for future work.

OBJECTIVES

In people with COPD, which interventions are effective at improving objectively-assessed physical activity?

METHODS

Criteria for considering studies for this review

Types of studies

We include randomised controlled trials (RCTs) of any intervention where objectively-assessed physical activity or sedentary behaviour was a measured outcome in people with COPD, as previous consensus statements (Watz 2014a) and systematic reviews (Dhillon 2015; Gimeno-Santos 2011) have failed to identify subjective tools that accurately reflect this in people with COPD.

We include studies reported as full-text articles, those published as abstract only and unpublished data. Physical activity could be either a primary or a secondary outcome of the study. We include cross-over trials where pre-cross-over data were available from study authors.

Types of participants

We include adults (18 years of age and over) with a diagnosis of COPD according to established criteria, regardless of disease severity. We planned to include studies that incorporated a mix of diagnostic groups, only if we could obtain data on any of the review outcomes separately for people with COPD.

Types of interventions

We include trials that objectively assessed physical activity as an outcome. These trials compared an intervention versus no intervention or a sham/placebo intervention, compared an intervention in addition to another standard intervention common to both groups or to a different intervention. Interventions could be supervised or unsupervised. Interventions could include, but were not limited to, physical activity counselling, education programmes and self-management strategies. Studies including exercise training undertaken as a stand-alone intervention or as part of a comprehensive pulmonary rehabilitation programme incorporating other components targeting chronic disease self-management (Hill 2013) were considered together. We analysed studies that included pulmonary rehabilitation (as defined by authors) separately from studies that did not include pulmonary rehabilitation. We also included studies in which both groups received pulmonary rehabilitation and which assessed the inclusion of an additional specific physical activity intervention in one group.

Comparisons

- One or more interventions versus no intervention
- One or more interventions versus sham/placebo intervention
- One or more interventions in addition to a standard intervention common to both groups
- One or more interventions versus a different intervention

Types of outcome measures

Primary outcomes

- Studies had to include variable(s) that reflected participation in physical activity or sedentary behaviour, as measured objectively using a pedometer, accelerometer or activity monitor. Outcomes of interest included but were not limited to step count, activity counts, energy expenditure and physical activity time (different intensities, range of thresholds used). Primary time points were at baseline (prior to start) and at the time of intervention completion; we used change in physical activity from baseline for analysis where possible. We also categorised any follow-up measurements reported following intervention completion as either short-term (within one month), medium-term (between one and six months) or long-term (longer than six months). We sought raw data from the study authors where possible to facilitate comparisons.

Secondary outcomes

- Health-related quality of life (measured using either a generic or disease-specific tool)
- Exercise capacity: measured using a laboratory or field exercise test, e.g. cardiopulmonary exercise test, six-minute walk test (6MWT)
- Adverse events, e.g. musculoskeletal injury
- Adherence to intervention

Search methods for identification of studies

Electronic searches

We identified studies from the Cochrane Airways Trials Register, which is maintained by the Information Specialist for the Group. The Cochrane Airways Trials Register contains studies identified from several sources:

- Monthly searches of the Cochrane Central Register of Controlled Trials (CENTRAL), through the Cochrane Register of Studies Online (crso.cochrane.org);
- Weekly searches of MEDLINE Ovid SP 1946 to June 2019;
- Weekly searches of Embase Ovid SP 1974 to June 2019;
- Monthly searches of PsycINFO Ovid SP 1967 to June 2019;
- Monthly searches of Cumulative Index to Nursing and Allied Health Literature (CINAHL EBSCO), 1937 to June 2019;
- Monthly searches of Allied and Complementary Medicine (AMED EBSCO), all years to June 2019;
- Handsearches of the proceedings of major respiratory conferences.

Studies contained in the Trials Register are identified through search strategies based on the scope of Cochrane Airways. Details of these strategies, as well as a list of handsearched conference proceedings, are in Appendix 1. See Appendix 2 and Appendix 3 for search terms used to identify studies for this review.

We also searched Physiotherapy Evidence Database (PEDro), www.clinicaltrials.gov, the WHO ICTRP portal (www.who.int/ictrp/en/) and the Australian New Zealand Clinical Trials Registry (www.anzctr.org.au/). We searched all databases from their inception to June 2019, and imposed no restriction on language of publication.

Searching other resources

We checked reference lists of all primary studies and review articles for additional references. We searched relevant manufacturers' websites for trial information.

We searched for errata or retractions from included studies published in full text on PubMed (www.ncbi.nlm.nih.gov/pubmed) on 12 July 2019.

Data collection and analysis

Selection of studies

Two review authors (AB and NC) independently screened titles and abstracts for inclusion of all the potentially eligible studies we identified from the search, and coded them as either 'retrieve' (eligible or potentially eligible/unclear) or 'do not retrieve'. We retrieved the full-text study reports/publications and two review authors (AB and NC) independently screened the full-text articles and identified studies for inclusion, recording reasons for exclusion of the ineligible studies. We resolved any disagreement through discussion or, if required, we consulted a third review author (AH). We identified and excluded duplicates and collated multiple reports of the same study so that each study rather than each report was the unit of interest in the review. We recorded the selection process in sufficient detail to complete a PRISMA flow diagram and Characteristics of excluded studies tables (Moher 2009).

Data extraction and management

We used a data collection form that was piloted on at least one study included in the review, to record study characteristics and outcome data. Two review authors (AB and NC) independently extracted the following study characteristics from included studies:

- Methods: study design, duration of study, study locations, study setting, date of study;
- Participants: number, mean age, age range, gender, severity of condition, diagnostic criteria, baseline lung function, smoking history, inclusion criteria, exclusion criteria, withdrawals;
- Interventions: intervention, comparison, concomitant interventions;
- Measurement tool;
- Outcomes: primary and secondary outcomes specified and collected (at baseline and at the time of intervention completion) and follow-up measurements at any other time points noted;
- Notes: funding for trial, declared conflicts of interest by trial authors.

We resolved disagreements by reaching consensus, or by involving a third review author (AH or MA). We noted in the Characteristics of included studies table if the included studies did not report outcome data in a useable way. We contacted study authors to verify extracted data when necessary and we provided details of missing data when possible. One review author (AB) transferred data into the Review Manager 5 (RevMan 5) file (Review Manager 2014). We double-checked that the review author had entered data correctly by comparing data presented in the systematic review with data provided in the study reports. A second review author (NC) spot-checked study characteristics for accuracy against the trial report.

Where meta-analyses of physical activity outcome were possible, we included figures in the review.

Assessment of risk of bias in included studies

Two review authors (AB and NC) independently assessed risks of bias for each included RCT, using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2017). We resolved disagreements by discussion or by involving another review author (AH or MA). Where conflicts of interest were present, an independent co-author conducted the assessment. We assessed risks of bias according to the following domains:

- Random sequence generation;
- Allocation concealment;
- Blinding of participants and personnel;
- Blinding of outcome assessment;
- Incomplete outcome data;
- Selective outcome reporting;
- Other potential bias.

For the 'blinding of outcome assessment' domain, we rated both primary and secondary outcomes as ‘objective’ for objectively-measured outcomes and ‘other’ for those outcomes with greater potential to be affected by lack of blinding (e.g. quality of life questionnaires).

We graded each potential source of bias as either high, low or unclear, and provided an extract from the study report together with a justification for our judgement. We resolved discrepancies by consensus. We summarised the 'Risk of bias' judgements across different studies for each of the domains listed and summarised results in a ’Risk of bias' table. When considering treatment effects, we took into account the risks of bias for studies that contributed to this outcome.

Assessment of bias in conducting the systematic review

We conducted the review according to this published protocol and have reported any deviations from it in the Differences between protocol and review section of the review.

Measures of treatment effect

We analysed all the data reported for each outcome, irrespective of dropout rate or use of intention-to-treat analysis.

We undertook meta-analyses only when this was meaningful, i.e. if treatments, participants and the underlying clinical question were similar enough for pooling to make clinical sense.

We intended to analyse dichotomous data as odds ratios (ORs) and 95% confidence intervals (CIs) but no data were available. For continuous data we calculated mean differences (MDs: same metric scale). To retain the units of measurement, we did not express any data as standardised mean differences (SMDs: different metric scales) with 95% CIs. We narratively described skewed data reported as medians and interquartile ranges.

Where multiple arms were reported in a single trial, we included only the relevant arms. We had intended to halve the control group to avoid double-counting in the event that we combined two comparisons (e.g. drug A versus placebo and drug B versus placebo) in the same meta-analysis, but this approach was not required.

Unit of analysis issues

Where studies randomly allocated individual participants to study groups, we considered the participant as the unit of analysis. We only included cross-over trials where data were available prior to cross-over, due to the potential carry-over effects of behavioural interventions. We had intended to consider the cluster as the unit of analysis for cluster-randomised studies, but this approach was not required.

Dealing with missing data

In the event of missing data, we contacted investigators or study sponsors to verify key study characteristics and to obtain missing numerical outcome data when possible, e.g. when a study was reported only as an abstract. If this was not possible, we had intended to analyse the impact of including studies with missing data that may be related to the intervention by performing a sensitivity analysis, but this approach was not required.

Assessment of heterogeneity

We used the I^2 statistic to measure heterogeneity among the trials in each analysis. Where we identified it, we considered statistical heterogeneity to be substantial if I^2 was greater than 50% (Deeks 2017), and explored possible causes using prespecified subgroup analyses.

Assessment of reporting biases

We had intended to create a funnel plot to explore possible small-study and publication biases if we could pool more than 10 included trials, but this was not possible.

Data synthesis

We performed a pooled quantitative synthesis where the trials were clinically homogeneous. We pooled data using a random-effects model to incorporate between-study heterogeneity into the meta-analysis. Where the trials were clinically heterogeneous, we performed a narrative synthesis. For instance, we analysed data for different types of interventions separately, and data for studies starting in the period following acute exacerbation separately from those in stable disease.

'Summary of findings' table

We created 'Summary of findings' tables using the following outcomes:

- time spent in moderate or moderate-to-vigorous physical activity at end intervention in participants with clinically-stable COPD.

We used the five Grading of Recommendations Assessment, Development and Evaluation (GRADE) working group considerations (study limitations, consistency of effect, imprecision, indirectness and publication bias) to assess the quality of a body of evidence as it related to studies that contributed data to the meta-analyses for prespecified outcomes. We used methods and recommendations described in Section 8.5 (Higgins 2017) and Chapter 12 (Schünemann 2017) of the *Cochrane Handbook for Systematic Reviews of Interventions*, and we used the GRADEpro Guideline Development Tool software (GRADEpro GDT 2014). We justified all decisions to downgrade or upgrade the quality of the evidence using footnotes, and we provide comments to aid the reader's understanding of the review where necessary. We did not include data from studies published only in abstract form or on clinical trial registries, due to inadequate assessment of risks of bias.

Subgroup analysis and investigation of heterogeneity

We planned to perform the following subgroup analyses.

- Duration of intervention (≤ 3 months versus > 3 months);
- Supervision of intervention (yes or no);
- Disease severity (mild disease, defined as forced expiratory volume in one second (FEV_1) % predicted ≥ 80%, forced expiratory ratio (FER) < 0.7, compared with other classifications).

We used physical activity as the outcome for subgroup analyses.

We used the formal test for subgroup interactions in Review Manager 5 (RevMan 5) (Review Manager 2014).

Sensitivity analysis

We examined the effects of methodological quality on the pooled estimate by removing studies that were at high or unclear risk of bias for the domains of blinding and incomplete outcome data. We had also intended to examine the effects of measurement device on the pooled estimate by removing studies that used pedometers, as previous studies suggest that these might be less accurate in detecting steps in people with COPD (Pitta 2006b).

RESULTS

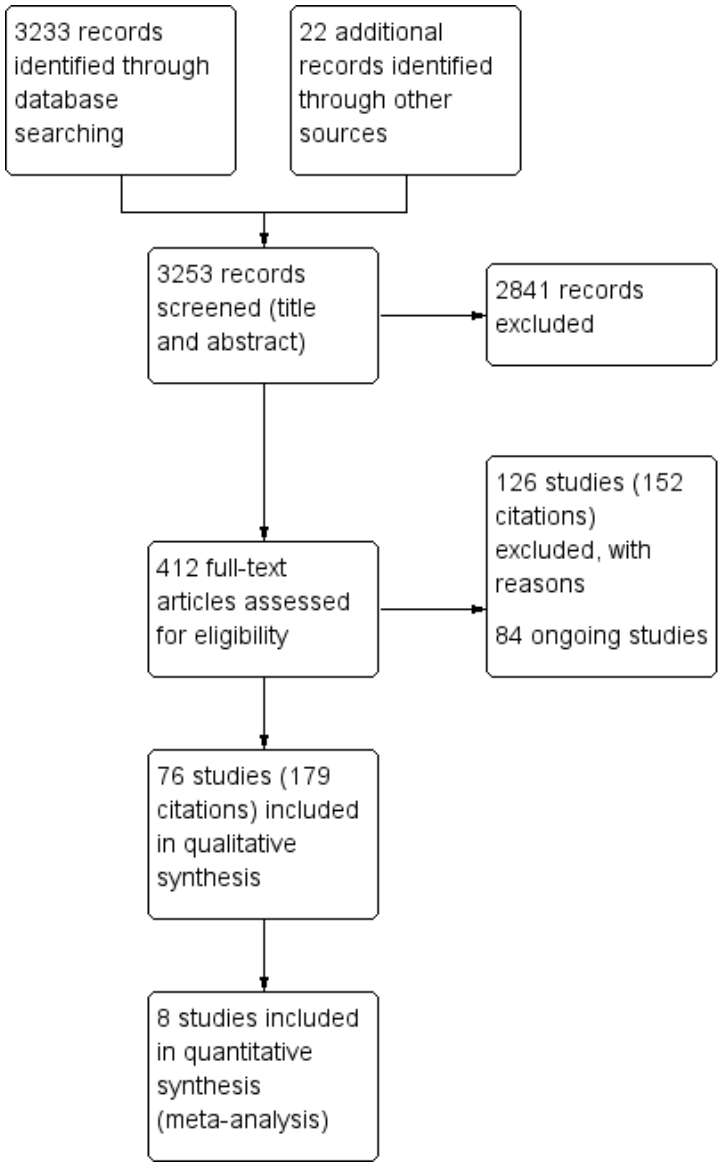
Description of studies

Details are available in the Characteristics of included studies and Characteristics of excluded studies tables.

Results of the search

The search yielded 3233 citations and ended with 76 studies included from 179 citations. These included 12 abstracts (see Figure 1).

Figure 1. Study flow diagram.



Eighty-four studies are currently underway and pending study completion/publication (see Ongoing studies).

Included studies

Of the 76 studies included, 24 studies compared an intervention to promote physical activity versus no intervention (comparison 1). These included pulmonary rehabilitation/exercise training (Borges 2014; De Roos 2017; Egan 2010; Louvaris 2016, Tahirah 2015; Tsai 2016; Vasilopoulou 2017; Wootton 2017), physical activity counselling (Altenburg 2015; Arbillaga-Etxarri 2018; Demeyer 2017; Hornikx 2015; Hospes 2009; Orme 2018; Priori 2017; Saini 2017; Wootton 2017), self-management (Jolly 2018; Kanabar 2015; Mitchell 2013; Tabak 2014b), nutritional supplementation (Goris 2003), gait aid (Ng 2015) and endobronchial valve surgery (Hartman 2016).

There were 10 studies that compared an intervention to promote physical activity to sham/placebo (comparison 2). These included self-management (Schuz 2015), pharmaceutical interventions (Beeh 2014; Magnussen 2017; NCT00144326; Watz 2016; Watz 2017), nutritional supplementation (Dal Negro 2012), supplemental oxygen (Sandland 2008), singing (Lord 2012) and neuromuscular electrical stimulation (Maddocks 2016).

There were 31 studies that compared an intervention to promote physical activity in addition to an intervention common to both groups (comparison 3). These included pulmonary rehabilitation/exercise training (Breyer 2010; Effing 2011; Larson 2014; Troosters 2018; Varas 2018), physical activity counselling (Altenburg 2015; Bender 2016; Cruz 2016; De Blok 2006; Kawagoshi 2015; Loeckx 2018; Mantoani 2018; Mendoza 2015; Moy 2015a; Nguyen 2009; Nolan 2017; Orme 2018; Singh 1998; Tabak 2014a; Vorrink 2016; Wan 2017), self-management (Benzo 2016; Larson 2014), pharmaceutical interventions (Curtis 2016; Troosters 2014; Troosters 2018), nutritional supplementation (Ogasawara 2018; Van de Bool 2017) supplemental oxygen (Alison 2019), non-invasive

ventilation (Duiverman 2008) and inspiratory muscle training (Charususin 2018).

Sixteen studies compared two interventions to increase physical activity with each other (comparison 4). These studies included alternative models of or alternatives to pulmonary rehabilitation/exercise training (Chaplin 2017; Felcar 2018; Gamper 2019; Holland 2017; O'Neill 2018; Polkey 2018; Probst 2011; Rinaldo 2017; Sena 2013; Steele 2019; Vasilopoulou 2017; Widyastuti 2018), self-management (Blumenthal 2014), pharmaceutical interventions (Nakamura 2016; NCT01351792) and a lightweight cylinder for supplemental oxygen (Casaburi 2012).

Of studies with more than two groups, four contributed to more than one comparison (Altenburg 2015; Larson 2014; Orme 2018; Vasilopoulou 2017).

The total number of participants involved in the included studies was 8018. The sample sizes ranged from eight participants (Nguyen 2009; Priori 2017; Sena 2013) to 289 participants (Jolly 2018). The mean age of participants was 66 years and mean FEV_1 54% predicted. On average, groups comprised 63% men, but details relating to the sex of participants were not reported in four abstracts (Egan 2010; Nakamura 2016; Priori 2017; Sena 2013), three papers (Larson 2014; Lord 2012; Polkey 2018) and two clinical trial registries (NCT00144326; NCT01351792). Interventions were provided in person and by telephone call, smart phone app, website, device or printed information. Study duration ranged from one day (surgical procedure) to 12 months, with follow-up provided in 11 studies (ranging from seven days to 12 months post-intervention). Three studies assessed interventions provided during inpatient admissions for acute exacerbation of COPD (AECOPD) and five studies in the post-admission phase. Of the 76 studies included, 38 had assessed physical activity as a primary outcome. Details are available in the Characteristics of included studies table.

Excluded studies

We excluded most of these 134 studies (n = 84) due to physical activity not being objectively assessed. We report reasons for exclusion in the Characteristics of excluded studies table.

Risk of bias in included studies

Overall, the domains with the highest risks of bias were performance bias, as the method of delivery of some interventions precluded participant blinding, and reporting bias. Domains with the lowest risks of bias were detection bias, as objective assessment of physical activity was an inclusion criterion, and selection bias, as most studies did report the method of random sequence generation (Figure 2).

Figure 2. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

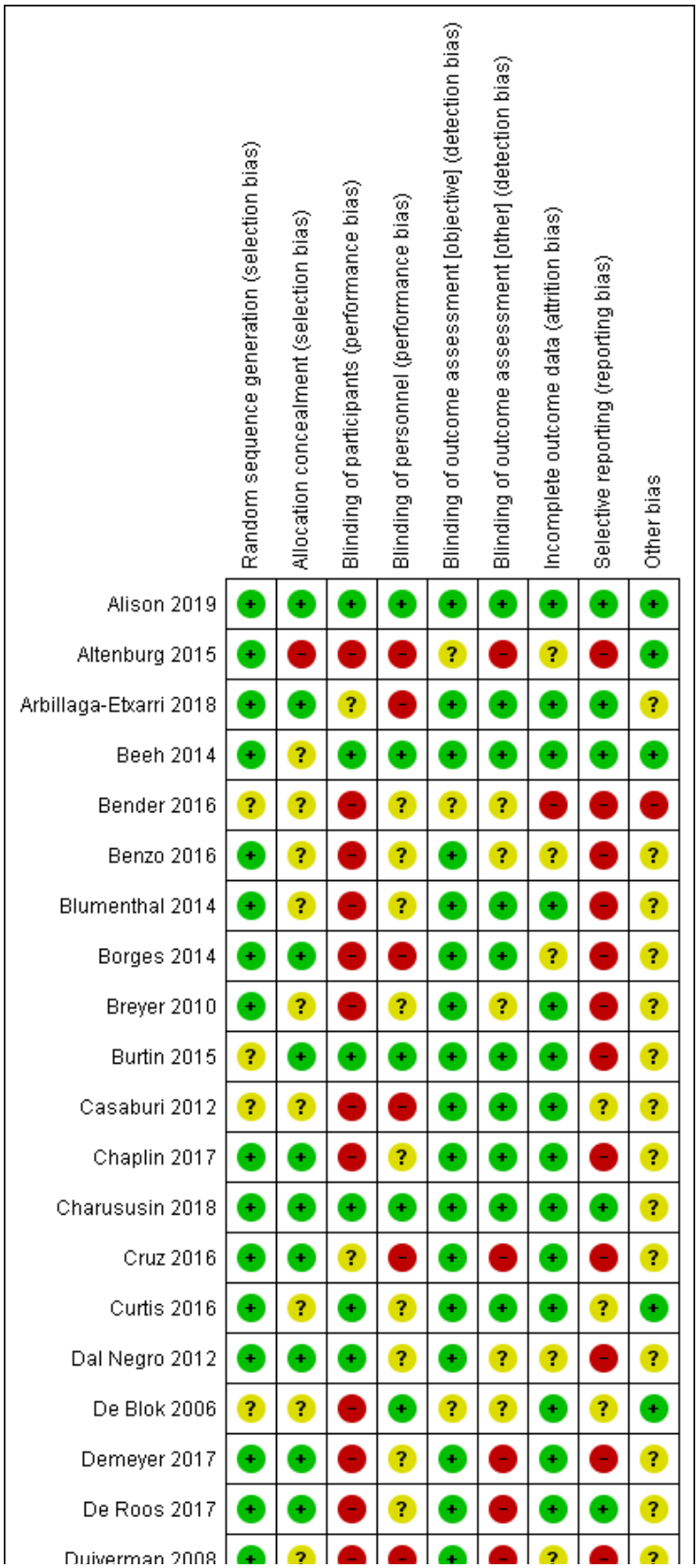


Figure 2. (Continued)

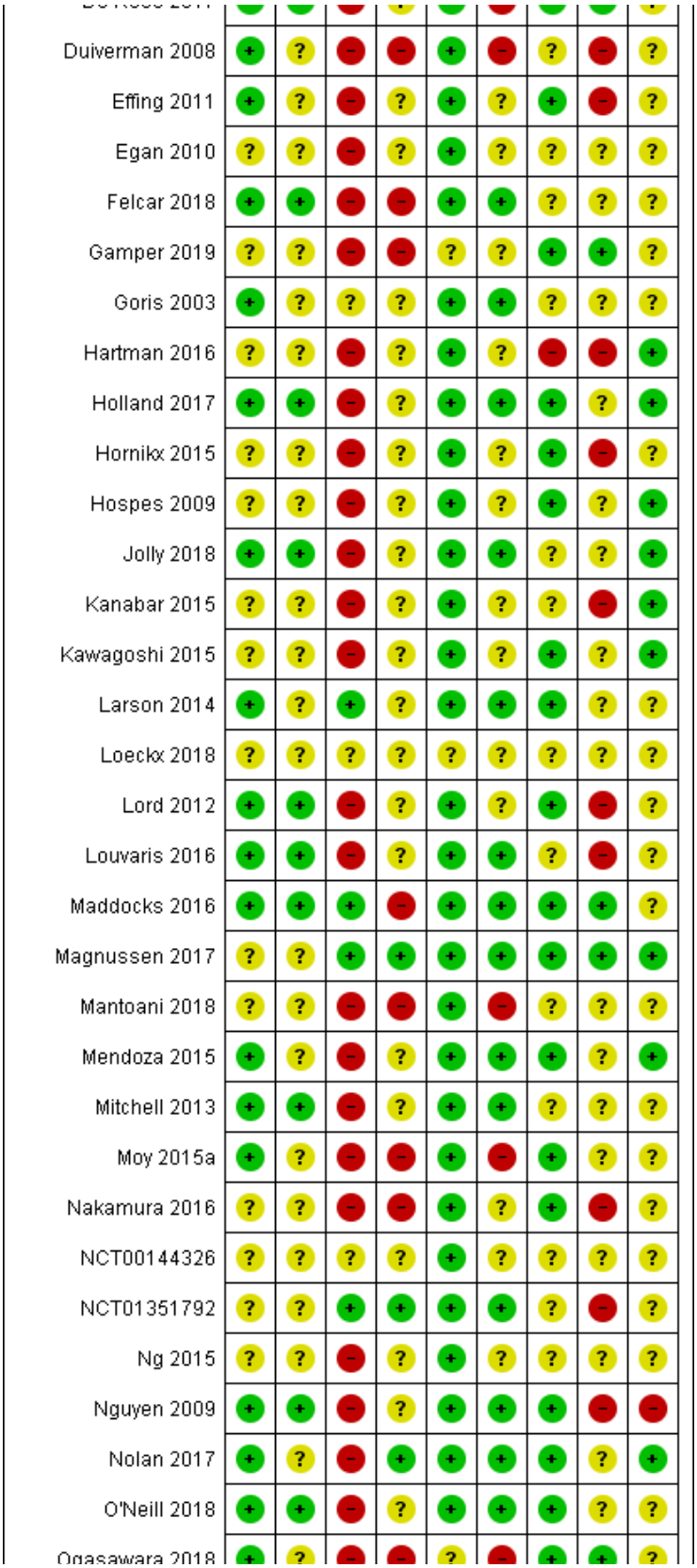
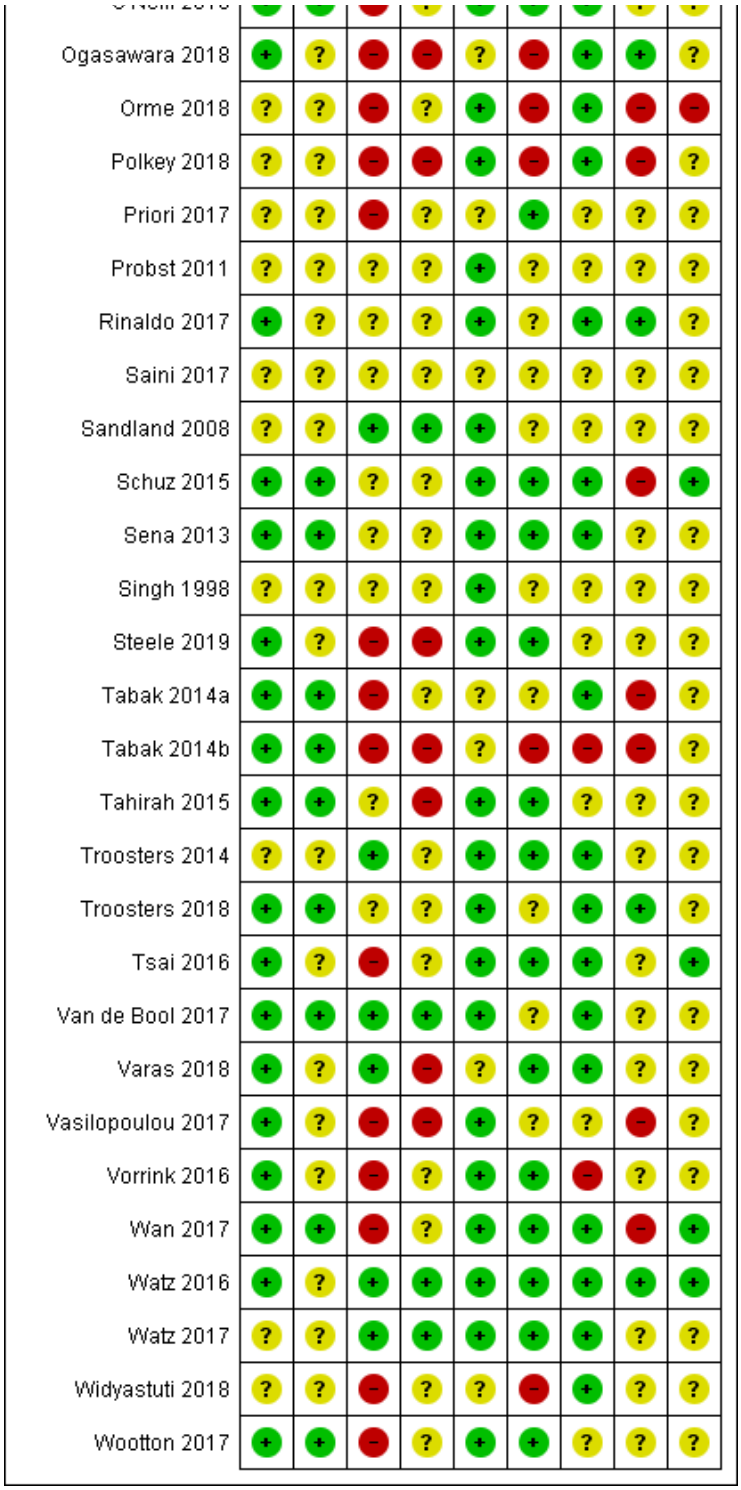


Figure 2. (Continued)



Allocation

For random sequence generation, 48 studies had a low risk of bias. Insufficient information was available to inform a decision for 17 studies (Bender 2016; Burtin 2015; Casaburi 2012; De Blok 2006; Gamper 2019; Hartman 2016; Hornikx 2015; Hospes 2009; Kawagoshi 2015; Magnussen 2017; Orme 2018; Polkey 2018; Probst 2011; Sandland 2008; Troosters 2014; Watz 2017; Widyastuti 2018), nine abstracts (Egan 2010; Kanabar 2015; Loeckx 2018; Mantoani 2018; Nakamura 2016; Ng 2015; Priori 2017; Saini 2017; Singh 1998) and studies from two clinical trial registries (NCT00144326; NCT01351792).

For allocation concealment, one study was assessed at high risk of bias (Altenburg 2015) and 28 at low risk of bias. Insufficient information was available to inform a decision in 36 studies (Beeh

2014; Bender 2016; Benzo 2016; Blumenthal 2014; Breyer 2010; Casaburi 2012; Curtis 2016; De Blok 2006; Duiverman 2008; Effing 2011; Gamper 2019; Goris 2003; Hartman 2016; Hornikx 2015; Hospes 2009; Kawagoshi 2015; Larson 2014; Magnussen 2017; Mendoza 2015; Moy 2015a; Nolan 2017; Ogasawara 2018; Orme 2018; Polkey 2018; Probst 2011; Rinaldo 2017; Sandland 2008; Steele 2019; Troosters 2014; Tsai 2016; Varas 2018; Vasilopoulou 2017; Vorrink 2016; Watz 2016; Watz 2017; Widyastuti 2018), nine abstracts (Egan 2010; Kanabar 2015; Loeckx 2018; Mantoani 2018; Nakamura 2016; Ng 2015; Priori 2017; Saini 2017; Singh 1998) and studies from two clinical trial registries (NCT00144326; NCT01351792).

Blinding

We assessed performance bias separately for participants and personnel.

Participants

We rated the risk of performance bias as high in 47 studies, in some cases due to the nature of the intervention precluding participant blinding. Most pharmaceutical interventions were able to blind participants and were assessed as being at low risk of performance bias (Beeh 2014; Curtis 2016; Magnussen 2017; NCT01351792; Troosters 2014; Watz 2016; Watz 2017), apart from the high risk assessment for Nakamura 2016 (lack of blinding) and unclear risk for NCT00144326 and Troosters 2018 (insufficient information). Similarly, studies involving nutritional supplementation were also able to blind participants and were assessed at low risk (Dal Negro 2012; Van de Bool 2017), apart from the high risk assessment for Ogasawara 2018 (lack of blinding) and unclear risk for Goris 2003 (insufficient information).

Other studies assessed as low risk were Alison 2019, Burtin 2015, Charususin 2018, Curtis 2016, Larson 2014, Maddocks 2016, Sandland 2008 and Varas 2018. Other studies with unclear risk due to insufficient information were Arbillaga-Etxarri 2018, Cruz 2016, Loeckx 2018, NCT00144326, Probst 2011, Rinaldo 2017, Saini 2017, Schuz 2015, Sena 2013, Singh 1998, and Tahirah 2015.

Personnel

We judged most studies (n = 45) to be subject to unclear risk due to insufficient information. Studies at low risk (n = 12) included pharmacological interventions (Beeh 2014; Magnussen 2017; NCT01351792; Watz 2016; Watz 2017), supplemental oxygen (Alison 2019; Sandland 2008) and nutritional supplementation (Van de Bool 2017), as well as studies involving an intervention in addition to pulmonary rehabilitation programs (Burtin 2015; Charususin 2018; Nolan 2017) and one physical activity counselling study (De Blok 2006). There were 19 studies assessed at high risk which was primarily attributable to personnel awareness of group allocation during the study (Altenburg 2015; Arbillaga-Etxarri 2018; Borges 2014; Casaburi 2012; Cruz 2016; Duiverman 2008; Felcar 2018; Gamper 2019; Maddocks 2016; Mantoani 2018; Moy 2015a; Nakamura 2016; Ogasawara 2018; Polkey 2018; Steele 2019; Tabak 2014b; Tahirah 2015; Varas 2018; Vasilopoulou 2017).

We assessed detection bias separately for outcomes that were or were not objectively assessed.

Objective outcomes

In line with the inclusion criteria, all studies objectively assessed physical activity. Most (n = 64) were therefore classified as low risk of detection bias. Studies at unclear risk were Altenburg 2015, Bender 2016, De Blok 2006, Gamper 2019, Loeckx 2018, Ogasawara 2018, Priori 2017, Saini 2017, Tabak 2014a, Tabak 2014b, Varas 2018 and Widyastuti 2018, as there was insufficient information to make an assessment.

Other outcomes

We rated 35 studies at low risk of detection bias (Alison 2019; Arbillaga-Etxarri 2018; Beeh 2014; Blumenthal 2014; Borges 2014; Burtin 2015; Casaburi 2012; Chaplin 2017; Charususin 2018; Curtis 2016; Felcar 2018; Goris 2003; Jolly 2018; Larson 2014; Louvaris 2016; Magnussen 2017; Mendoza 2015; Mitchell 2013; NCT01351792; Nguyen 2009; Nolan 2017; O'Neill 2018; Priori 2017; Schuz 2015; Sena 2013; Singh 1998; Steele 2019; Tahirah 2015; Troosters 2014; Tsai 2016; Varas 2018; Vorrink 2016; Wan 2017; Watz 2017; Wootton 2017). We judged 12 studies to be at high risk (Altenburg 2015; Cruz 2016; Demeyer 2017; De Roos 2017; Duiverman 2008; Mantoani 2018; Moy 2015a; Orme 2018; Ogasawara 2018; Polkey 2018; Tabak 2014b; Widyastuti 2018), due to lack of assessor blinding. Insufficient information was available to inform a decision on the remaining 29 studies.

Incomplete outcome data

We rated most studies (n = 46) at low risk of attrition bias. We assessed 14 studies (Altenburg 2015; Benzo 2016; Borges 2014; Dal Negro 2012; Duiverman 2008; Felcar 2018; Goris 2003; Jolly 2018; Louvaris 2016; Probst 2011; Sandland 2008; Steele 2019; Vasilopoulou 2017; Wootton 2017) and 10 abstracts (Egan 2010; Kanabar 2015; Loeckx 2018; Mantoani 2018; Mitchell 2013; Ng 2015; Priori 2017; Saini 2017; Singh 1998; Tahirah 2015) to be at unclear risk.

We judged four studies to have a high risk of bias where attrition was unevenly distributed between groups (Tabak 2014b), documented but not detailed (Bender 2016), specifically addressed by authors (Vorrink 2016) or clearly related to the intervention (Hartman 2016).

Selective reporting

Most studies (n = 58) had a registered or published trial protocol which facilitated assessment for risk of reporting bias, except for 11 studies (Altenburg 2015; Dal Negro 2012; De Blok 2006; Goris 2003; Hospes 2009; Kawagoshi 2015; Probst 2011; Rinaldo 2017; Varas 2018; Vorrink 2016; Widyastuti 2018) and seven abstracts (Kanabar 2015; Loeckx 2018; Nakamura 2016; Ng 2015; Saini 2017; Priori 2017; Sena 2013).

We rated 12 studies at low risk (Alison 2019; Arbillaga-Etxarri 2018; Beeh 2014; Charususin 2018; De Roos 2017; Gamper 2019; Maddocks 2016; Magnussen 2017; Ogasawara 2018; Rinaldo 2017; Troosters 2018; Watz 2016).

We judged 25 studies (Altenburg 2015; Bender 2016; Benzo 2016; Blumenthal 2014; Borges 2014; Breyer 2010; Burtin 2015; Chaplin 2017; Cruz 2016; Dal Negro 2012; Demeyer 2017; Duiverman 2008; Effing 2011; Hartman 2016; Hornikx 2015; Lord 2012; Louvaris 2016; Nguyen 2009; Orme 2018; Polkey 2018; Schuz 2015; Tabak 2014a; Tabak 2014b; Vasilopoulou 2017; Wan 2017), two abstracts (Kanabar 2015; Nakamura 2016) and one clinical trial registry

study (NCT01351792) to be at high risk. This was primarily due to discrepancies between trial registration and publications (including identification of primary and secondary outcomes), as well as between the way that outcomes were prespecified to be analysed and actually reported. Thirty-six studies were at unclear risk of reporting bias.

Other potential sources of bias

We rated most studies (n = 55) as being at unclear risk, or at low risk (n = 18; Alison 2019; Altenburg 2015; Beeh 2014; Curtis 2016; De Blok 2006; Hartman 2016; Holland 2017; Hospes 2009; Jolly 2018; Kanabar 2015; Kawagoshi 2015; Magnussen 2017; Mendoza 2015; Nolan 2017; Schuz 2015; Tsai 2016; Wan 2017; Watz 2016) from other potential sources of bias. We deemed three studies to be at high risk from other potential sources of bias (methodological concerns, Bender 2016, Nguyen 2009; lack of physical activity data by group, Orme 2018).

Effects of interventions

See: **Summary of findings for the main comparison** Pulmonary rehabilitation/exercise training versus no intervention; **Summary of findings 2** Comparison of types of pulmonary rehabilitation/exercise training; **Summary of findings 3** Physical activity counselling; **Summary of findings 4** Self-management; **Summary of findings 5** Pharmacological interventions

Structure of the analysis

After examining the data, we found that the included studies examined a wide range of interventions (Table 2) across the four defined comparisons (intervention versus no intervention; intervention versus placebo/sham; intervention with common intervention versus common intervention; intervention versus intervention).

We present results for the primary outcome of physical activity here. We present results for secondary outcomes in Appendix 4 (health-related quality of life), Appendix 5 (exercise capacity), Appendix 6 (adherence) and Appendix 7 (adverse events).

We present results by type of intervention, with precise comparison by clinical setting (clinically-stable disease, acute exacerbation). We define the following types of intervention to aid the reader in finding relevant data:

- pulmonary rehabilitation/exercise training;
- physical activity counselling;
- self-management;
- pharmacological;
- nutritional supplementation;
- supplemental oxygen;
- other interventions.

INTERVENTION: Pulmonary rehabilitation/exercise training

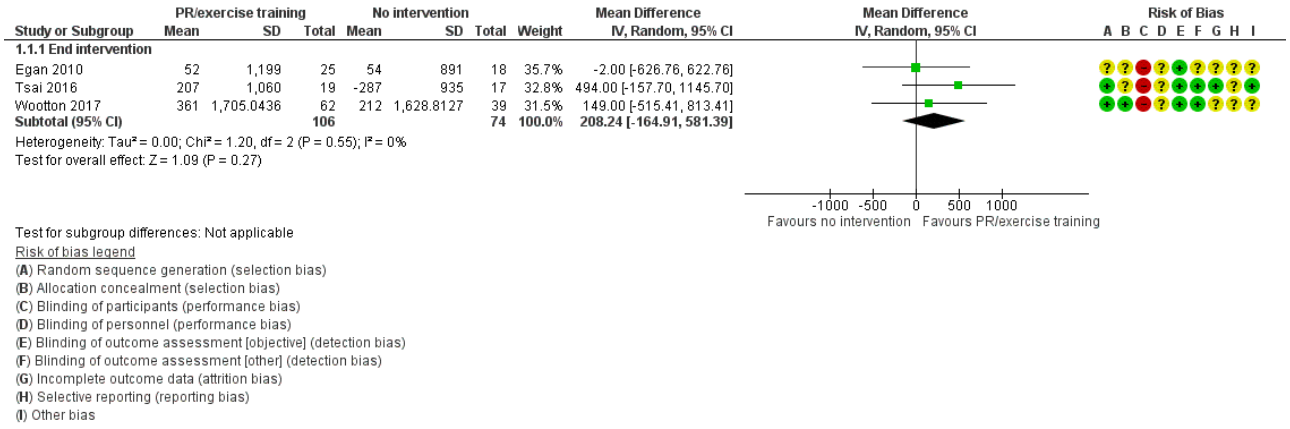
See Summary of findings for the main comparison and Summary of findings 2.

COMPARISON: Intervention versus no intervention (clinically-stable COPD)

Pulmonary rehabilitation versus no intervention

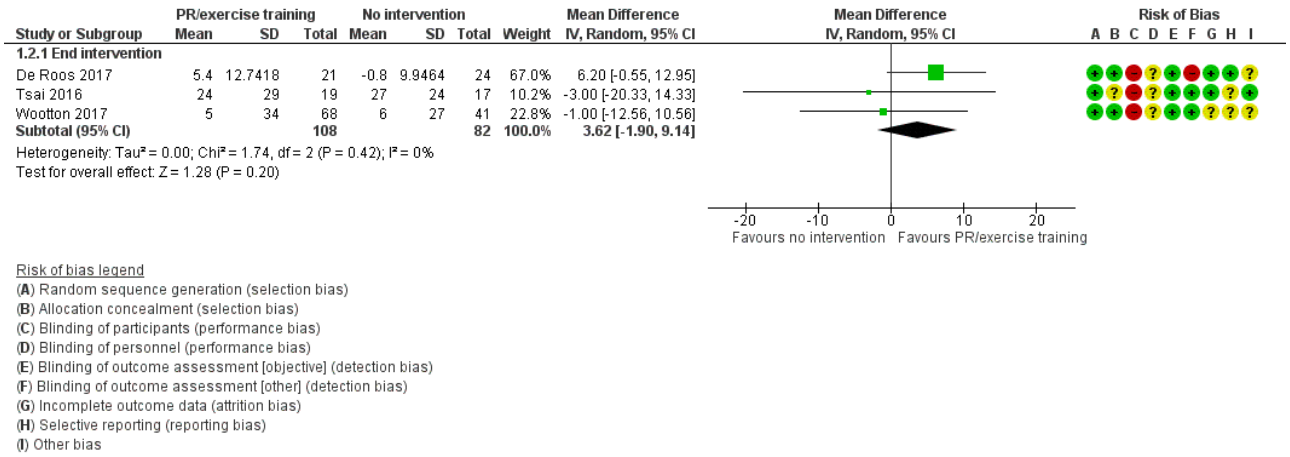
No clear improvement in physical activity was demonstrated following pulmonary rehabilitation compared to no intervention, with a single variable showing an increase. The mean difference (MD) in step count was 208 steps (95% confidence interval (CI) −165 to 581; 3 studies, 180 participants; low-certainty evidence; Analysis 1.1; Figure 3).

Figure 3. Forest plot of comparison 1: Intervention vs. no intervention Outcome 1.1: Physical activity: change in step count (steps per day)



The mean difference in time in moderate-to-vigorous intensity physical activity (MVPA) was 4 minutes (95% CI −2 to 9; 3 studies, 190 participants; low-certainty evidence; Analysis 1.2; Figure 4).

