Pulmonary rehabilitation following exacerbations of chronic obstructive pulmonary disease (Review)

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[Intervention Review]

Pulmonary rehabilitation following exacerbations of chronic obstructive pulmonary disease

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ABSTRACT

Background

Pulmonary rehabilitation has become a cornerstone in the management of patients with stable Chronic Obstructive Pulmonary Disease (COPD). Systematic reviews have shown large and important clinical effects of pulmonary rehabilitation in these patients. However, in unstable COPD patients who have recently suffered an exacerbation, the effects of pulmonary rehabilitation are less established.

Objectives

To assess the effects of pulmonary rehabilitation after COPD exacerbations on future hospital admissions (primary outcome) and other patient-important outcomes (mortality, health-related quality of life and exercise capacity).

Search methods

Trials were identified from searches of CENTRAL, MEDLINE, EMBASE, PEDRO and the Cochrane Airways Group Register of Trials. Searches were current as of March 2010.

Selection criteria

Randomized controlled trials comparing pulmonary rehabilitation of any duration after exacerbation of COPD with conventional care. Pulmonary rehabilitation programmes needed to include at least physical exercise. Control groups received conventional community care without rehabilitation.

Data collection and analysis

We calculated pooled odds ratios and weighted mean differences (MD) using random-effects models. We requested missing data from the authors of the primary studies.

Main results

We identified nine trials involving 432 patients. Pulmonary rehabilitation significantly reduced hospital admissions (pooled odds ratio 0.22 [95% CI 0.08 to 0.58], number needed to treat (NNT) 4 [95% CI 3 to 8], over 25 weeks) and mortality (OR 0.28; 95% CI 0.10 to 0.84), NNT 6 [95% CI 5 to 30] over 107 weeks). Effects of pulmonary rehabilitation on health-related quality of life were well above the minimal important difference when measured by the Chronic Respiratory Questionnaire (MD for dyspnea, fatigue, emotional function and mastery domains between 0.81 (fatigue; 95% CI 0.16 to 1.45) and 0.97 (dyspnea; 95% CI 0.35 to 1.58)) and the St. Georges Respiratory Questionnaire total score (MD -9.88; 95% CI -14.40 to -5.37); impacts domain (MD -13.94; 95% CI -20.37 to -7.51) and for activity limitation domain (MD -9.94; 95% CI -15.98 to -3.89)). The symptoms domain of the St. Georges Respiratory Questionnaire showed no significant improvement. Pulmonary rehabilitation significantly improved exercise capacity and the improvement was above the minimally important difference (six-minute walk test (MD 77.70 meters; 95% CI 12.21 to 143.20) and shuttle walk test (MD 64.35; 95% CI 41.28 to 87.43)). No adverse events were reported in three studies.

Authors' conclusions

Evidence from nine small studies of moderate methodological quality, suggests that pulmonary rehabilitation is a highly effective and safe intervention to reduce hospital admissions and mortality and to improve health-related quality of life in COPD patients who have recently suffered an exacerbation of COPD.

PLAIN LANGUAGE SUMMARY

Pulmonary rehabilitation for people who have been in hospital with an exacerbation of chronic obstructive pulmonary disease

We wished to determine the impact of pulmonary rehabilitation on hospital admissions and other patient-important outcomes such as quality of life. In order to be considered for our review, the clinical trials had to involve some sort of exercise program. However some of the programs also included emphasis on endurance and strength training or breathing exercises and education about COPD. We were interested only in studies which assessed the effects of courses of exercise therapy in people with Chronic Obstructive Pulmonary Disease (COPD), who had been in hospital following an exacerbation. We included nine studies. Pulmonary rehabilitation reduced hospital admissions and mortality compared with usual community care (no rehabilitation). Quality of life was also improved and the effect was substantially larger than the minimal important difference. Pulmonary rehabilitation appears to be a highly effective and safe intervention in COPD patients after suffering an exacerbation.

BACKGROUND

Exacerbations and hospitalisations in patients with Chronic Obstructive Pulmonary Disease (COPD) represent a major health burden in industrialized and developing countries, for patients as well as health care systems (Chan-Yeung 2004; Seemungal 1998; Sin 2002; Sullivan 2000). Acute exacerbations are the most common reason for hospital admissions and death among COPD patients (Mannino 2002). In addition, health-related quality of life (HRQL) is reduced in patients with COPD (Schlenk 1998) compared to the healthy population and it is further impaired by acute and repeated exacerbations (Seemungal 1998). Patients are at risk of early death and further exacerbations requiring hospitalisations. Mortality rates during the year following a hospitalisation are around 35% (Almagro 2002; Connors 1996; Groenewegen 2003; Seneff 1995; Vitacca 2001) and re-hospitalisation rates around 60% (Connors 1996; Cydulka 1997; Groenewegen 2003; Martin 1982).

From the health care provider's perspective, COPD is resource-consuming (Sullivan 2000). Acute exacerbations account for over 70% of COPD-related costs because of emergency visits and hospitalisations (NHLBI 2001; Oostenbrink 2004; Sullivan 2000). Thus the cost drivers for COPD care are emergency visits and hospital admissions for acute exacerbations.

Position papers of the American College of Physicians and American College of Chest Physicians provided recommendations on the management of acute exacerbations (Bach 2001; Snow 2001). However, the articles focused on acute therapeutic interventions and did not provide recommendations on recovery, or how future exacerbations and hospitalisations could be reduced, despite this

being one of the main goals of COPD management. Pulmonary rehabilitation could play an important role in the management of COPD patients with repeated exacerbations. Pulmonary rehabilitation combines interventions on the respiratory system (i.e. smoking cessation, medications), psychological support (i.e. patient education, psychological and social support) and physical exercise and there is a large body of evidence showing that pulmonary rehabilitation improves exercise capacity and health-related quality of life (HRQL) as measured by the COPD-specific Chronic Respiratory Disease Questionnaire (CRQ) (Lacasse 2006), and that it may be cost effective (Griffiths 2001).

Most studies on pulmonary rehabilitation have been done in stable patients and the effect of pulmonary rehabilitation in patients with unstable COPD is less clear. In addition, there might be concerns that pulmonary rehabilitation is not safe shortly after exacerbations of COPD. Therefore, our aim was to conduct a systematic review to assess the effectiveness and safety of pulmonary rehabilitation after exacerbations of COPD.

The protocol for this Cochrane review was initially based upon an non-Cochrane systematic review, which has been previously published (Puhan 2005).

OBJECTIVES

To assess the effects of pulmonary rehabilitation after COPD exacerbations on future hospital admissions (primary outcome) and other patient-important outcomes (mortality, health-related quality of life and exercise capacity).

METHODS

Criteria for considering studies for this review

Types of studies

Randomised controlled trials comparing pulmonary rehabilitation to conventional community care after acute exacerbation of COPD.

Types of participants

COPD patients after in- or out-patient care for acute exacerbation. More than 90% of study participants were required to be COPD patients.

Types of interventions

Any in-patient and/or out-patient pulmonary rehabilitation program, including at least physical exercise, delivered to patients who have received acute care for an exacerbation of COPD. The rehabilitation program must commence either from immediately after initiation of exacerbation treatment or up to three weeks after initiation of exacerbation treatment.

Types of outcome measures

Primary outcomes

Hospital admissions (at least one hospital admission during follow-up)

Secondary outcomes

1. Health-related quality of life as measured by generic (e.g. SF-36) or disease-specific (e.g. CRQ, SGRQ) questionnaires
2. Exacerbation rates (after discharge)
3. Number of outpatient visits
4. Length of readmissions
5. Mortality
6. Functional exercise capacity as measured by 2-, 4-, 6-, 12-minute-walk test or a shuttle walk test
7. Maximal exercise capacity
8. Exercise endurance
9. Withdrawals
10. Adverse events
11. Costs

Search methods for identification of studies

Electronic searches

We performed literature searches in the following electronic databases:
MEDLINE
EMBASE
PEDro (Physiotherapy Evidence Database)
The Cochrane Central Register of Controlled Trials (CENTRAL, Issue 2, 2008)
We performed a very broad literature search to identify any randomised controlled studies on pulmonary rehabilitation in COPD patients. The search strategy for MEDLINE and EMBASE can be found in Appendix 1. In addition, we used the Pub-med "related articles" function for included studies to identify further studies. Also, we performed a Science citation index search for studies that cite included studies as well as studies that are cited by included studies.

In addition, a search of the Cochrane Airways Group Specialised Register of COPD trials was carried out using the following terms: (rehabilitat* or fitness or exercis* or physical* or train* or kinesio* or endurance*) and (acute* or exacerb* or emerg* or hospital* or admit* or admis* or discharg*)
The databases have been searched from their inception up to March 2010.

Searching other resources

We screened reference lists from included primary studies, review articles and conference proceedings of American Thoracic Society (ATS) and European Respiratory Society (ERS) and contacted experts in the field to ask for further published or unpublished studies. There were no restrictions of language of the articles.

Data collection and analysis

Selection of studies

Two members of the review team independently assessed the titles and abstracts of all identified citations. Decisions of the two reviewers were recorded (order full text article or reject) and then compared. Any disagreements were resolved by consensus with close attention to the inclusion/exclusion criteria. Two reviewers evaluated the full text of all potentially eligible papers and made a decision whether to include or exclude each study according to the inclusion and exclusion criteria specified above. Any disagreements were resolved again by consensus with close attention to the inclusion/exclusion criteria. All studies that did not fulfil all of the criteria were excluded and their bibliographic details listed, with the reason for exclusion. A third reviewer resolved any discrepancies if the two reviewers disagree.

Data extraction and management

Two independent reviewers independently screened the full text of the included studies and recorded details about study design, interventions, patients and outcome measures in a predefined Windows Excel form. We tested the data collection forms on a small sample of studies with strong likelihood for inclusion and exclusion. A third reviewer resolved any disagreements between the two reviewers. Bibliographic details such as author, journal, year of publication and language, were registered. We contacted the authors of the studies to obtain missing information.

Assessment of risk of bias in included studies

We assessed the risk of bias in the included studies as either high, low or unclear using the Cochrane Collaboration's 'Risk of bias' tool (Higgins 2008) and the following headings 1) sequence generation; 2) allocation concealment; and 3) blinding.
We recorded the initial degree of discordance between the reviewers and corrected discordant scores based on obvious errors. We resolved discordant scores based on real differences in interpretation through consensus or third party arbitration. The reviewers were not blinded to names of authors, institutions, journals or the outcomes of the trials.

