Interventions to modify physical activity in patients with COPD: a systematic review

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ABSTRACT The broad range of interventions to increase physical activity (PA) in patients with chronic obstructive pulmonary disease (COPD) has not been systematically assessed. We aimed to perform a systematic review of the interventional studies that have assessed PA as an outcome in patients with COPD.

A systematic search in five different databases (Medline, Embase, PsycINFO, CINAHL and Web of Science) was performed in March 2015. Two independent reviewers analysed the studies against the inclusion criteria (COPD defined by spirometry; prospective, randomised/nonrandomised studies, cohort and experimental studies with interventions using PA as an outcome), extracted the data and assessed the quality of evidence.

60 studies were included. Seven intervention groups were identified. PA counselling increased PA levels in COPD, especially when combined with coaching. 13 studies showed positive effects of pulmonary rehabilitation (PR) on PA, while seven studies showed no changes. All three PR programmes >12 weeks in duration increased PA. Overall, the quality of evidence was graded as very low.

Interventions focusing specifically on increasing PA, and longer PR programmes, may have greater impacts on PA in COPD. Well-designed clinical trials with objective assessment of PA in COPD patients are needed.

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Introduction

Assessment of physical activity (PA) in daily life as an outcome has generated growing scientific interest in recent years, especially in chronic respiratory diseases [1, 2], due to its relationship with mortality [3]. It is well known that preserved PA levels may delay or even prevent the appearance of chronic diseases [4, 5]. Patients with chronic obstructive pulmonary disease (COPD) are characterised by a sedentary lifestyle and reduced PA levels [6]. This inactivity is an independent predictor of the risk of hospitalisations due to acute exacerbations and early mortality in this population [1, 2]. Therefore, improving PA levels has been considered a key component in the management of patients with COPD.

Pulmonary rehabilitation (PR) is the most successful intervention aimed at improving symptoms (dyspnoea, muscle fatigue), exercise capacity, health-related quality of life, healthcare utilisation and costs in individuals with chronic respiratory disease [7]. However, the translation of the improvements in exercise capacity into increments in PA levels is less evident and still controversial [8, 9]. The ability to increase PA levels using other therapeutic strategies, such as PA counselling [10, 11], nutritional supplementation [12], long-term oxygen therapy (LTOT) [13] and bronchodilators [13, 14], has also been explored in COPD and the effects to date are variable. These different types of interventions were cited in two recent reviews [15, 16] and comprise the majority of the interventions able to change PA levels in patients with COPD. Therefore, we chose to use them as part of the search strategy of the present systematic review, in order to summarise the wide range of interventions that could increase PA in this population. Currently, it is still unclear which is the best strategy to increase PA levels in patients with COPD.

Recent systematic literature reviews have addressed the determinants and outcomes of PA in COPD [15], investigated the effects of PA counselling on PA and health-related outcomes in chronic disease [16], and outlined the components of PA interventions other than PR aimed at increasing PA in patients with COPD [17]. These well-designed and well-conducted systematic reviews have generated important scientific knowledge. However, there has been no systematic summary of the interventions aimed at modifying PA levels in patients with COPD. Thus, the aims of the present study were to perform a systematic review of the interventional studies that have assessed PA as an outcome in patients with COPD.

Methods

Data sources and search strategy

This systematic review followed the handbook of the Centre for Reviews and Dissemination [18] and the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines [19] for reporting systematic review analysis. A computerised literature search was performed in the following databases in March 2015 (date of last update): Medline/PubMed, Embase, PsycINFO, CINAHL and Web of Science. We performed some pre-piloted searches prior to the final search strategy, based on two recently published systematic reviews on a related topic [15, 16]. We also performed a hand search of the studies based on the bibliographic references of the included articles and PubMed's "related articles" search filters.

Our search strategy included a wide range of modalities with variable levels of evidence for modifying PA levels in COPD (*e.g.* exercise training, PA counselling, nutritional supplementation, LTOT and bronchodilators) (see online supplementary material for details) [15]. Bibliographic details of all articles from the different databases were stored in a reference managing software file (EndNote X7; Thomson Reuters, New York, NY, USA). We used a simple symbol system in EndNote to record reviewers' decisions on inclusion or exclusion of each article. More details about the protocol of the present systematic review can be found in the supplementary material.

Eligibility and exclusion criteria

Eligible studies were included if they fulfilled the following *a priori* defined criteria. 1) Population/participants: patients with COPD defined by spirometry (*i.e.* post-bronchodilator forced expiratory volume in 1 s (FEV_1)/forced vital capacity <0.7). 2) Study design: i) prospective longitudinal studies; ii) randomised and nonrandomised clinical trials, both arms (intervention plus control) if the outcome was PA; iii) cohort studies; and iv) experimental or pilot studies of any type of intervention targeting PA in patients with COPD. 3) Studies with interventions that have assessed PA as an outcome, defined as "any bodily movement produced by skeletal muscles that results in energy expenditure" [20]. Exclusion criteria were articles in a non-English language, review articles, notes, editorials, qualitative studies and scientific congress abstracts.

Study selection

Two independent reviewers (L.C. Mantoani and N. Rubio) screened the titles and abstracts of every citation against the inclusion criteria. The reviewers' decisions on including or excluding all the retrieved articles were recorded in the EndNote file. Potentially eligible articles were highlighted and retrieved for full text evaluation. The same independent reviewers assessed the remaining articles and made a decision on

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inclusion or exclusion based on the eligibility criteria. Any disagreements between the reviewers were usually resolved by consensus. Persistent disagreements were resolved by a third independent reviewer (R.A. Rabinovich). We recorded the bibliographic details of all excluded studies with the specific reasons for excluding them from the final analysis (see supplementary material for details).

Data extraction and quality assessment

From each included study, we extracted and recorded the following information in an Excel file: authors, journal, year of publication, study design, setting, sample size, blindness, patient characteristics (sex, age, FEV_1 and body mass index (BMI)), interventions (type, frequency, intensity and duration), PA measurements, outcomes and results.

We used the GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach [21, 22] to assess the quality of the included studies. The GRADE system has been used by many international organisations and is a transparent approach created to help systematic reviewers and guideline authors to rate the quality of the evidence and the strength of recommendations [21]. The GRADE approach assesses the overall quality of the studies and provides a score for the body of evidence instead of a score for each study. Therefore, our judgement on the quality of the evidence across the included studies was based on each group of studies of the different interventions to modify PA levels in patients with COPD (*i.e.* exercise training category). Two reviewers (L.C. Mantoani and R.A. Rabinovich) assessed the quality of evidence and categorised it accordingly (high, moderate, low or very low) [21, 22]. The body of the evidence for each identified intervention category started with the high quality level on GRADE (high confidence between true and estimated effect) and was downgraded for specific reasons [21, 22]. Therefore, very low quality evidence is the lowest score for a body of evidence. This means there is very little confidence in the estimated effect and more studies are very likely to change the estimate. More details on how we used the GRADE system to judge the quality of included studies can be found in the supplementary material.

Analysis and data synthesis

As expected, there was marked heterogeneity among included studies, with a wide range of both different interventions to modify and different methods to assess PA, which precluded a meta-analysis. Findings were summarised using harvest plots [23, 24] of the retrieved eligible studies. Although it was not possible to statistically summarise the results of the included studies, we have calculated the average percentage change in PA levels according to each intervention's category. This was calculated using the percentage of change relative to baseline levels in each measured variable (subjective or objective) of each study, then calculating the average change (as a percentage) considering each study within every intervention category.

