# UNRAVELLING SELF-MANAGEMENT FOR PATIENTS WITH COPD

## LONG-TERM EFFECTS OF THE COPE-II STUDY

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**Unravelling self-management for patients with COPD**
Long-term effects of the COPE-II study

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## CONTENTS

# CHAPTER 1
GENERAL INTRODUCTION

## COPD

Chronic obstructive pulmonary disease (COPD) is a chronic, and usually progressive disease. It is characterised by persistent airflow limitation and an enhanced inflammatory response in the airways and lungs to noxious particles and gasses[1]. Common symptoms of COPD are chronic and progressive dyspnoea, cough and sputum production[1]. In the Western world, tobacco smoking is the principal and preventable cause of COPD. A worldwide study assessing the prevalence of spirometry-defined COPD, estimated that the prevalence of COPD was 10.1% in adults aged 40 years or older, and was higher in men than women[2]. However, prevalence varied across countries. In another study, it was estimated that COPD was the number three cause of death in 2010[3], and the number five cause of years lived in less than ideal health[4]. That COPD is a serious healthcare problem for society is also reflected in the high costs associated with it. In the European Union, €23.3 billion is spent on direct medical costs of primary and hospital healthcare, and €25.1 billion is spent on indirect costs of lost production annually[5].

## Exacerbations

Exacerbations of COPD are acute events that strongly determine the course of the disease. Exacerbations are associated with an increased decline in $FEV_1$[6], a decrease in health status[7;8], an increased risk for hospitalisation and death[9]. According to the Global Initiative for Chronic Obstructive Lung Disease (GOLD), an exacerbation is characterised by a worsening in respiratory symptoms that is beyond day-to-day variation and leads to a change in medication[1]. The frequency of exacerbations increases when disease severity increases, from less than one exacerbation per year in patients with GOLD stage 1 to two exacerbations per year in patients with GOLD stage 4[10]. Above that, there seems to be a group of patients that is susceptible to exacerbations, resulting in frequent exacerbations independent of GOLD stage[10]. Increased upper and lower airway inflammation, as well as systemic inflammation contribute to the increase in symptoms as observed during an exacerbation. These inflammations can be triggered by viral infections, bacterial infections, and/or environmental factors[11]. The nature of exacerbations is heterogeneous, and therefore not easy to capture in a definition. This is reflected in the variety of definitions in the literature. Roughly, a distinction can be made between symptom-based definitions and event-based definitions, the latter being mainly based on healthcare utilisation[12;13]. The definition used can relevantly influence effect sizes in clinical trials[13;14].

Exacerbations are routinely treated with short courses of antibiotics and/or oral prednisolone[1]. Antibiotics are usually prescribed when sputum is purulent or when sputum volume is increased, but scientific evidence for this approach is limited[15]. Timely treatment of exacerbations was suggested to lead to shorter recovery time and lower risk of hospitalisation[16]. That timely treatment is not as self-evident as it might seem, is underlined by the observations that 50-70% of the exacerbations are not reported to a physician[7;8;17;18], and that when exacerbations are reported this is done only several days after the onset[16;19]. A qualitative study found that although the majority of patients were able to recognise

symptoms that come with an exacerbation, only a small proportion of the patients changed medication or contacted a physician[20]. All these studies indicate that patients tend to act inadequately to the onset of exacerbations, and that there is a need for effective interventions that help patients to recognise and act promptly to the start of an exacerbation.

### Exercise capacity and physical activity

Besides symptoms of dyspnoea and chronic cough, patients with COPD often have impaired exercise capacity[21], and a decreased physical activity level[22]. In the Netherlands, half of the patients with chronic respiratory disease (asthma and COPD) does not meet the minimum of 30 minutes of physical activity at moderate intensity for at least five days per week as recommended for elderly adults with a clinically significant chronic condition[23;24]. In solely patients with COPD, the percentage not meeting this criterion is probably even higher[25]. Patients with COPD spend significantly less time walking and standing, and more time sitting and lying compared to healthy adults[22]. The physical activity level of patients with COPD gradually declines with the severity of disease[26], and declines faster in patients who exacerbate frequently[27;28]. Also, physical activity level is reduced during and after exacerbations[27-29]. A reduced physical activity level is associated with negative health outcomes such as accelerated lung function decline[30], and increased risk for COPD-related hospitalisations and mortality[31]. Moreover, in a study of Waschki et al., physical activity was the strongest predictor for all-cause mortality in patients with COPD[32]. Although the amount of research on the effects of exercise programmes on exercise capacity is extensive[33], the amount of research that also considers physical activity is increasing, but still limited[34-36]. The studies that did investigate physical activity showed contradictory results, which is probably due to the variation in length and content of the interventions. Whereas an increase in exercise capacity can be achieved with exercise programmes as short as four weeks[21], a sustained increase in daily physical activity level is only elicited by a change in habits and behaviours of the sedentary patient with COPD, and is thus most probably more time-consuming[21;36;37].

### Self-management

Treatment goals of patients with stable COPD are reduction of symptoms, and improving exercise tolerance and health status. Additional goals are preventing disease progression, preventing and treating exacerbations and a reduction of mortality[1]. Even with optimal pharmacological treatment and disease management, patients with COPD as a rule still experience symptoms and may have difficulties to cope with their disease. In view of this, self-management is increasingly recognised to be important in the treatment of patients with COPD. There is still no consensus on the exact definition of self-management, but in general, self-management programmes aim at helping patients to acquire, and practice the skills they need to carry out disease-specific medical regimens, to guide change in health behaviour and to provide emotional support to enable patients to adjust their roles for

optimal function and control of their disease[38;39]. Essential in self-management is that patients form a relationship with their healthcare provider in which disease management will be a combined responsibility, and in which there will be opportunities for feedback on set goals and actions taken. In order to manage their disease at a day-to-day basis, core skills that patients need include problem solving, decision making, resource utilisation and taking action based on a predefined action plan[40]. Earlier, patient education was seen as the major part of self-management programmes but nowadays it is recognised that transfer of knowledge alone is not sufficient to achieve the sustained behavioural change which should be aimed at in self-management. Cognitive behavioural therapy is suggested to be a relatively simple and effective technique to achieve behavioural change[21;39]. Self-efficacy is considered a key factor in achieving behavioural change, and is often described as the patient's confidence that he or she can successfully execute certain behaviour under specific conditions to achieve set goals[38;40]. Effective methods to increase self-efficacy include skills mastery, modelling, interpretation of symptoms and social persuasion[38]. Although there is a sound scientific and theoretical background on methods leading to behavioural change, evidence mainly comes from research in chronic diseases other than COPD. Apart from that, there are however a considerable number of (randomised) controlled studies on the efficacy of self-management interventions in COPD. In the previous update of the Cochrane review on self-management in patients with COPD, it was concluded that participation in a self-management programme increases health-related quality of life (HRQoL) and reduces hospital admissions[41]. The heterogeneity in interventions made it however impossible to make any recommendations on the most effective components of self-management, and restricted study follow-up times hindered conclusions about long-term effects[41]. Since the publication of the last update of this review in 2007, numerous new studies have been published and opinions concerning self-management have evolved. Therefore, we have updated the review with new studies that meet current standards (Chapter 2).

Action plans are often incorporated in self-management programmes for patients with COPD and can help patients to recognise symptoms that indicate an impending exacerbation, or identify an exacerbation earlier after the start. Action plans also describe how to act accordingly (e.g. change medication, or contact a healthcare provider). A Cochrane review on action plans with minimal or no self-management training included only five studies and concluded that such an intervention is effective in increasing the ability of patients with COPD to recognise and react appropriately to an exacerbation but does not affect healthcare utilisation[42]. The review on action plans is complementary to the Cochrane review on self-management in patients with COPD[41]. Subgroup analyses on programmes with and without action plans were however not possible since most included studies integrated an action plan in their self-management programme[41]. As a result, no statements could be made on the additional effect of action plans added to self-management programmes. In both reviews, the follow-up time of the majority of the included studies was no longer than 12 months[41;42]. Consequently, a scientific base for the additional effectiveness of action plans for self-treatment of exacerbations on the long-term

is lacking. Therefore, we have compared the effectiveness of self-treatment within a self-management programme to the effectiveness of self-management alone after two years of follow-up, and additionally we have performed a cost-effectiveness analysis (Chapter 3).

Self-management training is regularly combined with a standardised exercise programme. As was already stated above, exercise programmes are effective in increasing exercise capacity on the short term (i.e. directly after the end of the exercise programme)[33], but the evidence concerning its effectiveness on physical activity level is limited[35]. Also, the additional effect of exercise programmes as a component of self-management training is unknown[41]. Therefore, we have assessed the long-term effectiveness (Chapter 4) and cost-effectiveness (Chapter 5) of a self-management programme with versus without a community-based exercise programme that specifically aims for both an improvement in exercise capacity and a behavioural change towards exercise. It is increasingly recognised that maintenance of beneficial effects of exercise programmes in patients with COPD is problematic[43;44]. When the exercise programme ends, patients relapse to their sedentary life style, leading to rapid deconditioning. Even when patients have actually achieved an increase in exercise capacity, this does not automatically lead to a more active lifestyle[45]. It is therefore hypothesized that programmes should not aim solely at the improvement of exercise capacity but also at a behavioural change towards exercise and physical activity[21;44]. To underline the need for exercise programmes aiming both at an improvement in exercise capacity and physical activity, we have tested the hypothesis that a change in exercise capacity does not automatically lead to a change in physical activity level or vice versa, or in other words that there is a difference in what patients are functionally able to do and what they actually do in daily life (Chapter 6).

Chapters 3 until 6 were derived from the COPE-II study, which was conducted in Enschede, the Netherlands from 2004 to 2008. The general scheme of this study is outlined below.

## COPE-II study

Action plans and exercise training programmes are often incorporated in self-management programmes for patients with COPD, and are potentially valuable components. There is, however, a lack of knowledge concerning the solitary effects of components of self-management in COPD, and there is only scarce evidence on the long-term effects of these programmes. Therefore, the COPE-II study was designed to evaluate the independent effects of two different components of self-management, self-treatment of exacerbations and a community-based exercise programme (COPE-active), in one study[34;46]. Follow-up of the COPE-II study was set at two years to allow statements on long-term effectiveness of self-management.

### *Study design*

The two interventions were evaluated in one study using a 2x2 factorial design. This means that patients were randomised to one of four different study groups as depicted in Table 1.

In the comparison of self-treatment vs. self-management only, study groups two and four serve as the self-treatment group and study groups one and three serve as the control group (self-management only). In the comparison of COPE-active vs. self-management only, study groups three and four serve as the COPE-active group and study groups one and two serve as the control group. In both comparisons, patients receiving the intervention that is not evaluated are equally divided over the intervention and control group, and are therefore thought not to influence the comparison of interest. In other words, it was assumed that there would be no interaction between the two interventions. Outcome measurements were performed at baseline, 7, 12, 18 and 24 months of follow-up.

**Table 1** Assignment of interventions in the COPE-II study according to a 2x2 factorial design

| | Study group | | | |
|---|---|---|---|---|
| | 1 | 2 | 3 | 4 |
| Self-management programme | x | x | x | x |
| Self-treatment of exacerbations | | x | | x |
| COPE-active programme | | | x | x |

*Self-management sessions*

All patients participated in four self-management sessions supervised by a respiratory nurse and a physiotherapist. The goal of these sessions was to change the patient's disease behaviour by increasing knowledge and confronting them with consequences of specific behaviour. All information discussed during the courses was also provided to the patients in an educational booklet. Four, 13 26, 52, and 78 weeks after the last self-management session, patients were called by the respiratory nurse to reinforce the information discussed during the sessions.

*Self-treatment of exacerbations*

During the self-management sessions, all patients were taught to complete a daily symptom diary. Patients in group two and four (self-treatment group) additionally were taught to use an action plan that indicated how they could timely recognise the start of an exacerbation, and when they should start a course of oral prednisolone and/or antibiotics. Patients in group one and three (control group) were instructed to contact the research office in case of worsening symptoms that would otherwise have prompted them to contact their general practitioner or pulmonary physician. An appointment with a pulmonary physician was scheduled within 12 hours.

The (cost-)effectiveness of self-treatment of exacerbations after one year of follow-up was published previously[46]. As was hypothesised a priori, self-treatment of exacerbations did not lead to a difference in the *number* of exacerbations. The median number of exacerbation *days* was lower in patients who used the action plan compared to patients

who did not, but there was no difference in mean daily severity score and HRQoL. Regarding cost-effectiveness, self-management including self-treatment was the dominant strategy, with a lower probability for hospital admissions and healthcare contacts combined with cost savings in direct medical costs[46].

*COPE-active programme*

Patients in group one and three (the COPE-active group) participated in the COPE-active programme, a community-based exercise programme supervised by physiotherapists. The 11-month training period was divided in two parts. The first six months were compulsory, and consisted of three training sessions per week. The following five months of training were voluntary but recommended, and consisted of two training sessions per week. In both periods, one of the training sessions was performed at home to encourage exercise in the own environment. The training sessions consisted of cycling, walking, climbing stairs, and lifting weights. Besides improvement of exercise capacity, the main goal of COPE-active was a behavioural change towards exercise. The intensity of the programme was tailored to the individual patient's performance level by providing the physiotherapist with the baseline results of the cardio-pulmonary exercise test and the incremental shuttle walk test. After the 11-month supervised training period, patients in the COPE-active group were advised to continue with unsupervised training at home, but not to follow any formal physiotherapeutic exercise training programme. Instead, the patients were encouraged to participate in other forms of community-based exercise.

Effectiveness of the COPE-active programme after one year of follow-up was published previously[34]. After one year follow-up (directly after the end of the exercise programme), the walking distance in the incremental shuttle walk test of participants of the COPE-active programme was increased, whereas the walking distance of patients in the control group was decreased, resulting in a significant between-group difference in favour of the COPE-active group. No significant difference was found in walking distance in the endurance shuttle walk test. Patients in the COPE-active group had a higher daily physical activity level as measured by the number of steps/day over 12 months of follow-up, indicating that a behavioural change towards exercise was achieved. Apart from a statistically significant difference in CRQ dyspnoea score, no differences were found in health status.

## Aims and outline of this thesis

The aims of this thesis were:

To assess the current state of evidence concerning self-management programmes for patients with COPD (Chapter 2).

To assess the (cost-)effectiveness of self-treatment of exacerbations within a self-management programme compared to a self-management programme only in patients with COPD after two years of follow-up (Chapter 3).

To assess the effectiveness of a community-based exercise programme within a self-management programme compared to a self-management programme only in patients with COPD after two years of follow-up (Chapter 4).

To assess the cost-effectiveness of a community-based exercise programme within a self-management programme compared to a self-management programme only in patients with COPD after two years of follow-up (Chapter 5).

To determine the relationship between exercise capacity and daily physical activity level in patients with COPD (Chapter 6).

In Chapter 7, the results of the previous chapters are discussed and recommendations for clinical practice and future research are included. Finally, the main results of this thesis are summarised in Chapter 8.

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# CHAPTER 2

## SELF-MANAGEMENT FOR PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

COCHRANE DATABASE OF SYSTEMATIC REVIEWS 2014, ISSUE 3, ART. NO.: CD0029900

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## ABSTRACT


### Background
Self-management interventions help patients with chronic obstructive pulmonary disease (COPD) acquire and practise the skills they need to carry out disease-specific medical regimens, guide changes in health behaviour and provide emotional support to enable patients to control their disease. Since the first update of this review in 2007, several studies have been published. The results of the second update are reported here.

### Objectives
1. To evaluate whether self-management interventions in COPD lead to improved health outcomes.
2. To evaluate whether self-management interventions in COPD lead to reduced healthcare utilisation.

### Search methods
We searched the Cochrane Airways Group Specialised Register of trials (current to August 2011).

### Selection criteria
Controlled trials (randomised and non-randomised) published after 1994, assessing the efficacy of self-management interventions for individuals with COPD, were included. Interventions with fewer than two contact moments between study participants and healthcare providers were excluded.

### Data collection and analysis
Two review authors independently assessed trial quality and extracted data. Investigators were contacted to ask for additional information. When appropriate, study results were pooled using a random-effects model. The primary outcomes of the review were health-related quality of life (HRQoL) and number of hospital admissions.

### Main results
Twenty-nine studies were included. Twenty-three studies on 3189 participants compared self-management versus usual care; six studies on 499 participants compared different components of self-management on a head-to-head basis. Although we included non-randomised controlled clinical trials as well as RCTs in this review, we restricted the primary analysis to RCTs only and reported these trials in the abstract.

In the 23 studies with a usual care control group, follow-up time ranged from two to 24 months. The content of the interventions was diverse. A statistically significant effect of self-management on HRQoL was found (St George's Respiratory Questionnaire (SGRQ) total score, mean difference (MD) -3.51, 95% confidence interval (CI) -5.37 to -1.65, 10 studies, 1413 participants, moderate-quality evidence). Self-management also led to a lower

probability of respiratory-related hospitalisations (odds ratio (OR) 0.57, 95%CI 0.43 to 0.75, nine studies, 1749 participants, moderate-quality evidence) and all-cause hospitalisations (OR 0.60; 95%CI 0.40 to 0.89, 6 studies, 1365 participants, moderate-quality evidence). Over one year of follow-up, eight (95%CI 5 to 14) participants with a high baseline risk of respiratory-related hospital admission needed to be treated to prevent one participant with at least one hospital admission, and 20 (95%CI 15 to 35) participants with a low baseline risk of hospitalisation needed to be treated to prevent one participant with at least one respiratory-related hospital admission.

No statistically significant effect of self-management on mortality (OR 0.79, 95%CI 0.58 to 1.07, 8 studies, 2134 participants, very low-quality evidence) was detected. Also, dyspnoea measured by the (modified) Medical Research Council Scale ((m)MRC) was reduced in individuals who participated in self-management (MD -0.83, 95%CI -1.36 to -0.30, 3 studies, 119 participants, low-quality evidence). The difference in exercise capacity as measured by the six-minute walking test was not statistically significant (MD 33.69 m, 95%CI -9.12 to 76.50, 6 studies, 570 participants, low-quality evidence).

Subgroup analyses depending on the use of an exercise programme as part of the intervention revealed no statistically significant differences between studies with and without exercise programmes in our primary outcomes of HRQoL and respiratory-related hospital admissions.

We were unable to pool head-to-head trials because of heterogeneity among interventions and controls; thus results were presented narratively within the review.

### Authors' conclusions

Self-management interventions in patients with COPD are associated with improved health-related quality of life as measured by the SGRQ, a reduction in respiratory-related and all-cause hospital admissions, and improvement in dyspnoea as measured by the (m)MRC. No statistically significant differences were found in other outcome parameters. However, heterogeneity among interventions, study populations, follow-up time and outcome measures makes it difficult to formulate clear recommendations regarding the most effective form and content of self-management in COPD.

## PLAIN LANGUAGE SUMMARY

### Background

Symptoms of patients with COPD slowly worsen over the years. This leads to loss of well-being in these patients. In research, another word for well-being is health-related quality of life. Self-management training teaches patients the skills and behaviours they need to successfully manage their disease. Self-management training is becoming more and more important in the treatment of COPD. However, debate on the most effective content is ongoing. Therefore, we reviewed the evidence on the effects of self-management on health-related quality of life and on healthcare use in patients with COPD. The evidence is current to August 2011.

### Study characteristics

In this review, we assessed 29 studies that evaluated the effects of self- management. Patients in these studies were followed for two to 24 months. Twenty-three studies had a control group that received usual care. A total of 3189 patients participated in these studies. In six studies, different components of self- management were compared on a head-to-head basis. Content and duration of the self-management programmes were diverse.

### Key results

Analysis of the studies revealed that self-management training improved health-related quality of life in patients with COPD compared with usual care. Also, the number of patients with at least one hospital admission related to lung disease and other causes was reduced among those who participated in a self- management intervention. These patients also experienced less shortness of breath. We found trials that compared different types of self-management interventions versus each other. We had hoped that these trials would help us identify the most effective components of self-management. However, all interventions were different, and we were unable to draw out the key themes.

The studies assessed in this review were diverse. Self-management programmes differed in content and duration. Also, types of participants differed across studies. Therefore, no clear recommendations on the most effective content of self- management training can be made at this time.

## Summary of findings for the main comparison

**Self-management compared with control for participants with chronic obstructive pulmonary disease**

**Patient or population:** patients with chronic obstructive pulmonary disease
**Settings:** community, primary care, hospital outpatient
**Intervention:** self-management
**Comparison:** control
This table includes data from RCTs only; data from CCTs are presented in the review.

| Outcomes | Illustrative comparative risks* (95%CI) | | **Relative effect** (95%CI) | **No. of participants** (studies) | **Quality of the evidence** (GRADE) |
|---|---|---|---|---|---|
| | Assumed risk | Corresponding risk | | | |
| | Control | Self-management | | | |
| HRQoL: SGRQ total score. Scale ranges from zero to 100. Lower score indicates better HRQoL | Range of mean SGRQ total scores in the control group varied from 34.7 to 65.3 points | Mean SGRQ total score in the intervention group was 3.51 lower (5.37 to 1.65 lower) | **MD -3.51** (-5.37 to -1.65) | 1413 (10 studies) | ⊕⊕⊕⊖ **moderate**[1] |
| Respiratory-related hospital admissions: number of participants with at least one respiratory-related hospital admission | 293 per 1000 | 190 per 1000 (151 to 237) | **OR 0.57** (0.43 to 0.75 ) | 1749 (9 studies) | ⊕⊕⊕⊖ **moderate**[2] |
| All-cause hospital admissions: number of participants with at least one all-cause hospital admission | 428 per 1000 | 310 per 1000 (203 to 400) | **OR 0.60** (0.40 to 0.89) | 1365 (6 studies) | ⊕⊕⊕⊖ **moderate**[2] |
| Dyspnoea: (m)MRC score | Range of mean (m)MRC scores in the control group varied from 2.4 to 3.6 points | Mean (m)MRC total score in the intervention group was 0.83 lower (1.36 to 0.3 lower) | **MD -0.83** (-1.36 to -0.30) | 119 (3 studies) | ⊕⊕⊖⊖ **low**[3] |
| Courses of oral steroids: number of participants receiving at least one course of oral steroids | 541 per 1000 | 892 per 1000 (315 to 983) | **OR 4.42** (0.39 to 50.10) | 901 (3 studies) | ⊕⊕⊖⊖ **low**[4] |
| Exercise capacity: 6MWD | Range of mean 6MWD in the control group varied from 68.6 to 440.9 m | Mean 6MWD in the intervention group was 33.69 higher (9.12 lower to 76.50 higher) | **MD 33.69** (-9.12 to 76.50) | 570 (6 studies) | ⊕⊕⊖⊖ **low5**[5] |
| Mortality: number of deaths | 97 per 1000 | 79 per 1000 (59 to 103) | **OR 0.79** (0.58 to 1.07 ) | 2134 (8 studies) | ⊕⊖⊖⊖ **very low**[6] |

*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; HRQoL: Health-related quality of life; 6MWD: Six-minute walking distance.

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.

1 *Sensitivity analysis with CCTs shows that the outcome is still sensitive to inclusion of new studies.*
2 *Confidence intervals of several included studies were wide, and several studies showed low event rates (-1 imprecision).*
3 *Heterogeneity was substantial ($I^2$ = 58%). Only three small studies were included in this meta-analysis (inconsistency -1, imprecision -1).*
4 *Heterogeneity was high ($I^2$ = 96%). Only three studies were included in this meta-analysis, and the study of Rice et al heavily influenced the OR. The 95%CI was wide (inconsistency -1, imprecision -1).*
5 *Heterogeneity was high ($I^2$ = 89%) and sensitivity analysis with CCTs shows that the outcome is sensitive to inclusion of new studies (inconsistency -1, imprecision -1).*
6 *This meta-analysis was explorative and the number of events is relatively low. Numerous studies had no events and were not included in this analysis.*

## BACKGROUND

### Description of the condition

Chronic obstructive pulmonary disease (COPD) is characterised by persistent airflow limitation. The course of COPD is usually progressive, and it is associated with an enhanced inflammatory response in the airways and lungs to noxious particles or gasses[1]. COPD is a serious public health problem and a major cause of chronic morbidity and mortality worldwide. In 2010, COPD was the third leading cause of death worldwide[2]. Furthermore, COPD imparts a great economic burden on society, with exacerbations accounting for most of the costs[3].

### Description of the intervention

Mortality data do not provide a complete picture of the burden of the disease because many patients with COPD exhibit progressive disability rather than immediate death. In 2010, COPD was the number five cause of years of life lived in less than ideal health[4]. This is not surprising in that many patients with COPD experience slow development of functional impairment over many years and progressive loss of health-related quality of life[5]. In light of this, self-management training is considered increasingly important as treatment for patients with COPD. However, debate on the definition and the most effective content of self-management interventions is ongoing[6]. In general, self- management training aims to help patients acquire and practise the skills they need to carry out disease-specific medical regimens, to guide changes in health behaviour and to provide emotional support to enable patients to adjust their roles for optimal function and control of their disease[6;7]. Essential patient skills for successful self-management include problem solving, decision making, resource utilisation, forming a partnership between patient and healthcare provider, taking action and self tailoring[8]. Ideally, self-management training should be aimed at sustained behavioural change. Self-efficacy is seen as patients' confidence that they can effectively manage their health and has been recognised as a powerful factor in inducing new behaviours[8-10]. Skills mastery, modelling, interpretation of symptoms and social persuasion are believed to contribute to enhanced self-efficacy[8].

### Why it is important to do this review

The original Cochrane review regarding COPD self-management was published in 2003. In the first update of the review, published in 2007, it was concluded that self-management is associated with improved quality of life and reduced hospital admissions with no indication of detrimental effects on the other outcome measures. However, because of heterogeneity in study designs. it was not possible to make recommendations regarding the form and content of self- management interventions[6]. Since the first update, several studies have been published and new opinions have been formed regarding the contents of self-management interventions for patients with COPD. Therefore we report the results of the second update of the review. In this update of the review, we have chosen to exclude studies with education as the only active intervention. Although patient education is an indispensable component of self-management, education alone is insufficient to achieve

the goal of behavioural change[6;7;9;10]. To avoid ambiguity, we have removed the term 'education' from the title of the review.

## OBJECTIVES

1. To evaluate whether self-management interventions in COPD lead to improved health outcomes.
2. To evaluate whether self-management interventions in COPD lead to reduced healthcare utilisation.

## METHODS

### Criteria for considering studies for this review

*Types of studies*
We included randomised controlled trials (RCTs) and non-randomised controlled clinical trials assessing the efficacy of self-management interventions for individuals with COPD. Studies published before 1995 were excluded because we strongly believe that the primary focus of self-management programmes before 1995 consisted of improving knowledge through education rather than initiating and enabling sustained behavioural change.

*Types of participants*
Patients with a clinical diagnosis of COPD with symptoms and meeting agreed spirometry criteria (i.e. forced expiratory volume in one second ($FEV_1$)/forced vital capacity (FVC) $< 70\%$) were included[1]. Patients with asthma as a primary diagnosis were excluded.

*Types of interventions*
Self-management interventions were defined as structured interventions for individuals with COPD aimed at improvement of self health behaviours and self- management skills. These interventions required at least an iterative process of interaction between participant and healthcare provider, and ideally also included formulation of goals and provision of feedback. Interventions with fewer than two contact moments were therefore excluded. Furthermore, at least two of the following components had to be part of the intervention: smoking cessation, self- recognition and self treatment of exacerbations, an exercise or physical activity component, advice about diet, advice about medication or coping with breathlessness. Content could be delivered to study participants verbally, as written material (hardcopy or digital) or via audiovisual media. An action plan was defined as a guideline for participants describing when and how to change medication in case of worsening COPD-related symptoms, indicating (the start of) an exacerbation. Explicitly, interventions involving solely participant education were excluded. Disease management programmes classified as pulmonary rehabilitation offered in a hospital or rehabilitation centre, as well as community- or home-based pulmonary rehabilitation programmes solely directed towards exercise, were also excluded. Studies with usual care as a control group and those with an active intervention as a control group were included in this review.

*Types of outcome measures*

*Primary outcomes*
1. Health-related quality of life (HRQoL) scores.
2. Number of hospital admissions.

*Secondary outcomes*

1. Hospitalisation days.
2. Number of exacerbations requiring emergency department visits.
3. Use of (other) healthcare facilities.
4. Number of exacerbations requiring a course of oral corticosteroids or antibiotics.
5. Use of rescue medication.
6. Symptom scores.
7. Anxiety and depression.
8. Self-efficacy.
9. Days lost from work.
10. Lung function.
11. Exercise capacity.

## Search methods for identification of studies

*Electronic searches*

We identified trials from the Cochrane Airways Group Specialised Register (CAGR), which is maintained by the Trials Search Co-ordinator (TSC) for the Group. The Register contains trial reports identified through systematic searches of bibliographic databases, including the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, CINAHL, AMED and PsycINFO, and through handsearching of respiratory journals and meeting abstracts (please see Appendix 1 for further details). The TSC searched all records in the CAGR using the search strategy presented in Appendix 2. The most recent search was conducted in August 2011, with no restriction on language of publication.

*Searching other resources*

Additional trials were searched using the database of clinicaltrials.gov and the World Health Organization (WHO) trials database. Also, reference tracking of eligible studies was performed.

## Data collection and analysis

*Selection of studies*

Two review authors (MZ and TE) independently assessed titles and abstracts of all references retrieved. Two review authors (MZ and TE or JP or MB-K or PV) independently reviewed full-text versions of potentially relevant reports, and assessed these on definite eligibility for inclusion based on the criteria stated above. Disagreement was resolved by discussion between the two review authors. If consensus was not reached, a third review author was consulted.

*Data extraction and management*

Two review authors (MZ and TE or MB-K) independently extracted the following data from included studies: relevant outcome measures, sample size, demographics of included participants, disease severity, setting, duration and contents of the intervention.

*Assessment of risk of bias in included studies*

We assessed the risk of bias according to recommendations outlined in the *Cochrane Handbook for Systematic Reviews of Interventions*[11] for the following items.

1. Random sequence generation.
2. Allocation concealment.
3. Blinding of participants and personnel.
4. Blinding of outcome assessment.
5. Incomplete outcome data.
6. Selective outcome reporting.
7. Other bias.

For each included study, two review authors (MZ and TE or MB-K) independently assessed for all items above whether a high, low or unclear risk of bias was present. Unclear risk indicated that insufficient detail of what happened in the study was reported; that what happened in the study was known but the risk of bias was unknown; or that an entry was not relevant to the study at hand. Each judgement was supported by a short description of what was reported to have happened in the specific study.

*Measures of treatment effect*

For continuous outcomes, the mean difference (MD) or the standardised mean difference (SMD) with 95% confidence intervals (95%CI) was calculated as appropriate. For dichotomous outcomes, a pooled odds ratio (OR) was calculated. Numbers needed to treat for an additional beneficial outcome (NNTB) were calculated for hospital admissions using the pooled OR and control group data from individual studies to obtain study-specific NNTB, with Visual Rx.

*Unit of analysis issues*

Most studies included in this review were RCTs; therefore the unit of analysis in these trials is the participant. One study was cluster-randomised[12]. The cluster, and thus the unit of analysis, in this study was the general practice. We decided to include unadjusted values of this study in the meta-analysis because 1) we had no information from which to estimate a suitable intracluster correlation coefficient; and 2) excluding this trial from meta-analyses did not lead to clear changes in effect sizes.

*Dealing with missing data*

In cases of missing or incomplete data, we contacted the authors of the report. When the study authors did not respond, a second attempt was made. Trial authors who have contributed to this version or to previous versions of the review have been listed under the heading 'Acknowledgements'.

*Assessment of heterogeneity*
We explored variability among studies using the $I^2$ statistic[11]. When substantial heterogeneity ($I^2 > 50\%$) was detected, we discussed possible explanations and critically reconsidered the appropriateness of a meta-analysis. Furthermore, in meta-analyses, we used a random-effects model, rather than a fixed-effect model, to account for heterogeneity.

*Assessment of reporting biases*
We explored possible reporting bias by assessing asymmetry in funnel plots.

*Data synthesis*
When appropriate, we performed a meta-analysis using Review Manager[13]. A meta-analysis was considered when at least three studies reported sufficient data for the outcome. Because of the nature of the intervention analysed in this review, we expected heterogeneity between the studies. Therefore, we performed meta-analyses using a random-effects model rather than a fixed-effect model. Inclusion of controlled clinical trials (CCTs) in this review, resulted in higher risk of bias because of their non-randomised design, and may have introduced heterogeneity into the meta-analysis when data were pooled with findings of RCTs. Therefore meta-analyses were primarily performed without inclusion of CCTs. Sensitivity analyses with inclusion of CCTs were also performed.

Using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions*[11], we created a 'Summary of findings' table on the following outcomes: HRQoL measured with the St George's Respiratory Questionnaire (SGRQ), hospital admissions (respiratory-related and all-cause), courses of oral steroids, dyspnoea measured with the (modified) Medical Research Council Scale ((m)MRC), exercise capacity measured with the six-minute walking test and mortality.

*Subgroup analysis and investigation of heterogeneity*
Subgroup analyses of interest were defined a priori and were performed according to duration of follow-up ($<$ or $\geq$ 12 months), as well as use of an action plan, a standardised exercise programme, and behavioural components in the intervention.

*Sensitivity analysis*
We conducted sensitivity analyses to investigate robustness of effect sizes found in this review under different assumptions.

## MAIN RESULTS

### Description of studies

See Characteristics of included studies.

*Results of the search*

Searches identified 1300 titles and abstracts, which were screened by two review authors (MZ and TE) independently to identify 205 potentially eligible articles about self-management in COPD (Figure 1). Full-text versions of these papers were obtained and independently assessed by two review authors (MZ and TE or JP or MB-K or PV). Twenty-nine studies were included in this review. Eight studies that were included in earlier versions of this review were excluded in this update: four because they were published before 1995, two because they used only one component, one because it did not include participants with COPD as defined by the Global initiative for Obstructive Lung Disease (GOLD) (in the previous two reviews, spirometry data were not required) and one because its intervention could not be classified as self-management.

*Included studies*

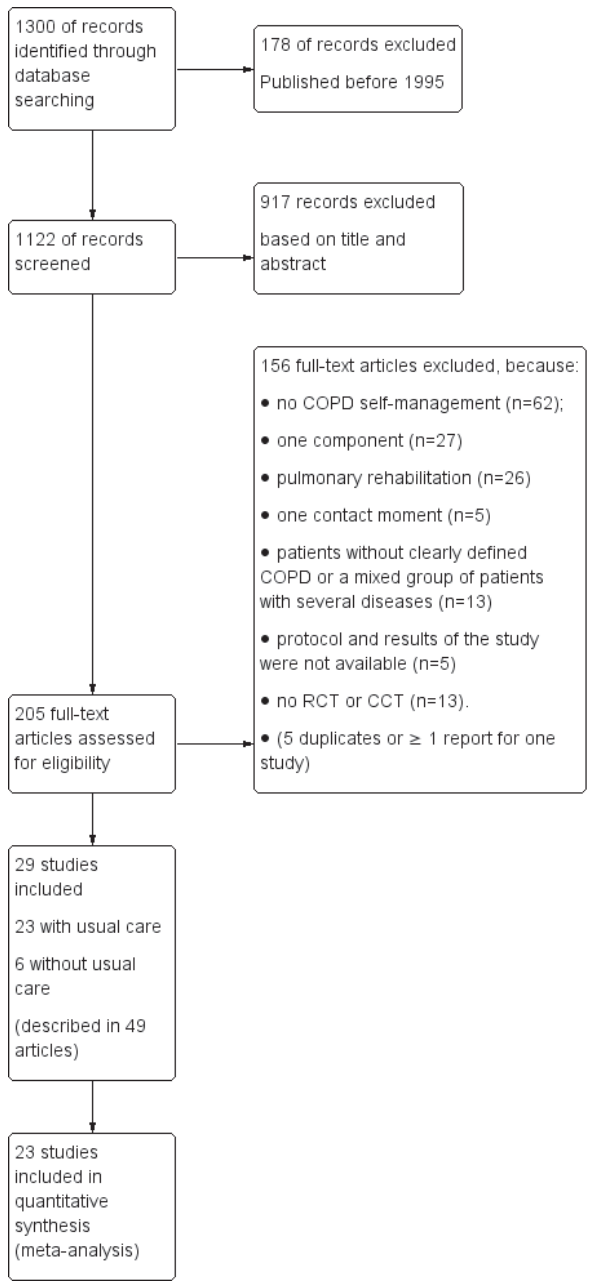
Of the 29 included studies, 23 compared self-management versus a usual care control group[12;14-35]. Twenty-five of the included studies were parallel RCTs, one study was a cluster-randomised trial and three studies were CCTs. The cluster-randomised trial and the CCTs all included a usual care control group. Six RCTs, including seven group comparisons, compared different components of self- management on a head-to-head basis[36-42]. Details of participant characteristics (Table 1) and characteristics of the interventions are tabulated (Table 2).

*Trials with a usual care control*

*Participants and recruitment*

Twenty-three studies on 3189 participants compared self-management versus usual care (Table 1). Drop out rates ranged from 0% to 39%, and 2751 (86%) participants completed the studies. Only eight (35%) studies reported details regarding adherence to the intervention. Four studies reported adherence as the number or percentage of sessions attended by participants. Participants in the intervention group in the study of Moullec et al attended 68.6% of the scheduled sessions[30]. Emery et al reported adherence of 88% in the intervention group[21]. All participants in the study of Hill et al attended the two scheduled education sessions[25]. Mean attendance frequency in the study of Monninkhof et al was 0.77 ± 0.22 sessions per week[29]. The other four studies reported the numbers of participants who were not adherent (according to different definitions); these numbers ranged from 5% to 40%.

**Figure 1** Study flow diagram



Fourteen studies recruited participants from a hospital (11 from the outpatient clinic and three from inpatient population). Six studies recruited participants from general practice or primary healthcare clinics; one study recruited participants from a rehabilitation centre, one from a health maintenance registration and one through advertisement in the community, combined with physician referral.

*Interventions*
Contents of the interventions assessed in the 23 included studies were diverse (Table 2). The duration of follow-up was two months or less in three (13%) studies and three months in five (22%), six months in one (4%), 12 months in 12 (52%) and 24 months in two (9%) studies. Self-management interventions were offered individually in 12 (52%) studies and in small groups in six (26%) studies, and included both individual and group sessions in five (22%) studies. In 17 (74%) studies, an action plan was part of the intervention, and a standardised exercise programme was part of the intervention in 11 (48%) studies. Smoking cessation was discussed in 17 (74%) studies, advice about diet and medication was given in 13 (57%) and 20 (87%) studies, respectively, and coping with breathlessness was discussed in 13 (57%) studies. In four (17%) studies, the use of cognitive-behavioural therapy was mentioned, in six (26%) motivational interviewing was used, and in 11 (48%) and 18 (78%) studies, respectively, goal setting or providing feedback to participants was used.

*Comparisons*
Self-management was compared with usual care in 23 studies. In one of these studies[20], two intervention groups and one usual care group were used. In meta-analyses, both intervention groups were compared with the same usual care group, resulting in one extra comparison[20].

*Head-to-head studies*
*Participants and recruitment*
The six head-to-head studies included 115[42], 17[40], 50[39], 98[41], 159[36;37], and 60[38] participants (Table 1). Percentages of drop outs in these studies ranged from 0% to 26%. Two studies recruited participants in the outpatient clinic of a hospital, one study recruited at a pulmonary rehabilitation site and three studies recruited in the community (e.g. via advertisements).

*Interventions*
Follow-up in the head-to-head studies was two months in one study (17%), six months in three (50%) studies and 12 months in two (33%) studies. In three (50%) studies, the intervention was offered in small groups, whereas in the other three (50%) studies, the intervention was offered individually. An exercise programme was part of the intervention in five (83%) studies, and an action plan was part of the intervention in two (33%) studies. Further details on the contents of separate interventions in the studies without a usual care control group are provided in the characteristics of included studies tables.

*Comparisons*
Six studies on 499 participants were head-to-head trials (i.e. they had no usual care control group; Table 2). One study assessed the mode of delivery by comparing a face-to-face self-management intervention with an Internet-based self-management intervention after six months of follow-up[39]. One study had three intervention groups, all of which included dyspnoea self-management training combined with different levels of exercise[42]. One study compared an exercise persistence intervention in which a mobile phone was used to coach the participant versus an exercise persistence intervention in which a mobile phone was used for self monitoring[40]. One study compared a dyspnoea management intervention versus general health education[41], and another study compared a structured participant education intervention versus giving educational advice only[38]. Finally, one study used a 2×2 factorial design, meaning that two independent interventions were evaluated using one design. This study compared self-management only versus self-management including an action plan for self treatment[36], and self-management only versus self-management including a community-based exercise programme[37].

*Outcomes*
See Table 3 for details on the number of studies reporting outcomes of interest.

*Missing data*
We received replies from all study authors listed in the 'Acknowledgements' section. However, not all of these authors could provide the additional requested information.

*Excluded studies*
One hundred fifty-one studies were excluded on the basis of full-text review (Figure 1). The main reasons for exclusion were as follows: interventions were not related to COPD self-management (n=62); interventions contained only one of the components (e.g. only exercise, only smoking cessation) (n=27); the studied intervention was classified as hospital-based pulmonary rehabilitation (n=26); the interventions contained only one contact moment between participant and healthcare provider (n=5); the study included participants without clearly defined COPD or a mixed group of participants with several diseases (n=13); the article was a protocol and results of the study were not available (n=5); or the study was neither an RCT nor a CCT (n=13). Further details can be found in the characteristics of excluded studies section.

### Risk of bias in included studies

An overview of our risk of bias judgements is presented in Figure 2.

*Allocation (selection bias)*
In most studies, computer-generated random number lists or other computerised methods were used to generate allocation sequences, some with stratification for potential confounders leading to a low risk of bias in these studies (n=17). Two studies were controlled clinical trials, and in one study group, assignment was based on place of residence; we judged that all would lead to a high risk of bias. In nine studies, information provided on generation of allocation sequences was not sufficient to allow judgement of the method.

In most studies, the allocation sequence was not known by investigators or staff, or randomisation was performed by an independent person not involved in the study, and the risk of bias was considered to be low (n=15). In 10 studies, it was not reported who performed the randomisation or which method was used; in these studies, the risk of bias was unclear. In three studies, group allocation was based on place of residence, and risk of bias due to allocation concealment was considered to be high. Risk of bias was also considered to be high in another study, which was a cluster-randomised trial.

*Blinding (performance bias and detection bias)*
Blinding of participants and personnel was not reported in any of the studies. Because of the nature of the intervention, it is difficult to blind participants and personnel to group assignment. Therefore, we assumed that in studies in which blinding was not reported, it was not performed. We evaluated as unclear the amount of bias that this would have caused.

When blinding of outcome assessment was not reported and we did not receive additional information from the study authors, we assumed that it was not done. In contrast to blinding of participants and personnel, seven studies reported blinding of outcome assessment and therefore were judged to have a low risk of bias. In five studies, outcome assessments were performed by independent research personnel who were not involved in the intervention, and so risk of bias was evaluated to be low. In four studies, outcome assessments were performed by study personnel who also provided the intervention or who were principal investigators, and the risk of bias was evaluated to be high.

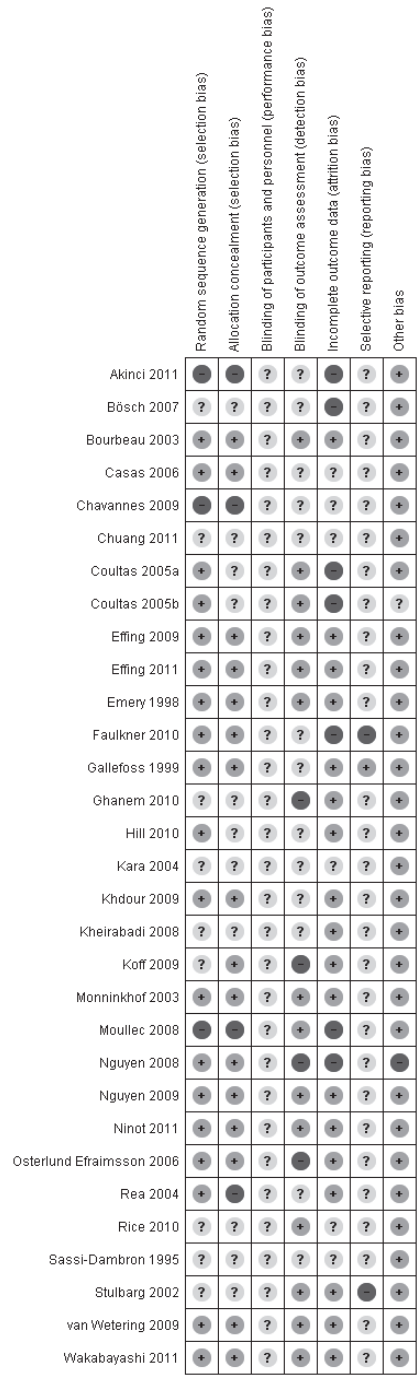



**Figure 2** Methodological quality summary: review authors' judgements about each methodological quality item for each included study

*Incomplete outcome data (attrition bias)*
In 17 studies, outcome data were complete or some outcome data were missing, but the quantities of missing data were equal in the intervention and control groups, and the reasons for missing data were comparable. In both situations, risk of bias was considered to be low. In one study, the quantities of missing outcome data were not equal in the intervention and control groups, and the reasons for this were not clear, leading to a high risk of bias. In five studies, the quantities of missing outcome data were > 25%, and risk of bias was considered to be high. In six studies, information was insufficient to allow assessment of the risk of bias, and the risk of bias was therefore considered to be unclear.

*Selective reporting (reporting bias)*
In most of the studies, it was difficult to determine whether outcomes were selectively reported because detailed study protocols often were not available. One paper reported an aim different from that reported in the original trial, and not all outcome measures were reported completely. The risk of bias in this study was therefore considered to be high. Other detected signs of selective reporting included missing domain scores on HRQoL questionnaires and outcome measures that were reported for the short term but not for the longer term. Risk of bias for selective outcome reporting in these studies was considered to be unclear.

*Other potential sources of bias*
We additionally assessed the study of Rea et al[12] on biases which are important in cluster-randomised trials. In Rea's study, general practices were randomly assigned to the interventions before the participants were included. For reasons unknown, the number of participants screened and included was lower in the intervention group than in the control group. The study authors state that baseline characteristics were not significantly different between groups. Therefore, risk of recruitment bias is unclear and risk of bias for baseline imbalance is low. The risk of bias due to loss of clusters is low because no clusters were lost after participant enrolment. Rea et al did not correct for clustering in their analyses, so risk of bias due to incorrect analysis is high.

No other potential sources of bias within studies were observed. Additionally, we explored reporting bias using funnel plots. We have created plots for our primary outcomes: HRQoL (Figure 3) and respiratory-related hospital admissions (Figure 4). The funnel plot of the MD in SGRQ total score per study plotted against the standard error of the MD seems to show a gap on the left side of the graph. This could indicate that smaller studies with effects in favour of the intervention group are less frequently published. The same could be suggested by the funnel plot of respiratory-related hospital admissions. Publication bias is just one reason for funnel plot asymmetry, so other study factors may have contributed to this.

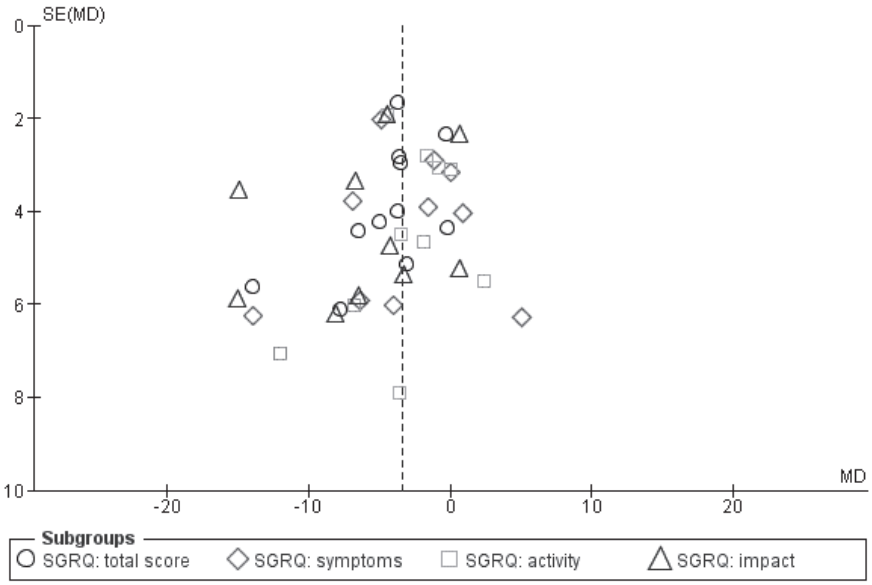



**Figure 3** Funnel plot of comparison: 1 Self-management versus control, outcome: 1.1 HRQoL: SGRQ.

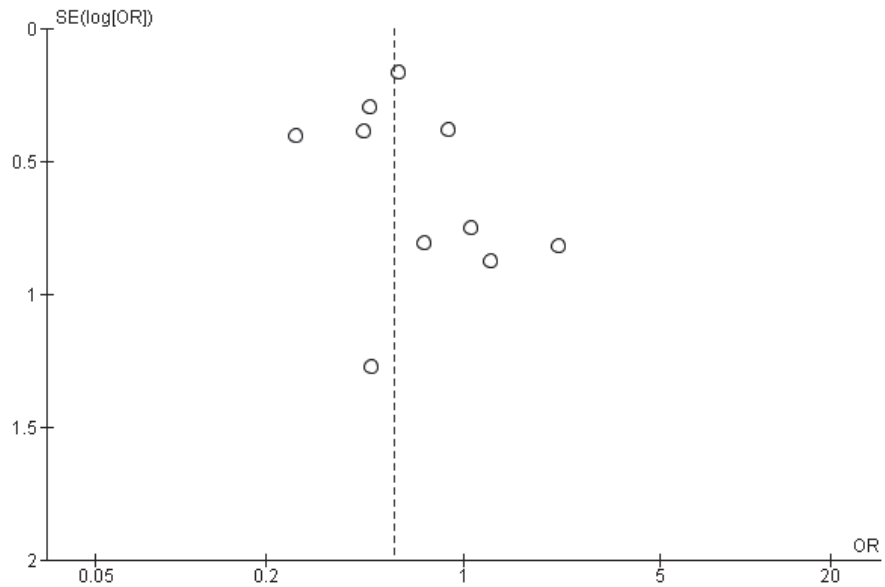



**Figure 4** Funnel plot of comparison: 1 Self-management versus control, outcome: 1.7 Respiratory-related hospital admissions.

## Effects of interventions

This review has been augmented with a 'Summary of findings' table, reflecting endpoints related to quality of life, healthcare use, exacerbations, dyspnoea, exercise capacity and mortality (Summary of findings table). The table was generated with GRADEpro software. As stated earlier, 23 studies compared self- management versus usual care, and six studies (with seven group comparisons) compared different components of self-management head-to-head. The latter studies are referred to as "studies without usual care" in the section below. Because of heterogeneity in the interventions, we were not able to pool studies without a usual care control group in the meta-analyses; therefore the results of these studies are described only qualitatively. Also, in the primary meta-analysis, CCTs were excluded. Sensitivity analyses with inclusion of CCTs were performed.