Measures of treatment effect

We used forest plots to compare results across the trials. When appropriate we explored sources of heterogeneity (i.e. differences between characteristics of the studies) using multivariable regression models (meta-regression analysis) where a priori defined clinical and methodological items from the quality assessment served as explanatory variables. These included severity of disease (GOLD criteria), in- or out-patient treatment of exacerbation, length of the intervention (< 6 months), length of follow-up and comprehensiveness of rehabilitation programme (whether patient education, psychosocial support, breathing exercises or relaxation therapies were added to physical exercise).
Whenever possible, estimates and confidence limits were related to the minimal important difference (MID) (Schunemann 2005) for each outcome. We assessed whether the estimates and 95% confidence limits for the difference between study groups exceeded the MID (Chronic Respiratory Questionnaire ± 0.5 on seven point scales and St. George's Respiratory Questionnaire ± 4 points; Schunemann 2003) or represented an important effect (six-minute walk distance ≥35 meters; Puhan 2008).
Numbers needed to treat (NNT) were calculated from the pooled OR and its 95% CI applied to a specified baseline risk using the formula NNT = (1-(CEER*(1-OR))) / ((1-CEER)*(CEER)*(1-OR)) where CEER is the expected event rate in the control group and OR the odds ratio. This approach converts the risk in the control group to the corresponding odds, applies the OR (and its 95% CI) to estimate the odds in the treated group, and converts the odds to the corresponding risk and calculates the absolute risk difference, the inverse of which is the NNT. These absolute differences were converted into Cates plots using Visual Rx (Cates 2003).

Data synthesis

We pooled trial results by calculating weighted Mean Differences (MD) and pooled Odds Ratios using random effects models in Review Manager 5.

RESULTS

Description of studies

See: Characteristics of included studies; Characteristics of excluded studies; Characteristics of ongoing studies.

Results of the search

We identified 1759 citations from searches of electronic databases in the original search. 1740 citations were excluded after title and abstract screening. A total of 22 studies were retrieved for detailed evaluation (19 from electronic database and 3 from handsearching). We included six reports in the original review (Behnke 2000; Kirsten 1998; Man 2004; Murphy 2005; Nava 1998; Troosters 2000).

The search for the update covered the period from July 2008 to March 2010. We identified 62 references from the electronic database search. Three from electronic database and one from handsearching were retrieved for the full text assessment. Three additional references (Carr 2009; Eaton 2009;; Seymour 2010) were included in the review update.

Included studies

Nine studies (drawn from eleven citations) met the eligibility criteria of the review. The studies involved a total of 432 participants who were in the recovery phase of a recent COPD exacerbation. In four studies (Behnke 2000; Eaton 2009; Kirsten 1998; Nava 1998), patients started an inpatient pulmonary rehabilitation within three to eight days of hospital admission, in one study (Carr 2009) patients started either an in- or out-patient rehabilitation program, in three studies (Man 2004; Seymour 2010; Troosters 2000) the outpatient rehabilitation was initiated after the inpatient exacerbation treatment and in one study (Murphy 2005) the outpatient rehabilitation was started after the hospital at home treatment of the exacerbation. Completion rates of the rehabilitation programme were reported in five studies and ranged from 40% to 94% (median 77%). None of the studies provided details about the exacerbation treatment provided to patients. See Characteristics of included studies for details of each included study.

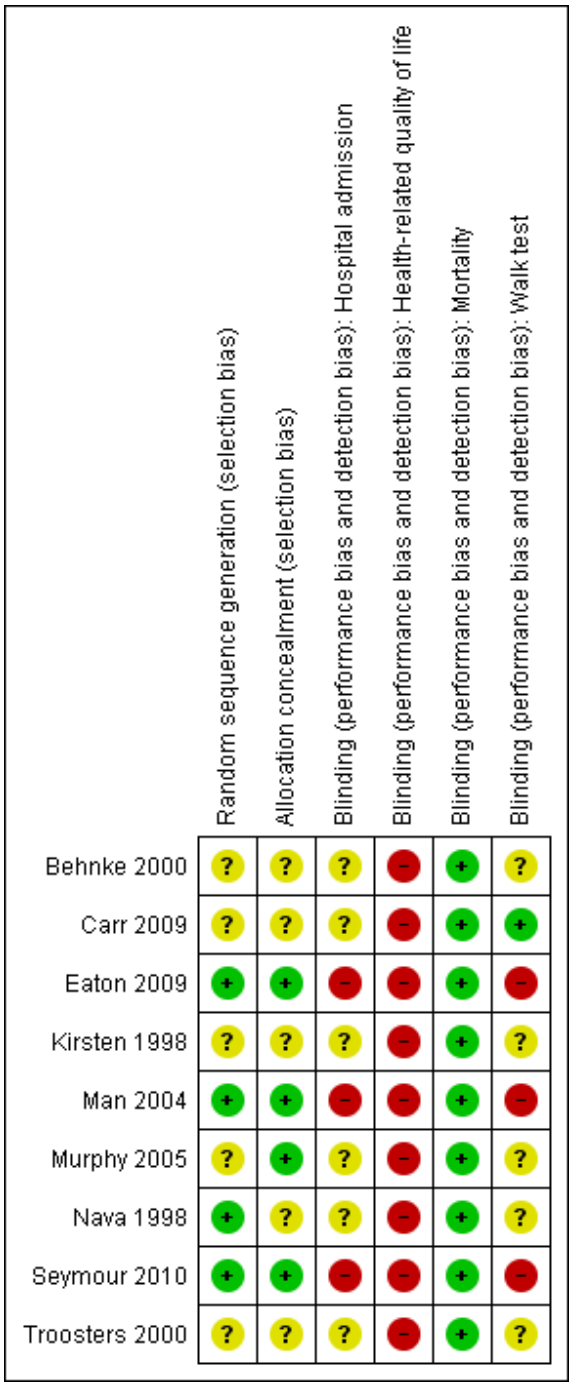
Excluded studies

The main reason for exclusion was that the study population did not have COPD. The reasons for exclusion are recorded in Characteristics of excluded studies.

Risk of bias in included studies

The available information regarding treatment group assignment and allocation concealment indicated a low risk of bias where this was reported. Patients could not be blinded in these studies, which may have introduced bias for outcomes such as HRQL, but is less likely to be an important source of bias for mortality and hospital admission (see Figure 1). Outcome assessors could be blinded for outcomes such as exercise endurance or six-minute walk distance, and this was done in one trial (Carr 2009).

Figure 1. Risk of bias summary: review authors' judgments about each risk of bias item for each included study.



Effects of interventions

Admission to hospital

Five studies involving 250 patients contributed data on admissions to hospital. There was a significant reduction in the odds of hospital re-admission (OR 0.22; 95% CI 0.08 to 0.58; I^2=51%) (Behnke 2000; Eaton 2009; Man 2004; Murphy 2005; Seymour 2010; Figure 2) with a NNT of 4 (95% CI 3 to 8) Figure 3. The follow-up period for these studies ranged from 3 to 18 months, with a mean duration of 25 weeks. In one trial (Eaton 2009) there was a large discrepancy between the intention-to-treat and the per-protocol analysis because only 19 (40%) patients assigned to early rehabilitation satisfied the a priori definition of adherence (attendance at 75% of rehabilitation sessions). Repeating the meta-analysis using the per-protocol data of that trial did not change the results of the meta-analysis significantly (OR 0.19; 95% CI 0.09 to 0.39, five studies, N = 222) but did reduce heterogeneity (I^2= 0%).

Figure 2. Forest plot of comparison: 1 Rehabilitation versus control, outcome: 1.1 Hospital admission (to end of follow-up).

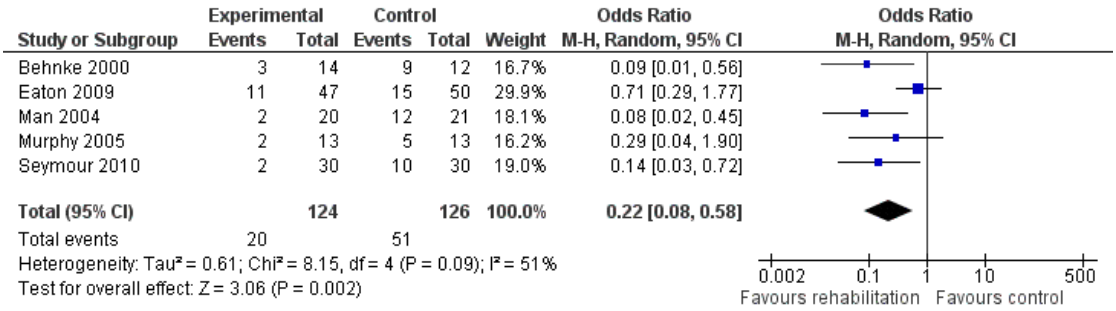
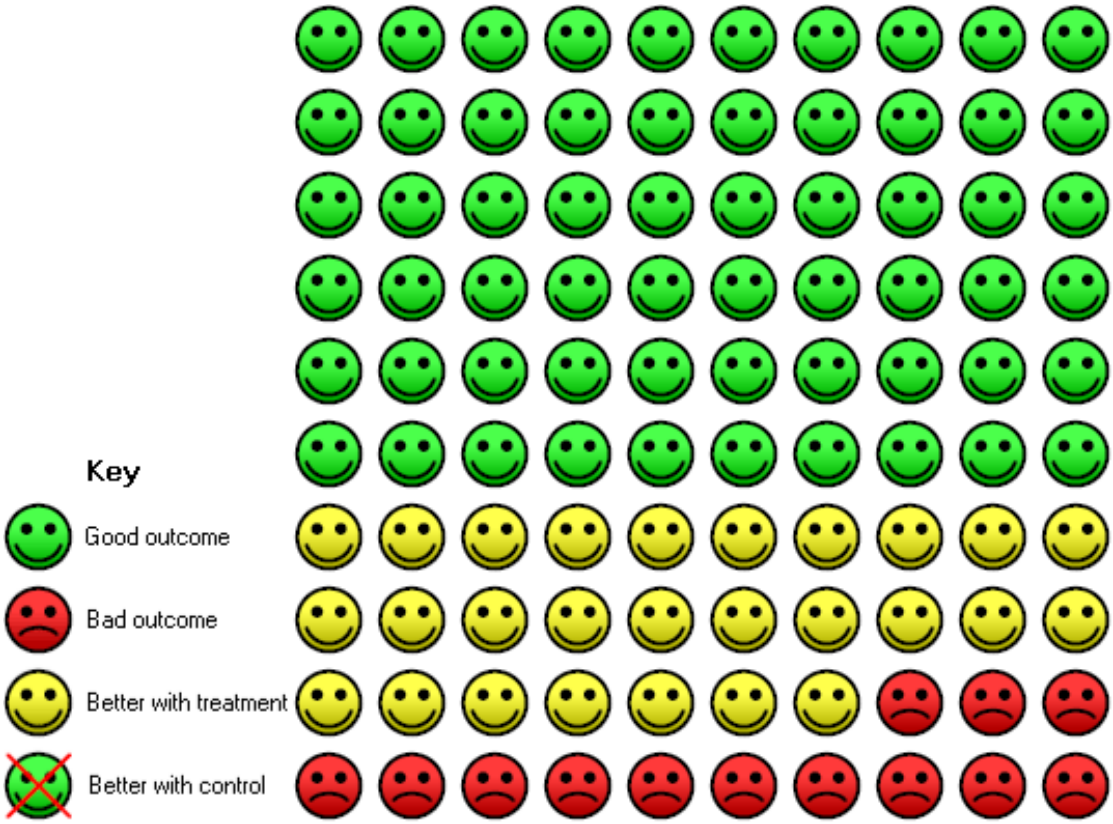


Figure 3. In the control group 40 people out of 100 had hospital admission over 25 weeks, compared to 13 (95% CI 5 to 28) out of 100 for the active treatment group. This represents an NNT(B) of 4 (95% CI 3 to 8) over 25 weeks.



