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McCarthy B, Casey D, Devane D, Murphy K, Murphy E, Lacasse Y

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[Intervention Review]

Pulmonary rehabilitation for chronic obstructive pulmonary disease

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ABSTRACT

Background

Widespread application of pulmonary rehabilitation (also known as respiratory rehabilitation) in chronic obstructive pulmonary disease (COPD) should be preceded by demonstrable improvements in function (health-related quality of life, functional and maximal exercise capacity) attributable to the programmes. This review updates the review reported in 2006.

Objectives

To compare the effects of pulmonary rehabilitation versus usual care on health-related quality of life and functional and maximal exercise capacity in persons with COPD.

Search methods

We identified additional randomised controlled trials (RCTs) from the Cochrane Airways Group Specialised Register. Searches were current as of March 2014.

Selection criteria

We selected RCTs of pulmonary rehabilitation in patients with COPD in which health-related quality of life (HRQoL) and/or functional (FEC) or maximal (MEC) exercise capacity were measured. We defined 'pulmonary rehabilitation' as exercise training for at least four weeks with or without education and/or psychological support. We defined 'usual care' as conventional care in which the control group was not given education or any form of additional intervention. We considered participants in the following situations to be in receipt of usual care: only verbal advice was given without additional education; and medication was altered or optimised to what was considered best practice at the start of the trial for all participants.

Data collection and analysis

We calculated mean differences (MDs) using a random-effects model. We requested missing data from the authors of the primary study. We used standard methods as recommended by The Cochrane Collaboration.

Main results

Along with the 31 RCTs included in the previous version (2006), we included 34 additional RCTs in this update, resulting in a total of 65 RCTs involving 3822 participants for inclusion in the meta-analysis.

We noted no significant demographic differences at baseline between members of the intervention group and those who received usual care. For the pulmonary rehabilitation group, the mean forced expiratory volume at one second (FEV₁) was 39.2% predicted, and for the usual care group 36.4%; mean age was 62.4 years and 62.5 years, respectively. The gender mix in both groups was around two males for each female. A total of 41 of the pulmonary rehabilitation programmes were hospital based (inpatient or outpatient), 23 were community based (at community centres or in individual homes) and one study had both a hospital component and a community component. Most programmes were of 12 weeks' or eight weeks' duration with an overall range of four weeks to 52 weeks.

The nature of the intervention made it impossible for investigators to blind participants or those delivering the programme. In addition, it was unclear from most early studies whether allocation concealment was undertaken; along with the high attrition rates reported by several studies, this impacted the overall risk of bias.

We found statistically significant improvement for all included outcomes. In four important domains of quality of life (QoL) (Chronic Respiratory Questionnaire (CRQ) scores for dyspnoea, fatigue, emotional function and mastery), the effect was larger than the minimal clinically important difference (MCID) of 0.5 units (dyspnoea: MD 0.79, 95% confidence interval (CI) 0.56 to 1.03; N = 1283; studies = 19; moderate-quality evidence; fatigue: MD 0.68, 95% CI 0.45 to 0.92; N = 1291; studies = 19; low-quality evidence; emotional function: MD 0.56, 95% CI 0.34 to 0.78; N = 1291; studies = 19; mastery: MD 0.71, 95% CI 0.47 to 0.95; N = 1212; studies = 19; low-quality evidence). Statistically significant improvements were noted in all domains of the St. George's Respiratory Questionnaire (SGRQ), and improvement in total score was better than 4 units (MD -6.89, 95% CI -9.26 to -4.52; N = 1146; studies = 19; low-quality evidence). Sensitivity analysis using the trials at lower risk of bias yielded a similar estimate of the treatment effect (MD -5.15, 95% CI -7.95 to -2.36; N = 572; studies = 7).

Both functional exercise and maximal exercise showed statistically significant improvement. Researchers reported an increase in maximal exercise capacity (mean Wmax (W)) in participants allocated to pulmonary rehabilitation compared with usual care (MD 6.77, 95% CI 1.89 to 11.65; N = 779; studies = 16). The common effect size exceeded the MCID (4 watts) proposed by [Puhan 2011\(b\)](#). In relation to functional exercise capacity, the six-minute walk distance mean treatment effect was greater than the threshold of clinical significance (MD 43.93, 95% CI 32.64 to 55.21; participants = 1879; studies = 38).

The subgroup analysis, which compared hospital-based programmes versus community-based programmes, provided evidence of a significant difference in treatment effect between subgroups for all domains of the CRQ, with higher mean values, on average, in the hospital-based pulmonary rehabilitation group than in the community-based group. The SGRQ did not reveal this difference. Subgroup analysis performed to look at the complexity of the pulmonary rehabilitation programme provided no evidence of a significant difference in treatment effect between subgroups that received exercise only and those that received exercise combined with more complex interventions. However, both subgroup analyses could be confounded and should be interpreted with caution.

Authors' conclusions

Pulmonary rehabilitation relieves dyspnoea and fatigue, improves emotional function and enhances the sense of control that individuals have over their condition. These improvements are moderately large and clinically significant. Rehabilitation serves as an important component of the management of COPD and is beneficial in improving health-related quality of life and exercise capacity. It is our opinion that additional RCTs comparing pulmonary rehabilitation and conventional care in COPD are not warranted. Future research studies should focus on identifying which components of pulmonary rehabilitation are essential, its ideal length and location, the degree of supervision and intensity of training required and how long treatment effects persist. This endeavour is important in the light of the new subgroup analysis, which showed a difference in treatment effect on the CRQ between hospital-based and community-based programmes but no difference between exercise only and more complex pulmonary rehabilitation programmes.

PLAIN LANGUAGE SUMMARY

Pulmonary rehabilitation for chronic obstructive pulmonary disease

Chronic obstructive pulmonary disease (COPD) describes a chronic lung condition that prevents the air supply from getting to the lungs. Symptoms include breathlessness, coughing, tiredness and frequent chest infection. Worldwide, COPD is a major cause of ill health.

Pulmonary rehabilitation programmes include exercise as a key component; some programmes contain other interventions such as assessment, education, psychological support and dietary advice. Pulmonary rehabilitation is one of the key recommended approaches in the treatment of COPD. This review compared the impact of pulmonary rehabilitation versus usual care on the health-related quality of life of people with COPD. We included 65 studies involving 3822 participants. Participants were randomly assigned to receive pulmonary rehabilitation or usual care. The quality of the studies was generally good.

This review highlights that pulmonary rehabilitation improves the health-related quality of life of people with COPD. Results strongly support inclusion of pulmonary rehabilitation as part of the management and treatment of patients with COPD.

Future studies should concentrate on identifying the most important components of pulmonary rehabilitation, the ideal length of a programme, the intensity of training required and how long the benefits of the programme last.

SUMMARY OF FINDINGS FOR THE MAIN COMPARISON *[Explanation]*

Rehabilitation versus usual care for chronic obstructive pulmonary disease					
Patient or population: patients with chronic obstructive pulmonary disease Settings: hospital and community Intervention: rehabilitation versus usual care					
Outcomes	Illustrative comparative effects* (95% CI)		Number of participants (studies)	Quality of the evidence (GRADE)	Comments
	Response on control	Treatment effect			
	Usual care	Rehabilitation versus usual care			
QoL - Change in CRQ (dyspnoea) CRQ Questionnaire. Scale from 1 to 7 (Higher is better and 0.5 unit is an important difference) Follow-up: median 12 weeks	Median change = 0 units	Mean QoL - change in CRQ (Dyspnoea) in the intervention groups was 0.79 units higher (0.56 to 1.03 higher)	1283 (19 studies)	⊕⊕⊕○ Moderate ^{1,2,3}	Sensitivity analysis from studies at lower risk of bias was similar (MD 0.99, 95% CI 0.64 to 1.34; participants = 384; studies = 5; I ² = 34%)
QoL - Change in SGRQ (total) Scale from 0 to 100 (Lower is better and 4 units is an important difference) Follow-up: median 12 weeks	Median change = 0.42 units	Mean QoL - change in SGRQ (total) in the intervention groups was 6.89 units lower (9.26 to 4.52 lower)	1146 (19 studies)	⊕⊕⊕○ Moderate ^{2,3,4}	Sensitivity analysis from studies at lower risk of bias was similar (MD -5.15, 95% CI -7.95 to -2.36; participants = 572; studies = 7; I ² = 51%)
Change in maximal exercise (Incremental Shuttle walk test (ISWT)) Distance metres Follow-up: median 12 weeks	Median change = 1 metre	Mean maximal exercise (incremental shuttle walk test) in the intervention groups was 39.77 metres higher	694 (8 studies)	⊕⊕⊕○ Moderate ^{2,3,5}	

weeks	(22.38 to 57.15 higher)			
Change in functional exercise capacity (6MWT)) Distance metres Follow-up: median 12 weeks	Median change = 3.4 metres	Mean functional exercise capacity (6MWT)) in the intervention groups was 43.93 metres higher (32.64 to 55.21 higher)	1879 (38 studies)	⊕○○○ Very low ^{2,3,6,7}
Change in maximal exercise capacity (cycle ergometer) Workmax (watt) Follow-up: median 12 weeks	Median change = -0.05 watts	Mean maximal exercise capacity (cycle ergometer) in the intervention groups was 6.77 watts higher (1.89 to 11.65 higher)	779 (16 studies)	⊕⊕○○ Low ^{2,3,8,9}

*The basis for the response on control is the median control group response across studies.

CI: confidence interval; MD: mean difference.

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.

¹17 studies reported random sequence generation (1 unclear), 12 reported allocation concealment 2 did not have allocation concealment and it is unclear in 5 studies. 4 studies did not blind assessors, 11 blinded assessors and 4 were unclear as to assessor blinding. 6 studies had attrition bias greater than 20%.

²Downgraded as there is a high level of heterogeneity within the results. Several factors may impact heterogeneity, including content of the intervention programme, setting of the programme and severity of COPD.

³Greater than optimal Information size (OIS). 95% confidence interval does not includes "no effect," nor does the confidence limit cross the MID, so no need to downgrade.

⁴18 studies reported random sequence generation (2 unclear), 10 reported allocation concealment, 2 did not have allocation concealment and it is unclear in 7 studies. 3 studies did not blind assessors, 9 blinded assessors and 7 were unclear as to assessor blinding. 7 studies had attrition bias greater than 20%.

⁵All 8 studies reported random sequence generation, 5 reported allocation concealment and it is unclear in 3 studies. 5 studies had blind assessors with 1 not blinded, and 2 were unclear as to assessor blinding. 4 studies had attrition bias greater than 20%.

⁶34 studies reported random sequence generation, 4 were unclear, 20 reported allocation concealment, 3 did not have allocation concealment and it is unclear in 15 studies. 5 studies did not blind assessors, 19 blinded assessors and 13 were unclear as to assessor blinding. 13 studies had attrition bias greater than 20% and 2 were unclear.

⁷Downgraded as bias indicated for 6-minute walk test: Egger: bias = 1.24304 (95% CI = 0.183967 to 2.302131; P value 0.0227). Begg-Mazumdar: Kendall's tau = 0.16074 (P value 0.1601).

⁸All 16 studies reported random sequence generation, 6 reported allocation concealment, 3 did not have allocation concealment and it is unclear in 7 studies. 2 studies did not blind assessors, 10 blinded assessors and 4 were unclear as to assessor blinding. 4 studies had attrition bias greater than 20%.

⁹Downgraded as bias indicated for cycle ergometer test: Egger: bias = 1.57164 (95% CI = 0.6053 to 2.337984; P value 0.0036). Begg-Mazumdar: Kendall's tau = -0.2666667 (P value 0.139).

BACKGROUND

Description of the condition

Chronic obstructive pulmonary disease (COPD) is a multi-factorial progressive chronic lung disease that causes obstruction in air-flow. This obstruction results in persistent and progressive breathlessness, productive coughing, fatigue and recurrent chest infection (GOLD 2014). COPD is also associated with extrapulmonary effects such as muscle wasting, osteopaenia (reduction in protein and mineral content of bone tissue), cardiovascular disease and depression and therefore is now best understood as a systemic disease (Agusti 2003; Agusti 2005). Worldwide, COPD is a major cause of morbidity. It is estimated that 210 million people are living with COPD (Franchi 2009), and it is projected that by the year 2030, COPD will be the third most frequent cause of death globally (WHO 2008). At this time, COPD is an incurable condition that is associated with significant economic costs due to progressive disease severity and frequent hospital admissions and readmissions (GOLD 2014; Guarascio 2013).

Risk factors for COPD are numerous and include genetics, recurrent respiratory infection, low socioeconomic status, exposure to air pollutants, poor nutrition and asthma (Eisner 2010; GOLD 2014). However smoking is recognised as a major cause of COPD, and the more a person smokes, the more likely he or she is to develop this condition (Forey 2011).

COPD is a heterogeneous condition with marked variation in progression between individuals (Casanova 2011; Nishimura 2013). The initial underlying pathology of COPD is confined to the lungs, and a clinical diagnosis is based on presenting symptoms and confirmation of airflow obstruction with a postbronchodilator spirometry forced expiratory volume in one second/forced vital capacity ratio (FEV_1/FVC) < 0.70 (GOLD 2014). The Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines are usually used to grade the severity of airflow limitations as mild ($FEV_1 \geq 80\%$ predicted: GOLD 1), moderate ($50\% \leq FEV_1 < 80\%$ predicted: GOLD 2), severe ($30\% \leq FEV_1 < 50\%$ predicted: GOLD 3) or very severe ($FEV_1 < 30\%$ predicted: GOLD 4) (GOLD 2014).

The symptoms of COPD make engagement in physical activity unpleasant as the result of air trapping and increased hyperinflation in the lungs, which result in increased breathlessness due to subsequent inefficient breathing (O'Donnell 2007). Increased breathlessness provokes anxiety, which inevitably leads to further breathlessness, exacerbation of COPD symptoms and panic. This causes a vicious circle whereby any activities that involve physical exertion are avoided, causing muscle de-conditioning, which further reduces capacity to engage in physical activity (Bourbeau 2007). Physical inactivity is therefore a key predictor of mortality in people with COPD (Garcia-Aymerich 2006; Spruit 2013; Waschki 2011). Consequently, the joint American Thoracic Society and European Respiratory Society (ATS/ERS) (Spruit 2013)

guidelines highlight the importance of exercise in the treatment and management of COPD.