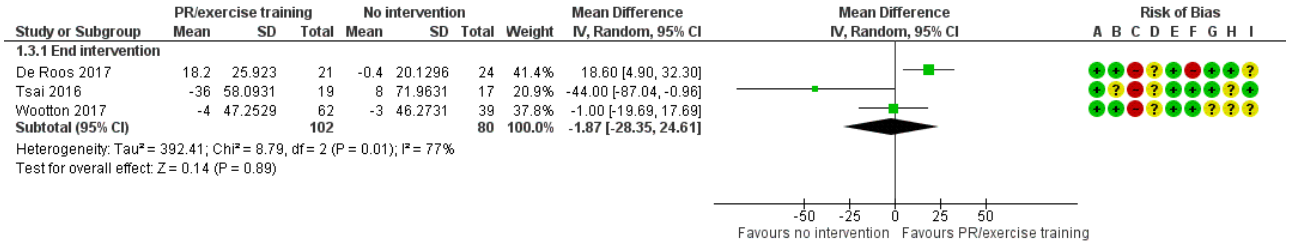
Figure 4. Forest plot of comparison 1: Intervention vs. no intervention Outcome 1.2: Physical activity: change in time in moderate-to-vigorous intensity physical activity (minutes per day)



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants (performance bias)
(D) Blinding of personnel (performance bias)
(E) Blinding of outcome assessment [objective] (detection bias)
(F) Blinding of outcome assessment [other] (detection bias)
(G) Incomplete outcome data (attrition bias)
(H) Selective reporting (reporting bias)
(I) Other bias

The mean difference in time in light-intensity physical activity (LIPA) was −2 minutes (95% CI −28 to 25; 3 studies, 182 participants; low-certainty evidence; Analysis 1.3; Figure 5), with substantial heterogeneity evident (I^2 = 77%) .

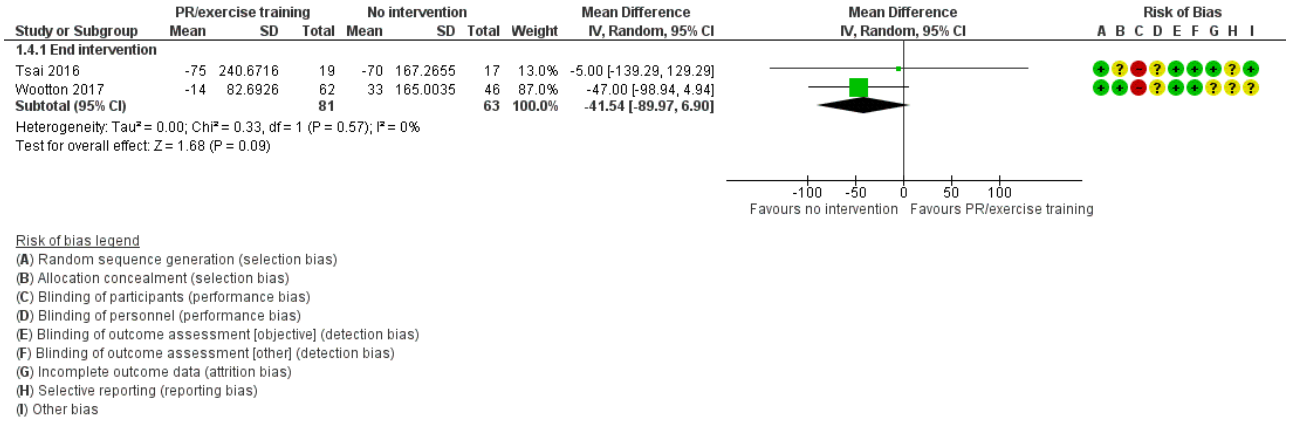
Figure 5. Forest plot of comparison 1: Intervention vs. no intervention Outcome 1.4: Physical activity: change in time in light-intensity physical activity (minutes per day)



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants (performance bias)
(D) Blinding of personnel (performance bias)
(E) Blinding of outcome assessment [objective] (detection bias)
(F) Blinding of outcome assessment [other] (detection bias)
(G) Incomplete outcome data (attrition bias)
(H) Selective reporting (reporting bias)
(I) Other bias

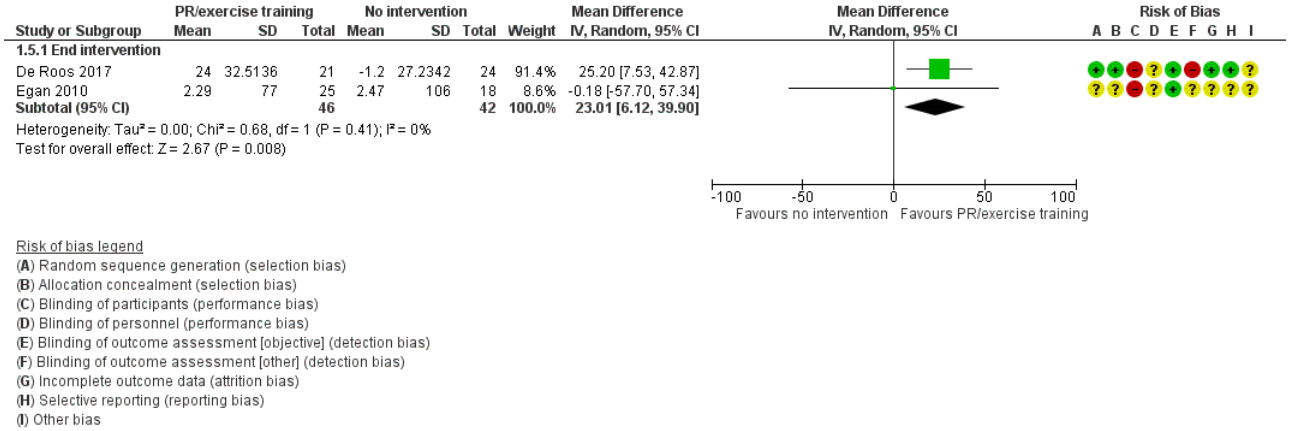
The mean difference in total energy expenditure was −42 kcal (95% CI −90 to 7; 2 studies, 144 participants; low-certainty evidence; Analysis 1.4; Figure 6).

Figure 6. Forest plot of comparison 1: Intervention vs. no intervention Outcome 1.3: Physical activity: change in total energy expenditure (kcal)



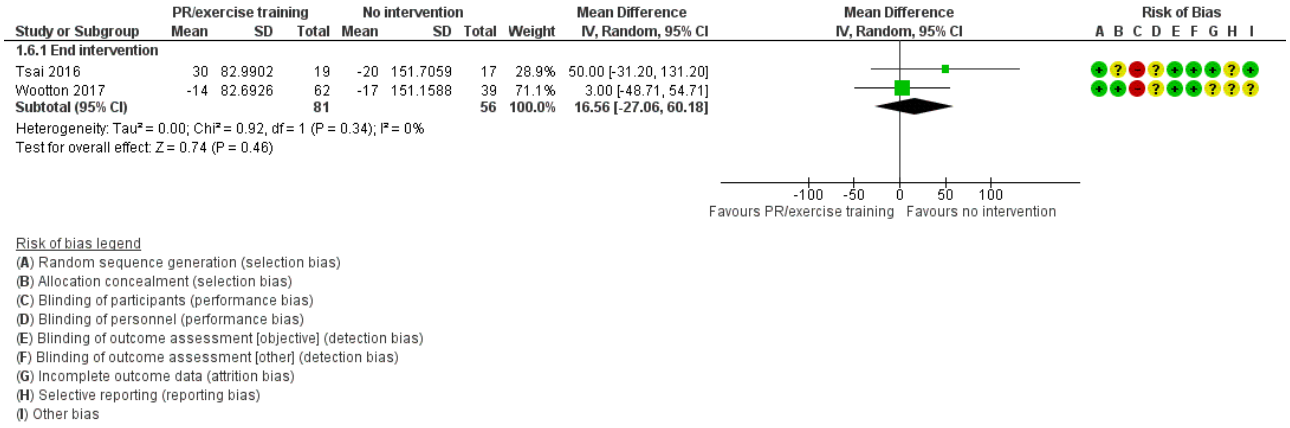
The mean difference in physical activity level (PAL) was 0.1 (95% CI −0.1 to 0.1; Tsai 2016, 36 participants; low-certainty evidence; Table 1) following telerehabilitation, consisting of pulmonary rehabilitation delivered by videoconferencing into the home. The only clear improvement in physical activity following pulmonary rehabilitation was a greater increase in total time spent in physical activity (MD 23 minutes, 95% CI 6 to 40; 2 studies, 88 participants; low-certainty evidence; Analysis 1.5; Figure 7).

Figure 7. Forest plot of comparison 1: Intervention vs. no intervention Outcome 1.6: Physical activity: change in time in physical activity (total, minutes per day)



The mean difference in change in sedentary time was 17 minutes (95% CI −27 to 60; 2 studies, 137 participants; low-certainty evidence; Analysis 1.6; Figure 8) following pulmonary rehabilitation compared to no intervention.

Figure 8. Forest plot of comparison 1: Intervention vs. no intervention Outcome 1.5: Physical activity: change in sedentary time (minutes per day)



High-intensity interval training versus no intervention

Improvements in physical activity were demonstrated following high-intensity interval training compared to no intervention in two studies from the same research team. Improvements in time in 'lifestyle' physical activity (MD 9 minutes, 95% CI 4 to 15; Analysis 1.7; Figure 9), in LIPA (MD 28 minutes, 95% CI 16 to 41; Analysis 1.8; Figure 10), in MVPA (MD 6 minutes, 95% CI 4 to 8; Analysis 1.9; Figure 11) and sedentary (MD −34 minutes, 95% CI −56 to −13; Analysis 1.10; Figure 12) were demonstrated at end intervention (2 studies, 275 participants; moderate-certainty evidence).

Figure 9. Forest plot of comparison 1: Intervention vs. no intervention Outcome: 1.8 Physical activity: time in "lifestyle" physical activity (minutes per day)

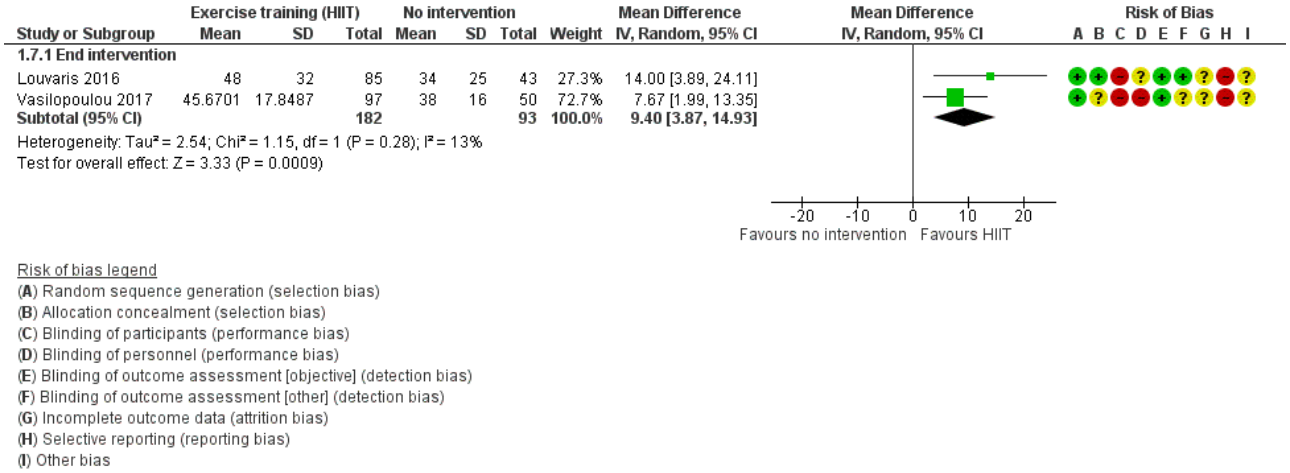
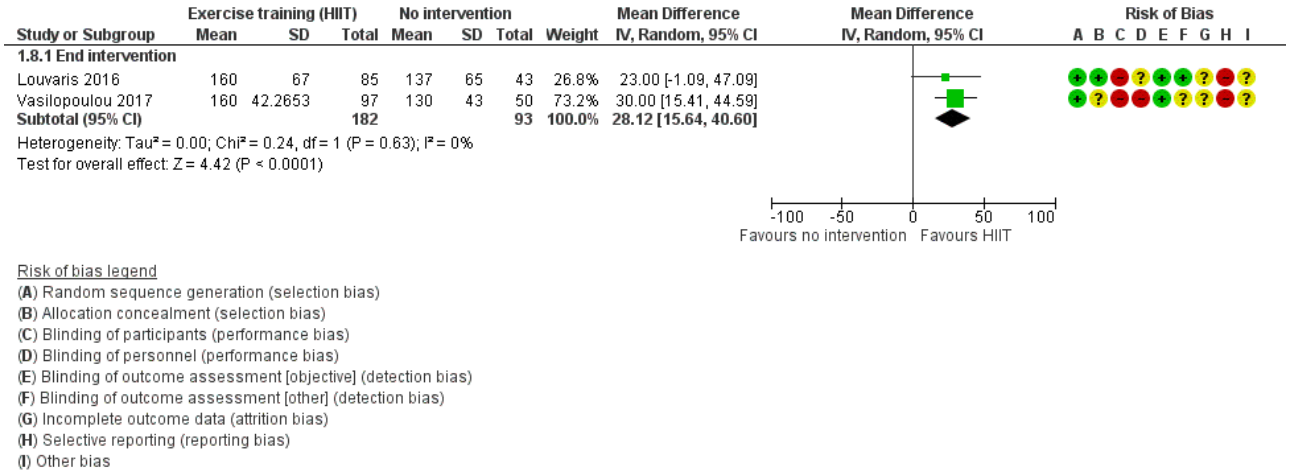
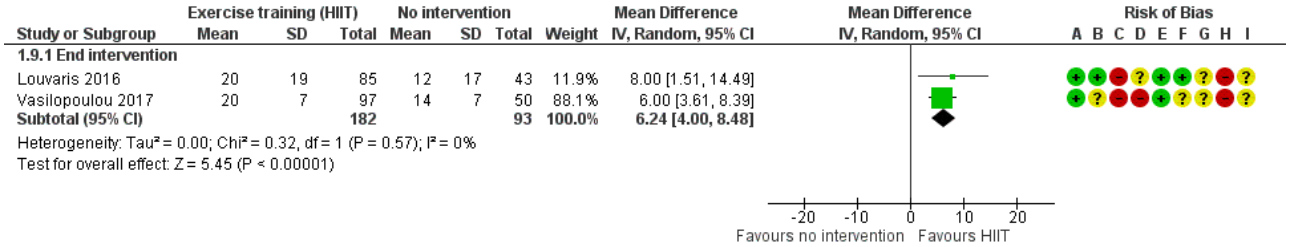


Figure 10. Forest plot of comparison: 1 Intervention vs. no intervention Outcome: 1.7 Physical activity: time in light-intensity physical activity (minutes per day)



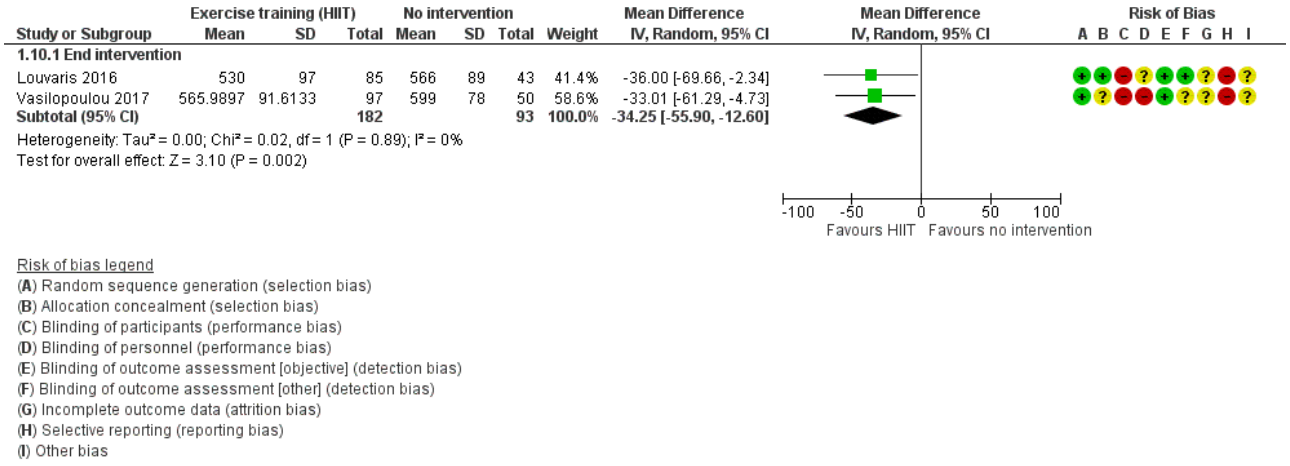
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants (performance bias)
(D) Blinding of personnel (performance bias)
(E) Blinding of outcome assessment [objective] (detection bias)
(F) Blinding of outcome assessment [other] (detection bias)
(G) Incomplete outcome data (attrition bias)
(H) Selective reporting (reporting bias)
(I) Other bias

Figure 11. Forest plot of comparison 1: Intervention vs. vs. no intervention Outcome 1.9: Physical activity: time in MVPA (minutes per day)



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants (performance bias)
(D) Blinding of personnel (performance bias)
(E) Blinding of outcome assessment [objective] (detection bias)
(F) Blinding of outcome assessment [other] (detection bias)
(G) Incomplete outcome data (attrition bias)
(H) Selective reporting (reporting bias)
(I) Other bias

Figure 12. Forest plot of comparison 1: Intervention vs. no intervention Outcome 1.10: Physical activity: sedentary time (minutes per day)



Additionally, improvements in step count (MD 1683 steps, 95% CI 721 to 2646) and vector magnitude units (VMU) (MD 89, 95% CI 13 to 165) were demonstrated following a 12-week intervention (moderate-certainty evidence; Louvaris 2016; 128 participants; Table 1).

Maintenance (telerehabilitation) following high-intensity interval training versus no intervention

Increased time in LIPA (MD 44 minutes, 95% CI 27 to 62), moderate-intensity (MD 7 minutes, 95% CI 4 to 10) and "lifestyle" physical activity (MD 7 minutes, 95% CI 1 to 13) were demonstrated following a 12-month telerehabilitation maintenance programme compared to no intervention (moderate-certainty evidence; Vasilopoulou 2017, 97 participants; Table 1). The mean difference in change in sedentary time was −31 minutes (95% CI −66 to 4; low-certainty evidence; Vasilopoulou 2017, 97 participants; Table 1) at end intervention.

Maintenance (centre-based) following high-intensity interval training versus no intervention

Increased time in LIPA (MD 46 minutes, 95% CI 29 to 63), moderate-intensity (MD 11 minutes, 95% CI 8 to 14) and "lifestyle" physical activity (MD 18 minutes, 95% CI 12 to 25) were demonstrated following a 12-month centre-based maintenance programme compared to no intervention. An improvement in sedentary time (MD −64 minutes, 95% CI −95 to −33; moderate-certainty evidence; Vasilopoulou 2017, 100 participants; Table 1) was also demonstrated at end intervention.

COMPARISON: Intervention versus sham intervention

No studies presented data for this comparison.

COMPARISON: Intervention versus standard common intervention (clinically-stable COPD)

A range of interventions have been tested in single studies such that meta-analysis was not possible.

Nordic walking with education versus education

Increased movement intensity was demonstrated following a 12-week Nordic walking programme with education compared to education alone (MD 0.51 m/s^2, 95% CI 0.27 to 0.75) and maintained at nine-month follow-up (MD 0.42 m/s^2, 95% CI 0.21 to 0.63; Breyer 2010, 60 participants; low-certainty evidence; Analysis 3.1). However, it was the only fully-reported physical activity variable in this study and no data were available for time sitting, standing and walking in the education group (Breyer 2010; Table 1).

Structured exercise training (COPE-active) with self-management versus self-management

The mean difference in step count was 565 steps (95% CI −354 to 1484) after seven months of an 11-month structured exercise training programme (COPE-active) with self-management compared to self-management. An increase in step count was demonstrated at end intervention (MD 1178 steps, 95% CI 260 to 2096) and this improvement was maintained at 24-month follow-up (MD 1193 steps, 95% CI 226 to 2160; Effing 2011, 110 participants; low-certainty evidence; Analysis 3.2).

Upper-limb exercise with education versus education

The mean difference in time in LIPA was 3 minutes (95% CI −31 to 38) at end intervention and 14 minutes (95% CI −36 to 64) at 12-month follow-up after a four-month study of upper-limb exercise with education compared to education alone (Larson 2014, 34 participants; low-certainty evidence; Analysis 3.3).

The mean difference in time spent in moderate-intensity physical activity was 1 minute (95% CI −1 to 3), sedentary time was −57 minutes (95% CI −133 to 19) and proportion of time spent sedentary was −2% (95% CI −8 to 4) at end intervention (Larson 2014, 34 participants; low-certainty evidence; Table 1).

Exercise training and long-acting muscarinic antagonist/long-acting beta agonist (LAMA/LABA) with behaviour modification versus placebo with behaviour modification

The mean difference in step count was −328 steps (95% CI −1214 to 558) after eight weeks and −541 steps (95% CI −1433 to 350) at end intervention following a 12-week study for exercise training and LAMA/LABA with behavioural modification compared to placebo with behavioural modification (Troosters 2018; *8 weeks*: 124 participants; *12 weeks*: 112 participants; moderate-certainty evidence; Analysis 3.4). The mean difference in walking time was

−3 minutes (95% CI −13 to 6) after eight weeks and −6 minutes (95% CI −15 to 4) at end intervention (Troosters 2018; *8 weeks*: 124 participants; *12 weeks*: 112 participants; moderate-certainty evidence; Analysis 3.5). The mean difference in walking intensity was −0.03 m/s^2 (95% CI −0.11 to 0.05) after eight weeks and −0.02 (95% CI −0.10 to 0.06) at end intervention (Troosters 2018; *8 weeks*: 124 participants; *12 weeks*: 112 participants; moderate-certainty evidence; Analysis 3.6).

Exercise training and LABA with LAMA and behaviour modification versus LAMA and behaviour modification

The mean difference in step count was −82 steps (95% CI −968 to 803) after eight weeks and 404 steps (95% CI −474 to 1281) at end intervention following a 12-week study for exercise training and LABA with LAMA and behaviour modification compared to LAMA and behaviour modification (Troosters 2018; *8 weeks*: 124 participants; *12 weeks*: 114 participants; moderate-certainty evidence; Analysis 3.7). The mean difference in walking time was −1 minute (95% CI −10 to 9) after eight weeks and 3 minutes (95% CI −6 to 13) at end intervention (Troosters 2018; *8 weeks*: 124 participants; *12 weeks*: 114 participants; moderate-certainty evidence; Analysis 3.8). The mean difference in walking intensity was −0.05 m/s^2 (95% CI −0.13 to 0.03) after eight weeks and 0.04 m/s^2 (95% CI −0.04 to 0.12) at end intervention (Troosters 2018; *8 weeks*: 124 participants; *12 weeks*: 113 participants; moderate-certainty evidence; Analysis 3.9).

Exercise training with LAMA/LABA and behaviour modification versus LAMA/LABA and behaviour modification

The mean difference in step count was −554 steps (95% CI −1432 to 325) after eight weeks and −837 steps (95% CI −1708 to 33) at end intervention following a 12-week study for exercise training with LAMA/LABA and behaviour modification compared to LAMA/LABA and behaviour modification (Troosters 2018; *8 weeks*: 126 participants; *12 weeks*: 117 participants; moderate-certainty evidence; Analysis 3.10).

The mean difference in walking time was −4 minutes (95% CI −14 to 5) after eight weeks and −8 minutes (95% CI −18 to 1) at end intervention (Troosters 2018; *8 weeks*: 126 participants; *12 weeks*: 117 participants; moderate-certainty evidence; Analysis 3.11).

Walking intensity was lower in the group without exercise training (−0.09 m/s^2, 95% CI −0.17 to −0.01) after eight weeks. The mean difference in walking intensity was −0.04 m/s^2 (95% CI −0.12 to 0.04) at end intervention (Troosters 2018; *8 weeks*: 126 participants; *12 weeks*: 115 participants; moderate-certainty evidence; Analysis 3.12).

Exercise training and physical activity counselling with pedometer versus pedometer alone

An increase in step count (MD 3174 steps, 95% CI 1453 to 4895) was demonstrated following an eight-week exercise training and physical activity counselling (in-person) programme with pedometer compared to pedometer alone. This improvement was maintained at three-month (MD 3841 steps, 95% CI 2225 to 5457) and 12-month follow-up (MD 2547 steps, 95% CI 927 to 4167; Varas 2018, 33 participants; moderate-quality evidence; Analysis 3.13).

COMPARISON: Intervention versus intervention (clinically-stable COPD)

Web-based pulmonary rehabilitation versus centre-based pulmonary rehabilitation

No data were presented in a seven-week study of web-based pulmonary rehabilitation compared to a centre-based program (Chaplin 2017, 54 participants; very low-certainty evidence; Table 1).

Exercise training (eccentric cycle training) versus exercise training (concentric cycle training)

No data were presented in a 10-week study of eccentric cycle training compared to concentric training (Sena 2013, 16 participants; very low-certainty evidence; Table 1).

Home-based pulmonary rehabilitation versus centre-based pulmonary rehabilitation

Similar results were demonstrated for change in step count (Analysis 4.1), time in MVPA (Analysis 4.2), number of MVPA bouts (Analysis 4.3), time in MVPA bouts (Analysis 4.4), sedentary time (Analysis 4.5), sedentary awake time (Analysis 4.6), number of sedentary bouts (Analysis 4.7), time in sedentary bouts (Analysis 4.8), METs (Analysis 4.9) and total energy expenditure (Analysis 4.10) at end intervention and 14-month follow-up in an equivalence study comparing an eight-week home-based pulmonary rehabilitation programme with a centre-based programme (Holland 2017, 58 participants; low-certainty evidence).

Water-based exercise training versus land-based exercise training

The mean difference in step count was 676 steps (95% CI −645 to 1997; Analysis 4.11) and total energy expenditure was 39 kcal (95% CI −14 to 92; Felcar 2018, Analysis 4.12). Ten participants in the water-based group and five participants in the land-based group were classified as "active" following a six-month study of water-based exercise training compared to a land-based programme (Felcar 2018, 36 participants; low-certainty evidence; Table 1).

Tai Chi versus pulmonary rehabilitation

An increase in step count was demonstrated in the Tai Chi group (MD 1349 steps, 95% CI 93 to 2605; Polkey 2018, 110 participants; moderate-certainty evidence; Analysis 4.13) following 22 weeks in a 24-week study of Tai Chi compared to pulmonary rehabilitation.

Calisthenics versus exercise training

"No significant differences" in step count, MVPA time, time walking, time standing, time sitting, time lying, active energy expenditure or total energy expenditure were reported following a 12-week callisthenics and breathing exercises programme compared to exercise training (Probst 2011, 40 participants; low-certainty evidence Table 1).

Exercise training (outdoor walking) versus exercise training (cycle ergometry)

The mean difference in step count was −928 steps (95% CI −2515 to 659) following a three-week study comparing outdoor walking and cycle ergometry. The mean difference in step count was −267 steps (95% CI −1622 to 1088) at three-month follow up (Gamper 2019, 16 participants; low-certainty evidence; Analysis 4.14).

Physical activity counselling versus pulmonary rehabilitation

The mean difference in step count was −92 steps (95% CI −1710 to 1526; Widyastuti 2018, 36 participants; low-certainty evidence; Table 1) following a six-week physical activity counselling intervention (in-person) compared to pulmonary rehabilitation.

The mean difference in step count was 1291 steps (95% CI −749 to 333) at end intervention following a 12-week physical activity counselling intervention (in-person) compared to six weeks of pulmonary rehabilitation. The mean difference in step count was 347 steps (95% CI −2216 to 2910) at three-month follow-up (O'Neill 2018, 26 participants; low-certainty evidence; Analysis 4.15).

An improvement in number in MVPA bouts was demonstrated in the physical activity counselling group (MD 0.5, 95% CI 0.3 to 0.8).

The mean difference in time in MVPA was 6 minutes (95% CI −10 to 22) and time in MVPA bouts was 10 minutes (95% CI −2 to 21) at end intervention (O'Neill 2018, 26 participants; low-certainty evidence; Table 1).

Exercise training with tapering supervision versus exercise training

The mean difference in total energy expenditure was 520 kcal (95% CI −105 to 1145) at end intervention and 400 kcal (95% CI −109 to 909) at 42-week follow-up after a 28-week study of exercise training with tapered supervision compared to supervised exercise training (Rinaldo 2017, 24 participants; moderate-certainty evidence; Analysis 4.16).

Adherence intervention versus pulmonary rehabilitation

The mean difference in step count was −159 steps (95% CI −1742 to 1424), time inactive was −2% (95% CI −9 to 5) and peak performance was 0 (95% CI −9 to 9) following six months of an adherence intervention compared to eight weeks of pulmonary rehabilitation (Steele 2019, 63 participants; low-certainty evidence; Table 1).

Maintenance following high-intensity interval training: telerehabilitation versus centre-based programme

Less time was spent in lifestyle (MD −11 minutes, 95% CI −18 to −4) and moderate-intensity physical activity (MD −4 minutes, 95% CI −7 to −1) in the telerehabilitation group compared to a centre-based group following a 12-month study of maintenance after eight weeks of high-intensity interval exercise training.

The mean difference in time in LIPA was −2 minutes (95% CI −19 to 15) and sedentary time was 33 minutes (95% CI −3 to 69; Vasilopoulou 2017, 100 participants; moderate-quality evidence; Table 1).

COMPARISON: Intervention versus no intervention (acute exacerbation of COPD)

Inpatient exercise training versus no intervention

No clear improvement in physical activity was demonstrated following two inpatient exercise-training interventions.

The median step count for the exercise training group was 4215 steps (interquartile range (IQR) 2133 to 6693) compared to no intervention (median 2198 steps (IQR 1242 to 4857; P = 0.07; low-certainty evidence; Tahirah 2015, 34 participants; Table 1) at discharge following inpatient walking and functional-resistance training compared to no intervention.

The mean difference for time in standing was 15 minutes (95% CI −57 to 87), sitting was −11 minutes (95% CI −94 to 72), walking was −19 minutes (95% CI −40 to 2) and lying was 21 minutes (95% CI −78 to 120; low-certainty evidence; Borges 2014, 29 participants; Table 1) four weeks after discharge following inpatient resistance training compared to no intervention.

INTERVENTION: Physical activity counselling

See Summary of findings 3.

COMPARISON: Intervention versus no intervention (clinically-stable COPD)

Physical activity counselling versus no intervention

We were unable to pool studies for quantitative synthesis due to data type (Altenburg 2015) and heterogeneous interventions (Arbillaga-Etxarri 2018; Demeyer 2017; Hospes 2009; Priori 2017; Saini 2017; Wootton 2017; see Characteristics of included studies).

An increased proportion of time spent in moderate-intensity physical activity (MD 32%, 95% CI 8 to 55; Priori 2017, 18 participants; very low-certainty evidence; Table 1) was demonstrated following an eight-week study of an automated coaching intervention compared to no intervention.

The same 12-week in-person intervention was used in three studies (two within this comparison). The mean difference in step count in one study was 1700 steps (95% CI −678 to 4078; Hospes 2009, 35 participants; low-certainty evidence; Analysis 1.11) compared to no intervention. In a subsequent study, the median change in step count in participants recruited from primary care was 537 steps (IQR −611 to 1740) in the physical activity counselling group and 431 steps (IQR −899 to 749) in the no-intervention group at end intervention (P = 0.48). The median change in step count was 157 steps (IQR −1679 to 994) in the physical activity counselling group and 48 steps (IQR −1004 to 885) in the no-intervention group (P = 0.90) at 12-month follow-up (Altenburg 2015; *12 weeks*: 40 participants; *12 months*: 38 participants; low-certainty evidence; Table 1). A greater median change in step count in participants recruited from secondary care was demonstrated in the physical activity counselling group (1002 steps, IQR −612 to 3077) compared to the no-intervention group (−814 steps, IQR −2827 to 1063) at end intervention (P = 0.007). The median change in step count was 1128 steps (IQR −1322 to 2707) in the physical activity counselling group and −217 steps (IQR −1951 to 1147) in the no-intervention group (P = 0.15) at 12-month follow-up (Altenburg 2015; *12 weeks*: 43 participants; *12 months*: 39 participants; low-certainty evidence; Table 1). Participants in secondary care had more severe disease, as indicated by a lower baseline FEV_1 (Characteristics of included studies). Subgroup analyses for participants with ≤ 10,000 steps per day at baseline revealed a similar pattern (Altenburg 2015; Table 1).

An increase in the mean difference for step count was 1548 steps (95% CI 1045 to 2051; Demeyer 2017; 280 participants; moderate-certainty evidence; Analysis 1.11) following a 12-week telecoaching intervention compared to no intervention. Improvements in walking time (MD 17 minutes, 95% CI 10 to 24), movement intensity (MD 0.09 m/s^2, 95% CI 0.04 to 0.14) and MVPA time (MD 11 minutes, 95% CI 7 to 15) were also demonstrated (Demeyer 2017, 280 participants; moderate-certainty evidence; Table 1).

The mean difference in step count was 177 steps (95% CI −828 to 1182; Arbillaga-Etxarri 2018, 280 participants; low-certainty evidence; Analysis 1.11) following a 12-month Urban Training intervention compared to no intervention.

The mean difference in change in proportion of time in moderate-intensity physical activity was −9% (standard deviation (SD) 24) in the physical activity counselling group and −21% (SD 21) in the no-intervention group (P = 0.116) following an eight-week physical activity counselling intervention compared to no intervention (Saini 2017, 28 participants; very low-certainty evidence; Table 1).

The mean difference in step count was −617 steps (95% CI −1669 to 453), time in LIPA was −27 min (95% CI −70 to 14), time in moderate-intensity physical activity was 20 minutes (95% CI −1 to 41), time in vigorous-intensity physical activity was 0 minutes (95% CI 0 to 1) and energy expenditure wads 17 kcal (95% CI −131 to 164) following 12 months of physical activity counselling compared to no intervention, which was completion of phase 2 of a 14-month study that all participants began with eight weeks of ground-based walking training (Wootton 2017, 43 participants; low-certainty evidence; Table 1).

COMPARISON: Intervention versus sham intervention

No studies presented data for this comparison.

COMPARISON: Intervention versus standard common intervention (clinically-stable COPD)

Physical activity counselling with optional supervised exercise versus optional supervised exercise

The mean difference in step count was 986 steps (95% CI −1553 to 3525; Tabak 2014a, 29 participants; low-certainty evidence; Table 1) following a three-week physical activity counselling intervention (telecoaching) with optional supervised exercise compared to optional supervised exercise.

The mean difference in step count was 240 steps (95% CI −417 to 897) at end intervention and −77 steps (95% CI −763 to 609) at 12-month follow-up of a study of a six-month physical activity counselling intervention (text message) following pulmonary rehabilitation with optional supervised exercise compared to optional supervised exercise (Vorrink 2016, 132 participants; low-certainty evidence; Analysis 3.14). The mean difference in METs was −0.08 (95% CI −0.22 to 0.06) at end intervention and 0.05 (95% CI −0.10 to 0.20) at 12-month follow-up (Vorrink 2016, 121 participants; low-certainty evidence; Analysis 3.15).

Pedometer with physical activity counselling versus physical activity counselling

An increase in step count was demonstrated (MD 2942 steps, 95% CI 1881 to 4003; Mendoza 2015, 97 participants; moderate-certainty evidence; Table 1) following a 12-week study of pedometer use with physical activity counselling (in-person) compared to physical activity counselling alone.

Physical activity counselling with pedometer versus pedometer

No data were presented for step count (completer data only) in a 12-week study of a physical activity counselling intervention (phone call) with pedometer compared to pedometer alone (Bender 2016, 99 participants; very low-certainty; Table 1).

The mean difference in step count was −75 steps (95% CI −1002 to 852; Wan 2017, 109 participants; low-certainty evidence; Analysis 3.16) following a 12-week physical activity counselling intervention (web-based) with pedometer compared to pedometer alone.

The mean difference in step count was 1427 steps (95% CI −1482 to 4336) after 12 weeks and −63 steps (95% CI −3080 to 2754) following a six-month physical activity counselling intervention (text message, coached) with pedometer compared to pedometer alone (Nguyen 2009, 17 participants; low-certainty evidence; Analysis 3.16.

The mean difference in active time was 6 minutes (95% CI −2 to 13) after 12 weeks and −0 minutes (95% CI −7 to 7) at end intervention (Nguyen 2009, 17 participants; low-certainty evidence; Analysis 3.17.

The mean difference in inactive time was −4 minutes (95% CI −15 to 8) after 12 weeks and 0 minutes (95% CI −12 to 1) at end intervention (Nguyen 2009, 17 participants; low-certainty evidence; Analysis 3.18).

The mean difference in peak performance was 0 steps/min (95% CI −15 to 15) after 12 weeks and −12 steps/min (95% CI −27 to 3) at end intervention (Nguyen 2009, 17 participants; low-certainty evidence; Analysis 3.19).

An increase in step count was demonstrated after four months (MD 793 steps, 95% CI 236 to 1350; 201 participants) but not at end intervention (MD 107 steps, 95% CI −498 to 712; Moy 2015a, 238 participants; low-certainty evidence; Analysis 3.16) following a 12-month physical activity counselling intervention (web-based) with pedometer compared to pedometer alone.

Pedometer during pulmonary rehabilitation

The mean difference in step count was 419 steps in a seven-day study of pedometer use during pulmonary rehabilitation with awareness of the purpose of the pedometer compared to lack of awareness (Singh 1998, 19 participants; very low-certainty evidence; Table 1).

Physical activity counselling with pulmonary rehabilitation versus pulmonary rehabilitation

An increase in step count was demonstrated (MD 1661 steps, 95% CI 552 to 2770; Mantoani 2018, 44 participants; very low-certainty evidence; Table 1) following a 12-week physical activity counselling intervention (web-based) with pulmonary rehabilitation compared to pulmonary rehabilitation.

The addition of the same 12-week physical activity counselling intervention (in-person) had mixed results in two studies where participants in both groups received pulmonary rehabilitation.

The mean difference in step count was 680 steps (95% CI −1105 to 2465; De Blok 2006, 16 participants; low-certainty evidence; Analysis 3.20) following a 12-week study of physical activity counselling with pulmonary rehabilitation compared to pulmonary rehabilitation alone. In a subsequent study, a greater median change in step count was demonstrated in the physical activity counselling and pulmonary rehabilitation group (547 steps, IQR 187 to 1323) compared to the pulmonary rehabilitation group (−211 steps, IQR −1337 to 1038) at end intervention (P = 0.03). The median change in step count was −569 steps (IQR −2512 to 1551) in the

physical activity counselling and pulmonary rehabilitation group, and −1137 steps (IQR −2376 to 1427) in the pulmonary rehabilitation group (P = 0.58) at 12-month follow-up (Altenburg 2015; *12 weeks*: 37 participants; *12 months*: 23 participants; low-certainty evidence; Table 1).

Longer studies have also had contradictory findings.

An increase in step count was demonstrated (MD 4010 steps, 95% CI 1407 to 6613) at 12 weeks and end intervention (MD 3267 steps, 95% CI 589 to 5944; Cruz 2016, 26 participants; moderate-certainty evidence; Analysis 3.20) following a six-month study of a physical activity counselling intervention (in-person) with 12 weeks of pulmonary rehabilitation compared to 12 weeks of pulmonary rehabilitation. An increase in MVPA time was demonstrated (MD 31 minutes, 95% CI 10 to 52) at 12 weeks and end intervention (MD 24 minutes, 95% CI 2 to 45; Cruz 2016, 26 participants; moderate-certainty evidence; Analysis 3.21). An increase in total physical activity time was demonstrated (MD 68 minutes, 95% CI 18 to 117) at 12 weeks and end intervention (MD 66 minutes, 95% CI 10 to 122; Cruz 2016, 26 participants; moderate-certainty evidence; Analysis 3.22). An improvement in sedentary time was demonstrated at 12 weeks (MD −90 minutes, 95% CI −159 to −20). The mean difference in sedentary time was 12 minutes (95% CI −73 to 97) at end intervention; Cruz 2016, 26 participants; moderate-certainty evidence; Analysis 3.23).

The median difference in accelerometer-assessed step count was 272 steps (IQR −342 to 782) in the physical activity counselling with pulmonary rehabilitation group and 155 steps (IQR −438 to 867) in the pulmonary rehabilitation group (P = 0.99) following a study of a six-month in-person physical activity counselling intervention with eight weeks of pulmonary rehabilitation compared to eight weeks of pulmonary rehabilitation alone. The median difference in pedometer-assessed step count was 727 steps (IQR −1493 to 3119) in the physical activity counselling with pulmonary rehabilitation group and 892 steps (IQR −1187 to 2534) in the pulmonary rehabilitation group (P = 0.55) at end intervention. The median difference in MVPA time was 11 minutes (IQR −1 to 33) in the physical activity counselling with pulmonary rehabilitation group and 11 minutes (IQR −2 to 28) in the pulmonary rehabilitation group (P = 0.62) at end intervention (Nolan 2017, 122 participants; low-certainty evidence; Table 1).

An improvement in change in walking time was demonstrated (MD 39 minutes, 95% CI 1 to 78) following a 12-month study of physical activity counselling with pulmonary rehabilitation compared to pulmonary rehabilitation alone. The mean difference in standing time was 11 minutes (95% CI −18 to 40), lying time was −24 minutes (95% CI −72 to 24), frequency of postural changes was 21 (95% CI −23 to 65) and sitting time was 53 minutes (95% CI −21 to 127) at end intervention (Kawagoshi 2015, 27 participants; low-certainty evidence; Table 1).

An improvement in change in step count was demonstrated (MD 1319 steps, standard error (SE) 571, P = 0.02) at end intervention and nine-month follow-up (MD 1348 steps, SE 628, P = 0.03) following 12 weeks of physical activity counselling with pulmonary rehabilitation compared to pulmonary rehabilitation after all participants undertook 12 weeks of pulmonary rehabilitation. The mean difference in change in MVPA time was 8 minutes (SE 4) (P = 0.11) at end intervention and an improvement in change in MVPA time was demonstrated at nine-month follow-up (MD 13 minutes, (SE 5), P = 0.02; Loeckx 2018, 50 participants; very low-certainty evidence; Table 1).

Physical activity counselling with pulmonary rehabilitation versus sham intervention with pulmonary rehabilitation

The mean difference in step count was 182 steps (95% CI −812 to 1176) after 12 weeks and −532 steps (95% CI −1584 to 520) following a six-month study of a physical activity counselling intervention (in-person) with pulmonary rehabilitation compared to a sham intervention with pulmonary rehabilitation (Burtin 2015; *12 weeks*: 61 participants; *6 months*: 50 participants; very low-certainty evidence; Analysis 3.24). The mean difference in time in MVPA was MD −1 minute (95% CI −13 to 12) after 12 weeks and −7 minutes (95% CI −16 to 3) at end intervention (Burtin 2015; *12 weeks*: 61 participants; *6 months*: 50 participants; very low-certainty evidence; Analysis 3.25). The mean difference in walking time was −3 minutes (95% CI −12 to 7) after 12 weeks and −1 minute (95% CI −18 to 16) at end intervention (Burtin 2015; *12 weeks*: 61 participants; *6 months*: 50 participants; very low-certainty evidence; Analysis 3.26). The mean difference in total physical activity time was −12 minutes (95% CI −39 to 15) after 12 weeks and −34 minutes (95% CI −48 to −20) at end intervention (Burtin 2015; *12 weeks*: 61 participants; *6 months*: 50 participants; very low-certainty evidence; Analysis 3.27).