Mortality

Three studies involving 110 patients contributed mortality data (Behnke 2000; Man 2004; Troosters 2000). Treatment with pulmonary rehabilitation led to a significant reduction in the odds of death between treatment and control: (OR 0.28; 95% CI 0.10 to 0.84; Figure 4) with an NNT of 6 (95% CI 5 to 30; Figure 5). The follow-up period for these studies varied from 3 to 48 months, with a weighted mean duration of 107 weeks.

Figure 4. Forest plot of comparison: 1 Rehabilitation versus control, outcome: 1.2 Mortality.

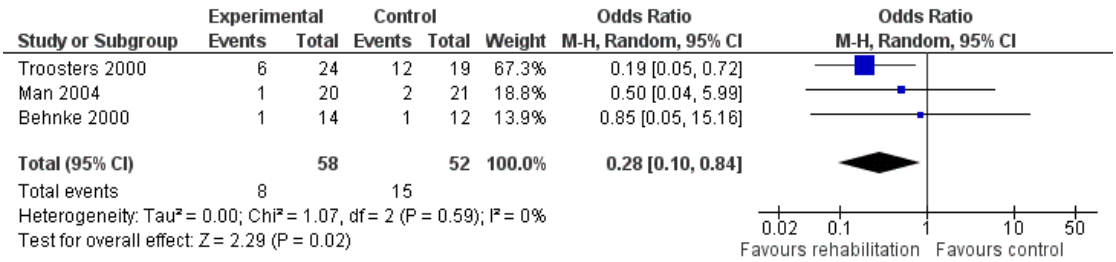
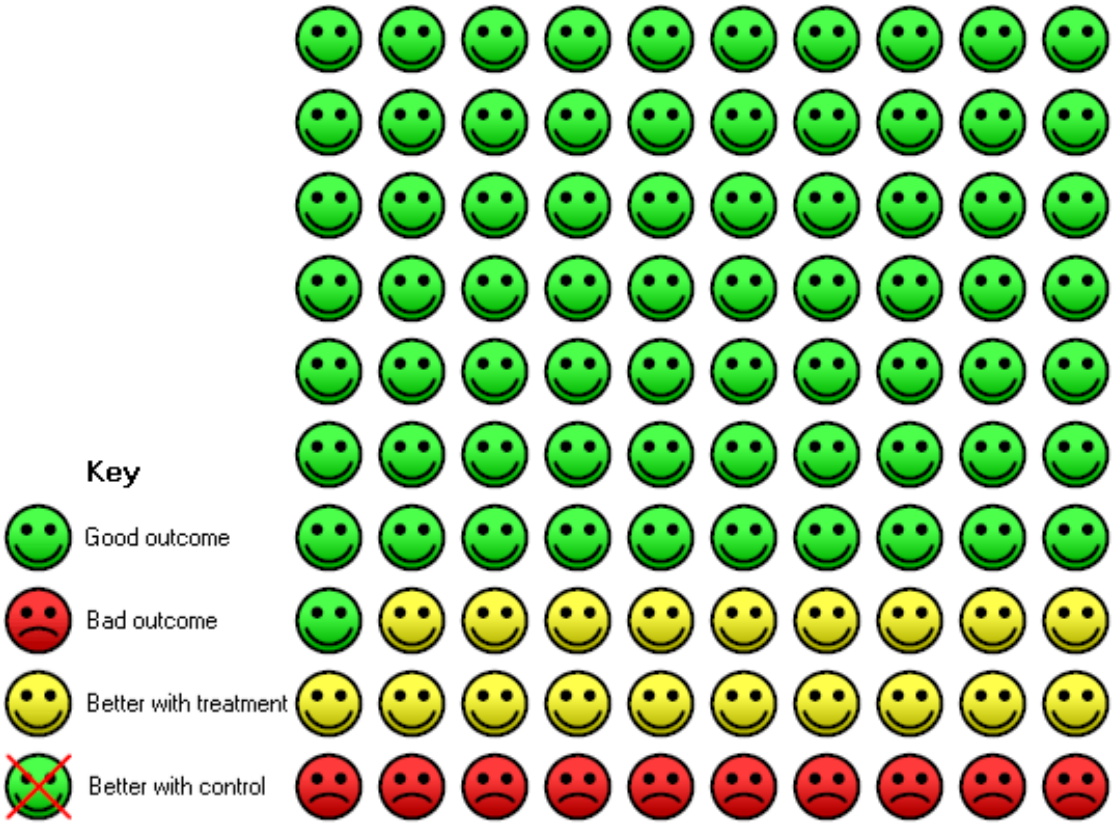


Figure 5. In the control group 29 people out of 100 had mortality over 107 weeks, compared to 10 (95% CI 4 to 26) out of 100 for the active treatment group. This represents an NNT(B) of 6 (95% CI: 5 to 30) over 107 weeks.

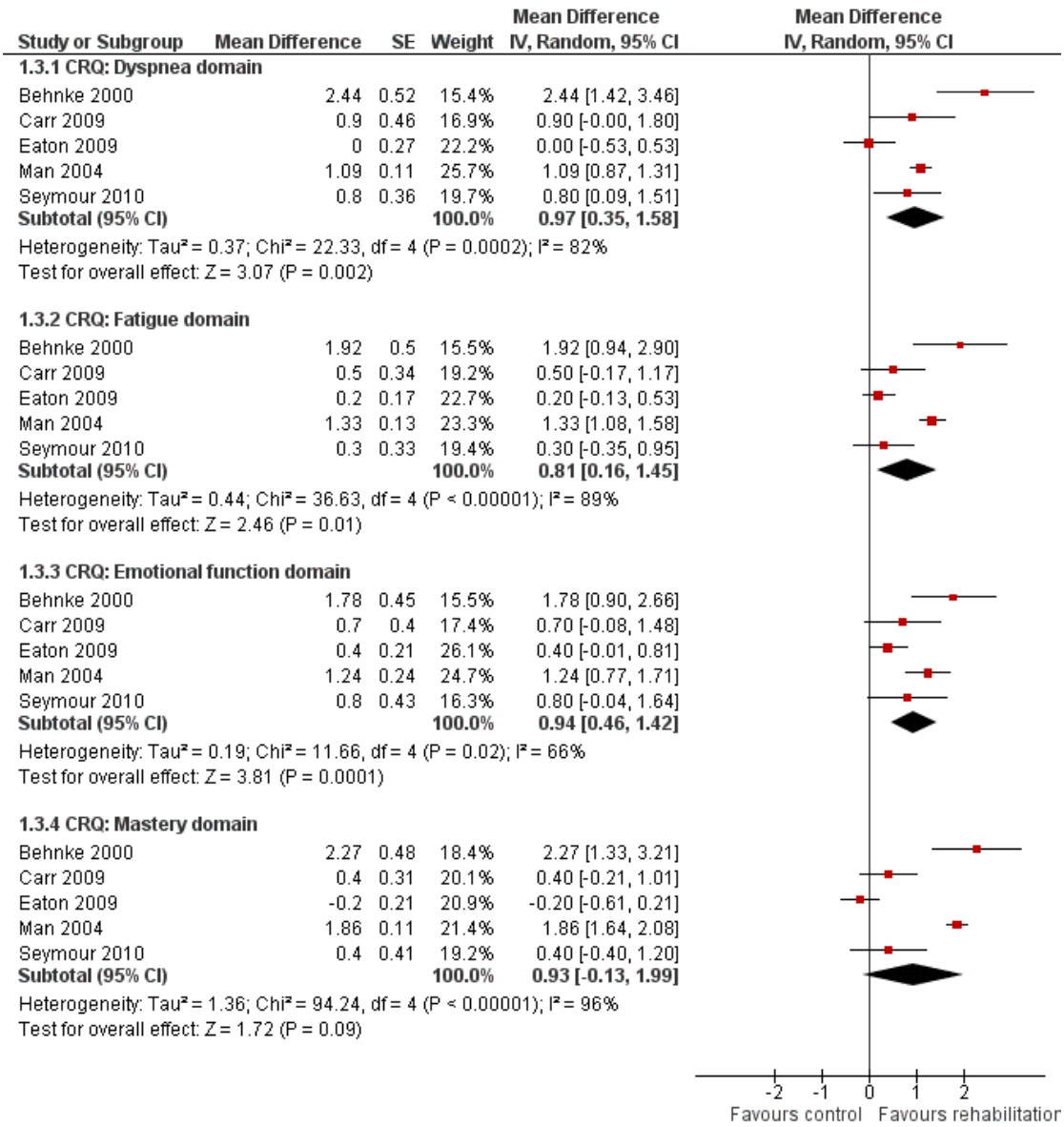


Health-related quality of life

Two instruments were used to measure this outcome; the Chronic Respiratory Questionnaire (CRQ) was used in five studies involving 259 patients (Behnke 2000; Carr 2009; Eaton 2009; Man 2004; Seymour 2010) and the St George's Respiratory Questionnaire (SGRQ) was used in three studies involving 128 patients (Man 2004; Murphy 2005; Seymour 2010).