Description of the intervention

Treatment interventions for COPD include smoking cessation, pharmacological and non-pharmacological therapies and, in specific circumstances, supplemental oxygen, ventilatory support, surgical treatment and palliative care (GOLD 2014). However, best evidence and all current international guidelines ratify the central role of pulmonary rehabilitation in the treatment of people with COPD (GOLD 2014; NICE 2010; Nici 2006; Ries 2007; Spruit 2013).

Pulmonary rehabilitation (PR), which was first defined by the American College of Chest Physicians Committee in 1974, is a proactive approach to minimising COPD symptoms, improving health-related quality of life (HRQoL) and increasing physical and emotional involvement in everyday life (GOLD 2014; Nici 2006; Ries 2007). The ATS in conjunction with the ERS has published numerous comprehensive statements on PR, with the most recent update in 2013. In the latest update, pulmonary rehabilitation was defined newly as a "...comprehensive intervention based on a thorough patient assessment followed by patient tailored therapies that include, but are not limited to, exercise training, education, and behaviour change, designed to improve the physical and psychological condition of people with chronic respiratory disease and to promote the long-term adherence to health-enhancing behaviours" (Spruit 2013). This new definition differs from the previous one (2006) in that it focuses on the interdisciplinary and therefore more holistic approach to PR rather than on the previous multi-disciplinary approach; highlights the importance of behaviour change; and places PR firmly within the concept of integrated care (Spruit 2013).

Depending on culture, healthcare systems and resources, the structure, personnel, content and settings of PR programmes may vary (Nici 2006; Spruit 2013). However, individually tailored exercise training is considered the cornerstone of PR (Nici 2006; Ries 2007; Spruit 2013). In particular, strength, low- and high-intensity training, exercise endurance and upper and lower extremity training are recommended (Nici 2006; Ries 2007, Spruit 2013). In addition to exercise, the typical comprehensive PR programme includes patient assessment, education, psychosocial support and nutritional counselling (ATS 1999; GOLD 2014; Spruit 2013). Pulmonary rehabilitation is typically delivered to groups of patients (rather than to individuals), but no evidence suggests the optimal size of the exercise group. However, the American Association of Cardiovascular and Pulmonary Rehabilitation (AACVPR 2011) recommends a staff-to-participant ratio of 1:4, and the British Thoracic Society (British Thoracic Society 2001) a ratio of 1:8. The setting for PR programmes varies; both community-based (Cambach 1997; Casey 2013; Wijkstra 1994a) and home-based programmes (Maltais 2008; Viera 2010) are available. However, traditionally,

most PR programmes have been hospital based (Bourbeau 2010), with participants attending as in-patients or on an out-patient basis.

The optimal duration of programmes, number of sessions offered per week and type of staff required to deliver PR programmes are unclear. Beauchamp 2011 concludes, following a systematic review, that available evidence is insufficient to show the optimal duration of PR programmes for people with COPD. However, a programme duration of at least eight weeks is recommended to attain a substantial effect (Beauchamp 2011). Likewise the number of times per week that programmes are offered differs; typically hospital-based out-patient programmes are offered two or three days per week, and in-patient programmes are offered over five days (Spruit 2013). The optimal number of sessions required remains unclear. However, the 2006 ATS/ERS guidelines specify three sessions per week or a twice-weekly supervised and one unsupervised home session (Nici 2006). Finally, key requirements for staff delivering the programme are that they are clinically competent, having the required skills and knowledge and maintain patient safety (Spruit 2013).

How the intervention might work

Pulmonary rehabilitation seeks to reduce COPD symptoms, reestablish and improve functional ability, enhance participation in everyday life, promote autonomy and improve HRQoL (Spruit 2013). It does this by focusing on the systemic aspects of the disease that are common among patients with COPD (AACVPR 2011). The exercise component of PR increases inspiratory volume and reduces dynamic hyperinflation, both of which reduce dyspnoea when the person is performing tasks (Casaburi 2009). Exercise also increases muscle function, delaying fatigue and resulting in increased exercise tolerance. Meanwhile, the educational component of PR focuses on collaborative self-management and behaviour change (Spruit 2013). It encompasses providing information and knowledge regarding COPD; building skills such as goal setting, problem solving and decision making; and developing action plans that allow individuals to better recognise and manage the disease (Spruit 2013). The behaviour change element focuses on modifying nutritional intake and smoking patterns; adhering to medication and regular exercise; and utilising effective breathing techniques and energy-saving strategies (Spruit 2013).

Why it is important to do this review

Review authors undertook the original version of this Cochrane review in 2001 in response to worldwide endorsement of PR as integral to the management of COPD and lack of clear evidence as to the impact of these programmes on HRQoL and exercise tolerance (Lacasse 2001). The review included 23 randomised controlled trials (RCTs), and review authors concluded that PR (exer-

cise training for a minimum of four weeks with or without education and/or psychological support) resulted in statistically significant improvement in HRQoL and modest improvement in exercise capacity (Lacasse 2001). This review was updated in 2006, included 31 RCTs and again reported statistically significant improvement in HRQoL. However, results for both functional and maximal exercise capacity were below the threshold of clinical significance. Lacasse 2006 concluded that further RCTs comparing PR versus usual care for patients with COPD were not needed. Despite this, a large number of RCTs published since 2006 have endorsed the need for this current update. Furthermore, recent RCTs tend to use disease-specific quality of life indices as primary outcome measures, combined with more refined maximal and functional exercise capacity measurement tools (Curtis 2003; de Torres 2002; Gross 2004; Jones 2003). Consequently in the current review, we will take a more focused approach to assessment of primary and secondary outcomes. In recent years, wide variation has been noted in the follow-up assessment times utilised within studies, and this may have an impact on study outcomes. Therefore in the current review, we will include only assessments completed up to and within three months of completion of the intervention. Also, risk of bias requirements for Cochrane reviews have been altered since the last update; review authors of this current update will ensure that these new requirements are met. Finally, as a separate systematic review examining the effects of PR following exacerbations of COPD has been undertaken (Puhan 2011(a)), we will exclude from this review studies that commenced within four weeks of an acute exacerbation of COPD.

OBJECTIVES

To compare the effects of pulmonary rehabilitation versus usual care on health-related quality of life and functional and maximal exercise capacity in persons with COPD.

METHODS

Criteria for considering studies for this review

Types of studies

All RCTs in which participants are randomly assigned at the individual or cluster level and in which researchers compare the effects of PR versus those of usual care.

Types of participants

We included RCTs in which more than 90% of participants had COPD defined as:

- a clinical diagnosis of COPD; and
- best recorded forced expiratory volume after one second (FEV₁)/forced vital capacity (FVC) (FEV₁/FVC) ratio of individual participants < 0.7.

We included RCTs in which:

- any or all participants were on continuous oxygen.

We excluded RCTs that focused on participants:

- who were mechanically ventilated; or
- who had an acute exacerbation within four weeks before commencement of the intervention.

Types of interventions

Pulmonary rehabilitation

Any in-patient, out-patient, community-based or home-based rehabilitation programme of at least four weeks' duration that included exercise therapy with or without any form of education and/or psychological support delivered to patients with exercise limitation attributable to COPD.

We included any exercise therapy that included physical activity considered to be aerobically demanding.

We excluded:

- interventions in which the physical activity component was considered to be not aerobically demanding (e.g. respiratory muscle training, breathing exercises, Tai Chi, yoga) (the degree of aerobic demand was assessed for each individual intervention by examining the detailed description of the intervention in identified studies); and
- programmes of less than 4 weeks' duration.

Usual care

For the purpose of this review, usual care was defined as conventional care. We excluded trials in which the control group was given education or any form of additional intervention. Participants in the following situations were considered to be in receipt of usual care.

- Only verbal advice was given. If the advice was accompanied by additional education provided in any way, for example, by video or by diary, then the study was excluded.
- Medication was altered or optimised to what was considered best practice at the start of the trial for all participants.

Types of outcome measures

We considered disease-specific HRQoL and/or maximal or functional exercise capacity (up to and including three months after the

end of the intervention). We defined 'maximal exercise capacity' as the peak capacity measured by an incremental cycle ergometry test. 'Functional exercise capacity' was defined according to the results of timed walk tests ([Holland 2014](#)).

Primary outcomes

Disease-specific health-related quality of life (HRQoL)

- Chronic Respiratory Disease Questionnaire (CRQ).
- St. George's Respiratory Questionnaire (SGRQ).

Secondary outcomes

Exercise testing

The classification of exercise testing is divided into functional and maximal exercise groups, which include the following ([Holland 2014](#)).

- Functional exercise capacity assessments.
 - Six-minute walk test/distance (6MWT/6MWD).
 - Incremental shuttle walk test (ISWT).
 - Endurance shuttle walk test (ESWT).
- Maximal exercise tests.
 - Incremental cycle ergometry.

Search methods for identification of studies

Electronic searches

We have detailed in [Appendix 1](#) the search methods used in the previous version of this review. The previously published version included searches up to July 2004. The search period for this update is July 2004 to March 2014.

For the current update, we identified trials from the Cochrane Airways Group Specialised Register (CAGR), which is maintained by the Trials Search Co-ordinator 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, the Cumulative Index to Nursing and Allied Health Literature (CINAHL), the Allied and Complementary Medicine Database (AMED) and PsycINFO, and by handsearching of respiratory journals and meeting abstracts (please see [Appendix 2](#) for further details). We searched all records in the CAGR using the search strategy described in [Appendix 3](#).

We also conducted a search of ClinicalTrials.gov (www.ClinicalTrials.gov) and the World Health Organization (WHO) trials portal (www.who.int/ictrp/en/). We

searched all databases from their inception to the present, with no restriction on the language of publication. We completed the latest searches in March 2014.

Searching other resources

We reviewed the reference lists of relevant articles and retrieved any potential additional citations. We contacted the authors of studies included in the meta-analysis and experts in the field of pulmonary rehabilitation to uncover unpublished material. We also included the papers suggested by the study authors contacted.

Data collection and analysis

The methods used in this review were designed in accordance with recommendations provided in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

Selection of studies

Two review authors (BMC, DC) independently tested the inclusion criteria and sought clarification on all areas of concern with the wider review team, which included the original author of the review (YL). When the review authors were confident of the clarity of the criteria and their skills, they assessed studies with respect to the identified criteria. The two review authors then independently assessed all citation titles and abstracts. Review authors electronically collated initial decisions with the use of Distiller SR and later with Early Reviewing Software (EROS); they coded each citation as:

- included to proceed;
- more information needed before inclusion decision;
- important article but not to be included in the review; or
- excluded (Appendix 4; Appendix 5).

Review authors held a meeting after every 100 reviewed citations during which they resolved disagreements by consensus. They used quadratic weighted Kappa statistics to measure agreement between coders (Kramer 1981). When consensus could not be reached, a third review author (DD) adjudicated. Review authors then retrieved full-text papers of all potentially eligible studies. Review authors maintained records on all studies that did not meet the inclusion criteria and provided the rationale for their exclusion.

Data extraction and management

The lead review author (BMC) extracted data from all original papers identified for inclusion in the meta-analysis using a developed data extraction form. The other members of the review group (DC, KM, DD, EM) independently extracted data from an equal share of the same studies. Extracted information included the following.

- Background characteristics of the research reports.

- Characteristics of participants in the study.
- The number and distribution of participants who dropped-out or withdrew from the study.
- A full description of the pulmonary rehabilitation programmes (setting, components and duration).
- Health-related quality of life measurement instruments and associated results.
- Exercise capacity measure outcomes and corresponding results.

The lead review author and co-review authors resolved discrepancies during the data extraction process through discussion; they consulted a third review author when unresolved issues remained. Review authors requested missing data from the authors of the primary studies. They asked these authors to provide additional information by filling in tables similar to the ones used by the review authors during the data extraction process. Two review authors (BMC, EM) entered all data into the Review Manager software (RevMan 2011) and checked them for accuracy. If a study reported multiple group comparisons (e.g. exercise therapy with inspiratory muscle training compared with exercise therapy alone or with conventional community care), treatment groups considered relevant to PR were combined as if one intervention group, and this group was compared with the group receiving conventional community care. Studies in which multiple group comparisons included interventions that were not considered relevant to PR such as acupuncture were not combined.

Assessment of risk of bias in included studies

The lead review author (BMC) assessed the risk of bias for all included studies. A second review author (DC, EM or KM) independently assessed the risk of bias for each study. The review authors followed the criteria for assessing risk of bias provided by The Cochrane Collaboration in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011) and contained in RevMan (RevMan 2011). We assessed risk of bias according to the following domains (Appendix 6).

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

We considered several important potential sources of bias that have proved to be major determinants of the magnitude of the effect size in clinical trials: unconcealed randomisation, unblinded study personnel, incomplete outcome data and attrition of more than 20% of those randomly assigned. The first of these has been associated with an overestimation of treatment effect by up to 40% (Schulz 1995), and the second may result in differential encouragement during performance testing, with the potential for dis-

tortion of the results (up to 30.5 metres in a six-minute walk test) (Guyatt 1984). Schulz 1995 argued that loss to follow-up of 20% or greater should be a matter of concern as it relates to the possibility of bias.

Review authors resolved disagreements by consensus. If details pertaining to randomisation, masking, drop-out and withdrawal were not specified or were unclear in the original trial publication, we contacted the study authors to clarify the issue.

Measures of treatment effect

Continuous data

Different measures of HRQoL and exercise capacity have been reported in the primary studies. Both primary outcomes (HRQoL) and secondary outcomes (exercise capacity) are continuous outcomes. For these continuous variables, we recorded mean change from baseline or mean postintervention values and standard deviation (SD) for each group for outcomes measured using the same metrics. When 95% confidence intervals (CIs) and standard errors (SEs) were reported, we calculated SDs as guided by the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). When SDs were missing from studies and it was not possible to obtain the results from study authors, we used a mean value for the SD of the other studies that reported that outcome. All outcomes were reported independently, so standardised mean differences (SMDs) for outcomes were not required. Mean differences (MDs) with 95% CIs were calculated for each study by using a random-effects model.

Dichotomous data

We did not plan to analyse dichotomous outcomes.

Unit of analysis issues

Cluster-randomised trials

We included cluster-randomised trials in the analysis for the current review alongside individually randomised trials. We made an adjustment to the sample size in these studies for each intervention based on the method described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). This method utilised the intracluster correlation co-efficient (ICC) as calculated from trial results.

Multi-armed trials

We included multi-armed trials in this review. To overcome potential issues due to multiple, correlated comparisons, we analysed

multi-armed trials using methods described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). When feasible, we combined multiple comparison groups to create one relevant intervention group and one relevant comparison group.