COMPARISON: Intervention versus intervention

No studies presented data for this comparison.

COMPARISON: Intervention versus no intervention (acute exacerbation of COPD)

Two studies have evaluated physical activity counselling following hospital admission for AECOPD.

Physical activity counselling versus no intervention

The mean difference in step count was −29 steps (95% CI −969 to 911), walking time was 0 minutes (95% CI −12 to 12) and walking intensity was −0.02 m/s^2 (95% CI −0.06 to 0.02; Hornikx 2015, 26 participants; low-certainty evidence; Table 1) after a four-week study comparing physical activity counselling to no intervention following hospital admission for AECOPD.

Feedback and education versus no intervention; education versus no intervention

No data were presented for a 14-day study of feedback and education compared to no intervention (14 participants) or education compared to no intervention (9 participants) following hospital admission for AECOPD (Orme 2018; very low-certainty evidence; Table 1).

COMPARISON: Intervention versus standard common intervention (acute exacerbation of COPD)

Feedback with education versus education

No data were presented in a 14-day study of feedback with education compared to education (Orme 2018; 11 participants; very low-certainty evidence; Table 1).

INTERVENTION: Self-management

See Summary of findings 4.

COMPARISON: Intervention versus no intervention (clinically-stable COPD)

Self-management versus no intervention

An increase in step count was demonstrated (MD 547 steps, 95% CI 12 to 1082) following a six-week SPACE programme compared to no intervention. The mean difference in sedentary time was −23 minutes (95% CI −77 to 31). The median time in bouts of physical activity was 142 minutes (95% CI 91 to 190) in the self-management group and 96 minutes (95% CI 56 to 135) in the no-intervention group at end intervention (P = 0.215). The mean difference in total energy expenditure was 16 kcal (95% CI −100 to 132) at end intervention (Mitchell 2013, 117 participants; very low-certainty evidence; Table 1).

Improvement in 'IMA' (time integral of the modulus of accelerometer output) was demonstrated (MD 176 cpm, 95% CI 53 to 298) after four weeks and at end intervention (MD 176 cpm, 95% CI 51 to 301) following a 12-week self-management intervention compared to no intervention (Tabak 2014b, 20 participants; moderate-certainty evidence; Analysis 1.12).

The mean difference in time in MVPA was 12 minutes (95% CI −21 to 45) at 12 months following a six-month self-management programme compared to no intervention (Jolly 2018, 411 participants; moderate-certainty evidence; Table 1).

COMPARISON: Intervention versus sham intervention (clinically-stable COPD)

Health mentoring versus sham intervention

The mean difference in step count was 61 steps (95% CI −951 to 1073) following a 12-month study of phone call-based health mentoring compared to a sham intervention (Schuz 2015, 120 participants; low-certainty evidence; Analysis 2.1).

COMPARISON: Intervention versus standard common intervention (clinically-stable COPD)

Self-efficacy training with upper-limb exercise versus education with upper-limb exercise

An increase in time in LIPA was demonstrated (MD 43 minutes, 95% CI 15 to 71) at end intervention and the mean difference was 32 minutes (95% CI −18 to 82) at 12-month follow-up after a four-month study of self-efficacy training with upper-limb exercise compared to upper-limb exercise alone (Larson 2014, 35 participants; low-certainty evidence; Analysis 3.28). The mean difference in time spent in moderate-intensity physical activity was 2 minutes (95% CI −1 to 5), sedentary time was 25 minutes (95% CI −49 to 99) and the proportion of time spent sedentary was 0% (95% CI −6 to 6) at end intervention (Larson 2014, 35 participants; low-certainty evidence; Table 1).

COMPARISON: Intervention versus intervention (clinically-stable COPD)

Self-management versus education and symptom monitoring

An increase in physical activity was demonstrated in the self-management group (mean 13 minutes (SE 1)) compared to the education and symptom-monitoring group (mean 11 minutes (SE 1); P = 0.045) following 16 weeks of self-management compared to education and symptom monitoring. An increase in total energy expenditure was also demonstrated in the self-management group (MD 3605 (SE 211)) compared to the education and symptom-monitoring group (MD 3113 (SE 212); P = 0.022) at end intervention. The mean difference in time in moderate-intensity physical activity was 0.5 minutes (95% CI −0.6 to 1.6) at end intervention (Blumenthal 2014, 326 participants; low-certainty evidence; Table 1).

COMPARISON: Intervention versus no intervention (acute exacerbation of COPD)

Self-management versus no intervention

The mean difference in step count was 310 steps (95% CI −1665 to 2285), time in physical activity was 15 minutes (95% CI −30 to 60), time in moderate-intensity physical activity was 13 minutes (95% CI −30 to 56), time in vigorous-intensity physical activity was 2 minutes (95% CI −1 to 5), sedentary time was 4 minutes (95% CI −75 to 83), active energy expenditure was 85 kcal (95% CI −108 to 278), and total energy expenditure was −30 kcal (95% CI −225 to 165) following a seven-day post-admission self-management programme of activity, coping and education (SPACE) compared to no intervention (Kanabar 2015, 25 participants; very low-certainty evidence; Table 1).

COMPARISON: Intervention versus standard common intervention (acute exacerbation of COPD)

Health coaching with pulmonary rehabilitation referral versus pulmonary-rehabilitation referral

No data were presented in a 12-month post-admission study of the addition of health coaching to pulmonary-rehabilitation referral compared to pulmonary-rehabilitation referral alone (Benzo 2016, 214 participants; very low-certainty evidence; Table 1).

INTERVENTION: Pharmacological treatments

See Summary of findings 5.

COMPARISON: Intervention versus no intervention

No studies presented data for this comparison.

COMPARISON: Intervention versus sham intervention (clinically-stable COPD)

LAMA versus placebo

Two three-week studies examined the impact of a long-acting muscarinic antagonist (LAMA) compared to placebo. Individual-level pre-cross-over data were obtained directly from the authors and used for combined analysis. The median change in step count was 104 steps (IQR −603 to 1228) in the LAMA group and 113 steps (IQR −936 to 1216) in the placebo group (P = 0.64) at end intervention. The median change in time in MVPA was −1 minute (IQR −17 to 24) in the LAMA group and −6 minutes (IQR −18 to 15) in the placebo group (P = 0.07) at end intervention. The median change in active energy expenditure was 15 kcal (IQR −103 to 117) in the LAMA group and −24 kcal (IQR −104 to 43) in the placebo group (P = 0.08) at end intervention. The median change in PAL was 0.00 (IQR −0.07 to 0.09) in the LAMA group and −0.01 (IQR −0.06 to 0.09) in the placebo group (P = 0.80) at end intervention (Beeh 2014; Magnussen 2017; 133 participants; moderate-certainty evidence; Table 1).

No data were presented in another 12-week study comparing LAMA with placebo (NCT00144326, 250 participants; very low-certainty evidence; Table 1).

LAMA/LABA versus placebo

Two short-term studies have assessed the effect of LAMA/long-acting beta$_2$ agonist (LABA); three weeks of indacaterol/glycopyrronium 110/50 µg once daily, Watz 2016; four weeks of aclidinium bromide/formoterol fumarate 400/12 µg twice daily, Watz 2017) compared to placebo. Meta-analyses demonstrated improvements in step count (MD 531 steps, 95% CI 167 to 895; 2 studies, 426 participants; high-certainty evidence; Analysis 2.2; Figure 13), time in MVPA (MD 10 minutes, 95% 4 to 15; 2 studies, 423 participants; high-certainty evidence; Analysis 2.3; Figure 14) and active energy expenditure (MD 44 kcal, 95% CI 18 to 70; 2 studies, 423 participants; high-certainty evidence; Analysis 2.4; Figure 15). Some heterogeneity was evident for step count (I^2 = 27%), but not for other outcomes. Additionally, a reduced odds ratio (OR) was demonstrated for being classified as 'inactive' post-intervention (OR 0.27, 95% CI 0.1 to 0.5; Watz 2017, 250 participants; high-certainty evidence; Table 1).

Figure 13. Forest plot of comparison 2: Intervention vs. placebo Outcome 2.2: Physical activity: change in step count (steps per day)

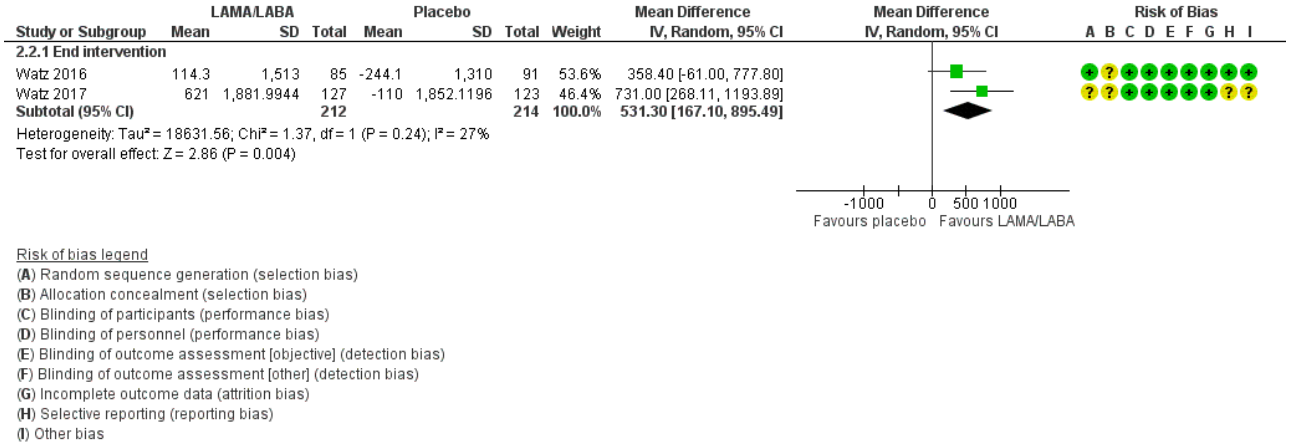


Figure 14. Forest plot of comparison 2: Intervention vs. placebo Outcome 2.3: Physical activity: change in time in moderate-to-vigorous intensity physical activity (minutes per day)

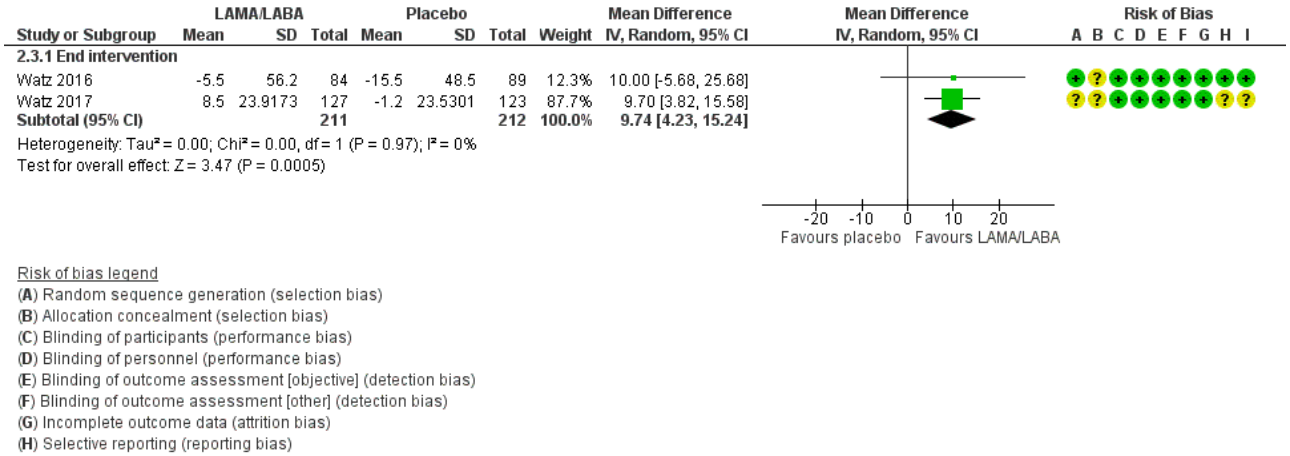
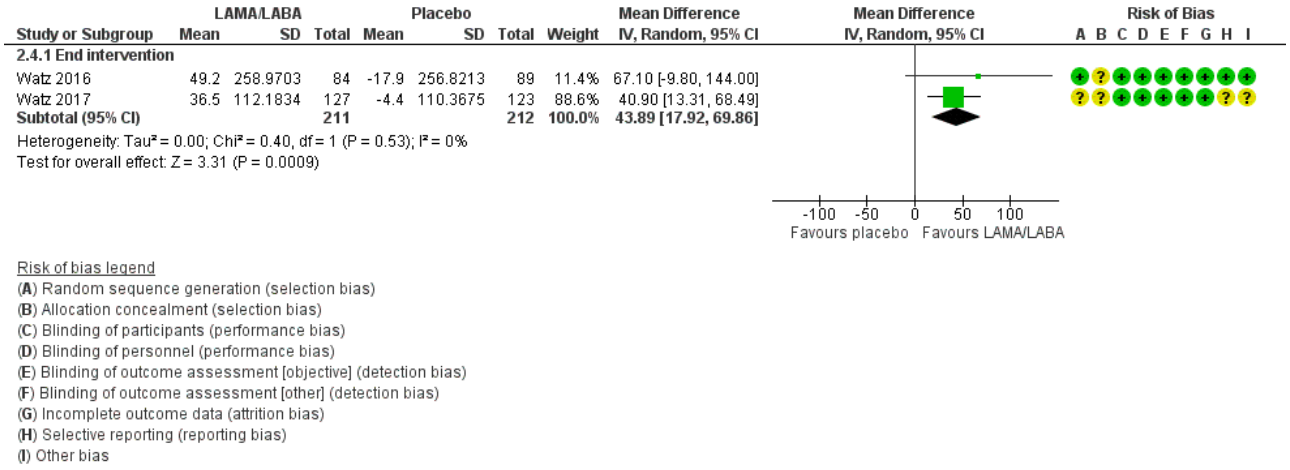


Figure 15. Forest plot of comparison 2: Intervention vs. placebo Outcome 2.4: Physical activity: change in active energy expenditure (kcal)



COMPARISON: Intervention versus standard common intervention (clinically-stable COPD)

LAMA with behaviour modification versus placebo with behaviour modification

The mean difference in time in MVPA was 8 minutes (95% CI −184 to 202), time in LIPA was 10 minutes (95% CI −6 to 26), odds ratio for being classified as 'inactive' post-intervention 0.86 (95% CI 0.57 to 1.30; P = 0.477) following a six-month study of LAMA compared to placebo (Troosters 2014, 426 participants; moderate-certainty evidence; Table 1).

The mean difference in step count was −245 steps (95% CI −1146 to 655) after eight weeks. A deterioration in step count was demonstrated in the intervention group (MD −945 steps, 95% CI −1836 to −54) at end intervention following a 12-week study for LAMA compared to placebo (Troosters 2018; *8 weeks*: 120 participants; *12 weeks:* 111 participants; moderate-certainty evidence; Analysis 3.29). The mean difference in walking time was −3 minutes (95% CI −12 to 7) after eight weeks and −9 minutes (95% CI −20 to 2) at end intervention (Troosters 2018; *8 weeks*: 120 participants; *12 weeks:* 112 participants; moderate-certainty evidence; Analysis 3.30). The mean difference in walking intensity was 0.02 m/s^2 (95% CI −0.06 to 0.10) after eight weeks and −0.06 m/s^2 (95% CI −0.14 to 0.02) at end intervention (Troosters 2018; *8 weeks*: 120 participants; *12 weeks:* 110 participants; moderate-certainty evidence; Analysis 3.31).

LAMA/LABA with behaviour modification versus placebo with behaviour modification

The mean difference in step count was 226 steps (95% CI −668 to 1119) after eight weeks and 296 steps (95% CI −585 to 1177) at end intervention following a 12-week study of LAMA/LABA compared to placebo (Troosters 2018; *8 weeks*: 122 participants; *12 weeks*: 115 participants; moderate-certainty evidence; Analysis 3.32. The mean difference in walking time was 1 minute (95% CI −8 to 11) after eight weeks and 3 minutes (95% CI −7 to 12) at end intervention (Troosters 2018; *8 weeks*: 122 participants; *12 weeks*: 115 participants; moderate-certainty evidence; Analysis 3.33). The mean difference in walking intensity was 0.06 m/s^2 (95% CI −0.02 to 0.14) after eight weeks and 0.02 m/s^2 (95% CI −0.06 to 0.10) at end intervention (Troosters 2018: *8 weeks*: 120 participants; *12 weeks*: 112 participants; moderate-certainty evidence; Analysis 3.34).

LABA with LAMA and behaviour modification versus LAMA and behaviour modification

The mean difference in step count was 471 steps (95% CI −422 to 1364) after eight weeks and 1241 steps (95% CI 370 to 2112) at end intervention following a 12-week study of LABA with LAMA and behaviour modification compared to LAMA and behaviour modification (Troosters 2018; *8 weeks*: 122 participants; *12 weeks*: 116 participants; moderate-certainty evidence; Analysis 3.35). The mean difference in walking time was 4 minutes (5%CI −6 to 13) after eight weeks and 11 minutes (95% CI 2 to 21) at end intervention (Troosters 2018; *8 weeks*: 122 participants; *12 weeks*: 117 participants; moderate-certainty evidence; Analysis 3.36). The mean difference in walking intensity was 0.04 m/s^2 (95% CI −0.04 to 0.12) after eight weeks and 0.08 m/s^2 (95% CI −0.00 to 0.16) at end intervention (Troosters 2018; *8 weeks*: 122 participants; *12 weeks*: 114 participants; moderate-certainty evidence; Analysis 3.37).

Angiotensin-converting enzyme (ACE) inhibitor with pulmonary rehabilitation versus placebo with pulmonary rehabilitation

The mean difference in change in step count was −943 steps (95% CI −2372 to 486) following a 10-week study of an ACE inhibitor and pulmonary rehabilitation compared to a placebo and pulmonary rehabilitation. A deterioration in PAL was demonstrated in the ACE inhibitor group (MD −0.10, 95% CI −0.20 to −0.00; Curtis 2016, 40 participants; moderate-certainty evidence; Table 1).

COMPARISON: Intervention versus intervention (clinically-stable COPD)

Inhaled corticosteroid and LABA versus inhaled corticosteroid and LABA

The mean difference in step count was 316 steps (95% CI −838 to 1470) following a 12-week study of inhaled corticosteroid (beclomethasone) and LABA compared to inhaled corticosteroid (budesonide) and LABA (NCT01351792, 59 participants; very low-certainty evidence; Table 1).

LAMA versus LAMA

No data were presented in an eight-week study of LAMA (aclidinium bromide) compared to LAMA (tiotropium; Nakamura 2016, 44 participants; very low-certainty evidence; Table 1).

INTERVENTION: Nutritional supplementation

COMPARISON: Intervention versus no intervention (clinically-stable COPD)

Nutritional supplement versus no intervention

The mean difference in PAL was 0.02 (95% CI −0.04 to 0.08) after four weeks and 0.06 (95% CI −0.12 to 0.24) after 12 weeks following pulmonary rehabilitation or hospital admission for nutritional supplementation compared to no intervention (Goris 2003: *4 weeks*: 20 participants; *12 weeks*: 19 participants; moderate-certainty evidence; Analysis 1.13). The mean difference in total energy expenditure was −0.6 MJ (95% CI −3.59 to 2.29) after four weeks and 0.5 MJ (95% CI −1.39 to 2.39) after 12 weeks (Goris 2003; *4 weeks*: 20 participants; *12 weeks*: 19 participants; moderate-certainty evidence; Analysis 1.14).

COMPARISON: Intervention versus sham intervention (clinically-stable COPD)

Nutritional supplement versus placebo

The mean difference in step count was 228 steps (95% CI −69 to 525) after four weeks of a 12-week study of essential amino acid supplementation compared to placebo. An increase in step count (MD 577 steps, 95% CI 341 to 813) was demonstrated at end intervention (Dal Negro 2012, 88 participants; low-certainty evidence; Analysis 2.5). An increase in energy expenditure for ambulation was demonstrated after four weeks (MD 0.6 kcal/step/FFM kg, 95% CI 0.3 to 1.0) and at end intervention (MD 2.3 kcal/step/FFM kg; 95% CI 1.8 to 2.8; Dal Negro 2012, 88 participants; low-certainty evidence; Analysis 2.6).

COMPARISON: Intervention versus standard common intervention (clinically-stable COPD)

Nutritional supplement and pulmonary rehabilitation versus placebo and pulmonary rehabilitation

The mean difference in change in step count was 719 steps (95% CI −635 to 2073) after four months of a 15-month study of nutritional supplementation and pulmonary rehabilitation compared to a placebo and pulmonary rehabilitation in people with low muscle mass. An increase in step count was demonstrated (MD 1030 steps, 95% CI 101 to 1959) after eight months. The mean difference in step count was 796 steps (95% CI −201 to 1793; Van de Bool 2017, 61 participants; moderate-certainty evidence; Analysis 3.38) at 15-month follow-up.

COMPARISON: Intervention versus intervention

No studies presented data for this comparison.

COMPARISON: Intervention versus standard common intervention (acute exacerbation of COPD)

Enriched nutritional supplement and inpatient pulmonary rehabilitation versus nutritional supplement and inpatient pulmonary rehabilitation

The mean difference in step count was 200 steps (95% CI −913 to 1313) following eicosapentaenoic acid-enriched nutritional supplement and inpatient pulmonary rehabilitation compared to an unenriched nutritional supplement and inpatient pulmonary rehabilitation during hospital admission for an acute exacerbation of COPD. The mean difference in energy expenditure was 80 kcal (95% CI −72 to 232; Ogasawara 2018, 45 participants; low-certainty evidence; Table 1).

INTERVENTION: Supplemental oxygen

COMPARISON: Intervention versus no intervention

No studies presented data for this comparison.

COMPARISON: Intervention versus sham intervention (clinically-stable COPD)

Supplemental oxygen versus placebo

The mean difference in "domestic activity counts" was 15 (95% CI −21 to 51) following an eight-week study of supplemental oxygen following pulmonary rehabilitation compared to placebo (Sandland 2008, 20 participants; moderate-certainty evidence; Table 1).

COMPARISON: Intervention versus standard common intervention (clinically-stable COPD)

Supplemental oxygen and pulmonary rehabilitation versus sham and pulmonary rehabilitation

The mean difference in change in step count was 340 steps (95% CI −145 to 825) following eight weeks of supplemental oxygen and pulmonary rehabilitation compared to sham and pulmonary rehabilitation in people with desaturation on the six-minute walk test (6MWT). The mean difference in change in step count was −316 steps (95% CI −865 to 233; Analysis 3.39) at six-month follow-up. The mean change in time in moderate-intensity physical activity was 3 minutes (95% CI −5 to 11) at end intervention and −2 minutes (95% CI −11 to 7; Analysis 3.40) at follow-up. The mean change in time in vigorous-intensity physical activity was −1 minute (95% CI −3 to 1) at end intervention and −1 minute (95% CI −3 to 1; Analysis 3.41) at follow-up. The mean change in LIPA time was −6 minutes (95% CI −35 to 23) at end intervention and −9 minutes (95% CI −41 to 23; Analysis 3.42) at follow-up. The mean change in total energy expenditure was −59 kcal (95% CI −166 to 48) at end intervention and −4 kcal (95% CI −127 to 199; Analysis 3.43) at follow-up. The mean change in sedentary time was 17 minutes (95% CI −28 to 62) at end intervention and 29 minutes (95% CI −25 to 75; Analysis 3.44) at follow-up (Alison 2019: *8 weeks*: 87 participants; *6 months*: 65 participants; moderate-certainty evidence).

COMPARISON: Intervention versus intervention (clinically-stable COPD)

Lightweight versus standard oxygen-cylinder use

The mean difference in "mid-day activity" was 34 VMU/min (95% CI −23 to 91) following a six-month study of lightweight ambulatory supplemental oxygen compared to supplemental oxygen with E-cylinder (Casaburi 2012, 17 participants; low-certainty evidence; Analysis 4.17).

INTERVENTION: Other interventions

COMPARISON: Intervention versus no intervention (clinically-stable COPD)

Four-wheeled walker versus no intervention

An increase in step count (MD 4081 steps, 95% CI 818 to 7344) was demonstrated over four weeks following pulmonary rehabilitation using a four-wheeled walker compared to no intervention (Ng 2015, 17 participants; very low-certainty evidence; Table 1).

Endobronchial valve surgery versus no intervention

An increase in step count (MD 1400 steps, 95% CI 655 to 2145), proportion of time walking MD 1% (95% CI 0 to 2) and movement intensity (MD 0.01 m/s^2, 95% CI 0.00 to 0.02) were demonstrated six months after endobronchial valve surgery compared to no intervention. The mean difference in the proportion of time sitting was −2% (95% CI −5 to 1) and time inactive was −1 minute (95% CI −3 to 1) after six months (Hartman 2016, 43 participants; moderate-certainty evidence; Table 1).

COMPARISON: Intervention versus sham intervention (clinically-stable COPD)

Singing versus sham intervention

A deterioration in step count (MD −1774 steps, 95% CI −2848 to −700) and activity-related energy expenditure (MD −373 kJ, 95% CI −625 to −121) were demonstrated in the intervention group following an eight-week singing intervention compared to a sham intervention. The mean difference in time in physical activity was −142 minutes (95% CI −263 to −22) and sedentary time was −9 minutes (95% CI −88 to 71) at end intervention (Lord 2012, 24 participants; low-certainty evidence; Table 1).

Neuromuscular electrical stimulation versus placebo

The mean difference in step count was 36 steps (95% CI −446 to 518) at end intervention and −160 steps (95% CI −692 to 372) at 12-week follow-up after a six-week neuromuscular electrical stimulation (NMES) programme compared to placebo (Maddocks 2016, 52 participants; low-certainty evidence; Analysis 2.7). The mean difference in change in number of up/down transitions was −5 (95% CI −12 to 3) at end intervention and −3 (95% CI −12 to 6) at 12-week follow-up (Maddocks 2016, 52 participants; low-certainty evidence; Analysis 2.8). The mean difference in upright time was 0.5 hours (95% CI −0.4 to 1.3) at end intervention and −0.4 (95% CI −1.2 to 0.4) at 12-week follow-up (Maddocks 2016, 52 participants; low-certainty evidence; Analysis 2.9).

COMPARISON: Intervention versus standard common intervention (clinically-stable COPD)

Non-invasive ventilation with pulmonary rehabilitation versus pulmonary rehabilitation

An increase in step count was demonstrated (MD 1269 steps, 95% CI 242 to 2296; Duiverman 2008, 56 participants; moderate-certainty evidence; Table 1) following a 12-week study of non-invasive ventilation with pulmonary rehabilitation compared to pulmonary rehabilitation in people with hypercapnia.

Inspiratory muscle training and pulmonary rehabilitation versus sham and pulmonary rehabilitation

The mean difference in step count was −206 steps (95% CI −923 to 512; Charususin 2018, 150 participants; moderate-certainty evidence; Table 1) following a 12-week study of the addition of inspiratory muscle training to pulmonary rehabilitation compared to a sham intervention with pulmonary rehabilitation in people with inspiratory muscle weakness.

COMPARISON: Intervention versus intervention

No studies presented data for this comparison

Subgroup analysis and investigation of heterogeneity

Insufficient data were available to perform subgroup analyses according to disease severity or duration of intervention.

Subgroup analyses were possible for supervised versus unsupervised pulmonary rehabilitation programmes in clinically-stable COPD for the following physical activity outcomes: step count; total energy expenditure; LIPA time; and total sedentary time.

Pulmonary rehabilitation: supervised versus unsupervised

The mean difference in step count in the supervised subgroup was 69 steps (95% CI −386 to 524; 2 studies, 144 participants) and unsupervised subgroup was 494 steps (95% CI −158 to 1146; Tsai 2016, 36 participants; low-certainty evidence; test for subgroup differences: P = 0.29; Analysis 1.15).

There was a significant difference (P = 0.02) between the supervised (MD 10 minutes, 95% CI −9 to 29; 2 studies, 146 participants) and unsupervised subgroups (MD −44 minutes, 95% CI −87 to −1; Tsai 2016, 36 participants; Analysis 1.16), but there was substantial heterogeneity within the supervised subgroup (I^2 = 64%) and between subgroups (I^2 = 80%).

The mean difference in total energy expenditure in the supervised subgroup was −47 kcal (95% CI −99 to 5; Wootton 2017, 108 participants) and in the unsupervised subgroup was −5 kcal (95% CI −139 to 129; Tsai 2016, 36 participants; low-certainty evidence; test for subgroup differences: P = 0.57; Analysis 1.17).

The mean difference in total sedentary time in the supervised subgroup was 3 minutes (95% CI −49 to 55; Wootton 2017, 101 participants) and in the unsupervised subgroup was 50 minutes (95% CI −31 to 131; Tsai 2016, 36 participants; low-certainty evidence; test for subgroup differences: P = 0.34; Analysis 1.18).

Sensitivity analysis

We considered physical activity as the appropriate outcome for sensitivity analyses, as it was the prespecified primary outcome for the review. Insufficient data were available to perform sensitivity analyses to examine the effects of the measurement device on the pooled estimate by removing studies that used pedometers. Sensitivity analyses for missing data were not required.

We planned to examine the effects of methodological quality on the pooled estimate by removing studies that were at high or unclear risk of bias for the domains of blinding and incomplete outcome data.

Sensitivity analyses could be considered for three comparisons in clinically-stable COPD: pulmonary rehabilitation versus no intervention; high-intensity interval training versus no intervention; and LAMA/LABA versus placebo.

Pulmonary rehabilitation versus placebo

For change in step count, sensitivity analyses for blinding were not possible as all three included studies were at high/unclear risk of bias for the domain of blinding of participants and at low risk of bias for the domain of blinding of personnel (Egan 2010; Tsai 2016; Wootton 2017). Following the removal of the two studies at unclear risk of bias for the domain of incomplete outcome data (Egan 2010; Wootton 2017), the mean difference was 494 steps (95% CI −158 to 1146; Tsai 2016; 36 participants; low-certainty evidence; Analysis 1.1).

For total physical activity time, sensitivity analyses for were not possible as both included studies were at high/unclear risk of bias for the domains of blinding of participants and personnel (Egan 2010; De Roos 2017). Following removal of the one study at unclear risk of bias for the domain of incomplete outcome data (Egan 2010), an improvement in total physical activity time was also demonstrated (MD 25 min, 95% CI 8 to 43; De Roos 2017, 45 participants; moderate-certainty evidence; Analysis 1.5).

Sensitivity analyses were not possible for blinding of participants and personnel for time in MVPA (Analysis 1.2), time in LIPA (Analysis 1.3), total energy expenditure (Analysis 1.4) or total sedentary time (Analysis 1.6), as all included studies were at high/unclear risk of bias for these domains (De Roos 2017; Tsai 2016; Wootton 2017). Following the removal of the one study at unclear risk of bias for the domain of incomplete outcome data (Wootton 2017), the mean difference in time in MVPA was 5 minutes (95% CI −1 to 11; 2 studies; 81 participants; low-certainty evidence; Analysis 1.2), the mean difference in time in LIPA was −9 minutes (95% CI −70 to 52; 2 studies; 81 participants; low-certainty evidence; Analysis 1.3), the mean difference in total energy expenditure was −5 kcal (95% CI – 139 to 129; Tsai 2016; 36 participants; low-certainty evidence; Analysis 1.4) and the mean difference in total sedentary time was – 50 minutes (95% CI –31 to 131; Tsai 2016; 36 participants; low-certainty evidence; Analysis 1.6).

High-intensity interval training versus placebo

Sensitivity analyses were not possible for blinding of participants and personnel or incomplete outcome data for time in “lifestyle” physical activity (Analysis 1.7), time in LIPA (Analysis 1.8), time in MVPA (Analysis 1.9) or sedentary time (Analysis 1.10), as both included studies were at high/unclear risk of bias for these domains (Louvaris 2016; Vasilopoulou 2017).

LAMA/LABA versus placebo

Sensitivity analyses were not possible for blinding of participants and personnel or incomplete outcome data for change in step count (Analysis 2.2), time in MVPA (Analysis 2.3) or active energy expenditure (Analysis 2.4), as both included studies were at low risk of bias for these domains (Watz 2016; Watz 2017).

DISCUSSION

This review has synthesised the available evidence for interventions that have measured physical activity and sedentary behaviour in people with COPD. The complexity of a behaviour like physical activity (Casperson 1985) was reflected in the wide range of interventions that have been used to date (Table 2).

Summary of main results

Pulmonary rehabilitation/exercise training

Despite documented deterioration in physical activity associated with acute exacerbations of COPD (Pitta 2006a), there has been limited work targeting participation for people with COPD at this vulnerable time. To date, no improvements in physical activity have been demonstrated following inpatient exercise training (Borges 2014; Tahirah 2015), enriched nutritional supplementation during inpatient pulmonary rehabilitation (Ogasawara 2018), short-term self-management post-discharge (Kanabar 2015; Orme 2018) or long-term health coaching (Benzo 2016). This remains a key area of interest for future work.

Pulmonary rehabilitation represents the most widely-studied intervention to improve physical activity to date. Findings in this review were consistent with clinically-important and consistent improvements in health-related quality of life and exercise capacity previously demonstrated across multiple trials (McCarthy 2015). However, translation of these benefits into improvement in physical activity was not clearly demonstrated. The appeal of using an existing intervention framework in an attempt to improve physical activity is clear. However, the addition of specific strategies underpinned by theoretical constructs to support behaviour change for physical activity is likely to be required. Meta-analyses revealed only an increase in total physical activity time following pulmonary rehabilitation, which was not undesirable, but not consistent with the increased intensity required to meet physical activity recommendations for improving health (WHO 2010).

Specific treatments for components of COPD have been added to pulmonary rehabilitation in attempts to improve physical activity with varying success. No clear benefits for physical activity were evident with the addition of inspiratory muscle training in people with inspiratory muscle weakness (Charususin 2018), and results numerically favoured the placebo group in a study looking at the addition of an ACE-inhibitor (Curtis 2016), although the confidence interval was wide. No clear benefit of supplemental oxygen was demonstrated in participants who desaturated during 6MWT (Alison 2019). However, increased step count was demonstrated following the addition of non-invasive ventilation in people with hypercapnia (Duiverman 2008) and nutritional supplementation in people with low muscle mass (Van de Bool 2017).

Alternatives to pulmonary rehabilitation/exercise training programmes have been investigated in a range of single studies, including home-based pulmonary rehabilitation (Holland 2017), water-based exercise training (Felcar 2018), low-intensity exercise training (Probst 2011), an exercise-training programme with tapering supervision (Rinaldo 2017), outdoor walking (Gamper 2019), and an adherence intervention (Steele 2019), without improvements demonstrated. Improvement in physical activity has been demonstrated in a study of Tai Chi compared to pulmonary rehabilitation and was accompanied by improvements in health-related quality of life and exercise capacity (Polkey 2018). Two studies assessed the impact of adding alternative models of exercise interventions to other components of pulmonary rehabilitation programmes (Nordic walking, COPE-active) and also demonstrated improved physical activity alongside improved

clinical outcomes (Breyer 2010; Effing 2011). At this stage, it appears that there are other exercise-based interventions that may be equally (if not more) effective in improving physical activity compared to conventional pulmonary rehabilitation/ exercise training programmes.

Use of a high-intensity interval training protocol delivered improvements in physical activity in association with health-related quality of life and exercise capacity at programme completion in two studies from the same group (Louvaris 2016; Vasilopoulou 2017). Mechanisms for these observed changes are yet to be clarified, longer-term outcomes have not been demonstrated and results need to be replicated in other studies prior to recommendations for clinical practice.

The only study that has looked at two models of maintenance exercise programmes following high-intensity interval training demonstrated that both telerehabilitation and centre-based programmes were superior to usual care across a range of physical activity variables; these findings were mirrored by improvements in health-related quality of life and exercise capacity. Comparing telerehabilitation and centre-based maintenance to each other, there were no differences in health-related quality of life, exercise capacity, time spent in light-intensity physical activity or sedentary time, but lifestyle and moderate-intensity physical activity were better in the centre-based group (Vasilopoulou 2017). These results indicate a direction for the development of effective and sustainable interventions.

Physical activity counselling

Improvements in physical activity following physical activity counselling were inconsistently demonstrated, with a wide range of programme durations, participant interfaces and intervention components used (Arbillaga-Etxarri 2018; Demeyer 2017; Hornikx 2015; Tabak 2014a; Vorrink 2016; Wootton 2017). The identification of effective components of interventions was complex. In some cases, clues to successful implementation were evident where the same intervention applied in different populations demonstrated (short-term) improvements in step count that were mirrored by improvements in other outcomes in people with more severe disease (Altenburg 2015; Hospes 2009). Several features were shared with other successful interventions (Demeyer 2017; Vorrink 2016), where participants received direct feedback from a step counter, tracking of participation in activity as well as individual goal-setting that was regularly revised. This was supported by some evidence specifically for the addition of a pedometer to physical activity counselling to increase step count (Mendoza 2015); however, evidence for the addition of physical activity counselling to use of a pedometer was less clear (Bender 2016; Moy 2015a; Nguyen 2009; Wan 2017). The components associated with success to date were not clearly linked to models of delivery or uniformly accompanied by improvements in health-related quality of life or exercise capacity or both, but offer may merit further exploration.

Physical activity counselling and pulmonary rehabilitation/ exercise training

Direct comparison of physical activity counselling with pulmonary rehabilitation was only undertaken in two studies. Whilst one compared interventions of equal duration (six weeks; Widyastuti 2018), the other compared a longer counselling programme (12 weeks) to pulmonary rehabilitation (six weeks; O'Neill 2018). The addition of physical activity counselling to pulmonary rehabilitation has been the subject of numerous studies. However, meta-analyses were not possible due to diversity in trial designs. Whilst negative studies showed a lack of improvement in physical activity and clinical outcomes (Burtin 2015; De Blok 2006; Nolan 2017), positive results for physical activity were variably accompanied by improvements in health-related quality of life and exercise capacity (Loeckx 2018; Mantoani 2018) or unaccompanied by these (Altenburg 2015; Cruz 2016; Kawagoshi 2015), maintained at follow-up (Cruz 2016; Loeckx 2018) or not maintained (Altenburg 2015). One study has demonstrated that the combined addition of physical activity counselling and exercise training to use of a pedometer resulted in improvements in step count, health-related quality of life and exercise capacity that were maintained at 12-month follow-up (Varas 2018), which provided a constructive indicator for programme development, suggesting that multifaceted interventions may be required for long-term success.

Self-management

Several shorter-term self-management interventions demonstrated some improvements in physical activity at end intervention compared to no intervention (Mitchell 2013; Tabak 2014b), as did education-based alternatives (Blumenthal 2014; Larson 2014). These improvements were not seen in longer studies (Jolly 2018; Schuz 2015), which may reflect the challenge of longer-term maintenance of this type of behaviour change.

Pharmacological treatments

There was mostly a lack of evidence for improvements in physical activity following LAMA treatment (Beeh 2014; Magnussen 2017). However, there was some evidence for a short-term increase in step count and active energy expenditure following LAMA/LABA combination treatment (Watz 2016; Watz 2017). In the multiple comparisons of one study in which all groups received behaviour modification, no comprehensive improvements in physical activity were demonstrated with the addition of LAMA, LAMA/LABA or exercise training in any combination over 12 weeks (Troosters 2018). These results suggest that meaningful change in and long-term adoption of regular participation in physical activity will require specific strategies targeting the behaviour of interest.

Endobronchial valve surgery

In one study assessing people six months after endobronchial valve surgery, expected improvement in exercise capacity was accompanied by improvement in a range of physical activity measures, but not measures of inactivity (Hartman 2016), which adds further evidence to the concept that improving physical capacity does not naturally result in comprehensive behaviour change.

Overall completeness and applicability of evidence

Study design

Of the 76 studies included, only 38 had physical activity as a primary outcome. In the context of the myriad of disparate interventions included in this review preventing meta-analyses for most comparisons, findings were largely presented from individual studies. As a result, whether studies were sufficiently powered presents an important consideration.

Additionally, protocols for activity monitor-wearing time resulted in fewer participants completing physical activity outcome assessments than health-related quality of life or exercise-capacity measures. Only 17 studies assessed physical activity after a post-intervention follow-up period, of which four studies demonstrated maintained improvements, so there was very limited information about the continued effect over time following interventions.

Methodology

A lack of comprehensive descriptions of interventions, particularly for physical activity counselling and exercise-training interventions, and a paucity of data for adherence also made it difficult to know whether interventions were delivered as intended and therefore limited the identification of effective treatment components. The evolution of behaviour change theory and identification of critical components deployed in the development of interventions post-dates some of this work (Michie 2013); future studies should provide sufficient detail to enable replication and implementation.

Devices

Rapid technological developments have led to a broad and ever-growing range of tools being used within this field of practice. The most commonly-used device to date (SenseWear Armband, 19 studies) is now obsolete, and the inaccuracy of step-count data from this device has been documented (Lee 2015). Financial considerations will inevitably factor into decisions about device selection, both in research settings and in clinical practice. However, the accuracy of data generated by different devices in people with COPD warrants consideration. Although we could not conduct sensitivity analyses as planned according to pedometer use, it is worth noting that a quarter of the studies in this review (15 studies) assessed step count using pedometers, despite evidence for poor accuracy at slower gait speeds (Furlanetto 2010). The impact of device selection on step count was highlighted in the results of Nolan 2017, who demonstrated different results for pedometer-assessed step count compared to another device.

Outcomes

Step count was the most commonly-assessed outcome (54 studies), followed by MVPA time (23 studies), sedentary time (12 studies) and LIPA time (10 studies). One challenge with synthesis of these variables was the variety and, in many cases, lack of specification of threshold values used to define intensity of activity. A range of wearing protocols were used and details about data handling were not routinely specified. In some cases, it appeared that post-intervention physical activity was assessed prior to completion (i.e. whilst participants were still undertaking the intervention).

Due to the small number of interventions that improved physical activity, it was not possible to evaluate whether improvements in physical activity were consistently accompanied by improvements in our secondary outcomes of health-related quality of life or exercise capacity.

Other factors

To date, there has not been widespread regard for personal factors beyond disease, physical or physiological features. Given the complexity of physical activity behaviour, factors such as motivation, readiness to change and self-efficacy are also likely to contribute to capacity to change physical activity, and therefore should be integrated into future design of interventions (Trost 2002).

Certainty of the evidence

In assessments of the quality of the evidence, most results were of low certainty, which was largely attributable to performance bias and imprecision. As expected, inclusion of studies that assessed physical activity objectively largely resulted in low risk of detection bias for physical activity outcomes. However, it is interesting to note that there were still instances where use of a device was subject to bias where participants were required to self-report daily measures. The nature of many interventions, including exercise training and physical activity counselling, will inevitably limit the capacity to blind participants to group allocation. This places more importance on the role of blinding outcome assessors for other outcomes such as exercise capacity. It is therefore concerning that we rated only 33 studies at low risk of bias for this domain. Another common observation was the frequency with which physical activity outcomes were not identified or were reported in a different manner to prespecified protocols.

Potential biases in the review process

Data extraction and 'Risk of bias' assessments were undertaken independently by two review authors, with clarification sought from other co-authors as required. The inclusion of data published only in conference abstracts ensured that we included all available data in the review. We sought additional information from 29 study authors to maximise accuracy of 'Risk of bias' assessment and data for inclusion, 21 of whom provided information (Characteristics of included studies).

Characteristics of the available data limited the application of prespecified analyses in this review, but it is likely that future versions will encompass these.

Use of cross-over study designs provides a challenge to inclusion where behavioural components to interventions are delivered. Despite the best efforts of co-operating authors, there were studies from which we could not obtain data that may have influenced estimates.