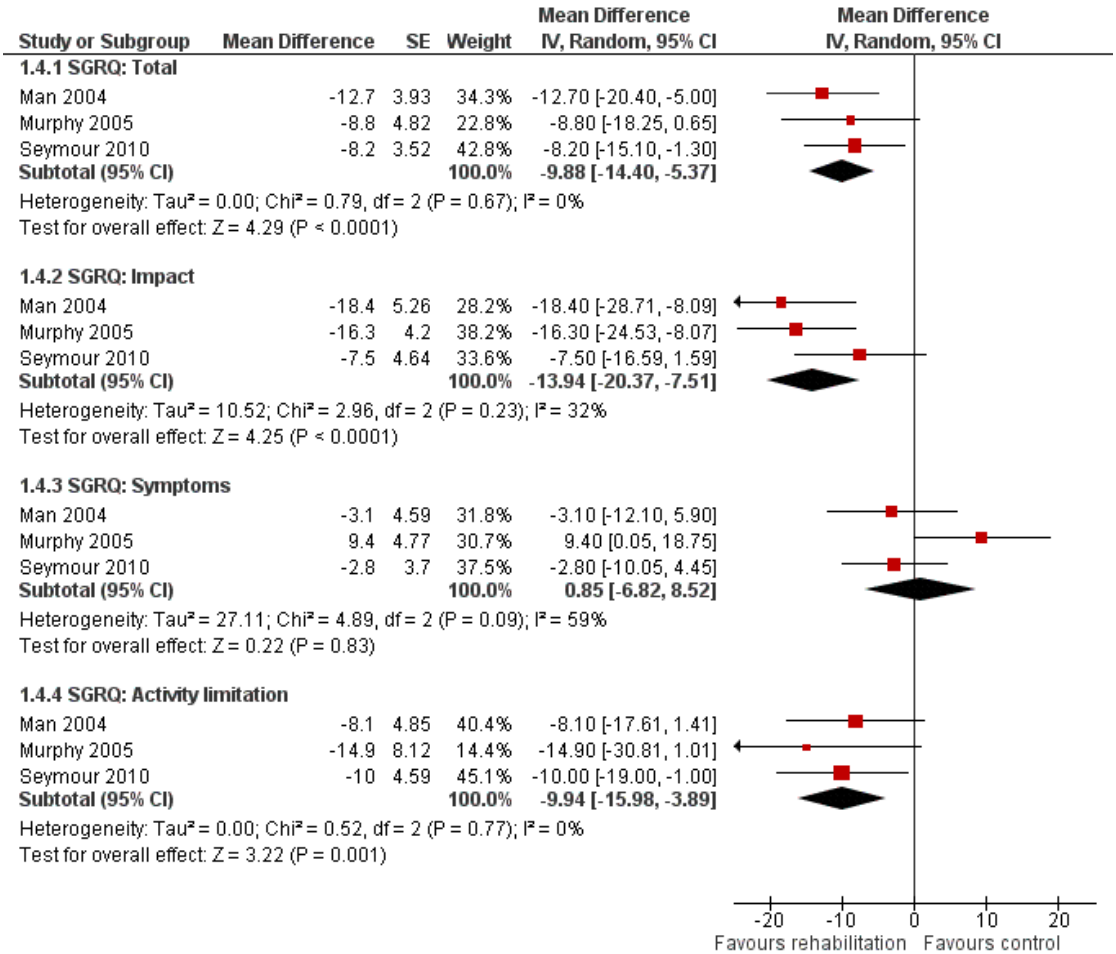
Although there was substantial heterogeneity across studies, the domains of the CRQ indicated a consistent, significant difference between treatment and control of between (MD 0.81; 95% CI 0.16 to 1.45) for the fatigue domain and (MD 0.97; 95% CI 0.35 to 1.58) for the dyspnea domain (Figure 6). Differences were well above the MID of 0.5 unit for all CRQ domains. We did not find a particular characteristic from either the methodological quality of the trials, differences in the populations of the trials, or difference in the rehabilitation programs that would explain the heterogeneity.

Figure 6. Forest plot of comparison: 1 Rehabilitation versus control, outcome: 1.3 Health-related quality of life: Chronic Respiratory Questionnaire (CRQ).



Results were more homogenous for the SRGQ results. Total scores for the SGRQ also significantly favoured pulmonary rehabilitation over usual care (MD -9.88; 95% CI -14.40 to -5.37; Figure 7). The sub domain scores for activity limitation and impact were consistent and favoured pulmonary rehabilitation with differences in units (MD -9.94; 95% CI -15.98 to -3.89) and (MD -13.94; 95% CI -20.37 to -7.51) respectively. Differences were above the MID of four units for the total score and for the impacts and activity limitation domains.There was no significant difference in the symptoms domain and a high degree of statistical heterogeneity (I^2 = 59%).

Figure 7. Forest plot of comparison: 1 Rehabilitation versus control, outcome: 1.4 Health-related quality of life: St George's Respiratory Questionnaire.



Exercise capacity

Six studies involving 300 patients used six-minute walk tests (Behnke 2000; Carr 2009; Eaton 2009; Kirsten 1998; Nava 1998; Troosters 2000) and three studies involving 128 patients (Man 2004; Murphy 2005; Seymour 2010) used shuttle walk tests to measure exercise capacity.

Six-minute walk distance was significantly improved by pulmonary rehabilitation (MD 77.70; 95% CI 12.21 to 143.20; Figure 8) and represented an important effect (≥ 35 meters). However, heterogeneity between studies was large with moderate to large effects in four trials (Behnke 2000; Kirsten 1998; Nava 1998; Troosters 2000) and no effect in two studies (Carr 2009; Eaton 2009). Shuttle walk tests also favoured rehabilitation significantly with a weighted mean difference (MD 64.35; 95% CI 41.28 to 87.43; Figure 9) and there was no statistical heterogeneity across studies.

Figure 8. Forest plot of comparison: 1 Rehabilitation versus control, outcome: 1.5 Change from baseline in 6 minute walking test.

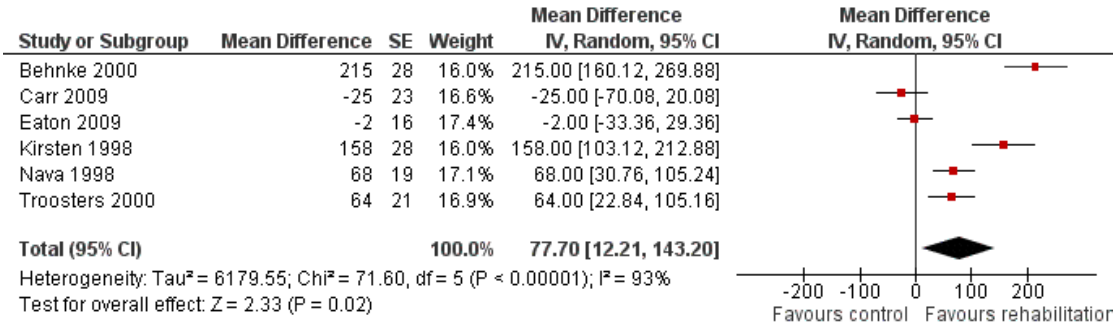
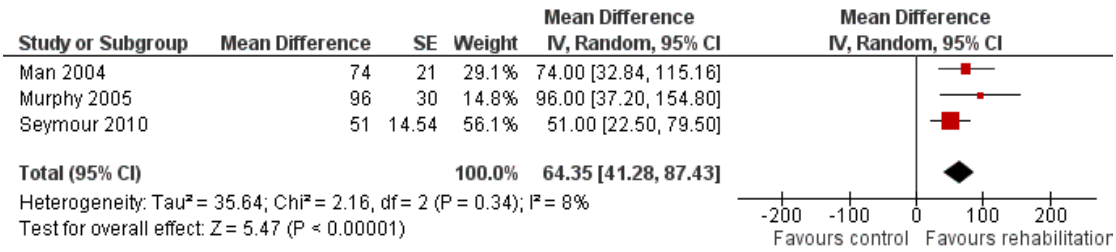


Figure 9. Forest plot of comparison: 1 Rehabilitation versus control, outcome: 1.6 Change from baseline in shuttle walk test.



Adverse events

Three trials involving 168 patients explicitly recorded adverse events (Behnke 2000; Eaton 2009; Man 2004). No adverse events during the rehabilitation programmes were reported in any of the trials.

DISCUSSION

Summary of main results

The meta-analyses showed that pulmonary rehabilitation after acute exacerbation of COPD reduced the risk for hospital admissions and mortality and improved health-related quality of life.

Effects on exercise capacity as measured by the six-minute and shuttle walking test were also statistically significant, but differed substantially between the trials.

The effect of pulmonary rehabilitation after acute exacerbation appears to be large. The number of unplanned hospital admissions and mortality was significantly reduced. When one assumes that pulmonary rehabilitation improves activity level in patients with COPD, it seems plausible that rehabilitation reduces readmission rate as inactivity has been shown to be a predictor of readmissions (Garcia-Aymerich 2003). Also, pulmonary rehabilitation addresses risk factors such as low exercise capacity or dyspnea well known to be associated with early death (Puhan 2009). In addition, the effects on health-related quality of life were well above the threshold for the minimal important difference for the CRQ (0.5 point difference Schunemann 2005) and the St. George's Respiratory Questionnaire (4 points Schunemann 2003, Jones 2005). Effects on six-minute walking distance were also above the threshold for an important effect (35 meters) although one needs to consider that estimate for the threshold for an important effect differ and may depend on the method to determine it and on the spectrum of patients (Puhan 2008).

Overall completeness and applicability of evidence

A word of caution is needed when interpreting the current analysis. A clear limitation of the trials is their relatively small sample size. All trials, in particular the trials reported by Behnke (Behnke 2000) and Kirsten (Kirsten 1998) showed large effects of pulmonary rehabilitation on health-related quality of life and exercise capacity. Small trials tend to overestimate the effect of an intervention compared to large trials (Cappelleri 1996; Ioannidis 1998; Kjaergard 2001; LeLorier 1997). This phenomenon may partly be attributed to a publication bias, that is, the fact that small trials are more likely to be published if they show statistically significant treatment effects (Egger 1998). On the other hand, methodological shortcomings of small trials such as inadequate generation of the randomisation code, insufficient concealment of random allocation and lack of blinding contribute to discrepancies between the results of single large trials and pooled estimates based on small trials (Kjaergard 2001). In our systematic review, the trials had methodological limitations and it cannot be excluded that the estimates provided by the meta-analyses represent overestimations of the effect of pulmonary rehabilitation after acute exacerbation. Conducting trials on pulmonary rehabilitation after an exacerbation is, however, challenging. Firstly, recruitment of patients is difficult because not all of them may want to be randomly allocated to different types of post-exacerbation management in a situation of poor health status. A trial on pulmonary rehabilitation after an exacerbation was recently stopped because only few patients could be recruited (van der Berg 2006). Also, recruitment was very slow in another trial comparing rehabilitation after exacerbation with rehabilitation in stable pulmonary state (Puhan 2006) and one trial had to be stopped before the recruitment target was reached (Spaar 2009). Secondly, patients willing to participate in a trial are likely to have a preference for pulmonary rehabilitation. If they are randomized to the control group or rehabilitation after a period of time, they might ask for pulmonary rehabilitation at any time during the follow-up. Given the clear benefits of this intervention in stable patients and confirmed in meta-analyses, patients can hardly be refused access to rehabilitative strategies. Whatever design investigators choose, a careful discussion of ethical and methodological issues is necessary before conducting large trials.

Quality of the evidence

A limitation is the small number of patients included in the trials and methodological shortcomings that limit firm conclusions.

Potential biases in the review process

Strengths of this systematic review include the extensive literature search, rigorous adherence to a predefined protocol and contact with authors of the included trials who all provided additional information about their data.