Results

A flow diagram of the study is shown in figure 1. In total, 2495 articles were retrieved. After removing the duplicates from the different database searches, 2091 articles were analysed. 1946 were excluded based on the titles and abstract screening, leaving 145 articles considered as potentially eligible for full text analysis. An additional 22 articles were identified from among the references of these 145 articles and from the related articles search filter in PubMed as suitable for full text assessment. After excluding 107 of these studies for the reasons specified in figure 1, 60 articles were considered for data extraction in this systematic review.

Summary of studies

From the 60 studies included in this systematic review, 33 were randomised controlled trials (RCTs), 18 were non-RCTs and nine were experimental or pilot studies (six of them with a randomisation). Table 1 shows the reference details, study design, number of participants, type of intervention and methods for measuring PA in each of these studies. Additional information on the patients' characteristics, performed interventions and methods of measuring PA for the 60 included studies is presented in table S1 of the supplementary material. Seven types of intervention with the potential to increase PA levels in patients with COPD were identified: PA counselling, nutritional supplementation (dietary intervention), LTOT, bronchodilator, nocturnal noninvasive ventilation (NIV), neuromuscular electrical stimulation (NMES) and exercise training (including PR programmes and other exercise interventions).

30 of the included studies used exercise training as the main intervention to modify PA levels (20 of them with PR alone). 14 studies used PA counselling, four exploited the benefits of nutritional supplementation, three used LTOT, six used bronchodilators, two used nocturnal NIV and one study used NMES as its main intervention. Seven studies combined two different types of interventions (*e.g.* PR plus PA counselling).

38 studies assessed the level of daily PA with objective measurements (accelerometers, multisensors and/or pedometers), while 27 studies measured PA levels using subjective assessments (questionnaires and/or scales).

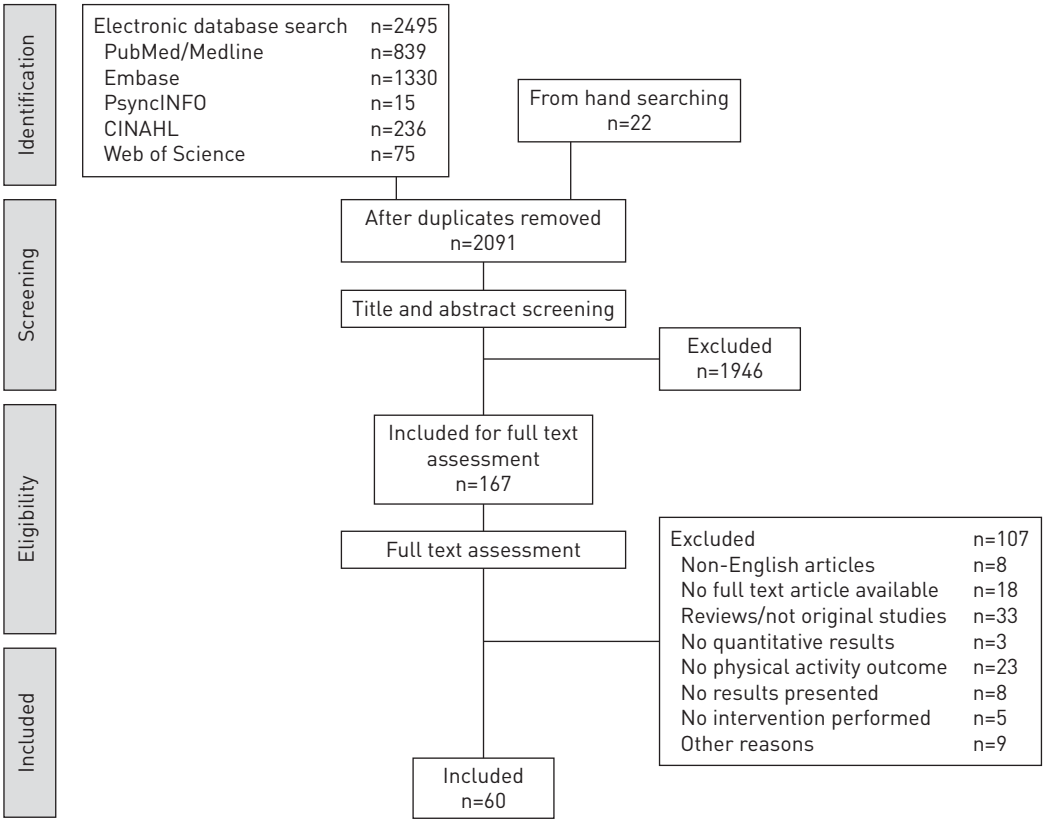

FIGURE 1 Flow diagram of the systematic review.

Four studies used both objective and subjective methods of measuring PA. More recent publications (from 2008 to date) chose more objective than subjective tools to measure daily PA levels in patients with COPD.

Overall, the quality of evidence across interventional studies to modify PA in patients with COPD was graded as very low (table 2). Serious imprecision and inconsistency across studies, as well as risk of bias (lack of blinding, concealment and/or randomisation process) and strongly suspected publication bias (studies with small sample size and absence of published negative results) were the main causes to downgrade the score for the quality of evidence. Directness was found across studies considering population, interventions and outcomes, regardless of intervention category.

Harvest plots and intervention characteristics

PA counselling

This category included three studies in which only advice on PA (PA advice) was given and 11 studies in which a coaching programme towards a more active life (PA coaching) was used with regular activity monitoring and incentive (figure 2a). Two studies in each category combined the PA intervention with exercise training. Almost half of the studies assessing the effect of PA counselling on PA levels were RCTs and most of these studies used objective tools to assess PA levels. Most studies were of a small sample size, included patients with moderate to very severe airflow limitation and had intervention periods of >8 weeks. The harvest plot shows that the most common intervention was PA coaching with the use of an activity monitor (figure 2a). The majority of the interventions (11 out of 14) increased PA levels, especially when they included objective activity monitoring. More details about the use of harvest plots in the present systematic review can be found in the supplementary material.

Nutritional supplementation

All the studies using nutritional supplementation were RCTs and 75% of the studies used objective tools to assess PA levels. All studies included patients with moderate to very severe airflow limitation with low BMI ($\leqslant$20 kg·m^{-2}). All studies provided nutritional supplementation to the patients for a minimum period of 8 weeks. 75% of the studies showed a positive impact on the levels of daily activities after treatment (figure 2b).

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TABLE 1 Reference details and study characteristics of the 60 studies included in the present systematic review