*Health-related quality of life - studies with usual care*
COPD-specific HRQoL was measured by the SGRQ in 15 studies[14;16-18;20;23;26;28-35]. The studies of van Wetering et al[34] and Österlund-Efraimsson et al[32] used the SGRQ but provided insufficient data for inclusion in the meta-analysis. The studies of Akinci et al[14], Chavannes et al[18] and Moullec et al[30] were CCTs and therefore were not included in the meta-analyses. Mean total scores of 10 studies could be included in the meta-analysis. All of these studies showed lower (meaning better quality of life) total scores in the intervention group compared with the control group. The MD of -3.51 (95%CI -5.37 to-1.65) was statistically significant at the 5% level (Analysis 1.1). Because Wakabayashi et al[35] reported no domain scores, only mean domain scores of nine of the 10 studies could be included in the meta-analysis. MDs in domain scores of the SGRQ were statistically significant, with MDs of -3.09 (95%CI -5.42 to -0.77), -2.75 (95%CI -4.93 to -0.56) and -5.71 (95%CI -9.17 to -2.25) for symptoms, activity and impact, respectively. The MD on the domain score of impact is considered to be clinically relevant because it reaches the minimal clinically important difference (MCID) of four points[43]. Meta-analyses of total scores and domain scores of symptoms and activity revealed only minimal heterogeneity, with $I^2$ statistics ranging from 0% to 4%. Moderate heterogeneity was detected in the meta-analysis of domain score impact ($I^2$ = 51%). For SGRQ total score, we also performed a meta-analysis on the change from baseline (Analysis 1.2). This analysis showed a statistically significant difference between intervention and control groups, with a somewhat smaller MD of -2.68 (95%CI -4.16 to -1.20), indicating that the total score on the SGRQ of the intervention group decreased by 2.68 points more from baseline compared with the score of the control group.

When we included the CCTs[14;18;30] in secondary meta-analyses, effect sizes for both total and domain scores increased, and all reached the MCID of four points (Analysis 2.1). However, heterogeneity was high, with $I^2$ statistics ranging from 60% to 79%. In particular, the study of Moullec et al[30] showed highly positive MDs in comparison with the other studies.

Van Wetering et al[34] and Österlund-Efraimsson et al[32] found statistically significantly lower total scores, so better HRQoL, in the intervention group compared with the control group. In the study of Österlund-Efraimsson[32], all domain scores also favoured the intervention group, whereas van Wetering et al found no statistically significant differences in the symptom domain.

In two studies[18;27], COPD-specific HRQoL was measured by the Clinical COPD Questionnaire (CCQ), on which a lower score again indicates better HRQoL. On total score, Kheirabadi et al[27] found no difference, and Chavannes et al[18] reported a lower score in the intervention group (0.92 ± 0.72) than in the control group (1.74 ± 0.95). Domain scores were reported only by Kheirabadi et al[18;27] and were comparable between groups after three months of follow-up.

Three studies measured HRQoL by means of the Chronic Respiratory Questionnaire (CRQ)[12;22;24]. Rea et al[12] did not report standard deviations (SDs) and therefore could not be included in a meta-analysis, leaving an insufficient number of studies to perform a meta-analysis. In the study of Rea et al[12], the dimensions of fatigue and mastery showed statistically significantly higher scores, meaning better HRQoL, in the intervention group (17.7 and 21.4, respectively) than in the control group (15.7 and 20.7, respectively) after 12 months of follow-up. The study of Ghanem et al[24] found statistically significantly higher scores in the intervention group than in the control group on all four domains (dyspnoea 19.6 ± 5.2 vs 13.5 ± 4.3, fatigue 17.4 ± 5.4 vs 13.2 ± 5.1, emotion 33.5 ± 7.2 vs 29.7 ± 11.4, mastery values not reported). However, Faulkner et al[22] found no significant differences between intervention and control groups on the CRQ.

Three studies measured generic HRQoL using the Short Form-36 (SF-36)[12;20;24]. Mean values and SDs were available only for the studies of Coultas et al[20] and Ghanem et al[24]; therefore, it was not considered appropriate to perform a meta-analysis. No differences were noted between intervention and control groups at the end of follow-up in the studies of Rea et a[12] and Coultas et al[20]. In the study of Ghanem et al[24], differences between intervention and control groups were reported, but these were already present at baseline. Therefore, the study authors mentioned significant improvement in the scales of physical functioning, role-physical, pain, vitality and role of emotions only in the intervention group. In the control group, no improvements were observed.

Generic HRQoL and health status were further measured using the short version of the questionnaire validated by the WHO (WHOQOL-BREF) in the study of Moullec et al[30], the Illness Intrusiveness Rating Scale (IIRS) in the study of Coultas et al[20], the Nottingham Health Profile (NHP) in the study of Ninot et al[31] and the Sickness Impact Profile (SIP) in the study of Emery et al[21]. Moullec et al[30] found statistically significantly higher scores on the physical domain of the WHOQOL-BREF in the intervention group compared with the control group after 12 months of follow-up (13.4 ± 1.9 vs 9.4 ± 2.2). No statistically significant differences were noted in the other domains. Coultas et al[20] found statistically significant

improvement in IIRS following nurse-assisted collaborative management compared with the usual care group. Ninot et al[31] found significant differences in NHP between the groups, in favour of the intervention group, on the energy and emotional reaction dimensions of the NHP, after adjustment for baseline values. Finally, Emery et al[21] found significant improvement in total function in the control group as measured by the SIP, whereas the intervention group showed no change.

*Health-related quality of life - head-to-head studies*
Only the study of Nguyen et al[40] measured HRQoL using the SGRQ and found no between-group differences in SGRQ total score. Three studies measured HRQoL using the disease-specific CRQ. Nguyen et al[39] observed statistically significant improvement after six months of follow-up in both study groups in total score, dyspnoea, fatigue and mastery score. Stulbarg et al[42] found statistically significantly greater improvement in mastery and dyspnoea in the group that received the most intensive exercise training compared with the groups that received less intense or no training, in addition to dyspnoea self-management. Effing et al[37] found a significantly higher CRQ dyspnoea score among individuals who participated in a community-based exercise programme in addition to self- management compared with those who participated only in self-management. No between-group differences were observed in other CRQ components. In the study of Effing et al[44] evaluating self treatment of exacerbation, no between-group differences in CRQ components were found. In the studies of Effing et al[36;37], HRQoL was also measured with the CCQ, but no between-group differences were reported.

The SF-36 was used in three studies. Stulbarg et al[42] found no statistically significant differences between groups in mental and physical component scores after 12 months of follow-up. The study of Nguyen et al[39] reported statistically significant improvement in both study groups on the SF-36 physical component scale but not on the mental component scale. In contrast, Nguyen et al[40] found no between-group differences in either physical or mental component scores of the SF-36. Sassi-Dambron et al[41] measured quality of life using the quality of well-being scale and found no differences among the three intervention groups.

*Hospital admissions - studies with usual care*
Respiratory-related hospital admissions were reported in 12 studies. Data on nine of these studies were suitable for inclusion in a meta-analysis[12;16;20;23;26;28;29;31;33]. A clinically relevant and statistically significant reduction in the probability of at least one respiratory-related hospital admission was noted among participants receiving self-management compared with those receiving usual care, with an OR of 0.57 (95%CI 0.43 to 0.75). Heterogeneity was low, with an $I^2$ of 13% (Analysis 1.7). Study-specific numbers needed to treat for a beneficial outcome (NNTBs) ranged from eight (95%CI 5 to 14) to 26 (95%CI 19 to 45). Differences between studies might be explained by differences in baseline risk, severity of disease and duration of follow-up (Table 4). Over one year of follow-up, eight (95%CI 5 to 14) participants with a high baseline risk of respiratory-related hospital admission needed to be

treated to prevent one participant with at least one hospital admission (Figure 6), and 20 (95%CI 15 to 35) participants with a low baseline risk of hospitalisation needed to be treated to prevent one participant with at least one respiratory-related hospital admission (Figure 7). The studies of van Wetering et al[34] and Bösch et al[15] could not be included in the meta-analysis because the trialists could not provide the numbers of participants with at least one hospital admission. Van Wetering et al[34] found a mean number of hospital admissions for COPD of 0.36 ± 1.00 in the intervention group and 0.40 ± 0.78 in the control group. The mean number of COPD-related hospitalisations significantly decreased during follow-up in the intervention group in the study of Bösch et al[15] to 0.3 ± 0.6, and was constant in the control group at 0.6 ± 0.7.

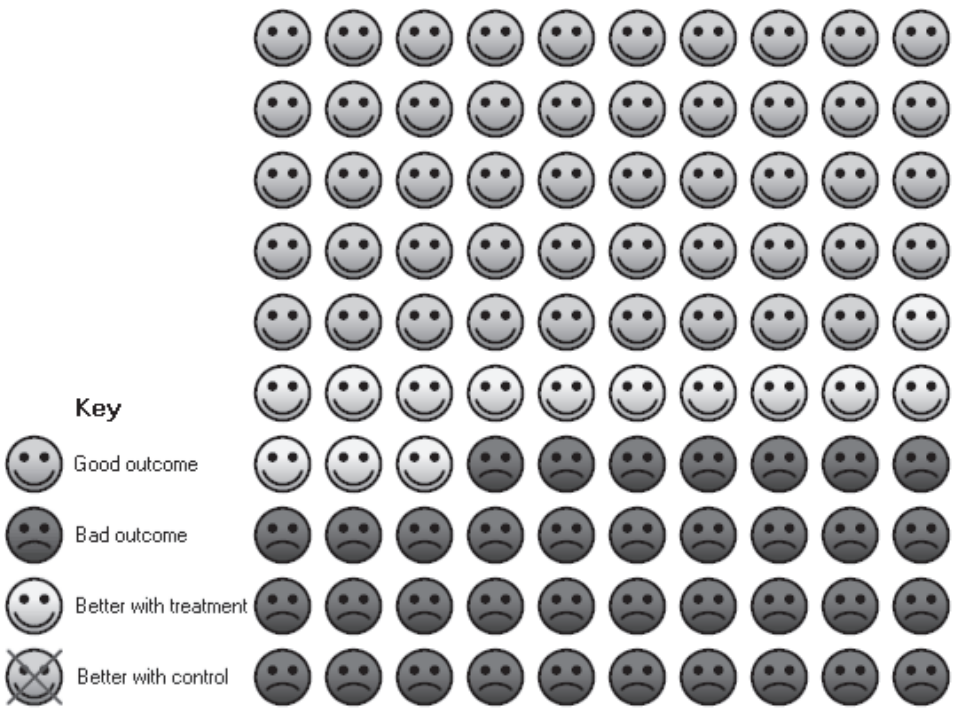



**Figure 5** High-risk participants: In the usual care group, 51 of 100 people had at least one respiratory-related hospital admission over 52 weeks, compared with 37 (95%CI 31 to 44) of 100 for the self-management group

The CCT of Moullec et al[30] reported zero respiratory-related hospital admissions among 11 participants in the intervention group and in two of 16 participants in the control group. We performed a sensitivity analysis by including this study in the meta-analysis on respiratory-related hospital admissions, and OR and heterogeneity were comparable with the primary analysis (0.57, 95%CI 0.44 to 0.73; $I^2 = 6\%$) (Analysis 2.3).

Six studies were included in the meta-analysis on all-cause hospital admissions[12;17;20;26;31;33]. The OR of having at least one all-cause hospital admission of 0.60 (95%CI 0.40 to 0.89) was statistically significant in favour of the self-management group (Analysis 1.8). The studies of van Wetering et al[34], Wakabayashi et al[35] and Chuang et al[19] could not be included in the meta-analysis for the reason stated in the paragraph above. Van Wetering et al[34] found a mean number of hospitalisations of 0.75 ± 1.29 in the intervention group and 0.96 ± 1.35 in the control group after 24 months of follow-up. Wakabayashi et al[35] found 0.07 ± 0.3 in the intervention group and 0.19 ± 0.8 in the control group after 12 months of follow-up. Chuang et al[19] reported fewer all-cause hospital admissions in the intervention group than in the control group (40 ± 27 vs 57 ± 27); however, this difference was not statistically significant.

The CCT of Moullec et al[30] reported three all-cause hospital admissions among 11 participants in the intervention group and four among 16 participants in the control group. We performed a sensitivity analysis by including this CCT in the meta-analysis, and the OR was comparable with that of the primary analysis: 0.61 (95%CI 0.42 to 0.89), with an $I^2$ of 41% (Analysis 2.4).

*Hospital admissions - head-to-head studies*
Effing et al[36] observed 14 all-cause hospital admissions in the self treatment intervention group and 24 hospital admissions in the self-management group, but this difference was not statistically significant. Effing et al[37] observed 15 hospital admissions in the exercise intervention group and 17 hospital admissions among participants who received solely self-management. Stulbarg et al[23;42] reported no differences between groups in the number of respiratory-related hospitalisations after 1 year of follow-up.

*Hospitalisation days - studies with usual care*
The number of respiratory-related hospitalisation days was reported in five studies. The studies of Gallefoss et al[23], Ninot et al[31] and van Wetering et al[34] were included in a meta-analysis. No difference in mean number of hospital days was found (MD 0.33, 95%CI -1.01 to 1.66) (Analysis 1.9). Moullec et al[30] reported zero hospital days in the intervention group; therefore, these data could not be included in a sensitivity analysis with CCTs. However, these investigators reported a statistically significantly lower number of hospital days in the intervention group compared with the control group (0 vs 6.4 ± 14.5). Rea et al[12] did not report SDs and therefore could not be included in the meta-analysis. Whereas Rea et al[12] reported no significant differences between groups in the number of bed days per participant per year, a statistically significant decrease in days per participant per year from

12 months before the trial to 12 months during the trial was noted in the intervention group; in contrast, a statistically significant increase was evident in the control group.

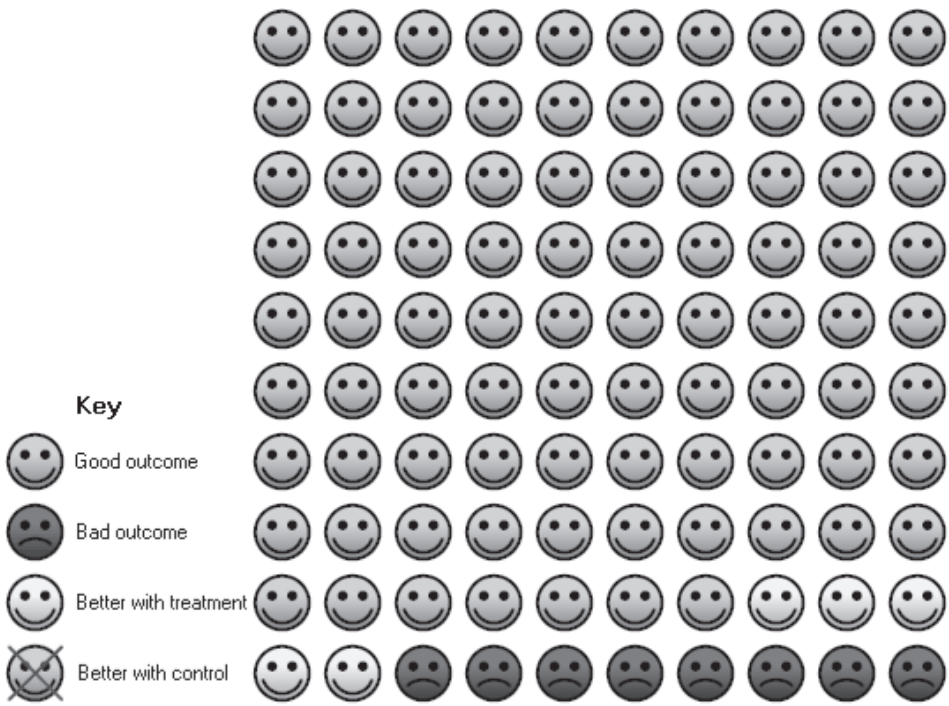



**Figure 6** Low-risk participants: In the usual care group, 13 of 100 people had at least one respiratory-related hospital admission over 52 weeks, compared with 8 (95%CI 6 to 10) of 100 for the self-management group.

The number of all-cause hospitalisation days was assessed in eight studies[12;16;19;26;30;31;33;34]. Five studies[16;26;31;33;34] were included in the meta-analysis, and we found no statistically significant difference between intervention and control group (MD -1.39, 95%CI -3.19 to 0.41) (Analysis 1.10). The study of Rea et al[12] could not be included in the meta-analysis because of the lack of SDs. The mean number of bed days in the study of Rea et al[12] was lower in the intervention group than in the control group (3.2 vs 6.8); however, this difference did not reach statistical significance. Chuang et al[19] reported a lower number of hospitalisation days in the intervention group compared with the control group (115 ± 105 vs 190 ± 110), but this difference was not statistically significant.

The CCT of Moullec et al reported a lower number of all-cause hospital days in the intervention group (1.5 ± 3.4) than in the control group (7.9 ± 16.1). We performed a sensitivity analysis by including this CCT in the meta-analysis, and the MD was -1.62 (95%CI -3.42 to 0.18), with heterogeneity comparable with that of the primary analysis (Analysis 2.5).

*Hospital days - head-to-head studies*
None of the studies without usual care reported the number of hospital days.

*Emergency department visits - studies with usual care*
Four studies[20;26;28;33] reported respiratory-related emergency department (ED) visits, but data could not be combined in a meta-analysis because different methods were used to report the outcome. Koff et al[28] reported one (5.3%) visit in the intervention group and three (15.8%) in the control group after three months of follow-up. Khdour et al[26] reported the total number of COPD-related visits and found a statistically significantly lower number in the intervention group than in the control group (40 vs 80) after 12 months of follow-up. Rice at al[33] found a significant difference between intervention and control groups (20.8, 95%CI 14.5 to 27.1 vs 42.4, 95%CI 31.4 to 53.4, per 100 person-years) after 12 months of follow-up. In contrast, Coultas et al[20] reported no differences between groups in COPD-related visits after six months of follow-up.

ED visits for all-causes were assessed in five studies[12;16;19;33;35], which also could not be included in a meta-analysis because different methods were used to report the outcomes. Rea et al[12] observed five (6%) visits in the intervention group and seven (13.5%) visits in the control group after 12 months of follow-up. Bourbeau et al[16] reported a significant treatment effect in favour of the intervention group (2.5 vs 3.2 per person per year) after 24 months. Rice et al[33] found significantly fewer visits in the intervention group than in the control group (67.0 vs 91.2 per 100 person-years). In the study of Wakabayashi et al[35], no significant changes in the frequency of ED visits were found during follow-up. Chuang et al[19] reported fewer ED visits in the intervention group than in the control group (92 ± 42 vs 71 ± 29), but this difference was not statistically significant.

*Emergency department visits - head-to-head studies*
Effing et al[36] reported a mean number of all-cause ED visits of 0.26 ± 0.61 per person per year in the self treatment group, and 0.53 ± 1.3 per person per year in the group receiving only self-management. Effing et al[37] reported 0.44 ± 0.92 ED visits per person per year in the group participating in the self-management exercise programme, and 0.41 ± 1.18 visits per person per year in the group that received solely self-management. These differences were not statistically significant.

*Use of other healthcare facilities - studies with usual care*
Doctor and nurse visits were reported in eight studies[16;19;20;23;26;29;30;34]. Only two of these studies[20;23] (three group comparisons) could be included in a meta-analysis; therefore a meta-analysis was considered to be not appropriate. After one year of follow-up, Gallefoss

et al[23] found a statistically significantly lower number of general practitioner consultations in the in the intervention group (0.5 ± 0.9) compared with the control group (3.4 ± 5.5). Coultas et al[20] found no statistically significant differences in doctor visits between any of the intervention groups and the control group. Khdour et al[26] reported a total number of 267 visits to the general practitioner in the intervention group and 258 visits in the control group. Whereas the number of scheduled general practice (GP) visits in this study was lower in the intervention group (145 vs 183), the number of unscheduled visits was somewhat higher in the intervention group (119 vs 75). Van Wetering et al[34] reported the mean number of GP visits over two years of follow-up; numbers in both study groups were comparable (intervention 7.2 ± 7.0; control 7.9 ± 8.1). Chuang et al[19] reported statistically significantly more GP visits in the intervention group than in the control group (683 ± 123 vs 887 ± 95). The studies of Bourbeau et al[16] and Monninkhof et al[29] could not be included in the meta-analysis because of the lack of SDs, but both showed a reduction in unscheduled doctor and nurse visits per person per year, with differences of -0.7 and -0.4, respectively. Moullec et al[30] found a statistically significant difference between intervention and control groups in home visits by the GP (0.0 vs 0.9 ± 3.0) but found no between-group differences in consultations with the GP or in consultations with a lung specialist.

*Use of other healthcare facilities - head-to-head studies*
Effing et al[37] (evaluating the self-management exercise component) reported no between-group differences in total healthcare contacts. Effing et al[36] reported a non–statistically significant reduction in healthcare contacts in the self treatment group compared with the self-management group (5.37 ± 3.75 vs 6.51 ± 3.89 contacts per participant per year). Total healthcare contacts included consults with the GP, outpatient visits and ED visits.

*Number and severity of exacerbations - studies with usual care*
In three studies[16;29;34], the numbers of exacerbations were reported. Van Wetering et al observed 3.02 exacerbations per participant in the intervention group and 2.18 in the control group after 24 months of follow-up. This difference was not statistically significant. Reported follow-up in the studies of Bourbeau et al[16] and Monninkhof et al[29] was 12 months. Whereas Bourbeau et al[16] found 299 exacerbations in the intervention group and 362 exacerbations in the control group, Monninkhof et al[29] found 360 exacerbations in the intervention group and 177 exacerbations in the control group.

*Number and severity of exacerbations - head-to-head studies*
Nguyen et al[40] reported that four participants experienced an exacerbation that required treatment with antibiotics or oral prednisone. In an earlier study, Nguyen et al[39] reported that they registered 11 exacerbations in 10 participants; however, they also stated that this number was too small to allow group comparisons. In the study of Effing et al[36], frequency, severity and number of exacerbations were assessed. Investigators found no between-group differences in the mean number of exacerbations (3.5 ± 2.7 in both study groups), nor in the mean severity of an exacerbation, over one year. However, participants in the self treatment group did report fewer exacerbation days (median 31, interquartile range (IQR)

8.9 to 67.5) compared with the control group (median 40, IQR 13.3 to 88.2). This difference was statistically significant in participants with a relatively high number of exacerbation days. In the study of Effing et al[37], again no statistically significant between-group differences were found in mean numbers of exacerbations (3.3 ± 2.5 vs 3.8 ± 2.8). Stulbarg et al[42] reported no differences between groups in numbers of exacerbations after one year of follow-up.

*Courses of oral steroids—studies with usual care*

Three studies reported the use of oral corticosteroids for respiratory problems[12;23;33] and could be included in a meta-analysis. Based on these three studies, the probability of having at least one course of oral steroids was higher in the self-management group compared with the control group, with an OR of 4.42 (95%CI 0.39 to 50.10). However, this OR was not statistically significant (P value 0.23), and heterogeneity was high ($I^2$ = 96%) (Analysis 1.13). The outlier in this meta-analysis was the study by Rice et al[33], which included many more participants than were included in the studies of Gallefoss et al[23] and Rea et al[12]. In addition, the proportion of participants with at least one course of oral steroids in the self-management group of the study of Rice et al[33] is relatively high (97.6%) compared with the studies of Gallefoss et al (69.2%) and Rea et al (47.6%). In the case that an event is common, the OR is an overestimation of the risk ratio and should be interpreted with caution. The latter is the case in the study of Rice et al, in which an OR of 32.7 was found. This meta-analysis therefore should be interpreted with caution.

*Courses of antibiotics - studies with usual care*

The use of antibiotics for respiratory problems was reported by three studies[12;23;33]; however, the number of people with at least one course of antibiotics was available for only two studies[12;33]; therefore a meta-analysis was not justified. Rea et al[12] reported fewer participants receiving at least one course of antibiotics in the intervention group than in the control group (59% vs 69%), whereas Rice et al[33] reported the opposite (92% vs 56%). Bösch et al[15] reported a significant reduction in the mean number of exacerbation-related antibiotic courses in the intervention group, with no changes observed in the control group. Khdour et al[26] reported mean number of oral steroids and antibiotic courses combined and found a significant difference, with less use in the intervention group compared with the control group (3.08, 95%CI 2.57 to 3.59 vs 4.03, 95%CI 3.37 to 4.69).

*Courses of oral steroids or antibiotics - head-to-head studies*

Nguyen et al[40] reported that four (23.5%) participants experienced an exacerbation that required treatment with antibiotics or oral prednisone. In the study of Effing et al[36], the median number of prednisolone (2.6, IQR 1.0 to 5.0 vs 1.7, IQR 1.0 to 3.2) and antibiotic courses (2.0, IQR 0.8 to 4.0 vs 1.1, IQR 0.0 to 2.9) was higher in the self treatment group than in the group that received only self-management. The difference in prednisolone courses was borderline non–statistically significant, whereas the difference in antibiotic courses was borderline statistically significant.

*Use of rescue medication - studies with usual care*
Gallefoss et al[23] reported the use of short-acting $\beta_2$-agonists as rescue medication. Use of rescue medication was coded as defined daily dosages (DDDs) for comparison of medications within the same chemical therapeutic group. In this study, participants receiving self-management used statistically significantly less rescue medication (median DDD 125, IQR 100 to 344) than the control group (median DDD 209, IQR 150 to 550). Rice et al[33] reported the use of short-acting $\beta_2$-agonists as the mean number of metered-dose inhalers and found no statistically significant differences between intervention and control groups (6.4 $\pm$ 8.3 vs 5.6 $\pm$ 8.0).

*Use of rescue medication - head-to-head studies*
None of the studies without usual care reported the use of rescue medication.

*Symptoms - studies with usual care*
The effect of self-management education on dyspnoea as measured by the (m)MRC was examined in six studies[15;17;18;22;34;35]. Three studies assessed dyspnoea using the MRC[17;18;22], and three studies assessed dyspnoea using the modified version of the MRC (mMRC)[15;34;35]. The outcomes of three studies were combined in a meta-analysis (Analysis 1.15). A statistically significant difference in favour of the intervention group was found, with an MD of -0.83 (95%CI -1.36 to -0.30). It is unclear whether this difference is also clinically relevant.

When we included the CCT of Chavannes et al in the meta-analysis, the MD decreased to -0.67 (95%CI -1.19 to -0.16) and heterogeneity was comparable with the primary analysis (Analysis 2.6).

The study of Wakabayashi et al could not be included in the meta-analysis because of irregularities in the SD; however, investigators reported an improvement in mMRC score in the intervention group and a worsening in the usual care group after 12 months of follow-up. Between-group differences were not statistically significant. Van Wetering et al[34] reported only changes from baseline and therefore could not be included in the meta-analysis. In this study, a statistically significant between-group difference in change from baseline MRC dyspnoea score of 0.21 $\pm$ 0.10 units in favour of the intervention group was found. Akinci et al[14] and Moullec et al[30] assessed dyspnoea using the Baseline Dyspnea Index (BDI) and a visual analogue scale (VAS) score for dyspnoea, respectively. In the study of Akinci et al[14], dyspnoea increased significantly in the intervention group, whereas it did not change in the control group after three months of follow-up. Moullec et al[30] observed a lower mean VAS score after 12 months of follow-up in the intervention group (1.3 $\pm$ 1.2) compared with the control group (4.0 $\pm$ 3.0) but did not report statistical significance for between-group differences.

In the study of Monninkhof et al[29], no significant between-group differences were seen in mean symptom scores for breathlessness and sputum production over two-week periods.

However, small differences in mean cough and sputum colour scores favoured the intervention group. Although these differences reached borderline significance, the study authors stated that differences probably were not clinically relevant. Finally, in the study by Bourbeau et al[16], symptoms during exacerbations were scored (breathlessness, sputum volume and sputum colour), but no significant differences were found between intervention and control groups.

*Symptoms - head-to-head studies*
Effing et al[37] measured dyspnoea with the MRC and found no differences in mean values between groups (2.2 ± 1.1 vs 2.5 ± 1.2). Stulbarg et al[42] assessed dyspnoea using the University of California San Diego (UCSD) Shortness of Breath Questionnaire (SOBQ) and the Transitional Dyspnea Index (TDI). For the total group, dyspnoea as measured with the SOBQ significantly improved after two months of follow-up. No statistically significant differences were observed on the TDI, in spite of improvements of 1.5 to 2.0 units in the three groups. Sassi-Dambron et al[41] measured dyspnoea using the TDI, the SOBQ, the American Thoracic Society Dyspnea Scale (ATS-DS), the Oxygen Cost Diagram (OCD), a VAS scale and the Borg Scale of Perceived Dyspnea. On the SOBQ, dyspnoea in both groups improved significantly over time. Furthermore, the group receiving dyspnoea management improved significantly over time on the TDI compared with the group that received solely education. The other measures did not change.

*Anxiety and depression - studies with usual care*
Faulkner et al[22] measured anxiety and depression using the Hospital Anxiety and Depression Scale (HADS). They found no significant differences in anxiety (3.8 ± 3.6 vs 3.3 ± 2.1) or depression (2.6 ± 2.4 vs 2.9 ± 2.6) between intervention and control groups. Emery et al[21] extensively assessed anxiety and depression. Depression was assessed by the Center for Epidemiological Studies–Depression inventory (CES-D), the depression subscale of the Hopkins Symptom Checklist and the Bradburn Affect-Balance Scale. Anxiety was assessed by the anxiety subscales of the State-Trait Anxiety Inventory (STAI) and the Hopkins Symptom Checklist. No statistically significant differences were found between education and stress management and waiting list groups after 10 weeks of follow-up[21].

*Anxiety and depression - head-to-head studies*
Effing et al[36;37] assessed anxiety and depression using the HADS. In both group comparisons, no statistically significant between-group differences were found. Sassi-Dambron et al[41] assessed anxiety using the STAI–Anxiety and Depression along with the CES-D and found no statistically significant between-group differences after six months of follow-up.

*Self-efficacy - studies with usual care*
Faulkner et al[22] measured self-efficacy using the Depression Coping Self-Efficacy Scale, but the results of the assessment were not reported.

*Self-efficacy - head-to-head studies*
Kara et al[38] assessed disease-specific self-efficacy using the COPD Self-Efficacy Scale (CSES). In the intervention group, statistically significant improvements in total score and in all domains of the CSES were noted in the intervention group. Differences varied from 0.95 to 1.46 points after two months of follow-up. In the intervention group, only total scores and scores on the domains of weather/environment and behavioural risk factors were statistically significantly improved. Stulbarg et al[42] measured two types of self-efficacy after two months of follow-up. Self-efficacy for walking was measured with the Self-Efficacy for Walking Questionnaire (SEWQ), and self-efficacy for managing shortness of breath was measured using the CSES and the Self-Efficacy for Managing Shortness of Breath instrument (SEMSOB). Self-efficacy for walking improved over time for all intervention groups, but no between-group differences were noted. No improvements were observed for self-efficacy for managing shortness of breath as measured by the CSES. In contrast, the SEMSOB showed statistically significant improvement in all groups. The SEMSOB showed no between-group differences in changes over time.

Nguyen et al[40] measured self-efficacy for overcoming barriers to exercise with the Exercise Barriers Efficacy Scale. No significant between-group differences were observed. Nguyen et al[39] assessed self-efficacy for managing dyspnoea with a single question ("How confident are you that you can keep your shortness of breath from interfering with what you want to do?") using a 0 to 10-point response scale. In both intervention groups, self-efficacy improved over six months of follow-up, but no between-group differences were found.

*Days lost from work - studies with usual care*
Three studies reported days lost from work[23;29;34]. Gallefoss et al reported no significant differences between groups. Almost 50% of participants with COPD in this study were employed. Only three of 14 participants in the intervention group and two of 13 in the control group reported absence from work. Monninkhof et al[29] used the term 'restrictive activity days', defined as days on which work was missed or days on which activities were significantly reduced because of health problems. A reduction in the average number of restricted activity days was seen in the education group compared with the control group ($4.1 \pm 4.2$ vs $5.3 \pm 5.3$), but no significant between-group differences were detected. Van Wetering et al[34] provided self reported hours unable to work and found a mean time of $22 \pm 89$ hours in the intervention group and a mean time of $6.8 \pm 40$ hours in the control group during 24 months of follow-up.

*Days lost from work - head-to-head studies*
None of the studies without usual care reported days lost from work.

*Lung function - studies with usual care*
Lung function was assessed as forced expiratory volume in one second ($FEV_1$) in litres in eight studies[14;15;21;22;26;30;31;35] and as percentage predicted for age, gender and height ($FEV_1$%) in eight studies[12;14;16;17;21-23;35]. Six and seven studies, respectively, could be included in the meta-analyses. The MD of $FEV_1$ was 0.08 (95%CI -0.03 to 0.19) (Analysis

1.17). No heterogeneity was observed, with an $I^2$ of 0%. In accordance with this, the MD of $FEV_1$% was 1.78 (95%CI -1.44 to 5.01), with an $I^2$ of 15% (Analysis 1.18). $FEV_1$/FVC was measured in five studies[14;17;22;31;35], and again no significant difference was found for this outcome (MD -0.84, 95%CI -5.04 to 3.36) (Analysis 1.20).

The CCTs of Moullec et al[30] and Akinci et al[14] reported no between-group differences for any of the lung function outcomes. Adding these two studies to the meta-analyses led to MDs of $FEV_1$ and $FEV_1$/FVC comparable with those of the primary analysis (Analysis 2.7; Analysis 2.8; Analysis 2.9).

*Lung function - head-to-head studies*
In both studies of Effing et al[36;37], no between-group differences were found in $FEV_1$ and $FEV_1$%. This corresponds with the results of Stulbarg et al[42], who found no significant changes in lung function after 12 months of follow-up.

*Exercise capacity and physical activity - studies with usual care*
Exercise capacity was measured in eight studies using the six-minute walking test (6MWT)[14-16;24;29-31]. Six studies were included in the meta-analysis. A between-group difference with an MD of 33.69 m (95%CI -9.12 to 76.50) was found (Analysis 1.20). Heterogeneity between the studies was high, with an $I^2$ of 89%. The studies of Bourbeau et al[16] and Monninkhof et al[29] found a lower mean distance walked in the intervention group compared with the control group, which seems to be the main contributor to the heterogeneity in this analysis.

The studies of Moullec et al[30] and Akinci et al[14] were excluded from the primary analysis because they were CCTs. Moullec et al[30] found a statistically significantly higher walking distance in the intervention group (510.6 ± 80.2) compared with the control group (436.3 ± 82.1) after one year of follow-up. Akinci et al[14] also found higher values in the intervention group (190.3 ± 65) than in the control group (170.6 ± 55.4). We performed a sensitivity analysis by including these two studies in the meta-analysis; the MD increased to 35.90 (95%CI 1.35 to 70.44) and became statistically significant, with comparable heterogeneity.

Activity level was measured using the Voorrips Questionnaire in the studies of Ninot et al[31] and Moullec et al[30]. Both groups in the study of Ninot et al[31] showed a significant increase in total Voorrips scores (meaning a higher activity level) after one year of follow-up, but participants in the intervention group had a significantly higher activity level compared with the control group (absolute values not reported). Ninot et al[31] also measured physical activity using a daily diary, but these data were not analysed because of non-compliance. Moullec et al[30] found a statistically significant improvement in total Voorrips score from low to moderate activity levels in the intervention group, whereas the score in the control group did not significantly change after six months of follow-up. Also, the intervention group was statistically significantly more active than the control group after 12 months of follow-up (12.0 ± 5.8 vs 5.1 ± 4.9). Faulkner et al[22] assessed physical activity using the seven-day

physical activity recall questionnaire and observed no statistically significant differences between intervention and control groups.

*Exercise capacity and physical activity - head-to-head studies*
Four studies without a usual care control group assessed exercise capacity using the 6MWT[39-42]. Nguyen et al[39] after six months of follow-up observed a decline in walking distance in the group that participated in a face-to-face dyspnoea self- management programme and an increase in walking distance among individuals who participated in an internet-based self-management programme. Nguyen et al[40] showed an increase in the self monitored intervention group and a decrease in the coached intervention group. This finding did not reach statistical significance. In the studies of Stulbarg et al[42] and Sassi-Dambron et al[41], no significant differences in changes in walking distance were reported between intervention groups after follow-up.

Effing et al[37] measured exercise capacity using the incremental shuttle walk test (ISWT) and the endurance shuttle walk test (ESWT). On the ISWT, they found a statistically significant between-group difference of 35.1 m in favour of the group participating in an exercise programme in addition to a self-management programme after 12 months of follow-up. The between-group difference of 145.8 m on the ESWT did not reach statistical or clinical significance. Stulbarg et al also assessed exercise capacity using both incremental and endurance walk tests, although these tests were performed on a treadmill. On both tests, the group that received exercise training in addition to dyspnoea self-management performed better than groups that received less exercise training, or no supervised exercise training at all. Nguyen et al[40] assessed exercise capacity using the incremental cycle ergometer test and found no significant differences between groups after six months of follow-up.

Effing et al[37] measured daily physical activity using pedometers. The mean between-group difference over 12 months of follow-up of 877 steps/d was statistically significant in favour of the group that participated in an exercise programme in addition to a self-management programme. Nguyen et al[40] assessed daily physical activity using a dual-axis accelerometer incorporated into an activity monitor. They found a decrease in the mean number of steps/d with the coached intervention and a lesser increase with the self monitored intervention.

*Mortality - studies with usual care*
Mortality was reported as an outcome measure in only two studies[17;33]. Therefore we extracted data on mortality mainly from sections describing the participant flow and reasons for loss to follow-up. Ten studies[14;18;21-23;25;27;28;31;35] reported zero deaths in the self-management and control groups; three studies provided no information on drop outs[19;24;32] and therefore could not be included in the meta-analysis. Eight studies[12;16;17;20;26;29;33;34] were included in a meta-analysis. No statistically significant differences in mortality were found between intervention and control groups, with an OR of 0.79 (95%CI 0.58 to 1.07) (Analysis 1.21).

Performing a sensitivity analysis with the CCT of Moullec et al[30], who reported zero deaths in the intervention group and one death in the control group, resulted in no change in the OR (Analysis 2.11).

*Subgroup analyses*
We planned to perform subgroup analyses on the duration of follow-up (less than 12 months vs 12 months or longer) and the contents of the intervention. Contents of particular interest were the use of an action plan, the use of a standardised exercise programme and the use of behavioural components. Subgroup analyses were considered possible when at least three studies could be included in each subgroup. Subgroup analyses were performed on our primary outcome measures HRQoL as measured with the SGRQ and respiratory-related hospital admissions.

Because of the relatively small number of studies with follow-up longer than 12 months, no subgroup analysis for duration of follow-up that met the criterion of at least three studies in a subgroup could be performed.

Action plans were used in most of the studies (17 of 23). HRQoL and respiratory-related hospital admissions were considered to be relevant outcome measures in subgroup analyses on the use of an action plan. However, because of the general use of action plans in the studies included in these meta-analyses, it was not possible to create subgroups of at least three studies that did not use an action plan in their intervention; therefore, subgroup analyses on studies with versus without an action plan could not be performed.

Subgroup analyses on the use of exercise programmes were performed on the outcomes of HRQoL and respiratory-related hospital admissions. In this specific subgroup analysis it would also be relevant to analyse exercise capacity as measured by the 6MWT, this was however not possible because the study of Wakabayashi et al[35] was the only study in that meta-analysis that did not include a standardised exercise programme. The subgroup difference in HRQoL between studies with and without exercise programmes was substantial but was not statistically significant. The MD of SGRQ total scores for studies with an exercise programme was -2.13 (95%CI -5.52 to 1.25), and the MD for studies without an exercise programme was -4.10 (95%CI -6.33 to -1.88) (Analysis 3.5). Subgroup differences in respiratory-related hospital admissions between studies with and without exercise programmes were not statistically significant. The OR for having at least one respiratory-related hospital admission was 0.75 (95%CI 0.37 to 1.53) for studies with an exercise programme and 0.54 (95%CI 0.41 to 0.71) for studies without an exercise programme (Analysis 3.6).

Studies with and without behavioural components showed no statistically significant subgroup differences in respiratory-related hospital admissions and HRQoL. The MD of SGRQ total score for studies with behavioural components was -3.61 (95%CI -7.65 to 0.44), and the MD of studies without behavioural components was -3.88 (95%CI -6.31 to -1.46)

(Analysis 3.9). The OR for respiratory-related hospital admissions in studies with behavioural components was 0.47 (95%CI 0.30 to 0.74), and the OR in studies without behavioural components was 0.65 (95%CI 0.48 to 0.89), both in favour of the intervention group (Analysis 3.10).

## DISCUSSION

### Summary of main results

This review is an update of a review published in 2007[45]. We have systematically evaluated 23 studies with a usual care control group and six studies comparing different components of self-management head-to-head. A statistically significant effect of self-management on quality of life as measured by the SGRQ was found, with the score on the impact domain reaching the MCID of four points. Also, individuals who participated in a self-management intervention were at lower risk for both one or more respiratory-related and all-cause hospitalisations, compared with individuals who received usual care. No effects of self-management on lung function were found, but dyspnoea as measured by the (m)MRC was significantly reduced in participants assigned to self-management. The mean difference between intervention and control groups in the distance walked on the 6MWT was not statistically significant.

Physiological and functional impairments in patients with COPD often go together with a reduced health-related quality of life[5;46]. In the included studies, health-related quality of life was the most frequently assessed outcome measure, with the SGRQ the most frequently used questionnaire. In the previous update of the review, total and impact scores on the SGRQ were statistically significant lower (meaning better HRQoL) in the intervention group than in the control group. In the current update, the positive effect of self-management on HRQoL of participants with COPD was even more distinct, with total and domain scores all significantly lower in the intervention group than in the control group. Only the score on the impact domain, which covers social, emotional and psychological impact of the disease, reached the MCID of four points and therefore can be considered as clinically relevant [47]. Whereas the MD of the SGRQ total score did not reach the MCID, we need to consider this more carefully. First, in the subgroup analysis, we found a clinically relevant MD of -4.10 (95%CI -6.33 to -1.88) in the interventions without an exercise programme. Second, in another Cochrane review on the use of tiotropium versus placebo, an MD of -2.89 (95%CI -3.35 to -2.44) in the SGRQ total score was found[48]. Secondary analysis revealed that statistically significantly more participants receiving tiotropium experienced a clinically relevant improvement of four points in SGRQ total score than participants given placebo. Based on this analysis, the study authors considered the effects of tiotropium on SGRQ total score to be clinically relevant. The mean effect on SGRQ total score in our meta-analysis was substantially greater than that in the review on tiotropium. We were not able to perform the same secondary analysis, but based on the reasoning above, we expect that significantly more individuals participating in self- management experienced clinically relevant improvement compared with participants receiving usual care.

The number of hospitalisations was analysed using the number of participants with at least one hospital admission. The odds ratio for having one or more respiratory-related hospital admissions favoured the intervention group. It is debatable whether this is clinically relevant

because there is no such thing as an MCID for hospitalisations. However, the OR of 0.57 indicates that individuals with COPD who participate in self-management are at substantially lower risk for one or more respiratory-related hospitalisations, meaning a reduction in the risk for a worse health outcome[49] and a reduction in costs[3]. It was expected that self- management interventions for participants with COPD would principally lead to a reduction in respiratory-related hospitalisations because the programmes focus on COPD-related self-management skills that aim to stimulate proper patient behaviours and actions, thereby preventing severe exacerbations and hospitalisations. However, our review data show that self-management interventions do also lead to a reduction in the odds ratio for having at least one all-cause hospital admission. This was less expected since all programmes were COPD-specific and not directed towards co-morbidities. Co-morbidities are more the rule than the exception in patients with COPD, with more than 90% of patients with COPD suffering from at least one co-morbidity (e.g. cardiovascular disease, diabetes, mental health issues)[50;51]. Co-morbidities in patients with COPD are associated with increased risk for any hospitalisation[52]. Future COPD self- management interventions should probably be more directed towards the individual patient's co-morbidities to further increase the benefit on all-cause hospitalisations among patients. The latter would most likely also further increase the safety of COPD self-management interventions. More generally, self- management should be tailored to the individual needs of each patient.

Exacerbations of COPD are negatively associated with disease progression and health-related quality of life and are positively associated with mortality[53-56]. Only three of the included studies assessed the effect of self-management on exacerbations[16;29;34]. Two of these three studies[29;34] reported a higher number of exacerbations in the intervention group than in the control group. Although this might seem remarkable, a plausible explanation can be found in the underreporting of COPD exacerbations in general. Earlier studies showed that approximately 50% to 70% of exacerbations of COPD are not reported to a physician[55;57-59]. Most self-management interventions include approaches to improve recognition of symptoms of a worsening of COPD. This might have led to improved recognition and improved reporting of exacerbations in the intervention group compared with the control group. Seventy-five percent of the studies in this review incorporated the use of an action plan into their self-management intervention. The primary goal of an action plan is to teach patients to recognise an exacerbation at an early stage and to act promptly to the worsening of symptoms. Because an action plan is used after the start of an exacerbation, it is not intended to prevent exacerbations. However, it could lead to less-severe exacerbations, which in turn lead to a reduced number of hospitalisations. The decrease in respiratory-related hospitalisations found in this review might be a reflection of this. Another point of attention is the diversity of definitions of 'exacerbation' used in clinical trials. Roughly, the definitions used can be classified as symptom-based or event-based[60;61]. This is reflected in the three studies discussed above, all of which used different definitions. No consensus has been reached on which definition is most accurate, but the chosen definition can seriously influence outcomes and even the statistical significance of effect sizes[44;61]. Outcome measures such as courses of oral steroids and/or antibiotics or

the use of rescue medication can serve as proxy variables for exacerbations of COPD because these variables indicate worsening of COPD. Two of the three studies[12;23;33] in the meta-analysis on this outcome reported that more participants had at least one course of oral corticosteroids in the intervention group than in the control group, with similar reversed causation, as discussed above.

In this update, we found an MD in distance walked on the 6MWT of 33.7 m. Although this difference exceeds the recently reported MCID of 25 m of Holland et al[62], it is not statistically significant. Because all but one study in this meta-analysis included some sort of standardised physical exercise programme, it is likely that these exercise programmes account for most of the improvement in walking distance. Heterogeneity in this analysis was high ($I^2$ = 86%). Major contributors to this high level of heterogeneity seem to be the studies of Moninnkhof et al[29] and Bourbeau et al[16], both of which show lower values in the intervention group compared with the control group. This contrasts with the findings of other studies included in this meta-analysis. Monninkhof and colleagues concluded at the end of their study that the frequency and intensity of the incorporated exercise intervention were too low to permit an increase in exercise capacity[29]. In the study of Bourbeau et al, the exercise programme was home-based, unsupervised and voluntary; this may have led to an intensity of the programme that was not sufficient to achieve an increase in exercise capacity[16].

As expected, no effect of self-management on lung function was found. A statistically significant effect on shortness of breath was found with the (m)MRC, but whether this difference is clinically relevant is not clear because studies on this topic are lacking. A reasonable explanation for the reduction in breathlessness score might be that patients learn strategies to cope with breathlessness during self-management education[63]. As a result, the anxiety that patients might have for becoming short of breath during activities of daily life is reduced; therefore patients may experience less dyspnoea during activities.

Subgroup analyses on the use of exercise programmes, the use of action plans and the use of behavioural components were performed to gain greater insight into the "black box" of self-management. Unfortunately, because most studies included an action plan for exacerbations, we were not able to create a subgroup of sufficient size to permit meta-analyses on the use of an action plan. Subgroup analyses on the use of an exercise programme revealed no statistically significant differences between studies with and without exercise programmes in HRQoL and respiratory-related hospital admissions. This indicates that improved HRQoL and reduced respiratory-related hospital admissions can thus be achieved solely with self-management training, and that a standardised exercise programme is not essential in this aspect.

In addition to the subgroup analyses, and in contrast to previous versions of the review, we did include studies comparing different components of self- management head-to-head. This gave us an extra opportunity to gain a better understanding of the effectiveness of the

separate self-management components. One study compared two methods of delivery of self-management to the participant, and the other studies assessed which combination of components was most effective. Unfortunately, whereas between-group differences were found, studies were too unique to allow general conclusions or recommendations on effective components.

The additional value of behavioural components, defined as cognitive-behavioural therapy, motivational interviewing, goal-setting and providing feedback to the participant, was difficult to determine because of lack of detailed information. We have created subgroups regarding the use of behavioural components based on global information received from authors about the use of these behavioural components. Whereas the literature provides a theoretical background for incorporating behavioural components into self-management interventions[8;10], we found no differences in HRQoL and respiratory-related hospital admissions between studies with and without behavioural components. This is probably a result of our definition of 'behavioural components', lack of information regarding these components and the limited number of studies in the subgroup analyses. Future studies should provide detailed information regarding the behavioural techniques. For example, this can be done by using an established taxonomy for behavioural change techniques[64].

Nowadays, studies focus predominantly on ultimate outcomes such as health status and physiological functioning. Intermediate outcomes linked to behaviour change, such as self-efficacy[8;10], are only incidentally measured. In this review, only one of 24 studies without a usual care control group reported the results of a questionnaire that assesses self-efficacy. The limited availability of valid and patient-friendly instruments to measure self-efficacy might explain in part the minimal use of these instruments[65]. Furthermore, in research on self-management, it is recommended that one select outcome measures that are in line with the goals and contents of the intervention. For example, effects on anxiety and depression most likely can be expected only when parts of the self-management intervention are targeted towards anxiety and/or depression.

When the effectiveness of self-management interventions is considered, it is appropriate to take into account adherence of patients to the intervention. Adherence was discussed in eight studies and was reported as the percentage of participants attending or not attending a certain percentage of sessions, or as the percentage of sessions attended by participants. In one study, participants were excluded from the analysis when they did not meet a prespecified attendance rate, with the consequence that a per-protocol analysis was performed. An intention-to-treat analysis including all randomly assigned participants is preferred because it will give a more realistic view of the intervention effect in real life, where there will always be poorly adhering patients. However, information about patient attendance should always be reported, so that some idea about the dose-response relationship can be obtained. Sohanpal et al studied reasons for low attendance in a self-management intervention for participants with COPD[66]. The main reasons for low attendance were that participants considered themselves not ill enough, or, conversely,

participants were too physically or psychologically disabled, or they had competing obligations. According to the tutors, low adherence was also caused by participants blaming others for their condition, having fear of making a change in their lives or lacking support from family or friends. Close to the concept of adherence is patient engagement to the programme (i.e. active involvement in tasks and processes); this is another requirement for achieving behavioural change in self-management[67].

### Overall completeness and applicability of evidence

Our searches were current up until August 2011. Since then, several new studies on the effectiveness of self-management have been published. The studies of Bucknall et al[68], Fan et al[69] and Bischoff et al[70] would have undoubtedly fitted our inclusion criteria; all had a reasonable follow-up of at least one year and were sufficiently powered to detect differences. The primary outcomes of two of these studies were related to hospital admissions for COPD , and one study primarily focused on HRQoL[69]. In the latter study, HRQoL was measured with the CRQ, and no differences were found between self-management and usual care group[69]. Bucknall et al[67] found no differences between self-management and control group in COPD-related hospital admissions and deaths. However, only 42% of participants in the intervention group could be classified as successful self- managers, which might clarify the lack of difference[67]. It is disturbing to note that the study of Fan et al[68] was stopped prematurely because of a higher number of deaths in the intervention group compared with the control group that could not be explained satisfactorily by the study authors. When we add the mortality data of Fan et al exploratively to our meta-analysis on mortality, the OR becomes 0.98 (95%CI 0.62 to1.54). This indicates that the results of Fan et al influence the effect size, but little meaningful difference in mortality is evident between self- management and control groups. However, these results need to be interpreted with caution because the analyses were just exploratory. Differences in study design and characteristics of included participants were not taken into account in these analyses; an analysis of individual participant data could contribute to the knowledge of factors influencing proper self-management. The additional results of these recently published studies do not automatically fit with the results reported in this review; therefore future updates should demonstrate how this recently gained knowledge influences the results of current meta-analyses.

### Potential biases in the review process

As we did in previous versions of this review, we included CCTs in this update. After due deliberation, we decided to exclude these CCTs from the primary meta-analyses because our data confirm the fact that their inclusion in meta-analyses led to a substantial increase in heterogeneity and therefore decreased the quality level of evidence. The main explanation for this can be found in differences in study design between CCTs and RCTs.