Dealing with missing data

For included studies, we noted the level of attrition; any study with greater than 20% attrition was considered at high risk of attrition bias. When standard deviations (SDs) of the change were missing from studies, and it was not possible to obtain the result from study authors, we used the mean value for the SD of other included studies that reported that outcome. We excluded from the analysis studies in which only medians and percentiles were available and study authors reported no other means of calculating mean change scores.

Assessment of heterogeneity

We assessed heterogeneity visually through inspection of forest plots, and statistical heterogeneity in each meta-analysis using τ^2 , I^2 and χ^2 statistics. We regarded heterogeneity as substantial when τ^2 was greater than zero and I^2 was greater than 30% or a low P value (< 0.10) was reported for the χ^2 test for heterogeneity.

Assessment of reporting biases

When 10 or more studies were included in the meta-analysis, we investigated reporting biases (such as publication bias) by using funnel plots. When asymmetry was suggested on visual assessment, we undertook exploratory analyses to investigate asymmetry using the test proposed by Egger 1997 (see Table 1).

Data synthesis

Review authors undertook statistical analysis by using Review Manager software (RevMan 2011). Throughout the analysis, we used mean differences (MDs) as determined (to take into account pre-experiment group differences) from the differences between preintervention and postintervention changes in treatment and control groups. We combined MDs according to random-effects analyses (Shadish 1994) and presented the results as average treatment effects with 95% CIs and estimates of τ^2 and I^2 . In the case of cross-over trials, we considered only the first study period and excluded from the analysis data obtained during the second study period. We explored heterogeneity through a priori specified subgroup analyses. When possible, for each outcome, we discussed the summary effect estimate in the context of its minimal clinically important difference (MCID). The MCID is defined as the smallest difference in score corresponding to the smallest difference perceived by the average patient that would mandate, in the absence of troublesome side effects and excessive costs, a change in management of a patient's condition (Jaesckhe 1989).

Subgroup analysis and investigation of heterogeneity

To explain anticipated heterogeneity among study results, we defined a set of three a priori hypotheses on which sensitivity analyses were to be based. We identified potential sources of heterogeneity in relation to the outcomes of exercise capacity and HRQoL. We then classified these hypotheses into subcategories as follows.

Interventions

The contribution of each of the components of PR programmes to patient improvement in exercise capacity and HRQoL is not known. We hypothesised that the more comprehensive the rehabilitation programme, the larger would be the effect size in improving exercise capacity and HRQoL. We also hypothesised that a difference in intervention effect may be noted between hospital only-based and community/home-based interventions. Therefore, we performed a subgroup analysis of:

- pulmonary rehabilitation and exercise only interventions versus PR plus a more comprehensive intervention within which education was included; and
- hospital only-based versus community/home-based programmes.

Methodological quality

We hypothesised that the results of trials would be influenced by their methodological quality. For the purpose of this subgroup analysis, we defined high-quality trials as those at low risk of bias for:

- allocation concealment; or
- incomplete outcome data (i.e. loss to follow-up $\geq 20\%$).

We assessed for subgroup differences by using interaction tests available within RevMan (RevMan 2011). We reported the results of subgroup analyses by quoting the statistic and the P value, and the interaction test by providing the I^2 value.

Sensitivity analysis

We performed sensitivity analyses on the basis of trial quality by repeating our analysis among only those trials judged to be of 'high

quality.' For the purposes of this review, 'high-quality' trials are defined as trials with low risk of bias due to allocation concealment or low risk of bias due to incomplete outcome data. We limited sensitivity analyses to primary outcomes (see [Types of outcome measures](#)).

RESULTS

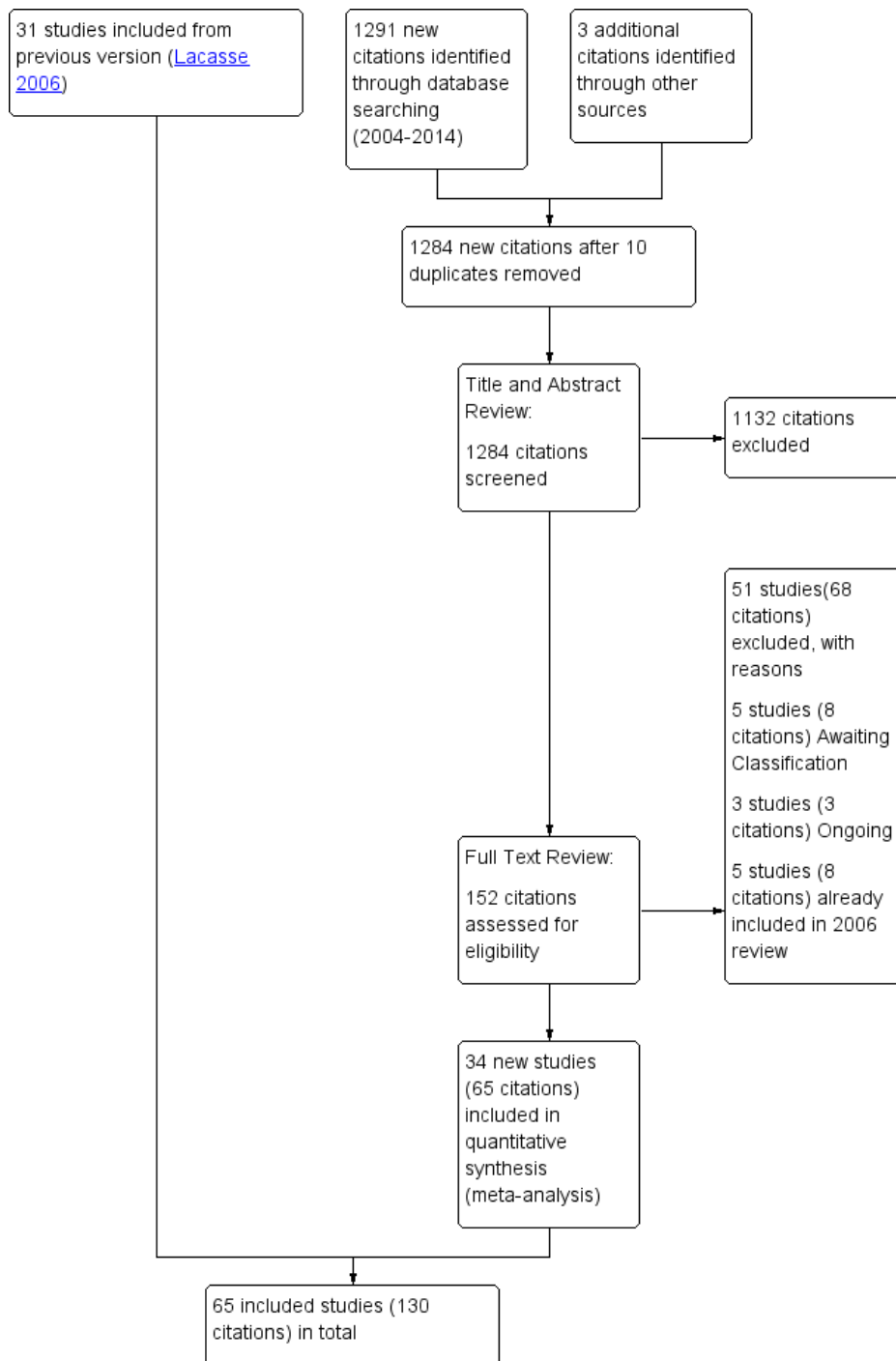
Description of studies

See [Characteristics of included studies](#) and [Characteristics of excluded studies](#) as well as baseline characteristics (Table 2) and study design (Table 3).

Results of the search

Our search yielded 1284 citations with potential for inclusion (see [Figure 1](#)). We excluded 1132 citations during the initial screening of titles and abstracts and assessed 98 studies (152 citations) on the basis of a full-text review. Of these, 51 studies (68 citations) failed to meet the inclusion criteria. A further five studies (eight citations) provided insufficient detail to allow a decision and are still awaiting classification (see [Characteristics of studies awaiting classification](#)). Of these, we conducted a teleconference with the author of two studies (Meshcheryakova 2010; Meshcheryakova 2012) and are awaiting additional unpublished information. We were not able to establish contact with the authors of the other three studies (Aksu 2006; D'Amico 2010; Ren 2011). Three studies were ongoing at the time of this review, and results were not yet published; the study authors wished to withhold results until after publication (Chang 2008; Gurgun 2011; Sathyapala 2008) (see [Characteristics of ongoing studies](#)). In addition, eight citations were related to five studies that were already included in the previous version of this review. Thus, 34 studies (65 citations) were included for the first time in this review, in addition to the 31 studies (65 citations) already included in the previous version of the review. We have provided details of the literature search for the previous version of the review in [Appendix 1](#).

Figure 1. Study flow diagram.



Included studies

We included the 31 RCTs from the 2006 version of the Cochrane review (Lacasse 2006). A total of 65 studies (represented by 130 citations) contributed to this meta-analysis, including 34 new studies (Barakat 2008; Baumann 2012; Borghi-Silva 2009; Casey 2013; Cebollero 2012; Chan 2011; Cochrane 2006; De Souto Araujo 2012; Deering 2011; Elci 2008; Faager 2004; Faulkner 2010; Fernandez 2009; Gohl 2006; Gomez 2006; Gottlieb 2011; Gurgun 2013; Hoff 2007; Karapolat 2007; Lindsay 2005; Liu 2012; McNamara 2013; Mehri 2007; Mendes De Oliveira 2010; Nalbant 2011; O'Shea 2007; Ozdemir 2010; Paz-Diaz 2007; Petty 2006; Sridhar 2008; Theander 2009; Van Wetering 2010; Vijayan 2010; Wen 2008), in addition to the 31 studies included in the original review (Behnke 2000a; Bendstrup 1997; Booker 1984; Boxall 2005; Busch 1988; Cambach 1997; Casaburi 2004; Chlumsky 2001; Clark 1996; Cockcroft 1981; Emery 1998; Engström 1999; Finnerty 2001; Goldstein 1994; Gosselink 2000; Griffiths 2000; Güell 1995; Güell 1998; Hernandez 2000; Jones 1985; Lake 1990; McGavin 1977; Reardon 1994; Ringbaek 2000; Simpson 1992; Singh 2003; Strijbos 1996; Vallet 1994; Weiner 1992; Wijkstra 1994; Xie 2003). We provided descriptions of these individual studies in the [Characteristics of included studies](#) table. These studies involved 3822 participants, 2090 of whom were randomly allocated to some form of exercise rehabilitation for a minimum duration of four weeks, and 1732 individuals who were randomly assigned to usual care. For a detailed account of the criteria required for inclusion, see [Criteria for considering studies for this review](#). The sample size in the included studies ranged from 12 participants (Hoff 2007) to 350 participants (Casey 2013) with a median of 45 participants (interquartile range (IQR) 29.5 to 67). We noted a large gender imbalance across all studies, with 69% of participants being male and with 10 studies including no female participants.

Only six studies reported patient-based programmes, three of which were combined with a home-based follow-up component. Thirty-seven studies were hospital out-patient based; eight of these

included a home-based element. In all, 21 programmes were community based, 11 of which were entirely home based, and one programme combined community- and home-based components. The venue for the programme run by Vijayan 2010 was unclear from the reports. The duration of the programmes ranged from four weeks (three studies) to one year (three studies). Eight- and 12-week programmes (18 studies of each) were most common. Timelines for assessment of participants followed a pattern identical to that of programme duration.

All but two trials that met the inclusion criteria used a standard parallel-group design. Casey 2013 utilised cluster samples from general practices, whereas Cambach 1997 conducted a cross-over trial. Most studies (48 trials) randomly assigned participants to two groups (i.e. rehabilitation and usual care), and three trials randomly assigned participants to three intervention groups, in addition to the usual care group (Casaburi 2004; Cochrane 2006; Lake 1990). The remaining 14 trials utilised two intervention groups and a usual care group (Cebollero 2012; De Souto Araujo 2012; Deering 2011; Emery 1998; Gomez 2006; Gurgun 2013; Jones 1985; Liu 2012; McNamara 2013; Mendes De Oliveira 2010; Petty 2006; Strijbos 1996; Weiner 1992; Wen 2008)

Excluded studies

We excluded 51 studies from the current update during the full-text screening process. The [Characteristics of excluded studies](#) table provides full details of the excluded studies.

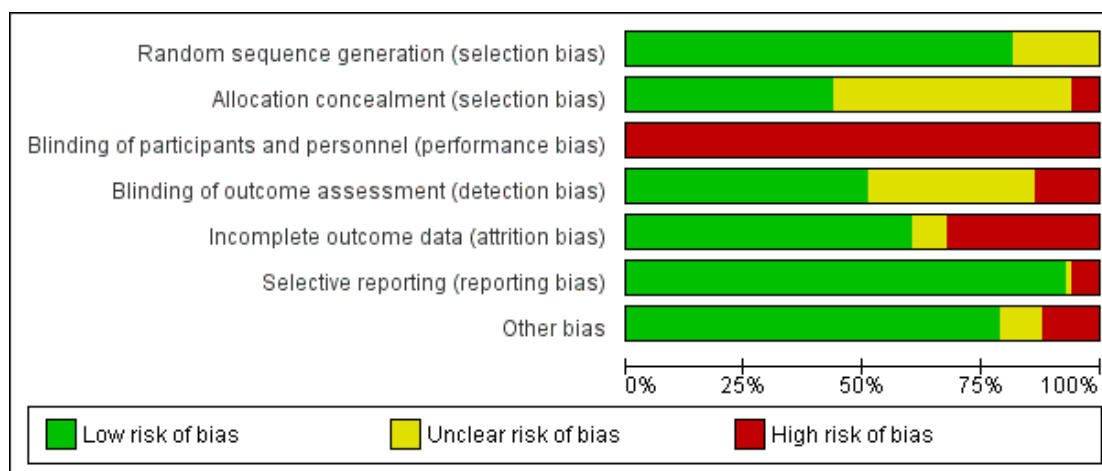
Risk of bias in included studies

As a result of the nature of the intervention, it was expected that blinding of participants and of professionals who delivered the interventions was not possible. Consequently, risk of performance bias in all studies was high. Risk of bias for other bias domains varied across included studies, and insufficient detail was provided to inform judgement in several included studies (see [Figure 2](#), Risk of bias summary table, and [Figure 3](#), Risk of bias graph, for an overview).