First author [ref.]	Year	Study design	Subjects n	Intervention type	PA measurement
Altenburg [25]	2015	RCT	155	PA counselling	Pedometer Yamax Digi-Walker SW-200
Barberan-Garcia [26]	2014	Non-RCT	143	PR plus telehealth care	Nonvalidated self-reported physical activity questionnaire
Bauldoff [27]	2002	Experimental/ RCT	24	Walking programme	Pedometer 342 and daily logs
Behnke [28]	2005	Non-RCT	88	Walking programme	Accelerometer Trictrac-R3D
Bendstrup [29]	1997	RCT	32	PR programme	Activities of Daily Living score specific for COPD
Berry [30]	2010	RCT	176	PR programme plus self-management	The Community Health Activities Model Program for Seniors
Borges [31]	2014	RCT	29	Resistance training	Accelerometer DynaPort Minimod
Breyer [32]	2010	RCT	60	Walking programme	Accelerometer DynaPort Activity Monitor
Casaburi [33]	2012	RCT	22	Oxygen therapy	Accelerometer RT3
Coronado [34]	2003	Non-RCT	15	PR programme	Accelerometer ADXL05
Dal Negro [35]	2010	RCT	32	Nutritional supplementation	Accelerometer SenseWear Armband PRO3
Dal Negro [36]	2012	RCT	88	Nutritional supplementation	Accelerometer SenseWear Armband PRO3
Dallas [37]	2009	Non-RCT	45	PR programme	Pedometer NL-200 Activity Monitor
Daly [38]	2011	Pilot/non-RCT	8	NMES	Accelerometer RT3
de Blok [10]	2006	Pilot/RCT	21	PA counselling plus PR programme	Pedometer Yamax Digi-Walker SW-200
Duiverman [39]	2008	RCT	66	Nocturnal NIPPV plus PR programme	Pedometer Yamax Digi-Walker SW-200
Duiverman [40]	2011	RCT	56	Nocturnal NIPPV plus physiotherapy	Groningen Activity and Restriction Scale
Effing [41]	2011	RCT	153	PR programme plus self-management	Pedometer Yamax Digi-Walker SW-200
Egan [42]	2012	Non-RCT	47	PR programme	Accelerometer Sense Wear Armband PRO3
Engström [43]	1999	RCT	50	PR plus walking programme	Sickness Impact Profile
Faager [44]	2004	Pilot/RCT	20	PR programme	Stanford Health Assessment Questionnaire
Faulkner [45]	2010	Pilot/RCT	14	PR programme plus PA counselling	7-day physical activity recall questionnaire
Goris [46]	2003	RCT	20	Nutritional supplementation	Accelerometer Tracmor
Hataji [14]	2013	Pilot/non-RCT	23	Bronchodilator	Accelerometer Lifecorder
Hospes [47]	2009	RCT	35	PA counselling	Pedometer Yamax Digi-Walker SW-200
Kesten [48]	2008	RCT	46	Bronchodilator	Nonvalidated activity questionnaire
Kozu [49]	2011	Non-RCT	45	PR programme	Activities of Daily Living score
Larson [50]	2014	RCT	49	Resistance training	Actigraph 7164
Mendoza [51]	2015	RCT	102	PA counselling	Tanita PD724 pedometer
Mercken [52]	2005	Non-RCT	11	PR programme	Accelerometer Physical Activity Monitor (Pam)
Mohammadi [53]	2013	RCT	106	Home-based rehabilitation	Barthel Index
Moy [54]	2010	Non-RCT	24	PA counselling	Pedometer Omron HJ-720ITC
Moy [55]	2012	Pilot/non-RCT	27	PA counselling	Pedometer Omron HJ-720ITC
Nguyen [11]	2009	Pilot/RCT	17	PA counselling	Accelerometer Stepwatch 3 Activity Monitor
Nield [56]	2005	Non-RCT	48	PR programme	Human Activity Profile
Nield [57]	2007	RCT	40	Breathing exercises	Human Activity Profile
Ninot [58]	2007	Non-RCT	23	PR programme	Physical Self Inventory-6
Nishijima [59]	2015	Non-RCT	18	Bronchodilator	Lifecorder Ex 4-second version
Pitta [8]	2008	Non-RCT	29	PR programme	Accelerometer DynaPort Activity Monitor
Pleguezuelos [60]	2013	RCT	125	PA counselling	Diary card
Pomidori [61]	2012	RCT	36	Walking programme	Accelerometer SenseWear Armband PRO3
Probst [62]	2011	RCT	40	PR programme	Accelerometer DynaPort Activity Monitor and SenseWear Armband PRO3
Ries [63]	1995	RCT	119	PR programme	Adapted form of the self-efficacy questionnaire
Sandland [64]	2008	RCT	20	Oxygen therapy	Accelerometer Gaehwiler Z80–32k V1
Sewell [65]	2005	RCT	180	PR programme	Accelerometer Gaehwiler Z80–32k V1 and Canadian Occupational Performance Measure
Sewell [66]	2010	RCT	95	PR programme	Accelerometer Gaehwiler Z80–32k V1
Shioya [67]	2008	RCT	17	Bronchodilator	London Chest Activities of Daily Living Scale
Skumlien [68]	2008	Non-RCT	40	PR programme	Hyrim Physical Activity Questionnaire and Glittre ADL-test
Steele [69]	2003	Non-RCT	38	PR programme	Accelerometer Tritrac R3D

Continued

TABLE 1 Continued

First author [ref.]	Year	Study design	Subjects n	Intervention type	PA measurement
Steele [70]	2008	RCT	102	Walking programme plus PA counselling	Accelerometer RT3 and Walking Self-Efficacy Questionnaire
Tabak [71]	2013	Pilot study/RCT	30	PA counselling	Pedometer Yamax Digi-Walker SW-200
Takigawa [72]	2007	Non-RCT	225	PR programme	Nonvalidated scale
Troosters [73]	2014	RCT	457	Bronchodilator	Accelerometer SenseWear Armband PRO3
Varga [74]	2007	Non-RCT	71	Home-based/continuous/ interval exercise training	Nonvalidated scale
Vergeret [75]	1989	RCT	159	Oxygen therapy	Nonvalidated questionnaire
Walker [76]	2008	Non-RCT	23	PR programme	Accelerometer Actiwatch and Dynaport Activity Monitor and Nottingham Extended Activities of Daily Living scale
Watz [77]	2014	RCT	83	Bronchodilator	Accelerometer SenseWear Armband
Weekes [12]	2009	RCT	59	Nutritional supplementation	Townsend score
Wewel [78]	2008	Non-RCT	21	PA counselling	Pedometer Kasper & Richter GmbH & Co. and accelerometer ActiTrac-Monitor
Yohannes [79]	2003	RCT	110	Walking programme plus oxygen therapy	The Barthel ADL index

PA: physical activity; RCT: randomised controlled trial; PR: pulmonary rehabilitation; COPD: chronic obstructive pulmonary disease; NMES: neuromuscular electrical stimulation; NIPPV: noninvasive positive pressure ventilation. Additional information on the patients' characteristics, performed interventions and methods of measuring PA is presented in supplementary table S1.

LTOT

All of the studies assessing the benefits of LTOT on PA levels in patients with COPD were RCTs. Two of the three included studies used accelerometers to measure PA levels. Patients were characterised by moderate to very severe airflow limitation, with low resting room air arterial oxygen saturation measured by pulse oximetry (<90%), and had been receiving LTOT at home over a period of ⩾8 weeks. The delivery of LTOT was diverse and included the use of ambulatory lightweight oxygen cylinders and oxygen concentrators. The use of ambulatory LTOT improved PA levels in COPD in only one out of the three studies (figure 2b).

Bronchodilators

Most of the studies of bronchodilators were RCTs including patients with moderate to very severe airflow limitation. Tiotropium and indacaterol were the most used bronchodilators and were compared to placebo or another bronchodilator. 67% of the studies measured PA levels with an objective tool and four out of the six studies delivered the interventions every day for ⩾12 weeks. As shown in the harvest plot (figure 2b), four out of the six bronchodilator studies resulted in increased PA levels in patients with COPD.