The non-randomised character of CCTs makes them more prone to biases such as selection bias, which, in turn, may lead to biased effect sizes. For this reason, we have chosen to include CCTs only in secondary sensitivity analyses. Although the exclusion of CCTs from the primary analysis led to reduced effect sizes in, for example, health-related quality of life as measured with the SGRQ, heterogeneity is also reduced, and we believe that this has contributed to the robustness of the results of this review. These observations on our data show that one should be very cautious about including CCTs in meta-analyses; for this reason, we will include only RCTs in future updates of this review.

In line with recent ideas regarding self-management training[6;7], we have made changes to the definition of self-management training before updating this review. The main objective of this change was to capture studies that do not focus purely on education but also have the potential to initiate behavioural change. Because the protocols of these interventions and the reasoning behind them are in general only globally described in the articles, we have chosen to exclude studies with only one contact moment between participants and healthcare providers (having only one contact moment makes it impossible to set goals and provide feedback, let alone change behaviour). For the same reason, we have chosen a priori to exclude studies published before 1995. We believe that evolving ideas about the goals and contents of self-management interventions over the years have resulted in substantially different interventions that are focused on more than just education. Moreover, healthcare in general has clearly changed over the past 25 years, leading to usual care groups and patient populations that are not comparable. Knowing this, we think that it would not be appropriate to pool the results of a study conducted in 1987 with results of a study conducted 24 years later, in 2011.

Although we have tried in this update to define more clearly criteria for self- management interventions, the included interventions are still diverse, both in name and in content. The simplest interventions that we have included in this review consisted of an educational session plus reinforcement by telephone or during routine outpatient visits. The most complex interventions consisted of several educational sessions combined with an exercise programme plus an optimisation of care plan. Furthermore, a large variety of topics were discussed during educational sessions. With this heterogeneity in interventions, it is difficult to determine the most effective parts of them. As Wagg[70] clearly presented in a diagram, disease management in patients with COPD requires a continuum of care in which self-management is part of both pulmonary rehabilitation and integrated disease management. Because it is a continuum of care, no clear borders can be seen between the disciplines, and some overlap is inevitable. Nevertheless, we decided to exclude hospital- and rehabilitation centre–based rehabilitation programmes because self-management often is only a minor part of these very intensive programmes. This will make it difficult or even impossible to filter the effects of self-management from other effects. We did, however, choose to include studies on home-based pulmonary rehabilitation that did not focus solely on exercise. In these programmes, training often is not supervised and action planning is

frequently included. Therefore, in our opinion, these programmes resemble self-management.

Topics that were discussed in the previous update are still relevant in this version of the review. The included studies used a broad spectrum of outcome measures. Meta-analyses often could not be performed because included studies used different methods to assess the outcome measure (e.g. different questionnaires) or calculated the same outcome in different ways (e.g. mean number of visits vs percentage of participants with ED visits). Lack of availability of data, even after contact was made with the study authors, hampered statistical combinations of data. The latter may have biased the effect estimates in the review. Furthermore, variation in follow-up was seen, the COPD population differed across studies and, as already stated, considerable variation was evident in the interventions provided. In future studies, it will be important to ensure greater homogeneity to allow comparisons with other studies and to permit the possibility of stronger recommendations.

## AUTHORS' CONCLUSIONS

### Implications for practice

Self-management interventions in patients with COPD are associated with improvement in health-related quality of life as measured by the SGRQ, reduction in both respiratory-related and all-cause hospital admissions and improvement in dyspnoea as measured by the (m)MRC. No statistically significant differences were found in other outcome parameters. Action plans were part of most of the studies included in the meta-analysis, and so are already considered to be an essential component of self-management. However, because of the low number of studies without an action plan, subgroup analyses could not be performed to confirm this. Also, the data indicate that self-management without exercise and self-management with exercise are equally effective in improving HRQoL. However, because of heterogeneity among interventions, study populations, follow-up times and outcome measures, and consequent limited possibilities to perform subgroup analyses, data remain insufficient to permit clear recommendations about the optimal form and content of self-management training for COPD.

### Implications for research

Future studies should focus on the following.

- Consensus on an operational definition for 'self-management'.
- Self-management training with the goal of acquisition of self-management skills and behavioural change.
- Comparison of self-management interventions and their different components to contribute to the definition of effective components in self- management interventions (e.g. programmes with and without self treatment of exacerbations, programmes with and without exercise).
- Homogeneity in outcome measures, with greater attention on standardised behavioural outcome measures.
- Integration of the handling of co-morbidities in self-management training for patients with COPD.
- Assessment of outcomes over the long-term (> 12 months).

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## CHARACTERISTICS OF STUDIES

### Characteristics of included studies

*Akinci 2011*

| | |
|---|---|
| **Methods** | **Design:** CCT **Follow-up:** three months **Control group:** usual care |
| **Participants** | **Recruitment:** university hospital (outpatient clinic)<br>**Eligible:** 68<br>**Randomly assigned:** 52<br>**Completed:** 32<br>**Mean age:** I: 71.8 (7.8) years; C: 65.1 (10.2) years<br>**Sex (% male):** not reported<br>**COPD:** clinically stable COPD stage three or four according to GOLD<br>**Major inclusion criteria:** clinically stable condition with no history of infection or exacerbation of respiratory symptoms and with no observable change in medication during the two months preceding the study<br>**Major exclusion criteria:** myocardial infarction within the preceding four months; unstable angina; severe congestive heart disease; severe hypertension; DM with complications; muscle and joint problems; cancer and asthma |
| **Interventions** | **Mode:** home-based, individual, face-to-face, educational booklet<br>**Professional:** nurse specialising in pulmonary rehabilitation<br>**Topics:** education regarding the disease, methods for smoking cessation, use of medication, coping with breathlessness, advice about exercise and activities<br>**Duration:** participant education: two to three sessions of two to three hours, four phone calls; exercise: daily, 30 to 60 minutes<br>**Action plan:** no<br>**Exercise programme:** yes<br>**Behavioural components:** providing feedback to the participant |
| **Outcomes** | 1. SGRQ<br>2. Baseline Dyspnoea CIndex<br>3. FEV1% of predicted<br>4. $FEV_1$/FVC<br>5. 6MWT |
| **Notes** | **Sources of funding:** not reported |

*Risk of bias table*

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | High risk | "These patients were divided into a rehabilitation group (n=27) and a control group (n=25)." page 160<br>Comment: The study is a CCT, so no random sequence was generated |
| Allocation concealment (selection bias) | High risk | "These patients were divided into a rehabilitation group (n=27) and a control group (n=25)." page 160<br>Comment: The study is a CCT, so no allocation concealment was provided |
| Blinding of | Unclear risk | Comment: Blinding of participants and personnel was |

| | | |
|---|---|---|
| participants and personnel (performance bias) | | not reported; the risk of bias of this is unclear |
| Blinding of outcome assessment (detection bias) | Unclear risk | Comment: Blinding of outcome assessment was not reported; the risk of bias of this is unclear |
| Incomplete outcome data (attrition bias) | High risk | "In the pulmonary rehabilitation group, five patents did not perform the assigned exercise, five patients had acute exacerbations of COPD, and one patient died. In the control group, five patients did not attend the second evaluation and four patients had exacerbation. Thus the study was conducted with 16 rehabilitation patients and 16 control patients." page 160<br>Comment: The number of drop outs was comparable in both groups but quite high (> 30%). Not clear why five participants did not perform the exercises and why five participants did not attend the second meeting. A per-protocol analysis was performed |
| Selective reporting (reporting bias) | Unclear risk | Comment: no signs of selective reporting; however, no protocol available |
| Other bias | Low risk | |

*Bourbeau 2003*

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|---|---|
| **Methods** | **Design:** RCT **Follow-up**: 12/24 months **Control group:** usual care |
| **Participants** | **Recruitment:** hospital (outpatients)<br>**Eligible:** 469<br>**Randomly assigned:** 191<br>**Completed:** 175<br>**Mean age:** I: 69.4 (6.5) years; C: 69.6 (7.4) years<br>**Sex (% male):** I: 52%; C: 59%<br>**COPD:** stable COPD with at least one hospitalisation for an exacerbation in preceding year<br>**Major inclusion criteria:** age >= 50 years; >= 10 pack-years; FEV1% (post): 25% to 70%; $FEV_1/VC < 70$<br>**Major exclusion criteria:** no previous diagnosis of asthma or left congestive heart failure, terminal disease, dementia, uncontrolled psychiatric disease, no pulmonary rehab < one year ago, no long-term facility stays |
| **Interventions** | **Mode:** individual sessions by an experienced health professional at the participant's home<br>**Professional:** nurse, respiratory therapist or respiratory physiotherapist<br>**Topics:** COPD knowledge, breathing and coughing techniques, energy conservation during day-by-day activities, relaxation exercises, preventing and controlling symptoms through inhalation techniques, understanding and using plan of action for acute exacerbations, adopting a healthy lifestyle, leisure activities and travelling, a simple home exercise programme, long-term oxygen therapy when appropriate<br>**Duration:** seven to eight weeks * one hour; first two months weekly telephone calls, from then, once-a-month telephone call. Exercise evaluation (not mandatory) and exercise teaching three times a week for 30 to 45 minutes<br>**Action plan:** yes<br>**Exercise programme:** yes (not mandatory)<br>**Behavioural components:** goal setting, motivational interviewing, providing feedback |
| **Outcomes** | 1. SGRQ<br>2. Exacerbations<br>3. Spirometry<br>4. $FEV_1$ (L)<br>5. Forced vital capacity<br>6. Hospital admissions<br>7. Symptoms<br>8. Emergency department visits<br>9. Outpatient visits<br>10. 6MWT |
| **Notes** | |

*Risk of bias table*

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | "...central computer-generated list of random numbers. Randomization was stratified per center and in blocks of 6, and patients were assigned to the self management |

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|---|---|---|
| | | program (intervention group) or to usual care." Bourbeau 2003, page 586<br>Comment: Random sequence generation was adequately performed |
| Allocation concealment (selection bias) | Low risk | "The blocking factor was not known by the investigators or their staff in each participating center." Bourbeau 2003, page 586<br>Comment: Allocation was adequately concealed |
| Blinding of participants and personnel (performance bias) | Unclear risk | "Since a double-blind design was impossible..." Bourbeau 2003, page 586<br>Comment: Participants and personnel were not blinded |
| Blinding of outcome assessment (detection bias) | Low risk | "...an independent evaluator unaware of the patient assignment was responsible for the evaluation process in each center. The evaluator was cautioned not to ask about the workbook modules and types of contact." Bourbeau 2003, page 586<br>Comment: Outcome assessment was blinded |
| Incomplete outcome data (attrition bias) | Low risk | "At the end of the 2nd yr of follow-up, data were available for 75 patients in the standard-care group (two subjects were lost to follow-up, nine patients died in the 1st yr and nine in the 2nd yr) and 83<br>patients following the self-management programme (five patients died in the 1st yr and eight in the 2nd yr)." Gadoury 2005, page 855<br>Comment: Drop out in the usual care group was somewhat higher than in the self management group; however, an intention-to-treat analysis was used |
| Selective reporting (reporting bias) | Unclear risk | Comment: no signs of selective reporting; however, no protocol available |
| Other bias | Low risk | |

*Bösch 2007*

| | |
|---|---|
| **Methods** | **Design:** RCT **Follow-up:** 12 months **Control group:** usual care |
| **Participants** | **Recruitment:** hospital (outpatient clinic)<br>**Eligible:** not reported<br>**Randomly assigned:** 50<br>**Completed:** 41<br>**Mean age:** I: 63.8 (8.4) years; C: 64.6 (6.8) years<br>**Sex (% male):** 63% of 41 participants who completed the study were male; the distribution in the groups is not reported<br>**COPD:** COPD with obstruction confirmed by spirometry and $FEV_1/FVC < 70\%$<br>**Major exclusion criteria:** co-morbidities that significantly influence symptoms, capacity or spirometry (symptomatic cardiopulmonary disease) |
| **Interventions** | **Mode:** group-based (six to eight participants), face-to-face, outpatient clinic<br>**Professional:** respiratory nurse under supervision of a respiratory specialist<br>**Topics:** education regarding the disease, smoking cessation, action plan with self treatment of exacerbations, advice about exercise, advice about nutrition, advice about medication, coping with breathlessness, travelling<br>**Duration:** four sessions of two hours<br>**Action plan:** yes<br>**Exercise programme:** no<br>**Behavioural components:** cognitive-behavioural therapy, motivational interviewing, goal setting, providing feedback to the participant |
| **Outcomes** | 1. mMRC<br>2. Courses of antibiotics<br>3. $FEV_1$ (L)<br>4. Hospital admissions<br>5. 6MWT |
| **Notes** | **Sources of funding:** not reported |

*Risk of bias table*

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Unclear risk | Comment: The method of random sequence generation was not clearly reported |
| Allocation concealment (selection bias) | Unclear risk | Information from the author: "Pick of envelope"<br>Comment: This information is too concise to assess risk of bias |
| Blinding of participants and personnel (performance bias) | Unclear risk | Comment: Blinding of participants and personnel was not reported |
| Blinding of outcome assessment (detection bias) | Unclear risk | Comment: Blinding of outcome assessment was not reported |
| Incomplete outcome data (attrition bias) | High risk | Comment: Eight participants in the intervention group and one participant in the control group dropped out. Reasons for drop out were not clearly reported, and only |

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|---|---|---|
| | | participants who completed follow-up were included in the analysis |
| Selective reporting (reporting bias) | Unclear risk | Comment: no signs of selective reporting; however, no protocol available |
| Other bias | Low risk | |

*Casas 2006*

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|---|---|
| **Methods** | **Design:** RCT **Follow-up:** 12 months **Control group:** usual care |
| **Participants** | **Recruitment:** hospital (inpatient clinic)<br>**Eligible:** 160<br>**Randomly assigned:** 155<br>**Completed:** 120<br>**Mean age:** I: 70 (9) years; C: 72 (9) years<br>**Sex (% male):** I: 77%; C: 88%<br>**COPD:** admitted because of an episode of exacerbation requiring hospitalisation > 48 hours<br>**Major exclusion criteria:** not living in the healthcare area or in a nursing home; severe co-morbid conditions; logistical limitations due to extremely poor social conditions |
| **Interventions** | **Mode:** group sessions and individual sessions, face-to-face, hospital-based and home-based<br>**Professional:** respiratory nurse<br>**Topics:** education regarding the disease, smoking cessation, action plan with self treatment of exacerbations, advice about exercise, advice about nutrition, advice about medication, coping with breathlessness, travelling, end-of-life decision making, interpretation of medical testing, irritant avoidance, anxiety and panic control<br>**Duration:** one group session of two hours, three individual sessions of 40 minutes, and one to 10 sessions of 20 minutes at home<br>**Action plan:** yes<br>**Exercise programme:** no<br>**Behavioural components:** cognitive-behavioural therapy, motivational interviewing, goal setting, providing feedback to the participant |
| **Outcomes** | 1. SGRQ<br>2. EQ-5D<br>3. MRC<br>4. $FEV_1$ (L)<br>5. $FEV_1$/FVC<br>6. Hospital admissions<br>7. Doctor and nurse visits<br>8. Courses of antibiotics |
| **Notes** | **Sources of funding:** The present study was supported by: the CHRONIC project (IST-1999/12158) from the European Union; Marato de TV3; Comissionat per a Universitats I Recerca de la Generalitat de Catalunya (SGR-00386); Red Respira Instituto de Salud Carlos III (ISCIII)-Redes Tematicas de Investigacion Cooperativa (RTIC)-03/11; and Red Telemedicina ISCIII-RTIC-03/117. A. Casas and T. Troosters were research fellows supported by CHRONIC (IST-1999/12158). T. Troosters is currently a postdoctoral research fellow of the Fonds voor Wetenschappelijk Onderzoek (Vlaanderen, Belgium). J. Garcia-Aymerich was supported by Red Respira (RTIC C03/11) and ICS III |

*Risk of bias table*

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence | Low risk | "All 155 patients included in the study were blindly |

| | | |
|---|---|---|
| generation (selection bias) | | assigned (1:1 ratio) using computer generated random numbers to either IC or usual care (UC)". page 124<br>Comment: Random sequence generation was adequately performed |
| Allocation concealment (selection bias) | Low risk | "Adequacy of the assignment process to either IC or UC was ensured by both the generation of the allocation sequence by a random process and preventing foreknowledge of the treatment assignments in the specialised team that implemented the allocation sequence". page 128<br>Comment: Allocation was adequately concealed |
| Blinding of participants and personnel (performance bias) | Unclear risk | Comment: Blinding of participants and personnel was not reported |
| Blinding of outcome assessment (detection bias) | Unclear risk | "Early assessment of patients at study admission was identical for both groups. Assessment included a blind administration of a questionnaire, described in detail elsewhere."<br>Comment: Only part of the baseline assessment was blinded; the other assessments were not blinded, and it is not clear who performed the measurements |
| Incomplete outcome data (attrition bias) | Unclear risk | "A strength of the present analysis was that there were no subjects lost to follow-up, since all drop outs were due to appearance of exclusion criteria or death and, in any case, valid information about re-hospitalisations was available from the national health services." Casas 2006, page XX<br>"During follow-up, a priori defined exclusion criteria, such as lung cancer, appeared in 9 subjects. Twenty-one subjects died, and 16 were lost to follow-up. Only 57% of subjects finished the study at 12 months". .... "Since data about outcome variables was not available in the lost subjects (whether due to exclusion, loss to follow-up or death), an intention-to-treat principle was not possible". Garcia-Aymerich 2007, page 1464<br>Comment: Data on healthcare utilisation reported in Casas et al 2006 were presented for all included participants, leading to a low risk of bias. However, > 40% of the data on functional status and HRQoL reported in Garcia-Aymerich et al 2006 was missing, leading to a high risk of bias |
| Selective reporting (reporting bias) | Unclear risk | Comment: no signs of selective reporting; however, no protocol available |
| Other bias | Low risk | |

*Chavannes 2009*

| | |
|---|---|
| **Methods** | **Design:** CCT **Follow-up:** 12 months **Control group:** usual care |
| **Participants** | **Recruitment:** general practise<br>**Eligible:** not reported<br>**Randomly assigned:** 162<br>**Completed:** 152<br>**Mean age:** I: 64 (11) years; C: 63 (11) years<br>**Sex (% male):** I: 59%; C: 67%<br>**COPD:** existing diagnosis, with chronic respiratory complaints in the absence of prior history of asthma or atopy, and had to fulfil former national guideline lung function criteria with a postbronchodilator $FEV_1 < 80\%$ predicted and/or a postbronchodilator $FEV_1/FVC$ ratio $< 0.7$<br>**Major exclusion criteria:** rapidly progressing or terminal disease, immobility, substance abuse or inability to fill in questionnaires |
| **Interventions** | **Mode:** group sessions and individual sessions, face-to-face, telephone, general practise<br>**Professional:** specialised physiotherapist, respiratory nurse, physician assistant, dietician, respiratory specialist, general practitioner<br>**Topics:** education regarding the disease, smoking cessation, action plan with self treatment of exacerbations, exercise programme, advice about nutrition, advice about medication<br>**Duration:** 10 group sessions, eight individual sessions, duration unknown<br>**Action plan:** yes<br>**Exercise programme:** yes<br>**Behavioural components:** goal setting, providing feedback to the participant |
| **Outcomes** | 1. SGRQ<br>2. CCQ<br>3. MRC |
| **Notes** | **Souces of funding:** PICASSO for COPD, an initiative of Boehringer Ingelheim, Pfizer and Caphri Research Institute, Maastricht University<br>**Note:** 106 (70%) of the participants had an $FEV_1/FVC > 70\%$ |

*Risk of bias table*

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | High risk | "Two primary health care centres serving two separate villages in the southern part of the Netherlands were recruited for epidemiological reasons: both had very similar patient populations with comparable regional living conditions, but these were traditionally self-sufficient communities with little risk of intervention contamination." page 172<br>Comment: The study is a CCT, so no random sequence was generated |
| Allocation concealment (selection bias) | High risk | "Two primary health care centres serving two separate villages in the southern part of the Netherlands were recruited for epidemiological reasons: both had very similar patient |

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|---|---|---|
| | | populations with comparable regional living conditions, but these were traditionally self-sufficient communities with little risk of intervention contamination." page 172<br>Comment: The study is a CCT, so no allocation concealment was provided |
| Blinding of participants and personnel (performance bias) | Unclear risk | Comment: Blinding of participants and personnel was not reported |
| Blinding of outcome assessment (detection bias) | Unclear risk | Comment: Blinding of outcome assessment was not reported |
| Incomplete outcome data (attrition bias) | Unclear risk | "We recruited 162 primary care COPD patients, of whom 152 had analysable data." page 173<br>Comment: It is not clear in which group participants dropped out and for what reason |
| Selective reporting (reporting bias) | Unclear risk | Domains of the SGRQ and the CCQ were not reported; further no signs of selective reporting |
| Other bias | Low risk | |

*Chuang 2011*

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|---|---|
| **Methods** | **Design:** RCT **Follow-up:** 12 months **Control group:** usual care |
| **Participants** | **Recruitment:** health maintenance registration<br>**Eligible:** 424<br>**Randomly assigned:** 282<br>**Completed:** not reported<br>**Mean age:** I: males: 76.8 (1.3) years, females: 75.4 (1.1) years<br>C: males: 76.9 (1.2) years, females: 75.6 (1.15) years<br>**Sex (% male):** I: 35%; C: 35%<br>**COPD:** clinical diagnosis<br>**Major exclusion criteria:** The participant or the primary care physician (PCP) declined or opted out, was no longer an active participant in the HCP health maintenance organisation; enrolled in hospice or institutionalised in custodial nursing facilities; was unable to participate because of severe dementia or organic brain disorder; was on long-term haemodialysis because of end-stage renal disease; or was undergoing chemotherapy for active malignancies |
| **Interventions** | **Mode:** individual sessions, face-to-face, telephone, written educational material, outpatient clinic<br>**Professional:** registered nurse/case manager<br>**Topics:** education regarding the disease, smoking cessation, action plan with self treatment of exacerbations, exercise programme, advice about exercise, advice about nutrition, advice about medication, coping with breathlessness<br>**Duration:** at least 10 educational calls 10 to 15 minutes each, at least one face-to-face 45 minutes<br>**Action plan:** yes<br>**Exercise programme:** yes<br>**Behavioural components:** motivational interviewing, providing feedback to the participant |
| **Outcomes** | 1. Hospital admissions<br>2. Hospital days<br>3. General practitioner visits<br>4. Emergency department visits<br>5. Costs |
| **Notes** | **Souces of funding:** not reported |

*Risk of bias table*

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Unclear risk | "A risk stratification tool (developed at SCAN Health Plan) helped prioritize patients for inclusion in the program with prospective designation of matched intervention and control groups. Nurse case managers then telephonically contacted the patients on the list in a 1-to-1 alternating fashion, to enroll patients into the intervention group until the end of the 6-month enrolment period". page 134<br>Additional information from the authors: "Stratified randomisation, with one to one assignment of patient to control vs intervention, stratified based on age, sex, |

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| | | risk/cost modelling and whether patient belongs to a group vs IPA practice"<br>Comment: unclear how the random sequence was generated |
| Allocation concealment (selection bias) | Unclear risk | Information from the authors: "See above and Patient selected sequentially from list, with stratification above, by project manager without influence from physicians or case managers"<br>Comment: unclear whether allocation was really concealed |
| Blinding of participants and personnel (performance bias) | Unclear risk | Comment: Blinding of participants and personnel was not reported |
| Blinding of outcome assessment (detection bias) | Unclear risk | Comment: Blinding of outcome assessment was not reported, and it was not clear who performed the outcome assessment |
| Incomplete outcome data (attrition bias) | Unclear risk | Comment: No information was given regarding the completeness of outcome data |
| Selective reporting (reporting bias) | Unclear risk | Comment: no signs of selective reporting; however, no protocol available |
| Other bias | Low risk | |

*Coultas 2005*

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| **Methods** | **Design:** RCT **Follow-up:** six months **Intervention one:** nurse-assisted medical management (MM) **Intervention two:** nurse-assisted collaborative management (CM) **Control group:** usual care (UC) |
| **Participants** | **Recruitment:** primary care clinics<br>**Eligible:** 217<br>**Randomly assigned:** 217<br>**Completed:** 151<br>**Mean age:** MM: 68.3 (6.6) years; CM: 70.1 (7.0) years; UC 68.8 (10.4) years<br>**Sex (% male):** MM: 42.9%; CM: 32.7%; UC: 53.8%<br>**COPD:** COPD-related diagnosis code (International Classification of Diseases, Ninth Revision: codes 491, 492, 496); current or former smoker (at least 20 pack-years); at least one respiratory symptom (cough, shortness of breath, wheeze) during the past 12 months; FEV1% < 80%; $FEV_1$/VC < 70%<br>**Major exclusion criteria:** not reported |
| **Interventions** | **Mode:** MM: nurse-assisted medical management = enhance patient knowledge; CM: nurse-assisted collaborative management = goals of MM + facilitating the adoption of healthy behaviour including lifestyle and self management skills<br>**Professional:** nurse<br>**Topics:** MM: COPD, symptoms, optimal medical management, smoking cessation, action plan for worsening symptoms. Finally, a letter was written to the participant's GP, describing the participant's status and providing suggestions of modifying management consistent with GOLD guidelines<br>**Duration (mean):** MM: 124 minutes (seven sessions); CM: 207 minutes (eight sessions)<br>**Action plan:** yes<br>**Exercise programme:** no<br>**Behavioural components:** providing feedback to the participant |
| **Outcomes** | 1. Health status<br>2. SGRQ<br>3. SF-36<br>4. Perceived illness intrusiveness<br>5. Doctor visits<br>6. ER visits<br>7. Hospital admissions |
| **Notes** | **Sources of funding:** a grant from Robert Wood Johnson Foundation<br>**Note 1:** Baseline characteristics are given only for the group of participants who completed the six-month follow-up period<br>**Note 2:** Drop out percentages are high: MM: 32.0%; CM: 29.2%; UC: 30.1%<br>**Note 3:** Participants who dropped out of the study had more severe airflow obstruction, higher levels of distress and lower quality of life compared with participants who completed the study<br>**Note 4:** Content of the interventions is not described properly, whereas the training of the nurses providing the intervention was described in detail<br>**Note 5:** Outcome measures of self efficacy and social support and BSI-18 and CES-D scores were measured but not reported in the article |

| *Risk of bias table* | | |
|---|---|---|
| **Bias** | **Authors' judgement** | **Support for judgement** |
| Random sequence generation (selection bias) | Low risk | "Patients were randomly assigned (...) using a computer-generated random list". page 2018<br>Comment: Random sequence generation was adequately performed |
| Allocation concealment (selection bias) | Unclear risk | Comment: It is unclear how allocation concealment was guaranteed |
| Blinding of participants and personnel (performance bias) | Unclear risk | Comment: Blinding of participants and personnel was not reported |
| Blinding of outcome assessment (detection bias) | Low risk | "Health outcomes in the intervention groups were assessed at baseline and after the 6-month intervention by two different trained interviewers who were not involved in the interventions and were blinded to group assignments". page 2019<br>"To limit interviewer bias, each interviewer who obtained the baseline and 6-month outcome data was blinded to the patient's treatment group". page 2023<br>Comment: The interviewers who performed the assessments were not involved in the intervention and were blinded to participants' treatment groups |
| Incomplete outcome data (attrition bias) | High risk | "Of the 217 patients enrolled in the study, 151 (69.6%) completed the 6-month intervention and follow-up data collection. The reasons for the failure to complete the study were patient was unavailable for follow-up (26.7%) and death (3.7%) [Fig 1]. The frequency of patients being unavailable for follow-up was equally distributed among the three intervention<br>groups (Fig 1). Overall, the demographic characteristics of the patients who dropped out of the study were similar to those who completed the study (data not shown). However, patients who dropped out of the study had more severe airflow obstruction, higher levels of distress, and lower quality of life, as measured with the SGRQ, compared with the patients<br>who had completed the study (data not shown)". page 2020<br>Comment: Approximately the same number of participants dropped out from each group, but the total number of drop outs was high (> 30%). Participants who dropped out were more severely diseased than those who did not drop out |
| Selective reporting (reporting bias) | Unclear risk | Comment: no signs of selective reporting; however, no protocol available |
| Other bias | Low risk | |

*Effing 2009*

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| **Methods** | **Design:** RCT **Follow-up:** 12 months **Intervention one:** self management programme and self treatment of exacerbations **Intervention two:** self management programme |
| **Participants** | **Recruitment:** hospital<br>**Eligible:** 421<br>**Randomly assigned:** 159<br>**Completed:** 139<br>**Mean age:** I: 63.1 (7.9) years; C: 63.7 (8.0) years<br>**Sex (% male):** I: 57.1%; C: 61.1%<br>**COPD:** clinical diagnosis of COPD according to the GOLD criteria; postbronchodilator $FEV_1$ 25% to 80% of predicted<br>**Major inclusion criteria:** no exacerbation in the month before enrolment; >= three exacerbations, defined as respiratory problems that required a course of oral corticosteroids and/or antibiotics, or one hospitalisation for respiratory problems in the two years preceding study entry; (ex)smoker; age 40 to 75 years<br>**Major exclusion criteria:** other serious disease with a low survival rate; other diseases influencing bronchial symptoms and/or lung function (e.g. cardiac insufficiency, sarcoidosis); severe psychiatric illness; uncontrolled diabetes mellitus during COPD exacerbation in the past or hospitalisation for diabetes mellitus in the two years preceding the study; need for regular oxygen therapy (> 16 hours/d or $pO_2$ < 7.2 kPa); maintenance therapy with antibiotics; known $\alpha_1$-antitrypsin deficiency; disorders or progressive disease seriously influencing walking ability (e.g. amputation, paralysis, progressive muscle disease) |
| **Interventions** | **Mode:** group and individual sessions, face-to-face, telephone, booklet, outpatient clinic<br>**Professional:** respiratory nurse, respiratory physiotherapist<br>**Topics:** education regarding COPD, action plan, advice about exercise, advice about nutrition, advice about medication, coping with breathlessness<br>**Duration:** Four weekly group sessions of two hours and three recall telephone calls<br>**Action plan:** yes<br>**Exercise programme:** yes<br>**Behavioural components:** goal setting, providing feedback to the participant |
| **Outcomes** | 1. CRQ<br>2. CCQ<br>3. HADS<br>4. Exacerbations (frequency, days, symptom score)<br>5. Courses of oral steroids<br>6. Courses of antibiotics<br>7. FEV1% of predicted<br>8. $FEV_1$/FVC<br>9. Hospital admissions<br>10. Hospital days<br>11. ED visits<br>12. Outpatient visits<br>13. GP visits |
| **Notes** | **Sources of funding:** a grant from the Dutch Asthma Foundation |

| *Risk of bias table* | | |
|---|---|---|
| **Bias** | **Authors' judgement** | **Support for judgement** |
| Random sequence generation (selection bias) | Low risk | "Patients were randomised into two study groups, using a minimisation programme, minimising differences between groups in gender, current smoking, FEV1 predicted (<= or >50%), use of inhaled corticosteroid, and current participation in a regular physiotherapy programme". page 957<br>Comment: Random sequence generation was adequately performed |
| Allocation concealment (selection bias) | Low risk | "Patients were randomised into two study groups, using a minimisation programme, minimising differences between groups in gender, current smoking, FEV1 predicted (<= or >50%), use of inhaled corticosteroid, and current participation in a regular physiotherapy programme". page 957<br>Comment: Allocation was adequately concealed |
| Blinding of participants and personnel (performance bias) | Unclear risk | Comment: Participants and personnel were not blinded |
| Blinding of outcome assessment (detection bias) | Low risk | Comment: Outcome assessment was not blinded; however, measurements were performed by an assessor who was independent of the study |
| Incomplete outcome data (attrition bias) | Low risk | "Between inclusion and the baseline measurements, three patients dropped out in each group and insufficient diary data were delivered by 11 patients. The baseline characteristics of the remaining 142 patients are shown in table 2, and were similar in both groups with respect to all measured prognostic factors. The 11 dropouts did not differ from the remaining group in any factors except the Medical Research Council dyspnoea scale (mean (SD) 2.3 (1.1) vs 3.0 (1.1) in drop outs versus remaining patients; P=0.041). During the 1-year follow-up period, three patients in the self-treatment group dropped out, of whom one died of an intracerebral haemorrhage. Thus, 67 patients in the self-treatment group and 72 patients in the control group completed the 1-year follow-up"<br>Comment: The number of drop outs and insufficient data were somewhat greater in the intervention group than in the control group. Reasons for drop out were comparable in the two groups, and overall drop out is low |
| Selective reporting (reporting bias) | Unclear risk | Comment: no signs of selective reporting; however, no protocol available |
| Other bias | Low risk | |

*Effing 2011*

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|---|---|
| **Methods** | **Design:** RCT **Follow-up:** 12 months **Intervention one:** self management programme and community-based physiotherapeutic exercise programme<br>**Intervention two:** self management programme |
| **Participants** | **Recruitment:** hospital<br>**Eligible:** 421<br>**Randomly assigned:** 159<br>**Completed:** 142<br>**Mean age:** I: 62.9 (8.1) years; C: 63.9 (7.8) years<br>**Sex (% male):** I: 58.4%; C: 57.9%<br>**COPD:** clinical diagnosis of COPD according to GOLD criteria, postbronchodilator $FEV_1$ 25% to 80% of predicted<br>**Major inclusion criteria:** no exacerbation in the month before enrolment; >= three exacerbations, defined as respiratory problems that required a course of oral corticosteroids and/or antibiotics, or one hospitalisation for respiratory problems in the two years preceding study entry; (ex)smoker; age 40 to 75 years<br>**Major exclusion criteria:** other serious disease with a low survival rate; other diseases influencing bronchial symptoms and/or lung function (e.g. cardiac insufficiency, sarcoidosis); severe psychiatric illness; uncontrolled diabetes mellitus during COPD exacerbation in the past or hospitalisation for diabetes mellitus in the two years preceding the study; need for regular oxygen therapy (> 16 hours/d or $pO_2$ < 7.2 kPa); maintenance therapy with antibiotics; known $\alpha_1$-antitrypsin deficiency; disorders or progressive disease seriously influencing walking ability (e.g. amputation, paralysis, progressive muscle disease) |
| **Interventions** | **Mode:** group and individual sessions, face-to-face, telephone, booklet, outpatient clinic, private physiotherapy practice<br>**Professional:** respiratory nurse, (respiratory) physiotherapist<br>**Topics:** education regarding COPD, action plan, advice about exercise, advice about nutrition, advice about medication, coping with breathlessness<br>**Duration:** Four weekly group sessions of two hours and three recall telephone calls<br>Six months: three times/wk training sessions = 72 sessions<br>Five months: two times/wk training sessions = 40 sessions<br>During the whole period, one training session of a half hour was provided at home<br>**Action plan:** yes<br>**Exercise programme:** yes<br>**Behavioural components:** goal setting, providing feedback to the participant |
| **Outcomes** | 1. CRQ<br>2. CCQ<br>3. HADS<br>4. Exacerbations (frequency, days, symptom score)<br>5. Courses of oral steroids<br>6. Courses of antibiotics<br>7. FEV1% of predicted<br>8. $FEV_1$/FVC<br>9. Hospital admissions<br>10. Hospital days<br>11. ED visits |

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|---|---|
| | 12. Outpatient visits<br>13. GP visits |
| **Notes** | **Sources of funding:** a grant from the Dutch Asthma Foundation |
| *Risk of bias table* | |
| **Bias** | **Authors' judgement** | **Support for judgement** |
| Random sequence generation (selection bias) | Low risk | "Patients were randomised into two study groups, using a minimisation programme, minimising differences between groups in gender, current smoking, FEV1 predicted (<= or >50%), use of inhaled corticosteroid, and current participation in a regular physiotherapy programme". page 419<br>Comment: Random sequence generation was adequately performed |
| Allocation concealment (selection bias) | Low risk | "Patients were randomised into two study groups, using a minimisation programme, minimising differences between groups in gender, current smoking, FEV1 predicted (<= or >50%), use of inhaled corticosteroid, and current participation in a regular physiotherapy programme". page 419<br>Comment: Allocation was adequately concealed |
| Blinding of participants and personnel (performance bias) | Unclear risk | Comment: Participants and personnel were not blinded |
| Blinding of outcome assessment (detection bias) | Low risk | Comment: Outcome assessment was not blinded; however, the measurements were performed by an assessor who was independent of the study |
| Incomplete outcome data (attrition bias) | Low risk | "Between the inclusion and the baseline measurements three patients dropped out in each study group (Fig. 1).....During the year after the baseline measurements, three patients dropped out in the intervention group, as did eight patients in the control group (see Fig. 1).<br>The three patients who dropped out of the intervention group during the one-year follow-up all dropped out directly after the baseline measurements before the start of COPE-active". page 421<br>Comment: The number of drop outs was somewhat higher in the control group than in the intervention group. Reasons for drop out were comparable in the two groups, and overall drop out was low. An intention-to-treat analysis was performed |
| Selective reporting (reporting bias) | Unclear risk | Coment: no signs of selective reporting; however, no protocol available |
| Other bias | Low risk | |

*Emery 1998*

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|---|---|
| **Methods** | **Design:** RCT **Follow-up:** two months **Control group:** usual care |
| **Participants** | **Recruitment:** announcements, word of mouth, advertisements in weekly newspapers for older adults and physician referral<br>**Eligible:** 92<br>**Randomly assigned:** 50<br>**Completed:** 49<br>**Mean age:** I: 67.4 (5.9) years C: 67.4 (7.1) years<br>**Sex (% male):** I: 40% C: 48%<br>**COPD:** stable COPD; > 50 years; $FEV_1/VC < 70$; > six months of clinical symptoms of COPD<br>**Major exclusion criteria:** significant cardiac disease; other diseases affecting exercise tolerance or learning skills last three months; asthma without fixed obstruction |
| **Interventions** | **Mode:** group education<br>**Profession:** clinical psychologist<br>**Topics:** COPD knowledge, therapy, coping, interpreting pulmonary function tests, understanding arterial blood gases, stress management<br>**Duration:** 26 hours<br>**Action plan:** no<br>**Exercise programme:** no<br>**Behavioural components:** cognitive-behavioural therapy |
| **Outcomes** | 1. Health status<br>2. SIP<br>3. HRQoL-MHLC<br>4. Health knowledge test<br>5. FEV1%pred |
| **Notes** | **Sources of funding:** grants from the National Heart Lung and Blood Institute (HL45290) and the National Institute on Aging (AG00029)<br>**Note 1:** The third arm was disregarded because it was focused on pulmonary rehabilitation |

*Risk of bias table*

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | "Group assignments were taken from a random number schedule..." page 233<br>Comment: Random sequence generation was adequately performed |
| Allocation concealment (selection bias) | Low risk | "...printed on a piece of paper, and placed in a sealed envelope. Participants were not given the envelope containing their group assignment until after completing the baseline assessment, and technical staff conducting the assessments were not aware of group assignments"<br>Comment: Allocation was adequately concealed |
| Blinding of participants and personnel (performance bias) | Unclear risk | Comment: Blinding of participants and personnel was not reported |

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|---|---|---|
| Blinding of outcome assessment (detection bias) | Low risk | "...technical staff conducting the assessments were not aware of group assignments". page 233<br>Comment: Blinding of outcome assessment was performed |
| Incomplete outcome data (attrition bias) | Low risk | "..and 2 dropped out of the ESM condition because of transportation problems". page 235<br>Comment: Drop out was low, two participants dropped out in the intervention group and zero participants dropped out in the control group. A per-protocol analysis was performed |
| Selective reporting (reporting bias) | Unclear risk | Comment: no signs of selective reporting; however, no protocol available |
| Other bias | Low risk | |

*Faulkner 2010*

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|---|---|
| **Methods** | **Design:** RCT **Follow-up:** 10 weeks **Control group:** usual care |
| **Participants** | **Recruitment:** general practise<br>**Eligible:** 215<br>**Randomly assigned:** 20<br>**Completed:** 14<br>**Mean age:** I: 70.8 (10.5) years; C: 71.3 (4.5) years<br>**Sex (% male):** I: 90%; C: 70%<br>**COPD:** clinical diagnosis of COPD GOLD stage II; $FEV_1$ 50% to 80% expected postbronchodilator and $FEV_1/FVC \leq 70\%$<br>**Major exclusion criteria:** BMI $>$ 35 kg $\cdot$ $m^2$ or $<$ 18 kg $\cdot$ $m^2$; history of asthma; recent respiratory tract infection; oxygen desaturation ($SaO_2$) at rest $<$ 90%; prior participation in a PR programme; serious co-morbid condition that would interfere with regular exercise training |
| **Interventions** | **Mode:** group sessions, face-to-face, booklet, University exercise facility<br>**Professional:** exercise practitioner<br>**Topics:** education regarding the disease, exercise programme, advice about exercise, coping with breathlessness<br>**Duration:** eight sessions of 90 minutes<br>**Action plan:** no<br>**Exercise programme:** yes<br>**Behavioural components:** cognitive-behavioural therapy, goal setting, providing feedback to the participant |
| **Outcomes** | 1. CRQ<br>2. HADS<br>3. Self-efficacy questionnaire<br>4. MRC<br>5. $FEV_1$ (L and % of predicted)<br>6. $FEV_1/FVC$<br>7. ISWT<br>8. Seven-day physical activity recall questionnaire<br>9. Physical self perception profile |
| **Notes** | **Sources of funding:** £137,256 from the International Primary Care Respiratory Group |

*Risk of bias table*

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | "The randomisation sequence, stratified for smoking status, was computer generated by a statistician who was independent of the trial". page 126<br>Comment: Random sequence generation was adequately performed |
| Allocation concealment (selection bias) | Low risk | "Group allocation was kept concealed by means of sealed envelopes which were only opened in sequence by the trial researcher following baseline assessment". page 126<br>Comment: Allocation was adequately concealed |
| Blinding of | Unclear risk | "It was not possible to blind patients or GPs to group |

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|---|---|---|
| participants and personnel (performance bias) | | allocation". page 126<br>Comment: Blinding of participants and personnel was not performed |
| Blinding of outcome assessment (detection bias) | Unclear risk | "Given the nature of the intervention it was also difficult to blind researchers from group allocation". page 126<br>Comment: Outcome assessment was not blinded; it is unclear who performed the outcome assessment |
| Incomplete outcome data (attrition bias) | High risk | "Following participant withdrawals post-randomisation – adverse event (n=4); personal commitments (n=2) – 14 participants attended the post-intervention follow-up assessment". page 127<br>Comment: Dropout was high (30%); reasons not clear |
| Selective reporting (reporting bias) | High risk | Comment: Selective reporting is possible; the report has a different aim than the original study. Of the HADS, only the anxiety part is reported, and other domain scores of the questionnaire are not reported. On page 126, the investigators name the self efficacy questionnaire (SEE) as an outcome measure; however, this is not reported in the results section |
| Other bias | Low risk | |

*Gallefoss 1999*

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|---|---|
| **Methods** | **Design:** RCT **Follow-up:** 12 months **Control group:** usual care |
| **Participants** | **Recruitment:** hospital (outpatient clinic)<br>**Eligible:** 68<br>**Randomly assigned:** 62<br>**Completed:** 53<br>**Mean age:** I: 57 (nine) years C: 58 (10) years<br>**Sex (% male):** I: 48%; C: 52%<br>**COPD:** FEV1% >= 40% and < 80%<br>**Major exclusion criteria:** any serious disease |
| **Interventions** | **Mode:** group sessions and patient brochure<br>**Professional:**<br>**Topics:** COPD knowledge, medication, symptoms, action plan, exacerbations, inhalation technique, smoking cessation, relaxation, coping<br>**Duration:** max 6.5 hours<br>**Action plan:** yes<br>**Exercise programme:** no<br>**Behavioural components:** providing feedback |
| **Outcomes** | 1. SGRQ<br>2. Other HRQoL instruments<br>3. Hospital admissions<br>4. Days lost from work<br>5. GP-consultation<br>6. FEV1%pred |
| **Notes** | **Sources of funding:** Norwegian Medical Association's Fund for Quality Improvement |

*Risk of bias table*

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | "The patients signed a written consent and were then randomly assigned using random number tables supplied by an external statistician in sealed envelopes". Gallefoss 2002, page 425<br>Comment: Random sequence generation was adequately performed |
| Allocation concealment (selection bias) | Low risk | "The patients signed a written consent and were then randomly assigned using random number tables supplied by an external statistician in sealed envelopes". Gallefoss 2002, page 425<br>Comment: Allocation was adequately concealed |
| Blinding of participants and personnel (performance bias) | Unclear risk | Comment: Blinding of participants and personnel was not reported |
| Blinding of outcome assessment (detection bias) | Unclear risk | Comment: Blinding of outcome assessment was not reported; not clear who performed the measurements |

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|---|---|---|
| Incomplete outcome data (attrition bias) | Low risk | "In the control group four patients were withdrawn (lack of co-operation (n = 2), diagnosis of rectal cancer (n = 1) and emigration (n = 1)). Two of the withdrawn control group patients were hospitalised for exacerbations of their COPD. This left us with 27 patients (84%) for the 1-year follow-up. In the intervention group, four patients failed to complete the educational program (social problems (n = 1), unannounced emigration (n = 1), failure to meet at educational group sessions for unknown reasons (n = 1) and serious myocardial infarction (n = 1)). Another patient was withdrawn from the study during the follow-up due to lymphoma (n = 1). This left us with 26 patients (81%) for a 1-year follow-up. The patients who were withdrawn from the intervention group did not, to our knowledge, have any serious deterioration in their obstructive lung disease, and none were hospitalised"<br>Comment: The number of drop outs was relatively low, and reasons for drop out were comparable over groups |
| Selective reporting (reporting bias) | Low risk | Comment: no signs of selective outcome reporting; study extensively described in various articles |
| Other bias | Low risk | |

*Ghanem 2010*

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|---|---|
| **Methods** | **Design:** RCT **Follow-up:** two months **Control group:** usual care |
| **Participants** | **Recruitment:** hospital (inpatient clinic)<br>**Eligible:** not reported<br>**Randomly assigned:** 39<br>**Completed:** 39<br>**Mean age:** I: 56.96 (11.59) years; C: 56.43 (9.03) years<br>**Sex (% male):** not reported<br>**COPD:** moderate to severe COPD according to GOLD<br>**Major exclusion criteria:** unable to read or write, locomotor problems, cognitive impairment, ischaemic heart disease, aortic valve disease, cancer or lung disease other than COPD |
| **Interventions** | **Mode:** individual sessions, face-to-face, booklet, home-based<br>**Professional:** respiratory nurse, respiratory specialist<br>**Topics:** education regarding the disease, exercise programme, advice about nutrition, advice about medication<br>**Duration:** four individual sessions of one hour, every other day exercise for two months<br>**Action plan:** no<br>**Exercise programme:** yes<br>**Behavioural components:** goal setting |
| **Outcomes** | 1. CRQ<br>2. SF-36<br>3. $FEV_1$ (L and % of predicted)<br>4. $FEV_1$/FVC<br>5. 6MWT |
| **Notes** | **Sources of funding:** none |

*Risk of bias table*

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Unclear risk | Comment: The method of random sequence generation was not reported; neither was the decision for the different group sizes |
| Allocation concealment (selection bias) | Unclear risk | Comment: The method of allocation concealment was not reported |
| Blinding of participants and personnel (performance bias) | Unclear risk | "Owing to the nature of the intervention, it was not possible to blind patients or assessors". page 20<br>Comment: Participants and personnel were not blinded |
| Blinding of outcome assessment (detection bias) | High risk | "Owing to the nature of the intervention, it was not possible to blind patients or assessors.The assessors were either the investigator responsible for assignment or members of the pulmonary rehabilitation team including the pulmonary specialist and the specialized nurses who were involved in the delivery of the intervention". page 20<br>Comment: Outcome assessment was not blinded; |

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|---|---|---|
| | | outcome assessors were involved in the intervention |
| Incomplete outcome data (attrition bias) | Low risk | "We analyzed data on an intention to treat basis". page 20<br>Comment: No information on dropouts was reported, but an intention-to-treat analysis was performed |
| Selective reporting (reporting bias) | Unclear risk | Comment: no signs of selective reporting; however, no protocol available |
| Other bias | Low risk | |

*Hill 2010*

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|---|---|
| **Methods** | **Design:** RCT **Follow-up:** three months **Control group:** usual care |
| **Participants** | **Recruitment:** primary care setting<br>**Eligible:** 131<br>**Randomly assigned:** 110<br>**Completed:** 93<br>**Mean age:** I: 63.4 (9.6) years; C: 65.7 (9.9) years<br>**Sex (% male):** I: 44%; C: 46.5%<br>**COPD:** postbronchodilator ratio of forced expiratory volume in one second ($FEV_1$) to forced vital capacity (FVC) $< 0.7$ and $FEV_1 < 80\%$ predicted<br>**Major exclusion criteria:** unable to perform spirometry for a medical reason; unable to communicate in written or spoken English |
| **Interventions** | **Mode:** individual sessions, face-to-face, written teaching manual, primary care practise<br>**Professional:** certified COPD educator<br>**Topics:** education regarding the disease, (strategies for) smoking cessation, recognition of an exacerbation, advice about exercise, advice about medication<br>**Duration:** two individual sessions of one hour<br>**Action plan:** no<br>**Exercise programme:** no<br>**Behavioural components:** none reported |
| **Outcomes** | Bristol COPD Knowledge Questionnaire |
| **Notes** | **Sources of funding:** Government of Ontario, Ontario Lung Association |

*Risk of bias table*

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | "Individuals were randomised to the experimental and control groups using a computer-generated random number sequence. The randomisation sequence was stratified according to the Medical Research Council (MRC) dyspnoea scale". page 15<br>Comment: Random sequence generation was adequately performed |
| Allocation concealment (selection bias) | Unclear risk | Comment: The method used to conceal allocation was not reported |
| Blinding of participants and personnel (performance bias) | Unclear risk | "Physicians at the three recruitment sites were unaware as to the group allocation of their patients" page 15<br>Comment: Personnel were blinded, and blinding of participants was not reported |
| Blinding of outcome assessment (detection bias) | Unclear risk | Comment: Blinding of outcome assessment was not reported; the questionnaire was self administered |
| Incomplete outcome data (attrition bias) | Low risk | "Analyses were performed according to the intention-to-treat principle using data from all participants for whom baseline and follow-up administrations of the BCKQ were available, irrespective of the time between the administrations". ....."Of the 55 people allocated to the |

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| | | experimental group, 5 withdrew before completing the study and of the 45 allocated to the control group, 2 withdrew before completing the study. Reasons for withdrawal included: moved away from the area (n = 2), medical problems precluding further participation (n = 2), language barrier (n = 1), lack of interest (n = 1), and deceased (n = 1)"<br>Comment: Study drop out was somewhat higher in the intervention group than in the control group, but overall it was quite low; an intention-to-treat analysis was performed |
| Selective reporting (reporting bias) | Unclear risk | "Given that the study selectively recruited individuals in the primary care setting, many of whom had only been recently diagnosed with COPD and were unlikely to be using inhaled steroids, they excluded the BCKQ questions in the domain that pertained to knowledge about this medication" page 15<br>Comment: further, no signs of selective reporting |
| Other bias | Low risk | |