Agreements and disagreements with other studies or reviews

Compared to pulmonary rehabilitation in stable COPD patients, the effect size of rehabilitation on health-related quality of life are similar in patients who have recently had an exacerbation of COPD. Weighted mean differences between the rehabilitation and control groups for CRQ dyspnea, fatigue, emotional function and mastery domains in this systematic review (0.97, 0.81, 0.94 and 0.93, respectively) were close to those observed in the stable COPD (1.00, 0.89, 0.70 and 0.93, respectively; Lacasse 2006). But the large improvements in exercise capacity and, in particular, the substantial risk reduction for hospital admissions, indicate that pulmonary rehabilitation may be may be a particularly attractive addition to the management of patients after an exacerbation. There are several possible explanations for this. First, as mentioned above, exacerbations lead to significant reductions in muscle function (Spruit 2003) and physical activity (Pitta 2006). This initial deterioration may render patients more likely to improve from pulmonary rehabilitation. Pulmonary rehabilitation is a particularly potent intervention to revert physical inactivity (Troosters 2010a) and it has been shown that patients who improve physical activity levels have less chance of being readmitted (Garcia-Aymerich 2006, Pitta 2006). Second, since eligible patients had been hospitalized for a COPD exacerbation, there may be an existing deficiency in self-management or education among

this group. This deficiency may be partially targeted with the rehabilitation intervention, and patient education may be of particular benefit to modify behaviour in these patients. Indeed, a major study of a patient management program including home exercises for COPD patients after acute exacerbations showed impressive results (Bourbeau 2003). In that study the mean number of hospital admissions per patient was reduced from 1.6 to 0.9 in the year following a hospital admission due to an acute exacerbation. It is well known from earlier studies that the recovery period is long even in patients who have no further exacerbations, and that another exacerbation within six months limits recovery markedly (Spencer 2003). A final explanation may be the effect of pulmonary rehabilitation on depressive symptoms after exacerbations. Depression is a significant risk factor for readmission and pulmonary rehabilitation has been shown to improve depressive symptoms in patients with depression (Coventry 2007; Trappenburg 2005). Our meta-analyses showed that pulmonary rehabilitation during the recovery period is superior compared with usual care in terms of prognosis and health-related quality of life.

Do we need more trials on pulmonary rehabilitation after COPD exacerbation? Larger trials may be justified because the trials included in this systematic review had several methodological limitations and because the small sample sizes do not allow estimating the treatment effect very precisely. In some countries a large trial may still be perceived to be ethically justifiable because pulmonary rehabilitation after exacerbation is uncommon. And indeed, there are four ongoing trials (Castelain 2008; Fanny 2006; van der Berg 2006; Young 2006) comparing pulmonary rehabilitation with usual care after a COPD exacerbation. On the other hand, observed effects are so large that it is unlikely that they can be attributed to bias only. Therefore, from an ethical point of view it may be difficult to withhold this intervention from patients. This may be particularly true in a number of European countries where pulmonary rehabilitation after exacerbation is common practice and where even more COPD patients follow a pulmonary rehabilitation after exacerbation than in stable pulmonary state (Puhan 2003).

If rehabilitation is effective in both stable pulmonary state and after exacerbations, the question arises at what point of time patients should be referred? An advantage of rehabilitation after exacerbation is that it may provide a window of opportunity for patient education because patients may be more willing to change their health behaviour after an exacerbation. Also, continuity of care is possible if patients are immediately referred to pulmonary rehabilitation. A disadvantage of rehabilitation after exacerbation is that patients often re-exacerbate within weeks so that the rehabilitation process is interrupted or even discontinued. Also, initiation of physical exercise is challenging in patients after exacerbation so that more time may be necessary to find the appropriate exercise protocol for the individual patient (Puhan 2005a; Puhan 2006). It is noteworthy that one recent randomized controlled trial has brought the provision of rehabilitation further forward, introducing specific resistance training during hospital admission. This intervention proved to be an adequate preventive strategy which may prevent some of the systemic consequences of the exacerbation on the skeletal muscle (Troosters 2010).

AUTHORS' CONCLUSIONS

Implications for practice

Pulmonary rehabilitation is an effective intervention for the post-exacerbation management of COPD patients. It is likely to reduce the risk for future hospital admissions and leads to large and clinically relevant improvements of health-related quality of life and exercise capacity.

Implications for research

Methodologically sound and large studies would provide more valid and precise estimates for the effects of pulmonary rehabilitation after COPD exacerbations. The decision to begin new trials of pulmonary rehabilitation should be taken against the background of perceived ethics about the benefit of rehabilitation after exacerbations and against the methodological and logistical challenges of such trials if placebo controlled, or compared to a no-exercise intervention. Formal cost effectiveness analyses should be conducted in order to estimate the financial benefit from rehabilitation after COPD exacerbations.

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Ongoing study Starting date of trial not provided. Contact author for more information.

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Ongoing study Starting date of trial not provided. Contact author for more information.

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Ongoing study Starting date of trial not provided. Contact author for more information.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Behnke 2000

Methods	Randomised parallel group trial
Participants	26 COPD patients (mean age 67 years, 77% males, mean FEV_1=36% predicted) after inpatient treatment for acute exacerbation
Interventions	**Rehabilitation:** Within 4-7 days after admission, inpatient pulmonary rehabilitation with endurance exercise (5 walking sessions/day for 10 days), followed by six months of supervised home-based endurance exercise (3 walking sessions/day for 6 months). Completion rate of pulmonary rehabilitation of 65.2% (15 out of 23 patients) **Usual care:** Standard inpatient care without exercise and standard community care with respirologist. Follow-up: 76 weeks
Outcomes	CRQ, Transition dyspnea index, 6MWD, hospital readmission, mortality
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Described as randomised; other information not available
Allocation concealment (selection bias)	Unclear risk	Information not available from trial report
Blinding (performance bias and detection bias) Hospital admission	Unclear risk	Information not available from trial report. Outcome may be affected by knowledge of treatment group assignment
Blinding (performance bias and detection bias) Health-related quality of life	High risk	Although unavoidable by definition, lack of blinding may affect outcome
Blinding (performance bias and detection bias) Mortality	Low risk	Information not available from trial report. Outcome unlikely to be affected by knowledge of treatment group assignment
Blinding (performance bias and detection bias) Walk test	Unclear risk	Information not provided in trial report. Potential lack of blinding likely to affect outcome assessment

Carr 2009

Methods	Randomised parallel group trial
Participants	34 COPD patients (mean age 68 years, 44% males, mean FEV_1= 0.91L) after inpatient treatment for acute exacerbation
Interventions	Rehabilitation: in- or out-patient pulmonary rehabilitation (based on subject preference or location of initial PR) (2 h/session over 3 weeks, completed between 9 or 15 sessions) with breathing exercise, strength and interval training, and corridor and treadmill walking or cycling; patient education (energy conservation, lung health, drugs and stress management). Completion rate of pulmonary rehabilitation of 94% (16 out of 17 patients). Follow-up: 12 weeks Usual care: Standard in-patient and community care without exercise (not further specified). Follow-up: 12 weeks
Outcomes	CRQ (primary outcome), 6MWD (secondary outcome)
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Described as randomised; additional information not available from trial report
Allocation concealment (selection bias)	Unclear risk	Information not available from trial report
Blinding (performance bias and detection bias) Hospital admission	Unclear risk	Information not reported
Blinding (performance bias and detection bias) Health-related quality of life	High risk	Although unavoidable by definition, lack of blinding may affect outcome
Blinding (performance bias and detection bias) Mortality	Low risk	Information not available from trial report. Outcome unlikely to be affected by knowledge of treatment group assignment
Blinding (performance bias and detection bias) Walk test	Low risk	'The investigator responsible for collecting outcome measures was unaware of group allocation'

Eaton 2009

Methods	Randomised parallel group trial
Participants	97 COPD patients (mean age 70 years, 44% males, mean FEV_1=36% predicted)
Interventions	**Rehabilitation:** The patient started inpatient programme as soon as medically appropriate as determined by the attending medical team. Inpatient programme: Supervised walking and upper-lower limb strengthening exercise at least 30 min/day until discharge, followed by outpatient programme: supervised exercise for 8 weeks (1 h session, twice weekly) and patient education (coping with dyspnea, the importance of a regular daily home exercise programme, management of activities of daily living, drugs, vaccines, airway clearance techniques, nutritional advice, self-management and action plans for exacerbations, stress and panic management, relaxation techniques, mood disturbance, adapting to a chronic illness and end-of-life care). Only 19 (40%) patients assigned to early rehabilitation satisfied the a priori definition of adherence (attendance at 75% of rehabilitation sessions) Follow-up: 12 weeks **Usual care:** Standardized care in accordance with the ATS/ERS COPD guidelines and standardized advice on exercise and maintaining daily activities, but not further specified. Follow-up:12 weeks
Outcomes	Hospital readmission and hospital days (primary outcomes); BODE index, 6MWD, CRQ (secondary outcomes)
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated randomization
Allocation concealment (selection bias)	Low risk	Information from computer only available at time of randomization
Blinding (performance bias and detection bias) Hospital admission	High risk	Outcome may be affected by knowledge of treatment group assignment
Blinding (performance bias and detection bias) Health-related quality of life	High risk	Although unavoidable by definition, lack of blinding may affect outcome
Blinding (performance bias and detection bias) Mortality	Low risk	Information not available from trial report. Outcome unlikely to be affected by knowledge of treatment group assignment

Blinding (performance bias and detection bias) Walk test	High risk	Lack of blinding likely to affect outcome assessment. 'The nature of intervention precluded blinding of participants and health care providers'

Kirsten 1998

Methods	Randomised parallel group trial
Participants	29 COPD patients (mean age 64 years, 90% males, mean FEV_1=36% predicted) after inpatient treatment for acute exacerbation
Interventions	**Rehabilitation:** Within 6-8 days after admission, inpatient pulmonary rehabilitation with endurance exercise (5 walking sessions/day for 10 days). Completion rate of pulmonary rehabilitation not reported **Usual care:** Standard inpatient care without exercise (not further specified). Follow-up: 11 days
Outcomes	Transition dyspnea index, 6MWD
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Described as randomised; additional information not available from trial report
Allocation concealment (selection bias)	Unclear risk	Information not available from trial report
Blinding (performance bias and detection bias) Hospital admission	Unclear risk	Information not reported
Blinding (performance bias and detection bias) Health-related quality of life	High risk	Information not available from trial report. Although unavoidable by definition, lack of blinding may affect outcome
Blinding (performance bias and detection bias) Mortality	Low risk	Information not available from trial report. Outcome unlikely to be affected by knowledge of treatment group assignment
Blinding (performance bias and detection bias) Walk test	Unclear risk	Information not provided in trial report. Potential lack of blinding likely to affect outcome assessment