TABLE 2 Quality of evidence for interventions used to modify physical activity levels in patients with chronic obstructive pulmonary disease

Intervention [ref.]	Studies n	Quality assessment					Quality
		Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	
Physical activity counselling [10, 11, 25, 47, 51, 54, 55, 60, 70, 71, 78]	11	Serious	Serious	Not serious	Serious	Strongly suspected	Very low
Nutritional supplementation [12, 35, 36, 46]	4	Serious	Serious	Not serious	Serious	Strongly suspected	Very low
Long-term oxygen therapy [33, 64]	2	Not serious	Serious	Not serious	Serious	Strongly suspected	Very low
Bronchodilator [14, 48, 59, 67, 73, 77]	6	Not serious	Serious	Not serious	Serious	Strongly suspected	Very low
Nocturnal NIV [39]	1	Serious	Not serious	Not serious	Serious	Strongly suspected	Very low
NMES [38]	1	Serious	Not serious	Not serious	Serious	Strongly suspected	Very low
Pulmonary rehabilitation [8, 10, 29, 34, 37, 39, 42, 44, 49, 52, 56, 58, 62, 63, 65, 66, 69, 72, 74, 76]	20	Serious	Serious	Not serious	Serious	Unsuspected	Very low
Other exercise training [30, 32, 41, 43, 50, 53, 57, 61, 62, 74, 79]	11	Serious	Serious	Not serious	Serious	Unsuspected	Very low

NIV: noninvasive ventilation; NMES: neuromuscular electrical stimulation.

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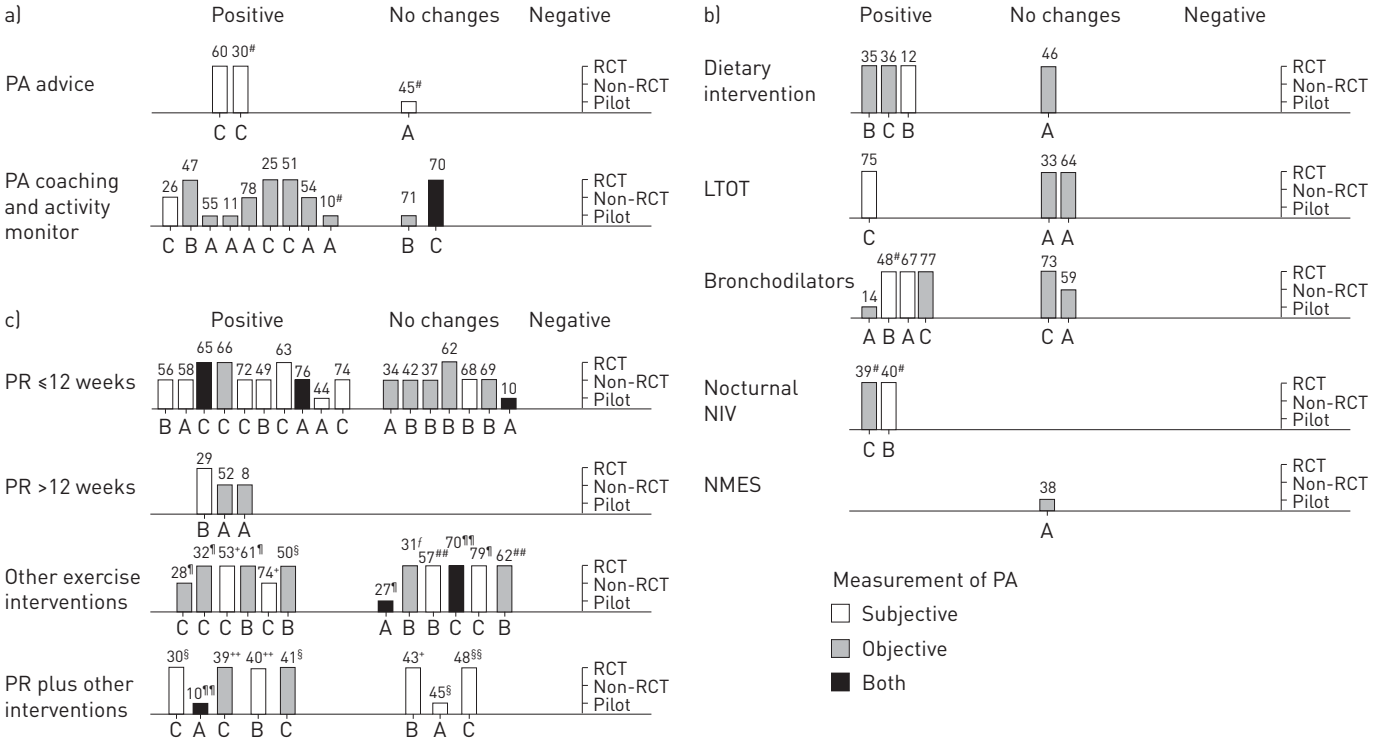

FIGURE 2 Harvest plots of the included studies. a) Studies that used physical activity (PA) counselling as the main intervention. b) Studies that used dietary intervention, long-term oxygen therapy (LTOT), bronchodilators, nocturnal noninvasive ventilation (NIV) and neuromuscular electrical stimulation (NMES) as the main intervention. c) Studies that used exercise training as the main intervention. A: studies with <30 patients; B: studies with 30–60 patients; C: studies with >60 patients; PR: pulmonary rehabilitation. The largest bars represent randomised controlled trials (RCTs), medium-sized bars represent non-RCTs and small bars represent pilot/experimental studies. The number on top of each bar represents the study's reference number in the present systematic review. #: addition of PR to the main intervention; ¶: walking programme; +: individualised/home training programme; §: self-management/PA advice programmes; *f*: resistance training alone; ##: breathing exercise; ¶¶: coaching programme (feedback on PA levels, individualised PA goals, and/or tailored motivational messages); ++: nocturnal NIV; §§: studies with bronchodilators.

Nocturnal NIV

Two studies assessed the impact of nocturnal NIV on PA levels in COPD patients. Both studies were RCTs and utilised exercise training in addition to the nocturnal NIV. One study assessed PA levels subjectively. Hypercapnic patients with severe and very severe airflow limitation were included in both studies. NIV was supplied *via* full face mask or nasal mask interface using a bilevel ventilator. Inspiratory and expiratory pressure with a spontaneous/timed mode with a backup frequency was applied. Interventions varied from 3 to 24 months' duration. All studies of nocturnal NIV in addition to exercise training increased PA levels of hypercapnic patients with COPD (figure 2b).

NMES

The only study performed in this area was a small pilot study, including eight patients with moderate to severe airflow obstruction. PA was measured with an accelerometer. NMES was applied on the quadriceps femoris of both legs through an electrical stimulation (impulses of tetanic frequency up to 19 Hz) for sessions of 1 h, 5 days per week over 8 weeks. NMES did not change daily activity levels of patients with COPD (figure 2b).

PR and other exercise interventions

PR alone

One third of the 60 included studies (n=20) used PR as the main intervention. 65% of the studies were non-RCTs and 11 of the 20 studies assessed PA levels with objective measurements. Most of the studies included patients with moderate to severe airflow limitation and involved high-intensity continuous exercise training (initial workload ⩾60% of exercise capacity) at least twice a week over a minimum period of 7 weeks. The prescription of training intensity was based on perceived effort scales (Borg scale), heart rate and exercise capacity (work rate or maximal oxygen consumption). 13 studies showed a positive effect on PA levels in patients with COPD, while seven studies showed no change. Interestingly, all the three studies that involved >12 weeks of PR programme showed a positive impact on PA levels of patients with COPD (figure 2c), while in programmes with ⩽12 weeks of training, only 10 out of 17 studies increased PA.