*Kara 2004*

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| **Methods** | **Design:** RCT **Follow-up:** two months **Control group:** educational advice |
| **Participants** | **Recruitment:** hospital (outpatient clinic)<br>**Eligible:** not reported<br>**Randomly assigned:** 60<br>**Completed:** 60<br>**Mean age:** I: 61.06 (11.33) years; C: 61.36 (11.06) years<br>**Sex (% male):** 78.3% in total group, distribution in groups was not reported<br>**COPD:** mild and moderate $FEV_1 < 85\%$, $FEV_1/FVC < 70\%$<br>**Major inclusion criteria:** at least two weeks after recovery from acute exacerbation of COPD; no evidence of ischaemic heart disease, musculoskeletal disorders or other disabling disease that could restrict the exercise; 45 or more years of age; literate, volunteer and coherent<br>**Major exclusion criteria:** none reported |
| **Interventions** | **Mode:** group and individual sessions, face-to-face, written teaching manual, hospital (outpatient clinic)<br>**Professional:** clinic nurse, respiratory physiotherapist<br>**Topics:** education regarding the disease, smoking cessation, exercise programme, advice about exercise, advice about nutrition, advice about medication, coping with breathlessness<br>**Duration:** 60 to 70 minutes, later 35 to 40 minutes three or four times per week in small groups<br>**Action plan:** no<br>**Exercise programme:** yes<br>**Behavioural components:** none reported |
| **Outcomes** | COPD self efficacy scale |
| **Notes** | **Sources of funding:** not reported |

*Risk of bias table*

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Unclear risk | "The patients were randomly assigned to the experimental and control group in order of referral up to 60 patients". page 116<br>Comment: The method of random sequence generation was not reported |
| Allocation concealment (selection bias) | Unclear risk | "The patients were randomly assigned to the experimental and control group in order of referral up to 60 patients". page 116<br>Comment: The method of allocation concealment was not reported |
| Blinding of participants and personnel (performance bias) | Unclear risk | Comment: Blinding of participants and personnel was not reported |
| Blinding of outcome assessment (detection bias) | Unclear risk | Comment: Blinding of outcome assessment was not reported. Questionnaires were self administered |

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| Incomplete outcome data (attrition bias) | Unclear risk | Comment: No information on drop outs was reported |
| Selective reporting (reporting bias) | Unclear risk | Comment: no signs of selective reporting, although only one outcome measure was reported |
| Other bias | Low risk | |

*Khdour 2009*

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| **Methods** | **Design:** RCT **Follow-up:** 12 months **Control group:** usual care |
| **Participants** | **Recruitment:** hospital (outpatient clinic)<br>**Eligible:** not reported<br>**Randomly assigned:** 173<br>**Completed:** 143<br>**Mean age:** I: 65.6 (10.1) years; C: 67.3 (9.2) years<br>**Sex (% male):** I: 43.7%; C: 44.2%<br>**COPD:** confirmed diagnosis of COPD (by the hospital consultant) for at least one year, having $FEV_1$ 30% to 80% of predicted and > 45 years old<br>**Major exclusion criteria:** congestive heart failure; moderate to severe learning difficulties (as judged by hospital consultant); attended a pulmonary rehabilitation programme in the last six months; severe mobility problems or terminal illness |
| **Interventions** | **Mode:** individual sessions, face-to-face, telephone, hospital (outpatient clinic)<br>**Professional:** clinical pharmacist<br>**Topics:** education regarding the disease, smoking cessation, action plan with self treatment of exacerbations, advice about exercise, advice about nutrition, advice about medication, coping with breathlessness<br>**Duration:** one session of one hour, reinforcement at each outpatient visit every six months, two telephone calls at three and nine months<br>**Action plan:** yes<br>**Exercise programme:** no<br>**Behavioural components:** motivational interviewing, feedback to the participant |
| **Outcomes** | 1. SGRQ<br>2. $FEV_1$<br>3. Hospital admissions for acute exacerbations<br>4. ED visits for acute exacerbations<br>5. GP visits, scheduled and unscheduled<br>6. COPD knowledge questionnaire<br>7. Adherence to prescribed medication |
| **Notes** | **Sources of funding:** Chest Heart and Stroke (N. Ireland) |

*Risk of bias table*

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | "Recruited patients were randomly assigned to one of two groups: the intervention group and the usual care (control group). Both groups were matched as closely as possible for the following parameters: severity of COPD (measured by FEV1), age, gender and other concomitant illness. The randomisation was carried out using the minimization method described by Gore". page 589<br>Comment: Random sequence generation was performed adequately |
| Allocation concealment (selection bias) | Low risk | "Recruited patients were randomly assigned to one of two groups: the intervention group and the usual care (control group). Both groups were matched as closely as possible for the following parameters: severity of COPD |

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|---|---|---|
| | | (measured by FEV1), age, gender and other concomitant illness. The randomisation was carried out using the minimization method described by Gore". page 589<br>Comment: Allocation was adequately concealed |
| Blinding of participants and personnel (performance bias) | Unclear risk | Comment: Blinding of participants and personnel was not reported |
| Blinding of outcome assessment (detection bias) | Unclear risk | "Baseline measurements were performed by the research pharmacist". ... "for operational reasons, the researcher could not be blinded to the group to which the patient belonged". page 590<br>Comment: Outcome assessment was not blinded; it was not clearly reported how the research pharmacist was related to the study |
| Incomplete outcome data (attrition bias) | Low risk | "A per-protocol analysis was used". page 590 "During the study period, three patients from the intervention group and five from the control group died and a total of 22 patients withdrew from the study; 12 patients from the intervention group and 10 from the control group". page 590<br>Comment: In both groups, 15 participants (17%) dropped out during the 12-month follow-up. Reasons for drop out were comparable across groups |
| Selective reporting (reporting bias) | Unclear risk | Comment: no signs of selective reporting; however, no protocol available |
| Other bias | Low risk | |

*Kheirabadi 2008*

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|---|---|
| **Methods** | **Design:** RCT **Follow-up:** three months **Control group:** usual care |
| **Participants** | **Recruitment:** hospital (outpatient clinic)<br>**Eligible:** not reported<br>**Randomly assigned:** 42<br>**Completed:** 42<br>**Mean age:** I: 56.6 (5.7) years; C: 56.2 (4.1) years<br>**Sex (% male):** I: 61.9%; C: 76.2%<br>**COPD:** diagnosed by a pulmonologist according to ATS<br>**Major exclusion criteria:** primary diagnosis of asthma; hospitalisation during the intervention; main treatment with oxygen; occurrence of serious unexpected stresses during the study |
| **Interventions** | **Mode:** group sessions, face-to-face, telephone, hospital (outpatient clinic)<br>**Professional:** psychologist, trained psychiatric residents<br>**Topics:** education regarding the disease, smoking cessation, exercise programme, action plan, advice about exercise, advice about nutrition, advice about medication<br>**Duration:** eight group sessions of 60 to 90 minutes; participants were followed up by phone<br>**Action plan:** yes<br>**Exercise programme:** no<br>**Behavioural components:** providing feedback to the participant |
| **Outcomes** | CCQ |
| **Notes** | **Sources of funding:** not reported |

*Risk of bias table*

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Unclear risk | Comment: The method of random sequence generation was not reported |
| Allocation concealment (selection bias) | Unclear risk | Comment: The method of allocation concealment was not reported |
| Blinding of partici-pants and personnel (performance bias) | Unclear risk | Comment: Blinding of participants and personnel was not reported |
| Blinding of outcome assessment (detection bias) | Unclear risk | Comment: Blinding of outcome assessment was not reported. Not clear who performed the measurements |
| Incomplete outcome data (attrition bias) | Low risk | "We also encouraged and followed up the patients by phone and even when someone was absent, we teached him/her over the phone. In this way, all patients accompanied us till the end of the course and no patient was excluded from the study". page 28<br>Comment: All participants completed follow-up |
| Selective reporting (reporting bias) | Unclear risk | Comment: no signs of selective reporting, although only one outcome measure was reported |
| Other bias | Low risk | |

*Koff 2009*

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|---|---|
| **Methods** | **Design:** RCT **Follow-up:** three months **Control group:** usual care |
| **Participants** | **Recruitment:** hospital (outpatient clinic)<br>**Eligible:** not reported<br>**Randomly assigned:** 40<br>**Completed:** 38<br>**Mean age:** I: 66.6 (9.1) years; C: 65.0 (8.2) years<br>**Sex (% male):** I: 45%; C: 50%<br>**COPD:** GOLD stage three or four<br>**Major exclusion criteria:** active treatment for lung cancer; illiteracy; non–English speaking; inability to complete a six-minute walk test |
| **Interventions** | **Mode:** individual sessions, face-to-face, telecommunication device, home-based<br>**Professional:** respiratory physiotherapist<br>**Topics:** education regarding the disease, exercise programme, action plan, advice about exercise, advice about medication<br>**Duration:** one individual session at enrolment; each weekday morning, a telehealth session with COPD-specific education of 20 minutes<br>**Action plan:** yes<br>**Exercise programme:** no<br>**Behavioural components:** goal setting, providing feedback to the participant |
| **Outcomes** | 1. SGRQ<br>2. COPD hospitalisations<br>3. COPD ER visits<br>4. Healthcare costs |
| **Notes** | **Sources of funding:** University of Colorado Hospital |

*Risk of bias table*

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Unclear risk | "Following informed consent, patients randomly selected their group assignment by choosing a blinded envelope that contained a group indicator". page 1032<br>Comment: The method of random sequence generation was not reported |
| Allocation concealment (selection bias) | Low risk | "Following informed consent, patients randomly selected their group assignment by choosing a blinded envelope that contained a group indicator". page 1032<br>Comment: Allocation was adequately concealed |
| Blinding of participants and personnel (performance bias) | Unclear risk | "Because of the type of intervention, it was not possible to blind the subjects or investigators as to whether they were randomised to the treatment or control arms of the trial". page 1032<br>Comment: Blinding of participants and personnel was not performed |
| Blinding of outcome assessment (detection bias) | High risk | "Because of the type of intervention, it was not possible to blind the subjects or investigators as to whether they were randomised to the treatment or control arms of the |

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| | | trial". page 1032<br>"This end-point (SGRQ) was collected by the coordinator...." page 1034<br>Comment: Blinding of outcome assessment was not performed; the assessor of the primary outcome was involved in the intervention |
| Incomplete outcome data (attrition bias) | Low risk | "A total of 40 patients were randomised; 20 to the PIC group and 20 to the UC control group, and one patient withdrew from each group". page 1034<br>Comment: The number of drop outs was low |
| Selective reporting (reporting bias) | Unclear risk | Comment: no signs of selective reporting; however, no protocol available |
| Other bias | Low risk | |

*Monninkhof 2003*

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|---|---|
| **Methods** | **Design:** RCT **Follow-up:** 12 months **Control group:** usual care |
| **Participants** | **Recruitment:** hospital (outpatients)<br>**Eligible:** 615<br>**Randomly assigned:** 248<br>**Completed:** 236<br>**Mean age:** I: 65 (seven) years C: 65 (seven) years<br>**Sex (% male):** I: 85% C: 84%<br>**COPD:** diagnosis of stable COPD (ATS); FEV1% pred (pre): 25% to 80%; $FEV_1$/VC (pre): < 60<br>**Major exclusion criteria:** no previous diagnosis of asthma; exacerbation in the months before inclusion; medical condition with low survival or serious psychiatric morbidity; any other lung disease; maintenance treatment of oral steroids or antibiotics |
| **Interventions** | **Mode:** outpatient at the hospital and community-based; group education; educational booklet<br>**Professional:** respiratory nurse<br>**Topics:** COPD knowledge; inhalation technique; importance of exercise; relaxation; nutrition; coping with breathlessness; ergonomic posture and energy conservation during daily activities or work; communication and social relationships; guidelines for self treatment for exacerbations (action plans). A fitness program was aimed at coping with disease, recognising participants' individual capacity, social interactions and behavioural changes<br>**Duration:** education: five * two hours. Exercise: duration one to two a week for 30 to 45 minutes<br>**Action plan:** yes<br>**Exercise programme:** yes<br>**Behavioural components:** goal setting, providing feedback |
| **Outcomes** | 1. SGRQ<br>2. EuroQol<br>3. Self confidence<br>4. Walking distance<br>5. 6MWT<br>6. Exacerbations<br>7. Symptoms<br>8. Doctor consultations<br>9. Hospital admissions<br>10. Symptoms<br>11. Days lost from work |
| **Notes** | **Sources of funding:** the Netherlands Asthma Foundation, Boehringer Ingelheim, Amicon Health Care Insurance Company and GlaxoSmithKline BV |

*Risk of bias table*

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | "Randomisation was performed in blocks of four, stratified by sex and smoking status, using sealed envelopes". page 816<br>Comment: Random sequence generation was |

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| | | adequately performed |
| Allocation concealment (selection bias) | Low risk | "Randomisation was performed in blocks of four, stratified by sex and smoking status, using sealed envelopes". page 816<br>Comment: Allocation was adequately concealed |
| Blinding of participants and personnel (performance bias) | Unclear risk | Comment: Participants and personnel were not blinded |
| Blinding of outcome assessment (detection bias) | Low risk | Comment: Outcome assessment was not blinded; however, measurements were performed by an assessor who was independent of the study |
| Incomplete outcome data (attrition bias) | Low risk | "In the intervention group five patients (three deaths, two other) dropped out, as did seven patients (three deaths, two carcinoma, two other) in the control group". page 818<br>Comment: The number of drop outs and reasons for drop out in both groups were comparable. Moreover, an intention-to-treat analysis was used and drop out was low |
| Selective reporting (reporting bias) | Unclear risk | Comment: no signs of selective reporting; however, no protocol available |
| Other bias | Low risk | |

*Moullec 2008*

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|---|---|
| **Methods** | **Design:** CCT **Follow-up:** 12 months **Control group:** usual care |
| **Participants** | **Recruitment:** rehabilitation centre<br>**Eligible:** 50<br>**Randomly assigned:** 40<br>**Completed:** 27<br>**Mean age:** I: 62.9 (7.4) years; C: 59.7(9.6) years<br>**Sex (% male):** I: 71%; C: 81%<br>**COPD:** moderate or severe COPD according to GOLD; postbronchodilator $FEV_1/FVC < 0.7$ and FEV1% 30% to 79% predicted<br>**Major inclusion criteria:** no indication for home oxygen therapy; no exacerbation or hospitalisation in the previous two months; participation in the 20 sessions of the four-week inpatient PR<br>**Major exclusion criteria:** significant medical or psychiatric disturbances that would interfere with full participation in the programme; previous diagnosis of asthma |
| **Interventions** | **Mode:** group sessions, face-to-face, community-based<br>**Professional:** respiratory physiotherapist, respiratory specialist, psychologist, peer-led, dietician, adapted physical activity professional (Faculty of Exercise Sciences)<br>**Topics:** education regarding the disease, smoking cessation, exercise programme, action plan, advice about exercise, advice about nutrition, advice about medication, coping with breathlessness<br>**Duration:** total 96 group sessions; individualised exercise training (3.5 hours/wk; 72 sessions), health education provided alternatively by all professionals of the healthcare network (two hours/mo; 12 sessions), psychosocial support (one hour/mo; 12 sessions)<br>**Action plan:** yes<br>**Exercise programme:** yes<br>**Behavioural components:** providing feedback to the participant |
| **Outcomes** | 1. SGRQ<br>2. WHQOL-BREF<br>3. $FEV_1$<br>4. Hospital days<br>5. Consultations with GP<br>6. Consultations with lung specialist<br>7. 6MWT<br>8. Voorrips questionnaire |
| **Notes** | **Sources of funding:** the Fond d'Aide a' la Qualite des Soins de Ville (FAQSV) of the Union Regionale des Caisses d'Assurance Maladie (URCAM) and the Agence Regionale de l'Hospitalisation (ARH) of the region Languedoc-Roussillon in France |

*Risk of bias table*

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | High risk | "The consecutive assignment of eligible patients to the follow-up groups was based on the unpredictable occurrence of their place of residence. The subjects |

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| | | assigned to the usual aftercare were those who lived in towns without an existing self help association". Moullec 2010, page 124<br>Comment: The method of random sequence generation was not adequate |
| Allocation concealment (selection bias) | High risk | "The consecutive assignment of eligible patients to the follow-up groups was based on the unpredictable occurrence of their place of residence. The subjects assigned to the usual aftercare were those who lived in towns without an existing self help association". Moullec 2010, page 124<br>Comment: The allocation was not concealed |
| Blinding of participants and personnel (performance bias) | Unclear risk | Comment: Blinding of participants and personnel was not reported |
| Blinding of outcome assessment (detection bias) | Low risk | "...the same trained research assistant visited the patients at home to supervise the completion of all quality of life questionnaires"...."The research assistant had no contact with participants other than during the evaluations". Moullec 2010, page 124<br>Comment: Blinding of outcome assessment was not reported. However, the measurements were performed by someone not directly involved in the intervention |
| Incomplete outcome data (attrition bias) | High risk | "At 1 year of individual follow-up, 13 subjects had not completed the scheduled sessions of assessment. In the SG, six patients had dropped out at the 6-month point for the following reasons: three exacerbation crises, one inpatient psychiatry admission, one death due to cardiac failure and one infectious arm. At 1-year, further four control subjects had dropped out because of acute exacerbation. In the MG, three patients were lost to follow-up evaluation (two because of acute chest exacerbation crises at 6-month, and one with myocardial aneurysm at 1 year)"<br>Comment: high number of drop outs compared with the number of participants included (> 30%) and a per-protocol analysis was performed |
| Selective reporting (reporting bias) | Unclear risk | Comment: no signs of selective reporting; however, no protocol available |
| Other bias | Low risk | |

*Nguyen 2008*

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|---|---|
| **Methods** | **Design:** RCT **Follow-up:** six months **Intervention one:** Internet-based dyspnoea self management programme **Intervention two:** face-to-face dyspnoea self management programme |
| **Participants** | **Recruitment:** community and clinic<br>**Eligible:** 84<br>**Randomly assigned:** 50<br>**Completed:** 38<br>**Mean age:** I: 68.0 (8.3) years; C: 70.9 (8.6) years<br>**Sex (% male):** I: 61%; C: 55%<br>**COPD:** diagnosis of COPD with spirometry showing at least mild obstructive disease defined as postbronchodilator $FEV_1/FVC < 0.70$ with $FEV_1 < 80\%$ predicted, or $FEV_1/FVC < 0.60$ with $FEV_1 > 80\%$ predicted<br>**Major inclusion criteria:** clinically stable for at least one month; ADL limited by dyspnoea; using the Internet and/or checking email at least once per week with a Windows operating<br>system; oxygen saturation > 85% on room air or ≤ 6 L/min of nasal oxygen at the end of a six-minute walk test<br>**Major exclusion criteria:** active symptomatic illness (i.e. cancer, heart failure, ischaemic heart disease with known coronary artery or valvular heart disease, psychiatric illness or neuromuscular disease); participation in a pulmonary rehabilitation programme in the last 12 months; participation in > two days of supervised maintenance exercise |
| **Interventions** | **Mode:** group and individual sessions, face-to-face, telephone or Internet, outpatient clinic and home-based<br>**Professional:** (respiratory) nurse<br>**Topics:** exercise programme, action plan, advice about exercise, advice about medication, coping with breathlessness<br>**Duration:**<br>1.5- to two-hour face-to-face consultation<br>Six one-hour weekly group sessions of structured education of dyspnoea management strategies via chat or face-to-face<br>Four times/wk 30-minute endurance, three times/wk arm strengthening<br>Reinforcement: via email or telephone weekly in month one, biweekly in months two through six<br>**Action plan:** yes<br>**Exercise programme:** yes<br>**Behavioural components:** motivational interviewing, goal setting, providing feedback to the participant |
| **Outcomes** | 1. SGRQ<br>2. WHQOL-BREF<br>3. $FEV_1$<br>4. Hospital days<br>5. Consultations with GP<br>6. Consultations with lung specialist<br>7. 6MWT<br>8. Voorrips questionnaire |

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| Notes | **Sources of funding:** This study was supported in part by Robert Wood Johnson Health e-Technologies Initiative grant RWJ49153 to Dr Carrieri-Kohlman, General Clinical Research Centers at the University of Washington (MO1-RR-000037) and UC San Francisco (MO1-RR-00079), and Grant Number 1KL2RR025015-01 from the National Center for Research Resources (NCRR), a component of the National Institutes of Health (NIH) and the NIH Roadmap for Medical Research<br>**Note:** "Both programs were designed to provide similar content and 'contact' time for ongoing reinforcement and support and differed only in the mode of delivery" |

*Risk of bias table*

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | "An investigator who was not involved in the day-to-day study operations generated the randomisation sequence using the SPSS version 14.0 random sequence generator feature and placed the randomisation in separate sealed opaque envelopes"<br>Comment: Random sequence generation was adequately performed. |
| Allocation concealment (selection bias) | Low risk | "An investigator who was not involved in the day-to-day study operations generated the randomisation sequence using the SPSS version 14.0 random sequence generator feature and placed the randomisation in separate sealed opaque envelopes"<br>Comment: Allocation was adequately concealed |
| Blinding of participants and personnel (performance bias) | Unclear risk | "Since registration and access to the Web questionnaires on the vendor-supported website required designation of a treatment group early in the baseline visit, the study nurse opened the randomisation envelope during the first half of the visit. While the study nurse was privy to the treatment assignment, participants were not informed of their assignment until the visit was complete"<br>Comment: Participants were blinded until the end of the baseline visit, and personnel were not blinded |
| Blinding of outcome assessment (detection bias) | High risk | "They returned to the medical center at 3 and 6 months for testing by study staff who were not involved in the intervention. Individual semi structured interviews were conducted either in person or via telephone at the final visit by the evaluation staff or investigators (HQN and VCK) who were not directly involved in the intervention"<br>Comment: Blinding of outcome assessment was not reported, and measurements were performed by study staff not directly involved in the intervention; however, staff members were investigators and therefore were involved in the study |

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| Incomplete outcome data (attrition bias) | High risk | Comment: A high percentage dropped out (> 20%), and not all randomly assigned participants were included in the intention-to-treat analysis |
| Selective reporting (reporting bias) | Unclear risk | Comment: no signs of selective reporting; however, no protocol available |
| Other bias | High risk | "The investigators stopped the study early due to the cumulative technical and usability challenges that peaked when three consecutive eDSMP participants had multiple difficulties accessing the Web application and subsequently withdrew. All enrolled participants were followed through 6 months according to the study protocol" |

*Nguyen 2009*

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|---|---|
| **Methods** | **Design:** RCT **Follow-up:** six months **Intervention one:** mobile coached cell phone–based exercise persistence intervention; **Intervention two:** self monitored cell phone–based exercise persistence intervention |
| **Participants** | **Recruitment:** pulmonary rehabilitation site<br>**Eligible:** 34<br>**Randomly assigned:** 17<br>**Completed:** 15<br>**Mean age:** I: 72 (nine) years; C: 64 (12) years<br>**Sex (% male):** I: 33%; C: 37%<br>**COPD:** stable moderate to severe COPD according to GOLD criteria<br>**Major exclusion criteria:** active symptomatic illness (e.g. cancer, heart failure, ischaemic heart disease, neuromuscular disease, psychiatric illness); inability (e.g. severe arthritis) or unwillingness to use the study issued cell phone; residence outside of the wireless coverage area |
| **Interventions** | **Mode:** individual sessions, face-to-face, booklet, telephone, outpatient clinic and home-based<br>**Professional:** respiratory nurse<br>**Topics:** exercise programme, action plan, advice about exercise<br>**Duration:** one individual session of 30 to 45 minutes, at least one or two phone calls of 10 minutes with participants in the coached group, and 24 weekly personalised (coached) or standard (self monitored) text message. 150 minutes of moderate-intensity endurance exercise per week in three to five sessions<br>**Action plan:** yes<br>**Exercise programme:** yes<br>**Behavioural components:** providing feedback to the participant |
| **Outcomes** | 1. SGRQ<br>2. Exercise barriers efficacy scale<br>3. 6MWT<br>4. Free-living ambulatory physical activity |
| **Notes** | **Sources of funding:** This study was supported in part by R03NR009361 and 1KL2RR025015-01; Omron Healthcare donated the pedometers |

*Risk of bias table*

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | "A biostatistician who was not involved in the day-to-day study operations generated the randomisation sequence and placed the randomisation in separate sealed opaque envelopes. The randomisation scheme was stratified by gender to ensure balanced allocation" page 303<br>Comment: Random sequence generation was adequately performed |
| Allocation concealment (selection bias) | Low risk | "A biostatistician who was not involved in the day-to-day study operations generated the randomisation sequence and placed the randomisation in separate sealed opaque envelopes. The randomisation scheme was stratified by gender to ensure balanced allocation". page 303<br>Comment: Allocation was adequately concealed |

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|---|---|---|
| Blinding of participants and personnel (performance bias) | Unclear risk | "The interventionist was not blind to group assignment..." page 303<br>Comment: Personnel was not blinded; blinding of participants was not reported |
| Blinding of outcome assessment (detection bias) | Low risk | "...however, the outcome assessments were performed by a research assistant who was blinded to this information". page 303<br>Comment: Outcome assessment was blinded; measurements were performed by study staff not directly involved in the intervention |
| Incomplete outcome data (attrition bias) | Low risk | Comment: Loss to follow-up was low, and an intention-to-treat analysis was used |
| Selective reporting (reporting bias) | Unclear risk | Comment: The domain scores of HRQoL questionnaires were not reported; further no signs of selective reporting were noted |
| Other bias | Low risk | |

*Ninot 2011*

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|---|---|
| **Methods** | **Design:** RCT **Follow-up:** 12 months **Control group:** usual care |
| **Participants** | **Recruitment:** hospital (university-based centre by flyers advertising the study)<br>**Eligible:** 61<br>**Randomly assigned:** 45<br>**Completed:** 38<br>**Mean age:** I: 65 (59 to 74) years; C: 61 (56 to 65) years<br>**Sex (% male):** I: 78%; C: 64%<br>**COPD:** stable COPD; $FEV_1$/FVC ratio < 0.70<br>**Major exclusion criteria:** previous diagnosis of asthma; oxygen dependence; unstable and/or uncontrolled cardiac disease; musculoskeletal problems precluding exercise training; terminal disease, dementia or an uncontrolled psychiatric illness |
| **Interventions** | **Mode:** group and Individual sessions, face-to-face, telephone, hospital on outpatient basis<br>**Professional:** health professional and qualified exercise trainer<br>**Topics:** smoking cessation, exercise programme, action plan, advice about exercise, advice about nutrition, advice about medication<br>**Duration:** eight group sessions of two hours, three phone calls<br>**Action plan:** yes<br>**Exercise programme:** yes<br>**Behavioural components:** goal setting, providing feedback to the participant |
| **Outcomes** | 1. CRQ<br>2. SF-36<br>3. Self efficacy for managing dyspnoea<br>4. 6MWT<br>5. Dyspnoea knowledge<br>6. Excercise stage of change |
| **Notes** | **Sources of funding:** a grant from the Hospital of Montpellier CHRU, PHRC (grant number UF7608) |

*Risk of bias table*

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | "Participants were randomly assigned either to the self-management program or usual care group. The trial statistician, MCP, generated the random allocation sequence using the random procedure in SAS (SAS v.9.1 e SAS Institute, Cary NC), with a 1:1 allocation using block size of 4…" page 379.<br>Comment: Random sequence generation was adequately performed |
| Allocation concealment (selection bias) | Low risk | "…..After the physician had obtained the patient's consent, he sent by fax the randomisation form to the Clinical Research Unit (AJ) for allocation consignment re-addressed by fax". page 379<br>Comment: Allocation was adequately concealed |
| Blinding of participants and | Unclear risk | "Due to the nature of the intervention conditions, it is not possible to blind research participants or assessors. |

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|---|---|---|
| personnel (performance bias) | | Several stratagems were adopted in an effort to ensure that objectivity was maintained as rigorously as possible. Participants were unaware of their group allocation until they had completed all of their pre-intervention assessment". page 379<br>Comment: Patients and personnel were not blinded |
| Blinding of outcome assessment (detection bias) | Low risk | "... The individuals carrying out the assessments were not part of the intervention team. Research participants were asked not to divulge information regarding their group allocation in conversation during assessments at 12 month"<br>Comment: Outcome assessment was not blinded; however, assessors were not part of the intervention team |
| Incomplete outcome data (attrition bias) | Low risk | "One patient from the intervention group did not fulfil our adherence criteria to the 4-week program, and also did not complete the 1-year evaluation. Six more patients were not available for follow-up evaluation: four in the usual care group, and two in the intervention group. The withdrawals were due to miscellaneous medical conditions (n = 3), and COPD exacerbation (n = 3). Due to the missing data, we did not retain these patients in our 1-year analyses"<br>Comment: The number of drop outs was relatively low and equally distributed over groups. Also, reasons for drop out in the two groups were comparable |
| Selective reporting (reporting bias) | Unclear risk | Comment: no signs of selective reporting; however, no protocol available |
| Other bias | Low risk | |

*Osterlund Efraimsson 2006*

| | |
|---|---|
| **Methods** | **Design:** RCT **Follow-up:** three to five months **Control group:** usual care |
| **Participants** | **Recruitment:** primary healthcare clinic<br>**Eligible:** 62<br>**Randomly assigned:** 52<br>**Completed:** 38<br>**Mean age:** I: 66 (9.4) years; C: 67 (10.4) years<br>**Sex (% male):** I: 50%; C: 50%<br>**COPD:** mild, moderate, severe or very severe COPD based on spirometry, lung capacity after bronchodilator use, based on GOLD criteria<br>**Major exclusion criteria:** Severe mental disorders such as schizophrenia, dementia and alcohol or drug abuse were excluded |
| **Interventions** | **Mode:** individual sessions, face-to-face, outpatient clinic<br>**Professional:** respiratory nurse<br>**Topics:** education regarding COPD, smoking cessation, action plan, advice about exercise, advice about nutrition, advice about medication, coping with breathlessness<br>**Duration:** two individual sessions of one hour<br>**Action plan:** yes<br>**Exercise programme:** no<br>**Behavioural components:** motivational interviewing, providing feedback to the participant |
| **Outcomes** | 1. SGRQ<br>2. COPD knowledge |
| **Notes** | **Sources of funding:** County of Council of Dalarna, Sweden |

*Risk of bias table*

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | "The randomisation was performed when two patients with the same variables agreed to participate in the study by assigning each individual an identity number. An independent person drew lots for allocation to either intervention or control group". pages 2 to 3<br>Comment: The random sequence generation was performed adequately |
| Allocation concealment (selection bias) | Low risk | "The randomisation was performed when two patients with the same variables agreed to participate in the study by assigning each individual an identity number. An independent person drew lots for allocation to either intervention or control group". pages 2 to 3<br>Comment: Allocation was adequately concealed |
| Blinding of participants and personnel (performance bias) | Unclear risk | Comment: Blinding of participants and personnel was not reported |

| | | |
|---|---|---|
| Blinding of outcome assessment (detection bias) | High risk | "Each visit lasted for about 1 hour and the same nurse (Eva Österlund Efraimsson) was responsible for all consultations. At the first and last visits, all patients responded to the two questionnaires, which were completed by each participant in an undisturbed area. The nurse in charge was available to answer questions and to check that the patients responded to all the items". page 180<br>Comment: Outcome assessment was not blinded, and measurements were performed/supervised by the same person who provided the intervention (who was also the principal investigator) |
| Incomplete outcome data (attrition bias) | Low risk | No participants were lost to follow-up |
| Selective reporting (reporting bias) | Unclear risk | Comment: All subscales of the two questionnaires used were reported; no signs of selective reporting were noted |
| Other bias | Low risk | |

*Rea 2004*

| | |
|---|---|
| **Methods** | **Design:** RCT (cluster) **Follow-up:** 12 months **Control group:** usual care |
| **Participants** | **Recruitment:** general practise<br>**Eligible:** 158<br>**Randomly assigned:** 135<br>**Completed:** 117<br>**Mean age of both groups:** 68 years (range 44 to 84)<br>**Sex (% male) of the whole study populations:** 41.5%<br>**COPD:** diagnosis of COPD by ICD-9-CM codes and GP records for a clinical diagnosis of moderate to severe COPD<br>**Major exclusion criteria:** chronic asthma; bronchiectasis; co-morbidity more significant than COPD; unable to give informed consent; prognosis < 12 months; long-term oxygen therapy or too unwell; deceased; no longer enrolled with GP practise or moved out; unable to contact participant; insufficient practise nurse |
| **Interventions** | **Mode:** timetable for regular maintenance checks; set achievable goals for lifestyle changes<br>**Professional:** general practitioner, practise nurse, respiratory physician, respiratory nurse specialist<br>**Topics:** an action plan detailing advice on how to manage worsening symptoms, when to call the GP and self medication options decided by the GP. Information about smoking cessation and the use of inhalers was given. Annual influenza vaccination and attendance at a pulmonary rehabilitation programme were recommended. Monthly visits with practise nurse, and three-monthly with the GP. More visits were demanded if worsening of symptoms occurred<br>**Duration:** 12 monthly visits to practise nurse, four three-monthly visits to GP, at least one home visit of respiratory nurse specialist and one following hospital admissions<br>**Action plans:** yes<br>**Exercise programme:** no<br>**Behavioural components:** goal setting, providing feedback |
| Outcomes | 1. SF-36<br>2. CRQ<br>3. ISWT<br>4. Hospital admissions<br>5. Spirometry<br>6. $FEV_1$<br>7. Medication<br>8. Courses of oral steroids<br>9. Courses of antibiotics<br>10. Smoking cessation |
| **Notes** | **Sources of funding:** provided by the Health Funding Authority, South Auckland Health, South-Med Ltd, ProCare Health Ltd and First Health Ltd<br>**Note:** Randomisation is done at the level of GP practise; analysis is performed at the level of participants |

*Risk of bias table*

| Bias | Authors' judgement | Support for judgement |
|---|---|---|

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|---|---|---|
| Random sequence generation (selection bias) | Low risk | "Fifty-one eligible practices with 116 GPs were randomised, using a set of computer-generated random numbers..." page 609<br>Comment: Random sequence generation was adequately performed |
| Allocation concealment (selection bias) | High risk | Comment: The study was cluster-randomised, so no allocation concealment was provided |
| Blinding of participants and personnel (performance bias) | Unclear risk | Comment: Blinding of participants and personnel was not reported |
| Blinding of outcome assessment (detection bias) | Unclear risk | "For all patients, an initial assessment with the GP and practice nurse included clinical history and the Short Form (SF)-36. Spirometry, the Shuttle Walk Test and the Chronic Respiratory Questionnaire (CRQ) were administered at the hospital outpatient clinic by a respiratory physician, respiratory nurses and experienced interviewers, respectively. At the completion of a 12-month trial period, an identical reassessment was undertaken". page 609<br>Comment: Blinding of outcome assessment was not reported; measurements were predominantly performed by study personnel at the outpatient clinic |
| Incomplete outcome data (attrition bias) | Low risk | "During the trial period, six patients died, six patients withdrew from the study, four patients developed cancer and two patients moved from the area. The 12 month follow-up assessment was completed by 117 patients (71 INT, 46 CON), although hospital admission data were available for all 135 patients". page 609<br>Comment: 12 participants dropped out in the intervention group (14%), six in the control group (12%). Reasons were comparable. Intention-to-treat analysis was performed on the primary outcome |
| Selective reporting (reporting bias) | Unclear risk | Comment: no signs of selective reporting; however, no protocol available |
| Other bias | Low risk | We additionally assessed this study on bias specifically important in cluster-randomised trials. In Rea's study, the general practises were randomly assigned before the participants were included. For reasons unknown, the number of participants screened and included was lower in the intervention group than in the control group. The study authors state that baseline characteristics were not significantly different between groups. Therefore, risk of recruitment bias is unclear, and risk of bias for baseline imbalance is low. The risk of bias due to loss of clusters is low because no clusters were lost after participant enrolment. Rea et al did not correct for clustering in their analyses, so risk of bias due to incorrect analysis is high |

*Rice 2010*

| | |
|---|---|
| **Methods** | **Design:** RCT **Follow-up:** 12 months **Control group:** usual care |
| **Participants** | **Recruitment:** hospital<br>**Eligible:** 1739<br>**Randomly assigned:** 743<br>**Completed:** 659<br>**Mean age:** I: 69.1 (9.4) years; C: 70.7 (9.7) years<br>**Sex (% male):** I: 97.6%; C: 98.4%<br>**COPD:** clinical diagnosis of COPD with postbronchodilator spirometry showing an $FEV_1 < 70\%$ predicted and an $FEV_1/FVC < 0.70$<br>**Major exclusion criteria:** inability to have access to a home telephone line or to sign a consent form; any condition that would preclude effective participation in the study or likely to reduce life expectancy to less than a year |
| **Interventions** | **Mode:** group and individual sessions, face-to-face, outpatient clinic<br>**Professional:** respiratory therapist case manager<br>**Topics:** education regarding COPD, smoking cessation, action plan with self treatment, advice about exercise, advice about medication, coping with breathlessness<br>**Duration:** one group session of one to 1.5 hours, 12 monthly phone calls of 10 to 15 minutes<br>**Action plan:** yes<br>**Exercise programme:** no<br>**Behavioural components:** providing feedback to the participant |
| **Outcomes** | 1. SGRQ<br>2. Use of short-acting beta-agonist, prednisone, antibiotics<br>3. Mortality<br>4. Hospitalisations<br>5. Hospital days<br>6. ED visits<br>7. ICU days |
| **Notes** | **Sources of funding:** an unrestricted grant from the Veterans Integrated Service Network 23 Primary Care and Research Services and by the Center for Chronic Disease Outcomes Research, a Veterans Affairs Health Services Research and Development Center of Excellence |

*Risk of bias table*

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Unclear risk | "We assigned subjects in equal proportions to each of the two treatment arms by permuted-block randomisation". Appendix 1, page 3<br>Comment: Information on the method of random sequence generation was not reported |
| Allocation concealment (selection bias) | Unclear risk | "We assigned subjects in equal proportions to each of the two treatment arms by permuted-block randomisation". Appendix 1, page 3<br>Comment: Information on the method of allocation concealment was not reported |

| | | |
|---|---|---|
| Blinding of participants and personnel (performance bias) | Unclear risk | Comment: Blinding of participants and personnel was not reported |
| Blinding of outcome assessment (detection bias) | Low risk | "Blinded pulmonologists independently reviewed all discharge summaries and ED reports and assigned a primary cause for each". page 891<br>Comment: Outcome assessment was blinded |
| Incomplete outcome data (attrition bias) | Unclear risk | "All patients were followed for 12 months or until the time of death if it occurred before 12 months". page 981<br>"Fifty-five percent of patients in the usual care group and 60% of patients in the disease management group returned a completed the Saint George's Respiratory Questionnaire in response to a single mailing at the end of the study". page 982<br>Comment: low response rates on SGRQ leading to a high risk of bias. However, data on healthcare utilisation seem complete with no risk of bias |
| Selective reporting (reporting bias) | Unclear risk | Comment: no signs of selective reporting; however, no protocol available |
| Other bias | Low risk | |

*Sassi-Dambron 1995*

| | |
|---|---|
| **Methods** | **Design:** RCT **Follow-up:** six months **Intervention one:** dyspnoea management programme **Intervention two:** general health education |
| **Participants** | **Recruitment:** community<br>**Eligible:** not reported, 497 persons were screened<br>**Randomly assigned:** 98<br>**Completed:** 80<br>**Mean age:** I: 67.5 (8.0) years; C: 67.3 (8.0) years<br>**Sex (% male):** I: 55 %; C: 41%<br>**COPD:** diagnosis of COPD confirmed with medical records and pulmonary function test evidence of expiratory obstruction<br>**Major exclusion criteria:** none reported |
| **Interventions** | **Mode:** group sessions, face-to-face<br>**Professional:** one: clinical nurse, graduate student in psychology; two: health professionals specialising in each subject<br>**Topics:** one: education regarding the disease, advice about exercise, coping with breathlessness; two: topics not directly related to lung disease: exercise, general medications, durable power of attorney, nutrition, Alzheimer's disease and medical insurance<br>**Duration:** six weekly group sessions, duration not reported<br>**Action plan:** no<br>**Exercise programme:** no<br>**Behavioural components:** not reported |
| **Outcomes** | 1. Quality of well-being scale<br>2. Spielberger state-trait anxiety inventory<br>3. The Centre of Epidemiologic Studies Depression<br>4. American Thoracic Society Dyspnea Scale<br>5. 6MWT<br>6. Shortness of Breath Questionnaire |
| **Notes** | **Sources of funding:** grant 2RT0268 from the University of California Tobacco Related Disease Research Program and grant R01 HL34732 from the National Heart Lung & Blood Institute |

*Risk of bias table*

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Unclear risk | "Study subjects were randomly assigned into either a treatment or an education-control group". page 725<br>Comment: Information on the method of random sequence generation was not reported |
| Allocation concealment (selection bias) | Unclear risk | "Study subjects were randomly assigned into either a treatment or an education-control group". page 725<br>Comment: Information on the method of allocation concealment was not reported |
| Blinding of participants and personnel (performance bias) | Unclear risk | Comment: Blinding of participants and personnel was not reported |

| | | |
|---|---|---|
| Blinding of outcome assessment (detection bias) | Unclear risk | Comment: Blinding of outcome assessment was not reported. Not clear who performed the measurement |
| Incomplete outcome data (attrition bias) | Unclear risk | "...nine dropped out before treatment, one from the treatment and eight from the control group. Reasons for dropping included illness (treatment = 1, control = 1), time conflict (control = 4), and lack of interest (control = 3). An additional nine subjects dropped out during treatment, five from the treatment and four from the control group. We attempted to follow up these subjects at the posttreatment and 6-month follow-up periods and included them as part of the study database resulting in 46 subjects in the treatment group and 43 subjects in the control group. However, only one subject returned to complete the 6-month follow-up examination". page 727<br>Comment: Drop out in the control group was higher than in the intervention group at 12 versus six; overall drop out is relatively low. Reasons for drop out after the start of treatment are not clear. A per-protocol analysis was performed |
| Selective reporting (reporting bias) | Unclear risk | Comment: no signs of selective reporting; however, no protocol available |
| Other bias | Low risk | |

*Stulbarg 2002*

| | |
|---|---|
| **Methods** | **Design:** RCT **Follow-up:** 12 months **Intervention one:** dyspnoea self management programme and training **Intervention two:** dyspnoea self management programme and exposure **Intervention three:** dyspnoea self management programme |
| **Participants** | **Recruitment:** community and practising physicians<br>**Eligible:** 115<br>**Randomly assigned:** 115<br>**Completed:** 103<br>**Mean age:** one: 66.2 (6.4) years; two: 67.2 (7.6) years; three: 65.7 (8.8) years<br>**Sex (% male):** one: 35.2%; two: 42.4%; three: 55.6%<br>**COPD:** diagnosis of moderate to severe COPD with clinical stability for at least one month, persistent moderate to severe airflow obstruction after inhalation of two puffs of albuterol (i.e. $FEV_1$ less than 60% of predicted or $FEV_1$/FVC less than 60%<br>**Major exclusion criteria:** cardiopulmonary (arrhythmias and desaturation (< 75) during incremental treadmill test) or musculoskeletal complications |
| **Interventions** | **Mode:** individual sessions, face-to-face, telephone, home-based<br>**Professional:** respiratory nurse<br>**Topics:** exercise programme, advice about exercise, advice about medication, coping with breathlessness<br>**Duration:** all: four individual educational sessions over the first eight weeks of one and one half-hour reinforcement sessions at four and eight months and >= four times walking per week for at least 20 minutes for 12 months. Biweekly nurse telephone calls<br>Two: four supervised exercise sessions once every other week for two months<br>Three: 24 supervised exercise sessions three times per week over two months<br>**Action plan:** no<br>**Exercise programme:** yes<br>**Behavioural components:** goal setting, providing feedback to the participant |
| **Outcomes** | 1. CRQ<br>2. SF-36<br>3. Self-efficacy for walking questionnaire<br>4. CES-D<br>5. Baseline and transitional dyspnoea index<br>6. $FEV_1$<br>7. $FEV_1$/FVC<br>8. 6MWT<br>9. Endurance treadmill test |
| **Notes** | **Sources of funding:** funded by National Institutes of Health NINR R01-NR02131-08; Nursing Research Training in Symptom Management National Institutes of Health/NINR 2T32 NR07088. This study was carried out in part in the General Clinical Research Center, Moffitt Hospital, University of California, San Francisco, with funds provided by the National Center for Research Resources, 5 M01 RR-00079, US Public Health Service |

| *Risk of bias table* | | |
|---|---|---|
| **Bias** | **Authors' judgement** | **Support for judgement** |
| Random sequence generation (selection bias) | Unclear risk | "In an attempt to control for disease severity, after baseline testing and before randomisation, subjects were stratified by oxygen saturation (SaO2) less than 85% or greater than or equal to 85% during incremental exercise testing and their ability (yes) or inability (no) to achieve anaerobic threshold (AT). Four strata were therefore created... A randomisation plan was created for each of the four strata". Stulbarg 2002, page 110<br>Comment: Information on the method of random sequence generation was not reported |
| Allocation concealment (selection bias) | Unclear risk | "In an attempt to control for disease severity, after baseline testing and before randomisation, subjects were stratified by oxygen saturation (SaO2) less than 85% or greater than or equal to 85% during incremental exercise testing and their ability (yes) or inability (no) to achieve anaerobic threshold (AT). Four strata were therefore created... A randomisation plan was created for each of the four strata". Stulbarg 2002, page 110<br>Comment: Information on the method of allocation concealment was not reported |
| Blinding of participants and personnel (performance bias) | Unclear risk | Comment: Blinding of participants and personnel was not reported |
| Blinding of outcome assessment (detection bias) | Low risk | "Research personnel who performed these measurements were blinded to patients' treatment group assignments". Carrieri-Kohlman 2005, page 275<br>Comment: Outcome assessment was blinded |
| Incomplete outcome data (attrition bias) | Low risk | "A total of 115 patients were randomised and 4 patients from each group dropped out before the first evaluation at 2 months....There were no significant differences between the 3 treatment groups in any of the baseline characteristics". Carrieri-Kohlman 2005, pages 278 to 279<br>Comment: A per-protocol analysis was performed; however, drop out was relatively low and equally distributed over groups |
| Selective reporting (reporting bias) | High risk | Comment: Several measures that were reported at two months were not reported at 12 months (CES-D, self efficacy, USCD shortness of breath questionnaire) |
| Other bias | Low risk | |

*van Wetering 2009*

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|---|---|
| **Methods** | **Design:** RCT **Follow-up:** 24 months **Control group:** usual care |
| **Participants** | **Recruitment:** hospital<br>**Eligible:** not reported<br>**Randomly assigned:** 199<br>**Completed:** 158<br>**Mean age:** I: 65.9 (8.8) years; C: 67.2 (8.9) years<br>**Sex (% male):** I: 71%; C: 71%<br>**COPD:** COPD GOLD stage two or three<br>**Major exclusion criteria:** prior rehabilitation; serious co-morbidity that precluded exercise therapy |
| **Interventions** | **Mode:** individual sessions, face-to-face, patient education book, community- and home-based<br>**Professional:** respiratory nurse, respiratory physiotherapist, dietician<br>**Topics:** education regarding COPD, smoking cessation, exercise programme, advice about exercise, advice about nutrition<br>**Duration:** 52 individual sessions of exercise training of 30 minutes. Daily home-based exercise sessions<br>**Action plan:** no<br>**Exercise programme:** yes<br>**Behavioural components:** providing feedback to the participant |
| **Outcomes** | 1. SGRQ<br>2. Number of exacerbations<br>3. mMRC<br>4. Hospitalisations<br>5. Hospital days<br>6. Time unable to work<br>7. GP visits<br>8. Nurse visits<br>9. Specialist visits<br>10. 6MWT |
| **Notes** | **Sources of funding:** the Netherlands Asthma Foundation (NAF 3.4.01.63), the ''Stichting Astma Bestrijding'' (SAB), Nutricia Netherlands, Pfizer and Partners in Care Solutions (PICASSO) for COPD |

*Risk of bias table*

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | "Patients were randomised to the INTERCOM programme or to usual care using a computerised procedure with concealed patient allocation". page 8<br>Comment: Random sequence generation was performed adequately |
| Allocation concealment (selection bias) | Low risk | "Patients were randomised to the INTERCOM programme or to usual care using a computerised procedure with concealed patient allocation". page 8<br>Comment: Allocation was adequately concealed |

| | | |
|---|---|---|
| Blinding of participants and personnel (performance bias) | Unclear risk | Comment: Participants and personnel were not blinded |
| Blinding of outcome assessment (detection bias) | Low risk | "All measurements were assessed single blind". page 8<br>Comment: Outcome assessment was blinded |
| Incomplete outcome data (attrition bias) | Low risk | "The analysis was performed according to an intention-to-treat (ITT) approach. All randomised patients who started the treatment (in the INTERCOM group) and who completed at least one post-randomisation outcome measurement (in both the INTERCOM group and usual care group) were included in the statistical analysis." page 8<br>"Thirteen of the 199 randomised patients did not start the treatment. The total<br>drop out rate was 24.5% (25 patients) in the INTERCOM group and 16.5% (16 patients) in the usual care group. This difference was not statistically significant (P=0.22)"<br>Comment: Reasons for drop out were comparable in the intervention and control groups |
| Selective reporting (reporting bias) | Unclear risk | Comment: no signs of selective reporting; however, no protocol available |
| Other bias | Low risk | |

*Wakabayashi 2011*

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|---|---|
| **Methods** | **Design:** RCT **Follow-up:** 12 months **Control group:** usual care |
| **Participants** | **Recruitment:** hospital (outpatient clinic)<br>**Eligible:** 118<br>**Randomly assigned:** 102<br>**Completed:** 85<br>**Mean age:** I: 72.9 (6.4) years; C: 70.4 (8.6) years<br>**Sex (% male):** I: 88.5%; C: 84%<br>**COPD:** clinical diagnosis of COPD including airflow obstruction assessed by pulmonary function tests with postbronchodilator inhalation<br>**Major exclusion criteria:** history of atopy or any apparent asthmatic features; illiterate or had a cognitive impairment score of less than 26 on the Mini-Mental State Examination (MMSE); lived in a residential care facility or a nursing home; had exacerbations during the preceding three months; had other respiratory diseases such as bronchiectasis, any type of pulmonary fibrosis or congestive heart failure |
| **Interventions** | **Mode:** individual sessions, face-to-face, booklet, outpatient clinic<br>**Professional:** respiratory nurse, pulmonary physician<br>**Topics:** education regarding COPD, smoking cessation, action plan with self treatment, advice about exercise, advice about nutrition, advice about medication, coping with breathlessness<br>**Duration:** six monthly individual sessions of at least 30 minutes<br>**Action plan:** yes<br>**Exercise programme:** no<br>**Behavioural components:** providing feedback to the participant |
| **Outcomes** | 1. SGRQ<br>2. LINQ<br>3. mMRC<br>4. FEV1% of predicted<br>5. Hospital admissions<br>6. Emergency department visits<br>7. 6MWT<br>8. Instrumental activities of daily living |
| **Notes** | **Sources of funding:** Environmental Restoration and Conservation Agency of Japan (2003 to 2005) |

*Risk of bias table*

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | "A case manager independent of the study randomly assigned patients to either group I or group U using a computer-generated list". page 423<br>Comment: Random sequence generation was performed adequately |
| Allocation concealment (selection bias) | Low risk | "A case manager independent of the study randomly assigned patients to either group I or group U using a computer-generated list. Patient allocations were sealed in numbered envelopes by an independent evaluator, not involved in the interventions, who assessed outcomes at |

| | | |
|---|---|---|
| | | the beginning of the study, after initial integrated education (6 months) and after the follow-up period (6 months)". page 423<br>Comment: Allocation was adequately concealed |
| Blinding of participants and personnel (performance bias) | Unclear risk | Comment: Blinding of participants and personnel was not reported |
| Blinding of outcome assessment (detection bias) | Low risk | "Patient allocations were sealed in numbered envelopes by an independent evaluator,<br>not involved in the interventions, who assessed outcomes at the beginning of the study, after initial integrated education (6 months) and after the follow-up period (6 months)". page 423<br>Comment: Outcome assessment was not blinded, but outcome assessment was performed by an independent evaluator |
| Incomplete outcome data (attrition bias) | Low risk | "A total of 125 patients fulfilled the inclusion criteria, and 102 were enrolled into the integrated or usual care groups. A total of 42 and 43 patients in group I and group U, respectively, completed the study. Withdrawal rates were similar for both groups". page 424<br>Comment: The number of drop outs was relatively low and equally distributed over groups; also the reasons for withdrawal were comparable |
| Selective reporting (reporting bias) | Unclear risk | Comment: no signs of selective reporting, although only one outcome measure was reported |
| Other bias | Low risk | |

## Characteristics of excluded studies

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|---|---|
| *Blake 1990* | |
| **Reason for exclusion** | In the update of 2007; now excluded because it was published before 1995 |
| *Boxall 2005* | |
| **Reason for exclusion** | In the update of 2007; now excluded because included participants did not have solely COPD |
| *Carone 2002* | |
| **Reason for exclusion** | No results |
| *Cockcroft 1987* | |
| **Reason for exclusion** | In the update of 2007; now excluded because it was published before 1995 |
| *de Toledo 2006* | |
| **Reason for exclusion** | No self management |
| *Gourley 1998* | |
| **Reason for exclusion** | In the update of 2007; now excluded because it provided no self management |
| *Hesselink 2004* | |
| **Reason for exclusion** | Participants with COPD and asthma included |
| *Jerant 2009* | |
| **Reason for exclusion** | Participants with several chronic diseases included |
| *Kunik 2008* | |
| **Reason for exclusion** | Self management directed towards depression |
| *Lamers 2010* | |
| **Reason for exclusion** | Self management directed towards depression |
| *Littlejohns 1991* | |
| **Reason for exclusion** | In the update of 2007; now excluded because it was published before 1995 |
| *Lorig 1999* | |
| **Reason for exclusion** | Participants with several chronic diseases included |
| *Lorig 2003a* | |
| **Reason for exclusion** | Participants with several chronic diseases included |
| *Martin 2004* | |
| **Reason for exclusion** | In the update of 2007; now excluded because it incorporated solely an action plan (= only one component) |
| *Martin 2008* | |
| **Reason for exclusion** | No self management; home- versus hospital-based rehabilitation |
| *McGeoch 2006* | |
| **Reason for exclusion** | Solely action plan (= only one component), with only one contact moment |
| *Rootmensen 2008* | |
| **Reason for exclusion** | Only one contact moment |
| *Sridhar 2008* | |
| **Reason for exclusion** | Hospital-based rehabilitation |
| *Watson 1997* | |
| **Reason for exclusion** | In the update of 2007; now excluded because it incorporated solely an action plan (= only one component), with only one contact moment |
| *Wood-Baker 2006* | |
| **Reason for exclusion** | Solely action plan (= only one component), with only one contact moment |

## Excluded studies

*Blake 1990*
Blake RL Jr, Vandiver TA, Braun S, Bertuso DD, Straub V. A randomized controlled evaluation of a psychosocial intervention in adults with chronic lung disease. Family Medicine 1990;22:365-70.