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

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Barakat 2008	●	●	●	●	●	●	●
Baumann 2012	●	●	●	●	●	●	●
Behrke 2000a	●	●	●	●	●	●	●
Bendstrup 1997	●	●	●	●	●	●	●
Booker 1984	●	●	●	●	●	●	●
Borghesi-Silva 2009	●	●	●	●	●	●	●
Boxall 2005	●	●	●	●	●	●	●
Busch 1988	●	●	●	●	●	●	●
Cambach 1997	●	●	●	●	●	●	●
Cassaboun 2004	●	●	●	●	●	●	●
Casey 2013	●	●	●	●	●	●	●
Cebalero 2012	●	●	●	●	●	●	●
Chan 2011	●	●	●	●	●	●	●
Chlumsky 2001	●	●	●	●	●	●	●
Clark 1996	●	●	●	●	●	●	●
Cochrane 2008	●	●	●	●	●	●	●
Cockcroft 1981	●	●	●	●	●	●	●
Deering 2011	●	●	●	●	●	●	●
De Souza Araujo 2012	●	●	●	●	●	●	●
Elci 2006	●	●	●	●	●	●	●
Emery 1998	●	●	●	●	●	●	●
Engstöm 1989	●	●	●	●	●	●	●
Faager 2004	●	●	●	●	●	●	●
Faulkner 2010	●	●	●	●	●	●	●
Fernandez 2009	●	●	●	●	●	●	●
Finnerty 2007	●	●	●	●	●	●	●
Gohl 2006	●	●	●	●	●	●	●
Gouldstein 1994	●	●	●	●	●	●	●
Gomez 2006	●	●	●	●	●	●	●
Gosselink 2000	●	●	●	●	●	●	●
Gottlieb 2011	●	●	●	●	●	●	●
Griffiths 2008	●	●	●	●	●	●	●
Gueli 1995	●	●	●	●	●	●	●
Gueli 1998	●	●	●	●	●	●	●
Gurgun 2013	●	●	●	●	●	●	●
Hernandez 2000	●	●	●	●	●	●	●
Hoff 2007	●	●	●	●	●	●	●
Jones 1985	●	●	●	●	●	●	●
Karapolat 2007	●	●	●	●	●	●	●
Lake 1998	●	●	●	●	●	●	●
Lindsay 2005	●	●	●	●	●	●	●
Liu 2012	●	●	●	●	●	●	●
McGavin 1973	●	●	●	●	●	●	●
McNamara 2013	●	●	●	●	●	●	●
Mehri 2007	●	●	●	●	●	●	●
Mendes De Oliveira 2010	●	●	●	●	●	●	●
Nalbant 2011	●	●	●	●	●	●	●
O'Shea 2007	●	●	●	●	●	●	●
Ozdemir 2010	●	●	●	●	●	●	●
Paz-Diaz 2007	●	●	●	●	●	●	●
Petty 2006	●	●	●	●	●	●	●
Reardon 1984	●	●	●	●	●	●	●
Ringbaek 2000	●	●	●	●	●	●	●
Simpson 1992	●	●	●	●	●	●	●
Singh 2003	●	●	●	●	●	●	●
Sridhar 2008	●	●	●	●	●	●	●
Strübos 1998	●	●	●	●	●	●	●
Theander 2006	●	●	●	●	●	●	●
Vallet 1994	●	●	●	●	●	●	●
Van Welering 2010	●	●	●	●	●	●	●
Vijayan 2010	●	●	●	●	●	●	●
Weiner 1992	●	●	●	●	●	●	●
Wien 2008	●	●	●	●	●	●	●
Wijkstra 1994	●	●	●	●	●	●	●
Xie 2002	●	●	●	●	●	●	●

Figure 3. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.



Allocation

We judged 53 included studies as having low risk of bias in random sequence generation. Information was insufficient to permit a decision in relation to 12 trials ([Bendstrup 1997](#); [Borghi-Silva 2009](#); [Clark 1996](#); [Faager 2004](#); [Fernandez 2009](#); [Hoff 2007](#); [Lindsay 2005](#); [Mehri 2007](#); [Nalbant 2011](#); [Paz-Diaz 2007](#); [Vijayan 2010](#); [Wen 2008](#)). With regard to allocation concealment, we judged 28 studies as having low risk of bias ([Behnke 2000a](#); [Booker 1984](#); [Boxall 2005](#); [Busch 1988](#); [Cambach 1997](#); [Casaburi 2004](#); [Casey 2013](#); [Cebollero 2012](#); [Cochrane 2006](#); [Cockcroft 1981](#); [De Souto Araujo 2012](#); [Emery 1998](#); [Engström 1999](#); [Faulkner 2010](#); [Finnerty 2001](#); [Goldstein 1994](#); [Gomez 2006](#); [Gosselink 2000](#); [Gottlieb 2011](#); [Griffiths 2000](#); [Gurgun 2013](#); [Karapolat 2007](#); [Liu 2012](#); [McNamara 2013](#); [Mendes De Oliveira 2010](#); [O'Shea 2007](#); [Theander 2009](#); [Van Wetering 2010](#)) and four studies as having high risk of bias ([Baumann 2012](#); [Güell 1995](#); [Güell 1998](#); [Jones 1985](#)); the remaining 33 studies provided insufficient information to inform judgements.

Blinding

Performance bias

As a result of the nature of the intervention, it was not possible to blind participants or professionals who delivered the interven-

tions. Consequently, we judged all studies as having high risk of performance bias.

Detection bias

Across studies, the level of reporting of whether outcome assessment was blinded was relatively poor. We judged 32 studies as having low risk of detection bias ([Barakat 2008](#); [Booker 1984](#); [Busch 1988](#); [Casaburi 2004](#); [Casey 2013](#); [Cebollero 2012](#); [Chan 2011](#); [Cochrane 2006](#); [De Souto Araujo 2012](#); [Deering 2011](#); [Elci 2008](#); [Emery 1998](#); [Engström 1999](#); [Finnerty 2001](#); [Goldstein 1994](#); [Gomez 2006](#); [Griffiths 2000](#); [Güell 1995](#); [Güell 1998](#); [Hernandez 2000](#); [Jones 1985](#); [Lake 1990](#); [Liu 2012](#); [McNamara 2013](#); [O'Shea 2007](#); [Petty 2006](#); [Reardon 1994](#); [Ringbaek 2000](#); [Simpson 1992](#); [Strijbos 1996](#); [Van Wetering 2010](#); [Weiner 1992](#)). In two of these studies ([Engström 1999](#); [Simpson 1992](#)), the primary outcome assessment (quality of life) was blinded but the secondary outcome assessment (exercise capacity) was not. In [Lake 1990](#), the cycle ergometer test was blinded, but the six-minute walk test was not. In [Busch 1988](#), the cycle ergometer test was not blinded and the 12-minute walk test was blinded. Among studies that reported blinding of outcome assessment, nine studies were judged as having high risk of detection bias ([Boxall 2005](#); [Cambach 1997](#); [Faulkner 2010](#); [Gosselink 2000](#); [Gottlieb 2011](#); [McGavin 1977](#); [Theander 2009](#); [Vallet 1994](#); [Wijkstra 1994](#)), and the remaining 23 studies provided insufficient information to inform judgements.

Incomplete outcome data

We judged 39 studies as having low risk of attrition bias (Barakat 2008; Borghi-Silva 2009; Boxall 2005; Cambach 1997; Casaburi 2004; Chlumsky 2001; Cockcroft 1981; Emery 1998; Engström 1999; Fernandez 2009; Goldstein 1994; Griffiths 2000; Güell 1995; Güell 1998; Gurgun 2013; Hoff 2007; Karapolat 2007; Lake 1990; Lindsay 2005; Liu 2012; McGavin 1977; McNamara 2013; Mehri 2007; O'Shea 2007; Ozdemir 2010; Paz-Diaz 2007; Petty 2006; Reardon 1994; Ringbaek 2000; Simpson 1992; Singh 2003; Strijbos 1996; Theander 2009; Vallet 1994; Van Wetering 2010; Vijayan 2010; Weiner 1992; Wijkstra 1994; Xie 2003) and 22 as having high risk (Baumann 2012 24% of people dropped out; Behnke 2000a 35%; Bendstrup 1997 24%; Booker 1984 27%; Busch 1988 30%; Casey 2013 24%; Chan 2011 23%; Cochrane 2006 43%; De Souto Araujo 2012 24%; Deering 2011 42%; Faager 2004 30%; Faulkner 2010 30%; Finnerty 2001 43%; Gohl 2006 44%; Gomez 2006 48%; Gosselink 2000 62%; Gottlieb 2011 32%; Hernandez 2000 38%; Jones 1985 26%; Mendes De Oliveira 2010 27%; Nalbant 2011 28%; Wen 2008 24%). Information was insufficient to inform judgements in five studies

(Cambach 1997; Cebollero 2012; Clark 1996; Elci 2008; Vijayan 2010).

Selective reporting

We found no trial registration protocol for most studies to check whether all prespecified outcomes were reported in the articles. However, outcomes listed in the methods section of the included studies were reported in the results section, with the exception of four studies that were judged to have high risk of reporting bias (i.e. Ozdemir 2010, whose results for the CRQ are incomplete; Paz-Diaz 2007, who did not provide results for the rehabilitation group for CRQ; Petty 2006, in which results of the six-minute walk test and Short Form (SF)-36 are not presented; and Weiner 1992, in which results of the SGRQ are not available). In relation to publication bias, we visually reviewed the funnel plots (Figure 1; Figure 4; Figure 5) and followed this by performing the Egger test (Egger 1997) (Table 1). Egger test results showed no significant publication bias across the studies included in the current meta-analysis.

Figure 4. Funnel plot of comparison: I Rehabilitation versus usual care, outcome: I.4 QoL - Change in CRQ (Dyspnoea) (see for Egger and Begg-Mazumdar: Kendall's test results).

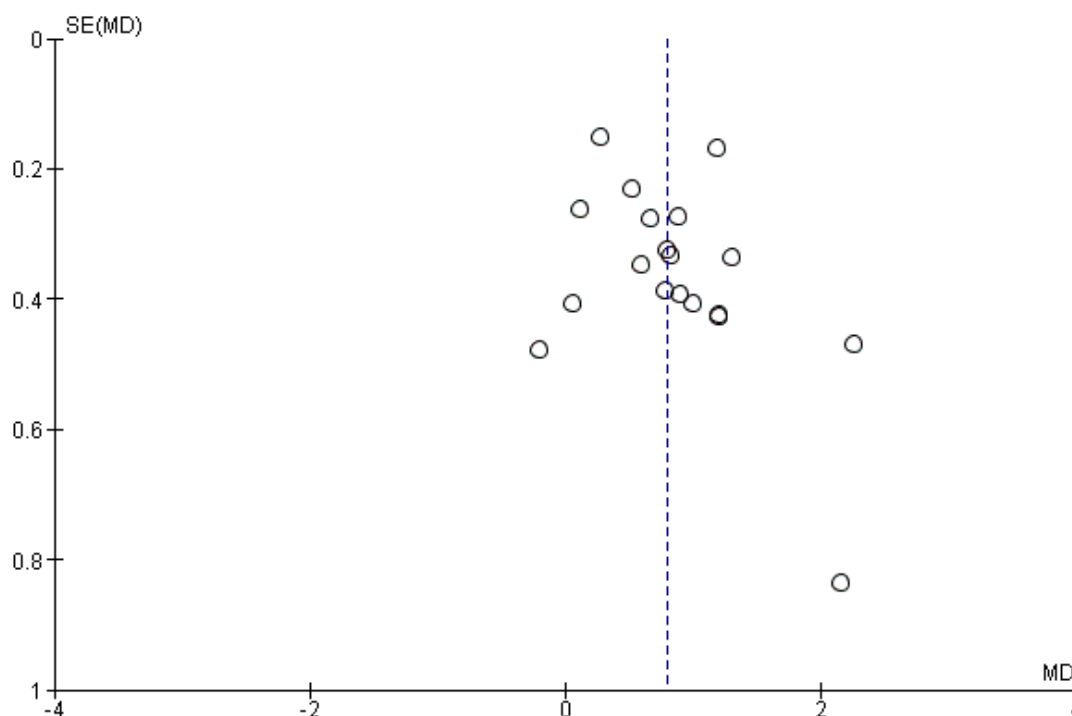
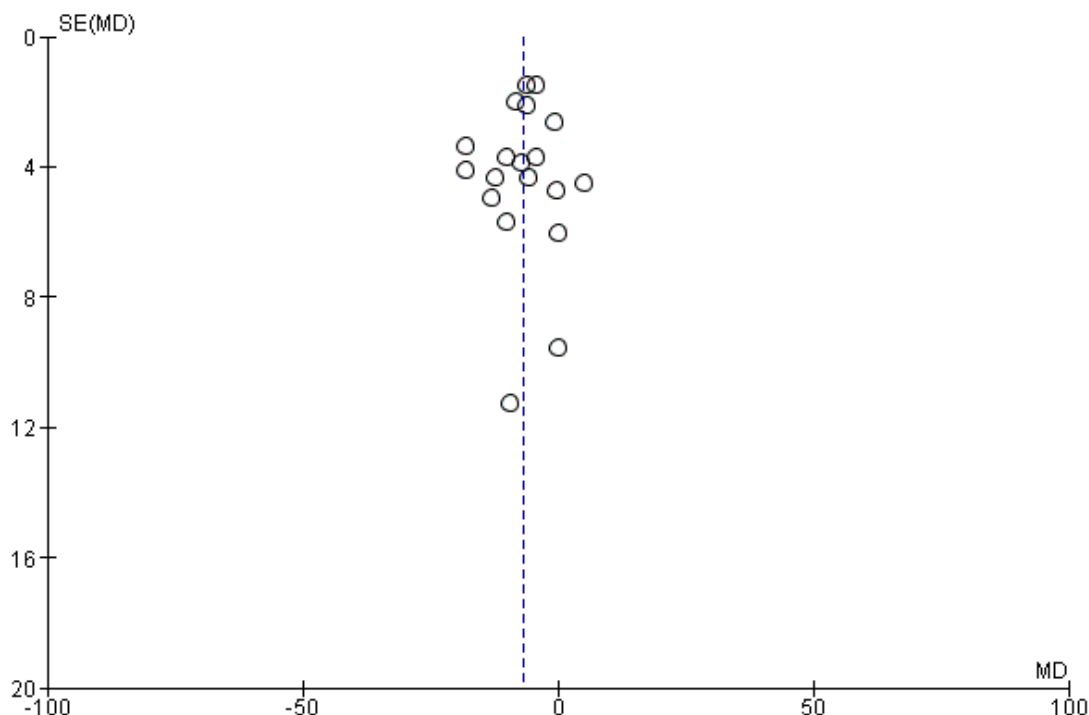


Figure 5. Funnel plot of comparison: I Rehabilitation versus usual care, outcome: I.5 QoL - Change in SGRQ (Total) (see for Egger and Begg-Mazumdar: Kendall's test results).