Cochrane Reviews often define study inclusion and exclusion criteria based on interventions; however, this review defined study criteria based on an outcome (objectively-assessed physical activity). In this relatively new field of measurement of this complex behaviour, it is as yet unclear which interventions clearly demonstrate benefit, and therefore inclusion of any approach was intended to inform a comprehensive review of available data.

Agreements and disagreements with other studies or reviews

Previously, the two most comprehensive reviews of interventions to promote physical activity in people with COPD were conducted by Mantoani 2016 (to March 2015; 60 studies), and Lahham 2016 (to May 2016; 37 studies). Consistent with this review, both reviews noted poor quality of available evidence. Study inclusion criteria for our review restricted studies to those assessing physical activity objectively and to RCTs, where both previous reviews had included subjective assessment and Mantoani 2016 included non-randomised, cohort and experimental designs. Previous observations about duration of pulmonary rehabilitation/

exercise training relating to increased physical activity could not be substantiated in this review, however preliminary evidence for combined interventions (e.g. physical activity counselling and pulmonary rehabilitation/exercise training) was confirmed by these results. However, preservation of the original units of outcomes for analysis (e.g. number of steps, time in physical activity rather than effect sizes), rigour of inclusion criteria, a rapidly-evolving area of clinical interest and concomitant increase in the number of papers have resulted in a unique body of evidence for the current review.

AUTHORS' CONCLUSIONS

Implications for practice

Awareness is rapidly progressing of the importance of increasing physical activity and decreasing sedentary behaviour for health outcomes. This is reflected in our understanding of the magnitude of the challenge for people with COPD to achieve the necessary behaviour changes. A diverse range of interventions have been assessed, mostly in single studies, but improvements have not been systematically demonstrated following any particular interventions. There was limited evidence for improvement in physical activity with strategies including exercise training, physical activity counselling, self-management, pharmacological interventions and endobronchial valve surgery, and in specific subgroups following nutritional supplementation and non-invasive ventilation. Where improvements were demonstrated in activity of at least moderate intensity, as recommended by guidelines (U.S. Department of Health and Human Services 2018), they were of relatively small magnitude. Compared to no intervention, high-intensity interval training did demonstrate an improvement of six minutes per day (Summary of findings for the main comparison) and physical activity counselling did demonstrate an improvement of 11 minutes per day (Summary of findings 3) after eight- to 12-week studies. Similarly, three to four weeks of LAMA/LABA resulted in an improvement of 10 minutes per day (Summary of findings 5). The greatest improvement was 24 minutes per day after a six-month study of physical activity counselling in addition to pulmonary rehabilitation in one study of 26 participants; this finding is at odds with similar studies (Summary of findings 3). These improvements were mirrored in the assessment of other physical activity outcomes.

Overall, assessment of quality was limited by a lack of methodological detail. The optimal timing, components, duration and models for interventions are still unclear. There was scant evidence for a continued effect over time following completion of interventions, a likely requirement for meaningful health benefits for people with COPD.

Implications for research

This review does not indicate one clear path forward, but does signal that optimisation of pharmacological management and physical function, as well as compliance with COPD care guidelines, may have an additional role in conjunction with physical activity counselling strategies. Future research should consider the design of interventions that are based on behaviour change constructs, with follow-up of physical activity outcomes after programme completion. Physical activity variables should be prospectively identified (ideally in a trial registry or published protocol) and reported accordingly. Outcomes should be selected according to intervention objectives, and consideration should be given to opportunities to inform longer-term cardiometabolic risk factor mitigation. Device outputs should align with the outcomes of interest (for example, using a validated device for step count in an intervention targeting increasing walking towards a step count goal) and wear-time protocols optimised to ensure data accuracy. A comprehensive description of intervention design and delivery, as well as physical activity data processing details, will be essential to move this field forward, particularly in the context of technological advancements.

ACKNOWLEDGEMENTS

We thank Elizabeth Stovold from the Cochrane Airways Group for her help with developing the search strategy.

We based the Background and Methods sections of this review on a standard template used by Cochrane Airways.

The authors and Airways Editorial Team are grateful to the following peer and consumer reviewers for their time and comments:

Andy Coles (consumer reviewer);
Dr Kylie Hill, Curtin University, Australia;
Marlies Zwerink, Medisch Spectrum Twente, the Netherlands;
Dr Rachael Evans, University of Leicester, UK.

This project was supported by the National Institute for Health Research (NIHR), via Cochrane Infrastructure funding to the Cochrane Airways Group. The views and opinions expressed therein are those of the protocol authors and do not necessarily reflect those of the Systematic Reviews Programme, the NIHR, the NHS, or the Department of Health.

Angela Burge was the recipient of the Lung Foundation Australia/ Cochrane Airways Australia Scholarship (2018).

We thank all authors who responded to requests for additional information, particularly Henrik Watz.

REFERENCES

References to studies included in this review

Alison 2019 *{published data only}*

Alison JA, McKeough ZJ, Jenkins SC, Holland AE, Hill K, Morris NR, et al. A randomised controlled trial of supplemental oxygen versus medical air during exercise training in people with chronic obstructive pulmonary disease: supplemental oxygen in pulmonary rehabilitation trial (SuppORT) [protocol]. *BMC Pulmonary Medicine* 2016;**1**:25.

* Alison JA, McKeough ZJ, Leung RW, Holland AE, Hill K, Morris NR, et al. Oxygen compared to air during exercise training in COPD with exercise-induced desaturation. *European Respiratory Journal* 2019;**53**:1802429.

Altenburg 2015 *{published data only}*

Altenburg W, Wempe J, De Greef M, Ten Hacken N, Kerstjens H. Short- and long-term effects of a physical activity counselling program in COPD [abstract]. *European Respiratory Journal* 2014;**44**:3490.

* Altenburg WA, Ten Hacken NH, Bossenbroek L, Kerstjens HA, De Greef MH, Wempe JB. Short- and long-term effects of a physical activity counselling programme in COPD: a randomized controlled trial. *Respiratory Medicine* 2015;**109**(1):112-21.

Arbillaga-Etxarri 2018 *{published data only}*

Arbillaga-Etxarri A, Gimeno-Santos E, Balcells E, Barberan-Garcia A, Benet M, Celorrio N, et al. Effectiveness of an intervention of urban training in patients with COPD: a randomized controlled trial [abstract]. *European Respiratory Journal* 2017;**50**:OA513.

* Arbillaga-Etxarri A, Gimeno-Santos E, Barberan-Garcia A, Balcells E, Benet M, Borrell E, et al. Long-term efficacy and effectiveness of a behavioural and community-based exercise intervention (Urban Training™) to increase physical activity in patients with COPD. A randomised controlled trial. *European Respiratory Journal* 2018;**52**(4):1800063.

Arbillaga-Etxarri A, Torrent-Pallicer J, Gimeno-Santos E, Barberan-Garcia A, Delgado A, Balcells E, et al. Validation of walking trails for the urban training of chronic obstructive disease patients. *PLoS ONE* 2016;**11**(1):e0146705.

Beeh 2014 *{published and unpublished data}*

Beeh KM, Watz H, Puente-Maestu L, De Teresa L, Jarreta D, Caracta C, et al. Aclidinium improves exercise endurance, dyspnea, lung hyperinflation, and physical activity in patients with COPD: a randomized, placebo-controlled, crossover trial. *BMC Pulmonary Medicine* 2014;**14**(1):209.

Bender 2016 *{published data only}*

* Bender BG, Depew A, Emmett A, Goelz K, Make B, Sharma S, et al. A patient-centered walking program for COPD. *Chronic Obstructive Pulmonary Diseases: Journal of the COPD Foundation* 2016;**3**(4):769-77.

Bender BG, Make BJ, Emmett A, Sharma S, Stempel D. Enhancing physical activity in patients with chronic obstructive pulmonary disease (COPD) through a program of patient selected goals [abstract]. *American Journal of Respiratory and Critical Care Medicine* 2015;**191**:A2458.

Benzo 2016 *{published data only (unpublished sought but not used)}*

Benzo R, McEvoy C. Effect of health coaching delivered by a respiratory therapist or nurse on self-management abilities in severe COPD: analysis of a large randomized study. *Respiratory Care* 2019;**64**(9):1065-72.

Benzo R, Vickers K, Ernst D, Tucker S, McEvoy C, Lorig K. Development and feasibility of a self-management intervention for chronic obstructive pulmonary disease delivered with motivational interviewing strategies. *Journal of Cardiopulmonary Rehabilitation and Prevention* 2013;**33**(2):113-22.

* Benzo R, Vickers K, Novotny PJ, Tucker S, Hoult J, Neuenfeldt P, et al. Health coaching and chronic obstructive pulmonary disease rehospitalization: a randomized study. *American Journal of Respiratory and Critical Care Medicine* 2016;**194**(6):672-80.

Blumenthal 2014 *{published data only}*

* Blumenthal JA, Emery CF, Smith PJ, Keefe FJ, Welty-Wolf K, Mabe S, et al. The effects of a telehealth coping skills intervention on outcomes in chronic obstructive pulmonary disease: primary results from the INSPIRE-II study. *Psychosomatic Medicine* 2014;**76**(8):581-92.

Blumenthal JA, Keefe FJ, Babyak MA, Fenwick CV, Johnson JM, Stott K, et al. Caregiver-assisted coping skills training for patients with COPD: background, design, and methodological issues for the INSPIREII study. *Clinical Trials* 2009;**6**(2):172-84.

Borges 2014 *{published and unpublished data}*

Borges R, Carvalho CR. Effect of resistance training during hospitalization in the systemic inflammation, functional capacity and muscle strength in COPD patients [abstract]. *European Respiratory Journal* 2011;**38**:1890.

* Borges RC, Carvalho CR. Impact of resistance training in chronic obstructive pulmonary disease patients during periods of acute exacerbation. *Archives of Physical Medicine and Rehabilitation* 2014;**95**(9):1638-45.

Breyer 2010 *{published data only (unpublished sought but not used)}*

* Breyer MK, Breyer-Kohansal R, Funk GC, Dornhofer N, Spruit MA, Wouters EF, et al. Nordic walking improves daily physical activities in COPD: a randomised controlled trial. *Respiratory Research* 2010;**11**:112.

Breyer MK, Kohansal R, Burghuber OC, Hartl S. The effects of Nordic walking on exercise capacity and physical activity in daily life (AoDL) in COPD [abstract]. *European Respiratory Journal* 2008;**32**(Supp 52):1754.

Burtin 2015 *{published data only}*

Burtin C, Lander D, Van Remoortel H, Gosselinki R, Decramer M, Janssens W, et al. Physical activity counseling and long-term effects of pulmonary rehabilitation [abstract]. *American Journal of Respiratory and Critical Care Medicine* 2012;**185**:A3675.

* Burtin C, Langer D, Van Remoortel H, Demeyer H, Gosselink R, Decramer M, et al. Physical activity counselling during pulmonary rehabilitation in patients with COPD: a randomised controlled trial. *PLOS One* 2015;**10**(12):e0144989.

Burtin C, Langer D, Van Remoortel J, Demeyer H, Gosselink R, Decramer M, et al. Correction: Physical activity counselling during pulmonary rehabilitation in patients with COPD: a randomised controlled trial. *PLOS One* 2016;**11**(2):e0148705.

Casaburi 2012 *{published data only}*

Casaburi R, Porszasz J, Hecht A, Tiep B, Albert RK, Anthonisen NR, et al: for the COPD Clinical Research Network. Influence of lightweight ambulatory oxygen on oxygen use and activity patterns of COPD patients receiving long-term oxygen therapy. *Journal of Chronic Obstructive Pulmonary Disease* 2012;**9**(1):3-11.

Chaplin 2017 *{published data only}*

Barnes A, Newby C, Chaplin E, Houchen-Wolloff, Singh SJ. Purposeful physical activity in COPD patients comparing standard and web based pulmonary rehabilitation [abstract]. *European Respiratory Journal* 2016;**48**(Supp 60):PA2056.

* Chaplin E, Hewitt S, Apps L, Bankart J, Pulikottil-Jacob R, Boyce S, et al. Interactive web-based pulmonary rehabilitation programme: a randomised controlled feasibility trial. *BMJ Open* 2017;**7**(3):e013682.

Chaplin E, Hewitt S, Apps L, Edwards K, Brough C, Glab A, et al. An interactive web-based programme: a randomised controlled feasibility trial [abstract]. *European Respiratory Journal* 2016;**48**(Suppl 60):PA2064.

Chaplin E, Hewitt S, Apps L, Edwards K, Brough C, Glab A, et al. The evaluation of an interactive web-based pulmonary rehabilitation programme: protocol for the WEB SPACE for COPD feasibility study. *BMJ Open* 2015;**5**(8):e008055.

Charususin 2018 *{published data only}*

* Charususin N, Gosselink R, Decramer M, Demeyer H, McConnell A, Saey D, et al. Randomised controlled trial of adjunctive inspiratory muscle training for patients with COPD. *Thorax* 2018;**73**(10):942-50.

Charususin N, Gosselink R, Decramer M, McConnell A, Saey D, Maltais F, et al. Inspiratory muscle training protocol for patients with chronic obstructive pulmonary disease (IMTCO study): A multicentre randomised controlled trial. *BMJ Open* 2013;**3**(8):e003101.

Cruz 2016 *{published data only}*

Cruz J, Brooks D, Marques A. Walk2Bactive: a randomised controlled trial of a physical activity-focused behavioural intervention beyond pulmonary rehabilitation in chronic obstructive pulmonary disease. *Chronic Respiratory Disease* 2016;**13**(1):57-66.

Curtis 2016 *{published data only}*

Curtis KJ, Meyrick VM, Mehta B, Haji GS, Li K, Montgomery H, et al. Angiotensin-converting enzyme inhibition as an adjunct to pulmonary rehabilitation in chronic obstructive pulmonary disease. *American Journal of Respiratory and Critical Care Medicine* 2016;**194**(11):1349-57.

Dal Negro 2012 *{published data only (unpublished sought but not used)}*

Dal Negro RW, Aquilani R, Bertacco S, Boschi F, Micheletto C, Tognella S. Comprehensive effects of supplemented essential amino acids in patients with severe COPD and sarcopenia. *Monaldi Archives of Chest Disease* 2010;**73**(1):25-33.

* Dal Negro RW, Testa A, Aquilani R, Tognella S, Pasini E, Barbieri A, et al. Essential amino acid supplementation in patients with severe COPD: a step towards home rehabilitation. *Monaldi Archives of Chest Disease* 2012;**77**(2):67-75.

De Blok 2006 *{published data only}*

De Blok BM, De Greef MH, Ten Hacken NH, Sprenger SR, Postema K, Wempe JB. The effects of a lifestyle physical activity counseling program with feedback of a pedometer during pulmonary rehabilitation in patients with COPD a pilot study [abstract]. *European Respiratory Journal* 2005;**26**(Suppl 49):548.

* De Blok BM, De Greef MH, Ten Hacken NH, Sprenger SR, Postema K, Wempe JB. The effects of a lifestyle physical activity counseling program with feedback of a pedometer during pulmonary rehabilitation in patients with COPD: a pilot study. *Patient Education and Counseling* 2006;**61**(1):48-55.

Demeyer 2017 *{published and unpublished data}*

* Demeyer H, Louvaris Z, Frei A, Rabinovich RA, De Jong C, Gimeno-Santos E, et al: on behalf of the Mr Papp PROactive study group and the PROactive consortium. Physical activity is increased by a 12-week semiautomated telecoaching programme in patients with COPD: a multicentre randomised controlled trial. *Thorax* 2017;**72**(5):415-23.

Demeyer H, Louvaris Z, Tanner R, Rubio N, Frei A, De Jong C, et al. Increasing physical activity in patients with COPD using a telecoaching program: a multicentre RCT [abstract]. *European Respiratory Journal* 2015;**46**:OA278.

Loeckx M, Louvaris Z, Tanner R, Rubio N, Frej A, De Jong C, et al. Contact time between patients with COPD and coach during an activity telecoaching intervention: Impact on the intervention effect [abstract]. *European Respiratory Journal* 2016;**48**(Suppl 60):OA4817.

Loeckx M, Louvaris Z, Tanner RJ, Yerramasu C, Busching G, Frei A, et al. Compliance with a three month telecoaching program to enhance physical activity in patients with Chronic Obstructive Pulmonary Disease [abstract]. *American Journal of Respiratory and Critical Care Medicine* 2015;**191**:A2007.

Loeckx M, Rabinovich RA, Demeyer H, Louvaris Z, Tanner R, Rubio N, et al. Smartphone-based physical activity telecoaching in chronic obstructive pulmonary disease: mixed-methods

study on patient experiences and lessons for implementation. *JMIR mHealth and uHealth* 2018;**6**(2):e200.

De Roos 2017 *{published and unpublished data}*

De Roos P, Lucas C, Strijbos JH, Van Trijffel E. Effectiveness of a combined exercise training and home-based walking programme on physical activity compared with standard medical care in moderate COPD: a randomised controlled trial. *Physiotherapy* 2017;**104**(1):116-21.

Duiverman 2008 *{published data only}*

Duiverman ML, Bladder G, Wempe JB, Kerstjens HA, Zijlstra JG, Wijkstra PJ. Chronic ventilatory support improves the outcomes of rehabilitation in hypercapnic COPD patients [abstract]. American Thoracic Society International Conference; 2008 May 16-21; Toronto. 2008:A557.

* Duiverman ML, Wempe JB, Bladder G, Jansen DF, Kerstjens HA, Zijlstra JG, et al. Nocturnal non-invasive ventilation in addition to rehabilitation in hypercapnic patients with COPD. *Thorax* 2008;**63**(12):1052-7.

Effing 2011 *{published data only}*

* Effing T, Zielhuis G, Kerstjens H, Van der Valk P, Van der Palen J. Community based physiotherapeutic exercise in COPD self-management: a randomised controlled trial. *Respiratory Medicine* 2011;**105**(3):418-26.

Zwerink M, Effing T, Kerstjens HA, Van der Valk P, Brusse-Keizer M, Zielhuis G, et al. Cost-effectiveness of a community-based exercise programme in COPD self-management. *Journal of Chronic Obstructive Pulmonary Disease* 2016;**13**(2):214-23.

Zwerink M, Van der Palen J, Kerstjens HA, Van der Valk P, Brusse-Keizer M, Zielhuis G, et al. A community-based exercise programme in COPD self-management: two years follow-up of the COPD-II study. *Respiratory Medicine* 2014;**108**(10):1481-90.

Zwerink M, Van der Palen J, Kerstjens HA, Van der Valk P, Brusse-Keizer M, Zielhuis G, et al. A community-based exercise programme in COPD self-management: two-year follow-up of the COPD-II study [abstract]. *European Respiratory Journal* 2014;**44**:1711.

Zwerink M, Van der Palen J, Van der Valk P, Brusse-Keizer M, Effing T. Relationship between daily physical activity and exercise capacity in patients with COPD. *Respiratory Medicine* 2013;**102**(2):242-8.

Egan 2010 *{published and unpublished data}*

* Egan C, Costello R, Deering B, McCormack NM, Blake C. Physical activity in COPD patients following pulmonary rehabilitation [abstract]. European Respiratory Society 20th Annual Congress; 2010 Sep 18-22; Barcelona. 2010:E3535.

Egan C, Deering BM, Blake C, Fullen BM, McCormack NM, Spruit MA, et al. Short term and long term effects of pulmonary rehabilitation on physical activity in COPD. *Respiratory Medicine* 2012;**106**(12):1671-9.

Felcar 2018 *{published data only}*

* Felcar JM, Probst VS, De Carvalho DR, Merli MF, Mesquita R, Vidotto LS, et al. Effects of exercise training in water and on land in patients with COPD: a randomised clinical trial. *Physiotherapy* 2018;**104**(4):408-16.

Felcar JM, Probst VS, De Carvalho DR, Merli MF, Mesquita RB, Vidotto LS, et al. Effects of exercise training in water and on land in patients with COPD [abstract]. *European Respiratory Journal* 2015;**46**(Suppl 59):PA2396.

Gamper 2019 *{published data only}*

Gamper E, Schmidt U, Bansi J, Kool J. Outdoor walking training compared to cycle ergometer training in severe COPD: a randomized controlled feasibility trial. *COPD: Journal of Chronic Obstructive Pulmonary Disease* 2019;**16**(1):37-44.

Goris 2003 *{published data only}*

Goris AH, Vermeeren MA, Wouters EF, Schols AM, Westerterp KR. Energy balance in depleted ambulatory patients with chronic obstructive pulmonary disease: the effect of physical activity and oral nutritional supplementation. *British Journal of Nutrition* 2003;**89**(5):725-9.

Hartman 2016 *{published data only}*

Hartman JE, Klooster K, Slebos DJ, Ten Hacken NH. Daily physical activity significantly improves after endobronchial valve treatment in patients with emphysema [abstract]. *European Respiratory Journal* 2015;**46**:OA1767.

* Hartman JE, Klooster K, Slebos DJ, ten Hacken NH. Improvement of physical activity after endobronchial valve treatment in emphysema patients. *Respiratory Medicine* 2016;**117**:116-21.

Holland 2017 *{published data only}*

* Holland AE, Mahal A, Hill CJ, Lee AL, Burge AT, Cox NS, et al. Home-based rehabilitation for COPD using minimal resources: a randomised, controlled equivalence trial. *Thorax* 2017;**72**(1):57-65.

Holland AE, Mahal A, Hill CJ, Lee AL, Burge AT, Cox NS, et al. Low cost home-based pulmonary rehabilitation for chronic obstructive pulmonary disease: a randomized controlled equivalence trial [abstract]. *American Journal of Respiratory and Critical Care Medicine* 2016;**193**:A2620.

Holland AE, Mahal A, Hill CJ, Lee AL, Burge AT, Moore R, et al. Benefits and costs of home-based pulmonary rehabilitation in chronic obstructive pulmonary disease - a multi-centre randomised controlled equivalence trial [protocol]. *BMC Pulmonary Medicine* 2013;**13**:57.

Lahham A, McDonald CF, Mahal A, Lee AL, Hill CJ, Burge AT, et al. Participation in physical activity during center and home-based pulmonary rehabilitation for people with COPD: a secondary analysis of a randomized controlled trial. *Journal of Cardiopulmonary Rehabilitation and Prevention* 2019;**39**:E1-4.

Liacos A, McDonald CF, Mahal A, Hill CJ, Lee AL, Burge AT, et al. The Pulmonary Rehabilitation Adapted Index of Self-Efficacy (PRAISE) tool predicts reduction in sedentary time following pulmonary rehabilitation in people with chronic obstructive pulmonary disease (COPD). *Physiotherapy* 2019;**105**(1):90-7.

Hornikx 2015 *{published data only}*

* Hornikx M, Demeyer H, Camillo CA, Janssens W, Troosters T. The effects of a physical activity counseling program after an exacerbation in patients with chronic obstructive pulmonary disease: a randomized controlled pilot study. *BMC Pulmonary Medicine* 2015;**15**:136.

Hornikx M, Demeyer H, Camillo CA, Janssens W, Troosters T. The effects of physical activity coaching in patients with COPD after an acute exacerbation [abstract]. *European Respiratory Journal* 2014;**44**:1920.

Hospes 2009 *{published data only (unpublished sought but not used)}*

* Hospes G, Bossenbroek L, Ten Hacken NH, Van Hengel P, De Greef MH. Enhancement of daily physical activity increases physical fitness of outclinic COPD patients: results of an exercise counseling program. *Patient Education and Counseling* 2009;**75**(2):274-8.

Hospes G, Ten Hacken NH, Van Hengel P, De Greef MH. Pedometer-based exercise counseling in COPD [abstract]. American Thoracic Society International Conference; 2007 May 18-23; San Francisco. 2007; Vol. 175:A601.

Jolly 2018 *{published data only}*

* Jolly K, Sidhu MS, Hewitt CA, Coventry PA, Daley A, Jordan R, et al. Self management of patients with mild COPD in primary care: randomised controlled trial. *BMJ* 2018;**361**:k2241.

Sidhu MS, Daley A, Jordan R, Coventry PA, Heneghan C, Jowett S, et al. Patient self-management in primary care patients with mild COPD – protocol of a randomised controlled trial of telephone health coaching. *BMC Pulmonary Medicine* 2015;**15**(1):16.

Kanabar 2015 *{published and unpublished data}*

Kanabar P, Warrington V, Houchen-Wolloff L, Singh SJ. Investigating the profile of physical activity in COPD patients 7 days post discharge from a respiratory-related admission. Does brief advice have an effect? [abstract]. *Thorax* 2015;**70**(Suppl 3):A146.

Kawagoshi 2015 *{published data only}*

Kawagoshi A, Kiyokawa N, Iwakura M, Okura K, Sugawara K, Takahashi H, Sakata S, Satake M, Shioya T. Effects of low-intensity exercise and home-based pulmonary rehabilitation with pedometer feedback on physical activity in elderly patients with COPD [abstract]. *European Respiratory Journal* 2015;**46**:PA3563.

* Kawagoshi A, Kiyokawa N, Sugawara K, Takahashi H, Sakata S, Satake M, et al. Effects of low-intensity exercise and home-based pulmonary rehabilitation with pedometer feedback on physical activity in elderly patients with chronic obstructive pulmonary disease. *Respiratory Medicine* 2015;**109**(3):364-71.

Larson 2014 *{published data only (unpublished sought but not used)}*

Covey MK, McAuley E, Kapella MC, Collins EG, Alex CG, Berbaum ML, et al. Upper-body resistance training and self-efficacy enhancement in COPD. *Journal of Pulmonary and Respiratory Medicine* 2012;**Suppl 9**:001.

* Larson JL, Covey MK, Kapella MC, Alex CG, McAuley E. Self-efficacy enhancing intervention increases light physical activity in people with chronic obstructive pulmonary disease. *International Journal of Chronic Obstructive Pulmonary Disease* 2014;**9**:1081-90.

Loeckx 2018 *{published data only}*

Loeckx M, Rodrigues F, Demeyer H, Janssens W, Troosters T. Improving physical activity to obtain sustainable benefits in extra-pulmonary consequences of COPD after pulmonary rehabilitation: a randomized controlled trial [abstract]. *American Journal of Respiratory and Critical Care Medicine* 2018;**197**:A2452.

Lord 2012 *{published data only (unpublished sought but not used)}*

Lord VM, Hume VJ, Kelly JL, Cave P, Silver J, Waldman M, et al. Effects of 'singing for breathing' in patients with chronic obstructive pulmonary disease (COPD) - a randomized controlled trial [abstract]. *American Journal of Respiratory and Critical Care Medicine* 2012;**185**:A5788.

* Lord VM, Hume VJ, Kelly JL, Cave P, Silver J, Waldman M, et al. Singing classes for chronic obstructive pulmonary disease: a randomized controlled trial. *BMC Pulmonary Medicine* 2012;**12**:69.

Louvaris 2016 *{published and unpublished data}*

Kortianou E, Louvaris Z, Spetsioti S, Vasilopoulou M, Chynkiamis N, Nasis I, et al. High-intensity interval exercise training improves daily physical activity levels in COPD [abstract]. *European Respiratory Journal* 2014;**44**(Suppl 58):1709.

Louvaris Z, Spetsioti S, Kortianou EA, Vasilopoulou M, Nasis I, Kaltsakas G, et al. Aerobic interval training induces clinically meaningful effects in daily physical activity in COPD [abstract]. *European Respiratory Journal* 2016;**48**:PA2053.

* Louvaris Z, Spetsioti S, Kortianou EA, Vasilopoulou M, Nasis I, Kaltsakas G, et al. Interval training induces clinically meaningful effects in daily activity levels in COPD. *European Respiratory Journal* 2016;**48**(2):567-70.

Maddocks 2016 *{published data only}*

Maddocks M, Nolan CM, Man WD, Polkey MI, Hart N, Gao W, et al. Neuromuscular electrical stimulation to improve exercise capacity in patients with severe COPD: a randomised double-blind, placebo-controlled trial. *Lancet Respiratory Medicine* 2016;**4**(1):27-36.

Magnussen 2017 *{published and unpublished data}*

* Magnussen H, Arzt M, Andrea S, Plate T, Ribera A, Seoane B, et al. Aclidinium bromide improves symptoms and sleep quality in COPD: a pilot study. *European Respiratory Journal* 2017;**49**(6):1700485.

Magnussen H, Arzt M, Andreas S, Plate T, Ribera A, Seoane B, et al. The effect of aclidinium bromide 400µg on lung function, sleep quality and physical activity in patients with chronic

obstructive pulmonary disease: results of a phase IV pilot study [abstract]. *American Journal of Respiratory and Critical Care Medicine* 2016;**193**:A6820.

Magnussen H, Arzt M, Andreas S, Plate T, Ribera A, Seoane B, et al. The effect of aclidinium bromide 400µg on sleep quality in COPD: a pilot study [abstract]. *European Respiratory Journal* 2016;**48**:PA4051.

Mantoani 2018 *{published data only}*

Mantoani L, McKinstry B, McNarry S, Mullen S, Begg S, Saini P, et al. Physical activity enhancing programme (PAEP) in COPD – a randomised controlled trial [abstract]. *European Respiratory Journal* 2018;**52**(Suppl 62):OA1986.

Mendoza 2015 *{published data only}*

Mendoza L, Aguilera M, Balmaceda N, Espinoza J, Horta P, Castro A, et al. Effect of a program of physical activity enhancement using pedometers in patients with chronic obstructive pulmonary disease [abstract]. *American Journal of Respiratory and Critical Care Medicine* 2013;**187**:A1360.

Mendoza L, Aguilera M, Espinoza J, Balmaceda N, Horta P, Castro A, et al. Effects of a program of physical activity encouragement using pedometers in COPD patients [abstract]. *European Respiratory Journal* 2013;**45**(2):A570.

* Mendoza L, Horta P, Espinoza J, Aguilera M, Balmaceda N, Castro A, et al. Pedometers to enhance physical activity in COPD: a randomised controlled trial. *European Respiratory Journal* 2015;**45**(2):347-54.

Mitchell 2013 *{published and unpublished data}*

Mitchell KE, Johnson-Warrington V, Apps LD, Bankart J, Sewell L, Williams JE, et al. A self-management programme for COPD: a randomised controlled trial. *European Respiratory Journal* 2014;**44**(6):1538-47.

* Mitchell KE, Warrington V, Sewell L, Bankart J, Williams JE, Steiner MC, et al. A randomised controlled trial of a self-management programme of activity coping and education - SPACE for COPD: impact on physical activity at 6 weeks [abstract]. *American Journal of Respiratory and Critical Care Medicine* 2013;**187**:A5952.

Mitchell-Wagg K, Warrington V, Apps L, Sewell L, Bankart J, Steiner MC, et al. A self-management programme of activity coping and education (SPACE) for COPD: results from a randomised controlled trial [abstract]. *Thorax* 2012;**67**(Suppl 2):A25.

Wagg K, Warrington V, Apps L, Sewell L, Bankart J, Steiner M, et al. A self-management programme of activity coping and education (SPACE) for COPD: 6 week results from a randomised controlled trial [abstract]. *European Respiratory Journal* 2012;**40**(Suppl 56):548s.

Wagg K, Wilcock E, Williams J, Sewell L, Steiner MC, Morgan M, et al. Pulmonary rehabilitation using the space (a self management programme of activity, coping and education) manual at home: a randomised controlled trial [abstract]. *Thorax* 2009;**64**:A97.

Moy 2015a *{published data only}*

Martinez CH, Moy ML, Nguyen HQ, Cohen M, Kadri R, Roman P, et al. Taking healthy steps: rationale, design and baseline characteristics of a randomized trial of a pedometer-based internet-mediated walking program in veterans with chronic obstructive pulmonary disease. *BMC Pulmonary Medicine* 2014;**14**:12.

* Moy ML, Collins RJ, Martinez CH, Kadri R, Roman P, Holleman RG, et al. An internet-mediated pedometer-based program improves health-related quality-of-life domains and daily step counts in COPD: a randomized controlled trial. *Chest* 2015;**148**(1):128-37.

Moy ML, Collins RJ, Martinez CH, Kadri R, Roman P, Holleman RG, et al. An internet-mediated, pedometer-based walking program improves HRQOL in veterans with COPD [abstract]. *American Journal of Respiratory and Critical Care Medicine* 2014;**189**:A3642.

Moy ML, Martinez CH, Kadri R, Roman P, Holleman RG, Kim HM, et al. Long-term effects of an internet-mediated pedometer-based walking program for chronic obstructive pulmonary disease: randomized controlled trial. *Journal of Medical Internet Research* 2016;**18**(8):e215.

Moy ML, Martinez CH, Kadri R, Roman P, Holleman RG, Kim HM, et al. Long-term effects of an internet-mediated pedometer-based walking program in COPD: a randomized controlled trial [abstract]. *American Journal of Respiratory and Critical Care Medicine* 2015;**191**:A2457.

Nakamura 2016 *{published data only}*

Nakamura H, Mori Y, Nanki N, Kamei T. Clinical benefits of aclidinium bromide twice daily compared with tiotropium once daily in patients with moderate to severe chronic obstructive pulmonary disease [abstract]. *American Journal of Respiratory and Critical Care Medicine* 2017;**195**:A5471.

NCT00144326 *{published data only}*

García Río F. A randomised, double-blind, placebo-controlled, 12 weeks trial to evaluate the effect of tiotropium inhalation capsules on the magnitude of exercise, measured using an accelerometer, in patients with chronic obstructive pulmonary disease. Boehringer Ingelheim Trial Results 2007; Vol. Trial number 205.269 (first received 5 September 2005).

NCT01351792 *{published data only}*

NCT01351792. Multicentre, randomized research study to test the safety and efficacy of Foster® compared to Symbicort® on small airway function in patients with COPD. Chiesi Clinical Study Report (first received 11 May 2011). [Study number CCD-1007-PR-0045]

Ng 2015 *{published and unpublished data}*

* Ng LW, Jenkins S, Cecins N, Eastwood P, Hill K. A wheeled walker improves physical activity in chronic obstructive pulmonary disease [abstract]. *Physiotherapy* 2015;**101**:eS1084.

Ng LW, Jenkins S, Cecins N, Eastwood P, Hill K. The effect of using a wheeled walker on physical activity in people with

COPD: preliminary data [abstract]. *Respirology* 2012;**17**(Suppl 1):60.

Nguyen 2009 *{published data only}*

Estrada EL, Silva K, Medina E, Desai S, Fan VS, Nguyen HQ. Depression and anxiety are associated with COPD patients' lower confidence for increasing physical activity but not with their motivation [abstract]. *American Journal of Respiratory and Critical Care Medicine* 2018;**197**:A7066.

Lee JS, Liu AI, Pounds D, Mahmud F, Flores C, Desai SA, et al. Characteristics of COPD patients who agree to participate in a pragmatic trial of physical activity coaching compared to non-participants [abstract]. *American Journal of Respiratory and Critical Care Medicine* 2018;**197**:A2642.

Mahmud F, Valmonte F, Medina E, Pounds D, Nguyen HQ. Real-world implementation of a physical activity coaching program [abstract]. *American Journal of Respiratory and Critical Care Medicine* 2018;**197**:A2728.

* Nguyen HQ, Gill DP, Wolpin S, Steele BG, Benditt JO. Pilot study of a cell phone-based exercise persistence intervention post-rehabilitation for COPD. *International Journal of Chronic Obstructive Pulmonary Disease* 2009;**4**:301-13.

Nolan 2017 *{published and unpublished data}*

* Nolan CM, Maddocks M, Canavan JL, Jones SE, Delogu V, Kaliaraju D, et al. Pedometer step count targets during pulmonary rehabilitation in chronic obstructive pulmonary disease: a randomized controlled trial. *American Journal of Respiratory and Critical Care Medicine* 2017;**195**(10):1344-52.

Nolan CM, Maddocks M, Canavan JL, Jones SE, Delogu V, Kaliaraju D, et al. Pedometer step count targets during pulmonary rehabilitation in chronic obstructive pulmonary disease: a randomized controlled trial [abstract]. *American Journal of Respiratory and Critical Care Medicine* 2016;**193**:A7862.

Nolan CM, Maddocks M, Canavan JL, Jones SE, Kon SS, Kaliaraju D, et al. Do pedometers maintain the benefits of pulmonary rehabilitation in COPD patients? [abstract]. *European Respiratory Journal* 2016;**48**:PA2058.

O'Neill 2018 *{published data only}*

O'Neill B, O'Shea OM, McDonough SM, McGarvey L, Bradbury I, Arden MA, et al. Physical activity intervention versus pulmonary rehabilitation in COPD: the LIVELY COPD project [abstract]. *Thorax* 2016;**71**(Suppl 3):A20.

* O'Neill B, O'Shea OM, McDonough SM, McGarvey L, Bradbury I, Arden MA, et al. Clinician-facilitated physical activity intervention versus pulmonary rehabilitation for improving physical activity in COPD: a feasibility study. *COPD: Journal of Chronic Obstructive Pulmonary Disease* 2018;**15**(3):254-64.

Ogasawara 2018 *{published data only}*

Ogasawara T, Marui S, Miura E, Sugiura M, Matsuyama W, Aoshima Y, et al. Effect of eicosapentaenoic acid on prevention of lean body mass depletion in patients with exacerbation of chronic obstructive pulmonary disease: a prospective randomized controlled trial. *Clinical Nutrition ESPEN* 2018;**28**:67-73.

Orme 2018 *{published data only}*

Orme MW, Weedon AE, Esliger DW, Saukko PM, Morgan MD, Steiner MC, et al. Study protocol for Chronic Obstructive Pulmonary Disease-Sitting and ExacerbAtions Trial (COPD-SEAT): a randomised controlled feasibility trial of a home-based self-monitoring sedentary behaviour intervention [protocol]. *BMJ Open* 2016;**6**:e013014.

* Orme MW, Weedon AE, Saukko PM, Esliger DW, Morgan MD, Steiner MC, et al. Findings of the Chronic Obstructive Pulmonary Disease - Sitting and Exacerbations Trial (COPD-SEAT) in reducing time using wearable and mobile technologies with educational support: randomized controlled feasibility trial. *JMIR mHealth and uHealth* 2018;**6**(4):e84.

Polkey 2018 *{published data only}*

Polkey MI, Qiu ZH, Zhou L, Zhu MD, Wu YX, Chen YY, et al. Tai Chi and pulmonary rehabilitation compared for treatment-naïve patients with COPD; a randomized controlled trial. *Chest* 2018;**153**(3):1116-24.

Priori 2017 *{published and unpublished data}*

* Priori R, Van Genugten L, Barretto C, Schonenberg H, Stut W, Miller B, et al. Automated coaching for physical activity in COPD patients: results from a pilot study [abstract]. *European Respiratory Journal* 2017;**50**:OA4868.

Saini PK, Dekker M, Van Genugten, Prior R, Klee M. Online coaching for physical activity in COPD patients: user engagement and determinants [abstract]. *European Respiratory Journal* 2018;**52**:PA3644.

Van Genugten L, Priori R, Barretto C, Schonenberg H, Dekker M, Klee M, et al. An online intervention to maintain physical activity levels in COPD patients after pulmonary rehabilitation [abstract]. *Bulletin of the European Health Psychology Society* 2016;**18**:635.

Probst 2011 *{published data only}*

Probst VS, Kovelis D, Hernandes NA, Camillo CA, Cavalheri V, Pitta F. Effects of 2 exercise training programs on physical activity in daily life in patients with COPD. *Respiratory Care* 2011;**56**(11):1799-807.

Rinaldo 2017 *{published data only}*

Rinaldo N, Bacchi E, Coratella G, Vitali F, Milanese C, Rossi A, et al. Effects of combined aerobic-strength training vs fitness education program in COPD patients. *International Journal of Sports Medicine* 2017;**38**(13):1001-8.

Saini 2017 *{published data only}*

Saini PK, Dekker M, Van Genugten L, Priori R, Klee M. Online coaching for physical activity in COPD patients: user engagement and determinants [abstract]. *European Respiratory Journal* 2018;**52**(Suppl 62):PA3644.

* Saini PK, Priori R, Barretto C, Delbressine J, Van Genugten L, Dekker M, et al. Activity maintenance after pulmonary rehabilitation - first results of an online coaching program

[abstract]. *American Journal of Respiratory and Critical Care Medicine* 2017;**195**:A4942.

Van Genugten L, Prior R, Barretto C, Schonenberg H, Dekker M, Klee M, et al. An online intervention to maintain physical activity levels after pulmonary rehabilitation [abstract]. European Health Psychologist 2016; Vol. 18.

Sandland 2008 *{published data only}*

Sandland CJ, Morgan MD, Singh SJ. Patterns of domestic activity and ambulatory oxygen usage in COPD. *Chest* 2008;**134**(4):753-60.

Schuz 2015 *{published and unpublished data}*

* Schuz N, Walters JA, Cameron-Tucker H, Scott J, Wood-Baker R, Walters EH. Patient anxiety and depression moderate the effects of increased self-management knowledge on physical activity: a secondary analysis of a randomised controlled trail on health-mentoring in COPD. *Journal of Chronic Obstructive Pulmonary Disease* 2015;**12**(5):502-9.

Walters JA, Cameron-Tucker H, Wills K, Schuz N, Scott J, Robinson A, et al. Effects of telephone health mentoring in community-recruited chronic obstructive pulmonary disease on self-management capacity, quality of life and psychological morbidity: a randomised controlled trial. *BMJ Open* 2013;**3**(9):e003097.

Walters JA, Wills K, Robinson A, Nelson M, Scott J, Turner P, et al. Effect of health-mentoring to increase daily physical activity in chronic obstructive pulmonary disease (COPD) [abstract]. *Respirology* 2012;**17**:TP079.

Sena 2013 *{published and unpublished data}*

Sena R, Baril J, Kapchinsky S, MacMillan NJ, Rocha DV, Ruddy R, et al. The effects of eccentric and concentric exercise training on muscle strength in COPD: preliminary results [abstract]. *European Respiratory Journal* 2012;**40**(Suppl 56):P482.

* Sena R, MacMillan NJ, Baril J, Rocha V, Richard R, Perrault H, et al. Short term effects of eccentric and concentric exercise training on strength muscle, exercise capacity and physical activity in patients with chronic obstructive pulmonary disease [abstract]. *Canadian Respiratory Journal* 2013;**20**(2):e36.

Singh 1998 *{published data only (unpublished sought but not used)}*

Singh SJ, Curcio A, Williams J, Morgan MD, Jones P. Does wearing an activity monitor influence daily activity recorded in patients with COPD? [abstract]. *Thorax* 1998;**53**(Suppl 4):A24.

Steele 2019 *{published data only}*

Kang Y, Steele BG, Burr RL, Dougherty CM. Mortality in advanced chronic obstructive pulmonary disease and heart failure following cardiopulmonary rehabilitation. *Biological Research for Nursing* 2018;**20**(4):429-39.

* Steele BG, Dougherty CM, Burr RL, Gylys-Colwell I, Hunziker J. A feasibility trial of two rehabilitation models in severe cardiopulmonary illness. *Rehabilitation Nursing* 2019;**44**(3):130-40.

Steele BG, Dougherty CM, Burr RL, Gylys-Colwell I, Hunziker J. An intervention to enhance function in severe cardiopulmonary illness [abstract]. *American Journal of Respiratory and Critical Care Medicine* 2012;**185**:A4879.

Tabak 2014a *{published data only}*

Tabak M, Vollenbroek-Hutten MM, van der Valk PD, van der Palen H, Hermens HJ. A telerehabilitation intervention for patients with chronic obstructive pulmonary disease: a randomized controlled pilot trial. *Clinical Rehabilitation* 2014;**28**(6):582-91.

Tabak 2014b *{published data only}*

Tabak M, Brusse-Keizer M, Van der Valk P, Hermens H, Vollenbroek-Hutten M. A telehealth program for self-management of COPD exacerbations and promotion of an active lifestyle: a pilot randomized controlled trial. *International Journal of Chronic Obstructive Pulmonary Disease* 2014;**9**:935-44.