*Boxall 2005*
Boxall AM, Barclay L, Sayers A, Caplan GA. 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(6):378-85.

*Carone 2002*
Carone M, Bertolotti G, Cerveri I, De Benedetto F, Fogliani V, Nardini S et al. EDU-CARE, a randomised, multicentre, parallel group study on education and quality of life in COPD. Monaldi Archives for Chest Disease 2002;57(1):25-9.

*Cockcroft 1987*
Cockcroft A, Bagnall P,Heslop A, Andersson N,Heaton R, Batstone J et al. Controlled trial of respiratory health worker visiting patients with chronic respiratory disability. British Medical Journal (Clin Res Ed) 1987;294(6566):225-8.

*de Toledo 2006*
de Toledo P, Jiménez S, del Pozo F, Roca J, Alonso A, Hernandez C. Telemedicine experience for chronic care in COPD. IEEE Transactions on Information Technology in Biomedicine 2006;10(3): 567-73.

*Gourley 1998*
Gourley GA, Portner TS, Gourley DR, Rigolosi EL, Holt JM,Solomon DK et al. Humanistic outcomes in the hypertension and COPD arms of a multicenter outcomes study. Journal of the American Pharmaceutical Association 1998;38(5):586-97.

*Hesselink 2004*
Hesselink AE, Penninx BW, van der Windt DA, van Duin BJ, de Vries P, Twisk JW et al. Effectiveness of an education programme by a general practice assistant for asthma and COPD patients: results from a randomised controlled trial. Patient Education and Counseling 2004;55(1):121-8.

*Jerant 2009*
Jerant A, Moore-Hill M, Franks P. Home-based, peer-led chronic illness self-management training: findings from a 1-year randomized controlled trial. Annals of Family Medicine 2009;7(4):319-27.

*Kunik 2008*
Kunik ME, Veazey C, Cully JA, Souchek J, Graham DP, Hopko D et al. COPD education and cognitive behavioral therapy group treatment for clinically significant symptoms of depression and anxiety in COPD patients: a randomized controlled trial. Psychological Medicine 2008;38(3):385-96.

*Lamers 2010*
Lamers F, Jonkers CC, Bosma H, Chavannes NH, Knottnerus JA, van Eijk JT. Improving quality of life in depressed COPD patients: effectiveness of a minimal psychological intervention. COPD 2010;7(5):315-22.

*Littlejohns 1991*
Littlejohns P, Baveystock CM, Parnell H, Jones P. Randomised controlled trial of the effectiveness of a respiratory health worker in reducing impairment, disability, and handicap due to chronic airflow imitation. Thorax 1991;46:559-64.

*Lorig 1999*
Lorig KR, Sobel DS, Stewart AL, Brown BW Jr, Bandura A, Ritter P et al. Evidence suggesting that a chronic disease self-management program can improve health status while reducing hospitalization: a randomized trial. Medical Care 1999;37(1):5-14.

*Lorig 2003a*
Lorig KR, Ritter PL, González VM. Hispanic chronic disease self-management: a randomized community-based outcome trial. Nursing Research 2003;52(6):361-9.

*Martin 2004*
Martin IR, McNamara D, Sutherland FR, Tilyard MW, Taylor DR. Care plans for acutely deteriorating COPD: a randomized controlled trial. Chronic Respiratory Disease 2004;1(4):191-5.

*Martin 2008*
Maltais F, Bourbeau J, Shapiro S, Lacasse Y, Perrault H, Baltzan M et al. Effects of home-based pulmonary rehabilitation in patients with chronic obstructive pulmonary disease: a randomized trial. Annals of Internal Medicine 2008;149(12):869-78.

*McGeoch 2006*
McGeoch GR, Willsman KJ, Dowson CA, Town GI, Frampton CM, McCartin FJ et al. Self-management plans in the primary care of patients with chronic obstructive pulmonary disease. Respirology 2006;11(5):611-8.

*Rootmensen 2008*
Rootmensen GN, van Keimpema AR, Looysen EE, van der Schaaf L, de Haan RJ, Jansen HM. The effects of additional care by a pulmonary nurse for asthma and COPD patients at a respiratory outpatient clinic: results from a double blind, randomized clinical trial. Patient Education and Counseling 2008;70(2):179-86.

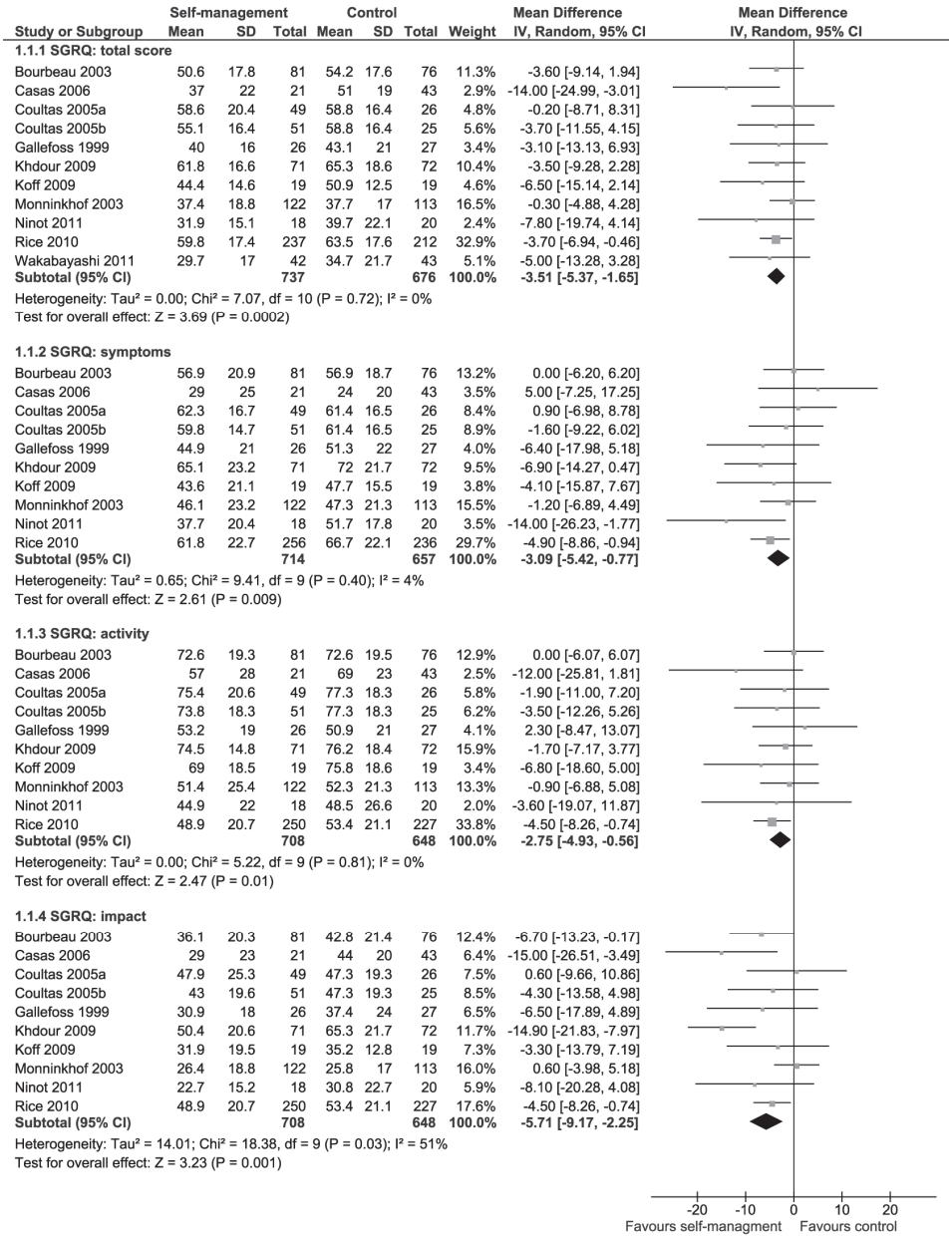
*Sridhar 2008*
Sridhar M, Taylor R, Dawson S, Roberts NJ, Partridge MR. A nurse led intermediate care package in patients who have been hospitalised with an acute exacerbation of chronic obstructive pulmonary disease. Thorax 2008;63(3):194-200.

*Watson 1997*
Watson PB, Town GI, Holbrook N, Dwan C, Toop LJ, Drennan CJ. Evaluation of a self-management plan for chronic obstructive pulmonary disease. European Respiratory Journal 1997;10(6):1267-71.

*Wood-Baker 2006*
Wood-Baker R, McGlone S, Venn A, Walters EH. Written action plans in chronic obstructive pulmonary disease increase appropriate treatment for acute exacerbations. Respirology 2006;11(5):619-26.

## DATA AND ANALYSES

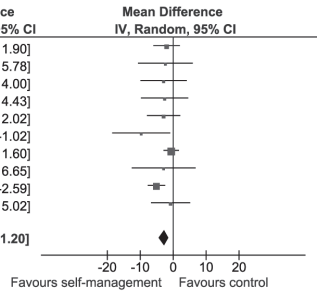
**Analysis 1.1** Comparison 1 Self management versus control, Outcome 1 HRQoL: SGRQ.



**Analysis 1.2** Comparison 1 Self management versus control, Outcome 2 HRQoL: SGRQ total score: change from baseline.

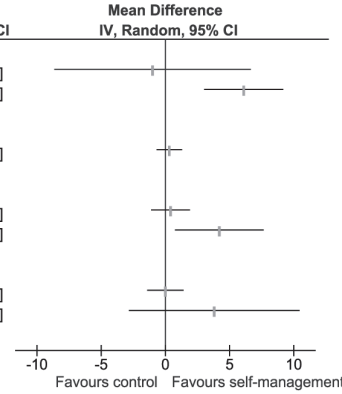
| Study or Subgroup | Mean Difference | SE | Self-management Total | Control Total | Weight | Mean Difference IV, Random, 95% CI |
|---|---|---|---|---|---|---|
| Bourbeau 2003 | -2 | 1.9898 | 81 | 76 | 12.5% | -2.00 [-5.90, 1.90] |
| Casas 2006 | -2.39 | 4.1684 | 21 | 41 | 3.2% | -2.39 [-10.56, 5.78] |
| Coultas 2005a | -2.9 | 3.5205 | 49 | 26 | 4.4% | -2.90 [-9.80, 4.00] |
| Coultas 2005b | -2.6 | 3.5871 | 51 | 26 | 4.2% | -2.60 [-9.63, 4.43] |
| Khdour 2009 | -2.9 | 2.5088 | 71 | 72 | 8.3% | -2.90 [-7.82, 2.02] |
| Koff 2009 | -9.7 | 4.4275 | 19 | 19 | 2.8% | -9.70 [-18.38, -1.02] |
| Monninkhof 2003 | -0.6 | 1.1225 | 122 | 113 | 30.7% | -0.60 [-2.80, 1.60] |
| Ninot 2011 | -2.9 | 4.8734 | 20 | 18 | 2.3% | -2.90 [-12.45, 6.65] |
| Rice 2010 | -5.1 | 1.28 | 233 | 204 | 25.5% | -5.10 [-7.61, -2.59] |
| Wakabayashi 2011 | -0.8 | 2.97 | 52 | 50 | 6.1% | -0.80 [-6.62, 5.02] |
| **Total (95% CI)** | | | **719** | **645** | **100.0%** | **-2.68 [-4.16, -1.20]** |

Heterogeneity: Tau² = 0.60; Chi² = 10.05, df = 9 (P = 0.35); I² = 10%
Test for overall effect: Z = 3.54 (P = 0.0004)



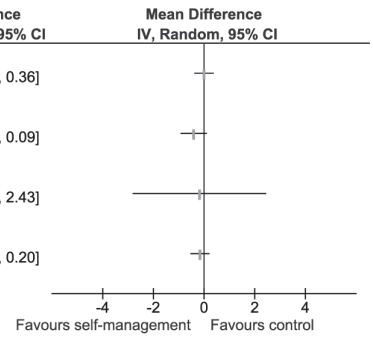

**Analysis 1.3** Comparison 1 Self management versus control, Outcome 3 HRQoL: CRQ.

| Study or Subgroup | Self-management Mean | SD | Total | Control Mean | SD | Total | Mean Difference IV, Random, 95% CI |
|---|---|---|---|---|---|---|---|
| **1.3.1 CRQ: dyspnoea** | | | | | | | |
| Faulkner 2010 | 13.5 | 7.6 | 6 | 14.5 | 6.6 | 8 | -1.00 [-8.61, 6.61] |
| Ghanem 2010 | 19.6 | 5.2 | 25 | 13.5 | 4.3 | 14 | 6.10 [3.06, 9.14] |
| **1.3.2 CRQ: mastery** | | | | | | | |
| Faulkner 2010 | 6.3 | 0.9 | 6 | 6 | 0.9 | 8 | 0.30 [-0.65, 1.25] |
| **1.3.3 CRQ: fatigue** | | | | | | | |
| Faulkner 2010 | 4.5 | 1.3 | 6 | 4.1 | 1.5 | 8 | 0.40 [-1.07, 1.87] |
| Ghanem 2010 | 17.4 | 5.4 | 25 | 13.2 | 5.1 | 14 | 4.20 [0.79, 7.61] |
| **1.3.4 CRQ: emotional function** | | | | | | | |
| Faulkner 2010 | 5.3 | 1.3 | 6 | 5.3 | 1.3 | 8 | 0.00 [-1.38, 1.38] |
| Ghanem 2010 | 33.5 | 7.2 | 25 | 29.7 | 11.4 | 14 | 3.80 [-2.80, 10.40] |



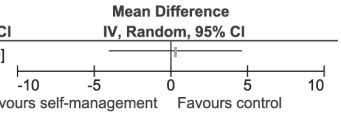

**Analysis 1.4** Comparison 1 Self management versus control, Outcome 4 HRQoL: CCQ.

| Study or Subgroup | Self-management Mean | SD | Total | Control Mean | SD | Total | Mean Difference IV, Random, 95% CI |
|---|---|---|---|---|---|---|---|
| **1.4.1 Total** | | | | | | | |
| Kheirabadi 2008 | 1.99 | 0.6 | 21 | 1.99 | 0.6 | 21 | 0.00 [-0.36, 0.36] |
| **1.4.2 Mental state** | | | | | | | |
| Kheirabadi 2008 | 1.9 | 0.77 | 21 | 2.31 | 0.87 | 21 | -0.41 [-0.91, 0.09] |
| **1.4.3 Symptoms** | | | | | | | |
| Kheirabadi 2008 | 2.01 | 6.1 | 21 | 2.19 | 0.37 | 21 | -0.18 [-2.79, 2.43] |
| **1.4.4 Functional state** | | | | | | | |
| Kheirabadi 2008 | 2.02 | 0.66 | 21 | 2.18 | 0.51 | 21 | -0.16 [-0.52, 0.20] |



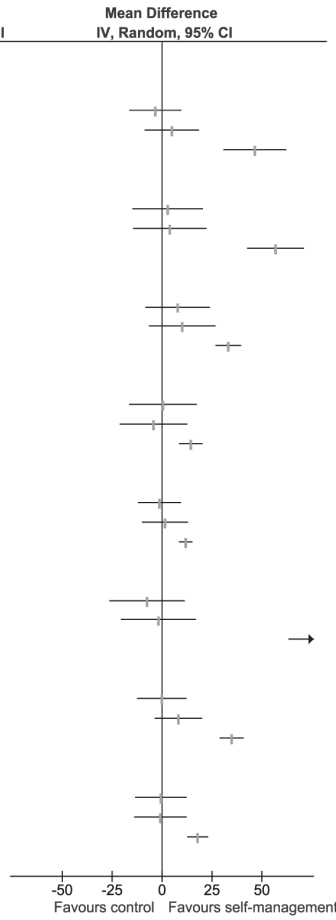
**Analysis 1.5** Comparison 1 Self management versus control, Outcome 5 HRQoL: SIP total score.

| Study or Subgroup | Self-management Mean | SD | Total | Control Mean | SD | Total | Mean Difference IV, Random, 95% CI |
|---|---|---|---|---|---|---|---|
| Emery 1998 | 10.7 | 7.4 | 23 | 10.4 | 7.8 | 25 | 0.30 [-4.00, 4.60] |




**Analysis 1.6** Comparison 1 Self management versus control, Outcome 6 HRQoL: SF-36.

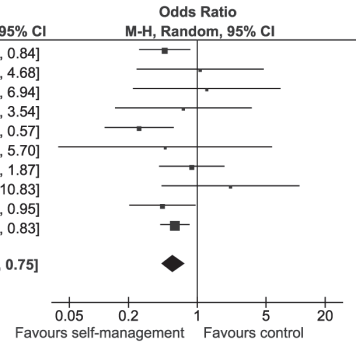
| Study or Subgroup | Self-management Mean | SD | Total | Control Mean | SD | Total | Mean Difference IV, Random, 95% CI |
|---|---|---|---|---|---|---|---|
| **1.6.1 SF-36—total** | | | | | | | |
| **1.6.2 SF-36—physical functioning** | | | | | | | |
| Coultas 2005a | 25.3 | 25.7 | 49 | 28.7 | 27.6 | 26 | -3.40 [-16.22, 9.42] |
| Coultas 2005b | 33.6 | 28.3 | 51 | 28.7 | 27.6 | 25 | 4.90 [-8.42, 18.22] |
| Ghanem 2010 | 75.08 | 14.31 | 25 | 28.58 | 27.51 | 14 | 46.50 [31.04, 61.96] |
| **1.6.3 SF-36—role limitations—physical** | | | | | | | |
| Coultas 2005a | 34.3 | 36.4 | 49 | 31.5 | 36.7 | 26 | 2.80 [-14.60, 20.20] |
| Coultas 2005b | 35.4 | 40 | 51 | 31.5 | 36.7 | 25 | 3.90 [-14.20, 22.00] |
| Ghanem 2010 | 64 | 26.1 | 25 | 7.14 | 18.16 | 14 | 56.86 [42.89, 70.83] |
| **1.6.4 SF-36—bodily pain** | | | | | | | |
| Coultas 2005a | 54.4 | 32.6 | 49 | 46.6 | 33.8 | 26 | 7.80 [-8.08, 23.68] |
| Coultas 2005b | 56.7 | 35.1 | 51 | 46.6 | 33.8 | 25 | 10.10 [-6.28, 26.48] |
| Ghanem 2010 | 61.2 | 11.3 | 25 | 28.01 | 8.14 | 14 | 33.19 [27.04, 39.34] |
| **1.6.5 SF-36—social limitations** | | | | | | | |
| Coultas 2005a | 70.8 | 37.6 | 49 | 70.3 | 33.7 | 26 | 0.50 [-16.19, 17.19] |
| Coultas 2005b | 66 | 37.1 | 51 | 70.3 | 33.7 | 25 | -4.30 [-20.98, 12.38] |
| Ghanem 2010 | 54.76 | 13.12 | 25 | 40.39 | 4.34 | 14 | 14.37 [8.75, 19.99] |
| **1.6.6 SF-36—mental health** | | | | | | | |
| Coultas 2005a | 69.7 | 19.6 | 49 | 71 | 23.5 | 26 | -1.30 [-11.87, 9.27] |
| Coultas 2005b | 72.5 | 23.6 | 51 | 71 | 23.5 | 25 | 1.50 [-9.76, 12.76] |
| Ghanem 2010 | 48 | 5.66 | 25 | 36.15 | 4.17 | 14 | 11.85 [8.74, 14.96] |
| **1.6.7 SF-36—role limitations—emotional** | | | | | | | |
| Coultas 2005a | 68.5 | 40.1 | 49 | 76 | 38.7 | 26 | -7.50 [-26.14, 11.14] |
| Coultas 2005b | 74.2 | 39 | 51 | 76 | 38.7 | 25 | -1.80 [-20.37, 16.77] |
| Ghanem 2010 | 96 | 20 | 25 | 13.27 | 33.37 | 14 | 82.73 [63.57, 101.89] |
| **1.6.8 SF-36—vitality, energy, fatigue** | | | | | | | |
| Coultas 2005a | 25.8 | 27.4 | 49 | 25.9 | 24.4 | 26 | -0.10 [-12.22, 12.02] |
| Coultas 2005b | 34.1 | 24.3 | 51 | 25.9 | 24.4 | 25 | 8.20 [-3.46, 19.86] |
| Ghanem 2010 | 79.6 | 10.89 | 25 | 44.78 | 7.33 | 14 | 34.82 [29.08, 40.56] |
| **1.6.9 SF-36—general health** | | | | | | | |
| Coultas 2005a | 40 | 27.1 | 49 | 40.6 | 26.4 | 26 | -0.60 [-13.27, 12.07] |
| Coultas 2005b | 39.8 | 27.9 | 51 | 40.6 | 26.4 | 25 | -0.80 [-13.67, 12.07] |
| Ghanem 2010 | 52 | 9.68 | 25 | 34.17 | 6.12 | 14 | 17.83 [12.86, 22.80] |



**Analysis 1.7** Comparison 1 Self management versus control, Outcome 7 Respiratory-related hospital admissions.

| Study or Subgroup | Self-management Events | Total | Control Events | Total | Weight | Odds Ratio M-H, Random, 95% CI |
|---|---|---|---|---|---|---|
| Bourbeau 2003 | 31 | 96 | 48 | 95 | 17.3% | 0.47 [0.26, 0.84] |
| Coultas 2005a | 6 | 49 | 3 | 26 | 3.4% | 1.07 [0.24, 4.68] |
| Coultas 2005b | 5 | 51 | 2 | 25 | 2.5% | 1.25 [0.23, 6.94] |
| Gallefoss 1999 | 3 | 31 | 4 | 31 | 2.9% | 0.72 [0.15, 3.54] |
| Khdour 2009 | 11 | 71 | 30 | 72 | 10.5% | 0.26 [0.12, 0.57] |
| Koff 2009 | 1 | 19 | 2 | 19 | 1.2% | 0.47 [0.04, 5.70] |
| Monninkhof 2003 | 15 | 127 | 16 | 121 | 11.5% | 0.88 [0.41, 1.87] |
| Ninot 2011 | 5 | 18 | 3 | 20 | 2.9% | 2.18 [0.44, 10.83] |
| Rea 2004 | 18 | 83 | 20 | 52 | 11.2% | 0.44 [0.21, 0.95] |
| Rice 2010 | 79 | 372 | 116 | 371 | 36.6% | 0.59 [0.43, 0.83] |
| **Total (95% CI)** | | **917** | | **832** | **100.0%** | **0.57 [0.43, 0.75]** |
| Total events | 174 | | 244 | | | |

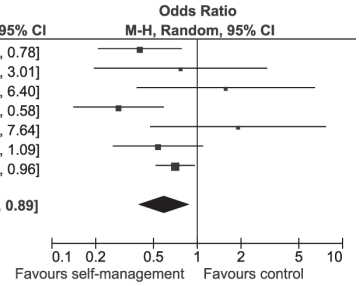
Heterogeneity: Tau² = 0.03; Chi² = 10.35, df = 9 (P = 0.32); I² = 13%
Test for overall effect: Z = 3.96 (P < 0.0001)




**Analysis 1.8** Comparison 1 Self management versus control, Outcome 8 All-cause hospital admissions.

| Study or Subgroup | Self-management Events | Total | Control Events | Total | Weight | Odds Ratio M-H, Random, 95% CI |
|---|---|---|---|---|---|---|
| Casas 2006 | 29 | 65 | 60 | 90 | 17.9% | 0.40 [0.21, 0.78] |
| Coultas 2005a | 6 | 49 | 4 | 26 | 6.8% | 0.77 [0.20, 3.01] |
| Coultas 2005b | 9 | 51 | 3 | 25 | 6.5% | 1.57 [0.39, 6.40] |
| Khdour 2009 | 18 | 71 | 39 | 72 | 16.6% | 0.29 [0.14, 0.58] |
| Ninot 2011 | 7 | 18 | 5 | 20 | 6.7% | 1.91 [0.48, 7.64] |
| Rea 2004 | 29 | 83 | 26 | 52 | 16.6% | 0.54 [0.26, 1.09] |
| Rice 2010 | 115 | 372 | 144 | 371 | 28.9% | 0.71 [0.52, 0.96] |
| **Total (95% CI)** | | **709** | | **656** | **100.0%** | **0.60 [0.40, 0.89]** |
| Total events | 213 | | 281 | | | |

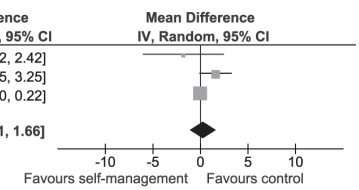
Heterogeneity: Tau² = 0.12; Chi² = 11.34, df = 6 (P = 0.08); I² = 47%
Test for overall effect: Z = 2.55 (P = 0.01)



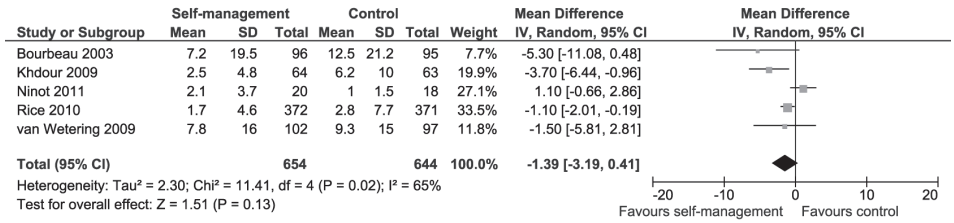

**Analysis 1.9** Comparison 1 Self management versus control, Outcome 9 Respiratory-related hospital admissions: days.

| Study or Subgroup | Self-management Mean | SD | Total | Control Mean | SD | Total | Weight | Mean Difference IV, Random, 95% CI |
|---|---|---|---|---|---|---|---|---|
| Gallefoss 1999 | 0.7 | 2 | 26 | 2.5 | 11 | 27 | 8.6% | -1.80 [-6.02, 2.42] |
| Ninot 2011 | 1.9 | 3.7 | 20 | 0.3 | 0.7 | 18 | 31.5% | 1.60 [-0.05, 3.25] |
| van Wetering 2009 | 0.36 | 1 | 102 | 0.4 | 0.78 | 79 | 59.9% | -0.04 [-0.30, 0.22] |
| **Total (95% CI)** | | | **148** | | | **124** | **100.0%** | **0.33 [-1.01, 1.66]** |

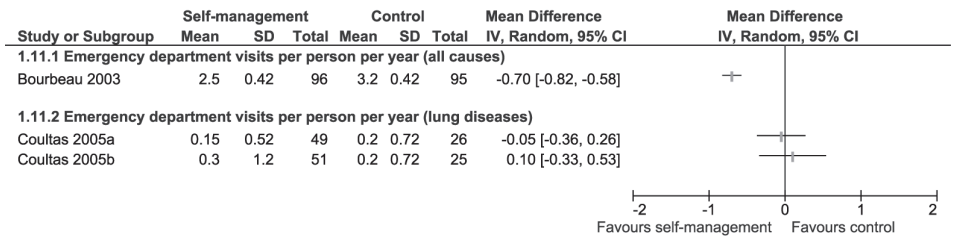
Heterogeneity: Tau² = 0.75; Chi² = 4.38, df = 2 (P = 0.11); I² = 54%
Test for overall effect: Z = 0.48 (P = 0.63)



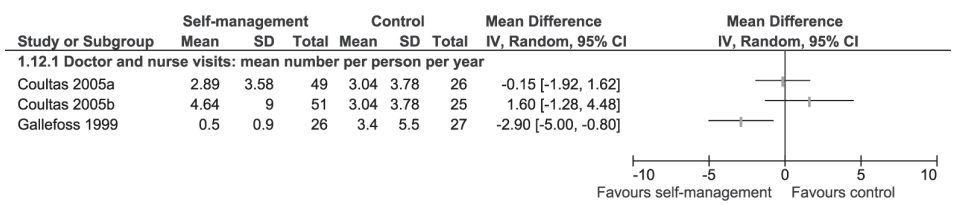
**Analysis 1.10** Comparison 1 Self management versus control, Outcome 10 All-cause hospital admissions: days.



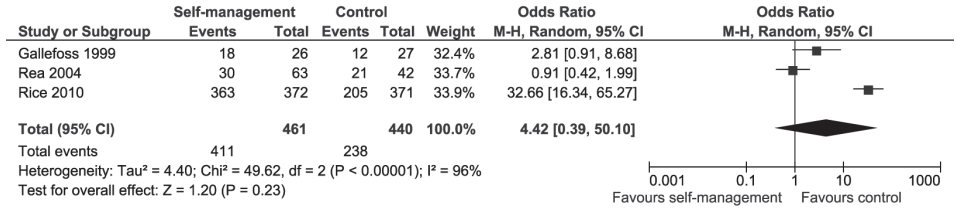

**Analysis 1.11** Comparison 1 Self management versus control, Outcome 11 Emergency department visits per person per year.



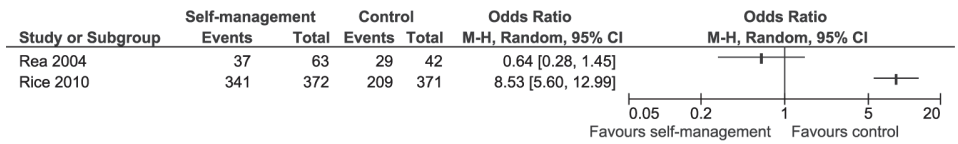

**Analysis 1.12** Comparison 1 Self management versus control, Outcome 12 Doctor and nurse visits: mean number per person per year.



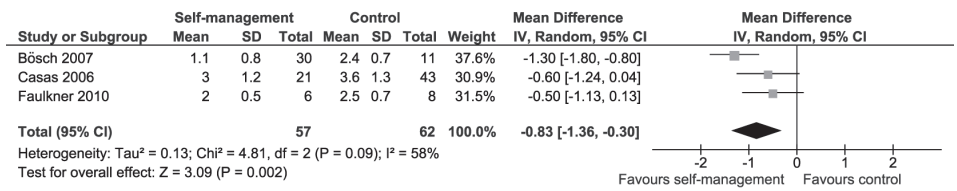
**Analysis 1.13** Comparison 1 Self management versus control, Outcome 13 Participants using at least one course of oral steroids.



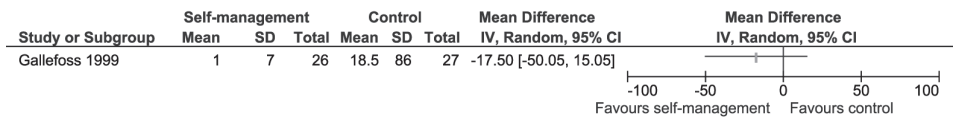

**Analysis 1.14** Comparison 1 Self management versus control, Outcome 14 Participants using at least one course of antibiotics.




**Analysis 1.15** Comparison 1 Self management versus control, Outcome 15 (Modified) Medical Research Council Dyspnoea Scale ((m)MRC).




**Analysis 1.16** Comparison 1 Self management versus control, Outcome 16 Days lost from work: mean number per person per year.



**Analysis 1.17** Comparison 1 Self management versus control, Outcome 17 Lung function: $FEV_1$ (litres).

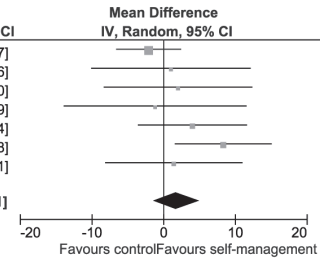
| | Self-management | | | Control | | | | Mean Difference | Mean Difference |
|---|---|---|---|---|---|---|---|---|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Random, 95% CI | IV, Random, 95% CI |
| Bösch 2007 | 1.2 | 0.5 | 30 | 1.3 | 0.5 | 11 | 10.2% | -0.10 [-0.45, 0.25] | |
| Emery 1998 | 1.07 | 0.46 | 23 | 1.04 | 0.4 | 25 | 20.2% | 0.03 [-0.21, 0.27] | |
| Faulkner 2010 | 1.94 | 0.52 | 6 | 1.69 | 0.48 | 8 | 4.3% | 0.25 [-0.28, 0.78] | |
| Khdour 2009 | 1.19 | 0.56 | 71 | 1.05 | 0.49 | 72 | 40.7% | 0.14 [-0.03, 0.31] | |
| Ninot 2011 | 1.71 | 0.56 | 20 | 1.46 | 0.6 | 18 | 8.8% | 0.25 [-0.12, 0.62] | |
| Wakabayashi 2011 | 1.53 | 0.6 | 42 | 1.57 | 0.7 | 43 | 15.8% | -0.04 [-0.32, 0.24] | |
| **Total (95% CI)** | | | **192** | | | **177** | **100.0%** | **0.08 [-0.03, 0.19]** | |

Heterogeneity: Tau² = 0.00; Chi² = 3.59, df = 5 (P = 0.61); I² = 0%
Test for overall effect: Z = 1.41 (P = 0.16)


**Analysis 1.18** Comparison 1 Self management versus control, Outcome 18 Lung function: $FEV_1$ (% of predicted).

| | Self-management | | | Control | | | | Mean Difference | Mean Difference |
|---|---|---|---|---|---|---|---|---|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Random, 95% CI | IV, Random, 95% CI |
| Bourbeau 2003 | 41 | 13.4 | 79 | 43.1 | 13.9 | 66 | 33.2% | -2.10 [-6.57, 2.37] | |
| Casas 2006 | 45 | 18 | 16 | 44 | 18 | 28 | 7.8% | 1.00 [-10.06, 12.06] | |
| Emery 1998 | 41 | 20 | 23 | 39 | 16 | 25 | 8.9% | 2.00 [-8.30, 12.30] | |
| Faulkner 2010 | 65.3 | 11.9 | 6 | 66.5 | 12.1 | 8 | 6.0% | -1.20 [-13.89, 11.49] | |
| Gallefoss 1999 | 62 | 14 | 26 | 58 | 14 | 27 | 15.3% | 4.00 [-3.54, 11.54] | |
| Rea 2004 | 53.9 | 19.2 | 71 | 45.6 | 17.2 | 46 | 18.6% | 8.30 [1.62, 14.98] | |
| Wakabayashi 2011 | 61.9 | 19.7 | 42 | 60.5 | 24.8 | 43 | 10.2% | 1.40 [-8.11, 10.91] | |
| **Total (95% CI)** | | | **263** | | | **243** | **100.0%** | **1.78 [-1.44, 5.01]** | |

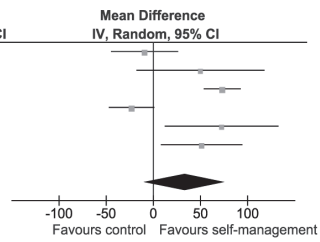
Heterogeneity: Tau² = 2.94; Chi² = 7.08, df = 6 (P = 0.31); I² = 15%
Test for overall effect: Z = 1.08 (P = 0.28)




**Analysis 1.19** Comparison 1 Self management versus control, Outcome 19 Exercise capacity: 6MWT.

| | Self-management | | | Control | | | | Mean Difference | Mean Difference |
|---|---|---|---|---|---|---|---|---|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Random, 95% CI | IV, Random, 95% CI |
| Bourbeau 2003 | 289.2 | 110 | 67 | 298.5 | 86 | 53 | 17.6% | -9.30 [-44.37, 25.77] | |
| Bösch 2007 | 436 | 94 | 30 | 386 | 99 | 11 | 13.3% | 50.00 [-17.48, 117.48] | |
| Ghanem 2010 | 141.7 | 23.1 | 25 | 68.6 | 32.1 | 14 | 19.2% | 73.10 [54.00, 92.20] | |
| Monninkhof 2003 | 415.5 | 104.7 | 127 | 438.6 | 85.3 | 120 | 18.8% | -23.10 [-46.86, 0.66] | |
| Ninot 2011 | 488.1 | 73.8 | 20 | 415.6 | 109 | 18 | 14.4% | 72.50 [12.65, 132.35] | |
| Wakabayashi 2011 | 492.2 | 90.5 | 42 | 440.9 | 109.9 | 43 | 16.7% | 51.30 [8.54, 94.06] | |
| **Total (95% CI)** | | | **311** | | | **259** | **100.0%** | **33.69 [-9.12, 76.50]** | |

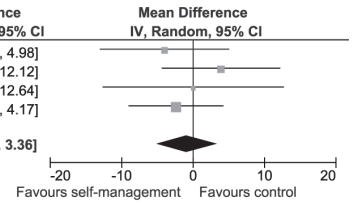
Heterogeneity: Tau² = 2388.69; Chi² = 46.56, df = 5 (P < 0.00001); I² = 89%
Test for overall effect: Z = 1.54 (P = 0.12)



**Analysis 1.20** Comparison 1 Self management versus control, Outcome 20 Lung function: $FEV_1/FVC$.

| Study or Subgroup | Self-management Mean | SD | Total | Control Mean | SD | Total | Weight | Mean Difference IV, Random, 95% CI |
|---|---|---|---|---|---|---|---|---|
| Casas 2006 | 45 | 16 | 17 | 49 | 15 | 38 | 21.9% | -4.00 [-12.98, 4.98] |
| Faulkner 2010 | 60.5 | 6.7 | 6 | 56.6 | 9 | 8 | 26.1% | 3.90 [-4.32, 12.12] |
| Ninot 2011 | 51.5 | 17.9 | 20 | 51.48 | 21.4 | 18 | 11.1% | 0.02 [-12.60, 12.64] |
| Wakabayashi 2011 | 56.5 | 15 | 42 | 58.9 | 15.9 | 43 | 40.9% | -2.40 [-8.97, 4.17] |
| **Total (95% CI)** | | | **85** | | | **107** | **100.0%** | **-0.84 [-5.04, 3.36]** |

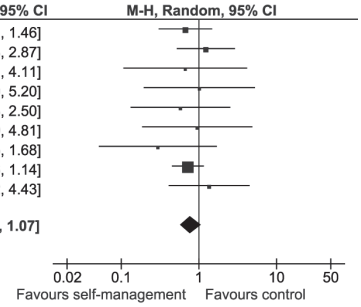
Heterogeneity: Tau² = 0.00; Chi² = 1.99, df = 3 (P = 0.58); I² = 0%
Test for overall effect: Z = 0.39 (P = 0.70)



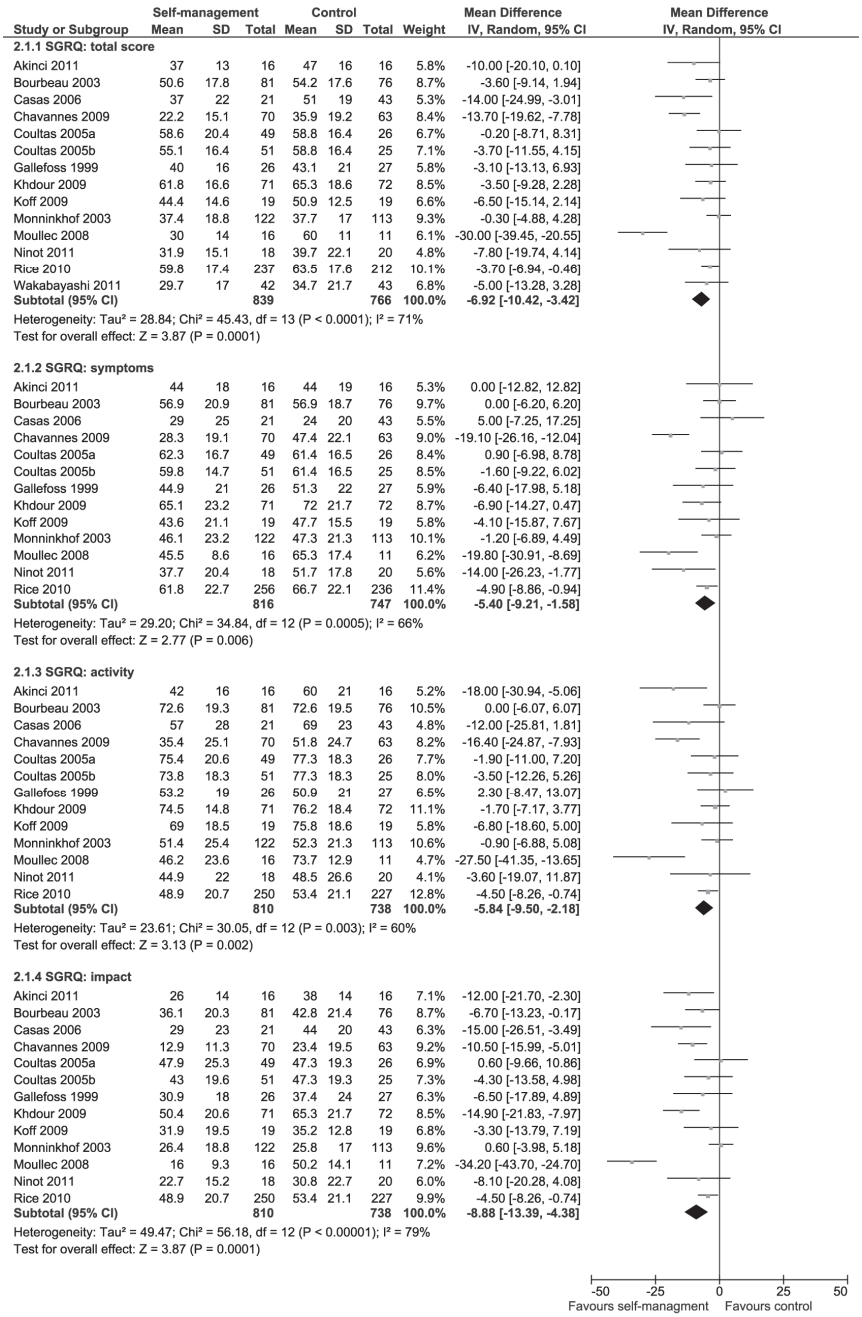

**Analysis 1.21** Comparison 1 Self management versus control, Outcome 21 Mortality.

| Study or Subgroup | Self-management Events | Total | Control Events | Total | Weight | Odds Ratio M-H, Random, 95% CI |
|---|---|---|---|---|---|---|
| Bourbeau 2003 | 13 | 96 | 18 | 95 | 15.9% | 0.67 [0.31, 1.46] |
| Casas 2006 | 12 | 65 | 14 | 90 | 13.4% | 1.23 [0.53, 2.87] |
| Coultas 2005a | 2 | 72 | 3 | 73 | 2.9% | 0.67 [0.11, 4.11] |
| Coultas 2005b | 3 | 72 | 3 | 73 | 3.6% | 1.01 [0.20, 5.20] |
| Khdour 2009 | 3 | 87 | 5 | 86 | 4.5% | 0.58 [0.13, 2.50] |
| Monninkhof 2003 | 3 | 127 | 3 | 121 | 3.7% | 0.95 [0.19, 4.81] |
| Rea 2004 | 2 | 83 | 4 | 52 | 3.2% | 0.30 [0.05, 1.68] |
| Rice 2010 | 36 | 372 | 48 | 371 | 45.9% | 0.72 [0.46, 1.14] |
| van Wetering 2009 | 7 | 102 | 5 | 97 | 6.9% | 1.36 [0.42, 4.43] |
| **Total (95% CI)** | | **1076** | | **1058** | **100.0%** | **0.79 [0.58, 1.07]** |
| Total events | 81 | | 103 | | | |

Heterogeneity: Tau² = 0.00; Chi² = 3.75, df = 8 (P = 0.88); I² = 0%
Test for overall effect: Z = 1.53 (P = 0.13)



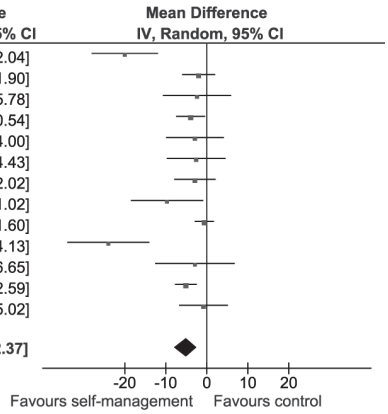
**Analysis 2.1** Comparison 2 Sensitivity analyses with inclusion of CCTs, Outcome 1 HRQoL: SGRQ (with CCTs).