Man 2004

Methods	Randomised parallel group trial
Participants	42 COPD patients (mean age 70 years, 41% males, FEV_1=39% predicted) after inpatient treatment for acute exacerbation
Interventions	**Rehabilitation:** Multidisciplinary outpatient pulmonary rehabilitation (within 10 days of discharge) with endurance and strength exercise and patient education for 12 weeks (2 sessions/week). Completion rate of pulmonary rehabilitation of 85.7% (18 out of 21patients) **Usual care:** Standard community care with respirologist. Follow-up: 12 weeks
Outcomes	CRQ, SGRQ, SF-36, ISWT, hospital readmission, hospital days, emergency admissions, mortality
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	'A random number generator was our tool to assign an intervention to the first patient entering the study. We used the minimisation method to assign patients further to the intervention group, taking into account five factors: age (< 70 years or 70 years), sex, length of hospital admission (<7 days or 7 days), incremental shuttle walk distance at discharge (< 100 metres or 100 metres), and predicted forced expiratory volume in one second (FEV_1; < 30% or 30%).'
Allocation concealment (selection bias)	Low risk	Used minimization where allocation is concealed
Blinding (performance bias and detection bias) Hospital admission	High risk	Lack of blinding may affect outcome assessment. 'Owing to the nature of the intervention... it was not possible to blind the patients or the assessors (investigator responsible and members of the pulmonary rehabilitation team)'
Blinding (performance bias and detection bias) Health-related quality of life	High risk	Although unavoidable by definition, lack of blinding may affect outcome
Blinding (performance bias and detection bias) Mortality	Low risk	Information not available from trial report. Outcome unlikely to be affected by knowledge of treatment group assignment
Blinding (performance bias and detection bias) Walk test	High risk	Lack of blinding likely to affect outcome assessment. 'Owing to the nature of the intervention... it was not possible to blind the patients or the assessors (inves-

		tigator responsible and members of the pulmonary rehabilitation team)'

Murphy 2005

Methods	Randomised parallel group trial
Participants	26 COPD patients (mean age 66 years, 65% males, mean FEV_1=40% predicted) after home for hospital treatment for acute exacerbation
Interventions	**Rehabilitation:** Supervised home-based pulmonary rehabilitation with endurance and strength exercise for 6 weeks (2 supervised sessions/week and daily unsupervised sessions) . Completion rate of pulmonary rehabilitation of 76.9% (10 out of 13 patients) **Usual care:** Standard community care with respirologist. Follow-up: 26 weeks
Outcomes	SGRQ, EQ-5D, MRC dyspnea scale, ISWT, 3-minute step test, hospital readmission
Notes	Dr Murphy provided standard deviations for SGRQ measurements

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"randomised" Although the process of generating randomisation schedule not specified, it was presumed done due to the efforts made with allocation concealment
Allocation concealment (selection bias)	Low risk	'...each patient was randomly assigned in a 1:1 ratio for the home exercise group or a control group (standard care group) using blinded sealed envelopes.'
Blinding (performance bias and detection bias) Hospital admission	Unclear risk	Information not reported
Blinding (performance bias and detection bias) Health-related quality of life	High risk	Although unavoidable by definition, lack of blinding may affect outcome
Blinding (performance bias and detection bias) Mortality	Low risk	Information not available from trial report. Outcome unlikely to be affected by knowledge of treatment group assignment
Blinding (performance bias and detection bias) Walk test	Unclear risk	Information not provided in trial report. Potential lack of blinding likely to affect outcome assessment

Nava 1998

Methods	Randomised parallel group trial
Participants	70 COPD patients (mean age 66 years, 73% males, mean FEV_1=32% predicted, 76% needed mechanical ventilation) admitted to inpatient care for treatment of acute exacerbation
Interventions	**Rehabilitation**: Within 3-5 days after admission, inpatient pulmonary rehabilitation with four steps of increasing intensity Step I, if unable to walk: Mobilisation and strength training for lower extremities Step II, if able to walk: Endurance exercise (walking) Step III, if possible: Endurance exercise (cycling and stair climbing) and respiratory muscle training IV, if possible: Endurance exercise (cycling at highest tolerated intensity, 2 sessions/day for 3 weeks) Completion rate of pulmonary rehabilitation of 85.4% (41 out of 48 patients) **Usual care**: Only steps I and II.Follow-up: 6 weeks
Outcomes	Dyspnea on exertion, 6MWD, mortality
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Described as randomised using computer program; additional information not available from trial report
Allocation concealment (selection bias)	Unclear risk	Information not available from trial report
Blinding (performance bias and detection bias) Hospital admission	Unclear risk	Information not available from trial report
Blinding (performance bias and detection bias) Health-related quality of life	High risk	Information not available from trial report. Although unavoidable by definition, lack of blinding may affect outcome
Blinding (performance bias and detection bias) Mortality	Low risk	Information not available from trial report. Outcome unlikely to be affected by knowledge of treatment group assignment
Blinding (performance bias and detection bias) Walk test	Unclear risk	Information not provided in trial report. Potential lack of blinding likely to affect outcome assessment

Seymour 2010

Methods	Randomised parallel group trial
Participants	60 COPD patients (mean age 66 years, 82% males, mean FEV_1=52% predicted) after inpatient treatment of acute exacerbation
Interventions	**Rehabilitation**: Within a week after hospital discharged, outpatient pulmonary rehabilitation twice-weekly exercise (limb strengthening and aerobic activities) and education sessions, during 8 weeks. Completion rate of pulmonary rehabilitation of 77% (23 out of 30). Patients were provided with general information about COPD and offered outpatient appointments with general practitioner or respiratory team. Follow-up: 12 weeks **Usual care**: Patients were provided with general information about COPD and offered outpatient appointments with general practitioner or respiratory team. Not referred further. Follow-up: 12 weeks
Outcomes	Exacerbation with hospitalization (primary outcome), ISW, ESW, CRQ and SGRQ (secondary)
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	'Participants were allocated by concealed randomisation by a statistician. The minimisation method matched groups for age (<70 years or ≥70 years), sex (male or female), predicted FEV_1 (<30% or ≥30%), duration of admission (<7 or ≥7 days) and baseline ISW (<100 m or ≥100 m).'
Allocation concealment (selection bias)	Low risk	Used minimization where allocation is concealed
Blinding (performance bias and detection bias) Hospital admission	High risk	Authors state: 'Due to the nature of the intervention, it was not possible to blind subjects to their allocation'
Blinding (performance bias and detection bias) Health-related quality of life	High risk	"Due to the nature of the intervention, it was not possible to blind subjects to their allocation" Although unavoidable by definition, lack of blinding may affect outcome
Blinding (performance bias and detection bias) Mortality	Low risk	Information not available from trial report. Outcome unlikely to be affected by knowledge of treatment group assignment
Blinding (performance bias and detection bias) Walk test	High risk	Authors state:'Due to the nature of the intervention, it was not possible to blind subjects to their allocation'

Troosters 2000

Methods	Randomised parallel group trial
Participants	43 COPD patients (mean age 62 years, 85% males, FEV_1 =39% predicted) after inpatient treatment for acute exacerbation
Interventions	**Rehabilitation:** Outpatient pulmonary rehabilitation with endurance and strength exercise for 6 months (3 sessions/week in first 3 months, then 2/week). Completion rate of pulmonary rehabilitation of 70.8% (17 out of 24 patients) **Usual care:** Standard community care with respirologist (not further specified). Follow-up: 208 weeks
Outcomes	6MWD, mortality
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Described as randomised; additional information not available from trial report
Allocation concealment (selection bias)	Unclear risk	Information not available from trial report
Blinding (performance bias and detection bias) Hospital admission	Unclear risk	Information not available from trial report. Outcome unlikely to be affected by knowledge of treatment group assignment
Blinding (performance bias and detection bias) Health-related quality of life	High risk	Information not provided in trial report. Although unavoidable by definition, lack of blinding may affect outcome
Blinding (performance bias and detection bias) Mortality	Low risk	Information not available from trial report. Outcome unlikely to be affected by knowledge of treatment group assignment
Blinding (performance bias and detection bias) Walk test	Unclear risk	Information not provided in trial report. Potential lack of blinding likely to affect outcome assessment

ATS: American Tohracic Society; COPD: Chronic obstructive pulmonary disease; CRQ: Chronic Respiratory Questionnaire; BODE index: body-mass index, airflow obstruction, dyspnea and exercise capacity Index; ERS: European Respiratory Society; FEV1: forced expiratory volume in 1 second; h: hour; SGRQ: St George's Respiratory Questionnaire; SF-36: short-form health survey; ISWT: incremental shuttle walk test; EQ-5D: EuroQoL questionnaire; MRC: Medical Reserach Council; ESWT: endurance shuttle walk test; 6MWD: six-minute walking distance.

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Rasekaba 2009	Not randomized trial

Characteristics of ongoing studies *[ordered by study ID]*

Benzo 2010

Trial name or title	
Methods	
Participants	
Interventions	
Outcomes	
Starting date	
Contact information	
Notes	Not open yet for recruitment

Castelain 2008

Trial name or title	
Methods	
Participants	
Interventions	
Outcomes	
Starting date	
Contact information	
Notes	Recruiting

Fanny 2006

Trial name or title	
Methods	
Participants	
Interventions	
Outcomes	
Starting date	
Contact information	
Notes	Recruiting

Ko 2006

Trial name or title	
Methods	
Participants	
Interventions	
Outcomes	
Starting date	
Contact information	
Notes	Recruiting

Puhan 2006

Trial name or title	
Methods	
Participants	
Interventions	
Outcomes	
Starting date	
Contact information	

Puhan 2006 (*Continued*)

Notes	Follow-up completed in June 2010

van der Berg 2006

Trial name or title	
Methods	
Participants	
Interventions	
Outcomes	
Starting date	
Contact information	
Notes	Trial was terminated prematurely because of failure of recruitment (personal communication as of May 25, 2010)

Young 2006

Trial name or title	
Methods	
Participants	
Interventions	
Outcomes	
Starting date	
Contact information	
Notes	Recruiting

DATA AND ANALYSES

Comparison 1. Rehabilitation versus control

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Hospital admission (to end of follow-up)	5	250	Odds Ratio (M-H, Random, 95% CI)	0.22 [0.08, 0.58]
2 Mortality	3	110	Odds Ratio (M-H, Random, 95% CI)	0.28 [0.10, 0.84]
3 Health-related quality of life: Canadian Respiratory Disease Questionnaire (CRQ)	5		Mean Difference (Random, 95% CI)	Subtotals only
3.1 CRQ: Dyspnea domain	5		Mean Difference (Random, 95% CI)	0.97 [0.35, 1.58]
3.2 CRQ: Fatigue domain	5		Mean Difference (Random, 95% CI)	0.81 [0.16, 1.45]
3.3 CRQ: Emotional function domain	5		Mean Difference (Random, 95% CI)	0.94 [0.46, 1.42]
3.4 CRQ: Mastery domain	5		Mean Difference (Random, 95% CI)	0.93 [-0.13, 1.99]
4 Health-related quality of life: St George's Respiratory Questionnaire	3		Mean Difference (Random, 95% CI)	Subtotals only
4.1 SGRQ: Total	3		Mean Difference (Random, 95% CI)	-9.88 [-14.40, -5.37]
4.2 SGRQ: Impact	3		Mean Difference (Random, 95% CI)	-13.94 [-20.37, -7.51]
4.3 SGRQ: Symptoms	3		Mean Difference (Random, 95% CI)	0.85 [-6.82, 8.52]
4.4 SGRQ: Activity limitation	3		Mean Difference (Random, 95% CI)	-9.94 [-15.98, -3.89]
5 Change from baseline in 6 minute walking test	6		Mean Difference (Random, 95% CI)	77.70 [12.21, 143.20]
6 Change from baseline in shuttle walk test	3		Mean Difference (Random, 95% CI)	64.35 [41.28, 87.43]

Analysis 1.1. Comparison 1 Rehabilitation versus control, Outcome 1 Hospital admission (to end of follow-up).