Other potential sources of bias

We found no other source of bias, with the exception of a tendency toward increased proportions of male participants, as was highlighted earlier.

Effects of interventions

See: [Summary of findings for the main comparison Rehabilitation versus usual care for chronic obstructive pulmonary disease](#)

Pulmonary rehabilitation versus usual care

For this comparison, we included all participants who were randomly assigned in the included studies and received PR (defined as exercise training for at least four weeks with or without educational and/or psychological support) and those allocated to usual care (see [Characteristics of included studies](#) for details). We also undertook subgroup analysis as discussed in the [Subgroup analysis and investigation of heterogeneity](#) section. All outcomes results utilised in the analyses were based on baseline assessment measure-

ments and the earliest follow-up assessment up to three months after completion of the intervention.

Primary outcomes

Health-related quality of life

Among the 65 trials that met the inclusion criteria of the meta-analysis, 44 made an attempt to measure HRQoL using eight different strategies. Only three of these strategies - the Transitional Dyspnoea Index (TDI; [Mahler 1984](#)), the Chronic Respiratory Disease Questionnaire (CRQ; [Guyatt 1987a](#)) and the St. Georges Respiratory Questionnaire (SGRQ; [Jones 1992](#)) - have been demonstrated to be valid and responsive. Of these, the CRQ and the SGRQ have become the recognised standard of assessment of HRQoL amongst patients with COPD and are reported here. We analysed the CRQ and the SGRQ separately. Not all subscales were fully completed by all participants, so the numbers of participants per outcome and per subscale varied.

Chronic Respiratory Disease Questionnaire (CRQ)

Scores for the CRQ are reported on a 7-point scale. Although 23 studies utilised the CRQ to assess HRQoL, only 19 studies (1291 participants) provided results suitable for analysis.

Participants allocated to rehabilitation programmes had, on average, significantly greater changes in HRQoL CRQ scores across all subscales when compared with participants allocated to control groups (Fatigue: MD 0.68, 95% CI 0.45 to 0.92; 19 trials; 1291 participants; $\text{Tau}^2 = 0.15$; $I^2 = 64\%$; [Analysis 1.1](#); Emotional function: MD 0.56, 95% CI 0.34 to 0.78; 19 trials; 1291 participants; $\text{Tau}^2 = 0.12$; $I^2 = 58\%$; [Analysis 1.2](#); Mastery: MD 0.71, 95% CI 0.47 to 0.95; 19 trials; 1212 participants; $\text{Tau}^2 = 0.16$; $I^2 = 63\%$; [Analysis 1.3](#); Dyspnoea: MD 0.79, 95% CI 0.56 to 1.03; 19 trials; 1283 participants; $\text{Tau}^2 = 0.15$; $I^2 = 63\%$; [Analysis 1.4](#)).

For each of the CRQ domains (dyspnoea, fatigue, emotional function and mastery), the common effect size exceeded the 'minimal clinically important difference' (MCID) (0.5 points on the 7-point scale) ([Jaeschke 1989](#)). The lower limit of the confidence interval around the common treatment effect of the dyspnoea domains ([Analysis 1.4](#)) exceeded the MCID, indicating not only statistical significance but also clinical significance in the effect of PR. The lower limits of the remaining domains were slightly below the MCID ([Analysis 1.1](#); [Analysis 1.2](#); [Analysis 1.3](#)).

Heterogeneity identified across all domains of the CRQ was substantial, as Tau^2 was greater than zero, and in all cases, I^2 was greater than 30% and the P value for the Chi^2 test was less than 0.10. We undertook subgroup and sensitivity analyses to try to explore heterogeneity; although findings are presented later, they did not explain the high level of heterogeneity.

St. George's Respiratory Questionnaire (SGRQ)

Scores for the SGRQ are reported on a 100-point scale. Twenty trials utilised the SGRQ to assess the HRQoL of participants. Results were available in a usable format from 19 trials (a maximum of 1153 participants) for inclusion in the meta-analysis. [Barakat 2008](#) was not included in the analysis, as clarification regarding the SD of the change is needed from the study authors.

Similar to the CRQ, participants allocated to PR programmes had, on average, significantly greater changes in SGRQ scores across all subscales when compared with participants allocated to control groups (SGRQ total: MD -6.89, 95% CI -9.26 to -4.52; 19 trials; 1146 participants; $\text{Tau}^2 = 13.17$; $I^2 = 59\%$; [Analysis 1.5](#); SGRQ symptoms: MD -5.09, 95% CI -7.69 to -2.49; 19 trials; 1153 participants; $\text{Tau}^2 = 7.79$; $I^2 = 26\%$; [Analysis 1.6](#); SGRQ impact: MD -7.23, 95% CI -9.91 to -4.55; 19 trials; 1149 participants; $\text{Tau}^2 = 17.94$; $I^2 = 58\%$; [Analysis 1.7](#); SGRQ activity: MD -6.08, 95% CI -9.28 to -2.88; 19 trials; 1148 participants; $\text{Tau}^2 = 27.01$; $I^2 = 64\%$; [Analysis 1.8](#)).

For each of the SGRQ domains (as well as the total SGRQ score), the common effect size exceeded the MCID of four ([Jones 1991](#);

[Quirk 1991](#)) ([Analysis 1.5](#); [Analysis 1.6](#); [Analysis 1.7](#); [Analysis 1.8](#)). All results of the analysis for all domains of the SGRQ were statistically significant. However, the extent of the 95% CI around the pooled treatment effect exceeds the MCID only for the SGRQ total and SGRQ impact domains of the SGRQ, demonstrating unequivocal clinical and statistical significance in these domains. Heterogeneity in results obtained from the total and all subscales of the SGRQ was substantial, with the exception of the symptoms subscale ([Analysis 1.6](#)).

Secondary outcomes

Maximal exercise capacity

A total of 34 trials measured maximal exercise capacity. We limited the meta-analysis to the 16 trials that used the incremental cycle ergometer test.

Investigators in 16 studies (779 participants) used the incremental cycle ergometer test. On average, a statistically significant increase in mean W_{max} (W) was reported among participants allocated to PR compared with those allocated to usual care (MD 6.77, 95% CI 1.89 to 11.65; $\text{Tau}^2 = 40.97$; $I^2 = 74\%$; [Analysis 1.10](#)). The common effect size exceeded the MCID (4 watts) proposed by [Puhan 2011\(b\)](#). The maximal exercise test showed substantial heterogeneity in the results obtained.

Functional exercise capacity

Of the included studies, 43 trials used the six-minute walk test as an outcome. Of these, 38 (1879 participants: 1012 actively treated, 867 controls) presented the results in a format that could be used for the meta-analysis (see [Analysis 1.11](#)). Investigators reported a statistically significant increase, on average, in the mean difference in metres walked associated with PR (MD 43.93 m, 95% CI 32.64 to 55.21; $\text{Tau}^2 = 713.49$; $I^2 = 74\%$; [Analysis 1.11](#)). Both the common effect and the lower limit of its confidence interval exceeded the MCID for the 6WMD of 30 metres, as recommended by [Holland 2014](#), indicating the clinical significance of the effect of PR.

Eight trials (694 participants) reported data on the incremental shuttle walk test (ISWT). These test results were analysed independently from those of the 6MWT. On average, a statistically significant increase in mean metres walked was noted among participants allocated to PR compared with those allocated to usual care (MD 39.77, 95% CI 22.38 to 57.15; $\text{Tau}^2 = 181.56$; $I^2 = 32\%$). This result is slightly below the MCID of 47.5 m ([Singh 2008](#); [Singh 2014](#)) to make this a finding of clinical significance. Similar to previous outcomes on maximal exercise, both the six-minute walk test and the analyses demonstrated substantial heterogeneity.

Several other outcome measures were used to measure functional capacity, but because of the limited numbers of trials providing

data for these other outcomes (endurance shuttle walk test: two trials; 12-minute walk test: four trials); four-minute walk test: one trial)), these findings were not included in the meta-analysis.

Subgroup and sensitivity analyses

Rehabilitation versus usual care (subgroup analysis hospital-versus community-based pulmonary rehabilitation)

In total, 39 included studies were considered to have a hospital-based PR intervention delivered on an in-patient or out-patient basis. A total of 25 studies focused on programmes that were delivered in the community at community centres or in individuals' homes. One study had both a community-based and an out-patient-based intervention group, so it was excluded from the subgroup analysis (Mendes De Oliveira 2010).

In the subgroup analysis for the CRQ domain outcomes, the 'community' subgroup included nine studies (Cambach 1997; Casey 2013; Faulkner 2010; Gomez 2006; Hernandez 2000; Lindsay 2005; O'Shea 2007; Singh 2003; Wijkstra 1994) and the 'hospital group' included 10 studies (Behnke 2000a; Cebollero 2012; Goldstein 1994; Gosselink 2000; Griffiths 2000; Güell 1995; Güell 1998; McNamara 2013; Simpson 1992; Sridhar 2008;). For SGRQ outcomes, the community subgroup included nine studies (Baumann 2012; Boxall 2005; Chan 2011; De Souto Araujo 2012; Elci 2008; Fernandez 2009; Gohl 2006; Gottlieb 2011; Van Wetering 2010) and the hospital subgroup included 10 studies (Chlumsky 2001; Deering 2011; Engström 1999; Finnerty 2001; Griffiths 2000; Gurgun 2013; Karapolat 2007; Paz-Diaz 2007; Ringbaek 2000; Theander 2009).

Evidence suggested a significant difference in treatment effect between subgroups for all domains of the CRQ, with higher mean values, on average, in the PR group in hospital than in the community-based group (Analysis 2.1; Analysis 2.2; Analysis 2.3; Analysis 2.4). No subgroup differences were reported for any of the SGRQ domains (Analysis 2.5; Analysis 2.6; Analysis 2.7; Analysis 2.8).

Rehabilitation versus usual care (subgroup analysis 'exercise only' vs 'exercise plus more comprehensive components')

A total of 31 trials were included in the 'exercise only' subgroup, and 34 trials in the 'exercise plus more comprehensive components' subgroup, of which 10 trials in the 'exercise only' subgroup (Cebollero 2012; Gosselink 2000; Güell 1995; Güell 1998; Hernandez 2000; McNamara 2013; O'Shea 2007; Simpson 1992; Singh 2003; Sridhar 2008), and nine in the more comprehensive subgroup (Behnke 2000a; Cambach 1997; Casey 2013; Faulkner 2010; Goldstein 1994; Gomez 2006; Griffiths 2000; Lindsay 2005; Wijkstra 1994) reported CRQ data.

For the SGRQ, five trials were included in the 'exercise only' subgroup (Chan 2011; Chlumsky 2001; De Souto Araujo 2012; Gohl 2006; Paz-Diaz 2007) and 14 trials in the more comprehensive

subgroup (Baumann 2012; Boxall 2005; Deering 2011; Elci 2008; Engström 1999; Fernandez 2009; Finnerty 2001; Gottlieb 2011; Griffiths 2000; Gurgun 2013; Karapolat 2007; Ringbaek 2000; Theander 2009; Van Wetering 2010).

No evidence was found of a significant treatment effect between subgroups for all domains of the CRQ (Analysis 3.1; Analysis 3.2; Analysis 3.3; Analysis 3.4) and the SGRQ (Analysis 3.5; Analysis 3.6; Analysis 3.7; Analysis 3.8).

Please see Table 4 for a summary of results of the subgroup analysis.

Sensitivity analysis

A sensitivity analysis included only studies of high quality (studies for which both allocation concealment and Incomplete outcome data were rated as low risk) (see risk of bias table in Figure 2). Thirteen studies met the criteria for high quality (Boxall 2005; Cambach 1997; Cockcroft 1981; Emery 1998; Engström 1999; Goldstein 1994; Griffiths 2000; Karapolat 2007; Liu 2012; McNamara 2013; O'Shea 2007; Theander 2009; Van Wetering 2010). Effect estimates were consistent with overall summary effect estimates for the two primary outcomes when contributing data were restricted to high-quality studies, with the exception of one domain, for which the confidence interval widened enough to include the possibility of no difference between rehabilitation and control. All domains for both the CRQ and the SGRQ continued to be statistically significant when restricted to studies of high quality, with the exception of the SGRQ symptoms domain, which was no longer statistically significant (MD -4.12, 95% CI -8.42 to 0.21; seven trials; 572 participants; $\tau^2 = 13.82$; $I^2 = 46\%$).

Neither subgroup analyses nor the sensitivity analysis based on quality had any impact on reducing or explaining high levels of heterogeneity.

DISCUSSION

This review summarised 65 studies involving 3822 participants with chronic obstructive pulmonary disease (COPD), 2090 of whom were randomly allocated to some form of exercise rehabilitation for a minimum duration of four weeks, and 1732 individuals randomly assigned to usual care. This is the second update of this review, which was last updated in 2006 (Lacasse 2006). Pulmonary rehabilitation is now accepted within the scientific community as an essential strategy in the ongoing management of people with COPD (GOLD 2014). Development of objective health-related quality of life (HRQoL) outcome measures (Kirshner 1985) and demonstration of a physiological rationale for exercise training in people with COPD (Casaburi 1991; Maltais 1996) have facilitated this acceptance. Results of the previous version of this meta-analysis strongly supported pulmonary rehabilitation (PR) in the

management of COPD, and results of this current update reconfirm these findings.

Three aspects of the meta-analysis warrant comment. First, we examined the short-term effects of PR in COPD, that is, the benefits of rehabilitation found at the completion of a programme. When the original review was undertaken, few investigators were examining the long-term benefits of rehabilitation (Guell 2000; Ries 1995; Troosters 2000; Wijkstra 1995). More recently, focus on this aspect of PR has increased and exploration of strategies to maintain early benefits continues (Brooks 2002; Foglio 2001; Ries 2003). This review does not attempt to examine these issues. Second, we have been conservative in concluding clear benefit only when the 95% confidence interval (CI) representing the smallest treatment effect was still greater than the minimal clinically important difference (MCID). Third, we excluded a number of well-conducted studies that have contributed to our understanding of PR, but in which control participants received interventions beyond what was considered conventional care. An example of this is Ries 1995, which was excluded on the grounds that control participants had been given an educational programme. Similarly, several studies in which an intervention such as inspiratory muscle training, psychosocial support or breathing exercises was compared with exercise training were excluded. Only studies in which usual care was directly compared with exercise rehabilitation were included for analysis.