**Analysis 2.2** Comparison 2 Sensitivity analyses with inclusion of CCTs, Outcome 2 HRQoL: SGRQ total score: change from baseline (with CCTs).

| Study or Subgroup | Mean Difference | SE | Weight | Mean Difference IV, Random, 95% CI |
|---|---|---|---|---|
| Akinci 2011 | -20 | 4.0619 | 5.9% | -20.00 [-27.96, -12.04] |
| Bourbeau 2003 | -2 | 1.9898 | 9.9% | -2.00 [-5.90, 1.90] |
| Casas 2006 | -2.39 | 4.1684 | 5.8% | -2.39 [-10.56, 5.78] |
| Chavannes 2009 | -3.94 | 1.7365 | 10.4% | -3.94 [-7.34, -0.54] |
| Coultas 2005a | -2.9 | 3.5205 | 6.8% | -2.90 [-9.80, 4.00] |
| Coultas 2005b | -2.6 | 3.5871 | 6.7% | -2.60 [-9.63, 4.43] |
| Khdour 2009 | -2.9 | 2.5088 | 8.8% | -2.90 [-7.82, 2.02] |
| Koff 2009 | -9.7 | 4.4275 | 5.4% | -9.70 [-18.38, -1.02] |
| Monninkhof 2003 | -0.6 | 1.1225 | 11.5% | -0.60 [-2.80, 1.60] |
| Moullec 2008 | -24 | 5.0379 | 4.6% | -24.00 [-33.87, -14.13] |
| Ninot 2011 | -2.9 | 4.8734 | 4.8% | -2.90 [-12.45, 6.65] |
| Rice 2010 | -5.1 | 1.28 | 11.3% | -5.10 [-7.61, -2.59] |
| Wakabayashi 2011 | -0.8 | 2.97 | 7.9% | -0.80 [-6.62, 5.02] |
| **Total (95% CI)** | | | **100.0%** | **-5.05 [-7.73, -2.37]** |

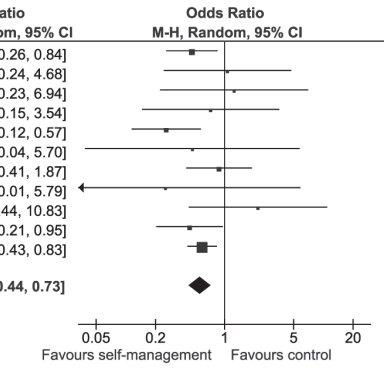
Heterogeneity: Tau² = 14.94; Chi² = 44.95, df = 12 (P < 0.0001); I² = 73%
Test for overall effect: Z = 3.69 (P = 0.0002)




**Analysis 2.3** Comparison 2 Sensitivity analyses with inclusion of CCTs, Outcome 3 Respiratory-related hospital admissions (with CCTs).

| Study or Subgroup | Self-management Events | Self-management Total | Control Events | Control Total | Weight | Odds Ratio M-H, Random, 95% CI |
|---|---|---|---|---|---|---|
| Bourbeau 2003 | 31 | 96 | 48 | 95 | 16.5% | 0.47 [0.26, 0.84] |
| Coultas 2005a | 6 | 49 | 3 | 26 | 2.9% | 1.07 [0.24, 4.68] |
| Coultas 2005b | 5 | 51 | 2 | 25 | 2.2% | 1.25 [0.23, 6.94] |
| Gallefoss 1999 | 3 | 31 | 4 | 31 | 2.5% | 0.72 [0.15, 3.54] |
| Khdour 2009 | 11 | 71 | 30 | 72 | 9.5% | 0.26 [0.12, 0.57] |
| Koff 2009 | 1 | 19 | 2 | 19 | 1.0% | 0.47 [0.04, 5.70] |
| Monninkhof 2003 | 15 | 127 | 16 | 121 | 10.5% | 0.88 [0.41, 1.87] |
| Moullec 2008 | 0 | 11 | 2 | 16 | 0.7% | 0.25 [0.01, 5.79] |
| Ninot 2011 | 5 | 18 | 3 | 20 | 2.5% | 2.18 [0.44, 10.83] |
| Rea 2004 | 18 | 83 | 20 | 52 | 10.2% | 0.44 [0.21, 0.95] |
| Rice 2010 | 79 | 372 | 116 | 371 | 41.6% | 0.59 [0.43, 0.83] |
| **Total (95% CI)** | | **928** | | **848** | **100.0%** | **0.57 [0.44, 0.73]** |
| Total events | 174 | | 246 | | | |

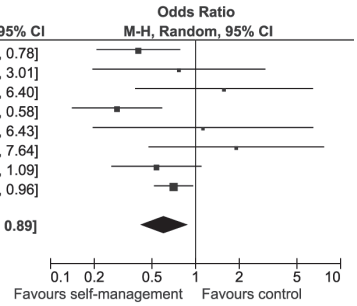
Heterogeneity: Tau² = 0.01; Chi² = 10.61, df = 10 (P = 0.39); I² = 6%
Test for overall effect: Z = 4.39 (P < 0.0001)



**Analysis 2.4** Comparison 2 Sensitivity analyses with inclusion of CCTs, Outcome 4 All-cause hospital admissions (with CCTs).

| Study or Subgroup | Self-management Events | Total | Control Events | Total | Weight | Odds Ratio M-H, Random, 95% CI |
|---|---|---|---|---|---|---|
| Casas 2006 | 29 | 65 | 60 | 90 | 17.1% | 0.40 [0.21, 0.78] |
| Coultas 2005a | 6 | 49 | 4 | 26 | 6.2% | 0.77 [0.20, 3.01] |
| Coultas 2005b | 9 | 51 | 3 | 25 | 6.0% | 1.57 [0.39, 6.40] |
| Khdour 2009 | 18 | 71 | 39 | 72 | 15.8% | 0.29 [0.14, 0.58] |
| Moullec 2008 | 3 | 11 | 4 | 16 | 4.1% | 1.13 [0.20, 6.43] |
| Ninot 2011 | 7 | 18 | 5 | 20 | 6.1% | 1.91 [0.48, 7.64] |
| Rea 2004 | 29 | 83 | 26 | 52 | 15.8% | 0.54 [0.26, 1.09] |
| Rice 2010 | 115 | 372 | 144 | 371 | 29.0% | 0.71 [0.52, 0.96] |
| **Total (95% CI)** | | **720** | | **672** | **100.0%** | **0.61 [0.42, 0.89]** |
| Total events | 216 | | 285 | | | |

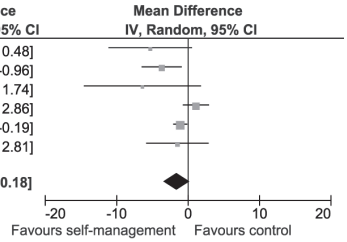
Heterogeneity: Tau² = 0.10; Chi² = 11.80, df = 7 (P = 0.11); I² = 41%
Test for overall effect: Z = 2.59 (P = 0.010)




**Analysis 2.5** Comparison 2 Sensitivity analyses with inclusion of CCTs, Outcome 5 All-cause hospital admissions: days (with CCTs).

| Study or Subgroup | Self-management Mean | SD | Total | Control Mean | SD | Total | Weight | Mean Difference IV, Random, 95% CI |
|---|---|---|---|---|---|---|---|---|
| Bourbeau 2003 | 7.2 | 19.5 | 96 | 12.5 | 21.2 | 95 | 7.6% | -5.30 [-11.08, 0.48] |
| Khdour 2009 | 2.5 | 4.8 | 64 | 6.2 | 10 | 63 | 19.2% | -3.70 [-6.44, -0.96] |
| Moullec 2008 | 1.5 | 3.4 | 11 | 7.9 | 16.1 | 16 | 4.3% | -6.40 [-14.54, 1.74] |
| Ninot 2011 | 2.1 | 3.7 | 20 | 1 | 1.5 | 18 | 25.8% | 1.10 [-0.66, 2.86] |
| Rice 2010 | 1.7 | 4.6 | 372 | 2.8 | 7.7 | 371 | 31.6% | -1.10 [-2.01, -0.19] |
| van Wetering 2009 | 7.8 | 16 | 102 | 9.3 | 15 | 97 | 11.6% | -1.50 [-5.81, 2.81] |
| **Total (95% CI)** | | | **665** | | | **660** | **100.0%** | **-1.62 [-3.42, 0.18]** |

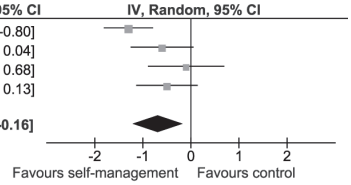
Heterogeneity: Tau² = 2.45; Chi² = 13.10, df = 5 (P = 0.02); I² = 62%
Test for overall effect: Z = 1.77 (P = 0.08)




**Analysis 2.6** Comparison 2 Sensitivity analyses with inclusion of CCTs, Outcome 6 (Modified) Medical Research Council Dyspnoea Scale ((m)MRC) (with CCTs).

| Study or Subgroup | Self-management Mean | SD | Total | Control Mean | SD | Total | Weight | Mean Difference IV, Random, 95% CI |
|---|---|---|---|---|---|---|---|---|
| Bösch 2007 | 1.1 | 0.8 | 30 | 2.4 | 0.7 | 11 | 29.1% | -1.30 [-1.80, -0.80] |
| Casas 2006 | 3 | 1.2 | 21 | 3.6 | 1.3 | 43 | 24.8% | -0.60 [-1.24, 0.04] |
| Chavannes 2009 | 2.1 | 2.6 | 80 | 2.2 | 2.3 | 70 | 20.9% | -0.10 [-0.88, 0.68] |
| Faulkner 2010 | 2 | 0.5 | 6 | 2.5 | 0.7 | 8 | 25.2% | -0.50 [-1.13, 0.13] |
| **Total (95% CI)** | | | **137** | | | **132** | **100.0%** | **-0.67 [-1.19, -0.16]** |

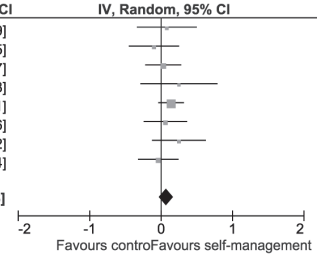
Heterogeneity: Tau² = 0.17; Chi² = 8.04, df = 3 (P = 0.05); I² = 63%
Test for overall effect: Z = 2.56 (P = 0.01)



**Analysis 2.7** Comparison 2 Sensitivity analyses with inclusion of CCTs, Outcome 7 Lung function: $FEV_1$ (liters) (with CCTs).

| Study or Subgroup | Self-management Mean | SD | Total | Control Mean | SD | Total | Weight | Mean Difference IV, Random, 95% CI |
|---|---|---|---|---|---|---|---|---|
| Akinci 2011 | 1.13 | 0.59 | 16 | 1.05 | 0.6 | 16 | 5.9% | 0.08 [-0.33, 0.49] |
| Bösch 2007 | 1.2 | 0.5 | 30 | 1.3 | 0.5 | 11 | 8.4% | -0.10 [-0.45, 0.25] |
| Emery 1998 | 1.07 | 0.46 | 23 | 1.04 | 0.4 | 25 | 16.7% | 0.03 [-0.21, 0.27] |
| Faulkner 2010 | 1.94 | 0.52 | 6 | 1.69 | 0.48 | 8 | 3.5% | 0.25 [-0.28, 0.78] |
| Khdour 2009 | 1.19 | 0.56 | 71 | 1.05 | 0.49 | 72 | 33.7% | 0.14 [-0.03, 0.31] |
| Moullec 2008 | 1.31 | 0.4 | 16 | 1.25 | 0.38 | 11 | 11.3% | 0.06 [-0.24, 0.36] |
| Ninot 2011 | 1.71 | 0.56 | 20 | 1.46 | 0.6 | 18 | 7.3% | 0.25 [-0.12, 0.62] |
| Wakabayashi 2011 | 1.53 | 0.6 | 42 | 1.57 | 0.7 | 43 | 13.1% | -0.04 [-0.32, 0.24] |
| **Total (95% CI)** | | | **224** | | | **204** | **100.0%** | **0.08 [-0.02, 0.18]** |

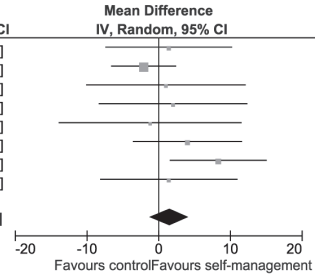
Heterogeneity: Tau² = 0.00; Chi² = 3.60, df = 7 (P = 0.82); I² = 0%
Test for overall effect: Z = 1.51 (P = 0.13)




**Analysis 2.8** Comparison 2 Sensitivity analyses with inclusion of CCTs, Outcome 8 Lung function: $FEV_1$ (% of predicted) (with CCTs).

| Study or Subgroup | Self-management Mean | SD | Total | Control Mean | SD | Total | Weight | Mean Difference IV, Random, 95% CI |
|---|---|---|---|---|---|---|---|---|
| Akinci 2011 | 40.7 | 13.2 | 16 | 39.3 | 12.1 | 16 | 9.5% | 1.40 [-7.37, 10.17] |
| Bourbeau 2003 | 41 | 13.4 | 79 | 43.1 | 13.9 | 66 | 35.7% | -2.10 [-6.57, 2.37] |
| Casas 2006 | 45 | 18 | 16 | 44 | 18 | 28 | 6.0% | 1.00 [-10.06, 12.06] |
| Emery 1998 | 41 | 20 | 23 | 39 | 16 | 25 | 6.9% | 2.00 [-8.30, 12.30] |
| Faulkner 2010 | 65.3 | 11.9 | 6 | 66.5 | 12.1 | 8 | 4.6% | -1.20 [-13.89, 11.49] |
| Gallefoss 1999 | 62 | 14 | 26 | 58 | 14 | 27 | 12.9% | 4.00 [-3.54, 11.54] |
| Rea 2004 | 53.9 | 19.2 | 71 | 45.6 | 17.2 | 46 | 16.3% | 8.30 [1.62, 14.98] |
| Wakabayashi 2011 | 61.9 | 19.7 | 42 | 60.5 | 24.8 | 43 | 8.1% | 1.40 [-8.11, 10.91] |
| **Total (95% CI)** | | | **279** | | | **259** | **100.0%** | **1.51 [-1.21, 4.23]** |

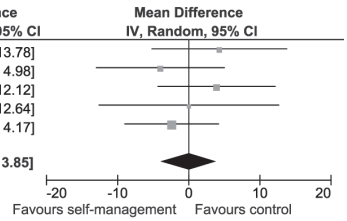
Heterogeneity: Tau² = 0.20; Chi² = 7.08, df = 7 (P = 0.42); I² = 1%
Test for overall effect: Z = 1.09 (P = 0.28)




**Analysis 2.9** Comparison 2 Sensitivity analyses with inclusion of CCTs, Outcome 9 Lung function: $FEV_1$/FVC (with CCTs).

| Study or Subgroup | Self-management Mean | SD | Total | Control Mean | SD | Total | Weight | Mean Difference IV, Random, 95% CI |
|---|---|---|---|---|---|---|---|---|
| Akinci 2011 | 49.7 | 12.8 | 16 | 45.4 | 14.5 | 16 | 16.4% | 4.30 [-5.18, 13.78] |
| Casas 2006 | 45 | 16 | 17 | 49 | 15 | 38 | 18.3% | -4.00 [-12.98, 4.98] |
| Faulkner 2010 | 60.5 | 6.7 | 6 | 56.6 | 9 | 8 | 21.8% | 3.90 [-4.32, 12.12] |
| Ninot 2011 | 51.5 | 17.9 | 20 | 51.48 | 21.4 | 18 | 9.3% | 0.02 [-12.60, 12.64] |
| Wakabayashi 2011 | 56.5 | 15 | 42 | 58.9 | 15.9 | 43 | 34.2% | -2.40 [-8.97, 4.17] |
| **Total (95% CI)** | | | **101** | | | **123** | **100.0%** | **0.01 [-3.83, 3.85]** |

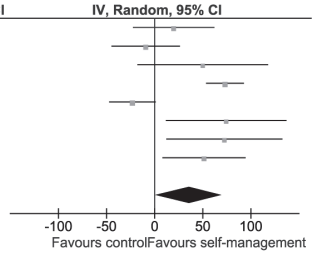
Heterogeneity: Tau² = 0.00; Chi² = 2.93, df = 4 (P = 0.57); I² = 0%
Test for overall effect: Z = 0.00 (P = 1.00)



**Analysis 2.10** Comparison 2 Sensitivity analyses with inclusion of CCTs, Outcome 10 Exercise capacity: 6MWT (with CCTs).

| | Self-management | | | Control | | | | Mean Difference |
|---|---|---|---|---|---|---|---|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Random, 95% CI |
| Akinci 2011 | 190.3 | 65 | 16 | 170.6 | 55.4 | 16 | 12.8% | 19.70 [-22.15, 61.55] |
| Bourbeau 2003 | 289.2 | 110 | 67 | 298.5 | 86 | 53 | 13.6% | -9.30 [-44.37, 25.77] |
| Bösch 2007 | 436 | 94 | 30 | 386 | 99 | 11 | 9.9% | 50.00 [-17.48, 117.48] |
| Ghanem 2010 | 141.7 | 23.1 | 25 | 68.6 | 32.1 | 14 | 15.1% | 73.10 [54.00, 92.20] |
| Monninkhof 2003 | 415.5 | 104.7 | 127 | 438.6 | 85.3 | 120 | 14.7% | -23.10 [-46.86, 0.66] |
| Moullec 2008 | 510.6 | 80.2 | 11 | 436.3 | 82.1 | 16 | 10.5% | 74.30 [12.13, 136.47] |
| Ninot 2011 | 488.1 | 73.8 | 20 | 415.6 | 109 | 18 | 10.7% | 72.50 [12.65, 132.35] |
| Wakabayashi 2011 | 492.2 | 90.5 | 42 | 440.9 | 109.9 | 43 | 12.7% | 51.30 [8.54, 94.06] |
| **Total (95% CI)** | | | **338** | | | **291** | **100.0%** | **35.90 [1.35, 70.44]** |

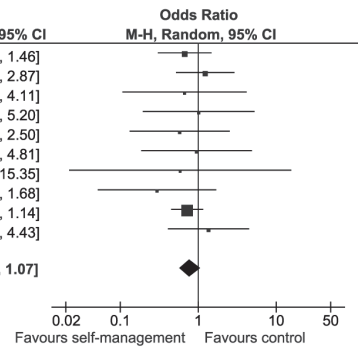
Heterogeneity: Tau² = 1964.68; Chi² = 48.64, df = 7 (P < 0.00001); I² = 86%
Test for overall effect: Z = 2.04 (P = 0.04)




**Analysis 2.11** Comparison 2 Sensitivity analyses with inclusion of CCTs, Outcome 11 Mortality (with CCTs).

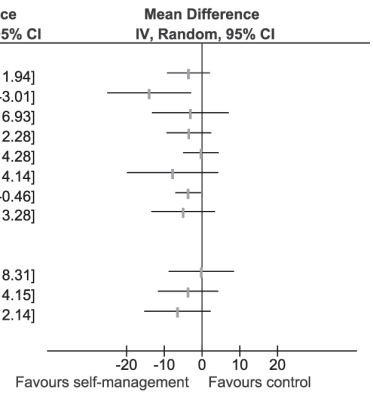
| | Self-management | | Control | | | Odds Ratio |
|---|---|---|---|---|---|---|
| Study or Subgroup | Events | Total | Events | Total | Weight | M-H, Random, 95% CI |
| Bourbeau 2003 | 13 | 96 | 18 | 95 | 15.8% | 0.67 [0.31, 1.46] |
| Casas 2006 | 12 | 65 | 14 | 90 | 13.3% | 1.23 [0.53, 2.87] |
| Coultas 2005a | 2 | 72 | 3 | 73 | 2.9% | 0.67 [0.11, 4.11] |
| Coultas 2005b | 3 | 72 | 3 | 73 | 3.6% | 1.01 [0.20, 5.20] |
| Khdour 2009 | 3 | 87 | 5 | 86 | 4.5% | 0.58 [0.13, 2.50] |
| Monninkhof 2003 | 3 | 127 | 3 | 121 | 3.6% | 0.95 [0.19, 4.81] |
| Moullec 2008 | 0 | 14 | 1 | 26 | 0.9% | 0.59 [0.02, 15.35] |
| Rea 2004 | 2 | 83 | 4 | 52 | 3.2% | 0.30 [0.05, 1.68] |
| Rice 2010 | 36 | 372 | 48 | 371 | 45.5% | 0.72 [0.46, 1.14] |
| van Wetering 2009 | 7 | 102 | 5 | 97 | 6.8% | 1.36 [0.42, 4.43] |
| **Total (95% CI)** | | **1090** | | **1084** | **100.0%** | **0.78 [0.57, 1.07]** |
| Total events | 81 | | 104 | | | |

Heterogeneity: Tau² = 0.00; Chi² = 3.78, df = 9 (P = 0.93); I² = 0%
Test for overall effect: Z = 1.55 (P = 0.12)



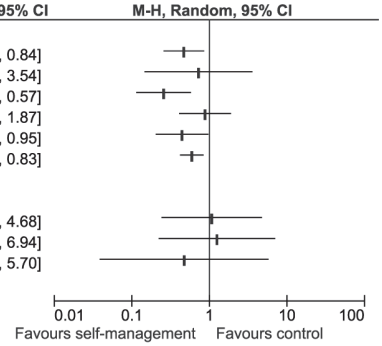
**Analysis 3.1** Comparison 3 Subgroup analyses, Outcome 1 HRQOL: SGRQ total (subgroup by follow-up).

| Study or Subgroup | Self-management Mean | SD | Total | Control Mean | SD | Total | Mean Difference IV, Random, 95% CI |
|---|---|---|---|---|---|---|---|
| **3.1.1 >= 12 months of follow-up** | | | | | | | |
| Bourbeau 2003 | 50.6 | 17.8 | 81 | 54.2 | 17.6 | 76 | -3.60 [-9.14, 1.94] |
| Casas 2006 | 37 | 22 | 21 | 51 | 19 | 43 | -14.00 [-24.99, -3.01] |
| Gallefoss 1999 | 40 | 16 | 26 | 43.1 | 21 | 27 | -3.10 [-13.13, 6.93] |
| Khdour 2009 | 61.8 | 16.6 | 71 | 65.3 | 18.6 | 72 | -3.50 [-9.28, 2.28] |
| Monninkhof 2003 | 37.4 | 18.8 | 122 | 37.7 | 17 | 113 | -0.30 [-4.88, 4.28] |
| Ninot 2011 | 31.9 | 15.1 | 18 | 39.7 | 22.1 | 20 | -7.80 [-19.74, 4.14] |
| Rice 2010 | 59.8 | 17.4 | 237 | 63.5 | 17.6 | 212 | -3.70 [-6.94, -0.46] |
| Wakabayashi 2011 | 29.7 | 17 | 42 | 34.7 | 21.7 | 43 | -5.00 [-13.28, 3.28] |
| **3.1.2 < 12 months of follow-up** | | | | | | | |
| Coultas 2005a | 58.6 | 20.4 | 49 | 58.8 | 16.4 | 26 | -0.20 [-8.71, 8.31] |
| Coultas 2005b | 55.1 | 16.4 | 51 | 58.8 | 16.4 | 25 | -3.70 [-11.55, 4.15] |
| Koff 2009 | 44.4 | 14.6 | 19 | 50.9 | 12.5 | 19 | -6.50 [-15.14, 2.14] |

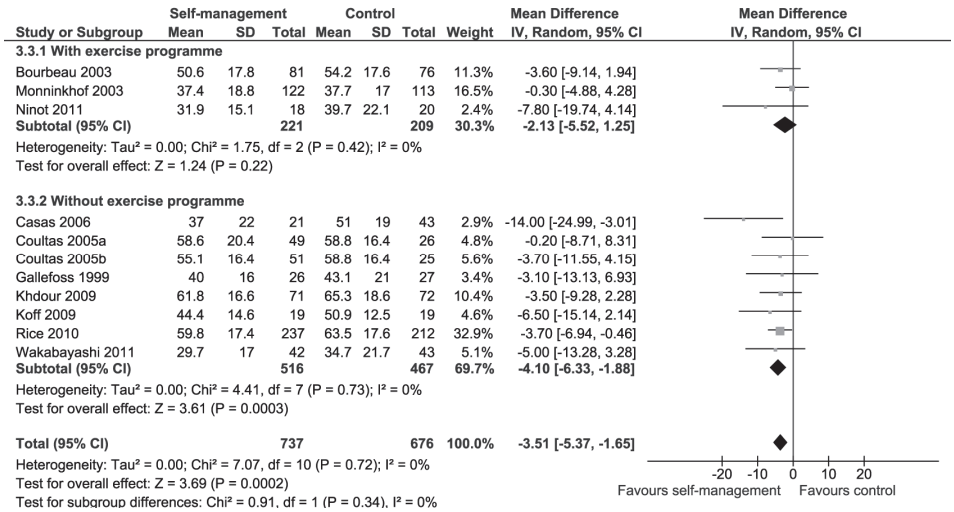



**Analysis 3.2** Comparison 3 Subgroup analyses, Outcome 4 Respiratory-related hospital admissions (subgroup by follow-up).

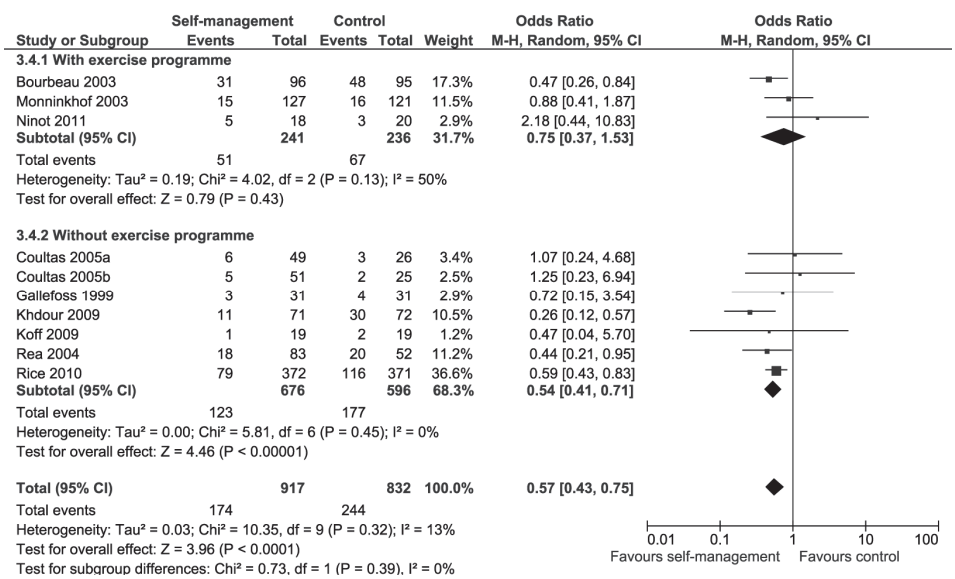
| Study or Subgroup | Self-management Events | Total | Control Events | Total | Odds Ratio M-H, Random, 95% CI |
|---|---|---|---|---|---|
| **3.2.1 >= 12 months of follow-up** | | | | | |
| Bourbeau 2003 | 31 | 96 | 48 | 95 | 0.47 [0.26, 0.84] |
| Gallefoss 1999 | 3 | 31 | 4 | 31 | 0.72 [0.15, 3.54] |
| Khdour 2009 | 11 | 71 | 30 | 72 | 0.26 [0.12, 0.57] |
| Monninkhof 2003 | 15 | 127 | 16 | 121 | 0.88 [0.41, 1.87] |
| Rea 2004 | 18 | 83 | 20 | 52 | 0.44 [0.21, 0.95] |
| Rice 2010 | 79 | 372 | 116 | 371 | 0.59 [0.43, 0.83] |
| **3.2.2 < 12 months of follow-up** | | | | | |
| Coultas 2005a | 6 | 49 | 3 | 26 | 1.07 [0.24, 4.68] |
| Coultas 2005b | 5 | 51 | 2 | 25 | 1.25 [0.23, 6.94] |
| Koff 2009 | 1 | 19 | 2 | 19 | 0.47 [0.04, 5.70] |



**Analysis 3.3** Comparison 3 Subgroup analyses, Outcome 5 HRQOL: SGRQ total (subgroup by exercise programme).

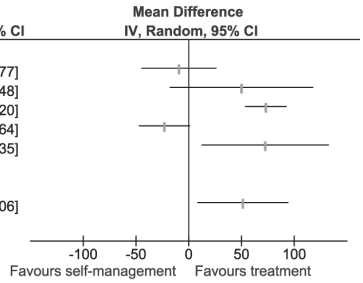



**Analysis 3.4** Comparison 3 Subgroup analyses, Outcome 6 Respiratory-related hospital admissions (subgroup by exercise programme).



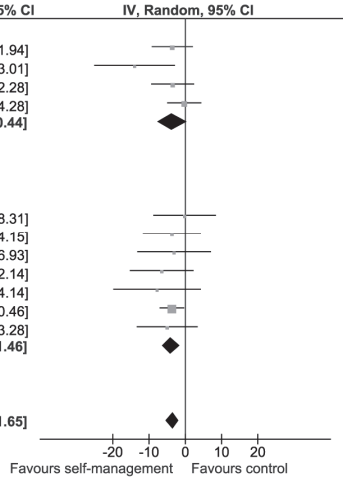
**Analysis 3.5** Comparison 3 Subgroup analyses, Outcome 7 Exercise capacity: 6MWT (subgroup by exercise programme).

| Study or Subgroup | Self-management Mean | SD | Total | Control Mean | SD | Total | Mean Difference IV, Random, 95% CI |
|---|---|---|---|---|---|---|---|
| **3.5.1 With exercise programme** | | | | | | | |
| Bourbeau 2003 | 289.2 | 110 | 67 | 298.5 | 86 | 53 | -9.30 [-44.37, 25.77] |
| Bösch 2007 | 436 | 94 | 30 | 386 | 99 | 11 | 50.00 [-17.48, 117.48] |
| Ghanem 2010 | 141.7 | 23.1 | 25 | 68.6 | 32.1 | 14 | 73.10 [54.00, 92.20] |
| Monninkhof 2003 | 415.5 | 104.7 | 127 | 438.62 | 85.3 | 120 | -23.12 [-46.88, 0.64] |
| Ninot 2011 | 488.1 | 73.8 | 20 | 415.6 | 109 | 18 | 72.50 [12.65, 132.35] |
| **3.5.2 Without exercise programme** | | | | | | | |
| Wakabayashi 2011 | 492.2 | 90.5 | 42 | 440.9 | 109.9 | 43 | 51.30 [8.54, 94.06] |

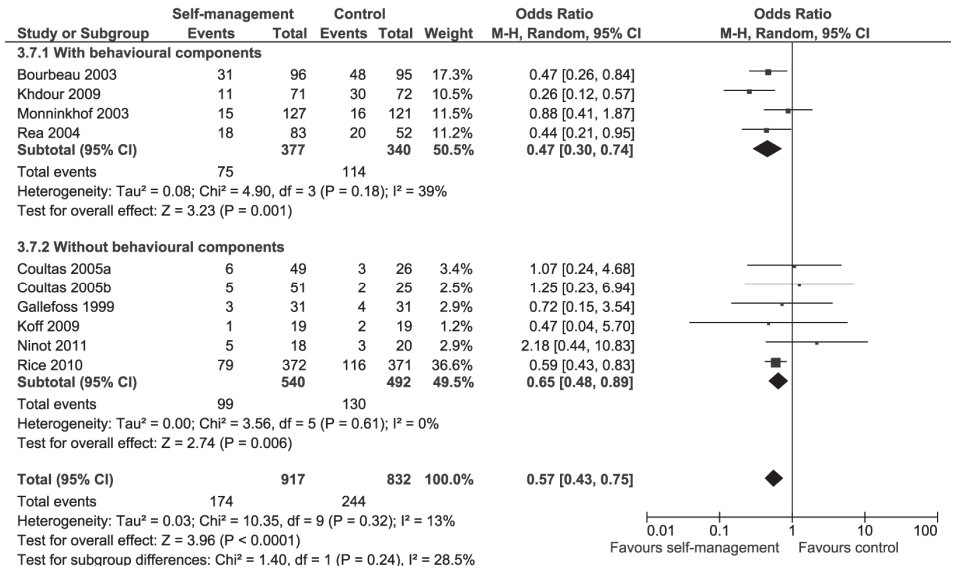



**Analysis 3.6** Comparison 3 Subgroup analyses, Outcome 9 HRQOL: SGRQ total (subgroup by behavioural components).

| Study or Subgroup | Self-management Mean | SD | Total | Control Mean | SD | Total | Weight | Mean Difference IV, Random, 95% CI |
|---|---|---|---|---|---|---|---|---|
| **3.6.1 With behavioural components** | | | | | | | | |
| Bourbeau 2003 | 50.6 | 17.8 | 81 | 54.2 | 17.6 | 76 | 11.3% | -3.60 [-9.14, 1.94] |
| Casas 2006 | 37 | 22 | 21 | 51 | 19 | 43 | 2.9% | -14.00 [-24.99, -3.01] |
| Khdour 2009 | 61.8 | 16.6 | 71 | 65.3 | 18.6 | 72 | 10.4% | -3.50 [-9.28, 2.28] |
| Monninkhof 2003 | 37.4 | 18.8 | 122 | 37.7 | 17 | 113 | 16.5% | -0.30 [-4.88, 4.28] |
| **Subtotal (95% CI)** | | | **295** | | | **304** | **41.1%** | **-3.61 [-7.65, 0.44]** |
| Heterogeneity: Tau² = 7.15; Chi² = 5.26, df = 3 (P = 0.15); I² = 43% | | | | | | | | |
| Test for overall effect: Z = 1.75 (P = 0.08) | | | | | | | | |
| **3.6.2 Without behavioural components** | | | | | | | | |
| Coultas 2005a | 58.6 | 20.4 | 49 | 58.8 | 16.4 | 26 | 4.8% | -0.20 [-8.71, 8.31] |
| Coultas 2005b | 55.1 | 16.4 | 51 | 58.8 | 16.4 | 25 | 5.6% | -3.70 [-11.55, 4.15] |
| Gallefoss 1999 | 40 | 16 | 26 | 43.1 | 21 | 27 | 3.4% | -3.10 [-13.13, 6.93] |
| Koff 2009 | 44.4 | 14.6 | 19 | 50.9 | 12.5 | 19 | 4.6% | -6.50 [-15.14, 2.14] |
| Ninot 2011 | 31.9 | 15.1 | 18 | 39.7 | 22.1 | 20 | 2.4% | -7.80 [-19.74, 4.14] |
| Rice 2010 | 59.8 | 17.4 | 237 | 63.5 | 17.6 | 212 | 32.9% | -3.70 [-6.94, -0.46] |
| Wakabayashi 2011 | 29.7 | 17 | 42 | 34.7 | 21.7 | 43 | 5.1% | -5.00 [-13.28, 3.28] |
| **Subtotal (95% CI)** | | | **442** | | | **372** | **58.9%** | **-3.88 [-6.31, -1.46]** |
| Heterogeneity: Tau² = 0.00; Chi² = 1.59, df = 6 (P = 0.95); I² = 0% | | | | | | | | |
| Test for overall effect: Z = 3.14 (P = 0.002) | | | | | | | | |
| **Total (95% CI)** | | | **737** | | | **676** | **100.0%** | **-3.51 [-5.37, -1.65]** |
| Heterogeneity: Tau² = 0.00; Chi² = 7.07, df = 10 (P = 0.72); I² = 0% | | | | | | | | |
| Test for overall effect: Z = 3.69 (P = 0.0002) | | | | | | | | |
| Test for subgroup differences: Chi² = 0.01, df = 1 (P = 0.91), I² = 0% | | | | | | | | |



**Analysis 3.7** Comparison 3 Subgroup analyses, Outcome 10 Respiratory-related hospital admissions (subgroup by behavioural components).



## ADDITIONAL TABLES

**Table 1** Characteristics of participants in included studies

| | Included participants (n) | | Lost to follow-up (%) | | Age (years) | | Sex (% male) | | $FEV_1$ (L or %) | |
|---|---|---|---|---|---|---|---|---|---|---|
| | SM | Control | SM | Control | SM | Control | SM | Control | SM | Control |
| **Comparison with usual care** | | | | | | | | | | |
| Akinci 2011 | 27 | 25 | 41 | 36 | 71.8 (7.8) | 65.1 (10.2) | n.a. | n.a | 0.9 (0.3) | 1.0 (0.4) |
| Bösch 2007 | 38 | 12 | 21 | 8 | 63.8 (8.4) | 64.6 (6.8) | 52 * | n.a. | 1.3 (0.5) | 1.4 (0.5) |
| Bourbeau 2003 | 96 | 95 | 10 | 17 | 69.4 (6.5) | 69.6 (7.4) | 52 | 59 | 1.0 (0.3) | 1.0 (0.3) |
| Casas 2006 | 65 | 90 | 26 | 20 | 70 (9) | 72 (9) | 77 | 88 | 43 (20) | 41 (15) |
| Chavannes 2009 | 79 | 73 | 14 | 18 | 64 (11) | 63 (11) | 59 | 67 | 62 (19) | 66 (16) |
| Chuang 2011 | 141 | 141 | n.a. | n.a. | n.a. | n.a. | 35 | 35 | n.a. | n.a. |
| Coultas 2005a | 72 | - | 29 | - | 68.3 (6.6) | - | 43 | | 46.2 (17.9) | - |
| Coultas 2005b | 72 | 73 | 32 | 30 | 70.1 (7.0) | 68.8 (10.4) | 33 | 54 | 42.2 (16.2) | 46.2 (17.2) |
| Emery 1998 | 25 | 25 | 8 | 0 | 67.4 (5.9) | 67.4 (7.1) | 40 | 48 | 1.1 (0.5) | 1.0 (0.4) |
| Faulkner 2010 | 10 | 10 | 40 | 20 | 70.8 (10.5) | 71.3 (4.5) | 90 | 70 | 2.0 (0.4) | 1.7 (0.5) |
| Gallefoss 1999 | 31 | 31 | 16 | 13 | 57 (9) | 58 (10) | 48 | 52 | 1.8 (0.5) | 1.7 (0.5) |
| Ghanem 2010 | 25 | 14 | 0 | 0 | 57 (11.6) | 56.4 (9) | n.a. | n.a. | 0.8 (0.4) | 0.6 (0.2) |
| Hill 2010 | 55 | 45 | 9 | 4 | 63.4 (9.6) | 65.7 (9.9) | 44 | 46 | 60.0 (14.3) | 58.2 (14.4) |
| Khdour 2009 | 86 | 87 | 17 | 17 | 65.6 (10.1) | 67.3 (9.2) | 44 | 44 | 1.0 (0.5) | 1.1 (0.5) |
| Kheirabadi 2008 | 21 | 21 | n.a. | n.a. | 56.6 (5.7) | 56.2 (4.1) | 62 | 76 | n.a. | n.a. |
| Koff 2009 | 20 | 20 | 5 | 5 | 66.6 (9.1) | 65.0 (8.2) | 45 | 50 | 33.6 (9.1) | 31.1 (10.2) |
| Monninkhof 2003 | 127 | 121 | 4 | 6 | 65 (7) | 65 (7) | 85 | 84 | 1.7 (0.6) | 1.8 (0.5) |
| Moullec 2008 | 14 | 26 | 21 | 38 | 62.9 (7.4) | 59.7 (9.6) | 71 | 81 | 49.3 (14.9) | 46.8 (18.2) |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Ninot 2011 | 23 | 22 | 13 | 18 | 65 (59 ; 74) | 61 (56 ; 65) | 78 | 64 | 1.69 (1.17; 2.01) | 1.52 (1.06; 1.85) |
| Osterlund 2006 | 26 | 26 | 0 | 0 | 66 (9.4) | 67 (10.4) | 50 | 50 | n.a. | n.a. |
| Rea 2004 | 83 | 52 | 14 | 12 | 68 (44 ; 48)* | n.a. | 42 * | n.a. | 1.2 (0.5) | 1.1 (0.5) |
| Rice 2010 | 372 | 371 | 10 | 13 | 69.1 (9.4) | 70.7 (9.7) | 98 | 98 | 1.1 (0.5) | 1.2 (0.5) |
| van Wetering 2009 | 102 | 97 | 25 | 17 | 65.9 (8.8) | 67.2 (8.9) | 71 | 71 | 58 (17) | 60 (15) |
| Wakabayashi 2011 | 52 | 50 | 19 | 14 | 72.9 (6.4) | 70.4 (8.6) | 88 | 84 | 1.5 (0.5) | 1.6 (0.7) |
| **Head-to-head trials** | | | | | | | | | | |
| Effing 2009 | 80 | 79 | 16 | 9 | 63.1 (7.9) | 63.7 (8.0) | 57 | 61 | 1.4 (0.6) | 1.4 (0.5) |
| Effing 2011 | 80 | 79 | 8 | 14 | 62.9 (8.1) | 63.9 (7.8) | 58 | 58 | 1.4 (0.5) | 1.4 (0.5) |
| Kara 2004 | 30 | 30 | n.a | n.a. | 61.1 (11.3) | 61.4 (11.1) | 78 * | n.a. | n.a. | n.a. |
| Nguyen 2008 | 26 | 24 | 27 | 17 | 68.0 (8.3) | 70.9 (8.6) | 61 | 55 | 49.0 (16.8) | 50.3 (17.6) |
| Nguyen 2009 | 9 | 8 | 0 | 0 | 72 (9) | 64 (12) | 33 | 37 | 46.7 (18.7) | 34.4 (15) |
| Sassi-Dambron 1995 | 47 | 51 | 13 | 24 | 67.5 (8.0) | 67.3 (8.0) | 55 | 45 | 1.1 (0.5) | 1.2 (0.6) |
| Stulbarg 2002 | 40;37 | 38 | 10; 11 | 11 | 66.2 (6.4); 67.2 (7.6) | 65.7 (6.8) | 50/38 | 32 | 1.1 (0.4); 1.2 (0.3) | 1.0 (0.3) |

**Total group; n.a. is not available; SM is self-management group.*

**Table 2** Characteristics of interventions in included studies

| Author | Follow-up | Comparison | Setting intervention | Duration intervention | Content intervention |
|---|---|---|---|---|---|
| **Comparison with usual care** | | | | | |
| Akinci 2011 | 3 months | Nurse-led home-based pulmonary rehab versus usual care | Home-based, individual, face-to-face, educational booklet | Participant education: two to three sessions of two to three hours, four phone calls; exercise: daily, 30 to 60 minutes | Education regarding the disease, methods for smoking cessation, use of medication, coping with breath-lessness, advice about exercise and activities |
| Bösch 2007 | 12 months | COPD outpatient education program versus usual care | Outpatient clinic, group-based (six to eight participants), face-to-face | Four small-group sessions of 120 minutes | Education regarding the disease, smoking cessation, action plan with self treatment of exacerbations, advice about exercise, advice about nutrition, advice about medication, coping with breath-lessness, travelling |
| Bourbeau 2003 | 24 months | Self management versus usual care | Home-based, individual | Seven to eight week one hour; first two months weekly telephone calls; from then, once-a-month telephone call. Exercise evaluation (not mandatory) and exercise teaching three times a week for 30 to 45 min. | COPD knowledge, breathing and coughing techniques, energy conservation during day-by-day activities, relaxation exercises, preventing and controlling symptoms through inhalation techniques, understanding and using plan of |

| | | | | | |
|---|---|---|---|---|---|
| | | | | | action for acute exacerbations, adopting a healthy lifestyle, leisure activities and travelling, a simple home exercise programme, long-term oxygen therapy when appropriate |
| Casas 2006 | 12 months | Integrated care versus usual care | Hospital-based and home-based, group sessions and individual sessions, face-to-face | One group session of two hours, three individual sessions of 40 minutes, and one to 10 sessions at home of 20 minutes | Education regarding the disease, smoking cessation, action plan with self treatment of exacerbations, advice about exercise, advice about nutrition, advice about medication, coping with breath-lessness, travelling, end-of-life decision making, interpretation of medical testing, irritant avoidance, anxiety and panic control |
| Chavannes 2009 | 12 months | Integrated disease management versus usual care | General practise, group sessions and individual sessions, face-to-face, telephone | One-month, twice-weekly individual education, five months twice weekly one-hour training in group sessions, one hour at home | Education regarding the disease, smoking cessation, action plan with self treatment of exacerbations, exercise programme, advice about nutrition, advice about medication |

| | | | | | |
|---|---|---|---|---|---|
| Chuang 2011 | 12 months | Participant-centric COPD programme versus usual care | Outpatient clinic, individual | ≥ One face-to-face 45 minutes, ≥ 10 educational calls 10 to 15 minutes each | Education regarding the disease, smoking cessation, action plan with self treatment of exacerbations, advice about exercise, advice about nutrition, advice about medication, coping with breathlessness |
| Coultas 2005a; Coultas 2005b | 6 months | Nurse-assisted medical management (MM) or nurse-assisted collaborative management (CM) versus usual care | Primary care | MM: 124 minutes (seven sessions); CM: 207 minutes (eight sessions) | Education regarding the disease, smoking cessation, action plan, advice about medication |
| Emery 1998 | 2 months | Education and stress management (ESM) versus usual care (exclude EXESM) | Duke University Center for living, group education | 16 one-hour-long educational lectures, 10 one-hour group meetings for stress management and social support | COPD knowledge, therapy, coping, interpreting pulmonary function tests, understanding arterial blood gases, stress management |
| Faulkner 2010 | 10 weeks | Health-enhancing physical activity programme versus usual care | University exercise facility, group sessions, face-to-face, booklet | Eight sessions of 90 minutes | Education regarding the disease, exercise programme, advice about exercise, coping with breathlessness |
| Gallefoss 1999 | 12 months | Standardised education programme and a self management programme versus usual care | Outpatient clinic, group and individual sessions, patient brochure | Two two-hour group sessions, two to four individual sessions of 40 minutes | COPD knowledge, medication, action plan, symptoms, exacerbations, inhalation technique, smoking cessation, relaxation, coping |

| | | | | | |
|---|---|---|---|---|---|
| Ghanem 2010 | 2 months | Home-based pulmonary rehabilitation programme versus usual care | Home-based, individual sessions, face-to-face, booklet | Four individual sessions of one hour, every other day exercise for two months | Education regarding the disease, exercise programme, advice about nutrition, advice about medication |
| Hill 2010 | 3 months | Brief disease-specific education programme versus usual care | Primary care practise, individual sessions, face-to-face, written teaching manual | Two individual sessions of one hour | Education regarding the disease, (strategies for) smoking cessation, recognition of an exacerbation, advice about exercise, advice about medication |
| Khdour 2009 | 12 months | Clinical pharmacy-led disease and medicine management programme versus usual care | Hospital (outpatient clinic), individual sessions, face -to-face, telephone | One session of one hour, reinforcement at each outpatient visit every six months, two telephone calls at three months and nine months | Education regarding the disease, smoking cessation, action plan with self treatment of exacerbations, advice about exercise, advice about nutrition, advice about medication, coping with breathlessness |
| Kheirabadi 2008 | 3 months | Self management and behaviour modification group education versus usual care | Hospital (outpatient clinic), group sessions, face-to-face, telephone | Eight group sessions of 60 to 90 minutes; participants were followed up by phone | Education regarding the disease, smoking cessation, exercise programme, action plan, advice about exercise, advice about nutrition, advice about medication |
| Koff 2009 | 3 months | Proactive integrated care versus usual care | Home-based, individual, face-to-face, tele-communication device | One individual session at enrolment, each weekday morning a telehealth session | Education regarding the disease, exercise programme, action plan, advice about exercise, advice |

| | | | | | |
|---|---|---|---|---|---|
| | | | | with COPD-specific education of 20 minutes | about medication |
| Monninkhof 2003 | 12 months | Comprehensive self management programme versus usual care | Outpatient at the hospital and community-based, group education, educational booklet | Five two-hour group sessions, one or two one-hour group training sessions | COPD knowledge, inhalation technique, importance of exercise, relaxation, nutrition, coping with breathless-ness, ergonomic posture and energy conservation during daily activities or work, communi-cation and social relationships, guidelines for self treatment for exacerbations (action plans), a fitness program aimed at coping with disease, recognising individual capacity, social interactions and behavioural change |
| Moullec 2008 | 12 months | Multidisciplinary maintenance programme after a first inpatient PR versus standard aftercare/ usual care | Community-based, group sessions, face-to-face | 3.5 hours exercise per week (72 sessions), two hours health education per month (12 sessions), one hour psycho-social support in discussion group per month (12 sessions) | Education regarding the disease, smoking cessation, exercise programme, action plan, advice about exercise, advice about nutrition, advice about medication, coping with breathlessness |

| | | | | | |
|---|---|---|---|---|---|
| Ninot 2011 | 12 months | Self management programme versus usual care | Hospital on outpatient basis, group and Individual sessions, face-to-face, telephone | Eight group sessions of two hours, three phone calls | Smoking cessation, exercise programme, action plan, advice about exercise, advice about nutrition, advice about medication |
| Osterlund Efraimsson 2006 | 3-5 months | Structured educational intervention versus usual care | Nurse-led primary healthcare clinic, individual sessions, face-to-face | Two visits that lasted for about one hour | Education regarding COPD, smoking cessation, action plan, advice about exercise, advice about nutrition, advice about medication, coping with breathlessness |
| Rea 2004 | 12 months | Chronic disease management versus usual care | Outpatient clinic, GP, home-based, individual | 12 monthly visits to practise nurse, four three-monthly visits to GP, at least one home visit of respiratory nurse specialist and one following hospital admissions | An action plan detailing advice on how to manage worsening symptoms, when to call the GP, and self medication options decided by the GP. Information about smoking cessation and the use of inhalers was given. Annual influenza vaccination and attendance at a pulmonary rehabilitation programme were recommended |
| Rice 2010 | 12 months | Simplified disease management programme versus usual care | Outpatient clinic, group and individual sessions, face-to-face. | One group session of one to 1.5 hours, 12 monthly phone calls of 10 to 15 minutes | Education regarding COPD, smoking cessation, action plan with self treatment, advice about exercise, advice about medication, coping |

| | | | | | |
|---|---|---|---|---|---|
| | | | | | with breathlessness |
| van Wetering 2009 | 24 months | Interdisciplinary community-based COPD management programme versus usual care | Community- and home-based, individual sessions, face-to-face, patient education book | 30 minutes of physiotherapy visits twice a week during the first four months, twice a day during 30 min. at home, education duration unknown. Once-a-month physiotherapy during the following 20 months | Education regarding COPD, smoking cessation, exercise programme, advice about exercise, advice about nutrition |
| Wakabayashi 2011 | 12 months | Integrated care focusing on participant information needs for the self management of COPD versus usual care | Outpatient clinic, individual sessions, face-to-face, booklet | Six monthly individual sessions of at least 30 minutes | Education regarding COPD, smoking cessation, action plan with self treatment, advice about exercise, advice about nutrition, advice about medication, coping with breathlessness |
| **Head-to-head trials** | | | | | |
| Kara 2004 | 2 months | Structured education programme versus educational advice | Hospital (outpatient clinic), group and individual sessions, face to-face, written teaching manual | 60 to 70 minutes, later 35 to 40 minutes three or four times per week in small groups | Education regarding the disease, smoking cessation, exercise programme, advice about exercise, advice about nutrition, advice about medication, coping withbreathlessness |
| Stulbarg 2002 | 12 months | Dyspnoea self management | Home-based walking, hospital-based (?) self management education | Three hours in four sessions over eight weeks, walk at least four times per week for minimum of 20 minutes | Individualised dyspnoea self management education, home-walking prescription |

| | | | | | |
|---|---|---|---|---|---|
| | | Dyspnoea self management and exposure | Home-based walking, hospital-based (?) self management education and exposure | Three hours in four sessions over eight weeks, walk at least four times per week for minimum of 20 minutes, four nurse-coached treadmill exercise sessions for 30 minutes once every other week for eight weeks | Individualised dyspnoea self management education, home-walking prescription, exposure to exercise-induced dyspnoea |
| | | Dyspnoea self management and training | Home-based walking, hospital-based (?) self management education and training | Three hours in four sessions over eight weeks, walk at least four times per week for minimum of 20 minutes, 24 nurse-coached treadmill exercise sessions for 30 minutes three times per week for eight weeks | Individualised dyspnoea self management education, home-walking prescription, exercise training |
| Nguyen 2009 | 6 months | Mobile-coached cell phone–based exercise persistence intervention | Outpatient clinic– and home-based, individual sessions, face-to-face, booklet, telephone | One individual session of 30 to 45 minutes, at least one or two phone calls of 10 minutes, 150 minutes of moderate-intensity endurance exercise over three to five sessions per week for six months | Action plan, advice about exercise and exercise programme with collaborative monitoring of symptoms and exercise and ongoing reinforcement feedback |
| | | Mobile-self monitored exercise persistence intervention | Outpatient clinic– and home-based, individual sessions, face-to-face, booklet, telephone | One individual session of 30 to 45 minutes, standard (self monitored) text message, 150 minutes of moderate-intensity | Action plan, advice about exercise and exercise programme with self monitoring |

| | | | | | |
|---|---|---|---|---|---|
| | | | | endurance exercise over three to five sessions per week for six months | |
| Nguyen 2008 | 6 months | Dyspnoea self management programme face-to-face | Outpatient clinic– and home-based, group and individual sessions, face-to-face, telephone | 1.5- to two-hour face-to-face consultation, six one-hour weekly group sessions of structured education of dyspnoea management strategies face-to-face, four times/wk 30 minutes endurance, three times/wk arm strengthening, reinforcement via telephone weekly in month one, biweekly in months two through six | Exercise programme, action plan, advice about exercise, advice about medication, coping with breathlessness |
| | | Dyspnoea self management programme Internet-based | Outpatient clinic and home-based, group and individual sessions, face-to-face, internet | 1.5- to two-hour face-to-face consultation, six one-hour weekly group sessions of structured education of dyspnoea management strategies via chat four times/wk 30 minutes endurance, three times/wk arm strengthening, reinforcement via email weekly in month one, biweekly in months two through six | Exercise programme, action plan, advice about exercise, advice about medication, coping with breathlessness |
| Sassi-Dambron 1995 | 12 months | Dyspnoea management | Group sessions, face-to-face | Six weekly sessions | Education regarding the disease, advice |

| | | | | | |
|---|---|---|---|---|---|
| | | | | | about exercise,coping with breathlessness |
| | | General health education | Group sessions, face-to-face | Six weekly general health education sessions | Topics not directly related to lung disease: exercise, general medications, durable power of attorney, nutrition, Alzheimer's disease, medical insurance |
| Effing 2011 | 12 months | Self management and community-based exercise programme | Outpatient clinic, private physiotherapy practise, group and individual sessions, face-to-face, telephone, booklet | Four weekly, two-hour small-group self management sessions with three follow-up phone calls, 11-month training, first six months two/wk at physiotherapy practise, one/wk at home, last five months one/wk at physiotherapy practice, one/wk at home | Education regarding COPD, action plan, advice about exercise, advice about nutrition, advice about medication, coping with breathlessness, exercise programme |
| | | Self management programme | Outpatient clinic, group and individual sessions, face-to-face, telephone, booklet | Four weekly, two-hour small-group self management sessions with three follow-up phone calls | Education regarding COPD, action plan, advice about exercise, advice about nutrition, advice about medication, coping with breathlessness |
| Effing 2009 | 12 months | Self management and self treatment | Outpatient clinic, group and individual sessions, face-to-face, telephone, booklet | Four weekly, two-hour small-group self management sessions with three follow-up phone calls | Education regarding COPD, action plan with self treatment of exacerbations, advice about exercise, advice about nutrition, advice about |

| | | | | |
|---|---|---|---|---|
| | | | | medication, coping with breathlessness |
| | Self management programme | Outpatient clinic, group and individual sessions, face-to-face, telephone, booklet | Four weekly, two-hour small-group self management sessions with three follow-up phone calls | Education regarding COPD, action plan, advice about exercise, advice about nutrition, advice about medication, coping with breathlessness |

**Table 3** Number of studies reporting outcome

| | Studies with usual care | Head-to-head trials |
|---|---|---|
| **Primary outcomes** | | |
| Health-related quality of life scores | 20 | 4 |
| Number of hospital admissions: respiratory-related | 12 | 1 |
| Number of hospital admissions: all-cause | 10 | 1 |
| **Secondary outcomes** | | |
| Symptom scores | 10 | 3 |
| Number of courses of oral corticosteroids or antibiotics | 5 | 2 |
| Use of rescue medication | 2 | 0 |
| Number of exacerbations | 3 | 4 |
| Hospitalisation days: respiratory-related | 5 | 0 |
| Hospitalisation days: all-cause | 8 | 0 |
| Emergency department visits | 8 | 1 |
| Doctor and nurse visits | 8 | 0 |
| Days lost from work | 3 | 0 |
| Lung function | 12 | 3 |
| Exercise capacity | 10 | 5 |
| Anxiety and depression | 2 | 2 |
| Self efficacy | 1 | 4 |

**Table 4** Study-specific number needed to treat for an additional beneficial outcome (NNTB) of respiratory-related hospital admissions

| Study | Baseline risk (% control) | Follow-up (weeks) | NNTB (95%CI) |
|---|---|---|---|
| Bourbeau 2003 | 51 | 52 | 8 (5 to 14) |
| Coultas 2005a; Coultas 2005b | 10 | 24 | 26 (19 to 45) |
| Gallefoss 1999 | 13 | 52 | 20 (15 to 35) |
| Khdour 2009 | 42 | 52 | 8 (6 to 15) |
| Koff 2009 | 11 | 12 | 24 (18 to 42) |
| Monninkhof 2003 | 13 | 52 | 20 (15 to 34) |
| Ninot 2011 | 15 | 52 | 18 (13 to 31) |
| Rea 2004 | 38 | 52 | 9 (6 to 16) |
| Rice 2010 | 31 | 52 | 10 (7 to 18) |

# APPENDICES

## Appendix 1. Sources and search methods for the Cochrane Airways Group Specialised Register (CAGR)

*Electronic searches: core databases*

| Database | Frequency of search |
|---|---|
| CENTRAL | Monthly |
| MEDLINE (Ovid) | Weekly |
| EMBASE (Ovid) | Weekly |
| PsycINFO (Ovid) | Monthly |
| CINAHL (EBSCO) | Monthly |
| AMED (EBSCO) | Monthly |

*Handsearches: core respiratory conference abstracts*

| Conference | Years searched |
|---|---|
| American Academy of Allergy, Asthma and Immunology (AAAAI) | 2001 onwards |
| American Thoracic Society (ATS) | 2001 onwards |
| Asia Pacific Society of Respirology (APSR) | 2004 onwards |
| British Thoracic Society Winter Meeting (BTS) | 2000 onwards |
| Chest Meeting | 2003 onwards |
| European Respiratory Society (ERS) | 1992, 1994, 2000 onwards |
| International Primary Care Respiratory Group Congress (IPCRG) | 2002 onwards |
| Thoracic Society of Australia and New Zealand (TSANZ) | 1999 onwards |

*MEDLINE search strategy used to identify trials for the CAGR COPD search*

1. Lung Diseases, Obstructive/
2. exp Pulmonary Disease, Chronic Obstructive/
3. emphysema$.mp.
4. (chronic$ adj3 bronchiti$).mp.
5. (obstruct$ adj3 (pulmonary or lung$ or airway$ or airflow$ or bronch$ or respirat$)).mp.
6. COPD.mp.
7. COAD.mp.
8. COBD.mp.
9. AECB.mp.
10. or/1-9

*Filter to identify RCTs*

1. exp "clinical trial [publication type]"/
2. (randomised or randomised).ab,ti.
3. placebo.ab,ti.
4. dt.fs.
5. randomly.ab,ti.
6. trial.ab,ti.
7. groups.ab,ti.
8. or/1-7
9. Animals/
10. Humans/
11. 9 not (9 and 10)
12. 8 not 11

The MEDLINE strategy and RCT filter are adapted to identify trials in other electronic databases

**Appendix 2. Search terms for Cochrane Airways Group Register**

educat* or self-manag* or "self manag*" or self-car* or "self car*" or train* or instruct* or "patient cent*" or patient-cent* or patient-focus* or "patient focus*" or patient-education or "patient education" or "management plan*" or "management program*" or behavior* or behaviour* or "disease management*" or management* or self-efficacy or empower*

*[Limited to records in the Register coded as 'COPD']*

## WHAT'S NEW

| Date / Event | Description |
|---|---|
| 31 August 2011<br>New citation: conclusions changed | Complete rewrite of the review conducted. Summary of findings table added. 14 new studies added. New risk of bias assessment completed for all included studies. References in background updated<br>Change of title—'education' removed |
| 31 August 2011<br>Updated | New literature search run |

## HISTORY

| Date / Event | Description |
|---|---|
| 25 March 2008<br>Amended | Converted to new review format. |
| 21 August 2007<br>New citation: conclusions changed | New studies: N = 7 (Bourbeau 2003; Boxall 2005; Coultas 2005a; Coutas 2005b; Martin 2004; Monninkhof 2003; Rea 2004)<br><br>What these studies have added:<br>Data on health related quality of life; exacerbations (hospitalisations, requirement for oral steroids); lung function (FEV1).<br><br>Quality of life scores and respiratory-related hospital admission now show significant benefits. Lung function parameters do not show a significant difference. Steroid-treated exacerbations were not significantly different.<br><br>How this has changed the review:<br>The review now demonstrates that from the self-management interventions assessed in the studies assembled in the review, patients were less likely to require hospital admissions when treated with this type of intervention. There was a small improvement in total quality of life scores measured by the St George's Respiratory Questionnaire. There were no indications of detrimental effects in other outcome parameters. The effects of different components of self-management interventions and their requisite intensity requires more research. |

# CHAPTER 3

## THE (COST-) EFFECTIVENESS OF SELF-TREATMENT OF EXACERBATIONS IN PATIENTS WITH COPD: TWO YEARS FOLLOW-UP OF A RANDOMISED CONTROLLED TRIAL

SUBMITTED

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HUIB KERSTJENS,
JOB VAN DER PALEN,
PAUL VAN DER VALK,
MARJOLEIN BRUSSE-KEIZER,
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# CHAPTER 4

## A COMMUNITY-BASED EXERCISE PROGRAMME IN COPD SELF-MANAGEMENT: TWO YEARS FOLLOW-UP OF THE COPE-II STUDY

RESPIRATORY MEDICINE 2014 AUG;
EPUB AHEAD OF PRINT

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## ABSTRACT

### Introduction
It is still unknown how best to maintain effects of exercise programmes in COPD in the long-term. We present the long-term effects of a community-based exercise programme incorporated in a self-management programme, compared to a self-management programme only in patients with COPD.