Tahirah 2015 *{published and unpublished data}*

Tahirah F, Jenkins S, Othman SK, Ismail R, Ismail T, Hill K. A randomised controlled trial of individualised, progressed early exercise in patients hospitalised with an acute exacerbation of chronic obstructive pulmonary disease (AECOPD) [abstract]. *European Respiratory Journal* 2015;**46**:PA743.

Troosters 2014 *{published data only (unpublished sought but not used)}*

Sciurba FC, Siafakas NM, Troosters T, Klioze SS, Sutradhar SC, Weisman IM, et al. The efficacy and safety of tiotropium handihaler 18 micrograms once daily plus prn salbutamol versus placebo plus prn salbutamol in COPD subjects naive to maintenance therapy [abstract]. *American Journal of Respiratory and Critical Care Medicine* 2011;**183**:A1589.

* Troosters T, Sciurba FC, Decramer M, Siafakas NM, Klioze SS, Sutradhar SC, et al. Tiotropium in patients with moderate COPD naive to maintenance therapy: a randomised placebo-controlled trial. *Primary Care Respiratory Medicine* 2014;**24**:14003.

Troosters T, Weisman I, Dobbels F, Giardino N, Valluri SR. Assessing the impact of tiotropium on lung function and physical activity in GOLD stage II COPD patients who are naïve to maintenance respiratory therapy: a study protocol. *Open Respiratory Medicine Journal* 2011;**5**:1-9.

Troosters 2018 *{published data only}*

Bourbeau J, Lavoie KL, Sedano M, De Sousa D, Erzen D, Hamilton A, et al. Behaviour-change intervention in a multicentre, randomised, placebo-controlled COPD study: methodological considerations and implementation [protocol]. *BMJ Open* 2016;**6**:e010109.

Bourbeau J, Sedeno M, Li PZ, Troosters T, Hamilton A, De Sousa D, et al. Impact of meeting behavioral targets in a self-management behaviour-modification program designed to improve physical activity in COPD patients [abstract]. *European Respiratory Journal* 2017;**50**:PA4899.

Frith P, Troosters T, Bourbeau J, Maltais F, Leidy N, Erzen D, et al. Effect of tiotropium and olodaterol, alone and with exercise

training, on exercise endurance in COPD [abstract]. *Respirology* 2017;**22**(Suppl 2):TO048.

Frith P, Troosters T, Lavoie KL, Leidy N, Maltais F, Sedeno M, et al. Bronchodilator therapy and exercise added to self-management behaviour-modifications: effects on physical activity in COPD [abstract]. *Respirology* 2017;**22**(Suppl 2):TO129.

Lavoie KL, Sedeno M, Li PZ, Troosters T, Hamilton A, De Sousa D, et al. Effects of bronchodilator therapy and exercise with self-management behaviour-modification on psychological and cognitive outcomes in COPD [abstract]. *European Respiratory Journal* 2017;**50**:OA4669.

Troosters T, Bourbeau J, Maltais F, Leidy N, Erzen D, De Sousa D, et al. Effect of 8 and 12 weeks' once-daily tiotropium and olodaterol alone and combined with exercise training, on exercise endurance during walking in patients with COPD [abstract]. *European Respiratory Journal* 2016;**48**:PA976.

Troosters T, Bourbeau J, Maltais F, Leidy N, Erzen D, De Sousa D, et al. Effect of 8 and 12 weeks' once-daily tiotropium and olodaterol, alone and combined with exercise training, on exercise endurance during walking in patients with COPD [abstract]. *Thorax* 2016;**71**(Suppl 3):A21-22.

Troosters T, Bourbeau J, Maltais F, Leidy N, Erzen D, De Sousa D, et al. Enhancing exercise tolerance and physical activity in COPD with combined pharmacological and non-pharmacological interventions: PHYSACTO randomised, placebo-controlled study design [protocol]. *BMJ Open* 2016;**6**:e010106.

Troosters T, Lavoie KL, Leidy N, Maltais F, Sedeno M, Janssens W, et al. Effects of bronchodilator therapy and exercise training, added to a self-management behaviour-modification programme, on physical activity in COPD [abstract]. *European Respiratory Journal* 2016;**48**:PA713.

Troosters T, Lavoie KL, Leidy N, Maltais F, Sedeno M, Janssens W, et al. Effects of bronchodilator therapy and exercise training, added to a self-management behaviour-modification programme, on physical activity in COPD [abstract]. *Pneumonologie* 2017;**71**(S01):37.

* Troosters T, Maltais F, Leidy N, Lavoie KL, Sedeno M, Janssens A, et al. Effect of bronchodilation and exercise training with behavior modification on exercise tolerance and downstream effects on symptoms and physical activity in COPD. *American Journal of Respiratory and Critical Care Medicine* 2018;**198**(8):1021-32.

Tsai 2016 *{published and unpublished data}*

* Tsai LL, McNamara RJ, Moddel C, Alison JA, McKenzie D, McKeogh ZJ. Home-based telerehabilitation via real-time videoconferencing improves endurance exercise capacity in patients with COPD: the randomized controlled TeleR study. *Respirology* 2017;**22**(4):699-707.

Tsai LL, McNamara RJ, Moddel C, Alison JA, McKenzie DK, McKeough ZJ. Home-based telerehabilitation via real-time videoconferencing improves endurance exercise capacity in patients with COPD: the randomized controlled TeleR sStudy [abstract]. *Respirology* 2016;**21**(S2):TP086.

Tsai LL, McNamara RJ, Moddel C, McKenzie D, Alison JA, McKeough ZJ. Telerehabilitation in people with chronic obstructive pulmonary disease (COPD): a randomised controlled trial [abstract]. *European Respiratory Journal* 2016;**48**(Suppl 60):PA2065.

Van de Bool 2017 *{published data only}*

Van Beers M, Rutten-van Molken MP, Van de Bool C, Boland M, Kremers SP, Franssen FM, et al. Clinical outcome and cost-effectiveness of 1-year nutritional intervention program in COPD [abstract]. *European Respiratory Journal* 2018;**52**(Suppl 62):PA723.

Van Beers M, Rutten-van Molken MP, Van de Bool C, Boland M, Kremers SP, Franssen FM, et al. Clinical outcome and cost-effectiveness of a 1-year nutritional intervention programme in COPD patients with low muscle mass: the randomized controlled NUTRAIN trial. *Clinical Nutrition* 2019;**39**(2):405-13.

* Van de Bool C, Rutten EP, Van Helvoort A, Franssen FM, Wouters EF, Schols AM. A randomized clinical trial investigating the efficacy of targeted nutrition as adjunct to exercise training in COPD. *Journal of Cachexia, Sarcopenia and Muscle* 2017;**8**(5):748-58.

Van de Bool C, Van Helvoort A, Franssen FM, Wouters EF, Schols AM. Physiological effects of nutritional supplementation as adjunct to exercise training in COPD patients with low muscle mass. The double blind, placebo controlled multi-centre NUTRAIN-trial [abstract]. *European Respiratory Journal* 2016;**48**(Suppl 60):OA266.

Varas 2018 *{published and unpublished data}*

Varas AB, Cordoba S, Rodriguez-Andonaegui I, Rueda MR, Garcia-Juez S, Vilaro J. Effectiveness of a community-based exercise training programme to increase physical activity level in patients with chronic obstructive pulmonary disease: a randomized controlled trial. *Physiotherapy Research International* 2018;**23**(4):e1740.

Vasilopoulou 2017 *{published and unpublished data}*

Vasilopoulou M, Papaioannou AI, Chynkiamis N, Vasilogiannakopoulou T, Spetsioti S, Louvaris Z, et al. Effectiveness of home telerehabilitation on functional capacity and daily physical activity in COPD patients [abstract]. *European Respiratory Journal* 2015;**46**:OA273.

* Vasilopoulou M, Papaioannou AI, Kaltsakas G, Louvaris Z, Chynkiamis N, Spetsioti S, et al. Home-based maintenance tele-rehabilitation reduces the risk of acute exacerbations of COPD, hospitalisations and emergency department visits. *European Respiratory Journal* 2017;**49**(5):pii:1602129.

Vorrink 2016 *{published data only}*

Vorrink S, Huisman C, Kort H, Troosters T, Lammers JW. Perceptions of patients with chronic obstructive pulmonary disease and their physiotherapists regarding the use of an ehealth intervention. *JMIR Human Factors* 2017;**4**(3):e20.

* Vorrink SN, Kort HS, Troosters T, Zanen P, Lammers JL. Efficacy of an mHealth intervention to stimulate physical activity in COPD patients after pulmonary rehabilitation. *European Respiratory Journal* 2016;**48**(4):1019-29.

Wan 2017 *{published and unpublished data}*

Kantorowski A, Wan ES, Homsy D, Kadri R, Richardson CR, Moy ML. Determinants and outcomes of change in physical activity in COPD. *ERJ Open Research* 2018;**4**(3):pii: 00054-2018.

Robinson SA, Shimada SL, Quigley KS, Moy ML. A web-based physical activity intervention benefits persons with low self-efficacy in COPD: results from a randomized controlled trial. *Journal of Behavioral Medicine* 2019;**42**(6):1082-90.

Wan ES, Kantorowski A, Homsy D, Kadri R, Richardson CR, Mori D, et al. Self-reported task-oriented physical activity: a comparison with objective daily step count in COPD. *Respiratory Medicine* 2018;**140**:63-70.

* Wan ES, Kantorowski A, Homsy D, Teylan M, Kadri R, Richardson CR, et al. Promoting physical activity in COPD: insights from a randomized trial of a web-based intervention and pedometer use. *Respiratory Medicine* 2017;**130**:102-10.

Wan ES, Kantorowski A, Teylan M, Kadri R, Richardson CR, Garshick E, et al. Patterns of change in daily step count among COPD patients enrolled in a 3-month physical activity intervention [abstract]. *American Journal of Respiratory and Critical Care Medicine* 2017;**195**:A4939.

Watz 2016 *{published and unpublished data}*

Watz H, Mailaender C, Kirsten AM. Effects of indacaterol/glycopyrronium on lung function and physical activity in patients with moderate to severe COPD [abstract]. *Thorax* 2015;**70**:A146-7.

* Watz H, Mailander C, Baier M, Kirsten AM. Effects of indacaterol/glycopyrronium (QVA149) on lung hyperinflation and physical activity in patients with moderate to severe COPD: a randomised, placebo-controlled, crossover study (The MOVE Study). *BMC Pulmonary Medicine* 2016;**16**(1):95.

Watz 2017 *{published data only}*

Watz H, Troosters T, Beeh KM, Garcia Aymerich J, Paggiaro P, Molins E, et al. ACTIVATE: effect of aclidinium/formoterol on physical activity in patients with COPD [abstract]. *European Respiratory Journal* 2017;**60**(Suppl 61):PA687.

Watz H, Troosters T, Beeh KM, Garcia Aymerich J, Paggiaro P, Molins E, et al. Effect of aclidinium/formoterol on lung hyperinflation, exercise capacity and physical activity in patients with COPD: results from ACTIVATE, a phase IV study [abstract]. *American Journal of Respiratory and Critical Care Medicine* 2017;**195**:A3593.

* Watz H, Troosters T, Beeh KM, Garcia-Aymerich J, Paggiaro P, Molins E, et al. ACTIVATE: the effect of aclidinium/formoterol on hyperinflation, exercise capacity and physical activity in patients with COPD. *International Journal of Chronic Obstructive Pulmonary Disease* 2017;**12**:2545-58.

Widyastuti 2018 *{published data only}*

Widyastuti K, Makhabah DN, Rima A, Sutanto YS, Suradi S, Ambrosino N. Home based pulmonary rehabilitation with pedometers in Indonesian COPD patients [abstract]. *European Respiratory Journal* 2017;**50**:PA777.

* Widyastuti K, Makhabah DN, Rima Setijadi A, Sutanto YS, Suradi S, Ambrosino N. Benefits and costs of home pedometer assisted physical activity in patients with COPD: a preliminary randomized controlled trial. *Pulmonology* 2018;**24**(4):211-8.

Wootton 2017 *{published and unpublished data}*

Hill K, Wootton SL, Ng LW, Jenkins S, Cecins N, Straker L, et al. High-intensity ground-based walking does not change time spent in physical activity or sedentary behaviour in people with chronic obstructive pulmonary disease [abstract]. *Respirology* 2016;**21**(Suppl 2):TP083.

Watts SL, Ng LW, McKeogh ZJ, Jenkins S, Hill K, Eastwood PR, et al. Effects of ground walking training in COPD: a randomized controlled trial [abstract]. *Respirology* 2013;**18**(Suppl 2):O064.

* Wootton SL, Hill K, Alison JA, Ng LW, Jenkins S, Eastwood PR, et al. Effects of ground-based walking training on daily physical activity in people with COPD: a randomised controlled trial. *Respiratory Medicine* 2017;**132**:139-45.

Wootton SL, Hill K, Alison JA, Ng LW, Jenkins S, Eastwood PR, et al. Effects of ongoing feedback during a 12-month maintenance walking program on daily physical activity in people with COPD. *Lung* 2019;**197**(3):315-9.

Wootton SL, Ng LW, McKeough ZJ, Jenkins S, Hill K, Eastwood PR, et al. Ground walking training in chronic obstructive pulmonary disease: a randomised controlled trial [abstract]. *American Journal of Respiratory and Critical Care Medicine* 2014;**189**:A4162.

Wootton SL, Ng LW, McKeough ZJ, Jenkins S, Hill K, Eastwood PR, et al. Ground-based walking training improves quality of life and exercise capacity in COPD. *European Respiratory Journal* 2014;**44**(4):885-94.

References to studies excluded from this review

ACTRN12611001034921 *{published data only}*

ACTRN12611001034921. A randomised controlled clinical trial in adults with Chronic Obstructive Pulmonary Disease on the effect of telephone health-mentoring, home-based walking and rehabilitation compared with rehabilitation only on health-related quality of life. www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=343303 (first received 29 November 2011).

Aksu 2006 *{published data only}*

Aksu B, Inanir M, Basyigit I, Dursun N, Yildiz F. Comparison of two different exercise programs in chronic obstructive pulmonary disease [abstract]. *European Respiratory Journal* 2006;**28**(Suppl 50):555s.

Arnedillo 1998 *{published data only}*

Arnedillo A, Puente L, Mangas A, Leaan A. Comparison of two exercise training programmes in patients with chronic obstructive pulmonary disease [abstract]. *Neumosur* 1998;**10**(4):223-9.

Atkins 1984 *{published data only}*

Atkins CJ, Kaplan RM, Timms RM, Reinsch S, Lofback K. Behavioral exercise programs in the management of chronic

obstructive pulmonary disease. *Journal of Consulting and Clinical Psychology* 1984;**52**(4):591-603.

Barnes-Harris 2019 *{published data only}*

Barnes-Harris M, Allgar V, Booth S, Currow D, Hart S, Phillips J, et al. Battery operated fan and chronic breathlessness: does it help?. *BMJ Supportive and Palliative Care* 2019;**May 8**:pii: bmjspcare-2018-001749.

Bartlett 2017 *{published data only}*

Bartlett YK, Webb TL, Hawley MS. Using persuasive technology to increase physical activity in people with chronic obstructive pulmonary disease by encouraging regular walking: a mixed-methods study exploring opinions and preferences. *Journal of Medical Internet Research* 2017;**19**(4):e124.

Baumann 2006 *{published data only}*

Baumann HJ, Rummel K, Schmoller T, Meyer A. Efficacy of a long term ambulatory interdisciplinary rehabilitation (AIR) program in moderate to severe COPD [abstract]. *European Respiratory Journal* 2006;**28**(Suppl 50):555s.

Behnke 2000 *{published data only}*

Behnke M. The effects of a home-based exercise training programme in patients with chronic obstructive lung disease. *Pneumologie* 2000;**53**:2-3.

Behnke 2005 *{published data only}*

Behnke M, Wewel AR, Kirsten D, Jorres RA, Magnussen H. Exercise training raises daily activity stronger than predicted from exercise capacity in patients with COPD. *Respiratory Medicine* 2005;**99**(6):711-7.

Bernardi 2017 *{published data only}*

Bernardi E, Merlo C, Bellotti F, Grazzi G, Cogo A. An exercise training program improves endothelial function in COPD patients [abstract]. *European Respiratory Journal* 2017;**50**(Suppl 61):OA1959.

Bertici 2013 *{published data only}*

Bertici N, Fira-Mladinescu O, Oancea C, Tudorache V. The usefulness of pedometry in patients with chronic obstructive pulmonary disease. *Multidisciplinary Respiratory Medicine* 2013;**8**(1):7.

Biscione 2009 *{published data only}*

Biscione G, Crigna G, Auciello L, Pasqua F, Cazzola M. Addition of tiotropium (T) to a regular treatment with long-acting beta-agonist + inhaled corticosteroid (LABA + ICS) in patients with severe to very-severe COPD under in-patient pulmonary rehabilitation program (PRP) [abstract]. European Respiratory Society 19th Annual Congress; 2009 Sep 12-15; Vienna. 2009:P526.

Bohning 1990 *{published data only}*

Bohning W, Wettengel R. Physical exercise training in COPD during a 4 -week rehabilitation programme [abstract]. *European Respiratory Journal* 1990;**3**(Suppl 10):212S.

Boland 2015 *{published data only}*

* Boland MR, Tsiachristas A, Rutten van Molken M. COPD performance indicators in an integrated care program and its impact on health outcomes: The Recode Cluster Randomized Trial [abstract]. *Value in Health* 2015;**18**(7):A505.

Kruis AL, Boland MR, Assendelft WJ, Gussekloo J, Tsiachristas A, Stijnen T, et al. Effectiveness of integrated disease management for primary care chronic obstructive pulmonary disease patients: Results of cluster randomised trial. *BMJ* 2014;**349**(7976):g5392.

Börekçi 2008 *{published data only}*

Börekçi S, Elci A, Ovayolu N, Elbeck O. Applicability and efficacy of the pulmonary rehabilitation program for COPD patients in a secondary-care community hospital [Abstract]. American Thoracic Society International Conference; 2008 May 16-21; Toronto. 2008; Vol. 5, issue 5:P416.

Borges 2012 *{published data only}*

Borges RC, Carvalho CR. Physical activity in daily life in Brazilian COPD patients during and after exacerbation. *Chronic Obstructive Pulmonary Disease* 2012;**9**(6):596-602.

Bourbeau 2000 *{published data only}*

Bourbeau J, Julien M, Rouleau M, Maltais F, Beaupre A, Begin R, et al. Impact of an integrated rehabilitative self-management program on health status of COPD patients: a multicentre randomised clinical trial [abstract]. *European Respiratory Journal* 2000;**16**(Suppl 31):159s.

Budnevskiy 2015 *{published data only}*

Budnevskiy AV, Chernov AV, Isaeva YV, Yu Malysh E. Clinical efficacy of pulmonary rehabilitation program in patients with chronic obstructive pulmonary disease and metabolic syndrome. *Pulmonologiya* 2015;**25**(4):447-55.

Bunker 2012 *{published data only}*

Bunker JM, Reddel HK, Dennis SM, Middleton S, Van Schayck C, Crockett AJ, et al. A pragmatic cluster randomized controlled trial of early intervention for chronic obstructive pulmonary disease by practice nurse-general practitioner teams: study protocol. *Implementation Science* 2012;**7**:83.

Bustamante 2013 *{published data only}*

Bustamante V, Lopez de Santamaria E, Marina N, Gorostiza A, Fernandez Z, Galdiz J. Neuromuscular magnetic stimulation of the quadriceps muscle after COPD exacerbations. *European Respiratory Journal* 2013;**42**:P3572.

Camillo 2011 *{published data only}*

Camillo CA, Laburu V de M, Gonçalves NS, Cavalheri V, Tomasi FP, Hernandes NA, et al. Improvement of heart rate variability after exercise training and its predictors in COPD. *Respiratory Medicine* 2011;**105**(7):1054-62.

Cebollero 2018 *{published data only}*

* Cebollero P, Anton M, Hernandez M, Hueto J. Walking program for COPD patients: clinical impact after two years of follow-up [Programa de paseos para pacientes con EPOC: impacto clínico

tras 2 anos de seguimiento]. *Archivos de Bronconeumología* 2018;**54**(8):431-3.

Hernandez Bonaga M, Zambom F, Cascante JA, Hueto J, Anton M, Cebollero Rivas P. Walking guide for COPD patients: a promoter of physical activity?. *European Respiratory Journal* 2014;**44**:p3681.

Hernandez M, Zambom F, Cascante JA, Hueto J, Anton M, Cebollero P. Walking guide for COPD patients: can be used as a promoter of physical activity?. *European Respiratory Journal* 2013;**42**:p3703.

Hernandez M, Zambom-Ferraresi F, Milagros Anton M, Hueto J, Cascante J, Cebollero P. Short and long term effects of a physical activity programa in COPD patients. *European Respiratory Journal* 2015;**46**(Suppl 59):PA 2213.

Chen 2018 *{published data only}*

Chen K-Y, Hung M-H, Chang M-C, Kuo C, Lin C-M, Chuang L-P, et al. Four-weeks remote pulmonary rehabilitation protocol with mobile apps of real-time heart rate monitoring for gold category B/C/D-A study design. *Respirology* 2018;**23**(Suppl 2):82.

Corrado 1995 *{published data only}*

Corrado A, Gorini M, De Paola E, Martorana P, Villella G, Augustynen A, et al. Effects of a short outpatient pulmonary rehabilitation program (PRP) in severe COPD patients with chronic respiratory insufficiency (CRI) [abstract]. *European Respiratory Journal* 1995;**8**(Suppl 19):126s.

Coultas 2011 *{published data only}*

Coultas D, Sloan J, Wilson D. Pilot study of effectiveness of home rehabilitation for homebound patients with severe COPD [abstract]. European Respiratory Society 21st Annual Congress; 2011 Sep 24-28; Amsterdam. 2011:881s.

Coultas 2017 *{published data only}*

Ashmore J, Russo R, Peoples J, Sloan J, Jackson BE, Bae S, et al. Chronic obstructive pulmonary disease self-management activation research trial (COPD-SMART): design and methods. *Contemporary Clinical Trials* 2013;**35**(2):77-86.

Coultas D, Russo R, Peoples J, Ashmore J, Sloan J, Jackson B, et al. A lifestyle physical activity intervention is associated with decline in health care utilization (HCU) among patients with COPD [abstract]. *European Respiratory Journal* 2014;**44**(Suppl 58):P611.

Coultas DB, Jackson BE, Russo R, Peoples J, Singh KP, Sloan J, et al. Home-based physical activity coaching, physical activity, and healthcare utilization in COPD: COPD-SMART secondary outcomes. *Annals of the American Thoracic Society* 2018;**15**(4):470-8.

Russo R, Coultas D, Ashmore J, Peoples J, Sloan J, Jackson BE, et al. Chronic obstructive pulmonary disease self-management activation research trial (COPD-SMART): results of recruitment and baseline patient characteristics. *Contemporary Clinical Trials* 2015;**41C**:192-201.

De Backer 2014 *{published data only}*

De Backer W, Vos W, Van Holsbeke C, Vinchurkar S, Claes R, Hufkens A, et al. The effect of roflumilast in addition to LABA/LAMA/ICS treatment in COPD patients [abstract]. *European Respiratory Journal* 2014;**44**(2):527-9.

Deering 2011 *{published data only}*

Deering BM, Fullen B, Egan C, McCormack N, Kelly E, Pender M, et al. Acupuncture as an adjunct to pulmonary rehabilitation. *Journal of Cardiopulmonary Rehabilitation and Prevention* 2011;**31**(6):392-9.

De Souza 2017 *{published data only}*

De Souza Y, Da Sliva KM, Condesso D, Figueira B, Alves RR, Costa CH, et al. Home-based pulmonary rehabilitation intervention: does it maintain the benefits achieved during the outpatient program [abstract]. *American Journal of Respiratory and Critical Care Medicine* 2017;**195**:A941.

Durheim 2015 *{published data only}*

Durheim MT, Smith PJ, Babyak MA, Mabe SK, Emery CF, Blumenthal JA, et al. Physical function as measured by 6-minute walk distance or accelerometry predicts clinical outcomes in COPD patients independent of GOLD 2011 [abstract]. *American Journal of Respiratory and Critical Care Medicine* 2014;**189**:A6679.

* Durheim MT, Smith PJ, Babyak MA, Mabe SK, Martinu T, Welty-Wolf KE, et al. Six-minute-walk distance and accelerometry predict outcomes in chronic obstructive pulmonary disease independent of Global Initiative for Chronic Obstructive Lung Disease 2011 Group. *Annals of the American Thoracic Society* 2015;**12**(3):349-56.

Dyer 2011 *{published data only}*

Dyer F, Flude L, Bazari F, Jolley C, Englebretsen C, Lai D, et al. Non-invasive ventilation (NIV) as an aid to rehabilitation in acute respiratory disease. *BMC Pulmonary Medicine* 2011;**11**:58.

EUCTR2016-003675-21-ES *{published data only}*

EUCTR2016-003675-21-ES. A study to test different doses of Danirixin in patients with COPD. www.clinicaltrialsregister.eu/ctr-search/trial/2016-003675-21/results (first received 18 April 2017).

Faulkner 2010 *{published data only}*

Faulkner J, Walshaw E, Campbell J, Jones R, Taylor R, Price D, et al. The feasibility of recruiting patients with early COPD to a pilot trial assessing the effects of a physical activity intervention. *Primary Care Respiratory Journal* 2010;**19**(2):124-30.

Fernandez 1998 *{published data only}*

Fernandez J, Martin M, Moreno LF. Evaluation of a home-based rehabilitation program controlled with pulse-meter in COPD. *Neumosur* 1998;**10**(1):54-5.

Foy 2006 *{published data only}*

Foy CG, Wickley KL, Adair N, Lang W, Miller ME, Rejeski WJ, et al. The Reconditioning Exercise and Chronic Obstructive Pulmonary Disease Trial II (REACT II): Rationale and study

design for a clinical trial of physical activity among individuals with chronic obstructive pulmonary disease. *Contemporary Clinical Trials* 2006;**27**(2):135-46.

Friis 2017 *{published data only}*

Friis AL, Steenholt CB, Lokke A, Hansen M. Dietary beetroot juice - effects on physical performance in COPD patients: a randomized controlled crossover trial. *International Journal of Chronic Obstructive Pulmonary Disease* 2017;**12**:1765-73.

Furness 2014 *{published data only}*

Furness T, Joseph C, Naughton G, Welsh L, Lorenzen C. Benefits of whole-body vibration to people with COPD: a community-based efficacy trial. *BMC Pulmonary Medicine* 2014;**14**(1):38.

Garcia Aymerich 2016 *{published data only}*

Garcia Aymerich J, Puham M, De Jongh C, Demeyer H, Erzen D, Gimeno Santos E, et al. Responsiveness of PROactive instruments to measure physical activity in COPD patients [abstract]. *European Respiratory Journal* 2016;**48**:PA1896.

Gohl 2004 *{published data only}*

Gohl O, Linz H, Otte B, Schonleben T, Weineck J, Worth H. Benefits of a multicomponent outpatient rehabilitation program for patients with chronic obstructive pulmonary disease [abstract]. American Thoracic Society 100th International conference; 2004 May 21-26; Orlando. 2004:D14.

* Gohl O, Linz H, Otte B, Schonleben T, Weineck J, Worth H. Effects of multicomponent outpatient rehabilitation program for patients with COPD [abstract]. *European Respiratory Journal* 2004;**24**(Suppl 48):208s.

Gohl 2006 *{published data only}*

Gohl O, Schacher C, Grensemann S, Worth H. Effects of inspiratory muscle training with the RESPIFIT S in addition to an outpatient exercise training program for patients with COPD [abstract]. *European Respiratory Journal* 2006;**28**(Suppl 50):556s.

Gomez 2006 *{published data only}*

Gomez A, Roman M, Larraz C, Esteva M, Mir I, Thomas V, et al. Efficacy of respiratory rehabilitation on patients with moderate COPD in primary care and maintenance of benefits at 2 years. *Atencion Primaria / Sociedad Espanola de Medicina de Familia y Comunitaria* 2006;**38**(4):230-3.

Gosselink 1990 *{published data only}*

Gosselink H, Van Keimpema A, Wagenaar R, Chadwick Straver R. The relative efficacy of a rehabilitation-programme in COPD patients [abstract]. *European Respiratory Journal* 1990;**10**(Suppl 10):212S.

Grabenhorst 2013 *{published data only}*

Grabenhorst M, Jehn M, Maldener N, Liebers U, Kohler F, Witt C. Telemedicine in patients with COPD: Feasibility and benefit of regular exercise testing via remote patient monitoring [abstract]. *Pneumologie* 2013;**67**:P377.

Greulich 2013 *{published data only}*

Greulich T, Augsten M, Kehr K, Nell C, Koehler U, Werner J. A randomized clinical trial to assess the influence of a three months training program (individualized vs. non-individualized) in patients with moderate to very severe COPD [abstract]. *American Journal of Respiratory and Critical Care Medicine* 2012;**185**:A4874.

* Greulich T, Kehr K, Nell C, Haid D, Koehler U, Koehler K, et al. A randomized clinical trial comparing the influence of two different training modalities (individualized vs. non-individualized) in patients with moderate to very severe COPD [abstract]. *American Journal of Respiratory and Critical Care Medicine* 2013;**187**:A1801.

Guell 2008 *{published data only}*

* Guell MR, De Lucas P, Galdiz JB, Montemayor T, Gonzalez-Moro JM, Gorostiza A, et al. Home versus hospital-based pulmonary rehabilitation for patients with chronic obstructive pulmonary disease: a Spanish multicenter trial. *Archivos de Bronconeumología* 2008;**44**(10):512-8.

Guell R, Delucas P, Galdiz JB, Montemayor T, Rodriguez JM, Gorostiza A, et al. Effectiveness of a home based pulmonary rehabilitation program compared to a hospital based pulmonary rehabilitation program in COPD patients, a Spanish multicenter randomized trial [abstract]. *European Respiratory Journal* 2006;**28**(Supp 50):298s.

Gurgun 2011 *{published data only}*

Gurgun A, Tuncel S, Korkmaz Ekren P, Deniz PS, Karapolat H, Kayahan B. Efficacy of an eight-week pulmonary rehabilitation in COPD patients: an experience of a single center in Turkey [abstract]. *American Journal of Respiratory and Critical Care Medicine* 2011;**183**:A5049.

Hartman 2012 *{published data only}*

Hartman JE, Boezen M, Heintzbergen S, De Greef MH, Klooster K, Ten Hacken NH, et al. Daily physical activity after bronchoscopic lung volume reduction: a pilot study. *European Respiratory Journal* 2012;**40**:1566-7.

Hataji 2017 *{published data only}*

Hataji O, Nishii Y, Ito K, Sakaguchi T, Saiki H, Suzuki Y, et al. Smart watch-based coaching with tiotropium and olodaterol ameliorates physical activity in patients with chronic obstructive pulmonary disease. *Experimental and Therapeutic Medicine* 2017;**14**(5):4061-4.

Herrejon 2010 *{published data only}*

Herrejon A, Catalan P, Palop J, Inchaurraga I, Blanquer R, Lopez A, et al. Effect of 8-week 320 mg Megestrol acetate daily administration In severe COPD and weight loss [abstract]. *American Journal of Respiratory and Critical Care Medicine* 2010;**181**:A4484.

Hillegass 2012 *{published data only}*

Hillegass E, Hayes D, Sanders D, Owens T, Langbehn C, Johnson M, et al. Continuous versus pulsed oxygen: is there a difference with activity? A pilot study [abstract]. *Chest* 2012;**142**(4):802A.

Horton 2018 *{published data only}*

Horton EJ, Mitchell KE, Johnson-Warrington V, Apps LD, Sewell L, Morgan M, et al. Comparison of a structured home-based rehabilitation programme withe conventional supervised pulmonary rehabilitation: a randomised non-inferiority trial. *Thorax* 2018;**73**:29-36.

Ichinose 2017 *{published data only}*

Ichinose M, Minakata Y, Motegi T, Ueki J, Gon Y, Seki T. Efficacy of tiotropium/olodaterol on lung volume, exercise capacity, and physical activityet al. *International Journal of Chronic Obstructive Pulmonary Disease* 2018;**13**:1407-19.

Ichinose M, Minakata Y, Motegi T, Ueki J, Gon Y, Seki T, et al. Efficacy of tiotropium/olodaterol on lung hyperinflation, exercise capacity, and physical activity in Japanese patients with Chronic Obstructive Pulmonary Disease (VESUTO Study): a randomized crossover trial [abstract]. *American Journal of Respiratory and Critical Care Medicine* 2018;**197**:A4243.

* Ichinose M, Minakata Y, Motegi T, Ueki J, Seki T, Anzai T, et al. Study design of VESUTO: efficacy of tiotropium/olodaterol on lung hyperinflation, exercise capacity and physical activity in Japanese patients with chronic obstructive pulmonary disease. *Advances in Therapy* 2017;**34**(7):1622-35.

Ichinose M, Minakata Y, Motegi T, Ueki J, Seki T, Anzai T, et al. Study design of VESUTO; study to evaluate the efficacy of tiotropium + olodaterol vs tiotropium on lung hyperinflation, exercise capacity, and physical activity in Japanese COPD patients [abstract]. *Respirology* 2016;**21**(S3):APSR6-0457.

Minakata Y, Motegi T, Ueki J, Gon Y, Seki T, Anzai T, et al. Efficacy of tiotropium/olodaterol on sedentary/active time in COPD patients: VESUTO study [abstract]. *European Respiratory Journal* 2018;**52**(Suppl 62):PA4390.

Ides 2012 *{published data only}*

Ides KM, De Backer L, Daems D, Boelen E, Leemans G, Vissers D, et al. Preliminary results of noninvasive ventilation during a pulmonary rehabilitation program in patients with COPD [abstract]. *European Respiratory Journal* 2012;**50**(Suppl 56):639s.

Innocenti 2000 *{published data only}*

Innocenti F, Fabbri A, Guerrini M, Fonseca D, Lippi P. Results of an outpatient pulmonary rehabilitation program in patients with COPD [abstract]. *European Respiratory Journal* 2000;**16**(Suppl 31):46s.

Johnson-Warrington 2016 *{published data only}*

Johnson-Warrington V, Rees K, Gedler C, Morgan MD, Singh SJ. Can a supported self-management program for COPD upon hospital discharge reduce readmissions? A randomized controlled trial. *International Journal of Chronic Obstructive Pulmonary Disease* 2016;**11**:1161-9.

Jonsdottir 2015 *{published data only}*

Jonsdottir H, Amundadottir OR, Gudmundsson G, Halldorsdottir BS, Hrafnkelsson B, Ingadottir TS, et al. Effectiveness of a partnership-based self-management programme for patients with mild and moderate chronic obstructive pulmonary disease: a pragmatic randomized controlled trial. *Journal of Advanced Nursing* 2015;**71**(11):2634-49.

Kato 2017 *{published data only}*

Kato D, Dobashi K, Fueki M, Tomioka S, Yamada H, Fueki N. Short-term and long-term effects of a self-managed physical activity program using a pedometer for chronic respiratory disease: a randomized controlled trial. *Journal of Physical Therapy Science* 2017;**89**:807-12.

Kim 2003 *{published data only}*

Kim DS, Na JO, Jegal YJ, Yoon SH, Shim TS, Lim CM, et al. Efficacy of home based pulmonary rehabilitation program for the patients with chronic lung diseases [abstract]. *European Respiratory Journal* 2003;**22**(Suppl 45):A1082.

Kruis 2014 *{published data only}*

Kruis AL, Boland MR, Assendelft WJ, Gussekloo J, Tsiachristas A, Stijnen T, et al. Effectiveness of integrated disease management for primary care chronic obstructive pulmonary disease patients: Results of cluster randomised trial. *BMJ Online* 2014;**349**(7976):g5392.

Langer 2018 *{published data only}*

Langer D, Ciavaglia C, Faisal A, Webb KA, Neder JA, Gosselink R, et al. Inspiratory muscle training reduces diaphragm activation and dyspnea during exercise in COPD. *Journal of Applied Physiology* 2018;**125**(2):381-92.

Larraz 2010 *{published data only}*

Larraz C, Esteva M, Ripoll J, Mir I, Gómez A, Román M. Efficacy of a rehabilitation program on moderate COPD conducted in primary care and the maintenance of benefits during two years [abstract]. *Primary Care Respiratory Journal* 2010;**19**(2):A22.

Lee 2007 *{published data only}*

Lee KH, Shin KC, Chung JH, Yu SK. Effects of self-efficacy promoting pulmonary rehabilitation program for chronic obstructive pulmonary disease patients [abstract]. American Thoracic Society International Conference; 2007 May 18-23; San Francisco. 2007:M60.

Liang 2018 *{published data only}*

Liang J, Abramson M, Zwar N, Russell G, Holland A, Bonevski B, et al. An interdisciplinary model of care for the early detection and management of chronic obstructive pulmonary disease (COPD) in primary care-the RADICALS trial [abstract]. *Respirology* 2016;**21**(Suppl 2):61.

* Liang J, Abramson MJ, Zwar NA, Russell GM, Holland AE, Bonevski M, et al. Diagnosing COPD and supporting smoking cessation in general practice: evidence–practice gaps. *Medical Journal of Australia* 2018;**208**(1):29-34.

Liu 2019 *{published data only}*

Liu X, Li P, Xiao L, Lu Y, Li N, Wang Z, et al. Effects of home-based prescribed pulmonary exercise by patients with chronic obstructive pulmonary disease: study protocol for a randomized controlled trial. *Trials* 2019;**20**(1):41.

Lum 2007 *{published data only}*

Lum CM, Woo J, Yeung F, Hui DS, Hui E. Semi-supervised, domiciliary pulmonary rehabilitation programme: a controlled clinical trial. *Hong Kong Medical Journal* 2007;**13**(Suppl 5):42-5.

Mahesh 2017 *{published data only}*

* Mahesh PA, Srikanth JN, Ananthakrishna MS, Parthasarathi G, Chaya SK, Rajgopal R, et al. Amelioration of quality of life and lung function of chronic obstructive pulmonary disease by pranic healing as adjuvant therapy: a randomised double blind placebo controlled pilot study. *Australasian Medical Journal* 2017;**10**(8):665-73.

Marques 2019 *{published data only}*

Marques A, Jacome C, Rebelo P, Paixao C, Oliveira A, Cruz J, et al. Improving access to community-based pulmonary rehabilitation: 3R protocol for real-world settings with cost-benefit analysis. *BMC Public Health* 2019;**19**(1):676.

Martinez 2008 *{published data only}*

Martinez G, Thogersen J, Brondum E, Ringaek T, Lange P. Effect of maintenance training after 7 weeks rehabilitation programme [abstract]. European Respiratory Society 18th Annual Congress; 2008 Oct 3-7; Berlin. 2008:E2805.

McGlone 2006 *{published data only}*

McGlone S, Venn A, Walters EH, Wood-Baker R. Physical activity, spirometry and quality-of-life in chronic obstructive pulmonary disease. *COPD* 2006;**3**(2):83-8.

McMahon 2000 *{published data only}*

McMahon S, Small T, Higgins BG, Corris PA. The use of a novel patient activity monitor to assess the therapeutic effect of adding salmeterol to regular therapy in patients with chronic obstructive pulmonary disease [abstract]. *Thorax* 2000;**55**(Suppl 3):A40.

Mesquita 2017 *{published data only}*

Mesquita R, Meijer K, Pitta F, Azcuna H, Goertz YM, Essers JM, et al. Changes in physical activity and sedentary behaviour following pulmonary rehabilitation in patients with COPD. *Respiratory Medicine* 2017;**126**:122-9.

Moore 2009 *{published data only}*

Moore R, Berlowitz D, Denehy L, Jackson B, McDonald CF. Comparison of pedometer and activity diary for measurement of physical activity in chronic obstructive pulmonary disease. *Journal of Cardiopulmonary Rehabilitation and Prevention* 2009;**29**(1):57-61.

Morris 2012 *{published data only}*

Atkinson C, Seale H, Walsh J, Adams L, Morris NR. The addition of a pedometer-guided intervention to pulmonary rehabilitation fails to improve physical activity levels in individuals with COPD [abstract]. *Respirology* 2012;**17**(Suppl 1):64.

* Morris NR, Atkinson C, Seale H, Walsh J. The addition of a pedometer guided intervention to pulmonary rehabilitation [abstract]. *American Journal of Respiratory and Critical Care Medicine* 2012;**185**:A2383.

Moy 2009 *{published data only}*

Moy ML, Matthess K, Stolzmann K, Reilly J, Garshick E. Free-living physical activity in COPD: assessment with accelerometer and activity checklist. *Journal of Rehabilitation Research and Development* 2009;**46**(2):277-86.

Moy 2012 *{published data only}*

Moy ML, Weston NA, Wilson EJ, Hess ML, Richardson CR. A pilot study of an Internet walking program and pedometer in COPD. *Respiratory Medicine* 2012;**106**(9):1342-50.

Murphy 2005 *{published data only}*

Murphy MC, Campbell M, Saunders JE, Jackson B. A randomized trial to compare the outcomes of a pulmonary rehabilitation program (PRP) weekly maintenance and the Stanford Model Chronic Disease Self Management Program (CDSMP) in COPD [abstract]. American Thoracic Society International Conference; 2005 May 20-25; San Diego. 2005:A26.

Nagata 2018 *{published data only}*

* Nagata K, Kikuchi T, Horie T, Shiraki A, Kitajima T, Kadowaki T, et al. Domiciliary high-flow nasal cannula oxygen therapy for patients with stable hypercapnic Chronic Obstructive Pulmonary Disease. A multicenter randomized crossover trial. *Annals of the American Thoracic Society* 2018;**15**(4):422-39.

Nagata K, Kikuchi T, Horie T, Shiraki A, Kitajima T, Kadowaki T, et al. Domiciliary high-flow nasal cannula oxygen therapy for stable hypercapnic chronic obstructive pulmonary disease: a prospective, multicentre, randomised crossover trial [abstract]. *European Respiratory Journal* 2017;**50**:OA4428.

NCT00620022 *{published data only}*

O'Donnell D, Casaburi R, Vincken W, Puente-Maestu L, Swales J, Lawrence D, et al. Effect of indacterol on exercise endurance and lung hyperinflation in COPD. *Respiratory Medicine* 2011;**105**(7):1030-6.

NCT01012765 *{published data only}*

Watz H, Krippner F, Kirsten A, Magnussen H, Vogelmeier C. Effects of indacaterol on lung volumes and physical activity In moderate chronic obstructive pulmonary disease [abstract]. *American Journal of Respiratory and Critical Care Medicine* 2012;**185**:A2257.

* Watz H, Krippner F, Kirsten A, Magnussen, Vogelmeier C. Indacaterol improves lung hyperinflation and physical activity in patients with moderate chronic obstructive pulmonary disease - a randomized, multicenter, double-blind, placebo-controlled study. *BMC Pulmonary Medicine* 2014;**14**(1):158.

NCT01380652 *{published data only}*

NCT01380652. Effects of whole body vibration training on physical activity in Chronic Obstructive Pulmonary Disease (COPD) III/IV patients during a three-week rehabilitation. clinicaltrials.gov/ct2/show/NCT01380652 (first received 27 June 2011).

NCT01486186 *{published data only}*

Wang M, Li J, Li S, Wang H, Yu X, Zhang H. Effect of traditional Chinese medicine on outcomes in patients with mild/moderate

chronic obstructive pulmonary disease: study protocol for a randomized placebo-controlled trial. *Trials* 2012;**13**:109.

NCT01722370 *{published data only}*

NCT01722370. Ambulatory oxygen effects on muscles in COPD (OM-COPD). clinicaltrials.gov/ct2/show/NCT01722370 (first received 6 November 2012).