Review: Pulmonary rehabilitation following exacerbations of chronic obstructive pulmonary disease

Comparison: 1 Rehabilitation versus control

Outcome: 1 Hospital admission (to end of follow-up)

Study or subgroup	Experimental n/N	Control n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Behnke 2000	3/14	9/12		16.7 %	0.09 [0.01, 0.56]
Eaton 2009	11/47	15/50		29.9 %	0.71 [0.29, 1.77]
Man 2004	2/20	12/21		18.1 %	0.08 [0.02, 0.45]
Murphy 2005	2/13	5/13		16.2 %	0.29 [0.04, 1.90]
Seymour 2010	2/30	10/30		19.0 %	0.14 [0.03, 0.72]
Total (95% CI)	**124**	**126**		**100.0 %**	**0.22 [0.08, 0.58]**

Total events: 20 (Experimental), 51 (Control)

Heterogeneity: $Tau^2 = 0.61$; $Chi^2 = 8.15$, df = 4 (P = 0.09); $I^2 = 51\%$

Test for overall effect: Z = 3.06 (P = 0.0022)

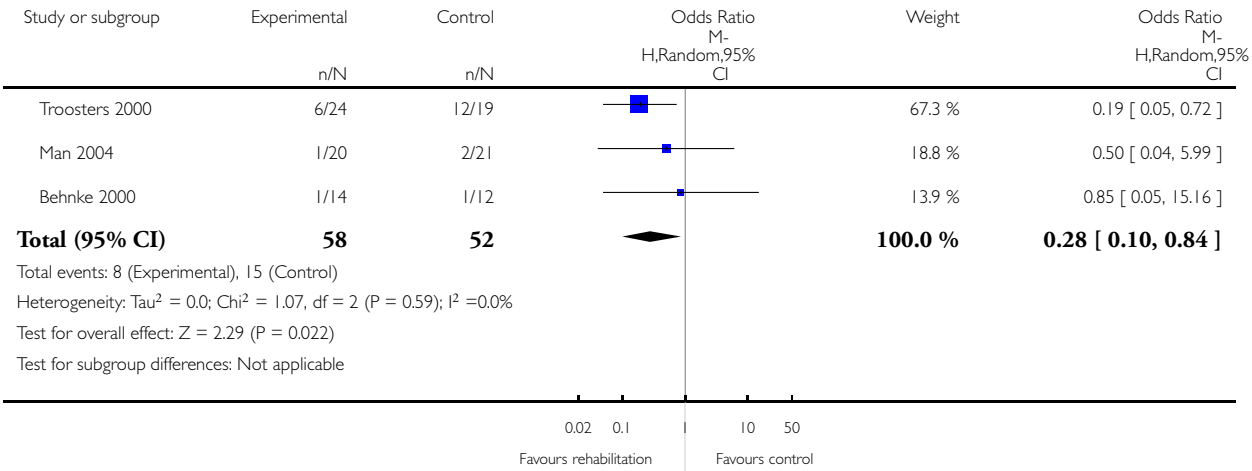
Test for subgroup differences: Not applicable

Analysis 1.2. Comparison 1 Rehabilitation versus control, Outcome 2 Mortality.

Review: Pulmonary rehabilitation following exacerbations of chronic obstructive pulmonary disease

Comparison: 1 Rehabilitation versus control

Outcome: 2 Mortality

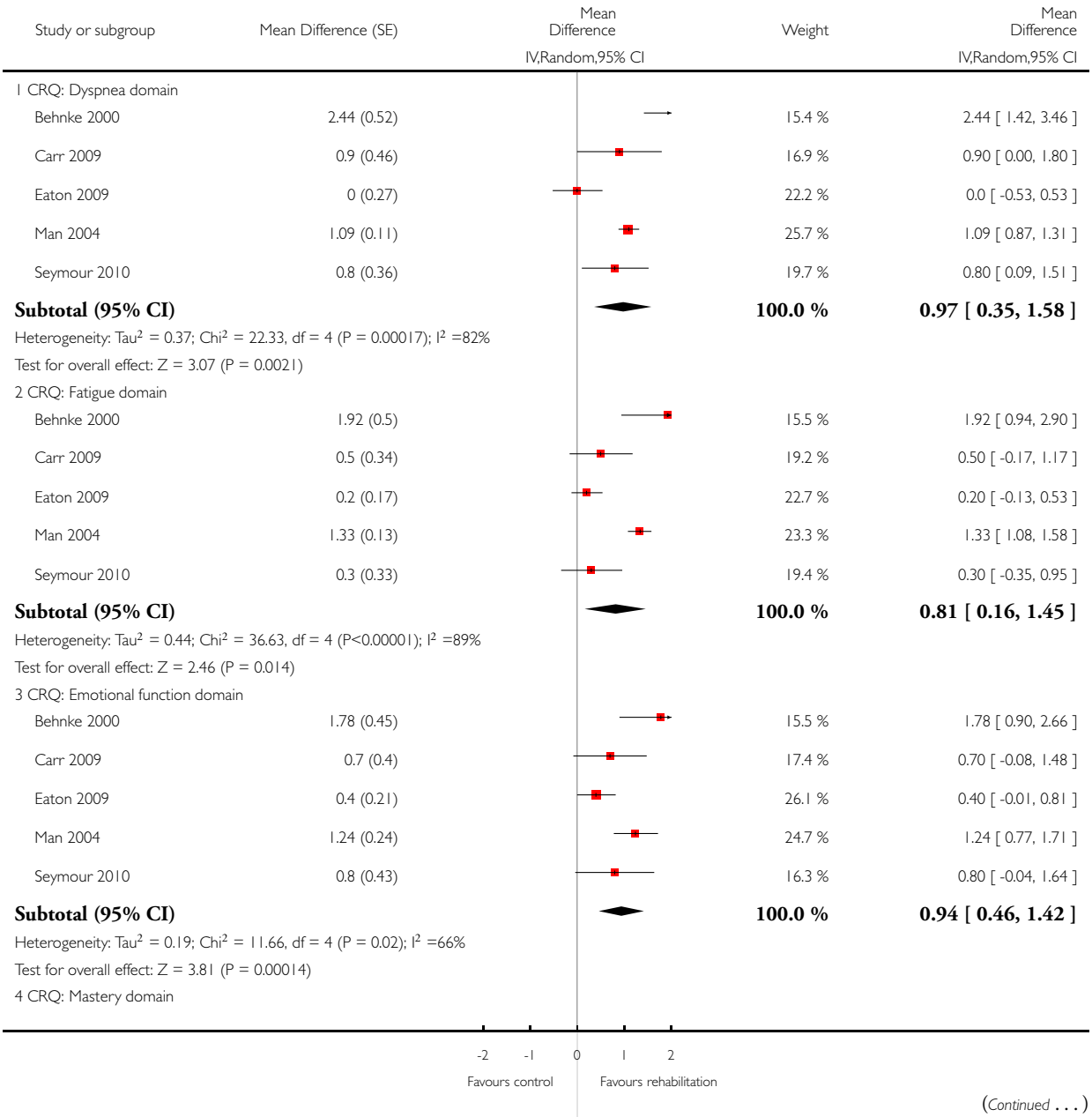


Analysis 1.3. Comparison 1 Rehabilitation versus control, Outcome 3 Health-related quality of life: Canadian Respiratory Disease Questionnaire (CRQ).

Review: Pulmonary rehabilitation following exacerbations of chronic obstructive pulmonary disease

Comparison: 1 Rehabilitation versus control

Outcome: 3 Health-related quality of life: Canadian Respiratory Disease Questionnaire (CRQ)