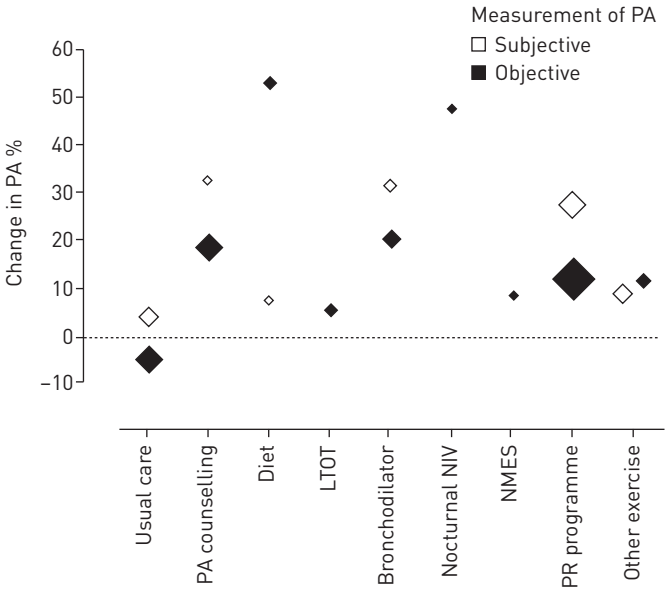

FIGURE 3 Percentage change in physical activity (PA) levels according to different intervention categories. The size of each square represents the number of studies within each category: the bigger the square, the higher the number of studies represented. Diet: dietary/nutritional intervention; LTOT: long-term oxygen therapy; NIV: noninvasive ventilation; NMES: neuromuscular electrical stimulation; PR: pulmonary rehabilitation; other exercise: other exercise programmes.

Other exercise interventions

12 studies used a wide range of exercise training including walking programmes, home training and self-management programmes (figure 2c). The majority of the interventions were based on walking exercise training, with a frequency of at least three times per week over a minimum period of 6 weeks. The intensity of the prescribed training was based on perceived dyspnoea (moderate to somewhat hard on the Borg scale), percentage of initial maximal heart rate or percentage of maximal distance/speed achieved in walking tests. Half of these studies showed no changes in PA levels in patients with COPD. This strategy was the intervention most commonly utilised in hospitalised patients.

PR combined with other exercise interventions

Eight studies combined PR programmes with other interventions. Five of these studies increased PA levels in patients with COPD (figure 2c).

Effects of different interventions on daily activity levels

Figure 3 summarises the percentage change relative to baseline in PA levels according to the seven identified categories of interventions. Overall, subjective methods showed higher percentage changes in PA in comparison to objective measurements within the same intervention category. PA counselling and bronchodilators produced similar improvements in PA levels after treatments (19% and 21%, respectively). NMES and LTOT produced 9% and 6% increase in daily activity levels in patients with COPD, respectively. Nutritional supplementation for undernourished patients and nocturnal NIV combined with exercise training in hypercapnic patients had the biggest impact on PA levels, increasing 53% and 48% respectively after treatment. Exercise training programmes (PR and other exercise programmes) increased daily activity levels by ~12%. Unsurprisingly, usual care did not increase PA levels in patients with COPD (average decrease of 4% after treatment).

Discussion

This systematic review provides information for researchers and clinicians by identifying and summarising the broad range of interventions to modify PA levels in patients with COPD. Unfortunately, it was not possible to perform a formal meta-analysis of the outcomes due to heterogeneity of the data. Additionally, the quality of the evidence remains very low, mainly because of serious imprecision and inconsistency across studies, as well as risk of bias.

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Interventions able to modify PA levels in patients with COPD

PA in COPD patients is limited by symptoms (*i.e.* dyspnoea, fatigue) but also by psychosocial/behavioural factors [80]. PA coaching is a common strategy to stimulate patients towards higher levels of daily activities by modifying their behaviour. Usually, these interventions [11, 25, 26, 47, 51, 54, 55, 71, 78] utilise some elements of the self-regulatory theory [81]. Using accurate assessment and feedback of PA levels, individualised PA goals and/or tailored motivational messages, patients are able to learn from successes and failures to develop an effective behavioural strategy to achieve their goal. Interestingly, PA coaching (with activity monitoring, *e.g.* use of a pedometer) is a very successful intervention for increasing daily activity levels of patients with COPD (figure 2a). This type of intervention is very promising and should be explored in bigger trials. Unfortunately, most of the studies in this category had a small sample size (figure 2a) [11, 47, 54, 55, 71, 78]. Other types of PA counselling interventions, such as PA advice alone [60] or in combination with exercise training [30, 45] or coaching [70], should also be further explored. To date, the results from the few available studies are still controversial and do not support a solid clinical decision [30, 45, 60, 70].

Four out of six bronchodilator studies have shown improvements in daily activity levels in patients with COPD [14, 48, 67, 77] (figure 2b). However, when considering studies using objective tools to assess PA levels, only half of the studies showed a positive impact [14, 77], while the other half showed no changes in PA [59, 73]. Rigorously conducted adequately powered RCTs with bronchodilators as the main intervention aiming at increasing PA levels, with objective measurement of daily activity, are required to clarify the role of bronchodilators in improving PA.

Although nutritional supplementation [12, 35, 36] and nocturnal NIV [39, 40] can increase PA levels of patients with COPD, the applicability of these approaches is limited to very specific subgroups of patients. Nocturnal NIV can increase PA levels in patients with hypercapnia when combined with exercise training [39, 40]. Unfortunately, no study has explored the effect of nocturnal NIV alone. Likewise, dietary interventions produced increases in PA levels in patients with COPD with low BMI ($\leqslant$20 kg·m^{-2}) [12, 35, 36]. The plausibility of such interventions is poor and these results cannot be extended to the whole population of patients with COPD. However, they do show that interventions targeted at specific aspects of the disease, such as nocturnal hypoventilation in the case of nocturnal NIV and poor nutritional status in the case of nutritional supplementation, can have a positive impact on the activity levels of COPD patients. Therefore, targeting specific subpopulations of patients might be necessary in specific interventions for specific patient phenotypes. More studies in these areas are needed in order to confirm this hypothesis.

LTOT [33, 64, 75] and NMES [38] were the interventions with the lowest impact on PA levels in patients with COPD. When considering objective measurement of PA, LTOT did not produce an increase in PA levels in this population. Likewise, NMES did not change PA levels in patients with COPD [38]. Perhaps these interventions may be useful in combination with other approaches (*e.g.* PA coaching) aiming specifically at increasing PA. More studies are needed to explore this possibility.

As expected, exercise training was the most commonly used strategy to modify PA levels in patients with COPD. However, the effect of PR programmes to increase PA levels is still controversial. 13 studies showed an increase in PA levels [8, 29, 44, 49, 52, 56, 58, 63, 65, 66, 72, 74, 76], while seven studies showed no effects after the intervention [10, 34, 37, 42, 62, 68, 69]. Interestingly, all the studies that failed to improve PA used programmes $\leqslant$12 weeks of duration. All studies involving programmes >12 weeks showed a positive impact on PA [8, 29, 52]. An even higher proportion of studies with programmes $\leqslant$12 weeks (six out of nine studies) showed no changes in PA levels when studies with objective measurements of PA were considered (figure 2c), whereas most of the studies that assessed PA with subjective tools showed positive effects of PR [44, 49, 56, 58, 63, 65, 72, 74, 76]. Since patients with COPD substantially overestimate their activity levels in daily life [82, 83], this finding may suggest that "short" PR programmes may impact positively on patients' perception of activities of daily living, but do not enhance their PA levels when objectively measured. In contrast, longer programmes (>12 weeks) seem to achieve better results [8, 29, 52]. Possibly, the translation of the gains (*i.e.* exercise capacity) of the PR programme into a more active lifestyle requires longer periods of training [8].