NCT01854008 *{published data only}*

* Pleguezuelos E, Pérez ME, Guirao L, Samitier B, Costea M, Ortega P, et al. Improving physical activity in patients with COPD with urban walking circuits. *Respiratory Medicine* 2013;**107**(12):1948-56.

Pleguezuelos E, Pérez ME, Guirao L, Samitier B, Costea M, Ortega P, et al. Improving physical activity in patients with severe COPD with urban walking circuits. A randomised trial [abstract]. European Respiratory Society Annual Congress; 2013 September 7-11; Barcelona. 2013; Vol. 42, issue Suppl 57:302s.

NCT01867970 *{published data only}*

* Van der Weegen S, Verwey R, Spreeuwenberg M, Tange H, Van der Weijden T, De Witte L. It's LiFe! Mobile and web-based monitoring and feedback tool embedded in primary care increases physical activity: a cluster randomized trial. *Journal of Medical Internet Research* 2015;**17**(7):e184.

Verwey R, Van der Weegen S, Spreeuwenberg M, Tange H, Van der Weijden T, De Witte L. A monitoring and feedback tool embedded in a counselling protocol to increase physical activity of patients with COPD or type 2 diabetes in primary care: study protocol of a three-arm cluster randomised controlled trial. *BMC Family Practice* 2014;**15**:93.

NCT01871025 *{published data only}*

Rodriguez DA, Rodopin A, Guerrero M, Coll R, Huerta A, Soler N, et al. Impact of step exercises as an early intervention during COPD exaverbation [abstract]. *European Respiratory Journal* 2016;**48**:PA2061.

NCT02100709 *{published data only}*

NCT02100709. The effect of NIV on QoL and exercise capacity in a COPD exercise rehabilitation program. clinicaltrials.gov/ct2/show/NCT02100709 (first received 27 March 2014).

NCT02172794 *{published data only}*

NCT02172794. Tiotropium inhalation capsules and salmeterol inhalation aerosol on muscular efficiency and resting energy expenditure in patients with stable chronic obstructive pulmonary disease. clinicaltrials.gov/ct2/show/NCT02172794 (first received 24 June 2014).

NCT02629965 *{published data only}*

NCT02629965. Comparing the efficacy of tiotropium + olodaterol fixed dose combination over tiotropium in improvement of lung hyperinflation, exercise capacity and physical activity in Japanese COPD patients. clinicaltrials.gov/ct2/show/NCT02629965 (first received 15 December 2015).

NCT02656667 *{published data only}*

Vivodtzev I, Debigaré R, Gagnon P, Mainguy V, Saey D, Dubé A, et al. Functional and muscular effects of neuromuscular electrical stimulation in patients with severe COPD: a randomized clinical trial. *Chest* 2012;**141**(3):716-25. [DOI: 10.1378/chest.11-0839; NCT02656667]

NCT03751670 *{published data only}*

NCT03751670. Pulmonary rehabilitation during acute exacerbations of Chronic Obstructive Pulmonary Disease: a mixed-methods approach. clinicaltrials.gov/ct2/show/NCT03751670 (first received 23 November 2018).

NL1729 *{published data only}*

NL1729. Effects of a phyisiotherapeutic exercise programme in patients with a combination of COPD and chronic heart failure: the CHEST-study. www.trialregister.nl/trial/1729 (first received 2009).

Norweg 2006 *{published data only}*

Norweg AM, Whiteson J, Malady R, Mola A, Rey M. The effectiveness of different combinations of pulmonary rehabilitation program components: a randomized controlled trial. *Journal of Cardiopulmonary Rehabilitation* 2006;**26**(2):120-1.

Nyberg 2017 *{published data only}*

Nyberg A, Wadell K, Lindgren H, Tistad M. Internet-based support for self-management strategies for people with COPD-protocol for a controlled pragmatic pilot trial of effectiveness and a process evaluation in primary healthcare. *BMJ Open* 2017;**7**(7):e016851.

Paneroni 2016 *{published data only}*

Paneroni M, Scalvini S, Bernocchi P, Galli T, Baratti D, La Rovere MT, et al. Home telerehabilitation maintenance program for patients affected by COPD and CHF [abstract]. *European Respiratory Journal* 2016;**48**(Suppl 60):OA268.

Pasqua 2010 *{published data only}*

Pasqua F, Biscione G, Crigna G, Auciello L, Cazzola M. Combining triple therapy and pulmonary rehabilitation in patients with advanced COPD: A pilot study. *Respiratory Medicine* 2010;**104**(3):412-7.

Pinnock 2013 *{published data only}*

Pinnock H, Hanley J, Lewis S, MacNee W, Pagliari C, Van der Pol M, et al. The impact of a telemetric chronic obstructive pulmonary disease monitoring service: Randomised controlled trial with economic evaluation and nested qualitative study. *Primary Care Respiratory Journal* 2009;**18**(3):233-5.

Pitta 2008 *{published data only}*

Pitta F, Takaki MY, Oliveira NH, Sant'anna TJ, Fontana AD, Kovelis D, et al. Relationship between pulmonary function and physical activity in daily life in patients with COPD. *Respiratory Medicine* 2008;**102**(8):1203-7.

Pomidori 2012 *{published data only}*

Pomidori L, Contoli M, Mandolesi G, Cogo A. A simple method for home exercise training in patients with chronic obstructive pulmonary disease: One-year study. *Journal of Cardiopulmonary Rehabilitation and Prevention* 2012;**32**(1):53-7.

Raphael 2014 *{published data only}*

Raphael Y, Maynard Da Silva K, Bessa EJ, Bartholo TP, Faria AC, Noronha Filho AJ, et al. Brazilian manual of home-based pulmonary rehabilitation: does it maintain the benefits achieved during the outpatient program? [abstract]. *American Journal of Respiratory and Critical Care Medicine* 2014;**189**:A1913.

Ringbaek 2009 *{published data only}*

Ringbaek T, Broendum E, Martinez G, Thoegersen J, Lange P. Effect of maintenance training after 7-weeks rehabilitation programme on hospitalisation [abstract]. European Respiratory Society 19th Annual Congress; 2009 Sep 12-15; Vienna. 2009:P576.

Robbins 2000 *{published data only}*

Robbins R. More evidence for the short-term beneficial effects of lung volume reduction surgery. *Critical Care* 2002;**2**(1):6379.

Rodriguez-Trigo 2011 *{published data only}*

Rodriguez-Trigo G, Cejudo P, Puy C, Galdiz JB, Bdeir K, Gorostiza A, et al. Long term pulmonary rehabilitation programs for chronic obstructive pulmonary disease (COPD). Two years follow-up [abstract]. *European Respiratory Journal* 2011;**38**(55):655s.

Romagnoli 2005 *{published data only}*

Romagnoli M, Dell'Orso D, Lubello R, Lucic S, Lugli D, Bellantone T, et al. Repeated pulmonary rehabilitation program (PRP) in severe and disabled COPD patients [abstract]. *European Respiratory Journal* 2005;**26**(Supp 49):A542.

Roman 2013 *{published data only}*

Roman M, Larraz C, Gomez A, Ripoll J, Mir I, Miranda EZ, et al. Efficacy of pulmonary rehabilitation in patients with moderate chronic obstructive pulmonary disease: a randomized controlled trial. *BMC Family Practice* 2013;**14**(1):21.

Schacher 2006 *{published data only}*

Schacher C, Dhein Y, Schoeffski O, Worth H. Comparison of two different exercise programs in chronic obstructive pulmonary disease [abstract]. *European Respiratory Journal* 2006;**28**(Suppl 50):555s.

Schönhofer 1997 *{published data only}*

Schönhofer B, Ardes P, Geibel M, Köhler D, Jones PW. Evaluation of a movement detector to measure daily activity in patients with chronic lung disease. *European Respiratory Journal* 1997;**10**(12):2814-9.

Senthilnathan 2018 *{published data only}*

Senthilnathan CV, Abinaya P, Rajalaxmi V, Mohan Kumar G, Subramanian SS. Efficacy of physical training program on chronic obstructive pulmonary disease [abstract]. *Biomedicine* 2018;**38**(2):240.

Sewell 2005 *{published data only}*

* Sewell L, Singh SJ, Williams JE, Collier R, Morgan MD. Can individualized rehabilitation improve functional independence in elderly patients with COPD?. *Chest* 2005;**128**(3):1194-200.

Sewell L, Singh SJ, Williams JE, Collier R, Morgan MD. Goal directed pulmonary rehabilitation does not significantly improve health status and domestic function. *European Respiratory Journal* 2001;**18**(Suppl 33):187s.

Sewell 2010 *{published data only}*

Sewell L, Singh SJ, Williams JE, Morgan MD. Seasonal variations affect physical activity and pulmonary rehabilitation outcomes. *Journal of Cardiopulmonary Rehabilitation and Prevention* 2010;**30**(5):329-33.

Sirichana 2013 *{published data only}*

Sirichana W, Moore-Gillon CE, Patel MH, Taylor M, Storer TW, Cooperr CB. Daily physical activity in COPD: quantification by tri-axial accelerometry [abstract]. *American Journal of Respiratory and Critical Care Medicine* 2013;**187**:A1361.

Soicher 2009 *{published data only}*

Soicher JE. A longitudinal study of physical activity behaviour in chronic disease: the example of chronic obstructive pulmonary disease [dissertation]. Montreal: McGill University, Montreal, 2009.

Spencer 2012 *{published data only}*

Spencer L, Mckeough Z, Alison J. Where are they now? Four years after the completion of a maintenance exercise programme in people with COPD [abstract]. *Respirology* 2012;**17**(Suppl 1):15.

Steele 2008 *{published data only}*

* Steele BG, Belza B, Cain KC, Coppersmith J, Lakshminarayan S, Howard J, et al. A randomized clinical trial of an activity and exercise adherence intervention in chronic pulmonary disease. *Archives of Physical Medicine and Rehabilitation* 2008;**89**(3):404-12.

Steele BG, Belza B, Coppersmith J, Cain K, Howard J, Lakshminarayan S. Promoting activity and exercise in chronic lung disease: an intervention study [abstract]. *American Journal of Respiratory and Critical Care Medicine* 2005;**191**:A2007.

Strijbos 1991 *{published data only}*

Strijbos JH, Koeter GH, Postma DS, Van Altena R. Reactivation of severe COPD patients. Long term results of a first line and a clinical rehabilitation program. *Nederlands Tijdschrift Fysiotherapie* 1991;**101**(4):105-10.

Sutanto 2018 *{published data only}*

Sutanto YS, Santi N, Makhabah DN, Aphridasari J, Kusumo H, Reviono R. Pedometer as a tool for quality of life improvement in COPD patients [abstract]. *Respirology* 2018;**23**(Suppl 2):244-5.

TCTR20170214002 *{published data only}*

TCTR20170214002. The effects of breathing with a positive expiratory pressure on physical activity in patients with Chronic Obstructive Pulmonary Disease. www.clinicaltrials.in.th/index.php?tp=regtrials&menu=trialsearch&smenu=fulltext&task=search&task2=view1& (first received 5 February 2017).

Troosters 2010 *{published data only}*

Troosters T, Sciurba F, Battaglia S, Langer D, Valluri SR, Martino L, et al. Physical inactivity in patients with COPD, a controlled multi-center pilot-study. *Respiratory Medicine* 2010;**104**(7):1005-11.

Troosters 2011 *{published data only}*

Troosters T, Sutradhar S, Sciurba FC, Klioze SS, Siafakas N, Yunis C, et al. Understanding physical activity in moderate COPD: results from a large, multicenter trial [abstract]. *American Journal of Respiratory and Critical Care Medicine* 2011;**183**:A3959.

Tse 2013 *{published data only}*

Tse HN, Raiteri L, Wong KY, Yee KS, Ng LY, Wai KY, et al. High-dose N-acetylcysteine in stable COPD: the 1-year, double-blind, randomized, placebo-controlled HIACE study. *Chest* 2013;**144**(1):106-18.

Turnbull 2013 *{published data only}*

* Turnbull J, McDonnell L, Bott J, Prevost T, Davidson C. Physical exercise and ambulatory oxygen device preference in patients' with exertional hypoxemia: a multicentre RCT [abstract]. *European Respiratory Journal* 2013;**42**(Suppl 57):772s.

Turnbull J, McDonnell L, Osman L, Bott J, Prevost T, Davidson AC. Patient activity levels and oxygen device preference: an RCT comparing refillable cylinders (HomefillTM) with usual ambulatory device [abstract]. *Thorax* 2012;**67**(Suppl 2):A83.

Turner-Lawlor 2005 *{published data only}*

Turner-Lawlor PJ, Shiels K, Griffiths TL. Randomized controlled trial of an 18 session pulmonary rehabilitation program delivered over 6 or 18 weeks, clinical outcomes [abstract]. American Thoracic Society International Conference; 2005 May 20-25; San Diego. 2005:C87.

U1111-1169-0718 *{published data only}*

U1111-1169-0718. Effect of training in vibrating platform in subjects with Chronic Obstructive Pulmonary Disease. www.ensaiosclinicos.gov.br/rg/RBR-3kxkzn/ (first received 7 April 2015).

UMIN000001833 *{published data only}*

Sakai K, Nakayama H, Hokari S, Suzuki R, Takiguchi A, Takada T, et al. The efficacy of the assistant use of short-acting Beta2 stimulant procaterol on the daily activity in COPD patients: Niigata multicentre study [abstract]. *European Respiratory Journal* 2011;**38**:862.

Valenson 2016 *{published data only}*

Valenson W, Valmonte F, Rodriguez O, Medina E, Lowrey M, Lew S, et al. Perceived barriers to physical activity in patients at high risk for COPD exacerbations. *Chest* 2016;**150**(4 Suppl 1):892A.

Voncken-Brewster 2013 *{published data only}*

Voncken-Brewster V, Tange H, De Vries H, Nagykaldi Z, Winkens B, Van der Weijden T. A randomised controlled trial testing a web-based, computer-tailored self-management intervention for people with or at risk for chronic obstructive pulmonary disease: a study protocol. *BMC Public Health* 2013;**13**:557.

* Voncken-Brewster V, Tange H, De Vries H, Nagykaldi Z, Winkens B, Van der Weijden T. A randomized controlled trial evaluating the effectiveness of a web-based, computer-tailored self-management intervention for people with or at risk for COPD. *International Journal of Chronic Obstructive Pulmonary Disease* 2015;**10**:1061-73.

Wilson 2015 *{published data only}*

Wilson AM, Browne P, Olive S, Clark A, Galey P, Dix E, et al. The effects of maintenance schedules following pulmonary rehabilitation in patients with chronic obstructive pulmonary disease: a randomised controlled trial. *BMJ Open* 2015;**5**(3):e005921.

Zanini 2002 *{published data only}*

Zanini A, Giorgetti G, Facchetti C, Mazzucchelli G, Conti S, Lucioni A, et al. Efficacy of a rehabilitation program based on circuit training in COPD subjects: A preliminary report [abstract]. *American Journal of Respiratory and Critical Care Medicine* 2002;**165**(Suppl 8):A738.

References to ongoing studies

ACTRN12615000121561 *{published data only}*

ACTRN12615000121561. Effect of opioids on outcomes of pulmonary rehabilitation. www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=367581 (first received 12 January 2015).

ACTRN 12616000360415 *{published data only}*

* Cox NS, McDonald CF, Alison JA, Mahal A, Wootton R, Hill CJ, et al. Telerehabilitation versus traditional centre-based pulmonary rehabilitation for people with chronic respiratory disease: protocol for a randomised controlled trial. *BMC Pulmonary Medicine* 2018;**18**:71.

ACTRN12616001534471 *{published data only}*

ACTRN12616001534471. A behaviour-change intervention to reduce sedentary time in people with chronic obstructive pulmonary disease. www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=371728 (first received 3 Nov 2016).

* Cheng SW, Alison JA, Dennis S, Stamatakis E, Spencer LM, McNamara RJ, et al. A behaviour change intervention to reduce sedentary time in people with chronic obstructive pulmonary disease: a protocol for a randomised controlled trial. *Journal of Physiotherapy* 2017;**63**:182.

ACTRN12616001586404 *{published data only}*

ACTRN12616001586404. Effect of a pulmonary rehabilitation program of 8 weeks duration compared to 12 weeks on exercise capacity in people with chronic obstructive pulmonary disease (PuRe Duration): a randomised controlled trial. www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=371612 (first received 16 November 2016).

ACTRN12617000242325 *{published data only}*

ACTRN12617000242325. Tai Chi for people with chronic obstructive pulmonary disease (COPD). www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=372216 (first received 16 February 2017).

ACTRN12617000499381 *{published data only}*

ACTRN12617000499381. Non drug interventions to reduce breathlessness in patients with chronic obstructive pulmonary disease (emphysema). www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=372467 (first received 6 April 2017).

ACTRN12617000653369 *{published data only}*

ACTRN12617000653369. Effect of cognitive behaviour therapy on anxiety, depression and breathlessness in patients with chronic obstructive pulmonary disease. www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=372765 (first received 5 May 2017).

ANZCTR12611000292976 *{published data only}*

ANZCTR12611000292976. Can changing the way people with chronic lung disease think about breathlessness improve and sustain health outcomes?. www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=336473 (first received 17 March 2011).

Williams MT, John D, Cafarella P, Frith P. No additional benefit for 6MWT or HADS in combining cognitive behavioural therapy and pulmonary rehabilitation [abstract]. *Respirology* 2017;**22**(S2):TO050.

* Williams MT, Paquet C, John D, Cafarella P, Frith P. No additional benefits for pulmonary rehabilitation including cognitive behavioural therapy [abstract]. *Respirology* 2018;**23**(S1):TO131.

Beekman 2014 *{published data only}*

Beekman E, Mesters I, Hendriks EJ, Muris JW, Wesseling G, Evers SM, et al. Exacerbations in patients with chronic obstructive pulmonary disease receiving physical therapy: a cohort-nested randomised controlled trial [protocol]. *BMC Pulmonary Medicine* 2014;**14**(1):71.

ChiCTR1800017405 *{published data only}*

ChiCTR1800017405. Effects of pulmonary rehabilitation prescription on COPD patients. www.chictr.org.cn/showprojen.aspx?proj=28343 (first received 28 July 2018).

DRKS00004931 *{published data only}*

DRKS00004931. "Medical Vulnerability" Impact of hospital room cooling in vulnerable patients with lung disease during periods of extreme weather (UCaHS). www.drks.de/drks_web/navigate.do?navigationId=trial.HTML&TRIAL_ID=DRKS00004931 (first received 26 April 2013).

DRKS00010777 *{published data only}*

DRKS00010777. The influence of the maintenance of physical activity on mental health of patients with occupational lung diseases after an inpatient rehabilitation in the BG clinic of Falkenstein. www.dguv.de/ifa/forschung/projektverzeichnis/ff-fb0227-2.jsp (first received 15 December 2017).

EUCTR2006-005534-20-GB *{published data only}*

EUCTR2006-005534-20-GB. Effect of erdosteine on inflammatory and oxidative biomarkers in sputum and exhaled breath in patients with COPD. www.clinicaltrialsregister.eu/ctr-search/trial/2006-005534-20/GB (first received 29 November 2007).

EUCTR2013-003619-24-ES *{published data only}*

EUCTR2013-003619-24-ES. Benefits of liquid oxygen in chronic obstructive pulmonary disease (COPD) patients without evidence of domiciliary oxygen therapy, presenting desaturation on exertion. www.clinicaltrialsregister.eu/ctr-search/trial/2013-003619-24/ES (first received 13 December 2013).

EUCTR2016-001238-89-ES *{published data only}*

EUCTR2016-001238-89-ES. Impact of iron replacement in patients with chronic obstructive pulmonary disease. www.clinicaltrialsregister.eu/ctr-search/trial/2016-001238-89/ES (first received 20 April 2016).

EUCTR2016-001805-18-SE *{published data only}*

EUCTR2016-001805-18-SE. A pilot study to explore safety and efficacy of NBMI treatment compared to placebo in patients with chronic obstructive pulmonary disease. www.clinicaltrialsregister.eu/ctr-search/trial/2016-001805-18/SE (first received 19 May 2016).

Fastenau 2014 *{published data only}*

Fastenau A. Exercise training and physical activity in patients with mild to moderate COPD in primary care [thesis]. Maastricht: Maastricht University, Maastricht, 2015.

* Fastenau A, Muris JW, De Bie RA, Hendriks EJ, Asijee GM, Beekman E, et al. Efficacy of a physical exercise training programme COPD in primary care: study protocol of a randomized controlled trial. *BMC Public Health* 2014;**14**:788.

Fastenau A, Van Schayck O, Winkens B, Gosselink R, Muris J. Effectiveness of a physical exercise training programme COPD in primary care: a randomized controlled trial [abstract]. *European Respiratory Journal* 2015;**46**:OA3287.

ISRCTN11017699 *{published data only}*

ISRCTN11017699. Investigation of steroid responsiveness in patients with chronic obstructive pulmonary disease. www.isrctn.com/ISRCTN11017699 (first received 15 November 2016).

ISRCTN13899108 *{published data only}*

ISRCTN13899108. Can a physical activity programme or pulmonary rehabilitation reduce the risk of heart and circulation disease in people with COPD?. www.isrctn.com/ISRCTN13899108 (first received 5 April 2019).

ISRCTN15949009 *{published data only}*

ISRCTN15949009. Humidified nasal high flow to improve clinical outcomes following severe exacerbations of chronic obstructive pulmonary disease. www.isrctn.com/ISRCTN15949009 (first received 19 February 2019).

ISRCTN17942821 *{published data only}*

Bourne CL, Kanabar P, Mitchell K, Schreder S, Houchen-Wolloff L, Bankart MJ, et al. A self-management programme of activity coping and education - SPACE for COPD(C) - in primary care: the protocol for a pragmatic trial. *BMJ Open* 2017;**7**(7):e014463.

ISRCTN17942821. A self-management programme of activity coping and education - SPACE FOR COPD - in primary care: a pragmatic trial. www.isrctn.com/ISRCTN17942821?q=&filters=conditionCategory:Respiratory,ageRange:All&sort=relevance&offset=1&totalResults=9&page=1&pageSize=10&searchType=basic-search (first received 17 November 2014).

ISRCTN19684749 *{published data only}*

Buttery S, Kemp SV, Shah PL, Waller D, Jordan S, Lee JT, et al. CELEB trial: Comparative effectiveness of lung volume reduction surgery for emphysema and bronchoscopic lung volume reduction with valve placement: a protocol for a randomised controlled trial. *BMJ Open* 2018;**8**:e021368.

ISRCTN19684749. CELEB: Lung volume reduction in COPD - surgery vs endobronchial valves. www.isrctn.com/ISRCTN19684749?q=&filters=conditionCategory:Respiratory&sort=&offset=9&totalResults=657&page=1&pageSize=10&searchType=basic-search (first received 23 May 2016).

ISRCTN27860457 *{published data only}*

ISRCTN27860457. ON-EPIC Oral nitrate supplementation to enhance pulmonary rehabilitation in chronic obstructive pulmonary disease. www.isrctn.com/ISRCTN27860457 (first received 22 September 2014).

Pavitt M, Lewis AP, Buttery SC, Fernandez BO, Mikus-Lelinska M, Feelisch M, et al. Dietary nitrate supplementation increases exercise endurance time in COPD patients using ambulatory oxygen [abstract]. *European Respiratory Journal* 2018;**52**(Suppl 62):PA4049.

* Pavitt M, Tanner RJ, Lewis AP, Buttery SC, Mehta B, Jefford H, et al. Dietary nitrate supplementation enhances the benefit of pulmonary rehabilitation in people with COPD [abstract]. *European Respiratory Journal* 2018;**52**(Suppl 62):PA4045.

Pavitt MJ, Tanner RJ, Lewis AP, Buttery SC, Mehta B, Jefford H, et al. Oral dietary nitrate supplementation to enhance pulmonary rehabilitation in chronic obstructive pulmonary disease: a multi-centre, double blind, placebo-controlled, parallel group study [abstract]. *Thorax* 2018;**73**(Suppl 4):A3.

ISRCTN45695543 *{published data only}*

Daynes E, Greening N, Sidiqqui S, Singh SJ. A randomised controlled trial to investigate the use of high-frequency airway oscillations as training to improve dyspnoea in COPD [protocol]. *ERJ Open Research* 2019;**5**:00064-2019.

ISRCTN45695543. Training to improve dyspnoea. www.isrctn.com/ISRCTN45695543 (first received 15 February 2017).

ISRCTN80279999 *{published data only}*

ISRCTN80279999. Domiciliary application of non-invasive positive pressure ventilation with average volume assured pressure support to subjects with chronic obstructive pulmonary disease (COPD) who remain hypercapnic following the application of non-invasive positive pressure ventilation (NPPV) for an acute exacerbation. www.isrctn.com/ISRCTN80279999 (first received 11 December 2008).

NCT01037387 *{published data only}*

NCT01037387. Effect of noninvasive ventilation on physical activity and inflammation in COPD patients. clinicaltrials.gov/ct2/show/NCT01037387 (first received 23 December 2009).

NCT01537627 *{published data only}*

NCT01537627. Long-term physical training in chronic obstructive pulmonary disease. clinicaltrials.gov/ct2/show/NCT01537627 (first received 23 February 2012).

NCT01539434 *{published data only}*

NCT01539434. Behavioral intervention to maintain physical capacity and activity in patients with chronic obstructive pulmonary disease (COPD). clinicaltrials.gov/ct2/show/NCT01539434 (first received 27 February 2012).

NCT01783808 *{published data only}*

NCT01783808. Intervention study to investigate supplemental oxygen in COPD. clinicaltrials.gov/ct2/show/NCT01783808 (first received 5 February 2013).

NCT01905982 *{published data only}*

NCT01905982. The effect of reflective breathing therapy compared with conventional breathing therapy in patients with chronic obstructive pulmonary disease (COPD) III-IV; part 2. clinicaltrials.gov/ct2/show/NCT01905982 (first received 23 July 2013).

NCT01998724 *{published data only}*

Moy ML, Wayne PM, Litrownik D, Beach D, Klings ES, Davis RB, et al. Long-term exercise after pulmonary rehabilitation (LEAP): design and rationale of a randomized controlled trial of Tai Chi. *Contemporary Clinical Trials* 2015;**45**(Part B):458-67.

NCT02099799 *{published data only}*

NCT02099799. The effect of physical activity promotion on short and long-term outcomes in COPD (WEB). clinicaltrials.gov/ct2/show/NCT02099799 (first received 31 March 2014).

NCT02205242 *{published data only}*

NCT02205242. BACE trial substudy 1 - PROactive substudy. clinicaltrials.gov/ct2/show/NCT02205242 (first received 31 July 2014).

NCT02398643 *{published data only}*

NCT02398643. Examine the impact of early education on COPD management. clinicaltrials.gov/ct2/show/NCT02398643 (first received 25 March 2015).

NCT02455206 *{published data only}*

NCT02455206. Counseling during pulmonary rehabilitation. clinicaltrials.gov/ct2/show/NCT02455206 (first received 27 May 2015).

Rausch-Osthoff AK, Greco N, Schwank A, Beyer S, Gisi D, Scheermesser M, et al. Effect of counselling during pulmonary rehabilitation on self-determined motivation towards physical activity in people with chronic obstructive pulmonary disease - protocol of a mixed methods study. *BMC Pulmonary Medicine* 2017;**17**(1):115.

NCT02471235 *{published data only}*

Ko FW, Chan K-P, Tam W, Wong I, Chan TO, Ip A, et al. Short-course pulmonary rehabilitation and exacerbations and activity of COPD patients over 1 year [abstract]. *European Respiratory Journal* 2018;**52**(Suppl 52):PA3353.

NCT02471235. Short-course out-patient pulmonary rehabilitation and COPD exacerbations. clinicaltrials.gov/ct2/show/NCT02471235 (first received 15 June 2015).

NCT02478359 *{published data only}*

Estrada EL, Silva K, Medina E, Desai S, Fan VS, Nguyen HQ. Depression and anxiety are associated with COPD patients' lower confidence for increasing physical activity but not with their motivation [abstract]. *American Journal of Respiratory and Critical Care Medicine* 2018;**197**:A7066.

Lee JS, Liu AI, Pounds D, Mahmud F, Flores C, Desai SA, et al. Characteristics of COPD patients who agree to participate in a pragmatic trial of physical activity coaching compared to non-participants [abstract]. *American Journal of Respiratory and Critical Care Medicine* 2018;**197**:A2642.

NCT02478359. Walk on! Physical activity coaching. clinicaltrials.gov/ct2/show/NCT02478359 (first received 23 June 2015).

* Nguyen HQ, Bailey A, Coleman KJ, Desai S, Fan VS, Gould MK, et al. Patient-centered physical activity coaching in COPD (Walk On!): a study protocol for a pragmatic randomized controlled trial. *Contemporary Clinical Trials* 2016;**46**:18-29.

Valenson W, Valmonte F, Rodriguez O, Medina E, Lowrey M, Lew S, et al. Perceived barriers to physical activity in patients at high risk for COPD exacerbations [abstract]. *Chest* 2016;**150**(4 Suppl 1):892A.

NCT02557178 *{published data only}*

NCT02557178. Home-based health management of COPD patients. clinicaltrials.gov/ct2/show/NCT02557178 (first received 23 September 2015).

NCT02667171 *{published data only}*

Hansen H, Bieler T, Beyer N, Godtfredsen N, Kallemose T, Frolich A. COPD online-rehabilitation versus conventional COPD rehabilitation - rationale and design for a multicenter randomized controlled trial study protocol (CORe trial). *BMC Pulmonary Medicine* 2017;**17**:140.

NCT02667171. COPD online rehabilitation (CORe) (CORe). clinicaltrials.gov/ct2/show/NCT02667171 (first received 28 January 2016).

NCT02691104 *{published data only}*

NCT02691104. Use of the SMART COPD physical activity app in pulmonary rehabilitation. clinicaltrials.gov/ct2/show/NCT02691104 (first received 25 February 2016).

NCT02702791 *{published data only}*

NCT02702791. Sustaining training effects through physical activity (STEP). clinicaltrials.gov/ct2/show/NCT02702791 (first received 9 March 2016).

NCT02707770 *{published data only}*

NCT02707770. The role of ambulatory oxygen in improving the effectiveness of pulmonary rehabilitation for COPD patients. clinicaltrials.gov/ct2/show/NCT02707770 (first received 14 March 2016).

NCT02720822 *{published data only}*

Currow D, Watts GJ, Johnson M, McDonald CF, Miners JO, Somogyi AA, et al. on behalf of the Australian National Palliative Care Clinical Studies Collaborative. A pragmatic, phase III, multisite, double-blind, placebo-controlled, parallel-arm, dose increment randomised trial of regular, low-dose extended-release morphine for chronic breathlessness: breathlessness, exertion And morphine sulfate (BEAMS) study protocol. *BMJ Open* 2017;**7**(7):e018100.

NCT02720822. Breathlessness exertion and morphine sulphate (BEAMS). clinicaltrials.gov/ct2/show/NCT02720822 (first received 28 March 2016).

NCT02864420 *{published data only}*

Levine DM, Ouchi K, Blanchfield B, Diamond K, Licurse A, Pu CT, et al. Hospital-level care at home for acutely ill adults: a pilot randomized controlled trial. *Journal of General Internal Medicine* 2018;**33**(5):729-36.

NCT02864420. Hospitalization at home: The acute care home hospital program for adults. clinicaltrials.gov/ct2/show/NCT02864420 (first received 12 August 2016).

NCT02895152 *{published data only}*

NCT02895152. Activity monitor use in COPD patients undergoing rehabilitation. clinicaltrials.gov/ct2/show/NCT02895152 (first received 9 September 2016).

NCT02917915 *{published data only}*

NCT02917915. The CaNadian Standardized Pulmonary Rehabilitation Efficacy trial (CoNSPiRE). clinicaltrials.gov/ct2/show/NCT02917915 (first received 28 September 2016).

Selzler AM, Jourdain T, Sedeno M, Wald J, Janaudis-Ferreira T, Goldstein R, et al. Development of the Canadian standardized pulmonary rehabilitation efficacy trial: a protocol update [abstract]. *Canadian Journal of Respiratory Critical Care and Sleep Medicine* 2017;**1**(3):170.

NCT02924870 *{published data only}*

NCT02924870. Long-term effect of an health education program on daily physical activity in patients with moderate to very severe chronic obstructive pulmonary disease (EA-EPOC). clinicaltrials.gov/ct2/show/NCT02924870 (first received 5 October 2016).

NCT02956213 *{published data only}*

NCT02956213. Indoor air quality and respiratory symptoms in former smokers. clinicaltrials.gov/ct2/show/NCT02956213 (first received 6 November 2016).

NCT02966561 *{published data only}*

Geidl W, Semrau J, Streber R, Lehbert N, Wingart S, Tallner A, et al. Effects of a brief, pedometer-based behavioral intervention for individuals with COPD during inpatient pulmonary rehabilitation on 6-week and 6-month objectively measured physical activity: study protocol for a randomized controlled trial. *Trials* 2017;**18**:396.

NCT02966561. Pedometer-based behavioural intervention for individuals with COPD to stay active after rehabilitation (STAR). clinicaltrials.gov/ct2/show/NCT02966561 (first received 17 November 2016).

NCT02999685 *{published data only}*

Benzo RP, Kramer KM, Hoult JP, Anderson PM, Begue IM, Seifert SJ. Development and feasibility of a home pulmonary rehabilitation program with health coaching. *Respiratory Care* 2018;**63**(2):131-40.

NCT02999685. Home-based health management of chronic obstructive lung Ddsease (COPD) patients. clinicaltrials.gov/ct2/show/NCT02999685 (first received 21 December 2016).

NCT03073954 *{published data only}*

NCT03073954. Working memory training in COPD patients: the Cogtrain-Trial. clinicaltrials.gov/ct2/show/NCT03073954 (first received 8 March 2017).

NCT03080662 *{published data only}*

NCT03080662. Impact of inspiratory muscle training on daily physical activity (INAF). clinicaltrials.gov/ct2/show/NCT03080662 (first received 15 March 2017).

NCT03084874 *{published data only}*

NCT03084874. Efficacy of a coaching program to promote physical activity and reduce sedentary behavior after a COPD hospitalization. clinicaltrials.gov/ct2/show/NCT03084874 (first received 21 March 2017).

NCT03114241 *{published data only}*

NCT03114241. Long-term effects of a 3-month pedometer-based program to enhance physical activity in patients with severe COPD. clinicaltrials.gov/ct2/show/NCT03114241 (first received 14 April 2017).

NCT03127878 *{published data only}*

NCT03127878. Effects of upper-limb training addition to a conventional ET program on PA level and ADL performance. clinicaltrials.gov/ct2/show/NCT03127878 (first received 25 April 2017).

NCT03201198 *{published data only}*

NCT03201198. Active for life: chronic obstructive pulmonary disease (ActiveCOPD). clinicaltrials.gov/ct2/show/NCT03201198 (first received 28 June 2017).

NCT03275116 *{published data only}*

NCT03275116. The effect of twice daily vs. once daily bronchodilation on hyperinflation in COPD patients during 24 hours (BOTH). clinicaltrials.gov/ct2/show/NCT03275116 (first received 7 September 2017).

NCT03280355 *{published data only}*

NCT03280355. The effects of singing training for patients with chronic obstructive pulmonary disease. clinicaltrials.gov/ct2/show/NCT03280355 (first received 12 September 2017).

NCT03321279 *{published data only}*

NCT03321279. Social incentives to increase mobility. clinicaltrials.gov/ct2/show/NCT03321279 (first received 25 October 2017).

NCT03359473 *{published data only}*

NCT03359473. Study to evaluate the safety and efficacy of 13 weeks of the selective androgen receptor modulator (SARM) GSK2881078 in chronic obstructive pulmonary disease. clinicaltrials.gov/ct2/show/NCT03359473 (first received 2 December 2017).

NCT03513068 *{published data only}*

NCT03513068. Portable oxygen concentrator improvements to physical activity, oxygen usage, and quality of life in chronic obstructive pulmonary disease patients using long-term oxygen therapy (POC-STEP). clinicaltrials.gov/ct2/show/NCT03513068 (first received 1 May 2018).

NCT03584269 *{published data only}*

NCT03584269. Innovation in non invasive ventilation in COPD patients treated by long term oxygen therapy (INOV-LTOT). clinicaltrials.gov/ct2/show/NCT03584269 (first received 12 July 2018).

NCT03584295 *{published data only}*

NCT03584295. Early extubation by $ECCO_2R$ compared to IMV in patients with severe acute exacerbation of COPD (X-COPD). clinicaltrials.gov/ct2/show/NCT03584269 (first received 12 July 2018).

NCT03620630 *{published data only}*

NCT03620630. Clinical efficacy and cost effectiveness of MYCOPD in patients with mild and moderate newly diagnosed COPD (EARLY). clinicaltrials.gov/ct2/show/NCT03620630 (first received 8 August 2018).

NCT03654092 *{published data only}*

Frei A, Radtke T, Lana KD, Braun J, Müller RM, Puhan MA. Effects of a long-term home-based exercise training programme using minimal equipment vs. usual care in COPD patients: a study protocol for two multicentre randomised controlled trials (HOMEX-1 and HOMEX-2 trials). *BMC Pulmonary Medicine* 2019;**19**:57.

NCT03655028 *{published data only}*

NCT03655028. Increasing physical activity in COPD through rhythmically enhanced music. clinicaltrials.gov/ct2/show/NCT03655028 (first received 31 August 2018).

NCT03660644 *{published data only}*

NCT03660644. Physical activity following pulmonary rehabilitation in COPD. clinicaltrials.gov/ct2/show/NCT03660644 (first received 6 September 2018).

NCT03746873 *{published data only}*

NCT03746873. Increase level of physical activity and decrease use of health care for people with COPD. clinicaltrials.gov/ct2/show/NCT03746873 (first received 20 November 2018).

NCT03749655 *{published data only}*

NCT03749655. Physical activity promotion added to standard care pulmonary rehabilitation and cognitive behavioural therapy. clinicaltrials.gov/ct2/show/NCT03749655 (first received 21 November 2018).

NCT03750292 *{published data only}*

NCT03750292. Residential cleaning of indoor air to protect COPD patients (CARE). clinicaltrials.gov/ct2/show/NCT03750292 (first received 23 November 2018).

NCT03793192 *{published data only}*

NCT03793192. Promoting activity after COPD exacerbations (aim 2, PACE2). clinicaltrials.gov/ct2/show/NCT03793192 (first received 4 January 2019).

NCT03794921 *{published data only}*

NCT03794921. COPD access to pulmonary rehabilitation intervention (CAPRI). clinicaltrials.gov/ct2/show/NCT03794921 (first received 7 January 2019).

NCT03807310 *{published data only}*

NCT03807310. Targeted nutrient supplement in COPD (NUTRECOVER-trial). clinicaltrials.gov/ct2/show/NCT03807310 (first received 16 January 2019).

NCT03810755 *{published data only}*

NCT03810755. EfiKroniK research program: physical exercise for people with chronic pathologies. clinicaltrials.gov/ct2/show/NCT03810755 (first received 22 January 2019).

NCT03817294 *{published data only}*

NCT03817294. Personalised exercise training in COPD. clinicaltrials.gov/ct2/show/NCT03817294 (first received 25 January 2019).

NCT03869112 *{published data only}*

NCT03869112. Physical activity intervention and cardiovascular risk markers in COPD (PARC). clinicaltrials.gov/ct2/show/NCT03869112 (first received 11 March 2019).

NCT03899558 *{published data only}*

NCT03899558. The role of HNHF to improve clinical outcomes following severe AECOPD. clinicaltrials.gov/ct2/show/NCT03899558 (first received 2 April 2019).

NL3827 *{published data only}*

NL3827. Pulmonary rehabilitation of COPD: a trial of sustained internet based self-management support (PRACTISS COPD). www.trialregister.nl/trial/3827 (first received 27 May 2013).

NL5277 *{published data only}*

NL5277. Efficacy of a physical activity coaching system for patients with COPD. www.trialregister.nl/trial/5277 (first received 30 October 2015).

RBR-3zmh3r *{published data only}*

RBR-3zmh3r. Effects of the inclusion of a functional circuit to aerobic and resistance training on functionality, physical activity in daily life and inflammation of patients with chronic obstructive pulmonary disease. www.ensaiosclinicos.gov.br/rg/RBR-3zmh3r/ (first received 7 March 2018).

UMIN000027190 *{published data only}*

UMIN000027190. The effect of the combination treatment with tiotropium and olodaterol compared to tiotropium on symptoms, respiratory functions and physical activity in maintenance naive Japanese patient with COPD. upload.umin.ac.jp/cgi-open-bin/ctr_e/ctr_view.cgi?recptno=R000031159 (first received 29 April 2017).

UMIN000031173 *{published data only}*

UMIN000031173. Combined effect of progressive resistance training and physical activity counseling in patients with chronic obstructive pulmonary disease: a randomized controlled crossover study. upload.umin.ac.jp/cgi-open-bin/ctr_e/ctr_view.cgi?recptno=R000035589 (first received 26 February 2018).

UMIN000033093 *{published data only}*

UMIN000033093. The effect of comprehensive respiratory rehabilitation using cloud system on exacerbation of patients with chronic obstructive pulmonary disease at home. upload.umin.ac.jp/cgi-open-bin/ctr_e/ctr_view.cgi?recptno=R000037694 (first received 1 July 2018).

Zanaboni 2016 *{published data only}*

Zanaboni P, Dinesen B, Hjalmarsen A, Hoaas H, Holland AE, Oliveira CC, et al. Long-term integrated telerehabilitation of COPD patients: A multicentre randomised controlled trial (iTrain) [protocol]. *BMC Pulmonary Medicine* 2016;**16**(1):126.

Additional references

Adeloye 2015

Adeloye D, Chua S, Lee C, Basquill C, Papana A, Theodoratou E, et al. Global and regional estimates of COPD prevalence: systematic review and meta-analysis. *Journal of Global Health* 2015;**5**(2):020415.

Alahmari 2015

Alahmari AD, Mackay AJ, Patel AR, Kowlessar BS, Singh R, Brill SE, et al. Influence of weather and atmospheric pollution on physical activity in patients with COPD. *Respiratory Research* 2015;**16**:71.

Andersson 2015

Andersson M, Stridsman C, Ronmark E, Lindberg A, Emtner M. Physical activity and fatigue in chronic obstructive pulmonary disease - a population based study. *Respiratory Medicine* 2015;**109**(8):1048-57.

Anton 2016

Anton A, Ratarasarn K. Pulmonary function testing and role of pulmonary rehabilitation in the elderly population with pulmonary diseases. *Current Geriatric Reports* 2016;**5**(2):117-23.

Arne 2009

Arne M, Janson C, Janson S, Boman G, Lindqvist U, Berne C, et al. Physical activity and quality of life in subjects with chronic obstructive pulmonary disease compared with rheumatoid arthritis and diabetes mellitus. *Scandinavian Journal of Primary Health Care* 2009;**27**(3):141-7.

Casperson 1985

Caspersen CJ, Powell KE, Christenson GM. Physical activity, exercise, and physical fitness: definitions and distinctions for health-related research. *Public Health Reports* 1985;**100**(2):126-31.

Choudhury 2014

Choudhury G, Rabinovich R, MacNee W. Comorbidities and systemic effects of chronic obstructive pulmonary disease. *Clinics in Chest Medicine* 2014;**35**(1):101-30.

Deeks 2017

Deeks JJ, Higgins JP, Altman DG, editor(s) on behalf of the Cochrane Statistical Methods Group. Chapter 9: Analysing data and undertaking metaanalyses. In: Higgins JP, Churchill R, Chandler J, Cumpston MS, editor(s), Cochrane Handbook for Systematic Reviews of Interventions version 5.2.0 (updated June 2017), The Cochrane Collaboration, 2017. Available from www.training.cochrane.org/handbook.