As the care of patients with COPD is largely concerned with treating symptoms (Pauwels 2001), we believe that HRQoL should be considered as the primary outcome in PR. The present meta-analysis reconfirms the findings of the previous version that PR is effective in relieving dyspnoea and fatigue, and in improving patients' emotional function and control over the disease. The magnitude of the improvement lies beyond the MCID.

In most trials, investigators measured HRQoL by using either the Chronic Respiratory Disease Questionnaire (CRQ) or the St. George's Respiratory Questionnaire (SGRQ). Head-to-head comparisons of these questionnaires have been published (Harper 1997; Rutten-van Mölken 1999). In both studies, analyses of reliability, validity and responsiveness did not clearly favour one instrument above the other. Rutten-van Mölken and colleagues (Rutten-van Mölken 1999) suggested that the choice between the CRQ and the SGRQ should be based on other considerations, such as the required sample size. Only one trial included in the meta-analysis reported results from both the CRQ and the SGRQ (Griffiths 2000), with no clear indication that one questionnaire is more sensitive to change than the other. Therefore, comparisons from this meta-analysis are only indirect. We found wider 95% CIs around the pooled treatment effect from the SGRQ - a situation that may be explained by the smaller number of participants contributing to this analysis.

Pulmonary rehabilitation programmes included in the meta-anal-

ysis differed in several aspects, including clinical setting, duration and composition. This we believe is responsible for the substantial heterogeneity observed in the results obtained and is in keeping with a recent study by Spruit 2014 and supported by Rochester 2014, who also identified this as an issue requiring further investigation. For instance, the contributions of educational activities and psychological support to exercise training remain uncertain. This information would be of outmost importance to physicians and allied healthcare professionals who prescribe rehabilitation and to those who allocate the resources. We addressed this issue in a systematic overview of the literature (Lacasse 1997). Since the time this review was published, further evidence from randomised controlled trials (RCTs) has been published to better define the type and intensity of exercise (Bernard 1999), as well as the influence of programme components, including patient education and self-management (Bourbeau 2003), nutritional support (Steiner 2003) and respiratory muscle training (Watson 1997). Sometimes, evidence even took the form of systematic reviews (Ferreira 2012; Lotters 2002; Taylor 2005). Such questions were too specific to be directly addressed in this meta-analysis, which aimed to investigate the overall effect of rehabilitation in COPD (not the effects of its components). Nevertheless, homogeneity among study results suggested that less sophisticated rehabilitation programmes may also be effective in improving HRQoL, although the between-study comparison from which this conclusion follows is relatively weak.

Investigators have identified an increase in exercise tolerance and functional activities such as walking as other relevant outcomes of rehabilitation (Fishman 1994; Pauwels 2001). Our current interpretation of the results of the six-minute walk test (6MWT) analysis differs from that of the previous version of the meta-analysis (Lacasse 2006). In 2006, results of the meta-analysis were compared with an MCID of 54 metres (95% CI 37 to 71 metres; Redelmeier 1997). From this comparison, the clinical significance of results obtained from the 2006 meta-analysis was interpreted as uncertain. Since 2006, several studies have further investigated the issue of the MCID in field walk tests in chronic respiratory disease. Results of these studies have recently been summarised in an important systematic review, which was supported by the European Respiratory and American Thoracic Societies (Holland 2014; Singh 2014). Although variability across studies and methods used to determine the MCID is evident, available evidence suggests that the MCID for the 6MWT lies between 25 and 33 metres (median estimate 30 metres). Results of our meta-analysis (i.e. MD of 43.93 metres with 95% CI between 36.24 and 55.21 metres) indicate the clinical significance of the effects of PR.

When compared with the treatment effects of other important modalities of care for patients with COPD, such as long-acting inhaled therapy or oral theophylline and its new derivatives (Kew 2014; Ram 2005), rehabilitation resulted in greater improvement in important domains of HRQoL and functional exercise capacity.

The importance of measures of maximal exercise capacity remains to be defined. An initial test may be useful in assisting with the prescription of an appropriate level of training. Retesting may provide physiological evidence that a training response has occurred and may be useful in adjustment of intensity levels during the programme (Jones 1988). As the results of maximal exercise tests correlate poorly with those of HRQoL measures (Guyatt 1985; Wijkstra 1994a), maximal exercise testing cannot serve as a substitute for such measures when the outcome of a rehabilitation programme is evaluated.

AUTHORS' CONCLUSIONS

Implications for practice

Results of this meta-analysis strongly support pulmonary rehabilitation, including at least four weeks of exercise training, as part of the spectrum of treatment for patients with COPD. We found clinically and statistically significant improvements in important domains of health-related quality of life, including dyspnoea, fatigue, emotional function and mastery, in addition to the six-minute walk/distance test - a measure of functional exercise.

Pulmonary rehabilitation has long been underused in patients with COPD (Brooks 2007; Puhan 2011(a); Yohannes 2004). With the support of current international statements or clinical practice guidelines targeting respiratory rehabilitation in COPD (Bolton 2013; Nici 2006; Spruit 2013), we hope that the results of this meta-analysis will encourage the implementation of new programmes.

Implications for research

Overall, the conclusions of this meta-analysis are in agreement with those of prior meta-analyses published in 1996 and in 2001 (Lacasse 1996; Lacasse 2001). The addition of 34 RCTs since the 2006 update resulted, as expected, in narrowing of the CIs around the common effects of rehabilitation in the outcomes examined. This update continues to support the strong argument that PR is beneficial in improving HRQoL. It also reiterates the view presented in the 2006 update that additional RCTs comparing PR and conventional care in COPD are no longer warranted. However findings of the subgroup analysis undertaken as part of this update do stimulate new questions in relation to PR. The subgroup anal-

ysis finding that identified a difference in treatment effect between hospital-based programmes and community-based programmes suggests that further research should be undertaken to compare these two approaches. Similarly, the fact that the subgroup analysis identified no differences between basic exercise PR programmes and those that provided more complex interventions suggests the need to examine and identify the most essential components of PR programmes for achieving the best patient outcomes. Other factors that remain uncertain include the degree of supervision, the intensity of the training and how long the treatment effect persists. Recent recommendations provided by current guidelines from the ATS or ACSM that at least three weekly sessions are necessary for a treatment effect raise issues that require consideration beyond this current review. These specific issues demand further elucidation through RCTs and further meta-analysis.

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The methods section of this review is based on a standard template used by the Cochrane Airways Group.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies [ordered by study ID]

Barakat 2008

Methods	Study design: RCT “Randomization was in blocks of 10, using random numbers” (pg 157)	
Participants	Setting: out-patients in France Inclusion criteria: <ul style="list-style-type: none">Participants accepted into the study were known to the respiratory team at the hospital as having long-standing airway disease, classified as COPD Exclusion criteria: <ul style="list-style-type: none">Unstable medical conditions such as congestive cardiac failure, cor pulmonale, malignancy or cerebrovascular accidentIndividuals with sleep apnoea syndrome Participant status: Age, years: RG: 63.7; CG: 65.9 Gender (M/F): 67/13 FEV ₁ % predicted: RG: 41.9; CG: 43.3 Participants randomly assigned: Randomised: 80 Analysed Rehab: 35 Control: 36	
Interventions	Pulmonary rehabilitation: Out-patient-based rehabilitation ULE, LLE, Edu Duration: 14-Week programme	
Outcomes	Assessed: baseline and 14 weeks Spirometry, SGRQ, 6MWT, Bode Index	
Notes		
<i>Risk of bias</i>		
Bias	Authors’ judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	“Randomization was in blocks of 10, using random numbers” (pg 157)
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	The nature of the intervention made it impossible to blind participants to their allocation

Barakat 2008 (Continued)

Blinding of outcome assessment (detection bias) All outcomes	Low risk	“All tests including SGRQ outcome assessment [were] blinded” (pg 150) “All of these tests were supervised by a blinded observer, who subsequently repeated this assessment before the study and at the end of the study (0 and 14 weeks)” (pg 156)
Incomplete outcome data (attrition bias) All outcomes	Low risk	Commenced: 80; completed: 71; attrition: 11.25%
Selective reporting (reporting bias)	Low risk	No protocol paper was registered, but all outcomes listed in the paper appear to have been reported
Other bias	Low risk	None noted

Baumann 2012

Methods	Study design: prospective, randomised, controlled, interventional, multi-centre trial
Participants	<p>Setting: Hamburg metropolitan area, multi-centre trial</p> <p>Inclusion criteria:</p> <ul style="list-style-type: none"> • Age between 50 and 80 years • COPD GOLD stage II-IV • Smoking history of > 20 pack-years • Pharmacological therapy according to current guidelines • Written informed consent <p>Exclusion criteria:</p> <ul style="list-style-type: none"> • Respiratory insufficiency, defined as $\text{PaO}_2 < 55$ mmHg and/or $\text{PaCO}_2 > 50$ mmHg breathing room air • Manifest cardiac insufficiency • Uncontrolled arterial hypertension • Active malignant disease • Symptomatic coronary heart disease or pathological test results in cycle ergometry • Limited physical capabilities • Musculoskeletal disorders as the cause • Unwillingness to return for follow-up • Previous or ongoing participation in exercise training programmes • Expected inability to attend at least 75% of sessions <p>Participant status: Age, years: RG: 65; CG: 63 Gender (M/F): 47/34 FEV₁ % predicted: RG: 45; CG: 47</p> <p>Participants randomly assigned: Randomised: 100 Analysed Rehab: 37</p>

	Control: 44	
Interventions	Pulmonary rehabilitation: Out-patient (hospital based) Aerobic exercise, ULE, LLE Edu, peer support Duration: 8 sessions of 20 minutes and 18 sessions of 60 minutes Usual care: Standard care consisted of referral back to the participant’s pulmonologist following baseline assessments. The control group did not take part in any components of the rehabilitation programme	
Outcomes	Assessed: baseline and 6 months 6-Minute walk test (6MWT) Cycle ergometry Short Form-12 (SF-12), SGRQ	
Notes		
<i>Risk of bias</i>		
Bias	Authors’ judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	”Randomisation was performed using a computer-generated list of random numbers to assign participants to either training or standard care“ (pg 3)
Allocation concealment (selection bias)	High risk	”Consecutive patients with COPD according to accepted criteria [5] were recruited“ (pg 3)
Blinding of participants and personnel (performance bias) All outcomes	High risk	”Due to the nature of the intervention it was not possible to blind subjects to their allocation (pg 2)
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Those supervising the 6MWT were not blinded, whereas those supervising cycle ergometry were blinded
Incomplete outcome data (attrition bias) All outcomes	High risk	Commenced: 42; completed: 32; attrition: 10 (24%)
Selective reporting (reporting bias)	Low risk	No protocol paper was registered, but all outcomes listed in the paper appear to have been reported
Other bias	Low risk	None noted

Methods	Study design: RCT	
Participants	Setting: work undertaken in Germany Inclusion criteria: <ul style="list-style-type: none">• Severe COPD• Following acute episode Exclusion criteria: <ul style="list-style-type: none">• Evidence of unstable cardiac disease, cor pulmonale decompensation• Other disabling diseases that prevented participation in the exercise programme, such as orthopaedic inabilities or peripheral vascular disease Participant status: Age, (years± SD): RG: 64.0 ± 1.9; CG: 68.0 ± 2.2 Gender (M/F): RG: 12/3; CG: 11/4 FEV ₁ % predicted (± SD): RG: 34.1 ± 7.4; 37.5 ± 6.6 Participants randomly assigned: In-patient and home-based Randomised: 46 Analysed Rehab: 15 Control: 15	
Interventions	Pulmonary rehabilitation: acute hospital admission followed by home exercise programme for 6 months LLE, Edu, Psy Duration: 24 weeks Usual care: Control participants were advised to perform exercise but without special instructions	
Outcomes	Assessment: baseline and 3, 6 months 6MWT, CRQ	
Notes		
Risk of bias		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation was in blocks of 10, using random numbers (from study authors)
Allocation concealment (selection bias)	Low risk	Randomisation process: sealed envelopes (from study authors)
Blinding of participants and personnel (performance bias) All outcomes	High risk	As a result of the nature of the intervention, both participants and those delivering the programme knew the allocation
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Does not provide information on blinding of assessors, other than that main researcher undertook assessments “the questionnaire was administered as a structured interview,

Behnke 2000a (Continued)

		and all interviews were performed by the same investigator (M. B.)” (pg 11867)
Incomplete outcome data (attrition bias) All outcomes	High risk	Commenced :46; completed: 30; attrition:16 (35%)
Selective reporting (reporting bias)	Low risk	No protocol paper was registered, but all outcomes listed in the paper appear to have been reported
Other bias	Low risk	None reported

Bendstrup 1997

Methods	Study design: RCT
Participants	<p>Setting: Patients came for out-patient rehabilitation to a hospital in Denmark</p> <p>Inclusion criteria:</p> <ul style="list-style-type: none"> • Forced expiratory volume in 1 second (FEV₁) between 25% and 55% of predicted value for age, gender and height • Tiffenau index (FEV₁/forced vital capacity (FVC) ratio) < 70% • Stable condition for at least 4 weeks • No change in exercise status, sputum colour and quantity; no changes in medication <p>Exclusion criteria:</p> <ul style="list-style-type: none"> • Heart disease (moderate or severe ischaemic heart disease, acute myocardial infarction within 3 months, cardiomyopathy and valvular heart disease) • Musculoskeletal disease limiting exercise • Intermittent claudication limiting exercise <p>Participant status: Age, (years ± SD): RG: 64 ± 3; CG: 65 ± 2 Gender (M/F): RG: 7/9; CG: 7/9</p> <p>Participants randomly assigned: Randomised: 42 Analysed Rehab: 16 Control: 16</p>
Interventions	<p>Pulmonary rehabilitation: out-patient LLE, ULE, IMT Duration: 12 weeks</p> <p>Control: Stated that care was provided by primary physician</p>
Outcomes	<p>Assessment: baseline and 12 weeks 6MWT, CRQ, activities of daily living, York QLQ</p>
Notes	

Bendstrup 1997 (Continued)