Other exercise interventions are also able to impact positively on PA levels of patients with COPD [10, 28, 30, 32, 39–41, 50, 53, 61, 74]. Walking programmes have been commonly used to enhance PA. Walking is a usual activity for patients and is easy to perform. When considering this strategy, duration ($\geqslant$30 min·day^{-1}) and frequency (at least three times per week over a minimum period of 3 months) of the intervention seem to be important. Similarly, the intensity of the intervention in walking programmes might be a key factor for success. When walking programmes involve activities with a high metabolic demand (*i.e.* 75% of maximal heart rate [32]), the results seem to be better [28, 32]. As shown in figure 2c, PR can also cause a positive effect on daily activity levels when combined with other interventions [10, 30, 39–41].

Percentage change in PA levels

Although the heterogeneity of the studies precludes a meta-analysis, figure 3 summarises the effects of different interventions on activity levels in patients with COPD. This figure must be interpreted with caution, since we calculated the average of changes relative to baseline PA levels for each intervention category for illustrative purpose only, to give an impression of the magnitude of the effect we found for the different interventions. However no correction by confounding factors (such as FEV_1, sex or age) was applied, due to data heterogeneity. As shown in figure 3, most interventions using objective measurements of PA were able to show 10–20% increments in activity levels. As expected [82, 83], subjective methods overestimated PA levels when compared with objective measurements in most of the studies.

Future research directions

Despite the importance of PA in COPD, studies assessing the effect of interventions on PA levels in this population are in general of low quality. Future research should focus on well-designed trials with proper randomisation, concealment and blinding processes. Apart from poor quality of evidence, the interpretation of the current literature on the topic may also be limited by publication bias (*i.e.* due to high probability of unreported studies). Studies with negative or with lack of impacting results are also necessary to elucidate the effect of the interventions on PA levels in patients with COPD. In addition, only a few studies have explored the benefits of interventions during hospitalisation [31, 79]. PA levels are affected in patients with COPD during and after hospitalisation for acute exacerbation [84]. Therefore, interventions aiming at increasing PA levels during and early after exacerbations are needed. Moreover, the benefits of other interventions, such as inspiratory muscle training [85], high-intensity interval training [86], downhill walking [87] and/or nonlinear exercise training [88], should be explored. Finally, the practice of PA is likely to have, as any other lifestyle habit, a strong behavioural factor. Consequently, in order to have improvements in PA levels of patients with COPD, it may be necessary to identify and reduce the time these patients spend in sedentary behaviour [89]. Furthermore, patients with COPD need adaptive behaviour change to achieve significant and lasting results on high levels of PA in daily life [90].

In conclusion, the benefit of exercise training on PA levels is still controversial. However, longer-lasting programmes are more effective than shorter programmes in increasing PA levels in COPD and might be needed to facilitate a change in behaviour. PA coaching with the feedback of an activity monitor is a very promising intervention to enhance daily activity levels in COPD. The combination of this type of programme with exercise training, particularly with long programmes, has the potential to enhance the effects by combining the increase in capacity provided by the exercise training with the behavioural changes facilitated by PA coaching programmes. Similarly, interventions directed at potential determinants of PA, such as dietary intervention for cachectic patients and nocturnal NIV with exercise training for hypercapnic patients, may contribute to increasing PA in very specific subgroups of patients with COPD. LTOT and NMES do not seem to enhance PA in this population, but may be useful in combination with other strategies. Bronchodilators might cause a positive impact on daily activity levels of COPD patients.

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References

1 Garcia-Aymerich J, Lange P, Benet M, *et al.* Regular physical activity reduces hospital admission and mortality in chronic obstructive pulmonary disease: a population based cohort study. *Thorax* 2006; 61: 772–778.
2 Yohannes AM, Baldwin RC, Connolly M. Mortality predictors in disabling chronic obstructive pulmonary disease in old age. *Age Ageing* 2002; 31: 137–140.
3 Wen CP, Wai JP, Tsai MK, *et al.* Minimum amount of physical activity for reduced mortality and extended life expectancy: a prospective cohort study. *Lancet* 2011; 378: 1244–1253.
4 Bravata DM, Smith-Spangler C, Sundaram V, *et al.* Using pedometers to increase physical activity and improve health: a systematic review. *JAMA* 2007; 298: 2296–2304.
5 Garber CE, Blissmer B, Deschenes MR, *et al.* American College of Sports Medicine position stand. Quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults: guidance for prescribing exercise. *Med Sci Sports Exerc* 2011; 43: 1334–1359.
6 Pitta F, Troosters T, Spruit MA, *et al.* Characteristics of physical activities in daily life in chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2005; 171: 972–977.
7 Spruit MA, Singh SJ, Garvey C, *et al.* An official American Thoracic Society/European Respiratory Society statement: key concepts and advances in pulmonary rehabilitation. *Am J Respir Crit Care Med* 2013; 188: e13–e64.
8 Pitta F, Troosters T, Probst VS, *et al.* Are patients with COPD more active after pulmonary rehabilitation? *Chest* 2008; 134: 273–280.
9 Cindy Ng LW, Mackney J, Jenkins S, *et al.* Does exercise training change physical activity in people with COPD? A systematic review and meta-analysis. *Chron Respir Dis* 2012; 9: 17–26.