Dhillon 2015

Dhillon SS, Sima CA, Kirkham AR, Syed N, Camp PG. Physical activity measurement accuracy in individuals with chronic lung disease: a systematic review with meta-analysis of method comparison studies. *Archives of Physical Medicine and Rehabilitation* 2015;**96**(11):2079-88.e.10.

Esteban 2010

Esteban C, Quintana JM, Aburto M, Moraza J, Equrrola M, Pérez-Izquierdo J, et al. Impact of changes in physical activity on health-related quality of life among patients with COPD. *European Respiratory Journal* 2010;**36**(2):292-300.

Esteban 2014

Esteban C, Arostequi I, Aburto M, Moraza J, Quintana JM, Aispiri S, et al. Influence of changes in physical activity on frequency of hospitalization in chronic obstructive pulmonary disease. *Respirology* 2014;**19**(3):330-8.

Fastenau 2013

Fastenau A, Van Schayck OC, Gosselink R, Aretz KC, Muris JW. Discrepancy between functional exercise capacity and daily physical activity: a cross-sectional study in patients with mild to moderate COPD. *Primary Care Respiratory Journal* 2013;**22**(4):425-30.

Furlanetto 2010

Furlanetto KC, Bisca GW, Oldemberg N, Sant'Anna TJ, Morakami FK, Camillo CA, et al. Step counting and energy expenditure estimation in patients with chronic obstructive pulmonary disease and healthy elderly: accuracy of 2 motion sensors. *Archives of Physical Medicine and Rehabilitation* 2010;**91**(2):261-7.

Furlanetto 2014

Furlanetto KC, Mantoani LC, Bisca G, Morita AA, Zabatiero J, Proença M, et al. Reduction of physical activity in daily life and its determinants in smokers without airflow obstruction. *Respirology* 2014;**19**(3):69-75.

Gagnon 2015

Gagnon P, Casaburi R, Saey D, Porszasz J, Provencher S, Milot J, et al. Cluster analysis in patients with GOLD 1 chronic obstructive pulmonary disease. *PLOS One* 2015;**10**(4):e012362.

Garcia-Aymerich 2006

Garcia-Aymerich J, Lange P, Benet M, Schohr P, Antó JM. Regular physical activity reduces hospital admission and mortality in chronic obstructive pulmonary disease: a population based cohort study. *Thorax* 2006;**61**(9):772-8.

Garcia-Rio 2012

Garcia-Rio F, Rojo B, Casitas R, Lores V, Madero R, Romero D, et al. Prognostic value of the objective measurement of daily physical activity in patients with COPD. *Chest* 2012;**142**(2):338-46.

Gimeno-Santos 2011

Gimeno-Santos E, Frei A, Dobbels F, Rüdell K, Puhan MA, Garcia-Aymerich J, et al. Validity of instruments to measure physical activity may be questionable due to a lack of conceptual frameworks: a systematic review. *Health and Quality of Life Outcomes* 2011;**9**:86.

GOLD 2019

Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global Strategy for the Diagnosis, Management and Prevention of COPD 2019. goldcopd.org/ (accessed 7 August 2019).

GRADEpro GDT 2014 [Computer program]

McMaster University (developed by Evidence Prime). GRADEpro GDT. Version accessed 29 September 2016. Hamilton (ON): McMaster University (developed by Evidence Prime), 2014.

Higgins 2017

Higgins JP, Altman DG, Sterne JA, editor(s). Chapter 8: Assessing risk of bias in included studies. In: Higgins JP, Churchill R, Chandler J, Cumpston MS, editor(s), Cochrane Handbook for Systematic Reviews of Interventions version 5.2.0 (updated June 2017), The Cochrane Collaboration, 2017. Available from www.training.cochrane.org/handbook.

Hill 2013

Hill K, Vogiatzis I, Burtin C. The importance of components of pulmonary rehabilitation, other than exercise training, in COPD. *European Respiratory Review* 2013;**22**(129):405-13.

Iwakura 2016

Iwakura M, Okura K, Shibata K, Kawagoshi A, Sugawara K, Takahashi H, et al. Relationship between balance and physical

activity measured by an activity monitor in elderly COPD patients. *International Journal of Chronic Obstructive Pulmonary Disease* 2016;**11**:1505-14.

Johnson-Warrington 2014

Johnson-Warrington V, Harrison S, Mitchell K, Steiner M, Morgan M, Singh S. Exercise capacity and physical activity in patients with COPD and healthy subjects classified as Medical Research Council dyspnoea scale grade 2. *Journal of Cardiopulmonary Rehabilitation and Prevention* 2014;**34**(2):150-4.

Lahham 2016

Lahham A, McDonald CF, Holland AE. Exercise training alone or with the addition of activity counseling improves physical activity levels in COPD: a systematic review and meta-analysis of randomized controlled trials. *International Journal of COPD* 2016;**11**:3121-36.

Langer 2016

Langer D, Demeyer H. Interventions to modify physical activity in patients with COPD: where do we go from here?. *European Respiratory Journal* 2016;**48**(1):14-7.

Lee 2012

Lee IM, Shiroma EJ, Lobelo F, Puska P, Blair SN, Katzmarzyk PT, et al. Effect of physical inactivity on major non-communicable diseases worldwide: an analysis of burden of disease and life expectancy. *Lancet* 2012;**380**(9838):219-29.

Lee 2015

Lee JA, Laurson KR. Validity of the SenseWear armband step count measure during controlled and free-living conditions. *Journal of Exercise Science and Fitness* 2015;**13**(1):16-23.

Lefebvre 2011

Lefebvre C, Manheimer E, Glanville J. Chapter 6: Searching for studies. In: Higgins JP, Green S, editor(s). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from handbook.cochrane.org. The Cochrane Collaboration.

Mantoani 2016

Mantoani LC, Rubio N, McKinstry B, Macnee W, Rabinovich PA. Interventions to modify physical activity in patients with COPD: a systematic review. *European Respiratory Journal* 2016;**48**(1):69-81.

Marcus 2006

Marcus BH, Williams DM, Dubbert PM, Sallis JF, King AC, Yancey AK, et al. Physical activity intervention studies: what we know and what we need to know. A scientific statement from the American Heart Association Council on Nutrition, Physical Activity and Metabolism. *Circulation* 2006;**114**(24):2739-52.

McCarthy 2015

McCarthy B, Casey D, Devane D, Murphy K, Murphy E, Lacasse Y. Pulmonary rehabilitation for chronic obstructive pulmonary disease. *Cochrane Database of Systematic Reviews* 2015, Issue 2. [DOI: 10.1002/14651858.CD003793.pub3]

Michie 2013

Michie S, Richardson M, Johnston M, Abraham C, Francis J, Hardeman W, et al. The behavior change technique taxonomy of 93 hierarchically clustered techniques: building an international consensus for the reporting of behaviour change interventions. *Annals of Behavioral Medicine* 2013;**46**(1):81-95.

Moher 2009

Moher D, Liberati A, Tetzlaff J, Altman D, PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLOS Medicine* 2009;**6**(7):e1000097. [DOI: 10.1371/journal.pmed.1000097]

Nasis 2015

Nasis I, Kortianou E, Vasilopoulou M, Spetsioti S, Louvaris Z, Kaltsakas G, et al. Hemodynamic effects of high intensity interval training in COPD patients exhibiting exercise-induced dynamic hyperinflation. *Respiratory Physiology and Neurobiology* 2015;**217**:8-16.

O'Donnell 2014

O'Donnell DE, Laveneziana P, Webb K, Neder JA. Chronic obstructive pulmonary disease: clinical integrative physiology. *Clinics in Chest Medicine* 2014;**35**(1):51-69.

Pitta 2005

Pitta F, Troosters T, Spruit M, Probst VS, Decramer M, Gosselink R. Characteristics of physical activities in daily life in chronic obstructive pulmonary disease. *American Journal of Respiratory and Critical Care Medicine* 2005;**171**(9):972-7.

Pitta 2006a

Pitta F, Troosters T, Probst VS, Spruit MA, Decramer M, Gosselink R. Physical activity and hospitalisation for exacerbation of COPD. *Chest* 2006;**129**(3):536-44.

Pitta 2006b

Pitta F, Troosters T, Probst VS, Spruit MA, Decramer M, Gosselink R. Quantifying physical activity in daily life with questionnaires and motion sensors in COPD. *European Respiratory Journal* 2006;**27**(5):1040-55.

Review Manager 2014 [Computer program]

Nordic Cochrane Centre, The Cochrane Collaboration. Review Manager 5 (RevMan 5). Version 5.3. Copenhagen: Nordic Cochrane Centre, The Cochrane Collaboration, 2014.

Schünemann 2017

Schünemann HJ, Oxman AD, Vist GE, Higgins JPT, Deeks JJ, Glasziou P, Akl E, Guyatt GH on behalf of the Cochrane Applicability and Recommendations Methods Group. Chapter 12: Interpreting results and drawing conclusions. In: Higgins JP, Churchill R, Chandler J, Cumpston MS, editor(s), Cochrane Handbook for Systematic Reviews of Interventions version 5.2.0 (updated June 2017). The Cochrane Collaboration, 2017. Available from www.training.cochrane.org/handbook.

Shrikrishna 2012

Shrikrishna D, Patel M, Tabber RJ, Seymour JM, Connolly BA, Puthucheary ZA, et al. Quadriceps wasting and physical

inactivity in patients with COPD. *European Respiratory Journal* 2012;**40**(5):1115-22.

Singh 2016

Singh S. One step at a time: lifestyle physical activity interventions. *Annals of the American Thoracic Society* 2016;**13**(5):586-7.

Trost 2002

Trost SG, Owen N, Cauman AE, Sallis JF, Brown W. Correlates of adults' participation in physical activity: review and update. *Medicine and Science in Sports and Exercise* 2002;**34**(12):1996-2001.

U.S. Department of Health and Human Services 2018

U.S. Department of Health and Human Services. Physical activity guidelines for Americans, 2nd edition. Washington, DC 2018.

UN 2015

United Nations, Department of Economic and Social Affairs, Population Division. World Population Prospects. Key findings & advance tables. 2015 revision. population.un.org/wpp/Publications/Files/WPP2015_DataBooklet.pdf (accessed 31 March 2020).

Vaes 2014

Vaes AW, Garcia-Aymerich J, Marott JL, Benet M, Groenen MT, Schnohr P, et al. Changes in physical activity and all-cause mortality in COPD. *European Respiratory Journal* 2014;**44**(5):1199-209.

Van Remoortel 2013

Van Remoortel H, Hornikx M, Demeyer H, Langer D, Burtin C, Decramer M, et al. Daily physical activity in subjects with newly diagnosed COPD. *Thorax* 2013;**68**(10):962-3.

Van Remoortel 2014

Van Remoortel H, Hornikx M, Langer D, Burtin C, Everaerts S, Verhamme P, et al. Risk factors and comorbidities in the preclinical stage of chronic obstructive pulmonary disease. *American Journal of Respiratory and Critical Care Medicine* 2014;**189**(1):30-8.

Vorrink 2011

Vorrink SN, Kort HS, Troosters T, Lammers JW. Level of daily physical activity in individuals with COPD compared to healthy controls. *Respiratory Research* 2011;**12**:33.

Waschki 2011

Waschki B, Kirsten A, Holz O, Mueller KC, Meyer T, Watz H, et al. Physical activity is the strongest predictor of all-cause mortality in patients with COPD: a prospective cohort study. *Chest* 2011;**140**(2):331-42.

Waschki 2015

Waschki B, Kirsten A, Holz O, Mueller KC, Schaper M, Sack AL, et al. Disease progression and changes in physical activity in patients with chronic obstructive pulmonary disease. *American Journal of Respiratory and Critical Care Medicine* 2015;**192**(3):295-306.

Watz 2009

Watz H, Waschki B, Meyer T, Magnussen H. Physical activity in patient with COPD. *European Respiratory Journal* 2009;**33**(2):262-72.

Watz 2014a

Watz H, Pitta F, Rochester CL, Garcia-Aymerich J, ZuWallack R, Troosters T, et al. An official European Respiratory Society statement on physical activity in COPD. *European Respiratory Journal* 2014;**44**(6):1521-37.

WHO 2010

World Health Organization. Global recommendations on physical activity for health. 2010. www.who.int/dietphysicalactivity/publications/9789241599979/en/ (accessed 29 September 2016).

WHO 2017

World Health Organization. The top 10 causes of death (fact sheet 310). www.who.int/mediacentre/factsheets/fs310/en/ (accessed 30 March 2017).

References to other published versions of this review

Burge 2017

Burge AT, Cox NS, Abramson MJ, Holland AE. Interventions for promoting physical activity in people with COPD. *Cochrane Database of Systematic Reviews* 2017, Issue 4. [DOI: 10.1002/14651858.CD012626]

* Indicates the major publication for the study

Chapter 3.

The impact of pulmonary rehabilitation on 24-hour movement behaviour in people with chronic obstructive pulmonary disease: New insights from a compositional perspective

Declaration of Authorship

Student declaration

The nature and extent of contributions to Chapter 3 were as follows:

Name	Nature of contribution	Extent of contribution
Angela Burge	Study concept and design, data cleaning, analysis and interpretation, manuscript preparation and review	70%
Sebastien Chastin	Study design, data interpretation, manuscript review	5%
Javier Palarea-Albaladejo	Study design, data analysis and interpretation, manuscript review	5%
Anne Holland	Study design, data interpretation, manuscript review	5%
Michael Abramson	Study design, data interpretation, manuscript review	5%
Christine McDonald	Original study design, manuscript review	1%
Ajay Mahal	Original study design, manuscript review	1%
Paul O'Halloran	Original study design, manuscript review	1%
Catherine Hill	Original data acquisition, manuscript review	1%
Annemarie Lee	Original data acquisition, manuscript review	1%
Narelle Cox	Original data acquisition, manuscript review	1%
Aroub Lahham	Original data acquisition, manuscript review	1%
Rosemary Moore	Original data acquisition, manuscript review	1%
Caroline Nicolson	Original data acquisition, manuscript review	1%
Rebecca Gillies	Original data acquisition, manuscript review	1%

Supervisor declaration

I hereby certify that the declaration above is a correct reflection of the extent and nature of contributions made toward Chapter 3 of this thesis by the student and all listed co-authors.

Name of Supervisor	Signature
Prof Anne Holland	

Preface

In Chapter 2, the overwhelming lack of change in physical activity following a myriad of interventions was evident. Pulmonary rehabilitation represented the most widely studied intervention to improve physical activity to date. Meta analyses revealed only a small increase in total physical activity time, which was not undesirable, but not consistent with the increased intensity required to meet physical activity recommendations for improving health. Alternatives to pulmonary rehabilitation/exercise training programs have been investigated in range of single studies (including home-based pulmonary rehabilitation) and were not inferior for physical activity or clinical outcomes. The relationships between time spent in sleep, sedentary behaviours and physical activity with health are usually studied without accounting for the fact that the total time in the day is finite, such that changes in one activity component necessitates changes in other components. As time spent in each of these behaviours are co-dependent, it has been proposed that analyses should be undertaken using a compositional analysis paradigm, which accounts for this intrinsic co-dependence.

The aims of Chapter 3 were to: (i) determine the impact of home- and centre-based pulmonary rehabilitation on movement behaviours; and
(ii) investigate associations between movement behaviours and participant characteristics, using both conventional and compositional analysis methods.

The manuscript in this chapter was submitted to *Journal of Physical Activity and Health* on 28th May 2020 for publication and has been formatted according to journal guidelines.

Chapter 4.

Application of the modified incremental step test for pulmonary rehabilitation

Declaration of Authorship

Student declaration

The nature and extent of contributions to Chapter 4 were as follows:

Name	Nature of contribution	Extent of contribution
Angela Burge	Study concept and design, data acquisition, analysis and interpretation, manuscript preparation and review	70%
Simone dal Corso	Study concept and design, data analysis and interpretation, manuscript review	8%
Anne Holland	Study concept and design, data analysis and interpretation, manuscript review	7%
Michael Abramson	Data interpretation, manuscript review	4%
Narelle Cox	Data acquisition, manuscript review	1%
Janet Bondarenko	Data acquisition, manuscript review	1%
Elizabeth Webb	Data acquisition, manuscript review	1%
Tunya Marceau	Data acquisition, manuscript review	1%
Emma Handley	Data acquisition, manuscript review	1%
Heather Macdonald	Data acquisition, manuscript review	1%
Annabel Askin	Data acquisition, manuscript review	1%
José Carlos Rodrigues-Junior	Data acquisition, manuscript review	1%
Geórgia Aparecida Santos Araújo Calasans	Data acquisition, manuscript review	1%
Daniel Pereira do Amaral	Data acquisition, manuscript review	1%
Julianna Dreger	Data acquisition, manuscript review	1%

Supervisor declaration

I hereby certify that the declaration above is a correct reflection of the extent and nature of contributions made toward Chapter 4 of this thesis by the student and all listed co-authors.

Name of Supervisor	Signature
Prof Anne Holland	

Preface

Previous research has demonstrated equivalent clinical outcomes and improved program completion for a model of pulmonary rehabilitation where the intervention was delivered entirely at home. However, the necessity for centre attendance for accurate assessment of exercise capacity prior to commencement (and following completion) continued to preclude delivery of an entirely home-based program. A feasible, reliable and responsive exercise test that could be safely undertaken in the home environment would help realise this model of service delivery. Preliminary work assessing a modified incremental step test (MIST) has been promising, but additional evidence was required for several outstanding applications for use in this setting.

The aims of Chapter 4 were to determine the feasibility of conducting home and centre-based MISTs in people chronic respiratory disease; to establish the reliability of home-based MIST undertaken in the home environment; to demonstrate responsiveness of the MIST to change in exercise capacity following pulmonary rehabilitation; to define what represents a meaningful change in the MIST by defining the minimal clinically important difference; and to investigate whether prescription of intensity for exercise training (based on MIST results) provides a physiological response within the recommended training range.

The manuscript in this chapter was submitted to *Physical Therapy* on 12th May 2020 for publication and has been formatted according to journal guidelines.

Aspects of this manuscript were presented at the following conferences:

Oral presentation: Thoracic Society of Australia and New Zealand Annual Scientific Meeting, March 2019 (Gold Coast, Australia)

> Published abstract: Burge A, Dal Corso S, Bondarenko J, Handley E, MacLachlan S, Abramson M, Holland A**.** Feasibility and reproducibility of the modified incremental step test for pulmonary rehabilitation**.** *Respirology* 2019;24:TO082**.**

Oral presentation: Hospital in the Home Society Conference, November 2018 (Brisbane, Australia)

Chapter 5.

Home-based pulmonary rehabilitation for COPD using minimal resources: An economic analysis

Declaration of Authorship

Student declaration

The nature and extent of contributions to Chapter 5 were as follows:

Name	Nature of contribution	Extent of contribution
Angela Burge	Study concept and design, data cleaning, analysis and interpretation, manuscript preparation and review	70%
Anne Holland	Study concept and design, data interpretation, manuscript review	7%
Ajay Mahal	Study concept and design, data analysis and interpretation, manuscript review	5%
Christine McDonald	Study concept and design, data interpretation, manuscript review	5%
Michael Abramson	Data interpretation, manuscript review	5%
Catherine Hill	Original data acquisition, manuscript review	1%
Annemarie Lee	Original data acquisition, manuscript review	1%
Narelle Cox	Original data acquisition, manuscript review	1%
Rosemary Moore	Original data acquisition, manuscript review	1%
Caroline Nicolson	Original data acquisition, manuscript review	1%
Aroub Lahham	Original data acquisition, manuscript review	1%
Rebecca Gillies	Original data acquisition, manuscript review	1%
Paul O'Halloran	Original study design, manuscript review	1%

Supervisor declaration

I hereby certify that the declaration above is a correct reflection of the extent and nature of contributions made toward Chapter 5 of this thesis by the student and all listed co-authors.

Name of Supervisor	Signature
Prof Anne Holland	

Preface

In Chapter 4, application of the MIST to facilitate home-based assessments to enable delivery of an entirely home-based pulmonary rehabilitation model was demonstrated. However, another important factor prior to recommendation for implementation in clinical practice was an economic evaluation to determine program delivery costs and whether completion of a home-based program gave rise to any reduction in costs following pulmonary rehabilitation. To date, no reliable cost-effectiveness data for a home-based program have been available.

The aim of Chapter 5 was to assess the impact of a new home-based model compared to centre-based practice using cost-effectiveness and cost-utility analyses. A secondary aim was to determine if pulmonary rehabilitation completion was associated with lower costs in the 12 months following the program.

The manuscript in this chapter has been published in Respirology which has an impact factor of 4.756.

> Burge, A, Holland A, McDonald C, Hill C, Lee A, Cox N, Moore R, Nicolson C, Lahham A, Gillies R, Abramson M, Mahal A. Home-based rehabilitation for COPD using minimal resources: an economic evaluation. Respirology 2020;25:183-190 doi: 10.1111/resp.13667

Aspects of this manuscript were presented at the following conferences:

Oral presentation: Asia Pacific Society of Respirology Congress, November 2017 (Sydney, Australia)

> Published abstract: Burge, A, Holland A, McDonald C, Hill C, Lee A, Cox N, Moore R, Nicolson C, Lahham A, Gillies R, Abramson M, Mahal A. Home-based rehabilitation for COPD using minimal resources: an economic evaluation. *Respirology* 2017;22:AO177

Oral presentation: Australian Physiotherapy Association Conference, October 2017 (Sydney, Australia)

Oral presentation: Thoracic Society of Australia and New Zealand Annual Scientific Meeting, March 2017 (Canberra, Australia)

Published abstract: Burge, A, Holland A, McDonald C, Hill C, Lee A, Cox N, Moore R, Nicolson C, Lahham A, Gillies R, Abramson M, Mahal A. Home-based rehabilitation for COPD using minimal resources: an economic evaluation. *Respirology* 2017;22:TO102

4

.

Chapter 6.

Discussion, conclusions and future directions

6.1 Overview of the main findings

The studies in this thesis present a body of work to underpin clinical implementation of entirely home-based pulmonary rehabilitation. Previously identified gaps in knowledge related to optimal methods to improve physical activity and analyse physical activity outcomes; robust tools for home-based assessment of exercise capacity; and the cost-effectiveness of home-based pulmonary rehabilitation for people with COPD. The main findings of this these were:

1. Despite pulmonary rehabilitation being the most widely-studied intervention to improve physical activity in COPD patients to date, there was limited evidence of benefit for this outcome, regardless of program location.

2. A compositional approach to analysis of physical activity outcomes did not conclusively demonstrate differences between pulmonary rehabilitation settings, but did identify associations between participant features and movement behaviours that were not identified in conventional analyses.

3. The MIST is feasible, reliable and responsive to pulmonary rehabilitation in the home-based setting.

4. Both home and centre-based pulmonary rehabilitation models offer similarly low-cost programs, and offer a significant reduction in healthcare costs in the 12 months following completion, regardless of program location.

6.2 Strengths and limitations

A strength of this thesis is the broad range of methodologies employed to encompass the diverse gaps in evidence required to support the clinical implementation of home-based pulmonary rehabilitation. The Cochrane systematic review (Chapter 2) used robust methods to synthesise objective physical activity data across a wide range of interventions, an approach that has not previously been used in COPD. Another strength was the unique application of the compositional data analysis approach in order to identify the impact of pulmonary rehabilitation on physical activity outcomes (Chapter 3). The study of clinimetric properties of the MIST provides new evidence for home-based exercise testing (Chapter 4). The comprehensive economic analysis (Chapter 5) received an editorial in *Respirology* where it was noted to "significantly strengthen the argument" for home-based pulmonary rehabilitation.[98]

Limitations to the work in this thesis include the inability to draw strong conclusions from the Cochrane systematic review (Chapter 2) due to the broad range of interventions and physical activity measures used across studies, which limited data synthesis (Chapter 2). This did however identify highly important methodological issues that should be addressed in future studies.

Compositional analysis of physical activity data (Chapter 3) was limited by the number of participants with physical activity data available (fewer than the number of participants with data for clinical outcomes). However, this work bolstered previous findings for a relationship between physical activity outcomes and baseline functional exercise capacity. Participant numbers were also a limitation in the MIST study (Chapter 4) where not all participants went on to commence or complete pulmonary rehabilitation, which is not unusual in a clinical context, but resulted in limited data availability for assessment of responsiveness. The results indicated that an appropriate prescription of sufficient intensity to induce training benefits is possible in people with chronic respiratory disease. However, the utility of this approach in clinical practice is yet to be tested. The peak heart rate across all exercise tests was low, so it remains possible that the prescribed training intensity may be lower than required for an effective exercise training dose. Future research should test whether exercise prescription based on the MIST delivers the expected improvements in exercise capacity following pulmonary rehabilitation. The analysis of economic outcomes (Chapter 5) took a health system perspective and thus the full costs to patients and to society were not represented, however the health system perspective is the most important for policy makers and funders.

6.3 Implications for future research

This thesis provides many prospects for future research in this area. The dearth of improvements in physical activity outcomes identified in the Cochrane systematic review (Chapter 2) strongly demonstrates the need to develop effective interventions and provides inducement to consider alternative analytical approaches. This work did indicate some promise from interventions incorporating physical activity counselling based on behaviour change constructs, aligned with the optimisation of pharmacological management and physical function. However, a lack of theoretical rationale and incomplete descriptions of interventions frequently hindered identification of the necessary components for effective strategies. The evolution of behaviour change theory[103] and developing understanding of requirements for behaviour change in people with COPD[104] provides a framework for the development and documentation of effective interventions in the future. It is also evident that interpretation of outcomes following interventions to improve physical activity was limited by a lack of methodological detail. Inconsistencies regarding definition of threshold values for classifying activity according to intensity, measurement device wearing protocols and data cleaning were all demonstrated and indicated the need to create a synthesised approach to physical activity data collection and reporting to inform protocol development.

Research studying the clinical implementation of entirely home-based pulmonary rehabilitation (including measures of program access, uptake and completion) is now possible subsequent to my work demonstrating the MIST is a feasible, reliable and responsive exercise test for this setting (Chapter 4). This direction is consistent with the Australian Government's Department of Health's National Lung Health Strategy Priority Area 6 which states the recommendation to "fund implementation research to drive the uptake of best evidence into routine patient care (e.g. pulmonary rehabilitation)" (Recommended Action 6.1).[22] The availability of the MIST would also allow the study of exercise capacity and home-based rehabilitation in new groups including those located in remote areas away from health care facilities, and groups in whom centre-based visits should be minimised, such as patients with immunosuppression. There are opportunities for further work assessing test utility across the spectrum of disease severity and in a wider range of chronic respiratory diseases for which people are referred to pulmonary rehabilitation. Investigation of the impact of clinical models where participants are provided with program options may also demonstrate an impact on uptake and outcomes.

The economic analysis presented in this thesis (Chapter 5) provides a detailed methodology that could be applied to other areas of pulmonary rehabilitation practice, and highlights the gaps in our understanding regarding the cost-benefit of this intervention. These gaps include an understanding of the health economic benefits of pulmonary rehabilitation following an acute exacerbation, maintenance pulmonary rehabilitation and repeat courses of pulmonary rehabilitation. The 6MWD was used as the measure of effectiveness as it was the primary outcome for the clinical trial, however use of a health-related quality of life measure would be an interesting application in future trials. The SF6D was chosen as the measure of utility as it had been demonstrated to be sensitive to health changes in people with COPD, but further investigation of alternative measures is another outstanding consideration. Whilst the study presented in this thesis used within-trial analyses, health economic modelling may also be a fruitful area for future research, to understand the costs and consequences of pulmonary rehabilitation over longer time periods.

6.4 Implications for clinical practice

An important finding for clinical practice from this thesis is the capability to deliver an entirely home-based pulmonary rehabilitation program using the MIST for assessment of exercise capacity (Chapter 4). Administration of this test is well within the scope of practice for pulmonary rehabilitation clinicians, who are accustomed to administering field exercise tests before and after the program. The test is feasible to administer in the home setting, allowing

participation of individuals who might not otherwise engage in pulmonary rehabilitation. Whilst this research showed that not all patients are able to undertake a MIST due to gait aid requirements or other medical conditions, it was feasible for 29% of patients who were typical of those seen in pulmonary rehabilitation programs. The original HomeBase paper[39] was identified by the American College of Physicians as 1 of the 7 most influential respiratory medicine papers globally in 2016, as a result of the potential to directly impact practice.[105] The work in this thesis directly contributes to further development of this model, by taking all aspects of the program into the home setting, underpinned by robust data.

Unfortunately, pulmonary rehabilitation does not necessarily result in improvements in physical activity, regardless of program location (Chapter 2, Chapter 3). However, higher levels of functional exercise capacity appear to be an important foundation in order for patients to increase participation in physical activity (Chapter 3). It is well established that functional exercise capacity can be improved by pulmonary rehabilitation in people with COPD, regardless of disease severity.[14, 106] This provides additional incentive for clinicians to ensure that all patients are referred to pulmonary rehabilitation in accordance with Australian COPD-X Guidelines (NHMRC level 1 evidence, strong recommendation).[11]

6.5 Implications for policy makers

The complexity of the healthcare system necessitates consideration of a range of factors to inform changes to service provision and funding models, in addition to evidence for clinical effectiveness. In the context of a healthcare system with a growing burden, cost-efficiency is a strong driver for health care reform and policy makers require strategic initiatives to support a fundamental shift in how we fund and deliver health care.[107, 108] Development of patient-centred services is supported by Australia's National Lung Health Strategy Priority Area 5 which highlights the need to ensure equitable access to evidence-based management for lung conditions.[22] The recommendation is to "expand service delivery of pulmonary rehabilitation beyond the hospital setting into the community and home setting to greatly increase access". Appropriate funding is essential for provision of pulmonary rehabilitation. The Australian and New Zealand Pulmonary Rehabilitation Guidelines call for major changes in funding models to enable wider program provision.[41] In consideration of the unsuccessful application for an Medicare Benefits Schedule Item Number for Pulmonary Rehabilitation, the Australian Government's Medical Services Advisory Committee highlighted the need for further "evidence of the effectiveness and cost-effectiveness of pulmonary rehabilitation".[109] As previously highlighted, a home-based model overcomes many of the patient-level barriers to participation

in pulmonary rehabilitation, and results from the economic analysis presented in this thesis provide crucial data to underpin future decisions by policy makers (Chapter 5).

Conclusion

Pulmonary rehabilitation is recommended for people with COPD, supported by strong evidence for improvements in exercise capacity and health-related quality of life. However, patient and system level barriers preclude widespread access. Home-based pulmonary rehabilitation delivers equivalent improvements in clinical outcomes, accompanied by an improved rate of program completion compared to traditional centre-based programs. This body of work addressed knowledge gaps that could facilitate clinical implementation of the HomeBase model. The studies in this thesis demonstrated persistently low levels of physical activity following pulmonary rehabilitation, regardless of program location but reinforced that exercise capacity appears to be a modifiable determinant of physical activity in people with COPD. The utility of the MIST for home-based assessment of exercise capacity and prescription of training intensity was also demonstrated, along with favourable cost-effectiveness compared to a traditional program model. This research provides new evidence to support the clinical implementation of home-based pulmonary rehabilitation as an alternative for people who cannot access centre-based programs.

References

1. Global Strategy for the Diagnosis, Management and Prevention of Chronic Obstructive Pulmonary Disease. Global Initiative for Chronic Obstructive Lung Disease (GOLD). 2020.

2. Adeloye D, Chua S, Lee C, Basquill C, Papana A, Theodoratou E, et al. Global and regional estimates of COPD prevalence: systematic review and meta-analyses. *Journal of Global Health*. 2015;5:020415.

3. Toelle B, Xuan W, Bird T, Abramson M, Atkinson D, Burton D, et al. Respiratory symptoms and illness in older Australians: the Burden of Obstructive Lung Disease (BOLD) study. *Medical Journal of Australia*. 2013;198:144-148.

4. Access Economics Pty Ltd. Economic impact of COPD and cost-effective solutions. 2008.

5. Hill K. Prevalence and underdiagnosis of chronic obstructive pulmonary disease among patients at risk in primary care. *Canadian Medical Association Journal*. 2010;182:673-678.

6. Australian Institute of Health and Welfare. COPD, associated comorbidities and risk factors. Canberra: Australian Government; 23 August 2016.

7. Global Burden of Disease Study Collaborators. Global, regional, and national age-sex specific all-cause and cause-specific mortality for 240 causes of death, 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet*. 2013;385:117-171.

8. Australian Institute of Health and Welfare. COPD snapshot. Canberra: Australian Government; 24 July 2018.

9. Global Burden of Disease 2013 DALYs and HALE Collaborators. Global, regional and national disability-adjusted life years (DALYs) for 306 diseases and injuries and healthy life expectancy (HALE) for 188 countries, 1990-2013: quantifying the epidemiological transition. *Lancet*. 2015;386:2145-2191.

10. Australian Institute of Health and Welfare. Chronic obstructive pulmonary disease (COPD). Canberra: Australian Government; 2019.

11. Yang I, Dabscheck E, George J, Jenkins S, McDonald C, McDonald V, et al. The COPD-X Plan: Australian and New Zealand Guidelines for the Management of Chronic Obstructive Pulmonary Disease. *Version 261*. 2020.

12. Zhang Y, Morgan R, Alonso-Coello P, Wiercioch W, Bata M, Jaeschke R, et al. A systematic review of how patients value COPD outcomes. *European Respiratory Journal*. 2018;52:1800222.

13. Spruit M, Singh S, Garvey C, ZuWallack R, Nici L, Rochester C, et al. An official American Thoracic Society/European Respiratory Society statement: key concepts and advances in pulmonary rehabilitation. *American Journal of Respiratory and Critical Care Medicine*. 2013;188:e13-64.

14. McCarthy B, Casey D, Devane D, Murphy K, Murphy E, Lacasse Y. Pulmonary rehabilitation for chronic obstructive pulmonary disease. *Cochrane Database of Systematic Reviews*. 2015;2:CD003793.

15. Puhan M, Gimeno-Santos E, Cates C, Troosters T. Pulmonary rehabilitation following exacerbations of chronic obstructive pulmonary disease. *Cochrane Database of Systematic Reviews*. 2016;10:CD005305.

16. Rochester C, Vogiatzis I, Holland A, Lareau S, Marciniuk D, Puhan M, et al. An official American Thoracic Society/European Respiratory Society policy statement: enhancing implementation, use, and delivery of pulmonary rehabilitation. *American Journal of Respiratory and Critical Care Medicine*. 2015;192:1373-1386.

17. Desveaux L, Janaudis-Ferreira T, Goldstein R, Brooks D. An international comparison of pulmonary rehabilitation: a systematic review. *COPD: Journal of Chronic Obstructive Pulmonary Disease*. 2015;12:144-153.

18. Marks G, Reddel H, Guevara-Rattray E, Poulos L, Ampon R. Monitoring pulmonary rehabilitation and long-term oxygen therapy for people with chronic obstructive pulmonary disease (COPD) in Australia: a discussion paper. Canberra: Australian Institute of Health and Welfare; 2013.

19. Keating A, Lee A, Holland A. What prevents people with chronic obstructive pulmonary disease from attending pulmonary rehabilitation? A systematic review. *Chronic Respiratory Disease.* 2011;8:89-99.

20. Cox N, Oliveira C, Lahham A, Holland A. Pulmonary rehabilitation referral and participation are commonly influenced by environment, knowledge, and beliefs about consequences: a systematic review using the Theoretical Domains Framework. *Journal of Physiotherapy*. 2017;63:84-93.

21. Keating A, Lee A, Holland A. Lack of perceived benefit and inadequate transport influence uptake and completion of pulmonary rehabilitation in people with chronic obstructive pulmonary disease: a qualitative study. *Journal of Physiotherapy*. 2011;57:183-190.

22. Department of Health. National strategic action plan for lung conditions. Canberra: Australian Government; February 2019.

23. Murphy N, Bell C, Costello R. Extending a home from hospital care programme for COPD exacerbations to include pulmonary rehabilitation. *Respiratory Medicine*. 2005;99:1297-1302.

24. Behnke M, Jörres R, Kirsten D, Magnussen H. Clinical benefits of a combined hospital and home-based exercise programme over 18 months in patients with severe COPD. *Monaldi Archives of Chest Disease*. 2003;59:44-51.

25. Ghanem M, Elaal E, Mehany M, Tolba K. Home-based pulmonary rehabilitation program: Effect on exercise tolerance and quality of life in chronic obstructive pulmonary disease patients. *Annals of Thoracic Medicine*. 2010;5:18-25.

26. Booker H. Exercise training and breathing control in patients with chronic airflow limitation. *Physiotherapy*. 1984;70:258-260.

27. Boxall A, Barclay L, Sayers A, Caplan G. Managing chronic obstructive pulmonary disease in the community. A randomized controlled trial of home-based pulmonary rehabilitation for elderly housebound patients. *Journal of Cardiopulmonary Rehabilitation*. 2005;25:378-385.

28. Xie S, Zhu M, Cui H, Liu H. Influence of home-based training program on patients with COPD. *Chinese Journal of Clinical Rehabilitation*. 2003;7:2554-2555.

29. Singh V, Khandelwal D, Khandelwal R, Abusaria S. Pulmonary rehabilitation in patients with chronic obstructive pulmonary disease. *Indian Journal of Chest Diseases and Allied Sciences*. 2003;45:13-17.

30. Fernández A, Pascual J, Ferrando C, Arnal A, Vergara I, Sevila V. Home-based pulmonary rehabilitation in very severe COPD: is it safe and useful? *Journal of Cardiopulmonary Rehabilitation and Prevention*. 2009;29:323-331.

31. Hernández M, Rubio T, Ruiz F, Riera H, Gil R, Gómez J. Results of a home-based training program for patients with COPD. *Chest*. 2000;118:106-114.

32. Jones D, Thomson R, Sears M. Physical exercise and resistive breathing training in severe chronic airways obstruction - are they effective? *European Journal of Respiratory Disease*. 1985;67:159-166.

33. McGavin C, Gupta S, Lloyd E, McHardy G. Physical rehabilitation for the chronic bronchitic: results of a controlled trial of exercises in the home. *Thorax*. 1977;32:307-311.

34. Güell M, de Lucas P, Gáldiz J, Montemayor T, Rodríguez González-Moro J, Gorostiza A, et al. Home vs hospital-based pulmonary rehabilitation for patients with chronic obstructive pulmonary disease: a Spanish multicenter trial. *Archivos de Bronconeumologia*. 2008;44:512-518.

35. Maltais F, Bourbeau J, Shapiro S, Lacasse Y, Perrault H, Maltsan M. Effects of home-based pulmonary rehabilitation in patients with chronic obstructive pulmonary disease: a randomized trial. *Annals of Internal Medicine*. 2008;149:869-878.

36. Mendes de Oliveira J, Studart Leitão Filho F, Malosa Sampaio L, Negrinho de Oliveira A, Hirata R, Costa D, et al. Outpatient vs. home-based pulmonary rehabilitation in COPD: a randomized controlled trial. *Multidisciplinary Respiratory Medicine*. 2010;5:401-408.

37. Puente-Maestu L, Sánz M, Sánz P, Cubillo J, Mayol J, Casaburi R. Comparison of effects of supervised versus self-monitored training programmes in patients with chronic obstructive pulmonary disease. *European Respiratory Journal*. 2000;15:517-525.

38. Strijbos J, Postma D, van Alterna R, Gimeno F, Koeter G. A comparison between an outpatient hospital-based pulmonary rehabilitation program and a home-case pulmonary rehabilitation program in patients with COPD: a follow-up of 18 months. *Chest*. 1996;109:366-372.

39. Holland A, Mahal A, Hill C, Lee A, Burge A, Cox N, et al. Home-based rehabilitation for COPD using minimal resources: a randomised, controlled equivalence trial. *Thorax*. 2017;72:57-65.

40. Horton E, Mitchell K, Johnson-Warrington V, Apps L, Sewell L, Morgan M, et al. Comparison of a structured home-based rehabilitation programme with conventional supervised pulmonary rehabilitation: a randomised non-inferiority trial. *Thorax*. 2018;73:29-36.

41. Alison J, McKeogh Z, Johnston K, McNamara R, Spencer L, Jenkins S, et al. Australian and New Zealand Pulmonary Rehabilitation Guidelines. *Respirology*. 2017;22:800-819.

42. Holland A, Mahal A, Hill C, Lee A, Burge A, Moore R, et al. Benefits and costs of home-based pulmonary rehabilitation in chronic obstructive pulmonary disease – a multi-centre randomised controlled equivalence trial. *BMC Pulmonary Medicine*. 2013;13:57.

43. Lahham A, McDonald C, Mahal A, Lee A, Hill C, Burge A, et al. Acceptability and validity of a home exercise diary used in home-based pulmonary rehabilitation: a secondary analysis of a randomised controlled trial. *Clinical Respiratory Journal*. 2018;12:2057-2064.

44. Lahham A, McDonald C, Mahal A, Lee A, Hill C, Burge A, et al. Home-based pulmonary rehabilitation for people with COPD: a qualitative study reporting the patient perspective. *Chronic Respiratory Disease*. 2018;15:123-130.

45. Rollnick S, Miller W, Butler C. *Motivational Interviewing in Health Care: helping patients change behaviour.* New York: Guildford Press; 2008.

46. Lahham A, McDonald C, Mahal A, Lee A, Hill C, Burge A, et al. Participation in physical activity during center and home-based pulmonary rehabilitation for people with COPD: a secondary analysis of a randomised controlled trial. *Journal of Cardiopulmonary Rehabilitation and Prevention*. 2019;39:e1-4.

47. Pitta F, Troosters T, Spruit M, Probst V, Decramer M, Gosselink R. Characteristics of physical activities in daily life in chronic obstructive pulmonary disease. *American Journal of Respiratory and Critical Care Medicine*. 2005;171:972-977.

48. Arne M, Janson C, Janson S, Boman G, Lindqvist U, Berne C, et al. Physical activity and quality of life in subjects with chronic obstructive pulmonary disease compared with rheumatoid arthritis and diabetes mellitus. *Scandinavian Journal of Primary Health Care*. 2009;27:141-147.

49. Vorrink S, Kort H, Troosters T, Lammers J. Level of daily physical activity in individuals with COPD compared to healthy controls. *Respiratory Research.* 2011;12:33.

50. Furlanetto K, Mantoani L, Bisca G, Morita A, Zabatiero J, Proenca M, et al. Reduction of physical activity in daily life and its determinants in smokers without airflow obstruction. *Respirology*. 2014;19:369-375.

51. Johnson-Warrington V, Harrison S, Mitchell K, Steiner M, Morgan M, Singh S. Exercise capacity and physical activity in patients with COPD and healthy subjects classified as Medical Research Council dyspnoea scale grade 2. *Journal of Cardiopulmonary Rehabilitation and Prevention*. 2014;34:150-154.

52. Shrikrishna D, Patel M, Tabber R, Seymour J, Connolly B, Puthucheary Z, et al. Quadriceps wasting and physical inactivity in patients with COPD. *European Respiratory Journal*. 2012;40:1115-1122.

53. Troosters T, Sciurba F, Battaglia S, Langer D, Valluri S, Martino L, et al. Physical inactivity in patients with COPD, a controlled multi-center pilot-study. *Respiratory Medicine*. 2010;104:1005-1011.

54. Waschki B, Kirsten A, Holz O, Mueller K, Schaper M, Sack A, et al. Disease progression and changes in physical activity in patients with chronic obstructive pulmonary disease. *American Journal of Respiratory and Critical Care Medicine*. 2015;192:295-306.

55. Van Remoortel H, Hornikx M, Langer D, Burtin C, Everaerts S, Verhamme P, et al. Risk factors and comorbidities in the preclinical stage of chronic obstructive pulmonary disease. *American Journal of Respiratory and Critical Care Medicine*. 2014;189:30-38.