### Methods
All included patients participated in four self-management sessions. Additionally, patients in the intervention group participated in an 11-month community-based exercise programme led by physiotherapists. Patients trained three times/week for six months and two times/week during the subsequent five months. To encourage a behavioural change towards exercise, one of these weekly training sessions was home-based (unsupervised). No formal exercise training was offered to intervention patients in the second year.

### Results
The intervention was assigned to 80 patients, and the control condition to 79 patients. 82.5% and 78.5% of the intervention and control group, respectively, completed 24 months follow-up. Modified intention-to-treat analyses were performed. Although statistically significant after 12 months (35.1 meters (95%CI: 8.4 to 61.8)), the between-group difference on maximal exercise capacity was not statistically significant after 24 months (12.2 meters (95%CI: -16.6 to 41.0)). Nevertheless, the between-group difference in daily physical activity was maintained after 24 months (1193 steps/day (95%CI: 203 to 2182)). A beneficial effect was also found on CRQ dyspnoea score but not on other CRQ domains, CCQ and HADS.

### Conclusions
Our intervention was effective in achieving a behavioural change reflected by a sustained increase in daily physical activity, not accompanied by a sustained increase in maximal exercise capacity after two years of follow-up (ISRCTN81447311).

## INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is not only characterized by symptoms of dyspnoea, chronic cough, and sputum production, but also and importantly by decreased exercise capacity[1] and a reduced physical activity level[2-4]. A large number of randomised controlled trials have investigated the effects of exercise training programmes, whether part of a formal pulmonary rehabilitation programme or not, on exercise capacity in patients with COPD. A meta-analysis of Lacasse et al.[5] included 31 randomised trials, and found that rehabilitation programmes including exercise therapy are effective in improving exercise capacity and quality of life. However, in this review only short-term effects (i.e. effects directly after the end of the intervention) were assessed. The results on the longer term are less unanimous[6-9].

It is increasingly recognised that the long-term maintenance of beneficial effects of exercise programmes in patients with COPD is problematic[1;10;11]. The leading hypothesis in this discussion is that one should not solely aim at the improvement of exercise capacity but also at a behavioural change towards exercise and physical activity[1;10;11]. Self-management training can play an important role in this context and is increasingly offered to patients with COPD, regularly combined with exercise programmes[1]. The goal of self-management is to teach patients the skills they need to carry out disease specific medical regimens, and to guide behavioural change to help patients control their own condition and improve their wellbeing[12;13]. Although self-management training is effective in improving health-related quality of life (HRQoL) and reducing respiratory-related hospitalisations, it remains unclear which components contribute most to its effectiveness[14].

The COPE-II study is a randomised controlled trial that evaluated the effects of a community-based physiotherapeutic exercise programme (COPE-active) within a self-management programme[15]. One of the main goals of the COPE-active programme was to achieve a behavioural change towards exercise in daily life. A relatively long training period of 11 months was chosen to facilitate the change from training under supervision of a physiotherapist to unsupervised exercise at home. To support this further, one training session was home-based and unsupervised during the entire training period. After one year of follow-up, patients who participated in the COPE-active programme showed an improved maximal exercise capacity and a positive change in daily physical activity in comparison with the control group[15]. On the short term, directly after the end of the structured exercise programme, the goal of behavioural change was therefore achieved. The current paper reports the long-term effects of the COPE-active programme on exercise capacity and daily physical activity in patients with COPD, i.e. after two years of follow-up.

## METHODS

### Study design

The detailed study design was published earlier[15;16]. In the COPE-II study a 2x2 factorial design was used. This means that two independent interventions, a community-based exercise programme and self-treatment of exacerbations, were evaluated in one design. In this report, the effectiveness at two years follow-up of a community-based exercise programme incorporated in a self-management programme was compared to the effectiveness of a self-management programme only. Both treatment regimens were allocated using a minimisation programme[17], and patients receiving guidelines for self-treatment were equally distributed over the COPE-active programme and the control group. Patients were assessed at baseline, after seven, 12, 18 and 24 months.

### Patients

From November 2004 through July 2006, participants were recruited from the outpatient department of pulmonary medicine[15]. Patients eligible for inclusion had a clinical diagnosis of COPD according to the GOLD criteria[18]; a post-bronchodilator $FEV_1$ between 25 and 80% of predicted; additionally, they had to have had at least three exacerbations or one hospitalisation for respiratory problems in the two years preceding study entry. Patients were excluded when they had a serious other disease with a low survival rate; another disease that influenced bronchial symptoms and/or lung function; a need for regular oxygen therapy; a disorder or progressive disease that seriously influenced walking ability. The study protocol was approved by the medical-ethical review committee of Medisch Spectrum Twente hospital and written informed consent was obtained from all participants[15]. The COPE-II study was registered in the ISRCTN register: ISRCTN81447311.

### Self-management sessions and COPE-active programme

All patients participated in four weekly 2-hour small-group (approximately 5 patients) self-management sessions led by a respiratory nurse and a physiotherapist. The goal of the course was to change the patients' disease behaviour by increasing their knowledge, confronting them with consequences of specific behaviour, and supplying them with tools to deal with different components of their disease. The respiratory nurse contacted all patients by telephone four, 13, 26, 52, and 78 weeks after the last course to recall the items addressed during the self-management course. Patients were supplied with a booklet with the content of the course[15].

Only patients in the intervention group participated in a community-based physiotherapeutic exercise programme (COPE-active), of which details were published earlier[15]. The COPE-active programme was divided in two parts: a ‘compulsory’ 6-month, and a subsequent optional but recommended 5-month training period. In the first period, patients trained three times per week, and in the second period patients trained two times per week. In both periods, one of these weekly training sessions was performed at home to

encourage the patients to exercise in their own environment. The training sessions consisted of cycling, walking, climbing stairs, and lifting weights. Besides improvement of physical condition, the main goal of COPE-active was a behavioural change towards exercise. The intensity of the programme was tailored to the individual patient's performance level by providing the physiotherapist with the baseline results of the cardio-pulmonary exercise test, and the incremental shuttle walk test. After the 11-month supervised training period, patients in the COPE-active group were advised to continue the unsupervised training at home, but not to follow any formal physiotherapeutic exercise training programme. Instead, the patients were encouraged to participate in other forms of community-based exercise.

### Outcome measures

The primary outcome was maximal exercise capacity measured with the incremental shuttle walk test (ISWT) according to the protocol of Singh et al.[19] using a 10-meter course. A practice walk was performed before the baseline measurement. According to current standard, an individual change of at least 47.5 meter is considered clinically important[20]. Endurance capacity was measured with the endurance shuttle walk test (ESWT) using a 10-meter course and a walking speed of 85% of the maximal ISWT walking speed[21]. Daily physical activity was assessed by the number of steps measured with a pedometer (Yamax Digi-Walker SW-200; Tokyo, Japan) during a 7-day period. HRQoL was measured by the self-administered standardised Chronic Respiratory Questionnaire (CRQ-SAS)[22]. An individual change of at least 0.5/domain (dyspnoea, fatigue, emotional functioning, mastery) is considered clinically important[23]. Health status was evaluated by the self-administrated Clinical COPD Questionnaire (CCQ)[24]. A change of 0.4 is considered to represent a minimal important difference at the individual level[25]. Anxiety and depression were measured with the Hospital Anxiety and Depression Scale (HADS)[26]. This instrument produces separate scores for anxiety and depression ranging from 0 to 21.

### Statistical analysis

Between-group differences in continuous variables over time were assessed by analysis of repeated measurements with fixed effects (SPSS procedure for mixed models, version 20). Baseline values were subtracted from follow-up values to correct for baseline differences. A modified intention-to-treat approach was used for all primary analyses, meaning that all patients who completed at least the baseline measurement were included in the analyses. Secondary, a per protocol analysis was performed on the primary outcome, maximal exercise capacity, in order to assess the effects of the programme in patients who adhered to the exercise programme. Adherence was defined as participation in at least 70% of the sessions.

The one year effects as presented in the text of the results section were obtained from the one year analyses as published earlier[15]. These values deviate from the one year values in the current two year analysis as presented in tables 2 and 4. Due to the additional data

collected in the second year of follow-up, estimations of missing values are slightly different in the first year compared to the second year, resulting in slightly different outcomes.

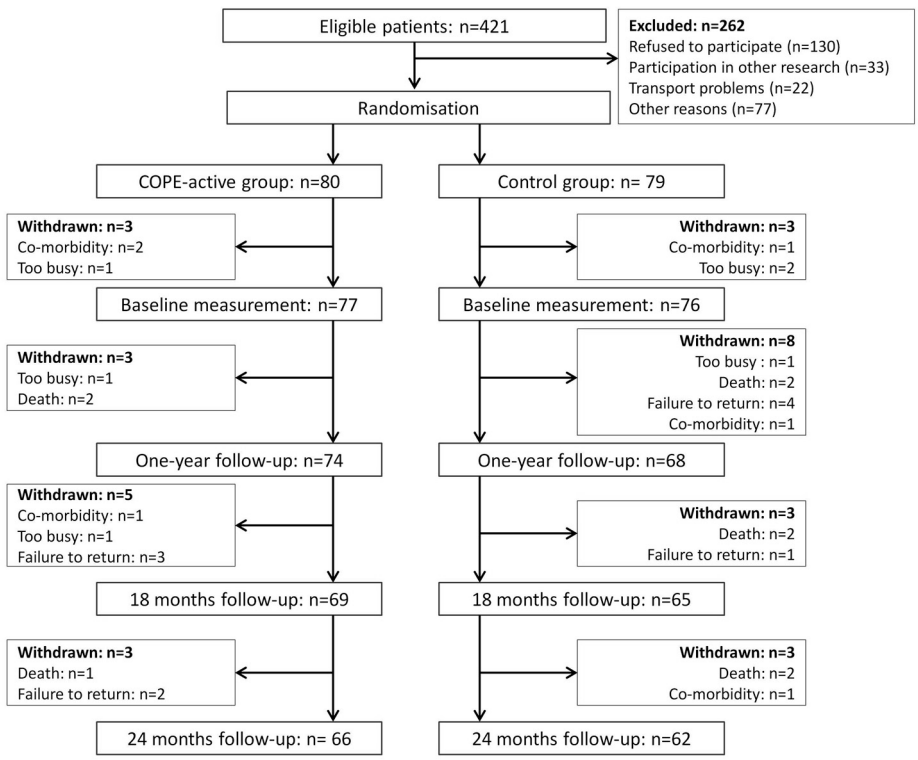


**Figure 1** Patient flow during 24 months follow-up.

## RESULTS

### Patients and follow-up

The intervention (community-based exercise programme) was assigned to 80 of the 159 included patients, while the control condition was assigned to 79 of them (Figure 1). After one year of follow-up, 74 (92.5%) patients in the intervention group and 68 (86.1%) patients in the control group still participated. In the second year of follow-up, an additional eight patients in the intervention group and six patients in the control group were lost-to-follow up, resulting in 66 (82.5%) and 62 (78.5%) patients, respectively, completing the two years follow-up (Figure 1). Reasons for drop out were comparable between the groups (Figure 1). Six patients dropped out before the baseline measurements, so baseline characteristics of 153 patients are presented in Table 1.

**Table 1** Baseline characteristics

| | COPE-active | Control |
|---|---|---|
| Number of patients | 77 | 76 |
| Age (years) | 63.1 ± 8.1 | 64.1± 7.7 |
| Gender (% male) | 58.4 % | 57.9 % |
| Body mass index (kg/m$^2$) | 26.1 ± 5.0 | 26.8 ± 4.4 |
| Smokers | 35 % | 34 % |
| Medical Research Council dyspnoea scale | 2.25 ± 1.05 | 2.50 ± 1.15 |
| $FEV_1$ (L) | 1.43 ± 0.54 | 1.40 ± 0.53 |
| $FEV_1$ (% of predicted) | 49.6 ± 14.2 | 50.5 ± 17.0 |
| VC (L) | 3.78 ± 1.05 | 3.47 ± 0.84 |

*Data are presented as mean ± standard deviation unless otherwise stated.*

### Exercise capacity

Maximal exercise capacity was measured with the ISWT. After one year of follow-up, directly after the end of the supervised exercise programme, there was a statistically significant between-group difference in mean change from baseline in walking distance of 35.1 meters (95%CI: 8.4 to 61.8). After two years of follow-up the between-group difference in mean change from baseline in walking distance was reduced to 12.2 meters (95%CI: -16.6 to 41.0) (Figure 2A), with better performance in the COPE-active group, but no longer statistically significant (Table 2).

Endurance capacity was measured with the ESWT. After one year of follow up, the between-group difference in mean change from baseline in walking distance was 145.8 meters (95%CI: -26.2 to 317.8) in favour of the intervention group, but not statistically significant. After two years this difference was reduced to 52.1 meters (95%CI: -145.6 to 249.8) (Table 2).

**Table 2** Baseline scores and mean differences from baseline at 12, 18 and 24 months of exercise capacity and physical activity in the COPE-active and control group

| | | | Difference from baseline* | | | Between-group difference (I vs. C) | |
|---|---|---|---|---|---|---|---|
| | | **Baseline** | **12 months** | **18 months** | **24 months** | **Δ 24 months** | **Overall*** |
| ISWT-I | Nr of patients | 77 | 69 | 66 | 62 | | |
| | Distance | 387.7 (350.3 ; 425.0) | 10.8 (-8.7 ; 30.4) | -14.7 (-34.5 ; 5.0) | -30.4 (-50.4 ; -10.3) | 12.2 (-16.6 ; 41.0) | 23.5 (-1.93 ; 49.0) |
| ISWT-C | Nr of patients | 74 | 66 | 60 | 57 | | |
| | Distance | 341.4 (306.0 ; 376.7) | -24.3 (-44.5 ; -4.1) | -37.9 (-58.5 ; -17.4) | -42.6 (-63.5 ; -21.7) | | |
| ESWT-I | Nr of patients | 77 | 68 | 66 | 62 | | |
| | Distance | 687.9 (553.3 ; 804.4) | 48.8 (-75.0 ; 172.6) | -73.5 (-212.0 ; 65.0) | -100.6 (238.8 ; 37.7) | 52.1 (-145.6 ; | 99.2 (-67.0 ; |
| ESWT-C | Nr of patients | 74 | 66 | 60 | 57 | | |
| | Distance | 629.5 (501.1 ; 757.9) | -92.8 (-220.5 ; 34.9) | -158.4 (-302.6 ; - | -152.7 (-296.5 ; -8.9) | | |
| Pedometer-I | Nr of patients | 62 | 55 | 50 | 47 | | |
| | Steps (n per | 4472 (3783 ; 5162) | 811 (145 ; 1478) | 584 (-100 ; 1267) | 648 (-56 ; 1352) | 1193 (203 ; 2182) | 924 (172 ; 1676) |
| Pedometer-C | Nr of patients | 65 | 55 | 47 | 47 | | |
| | Steps (n per | 5224 (4366 ; 6082) | -367 (-1029 ; 295) | -203 (-899 ; 493) | -545 (-1246 ; 157) | | |

*Data are presented as mean (95%CI); I: COPE-active group; C: control group; ISWT: Incremental Shuttle Walk Test; ESWT: Endurance Shuttle Walk Test; * Intention-to-treat analysis, results were obtained with repeated measurements analysis.*

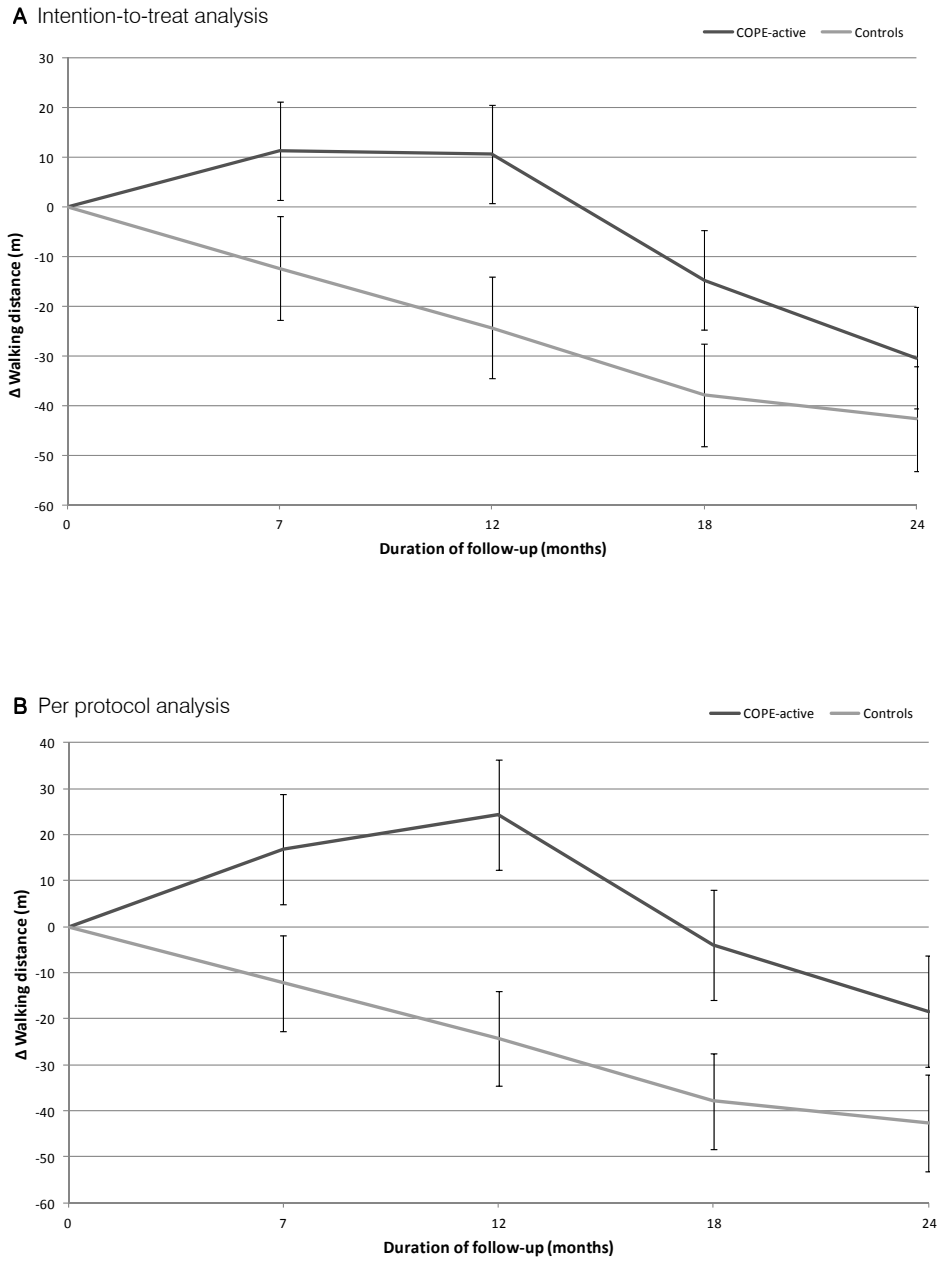


**Figure 2** Mean change from baseline in incremental shuttle walk test (ISWT) walking distance over 24 months of follow-up using an intention-to-treat analysis (A) and a per protocol analysis (B).

### Daily physical activity

Daily physical activity was measured with a pedometer. The change from baseline in mean number of steps per day was calculated over a 7-day period. After one year of follow-up, there was a statistically significant between-group difference in mean change from baseline in number of steps/day of 1190.4 (95%CI: 255.6 to 2125.2) in favour of the COPE-active group. After two years of follow-up this between-group difference was maintained, and still statistically significant, with 1193 steps/day (95%CI: 203 to 2183) (Figure 3 and Table 2).

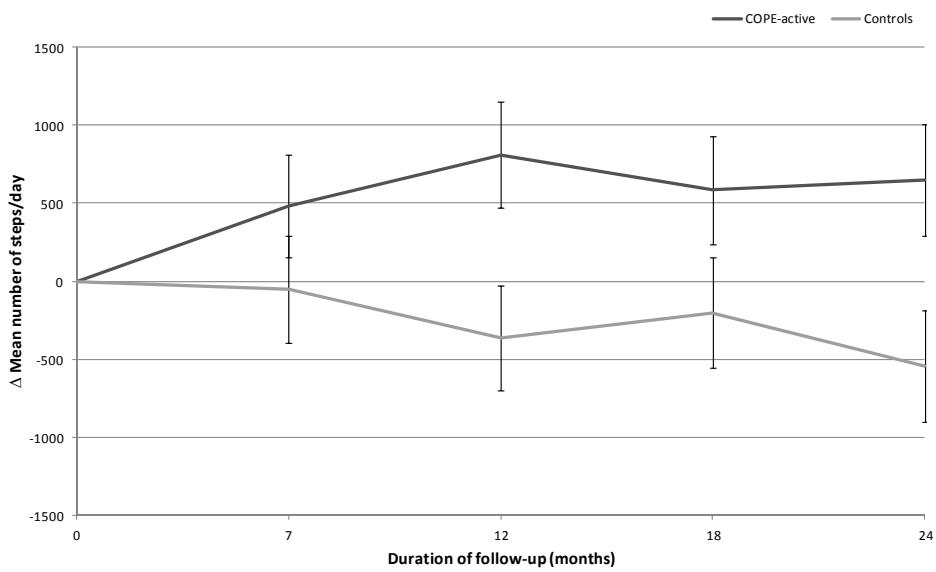


**Figure 3** Mean change from baseline in daily physical activity (mean number of steps/day) over 24 months of follow-up using an intention-to-treat analysis.

Pedometer data at 24 months were missing in 26 (34%) patients in both groups (28 due to drop out, and 24 due to other reasons). We assessed whether patients who had not completed the pedometer measurement at 24 months of follow-up were different with regard to baseline characteristics from patients who had completed the measurement. Patients with a missing pedometer measurement at 24 months follow-up were in a worse functional state at baseline than patients who had a pedometer measurement at that point of time (Table 3). The degree in which this influenced total group means was comparable in both groups and ranged from 0% to 8%.

**Table 3** Baseline characteristics of patients with and without a pedometer measurement at 24 months follow-up

| | COPE-active group | | Control group | |
|---|---|---|---|---|
| | **With** | **Without** | **With** | **Without** |
| Nr of patients | 51 | 25 | 50 | 25 |
| **Age (years)** | 63.2 ± 7.6 | 63.1 ± 9.3 | 63.9 ± 7.5 | 64.4 ± 8.5 |
| Nr of patients | 51 | 25 | 50 | 25 |
| **$FEV_1$ (L)** | 1.49 ± 0.53 | 1.29 ± 0.56 | 1.43 ± 0.51 | 1.35 ± 0.57 |
| Nr of patients | 51 | 26 | 50 | 26 |
| **$FEV_1$ (% of predicted)** | 50.1 ± 13.2 | 48.5 ± 16.3 | 50.6 ± 15.9 | 50.3 ± 19.4 |
| Nr of patients | 51 | 25 | 50 | 25 |
| **VC (L)** | 3.9 ± 1.1 | 3.5 ± 1.0 | 3.6 ± 0.8 | 3.2 ± 0.8 |
| Nr of patients | 51 | 26 | 48 | 26 |
| **ISWT** | 408.6 ± 166 | 346.5 ± 156.5 | 380.2 ± 142.2 | 269.62 ± 146.8 |
| Nr of patients | 51 | 26 | 48 | 26 |
| **ESWT** | 709.8 ± 565.6 | 618.2 ± 533.2 | 764.7 ± 612.8 | 379.8 ± 300.9 |
| Nr of patients | 47 | 15 | 47 | 18 |
| **Pedometer** | 4768 ± 2831 | 3547 ± 2141 | 5599 ± 3764 | 4244 ± 2329 |

*Data are presented as mean ± standard deviation; ISWT: Incremental Shuttle Walk Test; ESWT: Endurance Shuttle Walk Test.*

### Health status

As reported after one year, no between-group differences in mean scores were found in any domain of the CCQ or the domains of fatigue, emotional function and mastery of the CRQ after two years. The CRQ domain of dyspnoea showed a between-group difference in mean score of 0.30 points (95%CI: -0.14 to 0.74) after two years of follow-up, which was comparable to the difference after one year (0.32 points (95%CI: -0.03 to 0.67)). The overall difference over two years between the intervention and control group was statistically significant (0.35 (95%CI: 0.03 to 0.67)) but did not reach the minimal important difference of 0.5. Anxiety and depression were assessed with the HADS. There were no statistically significant differences in both these domains (Table 4).

### Per protocol analysis ISWT

In our secondary per protocol analysis on the ISWT, we pre-defined patients who participated in at least 70% of the physiotherapy sessions as treated per protocol, i.e. as patients who sufficiently adhered to the programme. This was the case in 67.5% of the patients. These patients who adhered well, increased their mean walking distance with 24.9 meters (95%CI: -2.0 to 51.8) after 12 months of follow-up as compared to 11.1 meters (95%CI: -10.0 to 32.2) in the group also including the poor adherers. After two years of follow-up, the loss in exercise capacity in the group with solely adherers was smaller than in the total group (-18.4 (95%CI: -42.4 to 5.7) vs. -30.4 (95%CI: -50.4 to -10.3) meters compared to baseline). The overall between-group difference of 34.1 meters (95%CI: 5.9 to 62.3) over 24 months was, in contrast to that in the intention-to-treat analysis, still statistically significant but did not reach the minimal clinically important difference of 35.1 meters (Figure 2B).

**Table 4** Baseline scores and mean differences from baseline at 12, 18 and 24 months of health status in the COPE-active and control group.

| | | | Difference from baseline* | | | Between-group difference | |
|---|---|---|---|---|---|---|---|
| | | **Baseline** | **12 months** | **18 months** | **24 months** | **Δ 24 months** | **Δ Overall*** |
| **CRQ - I** | Nr of patients | 77 | 71 | 68 | 65 | | |
| | Dyspnoea | 4.40 (4.08 ; 4.73) | 0.30 (0.06 ; 0.54) | 0.24 (-0.04 ; 0.52) | 0.08 (-0.24 ; 0.39) | 0.30 (-0.14 ; 0.74) | 0.35 (0.03 ; 0.67) |
| | Fatigue | 4.55 (4.27 ; 4.83) | 0.14 (-0.16 ; 0.43) | 0.09 (-0.21 ; 0.39) | -0.07 (-0.38 ; 0.23) | -0.02 (-0.45 ; 0.42) | 0.08 (-0.27 ; 0.43) |
| | Emotional function | 5.14 (4.88 ; 5.41) | 0.18 (-0.04 ; 0.4) | 0.04 (-0.19 ; 0.26) | 0.27 (0.05 ; 0.50) | 0.23 (-0.10 ; 0.55) | 0.12 (-0.12 ; 0.37) |
| | Mastery | 5.35 (5.09 ; 5.61) | 0.33 (0.08 ; 0.57) | 0.14 (-0.11 ; 0.39) | 0.13 (-0.12 ; 0.38) | 0.25 (-0.11 ; 0.61) | 0.16 (-0.13 ; 0.45) |
| **CRQ - C** | Nr of patients | 76 | 68 | 63 | 60 | | |
| | Dyspnoea | 4.52 (4.21 ; 4.84) | -0.01 (-0.26 ; 0.23) | -0.19 (-0.48 ; 0.1) | -0.22 (-0.54 ; 0.10) | | |
| | Fatigue | 4.13 (3.84 ; 4.42) | 0.06 (-0.24 ; 0.36) | -0.07 (-0.38 ; 0.24) | -0.06 (-0.37 ; 0.26) | | |
| | Emotional function | 4.90 (4.67 ; 5.13) | 0.09 (-0.14 ; 0.31) | -0.11 (-0.34 ; 0.12) | 0.05 (-0.19 ; 0.28) | | |
| | Mastery | 5.30 (5.05 ; 5.55) | 0.23 (-0.02 ; 0.47) | -0.03 (-0.29 ; 0.22) | -0.12 (-0.38 ; 0.14) | | |
| **CCQ - I** | Nr of patients | 77 | 70 | 68 | 65 | | |
| | Symptoms | 2.5 (2.12 ; 2.58) | -0.10 (-0.36 ; 0.15) | -0.06 (-0.29 ; 0.17) | 0.03 (-0.24 ; 0.29) | 0.30 (-0.07 ; 0.68) | 0.14 (-0.15 ; 0.43) |
| | Functional state | 2.14 (1.87 ; 2.41) | -0.05 (-0.29 ; 0.20) | 0.20 (-0.05 ; 0.45) | 0.21 (-0.05 ; 0.46) | 0.14 (-0.22 ; 0.51) | 0.04 (-0.27 ; 0.34) |
| | Mental state | 0.93 (0.71 ; 1.15) | -0.13 (-0.36 ; 0.10) | -0.12 (-0.37 ; 0.14) | 0.02 (-0.27 ; 0.30) | 0 (-0.40 ; 0.41) | -0.05 (-0.37 ; 0.26) |
| | Total | 1.81 (1.60 ; 2.01) | -0.10 (-0.28 ; 0.09) | 0.01 (-0.18 ; 0.19) | 0.09 (-0.10 ; 0.27) | 0.16 (-0.11 ; 0.43) | 0.04 (-0.18 ; 0.27) |
| | Nr of patients | 74 | 66 | 61 | 58 | | |
| | Symptoms | 2.92 (2.64 ; 3.21) | -0.17 (-0.43 ; 0.09) | -0.29 (-0.53 ; -0.03) | -0.28 (-0.55 ; 0.00) | | |
| | Functional state | 2.33 (2.03 ; 2.63) | 0.05 (-0.20 ; 0.31) | 0.13 (-0.13 ; 0.39) | 0.06 (-0.20 ; 0.33) | | |
| | Mental state | 1.03 (0.77 ; 1.28) | -0.11 (-0.35 ; 0.12) | -0.06 (-0.33 ; 0.20) | 0.02 (-0.28 ; 0.31) | | |
| | Total | 2.09 (1.87 ; 2.31) | -0.08 (-0.27 ; 0.11) | -0.07 (-0.27 ; 0.12) | -0.07 (-0.27 ; 0.13) | | |
| **HADS - I** | Nr of patients | 76 | 69 | 67 | 63 | | |
| | Anxiety | 4.26 (3.41 ; 5.12) | -0.69 (-1.37 ; -0.01) | 0.39 (-0.41 ; 1.19) | -0.24 (-0.99 ; 0.51) | -0.18 (-1.24 ; 0.89) | 0.09 (-0.69 ; 0.88) |
| | Depression | 3.96 (3.12 ; 4.80) | -0.72 (-1.32 ; -0.11) | 0.20 (-0.56 ; 0.96) | -0.28 (-1.0 ; 0.44) | -0.26 (-1.27 ; 0.75) | -0.27 (-1.00 ; 0.51) |
| **HADS - C** | Nr of patients | 76 | 68 | 63 | 60 | | |
| | Anxiety | 5.38 (4.56 ; 6.21) | -0.59 (-1.3 ; 0.10) | -0.10 (-0.92 ; 0.72) | -0.07 (-0.83 ; 0.70) | | |
| | Depression | 5.24 (4.35 ; 6.12) | -0.30 (-0.91 ; 0.31) | 0.76 (-0.02 ; 1.54) | -0.02 (-0.75 ; 0.72) | | |

*Data are presented as mean (95%CI); I: COPE-active group; C: control group; CRQ: Chronic Respiratory Questionnaire; CCQ: Clinical COPD Questionnaire; HADS: Hospital Anxiety and Depression Scale. * Intention-to-treat analysis. results were obtained with repeated measurements analysis.*

## DISCUSSION

The goal of this study was to compare the long-term effects of a community-based exercise programme incorporated in a self-management programme with the effects of a self-management programme only in patients with COPD. Maximal exercise capacity as measured with the ISWT was substantially better in the intervention group compared to the control group after one year of follow-up, but this initial increase was not maintained in the second year of follow-up. As a consequence, the overall benefit measured over two years was not statistically significantly different between the two groups. In contrast with this, the beneficial effect on daily physical activity was maintained after two years. After 24 months, the intervention still had a positive effect on the CRQ dyspnoea domain, but no statistically significant effects were seen on the other CRQ domains, the CCQ, the HADS, and the ESWT.

Only a few studies have used the ISWT to address long-term effects of exercise programmes, mainly classified as pulmonary rehabilitation, on exercise capacity in patients with COPD. Two of these studies, with intervention periods of six and eight weeks, found a decline in ISWT walking distance in the year following the initial intervention period in the intervention group, but also a more gradual decline in exercise capacity in the control group during the entire period of follow-up[8;9]. As a result, differences in walking distance between the intervention and the control group were still statistically significant after one year of follow-up[8]. Two other studies on long-term effects of exercise in patients with COPD measured exercise capacity with the six minute walking test (6MWT)[6;7]. Duration of the interventions in these studies was more comparable to that of our intervention, namely six and 12 months. Beneficial effects of these programmes on 6MWT distance were maintained after 18 and 24 months follow-up, respectively. The results of studies assessing long-term maintenance of exercise capacity after an exercise programme are therefore ambiguous.

The loss in exercise capacity in the second year of follow-up in our study is probably due to a combination of the discontinuation of regular exercise training and the progressive character of COPD. Patients in this study suffered from relatively severe disease with relatively frequent exacerbations, and it is known that each exacerbation negatively influences the functional state of the patient[27]. Patients were encouraged to participate in some sort of community-based exercise (e.g. general or respiratory specific exercise programmes not reimbursed as physiotherapy) at the end of the formal community-based exercise programme. However, the decrease in exercise capacity in the second year of follow-up suggests that most have failed to attend such programmes, or otherwise that training intensity and frequency of these programmes have been insufficient to maintain the gain in exercise capacity. Proper maintenance programmes might be preventing loss of beneficial effects after the initial exercise programme. In a systematic review of Beauchamp et al. regarding the effectiveness of supervised exercise programmes after an initial pulmonary rehabilitation programme in patients with COPD[10] only six studies could be included, and their meta-analysis showed a beneficial effect on 6MWT walking distance

after six months, but after 12 months follow-up, differences between study groups were no longer statistically significant[10]. This indicates that even formal (exercise) programmes after the end of the initial programme are no guarantee for maintenance of beneficial effects. More research on the optimal maintenance programme after a primary exercise programme is therefore needed.

A crucial factor in the success of exercise interventions is adherence of patients to the programmes[28]. In our per protocol analysis on the ISWT we excluded 26 (34%) patients who participated in less than 70% of the physiotherapeutic exercise sessions and were therefore classified as non-adherent. Per protocol analyses should be interpreted with extreme care since they most likely introduce selection bias. Our per protocol analysis suggests that patients who adhered are doing better than patients who did not, however non-adherent patients were worse at baseline than adherent patients (data not shown). It therefore remains to be seen whether this is an actual effect of the intervention or a result of selection bias. The primary intention-to-treat analysis gives probably the most realistic look on the effectiveness of the intervention in real life, since non-adherence is part of daily practice[29].

It is interesting to note that, although the improvement in maximal exercise capacity at one year was not maintained over two years, improvement in daily physical activity as measured with a pedometer, was maintained at two years. Maximal exercise capacity is a measure of what patients are able to do, and daily physical activity is a measure of what patients actually do. So, these are two different concepts[30]. It is known that an increase in exercise capacity can already be achieved with an exercise programme as short as four weeks[31], however changes in behaviour are usually not achieved in a couple of weeks[32;33]. Our data suggests that we not only achieved a change in activity behaviour, but that this effect was also maintained after two years of follow-up. However, our data also suggests that the intensity and/or frequency of this additional daily physical activity has most certainly been too low to actually contribute to maintenance of maximal exercise capacity. We were not able to assess the frequency and intensity of physical activity, since we used basic pedometers. A study that did assess walking intensity in patients with COPD concluded that 84% of the patients reached more than 30 minutes of walking time per day but that only less than a quarter of this time was walked at at least moderate intensity[34]. In another study[33;35;36] patients were classified as regular or irregular walkers, and compared with regard to long-term maintenance of effect of a pulmonary rehabilitation programme. Both regular and irregular walkers steadily declined in 6MWT distance during 24 months follow-up[36]. These findings seem to underline that walking is not sufficient to maintain an initial increase in exercise capacity.

We used pedometers to measure daily physical activity, which can be seen as a limitation since nowadays more sophisticated activity monitors are widely available, and pedometers tend to underestimate step counts at slow walking speed[37]. Also, we had a relatively large number of missing data for daily physical activity. Despite great efforts of the research personnel, there were issues with pedometers that did not work (either due to low battery or

mechanical defects), patients not returning the pedometer and diary, or patients just not wearing the pedometer for seven days. In general, patients who did not have a pedometer measurement at 24 months follow-up seemed to have a worse functional state at baseline compared to the patients who had a measurement. Possible underestimation due to the use of pedometers or overestimation due to the relatively large amount of missing data would be expected to be the same in both groups, and would therefore not have affected the between-group difference.

A statistically significant between-group difference was found on the CRQ dyspnoea domain, indicating that patients who participated in the COPE-active programme experienced less dyspnoea during activities than patients in the control group[23]. Breathing exercises and coping with breathlessness were part of the initial self-management programme, but patients in the intervention group had multiple opportunities to practice and acquire these methods during exercise under supervision of a physiotherapist. Also, improved exercise tolerance in the intervention group might have led to a reduction in exertional dyspnoea during activities which in turn might have contributed to the increase in daily physical activity[38]. As was expected based on the 12-month results, we did not find any between-group differences on the other CRQ domains or the CCQ. This is probably due to the already relatively good scores at baseline which left little room for improvement during follow-up[15]. The same accounts for anxiety and depression measured with the HADS.

We had already shown that in comparison to a self-management programme only, a community-based physiotherapeutic exercise programme was effective in achieving a behavioural change, reflected by an increase in daily physical activity after one year. We now show that the increase in daily physical activity could be maintained over the second year, but not the increase in exercise capacity. We still need further studies investigating how an initial increase in exercise capacity can be best maintained.

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# CHAPTER 5

## COST-EFFECTIVENESS OF A COMMUNITY-BASED EXERCISE PROGRAMME IN COPD SELF-MANAGEMENT

SUBMITTED

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# CHAPTER 6

## RELATIONSHIP BETWEEN DAILY PHYSICAL ACTIVITY AND EXERCISE CAPACITY IN PATIENTS WITH COPD

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## ABSTRACT

### Introduction
Exercise training programmes for patients with COPD are effective in improving exercise capacity. The few trials that have investigated the effects of exercise programmes on daily physical activity show contradictory results.

### Aim
To investigate the relation between daily physical activity level and exercise capacity in patients with COPD using data of a randomised controlled trial in which the exercise intervention was aimed at improvement of both physical activity and exercise capacity (the COPE-II study).

### Methods
These are secondary analyses of the COPE-II study, a randomised controlled trial in which a community-based physiotherapeutic exercise programme was evaluated. Daily physical activity was measured with a pedometer (steps/day). Exercise capacity was measured with an incremental maximal cycle ergometer test, the incremental (ISWT) and endurance shuttle walk test (ESWT). Pearson's correlation coefficients were calculated.

### Results
At baseline, correlations between steps/day and $VO_{2peak}$, ISWT (m), ESWT (m) and ESWT (s) were 0.54, 0.59, 0.44, and 0.34, respectively (all $p<0.01$). In the intervention group, correlations between change in steps/day over 7 months and change in ISWT (m), ESWT (m) and ESWT (s) were 0.47, 0.41, and 0.38, respectively (all $p<0.01$). In the control group, these same correlations were weak to non-existent.

### Conclusions
A moderate to weak relationship was found between daily physical activity and exercise capacity. These results strengthen our beliefs that exercise interventions need to target not only exercise capacity but also behavioural change with regard to daily physical activity to achieve improvements in both parameters.

## INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is not only characterized by symptoms of dyspnoea, chronic cough, and sputum production, but also by a decreased exercise performance[1] and reduced physical activity level[2-4]. There is a large number of randomised controlled trials investigating the effects of exercise training programmes, whether part of a pulmonary rehabilitation programme or not, on exercise capacity in patients with COPD. A meta-analysis of Lacasse et al[5] included 31 randomised trials and found that rehabilitation programmes including exercise therapy are effective in improving exercise capacity and quality of life. As a result, international guidelines recommend pulmonary rehabilitation for patients with chronic respiratory disease, and specifically for patients with COPD[1].

Most exercise training programmes for patients with COPD focus on improvement of exercise capacity which is reflected in the outcome measures. The incremental maximal cycle ergometry test is the 'gold standard' for measuring exercise capacity[6]. However, this laboratory-based test requires specialised equipment and knowledge, which makes it a relatively expensive test. Frequently used alternatives test are the field-based walking tests: the internally paced six-minute walk test (6MWT)[7] and the externally paced incremental and endurance shuttle walk tests (ISWT and ESWT)[8;9].

A minimum of 30 minutes of physical activity at a moderate intensity, on at least 5 days per week, is recommended for elderly adults, and adults with a clinically significant chronic condition to improve and maintain health[10]. In the Netherlands, half of the patients with chronic respiratory diseases (asthma and COPD) do not meet this criterion[11]. This percentage will probably even be higher in a population of solely patients with COPD[12]. Compared to healthy subjects, patients with COPD spend significantly less time walking and standing, and more time sitting and lying[2]. Recent studies show that physical activity level gradually declines with severity of disease[3;4]. In COPD patients, regular physical activity leads to general health benefits such as a reduced risk for cardiovascular disease, stroke, and colon cancer[13], but also to a lower risk for COPD-related hospitalisations and mortality[14]. Waschki and colleagues even state that the level of physical activity is the strongest predictor for all-cause mortality in patients with COPD[15]. On the shorter term, when participation in a rehabilitation programme leads to a permanent increase in daily physical activity, this might contribute to the maintenance of beneficial effects of the programme on exercise capacity. However, the latter is often not achieved with the current programmes[16;17].

Although there is an extensive amount of research on the effects of exercise programmes on exercise capacity, only a few trials investigated the effects on daily physical activity in patients with COPD[18-20]. These studies showed contradictory results, which is probably due to the variation in length and content of the interventions. Whereas an increase in exercise capacity can be achieved with exercise programmes as short as 4 weeks[1], an increase in daily physical activity is elicited by a change in habits and behaviours of the sedentary

patient with COPD, and is thus more time-consuming[17;19]. Therefore, it is likely that there is a difference in concept between exercise capacity and daily physical activity[21]. Hence, we hypothesise that a positive change in exercise capacity does not necessarily lead to an increase in daily physical activity and vice versa. Several earlier studies have investigated daily physical activity in relation to exercise capacity. In the majority of the studies the latter was measured with the 6MWT[2;15;22-28]. The relationship between physical activity and the ESWT and ISWT is less thoroughly investigated[26]. Using the data of a previous published randomised controlled trial in patients with COPD[20], in which the exercise intervention was aimed at change in both exercise capacity and daily physical activity, we further investigated the relationship between exercise capacity and daily physical activity. With these secondary analyses, we were among the first to investigate the relationship between change in exercise capacity and change in daily physical activity in patients who participated in the exercise programme and patients who received usual care. In addition, we have explored whether other patient characteristics were correlated with physical activity at baseline, and with change in physical activity.

## METHODS

Detailed methods of the COPE-II study have been published elsewhere [20;29].

### Subjects

Patients eligible for inclusion had a clinical diagnosis of COPD according to the GOLD criteria[30]; a post-bronchodilator $FEV_1$ between 25 and 80% of predicted; at least 3 exacerbations or one hospitalisation for respiratory problems in the two years preceding study entry. Patients were excluded when they had a serious other disease with a low survival rate; another disease that influenced bronchial symptoms and/or lung function; a need for regular oxygen therapy; a disorder or progressive disease that seriously influenced walking ability.

### Study design

All patients included in the COPE-II study participated in four self-management sessions. The intention was to change the patients' disease behaviour by increasing their knowledge, confronting them with consequences of specific behaviour, and helping patients acquire and practice skills to deal with different components of their disease. Subsequently, only the intervention group participated in a community-based physiotherapeutic exercise programme (COPE-active). This programme was divided in two parts: a 'compulsory' 6-month, and a subsequent optional but recommended 5-month training period. In the first period, patients trained three times per week, and in the second period patients trained two times per week. In both periods, one training session per week was performed at home to encourage the patients to exercise in their own environment. The training sessions consisted of cycling, walking, climbing stairs, and lifting weights. Besides improvement of physical condition, the main goal of COPE-active was a behavioural change towards exercise. The intensity of the programme was tailored to the individual patient's performance level by providing the physiotherapist with the baseline results of the incremental maximal cycle ergometry test, and the incremental shuttle walk test[20].

## Measurements

### *Exercise capacity*

*Incremental maximal cycle ergometer test*

At baseline, patients in the COPE-active group performed an incremental maximal cycle ergometer test on an electronically braked cycle ergometer. The tests started with two minutes of seated rest followed by three minutes of unloaded cycling. After this, the workload was increased with 10, 15 or 20 W each minute depending on the patient's height, weight and age. The patients were instructed to cycle at a speed of 60-70 rpm, and were encouraged to continue cycling until exhaustion. During the test, patients breathed through a facemask connected to a calibrated metabolic cart. Expired gas passed through a flow metre, oxygen ($O_2$) analyser and a carbon dioxide ($CO_2$) analyser. The flow metre and gas analysers were connected to a computer, which calculated breath-by-breath minute ventilation (VE), oxygen uptake ($VO_2$), carbon dioxide output ($VCO_2$) and the respiratory exchange ratio (RER = $VCO_2/VO_2$) from conventional equations. Heart rate (HR) was measured continuously during the exercise test by electrocardiogram (ECG). Peak oxygen consumption ($VO_{2peak}$) was calculated as the average value over the last 30 seconds before subjective exhaustion.

*Incremental shuttle walk test*

The ISWT was conducted according to the protocol of Singh et al[9]. Patients were instructed to walk along a 10-m course, and to turn around at the cones at either end in time with the audio signal. The test started at a walking speed of 0.5 m/s, and each minute the speed increased with 0.17 m/s. The maximum duration of the test was 12 minutes. However, the test was terminated earlier when the patient indicated not to be able to continue due to fatigue or dyspnoea, or when the patient failed to reach the cone in the time allowed. The ISWT was performed at baseline, seven, and 12 months. At baseline, each patient performed a practice walk[9].