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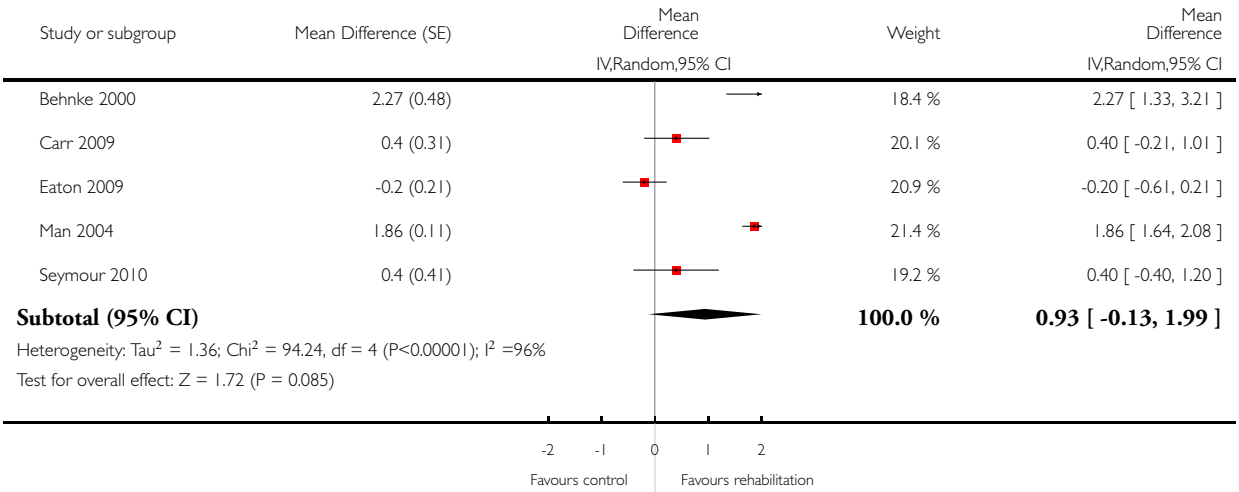
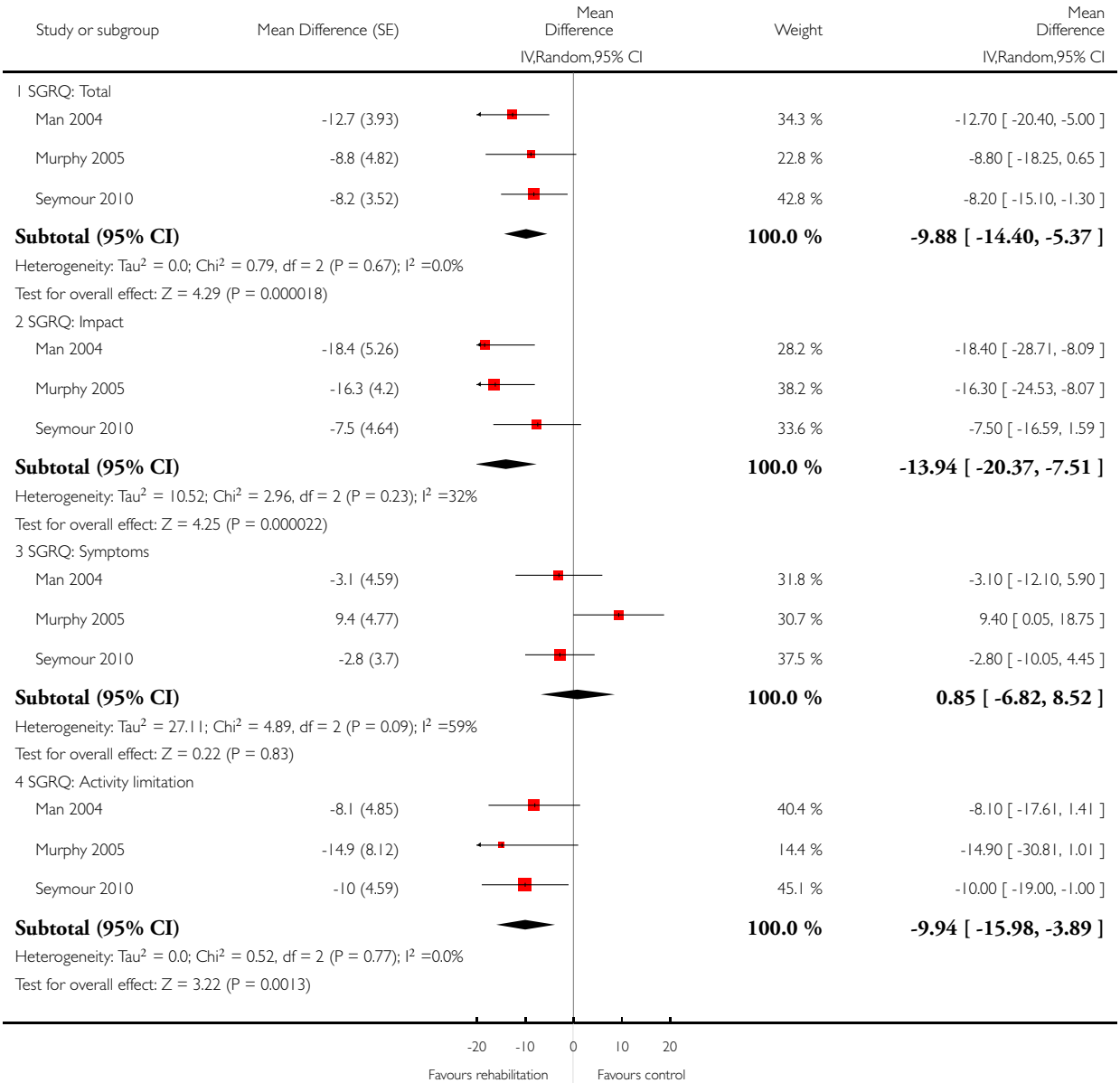


Analysis 1.4. Comparison 1 Rehabilitation versus control, Outcome 4 Health-related quality of life: St George's Respiratory Questionnaire.

Review: Pulmonary rehabilitation following exacerbations of chronic obstructive pulmonary disease

Comparison: 1 Rehabilitation versus control

Outcome: 4 Health-related quality of life: St George's Respiratory Questionnaire



Analysis 1.5. Comparison 1 Rehabilitation versus control, Outcome 5 Change from baseline in 6 minute walking test.

Review: Pulmonary rehabilitation following exacerbations of chronic obstructive pulmonary disease

Comparison: 1 Rehabilitation versus control

Outcome: 5 Change from baseline in 6 minute walking test

Study or subgroup	Mean Difference (SE)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Behnke 2000	215 (28)		16.0 %	215.00 [160.12, 269.88]
Carr 2009	-25 (23)		16.6 %	-25.00 [-70.08, 20.08]
Eaton 2009	-2 (16)		17.4 %	-2.00 [-33.36, 29.36]
Kirsten 1998	158 (28)		16.0 %	158.00 [103.12, 212.88]
Nava 1998	68 (19)		17.1 %	68.00 [30.76, 105.24]
Troosters 2000	64 (21)		16.9 %	64.00 [22.84, 105.16]
Total (95% CI)			**100.0 %**	**77.70 [12.21, 143.20]**

Heterogeneity: Tau^2 = 6179.55; Chi^2 = 71.60, df = 5 (P<0.00001); I^2 =93%

Test for overall effect: Z = 2.33 (P = 0.020)

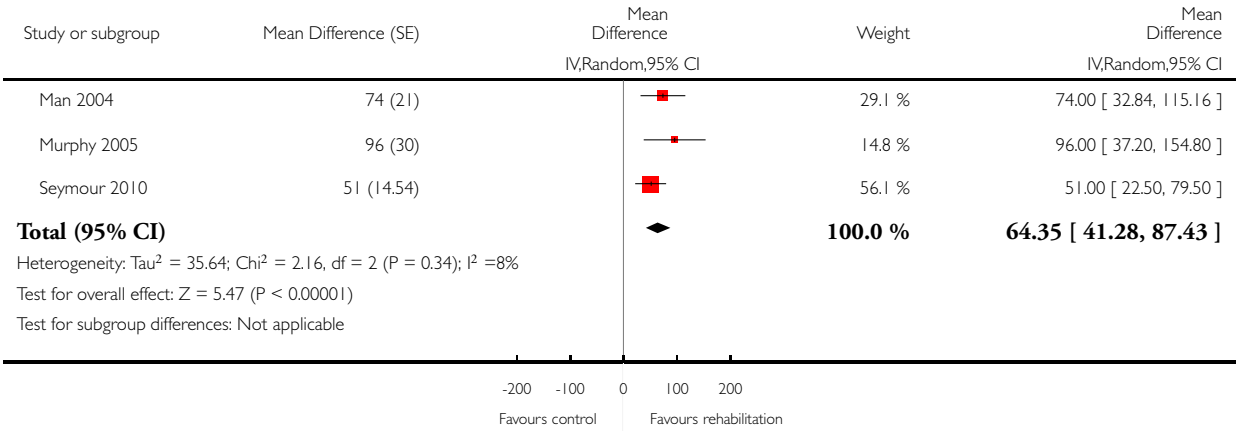
Test for subgroup differences: Not applicable

Analysis 1.6. Comparison 1 Rehabilitation versus control, Outcome 6 Change from baseline in shuttle walk test.

Review: Pulmonary rehabilitation following exacerbations of chronic obstructive pulmonary disease

Comparison: 1 Rehabilitation versus control

Outcome: 6 Change from baseline in shuttle walk test



APPENDICES

Appendix 1. MEDLINE & EMBASE search strategy

Search strategy
1 lung diseases obstructive.af.
2 chronic obstructive lung disease.af.
3 chronic obstructive pulmonary disease.af.
4 exp pulmonary disease chronic obstructive/
5 or/1-4
6 rh.fs.
7 rehabilitation.de.
8 exp exercise movement techniques/
9 exp exercise test/
10 exp physical endurance/
11 exp muscle training/
12 exp kinesiotherapy/

(*Continued*)

13 exp exercise/
14 or/6-13
15 5 and 14
16 clinical trial.pt.
17 exp epidemiologic methods/
18 exp controlled study/
19 exp major clinical study/
20 exp evidence based medicine/
21 or/16-20
22 15 and 21
23 comment.pt.
24 editorial.pt.
25 exp editorial/
26 or/23-25
27 22 not 26
28 remove duplicates from 27

FEEDBACK

Details of interventions administered in the studies, 6 July 2009

Summary

Thanks for a very helpful review. I am interested in using for my patients, but am puzzled by which program of "rehabilitation" to adopt. The table of characteristics shows considerable variation, which several combinations. Though most seem to be endurance exercise only rather than a more complex "rehabilitation" program. I was interested in any advice on what program I should implement with my patients. Could this (and a sample program) be included with the updated review?

Reply

Thank you for this comment. Based on our review we cannot make any statements about which rehabilitation programmes work best. However, there are systematic reviews on trials comparing different exercise programs that may help you defining your rehabilitation programme (for example, Puhan et al. Comparison of exercise modalities and intensities to treat skeletal muscle dysfunction during respiratory rehabilitation in COPD patients - A Systematic Review. *Thorax* 2005 May;60(5):367-75)

Contributors

Paul Glasziou

WHAT'S NEW

Last assessed as up-to-date: 11 July 2010.

Date	Event	Description
10 August 2011	New citation required but conclusions have not changed	The review has been published as a new citation version to correct an error in not doing so at the last update. The author byline changed at the last update

HISTORY

Protocol first published: Issue 2, 2005

Review first published: Issue 1, 2009

Date	Event	Description
12 July 2010	New search has been performed	Comments posted and incorporated into review. New literature search run and three new included studies incorporated (Eaton 2009; Carr 2009; Seymour 2010), increasing the total number of participants from 219 to 432. The conclusions are unchanged
8 April 2008	Amended	Converted to new review format.
20 February 2005	New citation required and major changes	Substantive amendment

CONTRIBUTIONS OF AUTHORS

Protocol writing: Puhan, Scharplatz, Gimeno-Santos, Steurer

Acquisition of data: Puhan, Gimeno-Santos, Scharplatz

Analysis and interpretation of data: Puhan, Gimeno-Santos, Scharplatz, Troosters, Steurer

Drafting of manuscript: Puhan

Critical revision of manuscript for important intellectual content: Puhan, Gimeno-Santos, Scharplatz, Troosters, Walters, Steurer

DECLARATIONS OF INTEREST

None declared.

SOURCES OF SUPPORT

Internal sources

- Helmut Horten Foundation, Switzerland.

Salary of Johann Steurer

External sources

- No sources of support supplied

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

Risk of Bias tables have been added for the 2010 update of this review.

INDEX TERMS

Medical Subject Headings (MeSH)

*Exercise Tolerance; Disease Progression; Health Status; Hospitalization [*statistics & numerical data]; Pulmonary Disease, Chronic Obstructive [mortality; *rehabilitation]; Quality of Life; Randomized Controlled Trials as Topic; Resistance Training [methods]

MeSH check words

Humans