 DOI: 10.1183/13993003.01744-2015

10 de Blok BM, de Greef MH, ten Hacken NH, *et al.* 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 Educ Couns* 2006; 61: 48–55.
11 Nguyen HQ, Gill DP, Wolpin S, *et al.* Pilot study of a cell phone-based exercise persistence intervention post-rehabilitation for COPD. *Int J Chron Obstruct Pulmon Dis* 2009; 4: 301–313.
12 Weekes CE, Emery PW, Elia M. Dietary counselling and food fortification in stable COPD: a randomised trial. *Thorax* 2009; 64: 326–331.
13 Garcia-Aymerich J, Félez MA, Escarrabill J, *et al.* Physical activity and its determinants in severe chronic obstructive pulmonary disease. *Med Sci Sports Exerc* 2004; 36: 1667–1673.
14 Hataji O, Naito M, Ito K, *et al.* Indacaterol improves daily physical activity in patients with chronic obstructive pulmonary disease. *Int J Chron Obstruct Pulmon Dis* 2013; 8: 1–5.
15 Gimeno-Santos E, Frei A, Steurer-Stey C, *et al.* Determinants and outcomes of physical activity in patients with COPD: a systematic review. *Thorax* 2014; 69: 731–739.
16 Vaes AW, Cheung A, Atakhorrami M, *et al.* Effect of "activity monitor-based" counseling on physical activity and health-related outcomes in patients with chronic diseases: a systematic review and meta-analysis. *Ann Med* 2013; 45: 397–412.
17 Wilson JJ, O'Neill B, Collins EG, *et al.* Interventions to increase physical activity in patients with COPD: a comprehensive review. *COPD* 2015; 12: 332–343.
18 Centre for Reviews and Dissemination (CRD). Systematic reviews: CRD's guidance for undertaking reviews in health care. York, CRD, University of York, 2009. Available from: www.york.ac.uk/media/crd/Systematic_Reviews.pdf
19 Liberati A, Altman DG, Tetzlaff J, *et al.* The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *Ann Intern Med* 2009; 151: W65–W94.
20 Caspersen CJ, Powell KE, Christenson GM. Physical activity, exercise, and physical fitness: definitions and distinctions for health-related research. *Public Health Rep* 1985; 100: 126–131.
21 Guyatt GH, Oxman AD, Schünemann HJ, *et al.* GRADE guidelines: a new series of articles in the *Journal of Clinical Epidemiology*. *J Clin Epidemiol* 2011; 64: 380–382.
22 Schünemann H, Hill S, Guyatt G, *et al.* The GRADE approach and Bradford Hill's criteria for causation. *J Epidemiol Community Health* 2011; 65: 392–395.
23 Crowther M, Avenell A, MacLennan G, *et al.* A further use for the Harvest plot: a novel method for the presentation of data synthesis. *Res Synth Methods* 2011; 2: 79–83.
24 Ogilvie D, Fayter D, Petticrew M, *et al.* The harvest plot: a method for synthesising evidence about the differential effects of interventions. *BMC Med Res Methodol* 2008; 8: 8.
25 Altenburg WA, ten Hacken NH, Bossenbroek L, *et al.* Short- and long-term effects of a physical activity counselling programme in COPD: a randomized controlled trial. *Respir Med* 2015; 109: 112–121.
26 Barberan-Garcia A, Vogiatzis I, Solberg HS, *et al.* Effects and barriers to deployment of telehealth wellness programs for chronic patients across 3 European countries. *Respir Med* 2014; 108: 628–637.
27 Bauldoff GS, Hoffman LA, Zullo TG, *et al.* Exercise maintenance following pulmonary rehabilitation: effect of distractive stimuli. *Chest* 2002; 122: 948–954.
28 Behnke M, Wewel AR, Kirsten D, *et al.* Exercise training raises daily activity stronger than predicted from exercise capacity in patients with COPD. *Respir Med* 2005; 99: 711–717.
29 Bendstrup KE, Ingemann Jensen J, Holm S, *et al.* Out-patient rehabilitation improves activities of daily living, quality of life and exercise tolerance in chronic obstructive pulmonary disease. *Eur Respir J* 1997; 10: 2801–2806.
30 Berry MJ, Rejeski WJ, Miller ME, *et al.* A lifestyle activity intervention in patients with chronic obstructive pulmonary disease. *Respir Med* 2010; 104: 829–839.
31 Borges RC, Carvalho CR. Impact of resistance training in chronic obstructive pulmonary disease patients during periods of acute exacerbation. *Arch Phys Med Rehabil* 2014; 95: 1638–1645.
32 Breyer MK, Breyer-Kohansal R, Funk GC, *et al.* Nordic walking improves daily physical activities in COPD: a randomised controlled trial. *Respir Res* 2010; 11: 112.
33 Casaburi R, Porszasz J, Hecht A, *et al.* Influence of lightweight ambulatory oxygen on oxygen use and activity patterns of COPD patients receiving long-term oxygen therapy. *COPD* 2012; 9: 3–11.
34 Coronado M, Janssens JP, de Muralt B, *et al.* Walking activity measured by accelerometry during respiratory rehabilitation. *J Cardiopulm Rehabil* 2003; 23: 357–364.
35 Dal Negro RW, Aquilani R, Bertacco S, *et al.* Comprehensive effects of supplemented essential amino acids in patients with severe COPD and sarcopenia. *Monaldi Arch Chest Dis* 2010; 73: 25–33.
36 Dal Negro RW, Testa A, Aquilani R, *et al.* Essential amino acid supplementation in patients with severe COPD: a step towards home rehabilitation. *Monaldi Arch Chest Dis* 2012; 77: 67–75.
37 Dallas MI, McCusker C, Haggerty MC, *et al.* Using pedometers to monitor walking activity in outcome assessment for pulmonary rehabilitation. *Chron Respir Dis* 2009; 6: 217–224.
38 Daly C, Coughlan GF, Hennessy E, *et al.* Effects of neuromuscular electrical stimulation on the activity levels and exercise capacity of patients with moderate to severe COPD. *Physiother Ireland* 2011; 32: 6–11.
39 Duiverman ML, Wempe JB, Bladder G, *et al.* Nocturnal non-invasive ventilation in addition to rehabilitation in hypercapnic patients with COPD. *Thorax* 2008; 63: 1052–1057.
40 Duiverman ML, Wempe JB, Bladder G, *et al.* Two-year home-based nocturnal noninvasive ventilation added to rehabilitation in chronic obstructive pulmonary disease patients: a randomized controlled trial. *Respir Res* 2011; 12: 112.
41 Effing T, Zielhuis G, Kerstjens H, *et al.* Community based physiotherapeutic exercise in COPD self-management: a randomised controlled trial. *Respir Med* 2011; 105: 418–426.
42 Egan C, Deering BM, Blake C, *et al.* Short term and long term effects of pulmonary rehabilitation on physical activity in COPD. *Respir Med* 2012; 106: 1671–1679.
43 Engström CP, Persson LO, Larsson S, *et al.* Long-term effects of a pulmonary rehabilitation programme in outpatients with chronic obstructive pulmonary disease: a randomized controlled study. *Scand J Rehabil Med* 1999; 31: 207–213.
44 Faager G, Larsen FF. Performance changes for patients with chronic obstructive pulmonary disease on long-term oxygen therapy after physiotherapy. *J Rehabil Med* 2004; 36: 153–158.