<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No information provided other than this: "The patients were randomly allocated to either an intervention or a control group"
Allocation concealment (selection bias)	Unclear risk	Information not available
Blinding of participants and personnel (performance bias) All outcomes	High risk	As a result of the nature of the intervention, both participants and those delivering the programme knew the allocation
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information was provided in relation to blinding of those carrying out outcome assessments
Incomplete outcome data (attrition bias) All outcomes	High risk	Commenced: 42; completed: 32; attrition: 10 (24%)
Selective reporting (reporting bias)	Low risk	No protocol paper was registered, but all outcomes listed in the paper appear to have been reported
Other bias	Low risk	None noted

Booker 1984

Methods	Study design: RCT
Participants	<p>Setting: home-based UK study in London</p> <p>Inclusion criteria:</p> <ul style="list-style-type: none"> Patients with CAL and exercise tolerance limited by breathlessness were accepted into the study <p>Exclusion criteria:</p> <ul style="list-style-type: none"> Not provided <p>Participant status:</p> <p>Age, (years±SD) : RG: 66± 8; CG: 65 ± 7</p> <p>Gender: not available</p> <p>Participants randomly assigned:</p> <p>Randomised: 69</p> <p>Analysed</p> <p>Rehab: 32</p> <p>Control: 37</p>
Interventions	<p>Pulmonary rehabilitation:</p> <p>LLE, BE, PD, Edu, Psy</p> <p>Duration: 9 weeks</p>

Booker 1984 (Continued)

Outcomes	Assessment: baseline and 3, 6, 12 months 6MWT, DSSI/SAD, daily activity questionnaire	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation process: coin toss
Allocation concealment (selection bias)	Low risk	Study investigators unaware as to order of treatment group assignment
Blinding of participants and personnel (performance bias) All outcomes	High risk	As a result of the nature of the intervention, both participants and those delivering the programme knew the allocation
Blinding of outcome assessment (detection bias) All outcomes	Low risk	All assessments were carried out by independent assessors who were unaware of the treatment received by each participant - "double-blind" (pg 258)
Incomplete outcome data (attrition bias) All outcomes	High risk	Commenced: 128; completed: 94 (73%); attrition: 27%
Selective reporting (reporting bias)	Low risk	No protocol paper was registered, but all outcomes listed in the paper appear to have been reported
Other bias	Low risk	None noted

Borghi-Silva 2009

Methods	Study design: prospective randomised controlled trial
Participants	<p>Setting: Brazil</p> <p>Inclusion criteria:</p> <ul style="list-style-type: none"> • Diagnosis of COPD according to criteria set forth by GOLD • Compliance with medical management • No change in medical management and no decompensation episodes for at least 1 month before study initiation • No participation in a regular physical exercise programme for at least 6 months before study initiation <p>Exclusion criteria:</p> <ul style="list-style-type: none"> • Presence of orthopaedic or neurological conditions that would preclude participation in an exercise programme • History of cardiac arrhythmias or potential ECG alterations • Past history consistent with heart disease, diabetes mellitus, uncontrolled

	hypertension or other concomitant respiratory diseases <ul style="list-style-type: none">● Failure to comply with the research protocol Participant status: Age (years): RG: 67 ±10; CG: 67 ± 10 Gender (M/F): RG: 13/7; CG: 12/8 FEV ₁ % predicted (± SD): RG: 64 ± 16; CG: 64 ± 18 Participants randomly assigned: Randomised: 40 Analysed: Rehab: 20 Control: 20	
Interventions	Pulmonary rehabilitation: Out-patient (hospital-based) supervised training programme Aerobic exercise, ULE, LLE Duration: 6-week programme Usual care	
Outcomes	Assessed: baseline and 6 weeks 6-Minute walk ReR intervals	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No information available
Allocation concealment (selection bias)	Unclear risk	No information available
Blinding of participants and personnel (performance bias) All outcomes	High risk	Unable to blind because of the nature of the intervention
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information available
Incomplete outcome data (attrition bias) All outcomes	Low risk	Commenced: 40; completed: 34; attrition: 6 (15%)
Selective reporting (reporting bias)	Low risk	No protocol paper was registered, but all outcomes listed in the paper appear to have been reported
Other bias	Unclear risk	None noted

Boxall 2005

Methods	Study design: RCT	
Participants	Setting: home-based PR programme in Australia Inclusion criteria: <ul style="list-style-type: none">• Diagnosis of COPD by 1 of 4 hospital respiratory specialists• Older than 60 years• Dyspnoea on exertion• Live locally• Free from worsening symptoms of disease over the past 2 weeks• Motivated to exercise daily unsupervised Exclusion criteria: <ul style="list-style-type: none">• Attending out-patient-based pulmonary rehabilitation• Restricted shoulder movement• Living in a nursing home• Previous lung volume reduction surgery• Pain limiting mobility Participant status: Gender (M/F): RG: 11/12; CG: 15/8 Age (years±SD): RG: 77.6 ±7.6; CG: 75.8 ±8.1 FEV ₁ % predicted (± SD): RG: 40.5 ±15.9; CG: 37.7 ±15.0 FEV ₁ /FVC % predicted (± SD): RG: 74.4 ± 21.3; CG: 70.4 ± 19.2 Participants randomly assigned: Randomised: 60 Analysed: Rehab: 23 Control: 23	
Interventions	Pulmonary rehabilitation: supervised home-based ULE, LLE, Edu Duration: 12 weeks Usual care: Control phase: Participants received no treatment in addition to usual medical care	
Outcomes	Assessed: baseline and 12 weeks 6MWT, SGRQ, dyspnoea	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	“computer-generated random numbers that were coded into opaque envelopes by a person independent from the study, they retained the envelopes until initial assessment was completed” (pg 380)
Allocation concealment (selection bias)	Low risk	Study investigators unaware as to order of treatment group: “computer-generated random numbers that were coded into

Boxall 2005 (Continued)

		opaque envelopes by a person independent from the study, they retained the envelopes until initial assessment was completed" (pg 380)
Blinding of participants and personnel (performance bias) All outcomes	High risk	"Neither assessors nor participants were blinded to group assignment in this study" (pg 380)
Blinding of outcome assessment (detection bias) All outcomes	High risk	"Neither assessors nor participants were blinded to group assignment in this study" (pg 380)
Incomplete outcome data (attrition bias) All outcomes	Low risk	Commenced: 60; completed: 46 (76.7%); attrition: 23.3%
Selective reporting (reporting bias)	Low risk	No protocol paper was registered, but all outcomes listed in the paper appear to have been reported
Other bias	High risk	"Had to live locally might bias the sample selection and be motivated to exercised daily" (pg 379)

Busch 1988

Methods	Study design: RCT stratified in a random manner
Participants	<p>Setting: home-based; Saskatchewan, Canada</p> <p>Inclusion criteria:</p> <ul style="list-style-type: none"> Severe, irreversible airway obstruction <p>Exclusion criteria:</p> <ul style="list-style-type: none"> Without apparent or symptomatic ischaemic heart disease or disablement from medical conditions other than COPD <p>Participant status: Age (years \pm SD): RG: 65 \pm16; CG: 66 \pm16 Gender (M/F): RG: 5/2; CG: 6/1 FEV₁ (\pm SD): RG: 26% \pm 9; CG: 27% \pm11</p> <p>Participants randomly assigned: Randomised: 14 Analysed: Rehab: 6 Control: 6</p>
Interventions	<p>Pulmonary rehabilitation: LLE, BE Duration: 18 weeks</p> <p>Usual care: Control group visited but did not follow the exercise programme</p>

Busch 1988 (Continued)

Outcomes	Assessment: baseline and at 18 weeks CRQ (dyspnoea only), ICET, multi-step stage test	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Letter received from study author: used a table of random numbers
Allocation concealment (selection bias)	Low risk	Study investigators unaware as to order of treatment group assignment
Blinding of participants and personnel (performance bias) All outcomes	High risk	Both participants and those delivering the intervention were aware of those allocated to the intervention group
Blinding of outcome assessment (detection bias) All outcomes	Low risk	“The testers did not know whether the patients were assigned to the Exercise Group or the Control Group” (pg 470)
Incomplete outcome data (attrition bias) All outcomes	High risk	Commenced: 20; completed: 14; attrition: 6 (30%)
Selective reporting (reporting bias)	Low risk	No protocol paper was registered, but all outcomes listed in the paper appear to have been reported
Other bias	Unclear risk	None noted

Cambach 1997

Methods	Study design: RCT
Participants	<p>Setting: 8 community-based local physiotherapy practices in The Netherlands</p> <p>Inclusion criteria:</p> <ul style="list-style-type: none"> • Evidence of dyspnoea and decreased exercise tolerance as a result of obstructive lung disease • Age 18-75 years • Ability to travel independently to the physiotherapy practice • Medication prescribed by a pulmonary physician; motivation to improve self-care • Informed consent <p>Exclusion criteria:</p> <ul style="list-style-type: none"> • Cardiac complaints or locomotor disabilities • Hypercapnia; arterial carbon dioxide tension (PaCO₂) > 6.0 kPa (45 mmHg))

	and/or hypoxia; arterial oxygen tension (PaO ₂ < 8.7 kPa (65 mmHg)) during rest and/or maximal bicycle exercise testing Participant status: Age, (years± SD): RG: 62 ± 5; CG: 62 ± 9 Gender (M/F): RG: 7/8; CG: 6/2 FEV ₁ % predicted (± SD): RG: 59% ± 16; CG: 60% ± 23 Participants randomly assigned: Randomised: 99 Analysed: Rehab: 15 Control: 8	
Interventions	Pulmonary rehabilitation: community based LLE, ULE, Edu, IMT Duration: 12 weeks. (3 days a week for 90 minutes) Usual care: medication management only	
Outcomes	Assessment: baseline, 3 months 6MWT, CRQ, ICET	
Notes		
<i>Risk of bias</i>		
Bias	Authors’ judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	“Within each physiotherapy practice, four out of eight patients were randomly allocated to group RC, and four patients to group CR (block randomisation procedure; four closed envelopes for condition RC and four closed envelopes for condition CR) Baseline assessments were carried out prior to randomisation” (pg 105)
Allocation concealment (selection bias)	Low risk	Study investigators unaware as to order of treatment group assignment “four closed envelopes for condition RC and four closed envelopes for condition CR” (pg 105)
Blinding of participants and personnel (performance bias) All outcomes	High risk	Both participants and those delivering the intervention were aware of those allocated to the intervention group
Blinding of outcome assessment (detection bias) All outcomes	High risk	Outcome assessments: not blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	No information available

Selective reporting (reporting bias)	Low risk	No protocol paper was registered, but all outcomes listed in the paper appear to have been reported
Other bias	Low risk	None identified

Casaburi 2004

Methods	Study design: RCT into 4 groups	
Participants	Setting: out-patient, Los Angeles Inclusion criteria: <ul style="list-style-type: none">• 55 to 80 years, FEV₁ of 60% predicted or less (13) and FEV₁ to vital capacity ratio of ≤ 60%• Screening serum testosterone was ≤ 400 ng/dL Exclusion criteria: <ul style="list-style-type: none">• Significant cardiovascular or orthopaedic impairment• Body weight < 75% or > 130% of ideal• Symptomatic benign prostatic hyperplasia, prostate cancer history, serum prostate specific antigen > 4 g/L or haemoglobin > 16 g/dL Participant status: Age (years± SD): RG: 69 (10); CG: 68 (9) Gender (M/F):RG: 12/0; CG: 12/0 FEV ₁ % predicted: RG: 36% (9); CG: 39% (12) Participants randomly assigned: Randomised: 26 Analysed: Rehab: 12 Control: 12	
Interventions	Pulmonary rehabilitation: out-patient (hospital) LLE, nutritional instruction provided Duration: 10 weeks (3 sessions/wk) Usual care: Placebo injections and no training	
Outcomes	Assessment: baseline and 10 weeks Peak work rate	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	“Subjects were randomly assigned to treatment groups based on randomisation tables; randomisation was stratified for age < or ≥ 67 years and FEV ₁ < or ≥ 40%

		predicted" (supplement)
Allocation concealment (selection bias)	Low risk	Study investigators unaware as to order of treatment group assignment (from study author)
Blinding of participants and personnel (performance bias) All outcomes	High risk	As a result of the nature of the intervention, it was not possible to blind participants to their allocation of exercise or to blind those delivering the exercise
Blinding of outcome assessment (detection bias) All outcomes	Low risk	"Investigators and study coordinators were blinded as to whether subjects received testosterone or placebo" (supplement)
Incomplete outcome data (attrition bias) All outcomes	Low risk	Commenced: 53; completed: 47 (88.7%); attrition: 6 (11.3%)
Selective reporting (reporting bias)	Low risk	No protocol paper was registered, but all outcomes listed in the paper appear to have been reported
Other bias	Low risk	None identified

Casey 2013

Methods	Study design: 2-Arm, cluster-randomised controlled trial
Participants	<p>Setting: community based, West of Ireland</p> <p>Inclusion criteria:</p> <ul style="list-style-type: none"> Postbronchial dilator FEV₁/FVC ratio < 70%* unless BMI > 30, in which case FEV₁/FVC ratio > 70% is acceptable provided other criteria are fully met and the postbronchial dilator predicted value of FEV₁ ≥ 30% and ≤ 80% <p>Exclusion criteria:</p> <ul style="list-style-type: none"> Underlying co-morbidities or mental health problems (based on the recorded judgement of practice staff), which are likely to impair their capacity to successfully participate in or assimilate new information as part of the rehabilitation programme, or which may pose a risk to health <p>Participant status:</p> <p>Age (years± SD): RG: 68.8 ±10.2; CG: 68.4 ± 10.3</p> <p>Gender (M/F): RG: 117/61; CG: 106/66</p> <p>FEV₁ % (pred ± SD): RG: 57.6 ±14.3 ; CG: 59.7 ±13.8</p> <p>Participants randomly assigned:</p> <p>Randomised: 350 (16 clusters in control and 16 clusters in intervention) (participants: 178 intervention; 172 control)</p> <p>Analysed:</p> <p>Rehab: 178</p> <p>Control: 172</p>
Interventions	Pulmonary rehabilitation: community based, structured, nurse-led and delivered in the primary healthcare setting

Casey 2013 (Continued)