*Endurance shuttle walk test*

The ESWT was also performed on a 10-m course[8]. After a warming up period of 120 s, walking speed increased and was constant during the test. Walking speed was set at 85% of the patient's maximum capacity as predicted from the distance walked during the ISWT. The maximal duration of the test was 20 minutes, and the criteria to stop the test were the same as described for the ISWT[9]. The ESWT was performed at baseline, seven, and 12 months.

### *Daily physical activity level*

*Pedometer*

Daily physical activity was assessed by the number of steps per day measured with the Yamax Digi-Walker SW-200 (Tokyo, Japan). Patients were instructed to wear a pedometer for a 7-day period, and to note the number of steps in a daily diary, at baseline, seven, and 12 months. Daily physical activity was calculated by summing up the number of steps over seven days, and then averaging it by that same number of days[20].

## Other measurements

At baseline, lung function was assessed using spirometry. The forced expiratory volume in one second ($FEV_1$) and vital capacity (VC) were measured. Also, the Medical Research Council (MRC) dyspnoea scale was administered[31], and anthropometry and demographic variables were collected.

## Statistical analysis

Baseline characteristics are reported as mean ± SD for continuous variables with a normal distribution, or as median and range when not normally distributed. Categorical variables are presented as number with percentage. The relationship between continuous variables was tested by calculating Pearson or Spearman correlation coefficients, depending on the normality of the distribution of the variables. Correlation coefficients were considered to be statistically significant when the p-value was smaller than 0.05. All analyses were performed using SPSS version 15.0.

## RESULTS

One hundred fifty nine patients were included in the COPE-II study, 80 patients were randomised to participation in the community-based physiotherapeutic exercise programme (COPE-active) and 79 patients were randomised to the control group. In both study groups, three patients dropped out between randomisation and baseline measurements. Table 1 shows the baseline characteristics of the remaining 153 patients.

**Table 1** Baseline characteristics

| | Total | COPE-active | Control |
|---|---|---|---|
| **Number of patients** | 153 | 77 | 76 |
| **Age (years)** | 63.6 ± 7.9 | 62.9 ± 8.1 | 63.9 ± 7.8 |
| **Male (%)** | 58.2 | 58.4 | 57.9 |
| **Smokers (%)** | 34.6 | 35.1 | 34.2 |
| **MRC dyspnoea scale** | 2.37 ± 1.11 | 2.25 ± 1.05 | 2.50 ± 1.15 |
| **$FEV_1$ (L)** | 1.41 ± 0.53 | 1.43 ± 0.54 | 1.40 ± 0.53 |
| **$FEV_1$% predicted value** | 50.2 ± 15.6 | 49.6 ± 14.2 | 50.5 ± 17.0 |
| **IVC (L)** | 3.63 ± 0.97 | 3.78 ± 1.05 | 3.47 ± 0.84 |
| **BMI ($kg/m^2$)** | 26.5 ± 4.72 | 26.1 ± 5.0 | 26.8 ± 4.4 |
| **Daily physical activity level (steps/day)[a]** | 4857 ± 3132 | 4472 ± 2716 | 5224 ± 3464 |
| **Incremental shuttle walk test (m)[b]** | 365.0 ± 159.9 | 387.7 ± 164.5 | 341.4 ± 152.4 |
| **Endurance shuttle walk test (m)[b]** | 654.7 ± 552.3 | 678.9 ± 553.1 | 629.5 ± 554.1 |
| **Endurance shuttle walk test (s)[b]** | 505.7 ± 370.3 | 503.7 ± 368.1 | 507.9 ± 375.1 |
| **$VO_{2peak}$ (ml/kg/min) [c]** | n.a. | 18.05 ± 5.03 | n.a. |
| **$W_{peak}$ (Watt)[d]** | n.a. | 93.38 ± 47.67 | n.a. |

*Medical Research Council (MRC); Forced Expiratory Volume in 1 second ($FEV_1$); Inspiratory Vital Capacity (IVC); Body Mass Index (BMI); Peak oxygen uptake ($VO_{2peak}$); Peak wattage ($W_{peak}$).*

*[a] Based on 62 patients in the COPE-active group and 65 patients in the control group*

*[b] Based on 77 patients in the COPE-active group and 74 patients in the control group*

*[c] Based on 69 patients in the COPE-active group*

*[d] Based on 71 patients in the COPE-active group*

### Relationship between daily physical activity and exercise capacity at baseline

The Pearson correlation coefficients between steps/day and ISWT (m), ESWT (m), and ESWT (s) at baseline were calculated for the patients in both study groups together (n=125), and were 0.59, 0.44, and 0.34, respectively ($p<0.01$ for all). Pearson correlation coefficients between steps/day on the one hand and $VO_{2peak}$ and $W_{peak}$ on the other hand were only calculated for the COPE-active group (n=57 and n=58, respectively), and were 0.54 ($p<0.001$) and 0.44 ($p=0.001$) respectively.

### Relationship between change in daily physical activity and change in exercise capacity at 7 and 12 months

The correlations between change in daily physical activity and change in the various measures of exercise capacity after 7 months of follow-up were moderate in the COPE-active group ($p<0.01$ for all), and negligible and not statistically significant in the control group (Table 2). After 12 months, only the correlation between change in ISWT distance and change in steps/day in the COPE-active group was moderate and statistically significant (Table 2).

**Table 2** Pearson correlation coefficients (r) between change in daily physical activity and change in exercise capacity from baseline to 7 and 12 months for the COPE-active and control group

| Δ 0-7 months | Daily physical activity (steps/day) | | | |
|---|---|---|---|---|
| | **COPE-active** (n=53) | | **Control** (n=48) | |
| | r | p | r | p |
| Incremental shuttle walk test (m) | 0.47 | < 0.001 | -0.11 | 0.48 |
| Endurance shuttle walk test (m) | 0.41 | 0.003 | -0.05 | 0.74 |
| Endurance shuttle walk test (s) | 0.38 | 0.006 | -0.05 | 0.74 |
| Δ 0-12 months | Daily physical activity (steps/day) | | | |
| | **COPE-active** (n=54) | | **Control** (n=54) | |
| | r | p | r | p |
| Incremental shuttle walk test(m) | 0.40 | 0.003 | 0.09 | 0.54 |
| Endurance shuttle walk test (m) | 0.18 | 0.21 | 0.10 | 0.46 |
| Endurance shuttle walk test (s) | 0.17 | 0.22 | 0.17 | 0.23 |

### Relationship between daily physical activity and patient characteristics at baseline

The Pearson correlation coefficients between steps/day on one hand and $FEV_1$, IVC, age, and Body Mass Index (BMI) at baseline on the other hand were calculated for the patients in both study groups together (n=127), and were 0.32 ($p<0.001$), 0.17 ($p=0.05$), -0.23 ($p=0.01$), and -0.09 ($p=0.29$) respectively.

### Relationship between change in daily physical activity from baseline to 7 months and patients characteristics at baseline

In the COPE-active group as well as in the control group, none of the variables measured at baseline was significantly correlated to change in daily physical activity from baseline to 7 months (Table 3).

**Table 3** Pearson correlation coefficients between change in daily physical activity from baseline to 7 months and patient characteristics at baseline for the COPE-active and control group

| Δ 0-7 months | Daily physical activity (steps/day) | | | |
|---|---|---|---|---|
| | **COPE-active** | | **Control** | |
| | r | p | r | p |
| $VO_{2peak}$ (ml/kg/min)[a] | 0.22 | 0.11 | n.a. | n.a. |
| $W_{peak}$ (watt)[b] | 0.21 | 0.12 | n.a. | n.a. |
| Incremental shuttle walk test(m)[c] | 0.05 | 0.70 | 0.04 | 0.78 |
| Endurance shuttle walk test (m)[c] | 0.08 | 0.53 | 0.07 | 0.64 |
| Endurance shuttle walk test (s) [c] | 0.1 | 0.47 | 0.07 | 0.60 |
| $FEV_1$ (L)[d] | 0.08 | 0.55 | 0.13 | 0.94 |
| IVC (L)[d] | 0.00 | 0.98 | - 0.06 | 0.69 |
| Age (years)[d] | 0.06 | 0.63 | 0.09 | 0.55 |
| BMI ($kg/m^2$)[d] | 0.19 | 0.14 | 0.02 | 0.89 |

*Peak oxygen uptake ($VO_{2peak}$); Peak wattage ($W_{peak}$); Forced Expiratory Volume in 1 second ($FEV_1$), Inspiratory Vital Capacity (IVC); Body Mass Index (BMI)*

[a] *Based on 54 patients in the COPE-active group*

[b] *Based on 55 patients in the COPE-active group*

[c] *Based on 59 patients in the COPE-active group and 50 patients in the control group*

[d] *Based on 59 patients in the COPE-active group and 52 patients in the control group*

## DISCUSSION

The current study showed that daily physical activity and exercise capacity were only moderately correlated in patients with COPD. Additionally, in patients with COPD who participated in a physiotherapeutic exercise programme, the relationship between change in exercise capacity and change in daily physical activity was moderate to weak. In the control group, change in exercise capacity and change in daily physical activity were not correlated.

Various earlier studies have investigated the relationship between daily physical activity and exercise capacity in patients with COPD. The studies that investigated the relationship between daily physical activity and $VO_{2peak}$ show divergent results with correlations varying from weak to moderate[2;24-26]. This variety in correlations might be due to differences in patient characteristics and the method of measuring physical activity. Hill and colleagues were recently the first to investigate daily physical activity in relation to performance on the incremental shuttle walk test[26]. In this study, daily physical activity was measured in 26 subjects with bi-axial accelerometers and expressed as daily energy expenditure in kcal. They found a statistically significant correlation of 0.52 between distance walked on the incremental shuttle walk test and daily energy expenditure[26]. Whereas we have measured daily physical activity with pedometers, we have found a similar correlation of 0.59 between steps per day and distance walked on the incremental shuttle walk test. Pedometers are relatively simple and inexpensive compared to other activity monitors such as accelerometers. In our study we used the Yamax Digi-Walker SW-200. The mechanism of the SW-200 is the same as the mechanism of the SW-701 and this latter pedometer was considered to be among the most accurate ones in comparison with 9 other models[32;33]. In a more recent study, Turner et al. compared a pedometer to an activity monitor with an accelerometer and both devices underestimated step counts at slow walking speed[34]. In the original COPE-II study pedometers were used to measure the level of physical activity in the intervention and control group, in case of underestimation this would be expected in the same amount in both groups, and would thus have not affected difference between the groups.

To our knowledge, we are the first to investigate daily physical activity in relation to the endurance shuttle walk test. The relationship between physical activity and endurance time of the ESWT at baseline seems weaker than the relationship between activity and distance walked during the ISWT, and it seems also weaker than the relationship between daily physical activity and $VO_{2peak}$. This is contrary to what we expected to find. Patients with COPD perform their activities of daily living at a submaximal level of intensity[26]. The ESWT measures endurance capacity also at a submaximal level of intensity, and therefore we assumed that performance on the ESWT would better reflect the level of daily physical activity. However, a recent other study of Hill et al. gives more insight by indicating that peak rates of oxygen uptake and peak heart rates that patients with moderate COPD

achieve during the ESWT are similar to rates achieved during the cycle ergometry test and the ISWT[35].

Opposite to the limited research on the relationship between daily physical activity and the shuttle walking tests, the six-minute walk test (6MWT) has been investigated more thoroughly. In the majority of the studies, daily physical activity relates slightly better with the 6MWT than that it relates with the ISWT and ESWT in our study[2;15;22-28]. During the 6MWT patients are instructed to walk at their own pace, and cover as much ground as they can within 6 minutes, moreover, patients are allowed to stop and rest during the test[7]. This differs from the ISWT and the ESWT, in which patients are instructed to walk at a predetermined speed until they are not able to continue due to dyspnoea or fatigue[8;9]. Pepin et al. showed a significantly higher heart rate, respiratory rate, minute ventilation and dyspnoea after completing the ESWT than after completing the 6MWT in patients with COPD[36]. In contrast, Hill and colleagues found no differences between $VO_{2peak}$ and heart rate after completion of the 6MWT, ESWT, ISWT and CPET in patients with COPD[35]. Patients in the latter study were functionally more impaired than the patients in the study of Pepin et al.. This might explain why the 6MWT seems to relate better to exercise behaviour and the submaximal intensity of daily physical activity in patients with mild COPD.

The strongest, although moderate, relation between change in physical activity and change in exercise capacity was found in the intervention group over the first 7 months. In this period, the number of moments for goal setting and feedback were the most frequent (four self-management sessions, and subsequently two training session per week at the physiotherapy practice and one training session per week at home). We therefore expected, and also detected a mean improvement in both exercise capacity and daily physical activity. During the following five months, the intervention was less intense (one exercise sessions at home, and one supervised physiotherapy session). We anticipated that the less intense training approach, but still frequent feedback and reinforcement would be necessary to maintain exercise capacity and further facilitate a shift towards being more active at home. After this second period, we observed a slight decrease in exercise capacity, this in contrast to a further increase in daily physical activity. Over 12 months, the relationship between activity and performance on the ISWT, and in particular the ESWT was weakened. The weakening of the relationship after including the period in which the intervention was primarily focused on improvement of daily physical activity, underlines the need to use interventions that target not only exercise capacity but also health behaviour regarding exercise in patients with COPD to achieve an increase in both parameters.

In the COPE-active group as well as in the control group, none of the patient characteristics measured at baseline were correlated with change in daily physical activity over 7 months. However, nearly all of these parameters were of a physiological nature, which are not the only variables influencing activities[37]. Daily activities are also influenced by environmental and personal factors[37]. Environmental factors make up the physical, social, and attitudinal environment in which people live and conduct their lives[37]. Personal factors are the

particular background of an individual's life and living and contribute to features of the individual. These factors include sex, race, age, but also lifestyle, coping styles, social background, education, overall behaviour patterns and other characteristics[37]. One of the main objectives in the COPE-II study was to assess the efficacy of a self-management programme, including a community-based physiotherapeutic exercise programme in increasing exercise capacity and daily physical activity. With the exception of steps per day no further (process) measures of behavioural change were measured. In future research on daily physical activity in patients with COPD, more attention should be paid to the role of behavioural characteristics and psychosocial factors such as self-efficacy, emotional status, and social functioning. Another remark that can be made, is that by including patients with at least three exacerbations in the two years preceding study entry, we have included relatively severe COPD patients. The COPE-II study was also designed to investigate the effectiveness of self-treatment of exacerbations[29], and the criterion of at least three exacerbations was used to ensure that a sufficient number of exacerbations could be detected during study follow-up. How this has affected the level of daily physical activity in our patients is hard to determine. Only few studies have assessed step count in patients with COPD using a pedometer, and the sample size of these studies was small. However, Hospes et al. also measured daily physical activity during 7 days with the Digi-Walker SW-200 in 39 Dutch patients with COPD. Compared to the patients in this study, the patients in our study reported on average fewer steps: 7087 ± 4058 steps versus 4857 ± 3132 steps, respectively[38]. This is probably due to the less restrictive inclusion criteria in the study of Hospes et al, which is also reflected in a higher mean $FEV_1$ % of predicted of 67.4 ± 17.5% versus 50.2 ± 15.6% in our study. A consequence for the current analyses might be that the results cannot be generalised to the general COPD population, but only to the more severe patients.

Although we found statistically significant correlations between daily physical activity and different measures of exercise capacity, these correlations were at best moderate. What do these results mean for clinical practice? The primary goal of exercise programmes for patients with COPD, as part of a pulmonary rehabilitation programme or not, is improvement of exercise capacity[1]. Intuitively it is logical to assume that an increased exercise capacity will subsequently lead to an increased physical activity level. An increased exercise capacity in patients with COPD reduces symptoms of dyspnoea and fatigue during and after exercise and therefore removes a barrier to be active. However, during the years that the severity of COPD gradually progresses, the patient develops a sedentary lifestyle that needs more than an increase in exercise capacity to change[21]. Behavioural techniques such as motivational interviewing and cognitive behavioural therapy are probably helpful in achieving and maintaining an improved daily physical activity level. However, future research has to investigate which tools are most effective in increasing daily physical activity.

In this study, a moderate to weak relationship was found between daily physical activity and exercise capacity. These results strengthen our beliefs that exercise interventions need to

target not only exercise capacity but also behavioural change with regard to daily physical activity, to achieve improvement in both parameters.

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# CHAPTER 7
GENERAL DISCUSSION

In this thesis, the body of evidence on self-management programmes for patients with COPD was updated. Also, the long-term (cost-)effectiveness of two major components of self-management, self-treatment of exacerbations and a community-based exercise programme, was investigated. In this chapter we will discuss the results, and the strengths and limitations of the studies in the light of the existing literature, and we will deliberate on what this means for clinical practice and future research.

## Self-management programmes

We have updated the Cochrane systematic review on self-management for patients with COPD (Chapter 1). One of the most prominent changes in this update was the removal of the term "education" from the title. Obviously, this was accompanied with changes to the in- and exclusion criteria of the review. The goal was to exclude programmes that purely focus on education, i.e. a transfer of knowledge. Although knowledge of the condition is indispensable, it is not sufficient to achieve the behavioural change that is judged to be necessary for successful and sustained self-management[1-3]. Despite this effort, details on the incorporation of techniques for behavioural change are often still lacking in study reports, obscuring subgroup analyses on the use of behavioural techniques[4]. Meta-analyses showed a beneficial effect of self-management on health-related quality of life (HRQoL) as measured with the St. George's Respiratory Questionnaire (SGRQ), and also the risk for both respiratory and all-cause hospital admissions was reduced through self-management interventions. Although we have tried to define stricter in- and exclusion criteria for COPD self-management, the included self-management interventions were still diverse in name and content. The simplest programme consisted of one educational session with telephone reinforcement, while the most complex intervention consisted of several educational sessions, an exercise programme, and an optimisation of care plan. The diversity in programmes is not surprising when looking at the spectrum of support for COPD as published by Wagg and presented in the latest ATS/ERS statement on pulmonary rehabilitation[5;6]. Self-management is located in the centre of this spectrum, and can therefore be offered as an independent treatment, but can also be offered as part of pulmonary rehabilitation or an integrated care programme. A broadly accepted operational definition of self-management training for patients with COPD would contribute to classification of self-management interventions. In the updated review, the included self-management interventions were often complex, meaning that several components (e.g. exercise programmes, education or action plans) were incorporated. The majority of the studies compared the comprehensive interventions with usual care, and as a consequence only statements on the effectiveness of complete interventions can be made, and not on their specific components. In this update, we have also included studies comparing specific components of self-management head-to-head, but the number of studies was too low, and the components were too diverse to draw any conclusions about the effectiveness of the individual components within self-management programmes. Also, 81% of the included studies with a usual control group had a follow-up of at most 12 months, leaving real long-term effectiveness (> 12 months) of self-management open to discussion. The latter emphasises that the COPE-II study, that assessed the long-term effects of self-

treatment of exacerbations (Chapter 3) and a community-based exercise programme (Chapter 4) within a self-management programme, is highly relevant.

Recently, a debate on the safety of self-management in patients with COPD was triggered by the study of Fan et al.[7]. This study was stopped prematurely because of a higher number of deaths in the intervention group compared to the control group. Despite additional analyses and data collection, no satisfactorily explanation for the increased mortality in the intervention group could be found[7]. However, several options were discussed including a baseline imbalance in prevalence of cardiovascular disease and marital status between both study groups, delay in treatment of severe COPD patients at an already high risk of mortality due to interference of a case manager, or overconfidence of patients in the intervention group, and last but not least early study termination at a "random high"[7;8]. Several recent studies that were not yet included in the Cochrane review on self-management failed to show beneficial effects of comprehensive self-management programmes on their respective primary outcomes health-related quality of life, hospital readmissions, and mortality[9;10]. One of the proposed explanations for this lack of effectiveness, is the low number of patients that could be classified as "successful self-managers"[8]. When a large proportion of the patients in a study does not act as prescribed in the action plan (i.e. fail to increase medication or contact a healthcare provider), evidently, further health benefits cannot be expected. Reasons for a (partial) lack of success of self-management interventions can be numerous[8;11]. The contents (e.g. components, duration and frequency of contact moments, behavioural change techniques, mode of delivery) of the intervention might have been suboptimal. However, it is also possible that the design of the intervention was optimal but that its implementation or execution was not. Each healthcare provider has a unique character, knowledge and experience, and especially in study-settings a new intervention is often an extra burden to the already high workload. This potentially leads to various levels of motivation and variation in execution, and thus suboptimal implementation of the self-management programme. To successfully execute self-management training, there is also a behavioural change needed of the healthcare provider, from the traditional role of all-knowing guide in COPD management to collaborator in partnership with patients. It is therefore essential, that healthcare providers are trained in the rationale, content, and (behavioural change) techniques of the new intervention.

Patient characteristics are also likely to play a role in the success or failure of self-management interventions. Bucknall et al. found that successful self-managers were younger and were less likely to live alone[10]. A younger age was also mentioned in the study of Bischoff et al., next to influenza vaccination, cardiac co-morbidity and more severe airflow limitation[12]. Motivation for behavioural change or adapting a new lifestyle might be low and, when this is not recognised and not incorporated as a treatment goal, success of self-management interventions is unlikely[1;6;13]. Also, low health literacy of patients is a factor that might contribute to the failure of self-management interventions. Health literacy is defined as the ability to read, understand and act on healthcare information[14]. Research on

health literacy in patients with COPD is still limited, and it is therefore not yet established to what degree low levels of health literacy affect the acquirement of self-management skills in this patient group. A study on adherence to daily symptom diaries found that patients with a low education level were less compliant in completing their daily diaries[15]. In our study, several patients were also not capable of filling in the daily diary independently, with the consequence that the action plan could not be used. This emphasises that to attain effective self-management training, educational tools should be designed in a way that is understandable for patients with lower levels of health literacy, or an alternative should be offered to this patient group.

The above indicates that although we have found a general beneficial effect of self-management on HRQoL and hospital admissions in patients with COPD, newly published studies do not uniformly report positive results, and not all patients benefit to an equal amount of self-management training. This can be attributed to the complex nature of self-management interventions, but also to the diversity of the patient groups it is offered to. To further increase effectiveness of self-management, and to enable patient-tailored interventions, it is essential to identify patient- and intervention- related factors that facilitate successful self-management. This is currently been worked on in the TASTE programme[16;17].

### Self-treatment of exacerbation

Action plans are among the most frequently used components in self-management programmes for patients with COPD, hindering subgroup analyses on self-management programmes with versus without action plans[4]. Action plans are guidelines that help patients with COPD to recognise, and act appropriately to exacerbations. Prescribed actions vary from increasing rescue medication to self-initiation of a course of prednisolone or antibiotics, or contacting a healthcare provider. The action plan in the COPE-II study was specifically directed towards self-treatment of exacerbations. The lower number of exacerbation days in the self-treatment group, combined with the equal number of exacerbations in the two study groups shows that the duration of exacerbations was decreased in the group that used the action plan. The severity of symptoms of an exacerbation was also lower in the self-treatment group. All this was accompanied by considerable cost savings due to a reduction in healthcare utilisation after two years of follow-up (Chapter 3). The number of courses of both prednisolone and antibiotics tended to be higher in the self-treatment group compared to the control group. In line with the findings of the Cochrane review on action plans[18], this indicates that use of the action plan leads to more appropriate treatment of exacerbations.

Overtreatment of exacerbations is a concern with the use of action plans. In our study, the number of courses of prednisolone and antibiotics both were noticeably lower than the number of exacerbations in the self-treatment group and control group, demonstrating that patients did not excessively treat themselves. Underreporting and the accompanying delay in treatment of exacerbations seem to be of a bigger concern than overtreatment of

exacerbations[19-21]. To prevent misuse of action plans resulting in under- or overtreatment of exacerbations, action plans should be offered within proper self-management programmes during which patients have the opportunity to become familiar with the plan and receive feedback on actions that were, or were not taken. A case-manager (e.g. a respiratory nurse) who regularly provides feedback, and who is easily accessible for patients in case of questions and uncertainties is indispensable in this aspect. Case-managers have a crucial role in communication with the patient. Pulmonary physicians and general practitioners are often restricted by a tight time schedule and less frequent control visits. In contrast, case-managers have more time to build a trust relationship with the patient, and to assess specific patient characteristics and needs. Moreover, they can facilitate the patients in behavioural change at their own level, by checking whether patients understood the information, setting goals and providing feedback on actions. Although current evidence for the additional value of case-managers in patients with COPD is limited, results from studies in other chronic diseases are promising with respect to their contribution in self-management behaviour[22].

During the COPE-II study, patients completed a daily symptom diary in which they had to indicate whether or not their symptoms were increased compared to normal. "Normal" or stable state was defined for each individual patient seperately, and was noted on a card that was provided to the patient. The symptoms that were scored were the major (breathlessness, sputum production, and sputum colour) and minor symptoms (cough, wheezing, running nose, sore throat and fever) as defined by Anthonisen[23]. Although completing a daily diary might seem intensive, the actual burden for the patients was low since they only had to answer one question each day when their COPD was stable. This is also reflected in the high completion rate over two years of follow-up of around 82%. The symptom diary was a tool helping patients to recognize, and self-treat their exacerbations, but it was also used to measure the number, duration and severity of exacerbations prospectively as was previously defined[24]. The heterogeneous nature of exacerbations has led to the use of numerous definitions of exacerbations in COPD studies. Event-based definitions are popular and are mainly based on change in medication use, or unscheduled healthcare utilisation with or without an increase in symptoms. Also, the severity of exacerbations is related to events. For example, an increase in rescue medication indicates a mild exacerbation, the start of a course of prednisolone and/or antibiotics indicate a moderate exacerbation, whereas emergency department visits or hospitalisations are defined as severe exacerbations[25]. A problem with event-based definitions is that patients tend to fail to report exacerbations to a physician, and event-based measures can thus lead to underestimation of exacerbations compared to symptom-based definitions. Our definition was symptom-based since we defined an exacerbation as a clear increase in two major symptoms or one major and one minor symptom compared to normal for at least two successive days. When we would have used an event-based definition instead, and for instance had defined the number of exacerbations as the number of courses prednisolone and antibiotics, the data would have suggested a difference in number of exacerbations in favour of the control group, when in fact there is none. Moreover, this would also have led

to an underestimation of the number of exacerbations, since the number of courses is clearly lower than the number of exacerbations. The variety in definitions of exacerbations can make a difference between statistically significant and non-significant effect size, both between event- and symptom-based definitions[26] but also between different symptom-based definitions[16]. A more clear symptom-based definition of exacerbations or a widely accepted patient reported outcome tool (e.g. the EXACT-PRO tool[27]) on exacerbations would contribute to more homogeneity in outcome measurement and thus comparability in studies on exacerbations.

Although data from the COPE-II study suggest that self-treatment of exacerbations is a relatively simple intervention that is both effective and cost-saving, a remark should be made on the type of COPD patient we have included in this study. These patients were a selection of the patients that are seen in the department of pulmonology of a large teaching hospital. They were selected on the occurrence of at least three exacerbations or one respiratory-related hospital admission in the two years preceding study entry, which implies that we have included patients that relatively frequently exacerbate. These patients benefit probably more from the use of an action plan than patients who only rarely exacerbate. Due to the limited number of exacerbations, the latter group of patients has less opportunity to become familiar with the action plan and receive feedback on taken actions. Furthermore, patients in our study were not allowed to have any serious co-morbidities. Co-morbidities such as cardiovascular disease, diabetes, and mental health issues are common in patients with COPD[28;29]. The action plan in the COPE-II study does not take co-morbidities into account and can for example not distinguish between an increase in dyspnoea caused by COPD or heart failure. Therefore, it is not recommended to use the current action plan in patients with COPD and relevant co-morbidities. An action plan that incorporates several frequently diagnosed co-morbidities is being evaluated in a randomised controlled trial at the time of writing[30].

### Community-based exercise programme

Exercise programmes are commonly offered in the continuum of COPD disease management[6], and can be combined with self-management training. The COPE-active programme in our self-management intervention was group-based and was offered near to the patients' homes in private physiotherapy practices. The proposed advantages of an exercise programme in this setting were easy accessibility, accompanied by less dependence on other persons for transportation, a safe environment to exercise under supervision of highly skilled and dedicated physiotherapists, and social support of peers. Patients with COPD perceive all these factors as supporting for participation in exercise, and this might have contributed to the high adherence of patients to the programme[31;32]. The goal of the exercise programme was not only an improvement of physical condition but also behavioural change towards exercise. Therefore, one home-based training session per week was deliberately incorporated to make patients feel comfortable exercising unsupervised in their own environment. Physiotherapists weekly discussed the home-

based sessions with the patient and provided feedback. Moreover, the relatively long training period of 11 months was chosen to further facilitate behavioural change toward exercise. Prior to the start of the COPE-active programme, participating physiotherapists were extensively trained in using the protocol, and regular evaluation sessions in which difficulties were discussed, were organised during the study. That the COPE-active programme was successfully executed by the physiotherapist was not only emphasised by the observed improvements in both exercise capacity and daily physical activity of the COPE-active group after one year of follow-up, but also by a qualitative study showing that adherence to the study protocol was excellent[33].

As anticipated, the improvement in exercise capacity in the COPE-active group was mainly gained in the first six months of the first year of follow up, and was maintained in the second half of that year with a lower training frequency[34]. Whereas exercise capacity was maintained during the second half of the first year (with one supervised physiotherapy session per week), a clear deterioration in exercise capacity was observed during the second year (with no supervised physiotherapy sessions) in the COPE-active group. In contrast to this, the increase in daily physical activity level was maintained over two years (Chapter 4). In the second year of follow-up, patients that participated in the exercise programme were not allowed to participate in a formal physiotherapeutic training programme, but they were encouraged to participate in any other sport activity. Although we have not actively registered sport activities of patients, the deterioration in exercise capacity suggests that the majority of the patients were not actively involved in regular sport activities. The lack of between-group difference in exercise capacity after two years of follow-up in combination with higher costs in the intervention group, led to the conclusion that the programme was not cost-effective with regard to its primary outcome (Chapter 5). However, we believe it has the potential to become cost-effective when patients in the COPE-active group continue supervised exercise for at least once a week in the second year of follow-up.

Daily physical activity level of patients in the COPE-active group after two years was still notably increased compared to patients in the control group. So, although the patients might have faced barriers to participate in organised sport activities they were still more physically active in their daily life. Although physical activity was not the primary outcome of the COPE-II study, this is a relevant finding since patients with COPD often have a reduced physical activity level[35-37], which is associated with negative health outcomes[38-40]. We measured daily physical activity with a pedometer, implying that only the number of steps during walking was counted and no other activities such as bicycling, or the intensity or frequency of the movements. Obviously, the increase in daily physical activity in the COPE-active group was not sufficient to maintain of the gain in exercise capacity, most likely because the training intensity of walking was not sufficient for the maintenance of maximal exercise capacity[41;42]. Although behavioural change towards daily physical activity is deemed essential with respect to maintenance of exercise capacity, when this change in behaviour only leads to an increase in every day leisure activities and not in sport or training

activities it appears not to be sufficient. Vice versa, it cannot be assumed that an increase in exercise capacity in patients with COPD will spontaneously lead to an increase in physical activity level, since there is only a moderate relationship between change in physical activity level and change in exercise capacity (Chapter 6). Although an improved exercise capacity can be facilitating in increasing physical activity, it will take more than that to change the generally sedentary lifestyle of patients with COPD[43]. Maintenance of improvement in physical condition after the end of an exercise programme is a challenge in patients with COPD. The question then remains how beneficial effects of exercise programmes can be best maintained. So-called "maintenance programmes" are suggested to contribute to the preservation of gains in exercise capacity. These programmes are however not yet uniformly successful[44], and continuing research on the optimal structure of these follow-up programmes is warranted.

### Recommendations for current clinical practice

We recommend that self-treatment of exacerbations guided by an action plan is offered to frequently exacerbating patients with COPD without co-morbidities. To prevent misuse of the action plan, and for safety in general, the plan should be offered within a proper self-management programme with support of a case-manager, allowing patients to become familiar with the plan.

We recommend participation of patients with COPD in standardised community-based exercise programmes supervised by physiotherapists (comparable to the COPE-active programme), since it is effective in improving exercise capacity on the short term, and daily physical activity level on the long term. On the longer term, patients should be encouraged to continue participating in supervised and specialised training activities of sufficient frequency and intensity to maintain benefits.

We recommend that standardised exercise programmes for patients with COPD not only focus on increasing exercise capacity (implicitly assuming that it will consequently lead to an increase in physical activity level), but also use specific behavioural changing techniques to increase daily physical activity level.

### Recommendations for future research

Although this thesis contributes to the evidence regarding the effectiveness of self-management for patients with COPD, there is still much to learn in this field of research/care. Most of all it is essential that an operational definition of self-management is agreed upon. This will add to the classification of interventions and transparency regarding comparability of study interventions. Another factor that will contribute to comparability of studies, is the use of uniform outcome measures (e.g. for exacerbations).

Furthermore, studies comparing different components of self-management head-to-head are needed. This will identify the components of self-management programmes that are most effective, and will contribute to the ideal package of self-management training.

Studies on self-management with follow-up times exceeding one year are needed, to present a complete and genuine picture of the effectiveness of self-management on the long term.

It is also essential that those patients are identified who benefit the most of self-management training. In other words, which patient characteristics predict successful self-management?

With respect to exercise programmes within self-management, and in general, it is essential to find methods to maintain benefits gained in exercise capacity on the long term. What are the optimal training frequency and intensity, and mode of support?

Since co-morbidities are common in patients with COPD, it is vital that these are taken into account in future self-management interventions to contribute to the safety and external validity of studied interventions. In line with this, interventions should be tailored, i.e. adapted to the specific needs of the individual patient.

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# CHAPTER 8

SUMMARY

SAMENVATTING

DANKWOORD

CURRICULUM VITAE

Chronic obstructive pulmonary disease (COPD) is a chronic, and usually progressive disease. It is characterized by persistent air flow limitation and an enhanced inflammatory response in the airways and lungs to noxious particles and gasses. Besides symptoms of dyspnoea, sputum production and chronic cough, patients with COPD often have impaired exercise capacity and a decreased physical activity level. Exacerbations of COPD are acute events that strongly determine the course of the disease. Despite optimal pharmacological treatment, patients with COPD still experience symptoms and may have difficulties to cope with their disease. In view of this, self-management is increasingly recognised to be important in the treatment of COPD. Scientific evidence on long-term effectiveness of self-management programmes remains scarce. Moreover, it is uncertain what the contribution of independent components of self-management is to its effectiveness. To assess the current state of evidence on the effectiveness of self-management for patients with COPD, we have updated the Cochrane review on this topic. Additionally, we have evaluated the long-term (i.e. after two years of follow-up) effectiveness of two frequently used components, self-treatment of exacerbations and a community-based exercise programme, within a self-management programme.

In **Chapter 2**, the results of the update of the Cochrane review on self-management for patients with COPD are presented. In this update, we explicitly excluded studies with education as the only active intervention, since education alone is not sufficient to achieve a behavioural change. For the same reason, studies with only one contact moment were excluded. To be able to make recommendations on effective components of self-management, we have included studies that compared different components of self-management head-to-head (without a usual care control group). Twenty-three studies (3189 participants) with a usual care control group and six head-to-head studies (115 patients) were included in the review. Follow-up of the studies ranged from two to 24 months. Randomised controlled trials were pooled in meta-analyses, when appropriate. Self-management had a beneficial effect on health-related quality of life (HRQoL) as measured with the St George's Respiratory Questionnaire (SGRQ) with a mean difference in total score of -3.51 (95%CI: -5.37 to -1.65). The mean difference on the domain score "impact" reached the minimally clinically important difference of four points: -5.71 (95%CI: -9.17 to -2.25). The probability of at least one respiratory-related or one all-cause hospital admission was also reduced in participants receiving self-management, with an OR of 0.57 (95%CI: 0.43 to 0.75) and 0.60 (95%CI 0.40 to 0.89), respectively. Also, a significant improvement was found in dyspnoea measured by the (modified) Medical Research Council scale. No significant differences were found in mortality, lung function or exercise capacity. Possibilities for subgroup analyses were restricted and revealed no statistically significant differences between subgroups. Also, studies comparing different components of self-management head-to-head were too diverse to perform any meta-analyses. Although it can be concluded that self-management interventions are effective in improving HRQoL and reducing both respiratory-related and all-cause hospital admissions, still no recommendations on the most effective components of self-management can be made.

In Chapters 3 to 5, the results of the COPE-II study after two years of follow-up were described. The COPE-II study was a randomised controlled trial that compared the (cost-)effectiveness of two independent interventions in one study using a two-by two factorial design. Self-treatment of exacerbations and the COPE-active programme were both compared to a self-management programme only. Self-treatment of exacerbations was linked to a daily symptom diary and an action plan indicating when a patient should start a course of antibiotics and/or prednisolone. The COPE-active programme was an 11-month community-based exercise programme supervised by physiotherapists, aiming at an increase in exercise capacity but also at a behavioural change towards exercise. In total, 159 patients with COPD according to GOLD, and at least three exacerbations or at least one hospitalisation in the two years preceding study entrance were included.

In **Chapter 3** the (cost-)effectiveness of a self-management programme with versus without self-treatment of exacerbations was assessed. Data of 142 patients were analysed. The number of exacerbation days and the mean symptom score of an exacerbation were significantly lower in patients who used an action plan for self-treatment of exacerbations. Apart from a significant between-group difference in CRQ dyspnoea score, no other differences were seen in HRQoL. The number of visits to the pulmonary physician and emergency department were significantly lower in the self-treatment group. The difference in hospital admissions was also in favour of the self-treatment group but did not reach statistical significance. The low programme costs combined with the reduced healthcare utilisation also led to a cost-saving in direct medical costs of €1081 per patient per two years. It was concluded that patients with COPD clearly benefit from self-treatment of exacerbations as regards the severity and length of exacerbations.

In **Chapter 4** the effectiveness of the addition of a community-based exercise programme to a self-management programme was compared to a self-management programme only. The data of 153 patients were analysed. After two years of follow-up, the between-group difference in exercise capacity as measured with the incremental shuttle walk test (ISWT) was diminished to a non-significant 12.2 meters (95%CI: -16.6 to 41.0). The between-group difference in daily physical activity was however still statistically significant after two years of follow-up: 1193 steps/day (95%CI: 203 to 2183) in favour of the COPE-active group. A beneficial effect was also found on CRQ dyspnoea score but not on other CRQ domains, the CCQ and HADS. Patients who participated in the COPE-active programme were thus more active over two years of follow-up, indicating that the programme was effective in achieving a behavioural change towards exercise. This was however not accompanied by a sustained increase in maximal exercise capacity.

In **Chapter 5** the cost-effectiveness of the COPE-active programme was evaluated. Due to the lack of between-group difference in distance walked on the ISWT after two years of follow-up, the additional costs of the community-based exercise programme were not outweighed by positive effects in this outcome. This is in contrast with the secondary outcome of daily physical activity. The costs per patient with a meaningful improvement in

daily physical activity was €1.564 wich is considered to be acceptable. The same was concluded for the costs of an additional quality adjusted life year, although the between-group difference was not significant.

In **Chapter 6** the relationship between exercise capacity and daily physical activity level was assessed. These were secondary analyses of the one year data of the COPE-II study. Pearson's correlations between (change in) daily physical activity measured as steps/day and (change in) exercise capacity as meters walked on the ISWT and the endurance shuttle walk test (ESWT) were calculated. Although statistically significant correlations were found between daily physical activity and exercise capacity, the strength of these correlations was only weak to moderate. This leads to the conclusion that exercise programmes should not only aim at an improvement in exercise capacity, but also should specifically target behavioural change toward daily physical activity to achieve improvements in both.

The findings of the studies in this thesis were discussed in **Chapter 7**. After critical appraisal of the result, we have composed the following recommendations for clinical practice for patients with COPD:

We recommend that self-treatment of exacerbations guided by an action plan is offered to frequently exacerbating patients with COPD without co-morbidities. To prevent misuse of the action plan, and for safety in general, the plan should be offered within a proper self-management programme with support of a case-manager, allowing patients to become familiar with the plan.

We recommend participation of patients with COPD in standardised community-based exercise programmes supervised by physiotherapists (comparable to the COPE-active programme), since it is effective in improving exercise capacity on the short term, and daily physical activity level on the long term. On the longer term, patients should be encouraged to continue participating in supervised and specialised training activities of sufficient frequency and intensity to maintain benefits.

We recommend that standardised exercise programmes for patients with COPD not only focus on increasing exercise capacity (implicitly assuming that it will consequently lead to an increase in physical activity level), but also use specific behavioural changing techniques to increase daily physical activity level.

COPD is een chronische en progressieve longaandoening gekenmerkt door een uitstroombelemmering van de luchtwegen, en een verhoogde ontstekingsreactie in de luchtwegen en longen op schadelijke deeltjes en gassen. Naast symptomen van kortademigheid, slijmproductie en chronisch hoesten, hebben patiënten met COPD ook vaak een verlaagde inspanningscapaciteit en zijn ze lichamelijk minder actief dan gezonde mensen. Exacerbaties van COPD (longaanvallen) treden acuut op, gaan gepaard met een verergering van de klachten en bepalen sterk het beloop van de ziekte. Ook met een optimale behandeling met medicijnen ervaren patiënten vaak nog symptomen en hebben ze geregeld moeite om in het dagelijkse leven met hun aandoening om te gaan. Zelfmanagement kan een belangrijke rol spelen in de behandeling van COPD. De wetenschappelijke onderbouwing voor de effectiviteit van zelfmanagement op de lange termijn is nog beperkt. Verder is het ook onbekend welke onderdelen van zelfmanagement het meest effectief zijn. Om de huidige wetenschappelijke stand van zaken rond de effectiviteit van zelfmanagement voor patiënten met COPD in kaart brengen, is de Cochrane overzichtsstudie over dit onderwerp geactualiseerd. Daarnaast zijn ook de langetermijneffecten (na twee jaar) van twee vaak toegepaste onderdelen van zelfmanagement, namelijk zelfbehandeling van exacerbaties en een bewegings-programma, binnen een zelfmanagement programma geëvalueerd.

In **hoofdstuk 2** worden de resultaten van de actualisatie van de Cochrane overzichtsstudie naar de effecten van zelfmanagement bij patiënten met COPD besproken. In deze actualisatie werden zelfmanagement-interventies die zich enkel richten op educatie uitgesloten omdat educatie alleen niet voldoende is om een gedragsverandering te bereiken. Vanwege dezelfde reden zijn ook de studies uitgesloten waarin de interventie uit maximaal één contactmoment bestond. Om meer inzicht te krijgen in de effectiviteit van de verschillende componenten van zelfmanagement-interventies zijn in deze versie voor het eerst studies geïncludeerd die verschillende componenten van zelfmanagement onderling vergelijken, dus waarin geen "standaard zorg" controlegroep is opgenomen. In totaal voldeden 29 studies aan alle criteria, hiervan hebben 23 studies een controlegroep die standaard zorg ontving en vergelijken zes studies verschillende componenten van zelfmanagement onderling. In de studies werden de deelnemers 2 tot 24 maanden gevolgd. Waar mogelijk werden de resultaten van gerandomiseerde gecontroleerde studies gecombineerd in meta-analyses. Deze analyses wijzen uit dat zelfmanagement leidt tot een betere kwaliteit van leven in patiënten die hebben deelgenomen aan een zelfmanagementprogramma vergeleken met patiënten die standaard zorg hebben ontvangen. In de zelfmanagementgroep was ook een afname te zien van het aantal patiënten met minimaal één ziekenhuisopname, zowel door longgerelateerde oorzaken als door andere oorzaken. Verder rapporteerden patiënten uit de zelfmanagementgroep minder kortademigheid, maar werden er geen verschillen gevonden tussen zelfmanagement en standaard zorg in longfunctie, inspanningscapaciteit of sterfte. De mogelijkheden voor subgroepanalyses waren beperkt en leverden geen statistisch significante verschillen op. De studies die verschillende componenten van zelfmanagement onderling vergeleken waren te divers om te combineren in meta-analyses. Hoewel er dus

geconcludeerd kan worden dat zelfmanagement een gunstig effect heeft op kwaliteit van leven, de kans op een ziekenhuisopname, en de mate van kortademigheid, kunnen er ook na deze actualisatie geen uitspraken worden gedaan over de bijdrage van de afzonderlijke componenten aan de effectiviteit van zelfmanagement.

In hoofdstuk drie tot en met vijf worden de langetermijneffecten (na twee jaar) van de COPE-II studie beschreven. De COPE-II studie is een gerandomiseerde gecontroleerde studie waarin de (kosten-)effectiviteit van twee onafhankelijke componenten van zelfmanagement zijn vergeleken in een 2x2 factorieel studieontwerp. Zelfbehandeling van exacerbaties en een bewegingsprogramma uitgevoerd in de eerstelijns fysiotherapie (COPE-actief programma) waren een toegevoegd onderdeel van een zelfmanagement-programma en werden elk afzonderlijk vergeleken met alleen het zelfmanagement-programma. Zelfbehandeling van exacerbaties werd uitgevoerd met behulp van een actieplan dat gekoppeld was aan een klachtendagboekje. Het actieplan gaf aan bij welke klachten de patiënt een kuur prednisolon en/of antibiotica moest starten. Het COPE-actief programma was een trainingsprogramma uitgevoerd in de eerstelijns fysiotherapie met een duur van 11 maanden. Het programma had als doel de inspanningscapaciteit te verbeteren, maar daarnaast ook een gedragsverandering met betrekking tot beweging te bereiken. In totaal werden 159 patiënten met COPD en minstens drie exacerbaties of minstens één ziekenhuisopname in de twee jaar voor deelname aan de studie, geïncludeerd.

In **hoofdstuk 3** werd de (kosten)effectiviteit van een zelfmanagementprogramma met en zonder zelfbehandeling van exacerbaties beschreven. De gegevens van 142 patiënten werden geanalyseerd. Het aantal exacerbatiedagen en de gemiddelde symptoomscore van een exacerbatie waren na twee jaar lager in de groep met een actieplan voor zelfbehandeling. Er werden geen verschillen gevonden tussen de groepen in kwaliteit van leven. Het aantal bezoeken aan de longarts en spoedeisende hulp was lager in de groep die zich zelf behandelde. Het totale aantal longgerelateerde ziekenhuis opnames was ook lager in de zelfbehandelgroep dan in de controlegroep, maar dit verschil was niet statistisch significant. De lage kosten van het actieplan en het zelfmanagementprogramma, gecombineerd met de vermindering in gezondheidszorggebruik heeft geleid tot een duidelijke kostenbesparing door zelfbehandeling van exacerbaties.

In **hoofdstuk 4** werd de effectiviteit van een zelfmanagementprogramma met en zonder het COPE-actief programma onderzocht. De gegevens van 153 patiënten werden geanalyseerd. Hoewel er eerder na één jaar (direct na het einde van de interventie) een significante verbetering in inspanningscapaciteit werd gevonden in de COPE-actief groep vergeleken met de controlegroep, was dit positieve effect na twee jaar niet meer zichtbaar. Dit in tegenstelling tot de dagelijkse fysieke activiteit, waar het positieve effect van het COPE-actief programma ook na 24 maanden follow-up nog duidelijk waarneembaar was. De patiënten die hadden deelgenomen aan het COPE-actief programma gaven ook aan minder benauwd te zijn in vergelijking met de patiënten in de controlegroep. Verder waren

er wat betreft kwaliteit van leven en angst en depressie geen verschillen tussen de twee studiegroepen. Uit deze studie kan dus geconcludeerd worden dat het COPE-actief programma heeft geleid tot een langdurige gedragsverandering in zijn deelnemers met betrekking tot fysieke activiteit. Dit ging echter niet samen met een behouden verbetering in inspanningscapaciteit.

In **hoofdstuk 5** werd onderzocht of het COPE-actief programma kosteneffectief is. Vanwege het verdwijnen van het positieve effect van het COPE-actief programma op inspanningscapaciteit na twee jaar follow-up, wegen de extra kosten die het programma met zich meebrengt niet op tegen de effecten. Voor dagelijkse fysieke activiteit ligt dit anders en zijn de kosten per patiënt met een klinisch relevante verbetering in dagelijkse fysieke activiteit acceptabel. Hetzelfde geldt voor de kosten per extra "quality adjusted life year", hoewel geen significant verschil werd gevonden in "quality adjusted life years" tussen de groepen.

In **hoofdstuk 6** wordt de relatie tussen inspanningscapaciteit en dagelijkse fysieke activiteit beschreven. Dit was een secundaire analyse op de gegevens verzameld in het eerste jaar van de COPE-II studie. Correlatie coëfficiënten tussen (verandering in) inspanningscapaciteit en (verandering in) dagelijkse fysieke activiteit werden berekend. Hoewel er statistisch significante correlaties werden gevonden tussen inspanningscapaciteit en dagelijkse fysieke activiteit, varieerde de sterkte van deze correlaties van zwak tot matig. Hieruit kan geconcludeerd worden dat de relatie tussen inspanningscapaciteit en fysieke activiteit hooguit matig is en dat bewegingsprogramma's zich niet alleen moeten richten op een verbetering van de inspanningscapaciteit, maar specifiek ook op een gedragsverandering met betrekking tot fysieke activiteit.

In **hoofdstuk 7** werden de bevindingen van de studies in dit proefschrift bediscussieerd en werden de onderstaande aanbevelingen gedaan voor de patiëntenzorg rondom COPD.

Het wordt aanbevolen dat zelfbehandeling van exacerbaties met behulp van een actieplan wordt aangeboden aan patiënten met COPD die frequent exacerbaties doormaken en verder geen significante additionele gezondheidsproblemen hebben. Het actieplan wordt hierbij bij voorkeur aangeboden als onderdeel van een zelfmanagementprogramma onder begeleiding van een case-manager, zodat patiënten leren het plan op een correcte manier te gebruiken.

Het wordt aanbevolen dat patiënten met COPD deelnemen aan een bewegingsprogramma (vergelijkbaar met het COPE-actief programma) in de eerstelijns fysiotherapie om de inspanningscapaciteit op de korte termijn te verbeteren, en een langdurige verandering in fysieke activiteit te behalen. Hierbij moeten de patiënten op de lange termijn gestimuleerd worden om deel te blijven nemen aan begeleide trainingsactiviteiten van voldoende intensiteit en frequentie om behaalde verbeteringen in inspanningscapaciteit te behouden.

Tenslotte wordt aanbevolen dat gestandaardiseerde bewegingsprogramma's voor patiënten met COPD niet enkel focussen op een verbetering van inspanningscapaciteit (impliciet ervan uitgaand dat dit automatisch leidt tot een verbetering in fysieke activiteit), maar ook technieken voor gedragsverandering toevoegen om de dagelijkse fysieke activiteit te verhogen.

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Marlies Zwerink was born on April 13, 1984 in Enschede, the Netherlands. After graduating from secondary school at the Bonhoeffer College in Enschede in 2002, she started the study Biomedical Sciences at the Radboud University Nijmegen. She graduated in 2007, and received a Master of Science in Biomedical Sciences, with a major in Clinical Human Movement Sciences. After graduation, she started her PhD project at the department of Pulmonary Medicine of Medisch Spectrum Twente, Enschede. Her research was on the long-term effects of self-management in patients with COPD. In the last phase of her PhD-project, she also worked as a researcher on the MICK-study at the department Health Technology and Services Research of the University of Twente. The aim of the MICK-study was to investigate the chain of emergency care with a focus on patients with myocardial infarction and cerebrovascular accidents. After her PhD defence, she will start as a researcher on Lyme disease at Gelre Ziekenhuis, Apeldoorn.

# UNRAVELLING SELF-MANAGEMENT FOR PATIENTS WITH COPD

LONG-TERM EFFECTS OF THE COPE-II STUDY

MARLIES ZWERINK