45 Faulkner J, Walshaw E, Campbell J, *et al.* The feasibility of recruiting patients with early COPD to a pilot trial assessing the effects of a physical activity intervention. *Prim Care Respir J* 2010; 19: 124–130.
46 Goris AH, Vermeeren MA, Wouters EF, *et al.* Energy balance in depleted ambulatory patients with chronic obstructive pulmonary disease: the effect of physical activity and oral nutritional supplementation. *Br J Nutr* 2003; 89: 725–731.
47 Hospes G, Bossenbroek L, Ten Hacken NH, *et al.* Enhancement of daily physical activity increases physical fitness of outclinic COPD patients: results of an exercise counseling program. *Patient Educ Couns* 2009; 75: 274–278.
48 Kesten S, Casaburi R, Kukafka D, *et al.* Improvement in self-reported exercise participation with the combination of tiotropium and rehabilitative exercise training in COPD patients. *Int J Chron Obstruct Pulmon Dis* 2008; 3: 127–136.
49 Kozu R, Senjyu H, Jenkins SC, *et al.* Differences in response to pulmonary rehabilitation in idiopathic pulmonary fibrosis and chronic obstructive pulmonary disease. *Respiration* 2011; 81: 196–205.
50 Larson JL, Covey MK, Kapella MC, *et al.* Self-efficacy enhancing intervention increases light physical activity in people with chronic obstructive pulmonary disease. *Int J Chron Obstruct Pulmon Dis* 2014; 9: 1081–1090.
51 Mendoza L, Horta P, Espinoza J, *et al.* Pedometers to enhance physical activity in COPD: a randomised controlled trial. *Eur Respir J* 2015; 45: 347–354.
52 Mercken EM, Hageman GJ, Schols AM, *et al.* Rehabilitation decreases exercise-induced oxidative stress in chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2005; 172: 994–1001.
53 Mohammadi F, Jowkar Z, Reza Khankeh H, *et al.* Effect of home-based nursing pulmonary rehabilitation on patients with chronic obstructive pulmonary disease: a randomised clinical trial. *Br J Community Nurs* 2013; 18: 398–403.
54 Moy ML, Janney AW, Nguyen HQ, *et al.* Use of pedometer and Internet-mediated walking program in patients with chronic obstructive pulmonary disease. *J Rehabil Res Dev* 2010; 47: 485–496.
55 Moy ML, Weston NA, Wilson EJ, *et al.* A pilot study of an Internet walking program and pedometer in COPD. *Respir Med* 2012; 106: 1342–1350.
56 Nield M, Hoo GS, Roper J, *et al.* Usefulness of the human activity profile, a functional performance measure, in people with chronic obstructive pulmonary disease. *J Cardiopulm Rehabil* 2005; 25: 115–121.
57 Nield MA, Soo Hoo GW, Roper JM, *et al.* Efficacy of pursed-lips breathing: a breathing pattern retraining strategy for dyspnea reduction. *J Cardiopulm Rehabil Prev* 2007; 27: 237–244.
58 Ninot G, Moullec G, Desplan J, *et al.* Daily functioning of dyspnea, self-esteem and physical self in patients with moderate COPD before, during and after a first inpatient rehabilitation program. *Disabil Rehabil* 2007; 29: 1671–1678.
59 Nishijima Y, Minami S, Yamamoto S, *et al.* Influence of indacaterol on daily physical activity in patients with untreated chronic obstructive pulmonary disease. *Int J Chron Obstruct Pulmon Dis* 2015; 10: 439–444.
60 Pleguezuelos E, Pérez ME, Guirao L, *et al.* Improving physical activity in patients with COPD with urban walking circuits. *Respir Med* 2013; 107: 1948–1956.
61 Pomidori L, Contoli M, Mandolesi G, *et al.* A simple method for home exercise training in patients with chronic obstructive pulmonary disease: one-year study. *J Cardiopulm Rehabil Prev* 2012; 32: 53–57.
62 Probst VS, Kovelis D, Hernandes NA, *et al.* Effects of 2 exercise training programs on physical activity in daily life in patients with COPD. *Respir Care* 2011; 56: 1799–1807.
63 Ries AL, Kaplan RM, Limberg TM, *et al.* Effects of pulmonary rehabilitation on physiologic and psychosocial outcomes in patients with chronic obstructive pulmonary disease. *Ann Intern Med* 1995; 122: 823–832.
64 Sandland CJ, Morgan MD, Singh SJ. Patterns of domestic activity and ambulatory oxygen usage in COPD. *Chest* 2008; 134: 753–760.
65 Sewell L, Singh SJ, Williams JE, *et al.* Can individualized rehabilitation improve functional independence in elderly patients with COPD? *Chest* 2005; 128: 1194–1200.
66 Sewell L, Singh SJ, Williams JE, *et al.* Seasonal variations affect physical activity and pulmonary rehabilitation outcomes. *J Cardiopulm Rehabil Prev* 2010; 30: 329–333.
67 Shioya T, Satake M, Sato K, *et al.* Long-term effect of the β_2-receptor agonist procaterol on daily life performance and exercise capacity in patients with stable chronic obstructive pulmonary disease. Clinical study with special reference to health-related quality of life and activities of daily living. *Arzneimittelforschung* 2008; 58: 24–28.
68 Skumlien S, Aure Skogedal E, Skrede Ryg M, *et al.* Endurance or resistance training in primary care after in-patient rehabilitation for COPD? *Respir Med* 2008; 102: 422–429.
69 Steele BG, Belza B, Hunziker J, *et al.* Monitoring daily activity during pulmonary rehabilitation using a triaxial accelerometer. *J Cardiopulm Rehabil* 2003; 23: 139–142.
70 Steele BG, Belza B, Cain KC, *et al.* A randomized clinical trial of an activity and exercise adherence intervention in chronic pulmonary disease. *Arch Phys Med Rehabil* 2008; 89: 404–412.
71 Tabak M, Vollenbroek-Hutten MM, van der Valk PD, *et al.* A telerehabilitation intervention for patients with chronic obstructive pulmonary disease: a randomized controlled pilot trial. *Clin Rehabil* 2013; 28: 582–591.
72 Takigawa N, Tada A, Soda R, *et al.* Comprehensive pulmonary rehabilitation according to severity of COPD. *Respir Med* 2007; 101: 326–332.
73 Troosters T, Sciurba FC, Decramer M, *et al.* Tiotropium in patients with moderate COPD naive to maintenance therapy: a randomised placebo-controlled trial. *NPJ Prim Care Respir Med* 2014; 24: 14003.
74 Varga J, Porszasz J, Boda K, *et al.* Supervised high intensity continuous and interval training *vs.* self-paced training in COPD. *Respir Med* 2007; 101: 2297–2304.
75 Vergeret J, Brambilla C, Mounier L. Portable oxygen therapy: use and benefit in hypoxaemic COPD patients on long-term oxygen therapy. *Eur Respir J* 1989; 2: 20–25.
76 Walker PP, Burnett A, Flavahan PW, *et al.* Lower limb activity and its determinants in COPD. *Thorax* 2008; 63: 683–689.
77 Watz H, Krippner F, Kirsten A, *et al.* Indacaterol improves lung hyperinflation and physical activity in patients with moderate chronic obstructive pulmonary disease – a randomized, multicenter, double-blind, placebo-controlled study. *BMC Pulm Med* 2014; 14: 158.
78 Wewel AR, Gellermann I, Schwertfeger I, *et al.* Intervention by phone calls raises domiciliary activity and exercise capacity in patients with severe COPD. *Respir Med* 2008; 102: 20–26.

DOI: 10.1183/13993003.01744-2015

79 Yohannes AM, Connolly MJ. Early mobilization with walking aids following hospital admission with acute exacerbation of chronic obstructive pulmonary disease. *Clin Rehabil* 2003; 17: 465–471.
80 Miravitlles M, Cantoni J, Naberan K. Factors associated with a low level of physical activity in patients with chronic obstructive pulmonary disease. *Lung* 2014; 192: 259–265.
81 Baumeister RF, Vohs KD, DeWall CN, *et al.* How emotion shapes behavior: feedback, anticipation, and reflection, rather than direct causation. *Pers Soc Psychol Rev* 2007; 11: 167–203.
82 Pitta F, Troosters T, Probst VS, *et al.* Quantifying physical activity in daily life with questionnaires and motion sensors in COPD. *Eur Respir J* 2006; 27: 1040–1055.
83 Pitta F, Troosters T, Spruit MA, *et al.* Activity monitoring for assessment of physical activities in daily life in patients with chronic obstructive pulmonary disease. *Arch Phys Med Rehabil* 2005; 86: 1979–1985.
84 Pitta F, Troosters T, Probst VS, *et al.* Physical activity and hospitalization for exacerbation of COPD. *Chest* 2006; 129: 536–544.
85 Charususin N, Gosselink R, Decramer M, *et al.* Inspiratory muscle training protocol for patients with chronic obstructive pulmonary disease (IMTCO study): a multicentre randomised controlled trial. *BMJ Open* 2013; 3: e003101.
86 Vogiatzis I, Nanas S, Roussos C. Interval training as an alternative modality to continuous exercise in patients with COPD. *Eur Respir J* 2002; 20: 12–19.
87 Camillo CA, Burtin C, Hornikx M, *et al.* Physiological responses during downhill walking: a new exercise modality for subjects with chronic obstructive pulmonary disease? *Chron Respir Dis* 2015; 12: 155–164.
88 Klijn P, van Keimpema A, Legemaat M, *et al.* Nonlinear exercise training in advanced chronic obstructive pulmonary disease is superior to traditional exercise training. A randomized trial. *Am J Respir Crit Care Med* 2013; 188: 193–200.
89 Cavalheri V, Straker L, Gucciardi DF, *et al.* Changing physical activity and sedentary behaviour in people with COPD. *Respirology* 2016; 21: 419–426.
90 Spruit MA, Pitta F, McAuley E, *et al.* Pulmonary rehabilitation and physical activity in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2015; 192: 924–933.