56. Watz H, Waschki B, Meyer T, Magnussen H. Physical activity in patient with COPD. *European Respiratory Journal*. 2009;33:262-272.

57. Waschki B, Kirsten A, Holz O, Muller K, Meyer T, Watz H, et al. Physical activity is the strongest predictor of all-cause mortality in patients with COPD: a prospective cohort study. *Chest*. 2011;140:331-342.

58. Vaes A, Garcia-Aymerich J, Marott J, Benet M, Groenen M, Schnohr P, et al. Changes in physical activity and all-cause mortality in COPD. *European Respiratory Journal*. 2014;44:1199-1209.

59. Garcia-Rio F, Rojo B, Casitas R, Lores V, Madero R, Romero D, et al. Prognostic value of the objective measurement of daily physical activity in patients with COPD. *Chest*. 2012;142:338-346.

60. Fastenau A, van Schayck O, Gosselink R, Aretz K, Muris J. Discrepancy between functional exercise capacity and daily physical activity: a cross-sectional study in patients with mild to moderate COPD. *Primary Care Respiratory Journal.* 2013;22:425-430.

61. Gagnon P, Casaburi R, Saey D, Porszasz J, Provencher S, Milot J, et al. Cluster analysis in patients with GOLD 1 chronic obstructive pulmonary disease. *PLoS ONE*. 2015;10:e012362.

62. Van Remoortel H, Hornikx M, Demeyer H, Langer D, Burtin C, Decramer M, et al. Daily physical activity in subjects with newly diagnosed COPD. *Thorax*. 2013;68:962-963.

63. Spruit M, Pitta F, McAuley E, ZuWallack R, Nici L. Pulmonary rehabilitation and physical activity in patients with chronic obstructive pulmonary disease. *American Journal of Respiratory and Critical Care Medicine*. 2015;192:924-933.

64. Mantoani L, Rubio N, McKinstry B, MacNee W, Rabinovich R. Interventions to modify physical activity in patients with COPD: a systematic review. *European Respiratory Journal*. 2016;48:14-17.

65. Lahham A, McDonald C, Holland A. Exercise training alone or with the addition of activity counseling improves physical activity levels in COPD: a systematic review and meta-analysis of randomized controlled trials. *International Journal of COPD*. 2016;11:3121-3136.

66. Pedišić Ž. Measurement issues and poor adjustments for physical activity and sleep undermine sedentary behaviour research - the focus should shift to the balance between sleep, sedentary behaviour, standing and activity. *Kinesiology*. 2014;46:135-146.

67. Gottlieb D, Redline S, Nieto F, Baldwin C, Newman A, Resnick H, et al. Association of usual sleep duration with hypertension: the Sleep Heart Health study. *Sleep*. 2006;29:1009-1014.

68. Chastin S, Palarea-Albaladejo J, Dontje M, Skelton, D. Combined effects of time spent in physical activity, sedentary behaviors and sleep on obesity and cardio-metabolic health markers: a novel compositional data analysis approach. *PLos ONE*. 2015;10:e0139984.

69. Aitchison J. The statistical analysis of compositional data. *Journal of the Royal Statistical Society Series B (Methodological)*. 1982;44:139-177.

70. Dumuid D, Stanford T, Martin-Fernández J, Pedišić Ž, Maher C, Lewis L, et al. Compositional data analysis for physical activity, sedentary time and sleep research. *Statistical Methods in Medical Research*. 2018;27:3726-3738.

71. Hunt T, Williams M, Olds T, Dumuid D. Patterns of time use across the chronic obstructive pulmonary disease severity spectrum. *International Journal of Environmental Research and Public Health*. 2018;15:533.

72. Lewthwaite H, Olds T, Williams M, Effing T, Dumuid D. Use of time in chronic obstructive pulmonary disease: Longitudinal associations with symptoms and quality of life using a compositional analysis approach. *PLoS ONE*. 2019;14:e0214058.

73. Reibe D, Franklin B, Thompson P, Garber C, Whitfield G, Magal M, et al. Updating ACSM's recommendations for exercise preparticipation health screening. *Medicine and Science in Sports and Exercise*. 2015;47:2473-2479.

74. Garber C, Blissmer B, Deschenes M, Franklin B, Lamonte M, Lee I, et al. Quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults: guidance for prescribing exercise. *Medicine and Science in Sports and Exercise*. 2011;43:1334-1359.

75. Singh S, Puhan M, Andrianopoulos V, Hernandes N, Mitchell K, Hill C, et al. An official systematic review of the European Respiratory Society/American Thoracic Society: measurement properties of field walking tests in chronic respiratory disease. *European Respiratory Journal*. 2014;44:1447-1478.

76. Holland A, Rasekaba T, Fiore J, Burge A, Lee A. The 6-minute walk distance cannot be accurately assessed at home in people with COPD. *Disability and Rehabilitation*. 2015;37:1102-1106.

77. de Andrade C, de Camargo A, de Castro B, Malaguti C, Dal Corso S. Comparison of cardiopulmonary responses during 2 incremental step tests in subjects with COPD. *Respiratory Care*. 2012;57:1920-1926.

78. Dal Corso S, de Camargo A, Izbicki M, Malaguti C, Nery L. A symptom-limited incremental step test determines maximum physiological responses in patients with COPD. *Respiratory Medicine*. 2013;107:1993-1999.

79. José A, Dal Corso S. Step tests are safe for assessing functional capacity in patients hospitalized with acute lung diseases. *Journal of Cardiopulmonary Rehabilitation and Prevention*. 2016;36:56-61.

80. Carmago A, Lanza F, Tupinamba T, Dal Corso S. Reproducibility of step tests in patients with bronchiectasis. *Brazilian Journal of Physical Therapy*. 2013;17:255-262.

81. Jose A, Holland A, de Oliveira C, Selman J, Castro R, Athanazio R, et al. Does home-based pulmonary rehabilitation improve functional capacity, peripheral muscle strength and quality of life in patients with bronchiectasis compared to standard care? *Brazilian Journal of Physical Therapy*. 2017;21:473-480.

82. Schunemann H, Guyatt G. Commentary - Goodbye M(C)ID! Hello MID, Where do you come from? *Health Services Research*. 2005;40:593-597.

83. Deyo R, Diehr P, Patrick D. Reproducibility and responsiveness of health status measures. Statistics and strategies for evaluation. *Controlled Clinical Trials.* 1991;12:142S-158S.

84. Wyrwich K, Nienaber N, Tierney W, Wolinsky F. Linking clinical relevance and statistical significance in evaluating intra-individual changes in health-related quality of life. *Medical Care*. 1999;37:469-478.

85. Kazis L, Anderson J, Meenan R. Effect sizes for interpreting changes in health status. *Medical Care*. 1989;27:S178-189.

86. Beaton D, Boers M, Wells G. Many faces of the minimal clinically important difference (MCID): a literature review and directions for future research. *Current Opinion in Rheumatology*. 2002;14:109-114.

87. Casaburi R, Patessio A, Ioli F, Zanaboni S, Donner C, Wasserman K. Reductions in exercise lactic acidosis and ventilation as a result of exercise training in patients with obstructive lung disease. *American Review of Respiratory Disease*. 1991;143:9-18.

88. Maltais F, LeBlanc P, Jobin J, Bérubé C, Bruneau J, Carrier L, et al. Intensity of training and physiologic adaptation in patients with chronic obstructive pulmonary disease. *American Journal of Respiratory and Critical Care Medicine*. 1997;155:555-561.

89. California Pulmonary Rehabilitation Collaborative Group. Effects of pulmonary rehabilitation on dyspnoea, quality of life and healthcare costs in California. *Journal of Cardiopulmonary Rehabilitation.* 2004;24:52-62.

90. Chakravorty I, Fasakin C, Paine T, Narasimhaiah D, Austin G. Outpatient-based pulmonary rehabilitation for COPD: a cost of illness study. *ISRN Pulmonology.* 2011:364989

91. Golmohammadi K, Jacobs P, Sin D. Economic evaluation of a community-based pulmonary rehabilitation program for chronic obstructive pulmonary disease. *Lung.* 2004;182:187-196.

92. Reina-Rosenbaum R, Bach J, Penek J. The cost/benefits of pulmonary rehabilitation. *Archives of Physical Medicine and Rehabilitation*. 1997;78:240-244.

93. Farias C, Resqueti V, Dias F, Borghi-Silva A, Arena R, Fregonezi G. Costs and benefits of pulmonary rehabilitation in chronic obstructive pulmonary disease: a randomized controlled trial. *Revista Brasileira de Fisioterapia*. 2014;18:165-173.

94. Gillespie P, O'Shea E, Casey D, Murphy K, Devance D, Cooney A, et al. The cost-effectiveness of a structured education pulmonary rehabilitation programme for chronic obstructive pulmonary disease in primary care: the PRINCE cluster randomised trial. *BMJ Open.* 2013;3:e003479.

95. Griffiths T, Phillips C, Davies S, Burr M, Campbell I. Cost effectiveness of an outpatient multidisciplinary pulmonary rehabilitation programme. *Thorax.* 2001;56:779-784.

96. Hoogendoorn M, van Wetering C, Schols A, Rutten-van Molken M. Is INTERdisciplinary COMmunity-based COPD management (INTERCOM) cost-effective. *European Respiratory Journal*. 2010;35:79-97.

97. Waterhouse J, Walters S, Oluboyede Y, Lawson R. A randomised 2x2 trial of community versus hospital pulmonary rehabilitation, followed by telephone or conventional follow-up. *Health Technology Assessment.* 2010;14:1-140.

98. Calverley P. Home economics for COPD care. *Respirology*. 2020;25:124-125.

99. Drummond M, Sculpher M, Claxton K, Stoddart G, Torrance G. *Methods for the economic evaluation of health care programmes (fourth edition)*. Oxford: Oxford University Press; 2015.

100. Cazzola M, Macnee W, Martinez F, Rabe K, Franciosi L, Barnes P, et al. Outcomes for COPD pharmacological trials: from lung function to biomarkers. *European Respiratory Journal*. 2008;31:416-469.

101. Gray A, Clarke P, Wolstenholme J, Wordsworth S. *Applied methods of cost-effectivess analysis in health care*. Oxford: Oxford University Press; 2011.

102. Wang S, Gum D, Merlin T. Comparing the ICERs in medicine reimbursement submissions to NICE and PBAC - does the presence of an explicit threshold affect the ICER proposed? *Value in Health*. 2018;21:938-943.

103. Michie S, Richardson M, Johnston M, Abraham C, Francis J, Hardeman W, et al. The Behavior Change Technique Taxonomy (v1) of 93 hierarchically clustered techniques: building an international consensus for the reporting of behavior change interventions. *Annals of Behavioral Medicine*. 2013;46:81-95.

104. Williams M, Effing T, Paquet C, Gibbs C, Lewthwaite H, Li L, et al. Counseling for health behavior change in people with COPD: systematic review. *International Journal of COPD* 2017;12:2165-2178.

105. Howard C, Guntupalli K. Update in Pulmonary Medicine: Evidence Published in 2016. *Annals of Internal Medicine*. 2017;166:W40-43.

106. Rochester C. Patient assessment and selection for pulmonary rehabilitation. *Respirology*. 2019;24:844-853.

107. Commonwealth Scientific and Industrial Research Organisation. Future of Health. Canberra: CSIRO Futures; 2018.

108. PwC. Reimaging health reform in Australia. National Health Practice, PwC (Australia); 2016.

109. Medical Services Advisory Committee. Public Summary Document: Application No. 1405 - MBS Item Number for Pulmonary Rehabilitation. Canberra: Australian Government; 2016.

Appendices

Appendix A: Ethics approvals

Appendix A1: Modified Incremental Step Test

The Alfred

theAlfred

Ethics Committee

Certificate of Approval of Amendments

This is to certify that amendments to

Project: 58358 (Local reference: **207/16**) **Clinical applications of the modified incremental step test for people with Chronic Obstructive Pulmonary Disease**

Coordinating Principal Investigator:
Professor Anne Holland

Amendment:
Conversion to SERP
Addition of site: Wimmera Base Hospital (Wimmera Health Care Group)
(Site PI: Ms Heather Macdonald)

Attachments:
Protocol version **4** dated **2-Sep-2019**
PICF (sub-study) version **7** dated **22-Sep-2019**

have been approved under the Victorian Streamlined Ethics Review Process (SERP) in accordance with your amendment application dated **2-Sep-2019** on the understanding that you observe the National Statement on Ethical Conduct in Human Research.

It is now your responsibility to ensure that all people associated with this particular research project are made aware of what has actually been approved and any caveats specified in correspondence with the Ethics Committee. Any further change to the application which is likely to have a significant impact on the ethical considerations of this project will require approval from the Ethics Committee.

Professor John J. McNeil
Chair, Ethics Committee

Date: **26-Sep-2019**

All research subject to Alfred Hospital Ethics Committee review must be conducted in accordance with the National Statement on Ethical Conduct in Human Research (2007).

The Alfred Ethics Committee is a properly constituted Human Research Ethics Committee operating in accordance with the National Statement on Ethical Conduct in Human Research (2007).

58358

Page 1 of 1

Wimmera
Health Care
Group

Incorporating Wimmera Base Hospital
and Dimboola District Hospital
Baillie Street, Horsham, Victoria 3400
Telephone (03) 5381 9111
Facsimile (03) 5382 0829
www.whcg.org.au
ceo@whcg.org.au

19 December 2019

Mrs Heather Macdonald
WHCG
HORSHAM VIC 3400
Heather.macdonald@whcg.org.au

Dear Heather

Re: Clinical applications of the modified incremental step test for people with chronic lung disease- assessing exercise prescriptions. (CRC 19/6)

The Wimmera Health Care Group Clinical Research Committee has reviewed and formally approved the above project application at its most recent meeting.

You should note that the following standard conditions apply to all projects approved by this hospital:

a. Limit of approval: approval is limited strictly to the research proposal as submitted on your application.

b. Variation to Project: any subsequent variations or modifications you may wish to make to your project must be notified formally to this committee for further consideration and approval. If the committee considers that the proposed changes are significant you may be required to submit a new application for approval of the revised project.

c. Incidents or Adverse Effects: researchers must report immediately to the committee anything which might affect the ethical acceptance of the protocol including adverse effects on the subjects or unforseen events that might affect continued ethical acceptability of the project.

d. Progress Reporting: Please be aware that the Clinical Research Committee requires all researchers to submit a report on each of their projects yearly, or at the conclusion of the project if it continues for less than a year. A report must also be submitted if the project is discontinued. Failure to submit a progress report may mean that approval for this project will lapse. **The next progress report for this project is due 19th December 2020.**

e. Auditing: all projects may be subject to audit by members of the committee

If you have any further queries on this matter, or require additional information, please contact me.

Yours sincerely

Alan

Professor Alan Wolff
Chairperson, Clinical Research Committee

Cc: Ms Briana Farr, Manager Health Information Services- WHCG

UNIVERSIDADE NOVE DE JULHO - UNINOVE

PARECER CONSUBSTANCIADO DO CEP

DADOS DA EMENDA

Título da Pesquisa: VALIDAÇÃO DO TESTE DO DEGRAU ENDURANCE E AVALIAÇÃO DE SUA RESPONSIVIDADE APÓS UM PROGRAMA DE REABILITAÇÃO PULMONAR EM PACIENTES COM DOENÇA PULMONAR OBSTRUTIVA CRÔNICA

Pesquisador: José Carlos Rodrigues Júnior

Área Temática:

Versão: 3

CAAE: 59148716.7.0000.5511

Instituição Proponente: ASSOCIACAO EDUCACIONAL NOVE DE JULHO

Patrocinador Principal: Financiamento Próprio

DADOS DO PARECER

Número do Parecer: 1.912.086

Apresentação do Projeto:

Introdução: O teste de caminhada de seis minutos (TC6) e o shuttle walk test (SWT) são vastamente utilizados para a avaliação da capacidade funcional em pacientes com doença pulmonar obstrutiva crônica (DPOC), entretanto sua execução pode ser limitada pelo espaço físico. Nesse contexto, o teste do degrau possui a facilidade de poder ser aplicado em qualquer ambiente, inclusive o domiciliar. Entretanto, não há na literatura um teste do degrau para avaliar o limite de tolerância (endurance) a este teste.

Objetivo da Pesquisa:

Objetivos: 1) elaborar um teste do degrau endurance (TDE) para pacientes com DPOC, 2) estabelecer os determinantes do desempenho obtido no TDE, 2) investigar sua responsividade para demonstrar aumento da capacidade de exercício após treinamento físico; 3) testar a reprodutibilidade do TDE 4) determinar a diferença mínima clinicamente importante
após um programa de reabilitação pulmonar.

Avaliação dos Riscos e Benefícios:

Pode acontecer sensação de dispneia e dessaturação de oxigênio durantes a realização dos testes ou dos exercícios físicos.

Endereço: VERGUEIRO nº 235/249
Bairro: LIBERDADE **CEP:** 01.504-001
UF: SP **Município:** SAO PAULO
Telefone: (11)3385-9197 **E-mail:** comitedeetica@uninove.br

Melhora da capacidade funcional após o programa de treinamento físico.

Comentários e Considerações sobre a Pesquisa:
Documentos apresentados de maneira satisfatória. Trata-se de uma emenda.

Considerações sobre os Termos de apresentação obrigatória:
TCLE apresentado satisfatoriamente.

Conclusões ou Pendências e Lista de Inadequações:
Emenda aprovada.

Considerações Finais a critério do CEP:
Para início da coleta dos dados, o pesquisador deverá se apresentar na mesma instância que autorizou a realização do estudo (Coordenadoria, Supervisão, SMS/Gab, etc). O sujeito de pesquisa (ou seu representante) e o pesquisador responsável deverão rubricar todas as folhas do Termo de Consentimento Livre e Esclarecido - TCLE apondo sua assinatura na última página do referido Termo, conforme Carta Circular no 003/2011 da CONEP/CNS. Salientamos que o pesquisador deve desenvolver a pesquisa conforme delineada no protocolo aprovado. Eventuais modificações ou emendas ao protocolo devem ser apresentadas ao CEP de forma clara e sucinta, identificando a parte do protocolo a ser modificada e suas justificativas. Lembramos que esta modificação necessitará de aprovação ética do CEP antes de ser implementada.
Ao pesquisador cabe manter em arquivo, sob sua guarda, por 5 anos, os dados da pesquisa, contendo fichas individuais e todos os demais documentos recomendados pelo CEP (Res. CNS 466/2012).
De acordo com a Res. CNS 196, IX.2.c, o pesquisador deve apresentar a este CEP/SMS os relatórios semestrais. O relatório final deverá ser enviado através da Plataforma Brasil, ícone Notificação. Uma cópia digital (CD/DVD) do projeto finalizado deverá ser enviada à instância que autorizou a realização do estudo, via correio ou entregue pessoalmente, logo que o mesmo estiver concluído.

Este parecer foi elaborado baseado nos documentos abaixo relacionados:

Tipo Documento	Arquivo	Postagem	Autor	Situação
Informações Básicas do Projeto	PB_INFORMAÇÕES_BÁSICAS_804494_E1.pdf	31/01/2017 15:44:36		Aceito
Outros	adendo.docx	31/01/2017 15:42:16	José Carlos Rodrigues Júnior	Aceito

Endereço: VERGUEIRO nº 235/249
Bairro: LIBERDADE **CEP:** 01.504-001
UF: SP **Município:** SAO PAULO
Telefone: (11)3385-9197 **E-mail:** comitedeetica@uninove.br

Projeto Detalhado / Brochura Investigador	Projeto_detalhado.docx	13/09/2016 13:28:13	José Carlos Rodrigues Júnior	Aceito
TCLE / Termos de Assentimento / Justificativa de Ausência	TCLE.doc	13/09/2016 13:27:50	José Carlos Rodrigues Júnior	Aceito
Folha de Rosto	folha.pdf	13/09/2016 13:26:43	José Carlos Rodrigues Júnior	Aceito

Situação do Parecer:
Aprovado

Necessita Apreciação da CONEP:
Não

SAO PAULO, 08 de Fevereiro de 2017

Assinado por:
Andrey Jorge Serra
(Coordenador)

Endereço: VERGUEIRO nº 235/249
Bairro: LIBERDADE **CEP:** 01.504-001
UF: SP **Município:** SAO PAULO
Telefone: (11)3385-9197 **E-mail:** comitedeetica@uninove.br

LA TROBE UNIVERSITY

University Human Ethics Committee

RESEARCH OFFICE

MEMORANDUM

To: **Professor Anne Holland, School of Allied Health, College of SHE**

From: **Senior Human Ethics Officer, Ethics and Integrity**

Subject: **Externally approved project - A Holland - Alfred - June 2016**

Title: **Clinical applications of the modified incremental step test for people with Chronic Obstructive Pulmonary Disease**

Date: **23 June 2016**

Thank you for submitting the above protocol to the University Human Ethics Committee (UHEC). Your material was forwarded to the UHEC Chair for consideration. Following evidence of a full review and subsequent final approval by the **The Alfred HREC**, the UHEC Chair agrees that the protocol complies with the National Health and Medical Research Council's *National Statement on Ethical Conduct in Human Research* and is in accordance with La Trobe University's *Human Research Ethics Guidelines*.

Endorsement is given for you to take part in this study in line with the conditions of final approval outlined by **The Alfred HREC.**

Limit of Approval. La Trobe UHEC endorsement is limited strictly to the research protocol as approved by **The Alfred HREC**.

Variation to Project. As a consequence of the previous condition, any subsequent modifications approved by **The Alfred HREC** for the project should be notified formally to the UHEC.

Annual Progress Reports. Copies of all progress reports submitted to **The Alfred HREC** must be forwarded to the UHEC. Failure to submit a progress report will mean that endorsement for your involvement this project will be rescinded. An audit related to your involvement in the study may be conducted by the UHEC at any time.

Final Report. A copy of the final report is to be forwarded to the UHEC within one month of it being submitted to **The Alfred HREC.**

If you have any queries on the information above please e-mail: humanethics@latrobe.edu.au or

contact me by phone.

On behalf of the La Trobe University Human Ethics Committee, best wishes with your research!

Kind regards,

Sara Paradowski
Senior Human Ethics Officer
Executive Officer – University Human Ethics Committee
Ethics and Integrity / Research Office
La Trobe University Bundoora, Victoria 3086
P: (03) 9479 – 1443 / F: (03) 9479 - 1464
http://www.latrobe.edu.au/researchers/ethics/human-ethics

Appendix A2: HomeBase (data for compositional data analysis and economic analysis)

The Alfred

TheAlfred

ETHICS COMMITTEE CERTIFICATE OF APPROVAL

This is to certify that

Project No: 261/11

Project Title: Benefits and costs of home-based pulmonary rehabilitation for people with chronic obstructive pulmonary disease

Principal Researcher: A/Professor Anne Holland

Participant Information and Consent Form version 2 **dated:** 18-Jul-2011

was considered by the Ethics Committee on ***28-Jul-2011*** *and* ***APPROVED*** *on* **28-Jul-2011**

It is the Principal Researcher's responsibility to ensure that all researchers associated with this project are aware of the conditions of approval and which documents have been approved.

The Principal Researcher is required to notify the Secretary of the Ethics Committee, via amendment or progress report, of

- Any significant change to the project and the reason for that change, including an indication of ethical implications (if any);
- Serious adverse effects on participants and the action taken to address those effects;
- Any other unforeseen events or unexpected developments that merit notification;
- The inability of the Principal Researcher to continue in that role, or any other change in research personnel involved in the project;
- Any expiry of the insurance coverage provided with respect to sponsored clinical trials and proof of re-insurance;
- A delay of more than 12 months in the commencement of the project; and,
- Termination or closure of the project.

Additionally, the Principal Researcher is required to submit

- A Progress Report on the anniversary of approval and on completion of the project *(forms to be provided)*;

The Ethics Committee may conduct an audit at any time.

All research subject to the Alfred Hospital Ethics Committee review must be conducted in accordance with the National Statement on Ethical Conduct in Human Research (2007).

The Alfred Hospital Ethics Committee is a properly constituted Human Research Ethics Committee in accordance with the National Statement on Ethical Conduct in Human Research (2007).

SPECIAL CONDITIONS

None

SIGNED: _____
Chair, Ethics Committee (or delegate)

R. FREW
SECRETARY
ETHICS COMMITTEE

Please quote Project No and Title in all correspondence

Austin Health

Austin Hospital

145 Studley Road
PO Box 5555 Heidelberg
Victoria Australia 3084
Telephone 03 9496 5000
Facsimile 03 9458 4779
www.austin.org.au

Human Research Ethics Committee
Research Ethics Unit
Henry Buck Building
Austin Hospital

TO:	**A/Prof Anne Holland** **Alfred Health Clinical School, LaTrobe University** **Level 4, The Alfred Centre, Commercial Rd Melbourne VIC 3004**
PROJECT:	Benefits and costs of home-based pulmonary rehabilitation in chronic obstructive pulmonary disease
PROTOCOL NO: **PROJECT NO:**	H2011/04364
FROM:	**Ms Jill Davis, Research Ethics Unit Manager**
DATE:	22 September 2011
RE:	**Protocol Version 2 dated 20 June 2011** **Participant Information and Consent Form Version 2 dated 20 July 2011** **Advertisement** **Modified Medical Research Council Dyspnoea Scale** **Chronic Respiratory Questionnaire (Self Reported) Follow Up** **Your Health and Well-Being Survey** **Home Exercise Diary**
Approval Period:	**22 September 2011 to 22 September 2014**

Agenda Item:

Further to my letter dated 25 August 2011 concerning the above detailed project, I am writing to acknowledge that your response to the issues raised by the Human Research Ethics Committee at their meeting on 18 August 2011 is satisfactory. This project now has full ethical approval for a period of three years from the date of this letter.

Before the study can commence you must ensure that you have:

- For trials involving radiation it is your responsibility to ensure the research is added to the Austin Health Management Licence issued by Department of Human Services – Radiation Safety Section prior to study commencement should it be required (check your Medical Physicist Report). The HREC must be notified when the research has been added to the licence.
- It is a requirement that a progress report is submitted to the Committee annually, or more frequently as directed. Please note a final report must be

submitted for all studies. Should you plan for your study to go beyond the 3-year ethics approval, please request in writing an extension of ethics approval prior to its lapsing. If your study will not commence within 12 months, a request must be forwarded to the HREC justifying the delay beyond 12 months. Should such a request not be received, ethics approval will lapse and a resubmission to the HREC will then be necessary.

- After commencement of your study, should the trial be discontinued prematurely you must notify the HREC of this, citing the reason.
- Any changes to the original application will require a submission of a protocol amendment for consideration as this approval only relates to the original application as detailed above.
- Please notify the HREC of any changes to research personnel. All new investigators must be approved prior to performing any study related activities.
- It is now your responsibility to ensure that all people (i.e. all investigators, sponsor and other relevant departments in the hospital) associated with this particular study are made aware of what has been approved.

The Committee wishes to be informed as soon as practicable of any untoward effects experienced by any participant in the trial where those effects in degree or nature were not anticipated by the researchers. The HREC has adopted the NHMRC Australian Health Ethics Committee (AHEC) Position Statement 'Monitoring and reporting of safety for clinical trials involving therapeutic products' May 2009

Please ensure you frequently refer to the Research Ethics Unit website http://www.austin.org.au/Page.aspx?ID=415 for all up to date information about research and ethical requirements.

DETAILS OF ETHICS COMMITTEE:
It is the policy of the Committee not to release personal details of its members. However I can confirm that at the meeting at which the above project was considered, the Committee fulfilled the requirements of the National Health and Medical Research Council in that it contained men and women encompassing different age groups and included people in the following categories:

Chairperson
Ethicist
Lawyer
Lay Man
Lay Woman
Person fulfilling a Pastoral Care Role
Person with Counselling Experience
Person with Research Experience

Additional members include:

- Chairs of all sub committees, or nominees
- Other persons as considered appropriate for the type/s of research usually being considered

I confirm that the Principal Investigator or Co-Investigators were not involved in the approval of this project. I further confirm that all relevant documentation relating to this study is kept on the premises of Austin Health for more than three years.

The Committee is organised and operates according to the National Statement on Ethical Conduct in Human Research (NHMRC The National Statement) and the Note for Guidance on Good Clinical Research Practice (CPMP/ICH/135/95) annotated with TGA comments (July 2008) and the applicable laws and regulations; and the Health Privacy Principles in The Health Records Act 2001.

PLEASE NOTE: The Committee requests that the Research Ethics Unit ethics@austin.org.au) is informed of the actual starting date of the study as soon as the study commences. A written notice (e-mail, fax or letter) is considered the appropriate format for notification.

Jill Davis

This HREC is constituted and operates in accordance with the National Health and Medical Research Council's (NHMRC) National Statement on Ethical Conduct in Human Research (2007), NHMRC and Universities Australia Australian Code for the Responsible Conduct of Research (2007) and the CPMP/ICH Note for Guidance on Good Clinical Practice. The process this HREC uses to review multi-centre research proposals has been certified by the NHMRC.

La Trobe University
Faculty of Health Sciences
MEMORANDUM

TO: Dr Anne Holland, Christine McDonald, Ajay Mahal, Catherine Hill, Annemarie Lee, Angela Burge — School of Physiotherapy

SUBJECT: *Reference:* **FHEC11/134**

Student or Other Investigator:

Title: **Benefits and costs of home-based pulmonary rehabilitation in chronic obstructive pulmonary disease**

DATE: 24 August, 2011

The Faculty Human Ethics Committee's (FHEC) reviewers have considered and approved the above project. You may now proceed.

Please note that the Informed Consent forms need to be retained for a minimum of 5 years. Please ensure that each participant retains a copy of the Informed Consent form. Researchers are also required to retain a copy of all Informed Consent forms separately from the data. The data must be retained for a period of 15 years.

Please note that any modification to the project must be submitted in writing to FHEC for approval. You are required to provide an annual report (where applicable) and/or a final report on completion of the project. A copy of the progress/final report can be downloaded from the following website: http://www.latrobe.edu.au/rgso/forms-resources/forms/ethic-prog-final.rtf

Please return the completed form to The Secretary, FHEC, Faculty of Health Sciences Office, La Trobe University, Victoria 3086.

If you have a student/s involved in this project, a copy of this memorandum is enclosed for you to forward to the student(s) concerned.

Dr Ellie Fossey
Chair
Faculty Human Ethics Committee
Faculty of Health Sciences

Appendix B: Copyright approvals

Appendix B1: For Chapter 2 – Interventions for promoting physical activity in people with chronic obstructive pulmonary disease

The paper from Chapter 2 was published in the *Cochrane Database of Systematic Reviews* in 2020 and the citation is as follows:

Burge AT, Cox NS, Abramson MJ, Holland AE. Interventions for promoting physical activity in people with chronic obstructive pulmonary disease (COPD). *Cochrane Database of Systematic Reviews* 2020;4;CD012626. doi: 10.1002/14651858.CD012626.pub2.

See the next pages for relevant copyright agreement terms for use in this thesis.

JOHN WILEY AND SONS LICENSE TERMS AND CONDITIONS

Sep 05, 2020

This Agreement between Angela Burge ("You") and John Wiley and Sons ("John Wiley and Sons") consists of your license details and the terms and conditions provided by John Wiley and Sons and Copyright Clearance Center.

License Number

4902850399185

License date

Sep 05, 2020

Licensed Content Publisher

John Wiley and Sons

Licensed Content Publication

Cochrane Database of Systematic Reviews

Licensed Content Title

Interventions for promoting physical activity in people with chronic obstructive pulmonary disease (COPD)

Licensed Content Author

Angela T Burge, Narelle S Cox, Michael J Abramson, et al

Licensed Content Date

Apr 16, 2020

Type of use

Dissertation/Thesis

Requestor type

Author of this Wiley article

Format

Print and electronic

Portion

Text extract

Number of Pages

73

Institution name

La Trobe University

Expected presentation date

Sep 2020

Portions

pg 1-64, Tables 1&2

TERMS AND CONDITIONS

This copyrighted material is owned by or exclusively licensed to John Wiley & Sons, Inc. or one of its group companies (each a"Wiley Company") or handled on behalf of a society with which a Wiley Company has exclusive publishing rights in relation to a particular work (collectively "WILEY"). By clicking "accept" in connection with completing this licensing transaction, you agree that the following terms and conditions apply to this transaction (along with the billing and payment terms and conditions established by the Copyright Clearance Center Inc., ("CCC's Billing and Payment terms and conditions"), at the time that you opened your RightsLink account (these are available at any time at http://myaccount.copyright.com).

Terms and Conditions

- The materials you have requested permission to reproduce or reuse (the "Wiley Materials") are protected by copyright.
- You are hereby granted a personal, non-exclusive, non-sub licensable (on a stand-alone basis), non-transferable, worldwide, limited license to reproduce the Wiley Materials for the purpose specified in the licensing process. This license, **and any CONTENT (PDF or image file) purchased as part of your order,** is for a one-time use only and limited to any maximum distribution number specified in the license. The first instance of republication or reuse granted by this license must be completed within two years of the date of the grant of this license (although copies prepared before the end date may be distributed thereafter). The Wiley Materials shall not be used in any other manner or for any other purpose, beyond what is granted in the license. Permission is granted subject to an appropriate acknowledgement given to the author, title of the material/book/journal and the publisher. You shall also duplicate the copyright notice that appears in the Wiley publication in your use of the Wiley Material. Permission is also granted on the understanding that nowhere in the text is a previously published source acknowledged for all or part of this Wiley Material. Any third party content is expressly excluded from this permission.

- With respect to the Wiley Materials, all rights are reserved. Except as expressly granted by the terms of the license, no part of the Wiley Materials may be copied, modified, adapted (except for minor reformatting required by the new Publication), translated, reproduced, transferred or distributed, in any form or by any means, and no derivative works may be made based on the Wiley Materials without the prior permission of the respective copyright owner.**For STM Signatory Publishers clearing permission under the terms of the STM Permissions Guidelines only, the terms of the license are extended to include subsequent editions and for editions in other languages, provided such editions are for the work as a whole in situ and does not involve the separate exploitation of the permitted figures or extracts,** You may not alter, remove or suppress in any manner any copyright, trademark or other notices displayed by the Wiley Materials. You may not license, rent, sell, loan, lease, pledge, offer as security, transfer or assign the Wiley Materials on a stand-alone basis, or any of the rights granted to you hereunder to any other person.

- The Wiley Materials and all of the intellectual property rights therein shall at all times remain the exclusive property of John Wiley & Sons Inc, the Wiley Companies, or their respective licensors, and your interest therein is only that of having possession of and the right to reproduce the Wiley Materials pursuant to Section 2 herein during the continuance of this Agreement. You agree that you own no right, title or interest in or to the Wiley Materials or any of the intellectual property rights therein. You shall have no rights hereunder other than the license as provided for above in Section 2. No right, license or interest to any trademark, trade name, service mark or other branding ("Marks") of WILEY or its licensors is granted hereunder, and you agree that you shall not assert any such right, license or interest with respect thereto

- NEITHER WILEY NOR ITS LICENSORS MAKES ANY WARRANTY OR REPRESENTATION OF ANY KIND TO YOU OR ANY THIRD PARTY, EXPRESS, IMPLIED OR STATUTORY, WITH RESPECT TO THE MATERIALS OR THE ACCURACY OF ANY INFORMATION CONTAINED IN THE MATERIALS, INCLUDING, WITHOUT LIMITATION, ANY IMPLIED WARRANTY OF MERCHANTABILITY, ACCURACY, SATISFACTORY QUALITY, FITNESS FOR A PARTICULAR PURPOSE, USABILITY, INTEGRATION OR NON-INFRINGEMENT AND ALL SUCH WARRANTIES ARE HEREBY EXCLUDED BY WILEY AND ITS LICENSORS AND WAIVED BY YOU.

- WILEY shall have the right to terminate this Agreement immediately upon breach of this Agreement by you.

- You shall indemnify, defend and hold harmless WILEY, its Licensors and their respective directors, officers, agents and employees, from and against any actual or threatened claims, demands, causes of action or proceedings arising from any breach of this Agreement by you.

- IN NO EVENT SHALL WILEY OR ITS LICENSORS BE LIABLE TO YOU OR ANY OTHER PARTY OR ANY OTHER PERSON OR ENTITY FOR ANY SPECIAL, CONSEQUENTIAL, INCIDENTAL, INDIRECT, EXEMPLARY OR PUNITIVE DAMAGES, HOWEVER CAUSED, ARISING OUT OF OR IN CONNECTION WITH THE DOWNLOADING, PROVISIONING, VIEWING OR USE OF THE MATERIALS REGARDLESS OF THE FORM OF ACTION,

WHETHER FOR BREACH OF CONTRACT, BREACH OF WARRANTY, TORT, NEGLIGENCE, INFRINGEMENT OR OTHERWISE (INCLUDING, WITHOUT LIMITATION, DAMAGES BASED ON LOSS OF PROFITS, DATA, FILES, USE, BUSINESS OPPORTUNITY OR CLAIMS OF THIRD PARTIES), AND WHETHER OR NOT THE PARTY HAS BEEN ADVISED OF THE POSSIBILITY OF SUCH DAMAGES. THIS LIMITATION SHALL APPLY NOTWITHSTANDING ANY FAILURE OF ESSENTIAL PURPOSE OF ANY LIMITED REMEDY PROVIDED HEREIN.

- Should any provision of this Agreement be held by a court of competent jurisdiction to be illegal, invalid, or unenforceable, that provision shall be deemed amended to achieve as nearly as possible the same economic effect as the original provision, and the legality, validity and enforceability of the remaining provisions of this Agreement shall not be affected or impaired thereby.

- The failure of either party to enforce any term or condition of this Agreement shall not constitute a waiver of either party's right to enforce each and every term and condition of this Agreement. No breach under this agreement shall be deemed waived or excused by either party unless such waiver or consent is in writing signed by the party granting such waiver or consent. The waiver by or consent of a party to a breach of any provision of this Agreement shall not operate or be construed as a waiver of or consent to any other or subsequent breach by such other party.

- This Agreement may not be assigned (including by operation of law or otherwise) by you without WILEY's prior written consent.

- Any fee required for this permission shall be non-refundable after thirty (30) days from receipt by the CCC.

- These terms and conditions together with CCC's Billing and Payment terms and conditions (which are incorporated herein) form the entire agreement between you and WILEY concerning this licensing transaction and (in the absence of fraud) supersedes all prior agreements and representations of the parties, oral or written. This Agreement may not be amended except in writing signed by both parties. This Agreement shall be binding upon and inure to the benefit of the parties' successors, legal representatives, and authorized assigns.

- In the event of any conflict between your obligations established by these terms and conditions and those established by CCC's Billing and Payment terms and conditions, these terms and conditions shall prevail.

- WILEY expressly reserves all rights not specifically granted in the combination of (i) the license details provided by you and accepted in the course of this licensing transaction, (ii) these terms and conditions and (iii) CCC's Billing and Payment terms and conditions.

- This Agreement will be void if the Type of Use, Format, Circulation, or Requestor Type was misrepresented during the licensing process.

- This Agreement shall be governed by and construed in accordance with the laws of the State of New York, USA, without regards to such state's conflict of law rules. Any legal action, suit or proceeding arising out of or relating to these Terms

and Conditions or the breach thereof shall be instituted in a court of competent jurisdiction in New York County in the State of New York in the United States of America and each party hereby consents and submits to the personal jurisdiction of such court, waives any objection to venue in such court and consents to service of process by registered or certified mail, return receipt requested, at the last known address of such party.

WILEY OPEN ACCESS TERMS AND CONDITIONS

Wiley Publishes Open Access Articles in fully Open Access Journals and in Subscription journals offering Online Open. Although most of the fully Open Access journals publish open access articles under the terms of the Creative Commons Attribution (CC BY) License only, the subscription journals and a few of the Open Access Journals offer a choice of Creative Commons Licenses. The license type is clearly identified on the article.

The Creative Commons Attribution License

The Creative Commons Attribution License (CC-BY) allows users to copy, distribute and transmit an article, adapt the article and make commercial use of the article. The CC-BY license permits commercial and non-

Creative Commons Attribution Non-Commercial License

The Creative Commons Attribution Non-Commercial (CC-BY-NC)License permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes.(see below)

Creative Commons Attribution-Non-Commercial-NoDerivs License

The Creative Commons Attribution Non-Commercial-NoDerivs License (CC-BY-NC-ND) permits use, distribution and reproduction in any medium, provided the original work is properly cited, is not used for commercial purposes and no modifications or adaptations are made. (see below)

Use by commercial "for-profit" organizations

Use of Wiley Open Access articles for commercial, promotional, or marketing purposes requires further explicit permission from Wiley and will be subject to a fee.

Further details can be found on Wiley Online Library http://olabout.wiley.com/WileyCDA/Section/id-410895.html

v1.10 Last updated September 2015

Appendix B2: For Chapter 5 – Home-based rehabilitation for COPD using minimal resources: an economic evaluation

The paper from Chapter 5 was published in *Respirology* in 2020 and the citation is as follows:

Burge, A, Holland A, McDonald C, Hill C, Lee A, Cox N, Moore R, Nicolson C, Lahham A, Gillies R, Abramson M, Mahal A. Home-based rehabilitation for COPD using minimal resources: an economic evaluation. Respirology 2020;25:183-190 doi: 10.1111/resp.13667

See the next page for relevant copyright agreement terms which include a 12-month embargo on the accepted version.

C. PERMITTED USES BY CONTRIBUTOR

1. Submitted Version. The Owner licenses back the following rights to the Contributor in the version of the Contribution as originally submitted for publication (the "Submitted Version"):

a. The right to self-archive the Submitted Version on the Contributor's personal website, place in a not for profit subject-based preprint server or repository or in a Scholarly Collaboration Network (SCN) which has signed up to the STM article sharing principles [http://www.stm-assoc.org/stm-consultations/scn-consultation-2015/] ("Compliant SCNs"), or in the Contributor's company/ institutional repository or archive. This right extends to both intranets and the Internet. The Contributor may replace the Submitted Version with the Accepted Version, after any relevant embargo period as set out in paragraph C.2(a) below has elapsed. The Contributor may wish to add a note about acceptance by the Journal and upon publication it is recommended that Contributors add a Digital Object Identifier (DOI) link back to the Final Published Version.

b. The right to transmit, print and share copies of the Submitted Version with colleagues, including via Compliant SCNs, provided that there is no systematic distribution of the Submitted Version, e.g. posting on a listserve, network (including SCNs which have not signed up to the STM sharing principles) or automated delivery.

2. Accepted Version. The Owner licenses back the following rights to the Contributor in the version of the Contribution that has been peer-reviewed and accepted for publication, but not final (the "Accepted Version"):

a. The right to self-archive the Accepted Version on the Contributor's personal website, in the Contributor's company/institutional repository or archive, in Compliant SCNs, and in not for profit subject-based repositories such as PubMed Central, subject to an embargo period of 12 months for scientific, technical and medical (STM) journals and 24 months for social science and humanities (SSH) journals following publication of the Final Published Version. There are separate arrangements with certain funding agencies governing reuse of the Accepted Version as set forth at the following website: http://www.wileyauthors.com/funderagreements. The Contributor may not update the Accepted Version or replace it with the Final Published Version. The Accepted Version posted must contain a legend as follows: This is the accepted version of the following article: FULL CITE, which has been published in final form at [Link to final article]. This article may be used for non-commercial purposes in accordance with the Wiley Self-Archiving Policy [http://www.wileyauthors.com/self-archiving].

b. The right to transmit, print and share copies of the Accepted Version with colleagues, including via Compliant SCNs (in private research groups only before the embargo and publicly after), provided that there is no systematic distribution of the Accepted Version, e.g. posting on a listserve, network (including SCNs which have not signed up to the STM sharing principles) or automated delivery.