	Aerobic exercise, ULE, LLE, Edu, phone support, respiratory muscle training Duration: 8 weeks, 2 hours per week Usual care: routine GP care	
Outcomes	Assessment: baseline and 12 weeks Incremental shuttle walking test, CRQ, Self-Efficacy for Managing Chronic Disease 6-item scale EuroQol EQ-5D, utilisation of healthcare service	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Random allocation using computerised random sequence generation" (Casey 2013 , pg 3)
Allocation concealment (selection bias)	Low risk	"Group allocation concealment was achieved by giving responsibility for computerised allocation sequence generation and group allocation to a researcher independent of the research team and blinded to baseline outcome data" (Casey 2013 , pg 3)
Blinding of participants and personnel (performance bias) All outcomes	High risk	As a result of the nature of the intervention, unable to blind participants
Blinding of outcome assessment (detection bias) All outcomes	Low risk	"Research assistants trained in outcome assessment, blinded to group allocation" (Casey 2013 , pg 3)
Incomplete outcome data (attrition bias) All outcomes	High risk	Commenced: 350; completed: 277 (79%) ; attrition: 73 (21%)
Selective reporting (reporting bias)	Low risk	Outcomes reported matched the protocol
Other bias	Low risk	None identified

Methods	Study design: RCT; randomisation into 3 groups	
Participants	Setting: 2 centres in Spain Inclusion criteria: <ul style="list-style-type: none">• Dyspnoea (MMRC grades II-III)• Current non-smoker status• Age 60-80 years Exclusion criteria: <ul style="list-style-type: none">• Never smoked• Exacerbation of symptoms in the preceding 3 months• Co-existing conditions that might limit exercise tolerance Participant status: Age (years): PG: 68 (7); CG: 69 (5) Gender (M/F): all male FEV ₁ % (pred): RG: 47.8 (5); REG: 44.3 (11.9); CG: 38.7 (5) Participants randomly assigned: Randomised: 36 Combined resistance and endurance group: 14 Resistance alone group: 14 Control: 8 Did not include anyone who did not finish the intervention	
Interventions	Pulmonary rehabilitation: out-patient programme (hospital-based PR); 3 groups: resistance training alone (n = 14); combined resistance and endurance training (n = 14); and control group (n = 8) Duration: 12 weeks. (twice a week 45-60 minutes) Usual care	
Outcomes	Assessment: baseline and 12 weeks CRQ, 6MWT	
Notes	Combined group of REG/RG used in the analysis	
Risk of bias		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"For each subject included in the study, a researcher picked closed ticket with a number inside (from 1 to 3). The number corresponded to one of the three study groups" (additional information from study author)
Allocation concealment (selection bias)	Low risk	Allocation: closed ticket with a number inside (additional information from study author)

Blinding of participants and personnel (performance bias) All outcomes	High risk	As a result of the nature of the intervention, it is not possible to blind participants
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Yes, according to the study authors
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Did not include anyone who did not finish the intervention; unclear as to attrition
Selective reporting (reporting bias)	Low risk	Provided summary of all outcomes
Other bias	Low risk	

Chan 2011

Methods	Study design: single-blind, randomised controlled trial Randomly assigned to 1 of 3 groups (TCQ group, exercise, control)
Participants	Setting: 5 general outpatient clinics in Hong Kong Inclusion criteria: <ul style="list-style-type: none"> • Clinically diagnosed with COPD according to the ATS Exclusion criteria: <ul style="list-style-type: none"> • Could not walk independently • Suffered from severe sensory or cognitive impairment • Symptomatic ischaemic heart disease • Practiced TCQ within a year prior Participant status: Age (years \pm SD): RG: 73.6 \pm 7.5; CG: 73.6 \pm 7.4 Gender (M/F): RG: 61/8; CG: 58/9 FEV ₁ % (pred \pm SD): RG: 91 \pm .39; CG: 89 \pm .39 Participants randomly assigned: Randomised: 206 (TCQ 70, exercise 69, control 67) Analysed: (only exercise group) Rehab:69 Control: 67
Interventions	Pulmonary rehabilitation: community (primary care setting) ULE, LLE, respiratory muscle training (Tai chi Qigong + exercise) Duration: completed 60 minutes twice a week for 3 months Usual care: instructed to maintain usual activities
Outcomes	Assessment: baseline and 3 months Spirometry results, 6MWD, SGRQ, multi-dimensional scale of perceived social support (MSPSS) Secondary outcomes Number of exacerbations, hospital admissions, Borg scale, SaO ₂

Notes	TCQ group not included in the analysis	
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Random allocation was done using a randomizer software" (pg 5)
Allocation concealment (selection bias)	Unclear risk	Not informed
Blinding of participants and personnel (performance bias) All outcomes	High risk	As a result of the nature of the intervention, unable to blind participants and those delivering the intervention
Blinding of outcome assessment (detection bias) All outcomes	Low risk	"Research assistants (RAs) for data collection were blind to the study in order to minimize researcher bias" (pg 6)
Incomplete outcome data (attrition bias) All outcomes	High risk	Commenced: 206; completed: 158 (76.7%); attrition: 48 (23.3%)
Selective reporting (reporting bias)	Low risk	All outcomes were reported between Chan 2010 and Chan 2011 articles and protocol paper
Other bias	Low risk	None noted

Chlumsky 2001

Methods	Study design: RCT into 2 groups
Participants	<p>Setting: out-patient</p> <p>Inclusion criteria:</p> <ul style="list-style-type: none"> Moderate to severe COPD <p>Exclusion criteria:</p> <p>Participant status:</p> <p>Age (years \pm SD): RG: 63 \pm11 ; CG: 65 \pm13</p> <p>Gender (M/F): RG: 12/1; CG: 5/1</p> <p>FEV₁ % (pred \pm SD): RG: 43% \pm21; CG: 51% \pm17</p> <p>Participants randomly assigned:</p> <p>Randomised: 19</p> <p>Analysed:</p> <p>Rehab: 13</p> <p>Control: 6</p>

Chlumsky 2001 (Continued)

Interventions	Pulmonary rehabilitation: outpatient hospital LLE, BE Duration: 8 weeks (60 minutes a week) Usual care: conventional care	
Outcomes	Assessment: baseline and 8 weeks ICET, SGRQ, 6MWT	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	“Randomized using specific PC program taking into consideration severity of bronchial obstruction and aimed at desired ratio 2:1” (letter from study author)
Allocation concealment (selection bias)	Unclear risk	No information provided
Blinding of participants and personnel (performance bias) All outcomes	High risk	Both participants and those delivering the intervention had to be aware of those who were in the intervention group
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information provided
Incomplete outcome data (attrition bias) All outcomes	Low risk	No information provided in relation to attrition, and no indication in results that any participants did not complete the second assessment
Selective reporting (reporting bias)	Low risk	No trial registration protocol was found at http://www.controlled-trials.com/mrct/ or www.who.int/trialsearch (searched for author names and parts of title of paper or intervention)
Other bias	Low risk	None noted

Clark 1996

Methods	Study design: RCT	
Participants	Setting: hospital in Glasgow recruited from a hospital chest clinic; recruited for home-based exercise Inclusion criteria: <ul style="list-style-type: none">• COPD as defined by the American Thoracic Society• Minimum treatment consisted of inhaled bronchodilator and inhaled steroid; maximum treatment included nebulised bronchodilators and long-term oral steroids Exclusion criteria: Participant status: Age (years± SD): RG: 58 ± 8 ; CG: 55 ± 8 Gender (M/F): N/A FEV ₁ ± SD : RG: 1.72 L ± 0.83; CG: 1.44 L ±0.59 Participants randomly assigned: Randomised: 48 Analysed: Rehab: 32 Control: 16	
Interventions	Pulmonary rehabilitation: home exercise LLE, ULE Duration: 12 weeks once a week Usual care: Control group asked to continue with their usual daily routine	
Outcomes	Assessment: baseline and 12 weeks ICET, ITT QoL: not measured	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Information not available “The 48 patients were randomly allocated into training (n=32) or control (n=16) groups, with a 2:1 training versus control ratio” (pg 2591)
Allocation concealment (selection bias)	Unclear risk	Information not available
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants undertaking the exercise had to be aware that they were receiving same
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not mentioned whether assessors were blinded

Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No account provided of any attrition after allocation; difficult to interpret from the graphs and tables how many completed
Selective reporting (reporting bias)	Low risk	No protocol paper was registered, but all outcomes listed in the paper appear to have been reported
Other bias	Low risk	None noted

Cochrane 2006

Methods	Study design: RCT, randomly assigned to 1 of 4 interventions
Participants	<p>Setting: North Tyneside and South Northumberland from primary and secondary care</p> <p>Inclusion criteria:</p> <ul style="list-style-type: none"> • Males and females between the ages of 40 and 85 years (inclusive) • Diagnosis of COPD ($FEV_1 < 80\%$ of predicted and FEV_1/FVC ratio $< 70\%$) <p>Exclusion criteria:</p> <ul style="list-style-type: none"> • Uncontrolled angina • Unable to mobilise (because of severe COPD or other disability) • Had previously attended pulmonary rehabilitation • Current exacerbation of COPD (antibiotics and/or steroids in previous 6 weeks) • Other co-morbidities or communication difficulties that prevented rehabilitation <p>Participant status:</p> <p>Age (years \pm SD): 68.9 \pm 7.3 across all groups</p> <p>Gender:</p> <p>male 113 (44.1%): combined 32, exercise 32, CBSM 31, cont 18</p> <p>Female 143 (55.9%): combined 42, exercise 35, CBSM 33, cont 32</p> <p>FEV_1 % (pred \pm SD): 52.4% \pm 15.7 across all groups</p> <p>Participants randomly assigned:</p> <p>Commenced: 256</p> <p>Group 1: allocated combined: 74</p> <p>Group 2: allocated exercise: 67</p> <p>Group 3: allocated CBMS: 65</p> <p>Group 4: allocated control: 50</p>
Interventions	<p>Pulmonary rehabilitation: out-patient programme (hospital-based PR)</p> <p>Aerobic, ULE, LLE, cognitive behavioural self-management</p> <p>Duration: 6 weeks (twice weekly, sessions lasting 2 hours)</p> <p>Usual care: This group of participants received no intervention, except standard care</p>
Outcomes	<p>Assessment: baseline and 6 weeks, 6, 12 months</p> <p>CRQ, Short Form-12 (SF-12), Psychological State Hospital Anxiety and Depression Scale, COPD Self-Efficacy Scale (COPD-SES)</p>
Notes	Incomplete results available for analysis of CRQ (reported as medians)
Risk of bias	

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"The random allocation sequence was generated using cards numbered one to four, which were picked at random. Randomisation was stratified according to site and cohort. There were different sequences for each site (Northumberland and North Tyneside) and a new sequence was started for each of the five cohorts" (pg 34)
Allocation concealment (selection bias)	Low risk	Sealed envelopes: "Letters detailing the group the subject had been randomised to and details of the intervention were then placed in envelopes. Only the patient ID number was visible on the outside of the envelopes" (pg 34)
Blinding of participants and personnel (performance bias) All outcomes	High risk	"Study participants and the practitioners running the interventions could not be blinded to which intervention they were receiving" (pg 34)
Blinding of outcome assessment (detection bias) All outcomes	Low risk	"However, both the subjects and the researchers were blinded to the results of previous assessments (they were not allowed to see previous answers to questionnaires for example)" (pg 34)
Incomplete outcome data (attrition bias) All outcomes	High risk	Commenced: 256; completed: 46 (57%); attrition: 43%
Selective reporting (reporting bias)	Low risk	Appeared to report what had been identified for reporting
Other bias	Low risk	None reported

Cockcroft 1981

Methods	Study design: RCT The first 20 were allocated entirely randomly, and the remaining 19 by a method known as "minimisation," which ensured an even spread of certain variables between groups Randomisation process: sealed envelopes Outcome assessments: blinded
Participants	Setting: in-patient graduated exercise Inclusion criteria: <ul style="list-style-type: none"> Breathless on exertion but no upper limit (FEV₁) for entry into the study

	Exclusion criteria: <ul style="list-style-type: none">• Men over the age of 70 years• Other disabling conditions such as severe arthritis• Those who required domiciliary oxygen Participant status: Age (years ± SD): RG: 61± 5; CG: 60 ± 5 Gender (M/F): RG: 18/0; CG: 16/0 FEV ₁ ± SD: RG: 1.53 L ±0.70; CG: 1.32 L ± 0.44 Participants randomly assigned: Randomised: 39 Analysed: Rehab: 18 Control: 16	
Interventions	Pulmonary rehabilitation: out-patient rehabilitation centre LLE, ULE Duration: 6 weeks Usual care: given no special advice to exercise	
Outcomes	Assessment: baseline and 2, 4 months 12-Minute WT, ITT Interviews, POMS, Eysenck	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation process: sealed envelopes (letter from study author)
Allocation concealment (selection bias)	Low risk	Study investigators unaware as to order of treatment group assignment (Cochrane Grade A)
Blinding of participants and personnel (performance bias) All outcomes	High risk	As participants had to undertake exercise, they were aware of the group allocation
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information on blinding
Incomplete outcome data (attrition bias) All outcomes	Low risk	Commenced: 39; 3completed: 4; attrition: 12%
Selective reporting (reporting bias)	Low risk	No protocol paper was registered, but all outcomes listed in the paper appear to have

Cockcroft 1981 (Continued)

		been reported
Other bias	Low risk	Gender selection: male only

De Souto Araujo 2012

Methods	<p>Study design: RCT; participants were allocated to 3 experimental groups: control group (CG), floor group (FG) and aquatic group (AG)</p> <p>The randomisation process was conducted by a researcher who was not involved in data collection, through the use of opaque envelopes sealed and numbered consecutively in the ratio 1:1:1 and containing study group assignment</p>
Participants	<p>Setting: Brazil</p> <p>Inclusion criteria:</p> <ul style="list-style-type: none"> • Diagnosis of moderate to severe COPD • Informed consent • Clinically stable without periods of exacerbation for at least 8 weeks • Non-smokers or ex-smokers for at least 3 months • Free of lung infection • Medical supervision and authorisation <p>Exclusion criteria:</p> <ul style="list-style-type: none"> • Presented with exacerbation of the disease • Neuromuscular, renal and cardiac disease • Uncontrolled hypertension and diabetes mellitus • Did not perform functional tests or did not complete the 24 sessions <p>Participant status:</p> <p>Age (years): RG: [FG: 56.9; AG: 62.4]; CG: 71.1</p> <p>Gender (M/F): RG:[FG: 8/5; AG: 4/4]; CG: 8/3</p> <p>FEV₁ % (pred± SD): RG:[FG: 39.2 ± 11.4; AG: 43.9 ± 10.3]; CG: 45.1 ± 12.6</p> <p>Participants randomly assigned:</p> <p>32 participants were randomly assigned</p> <p>Analysed:</p> <p>Floor group (FG): 13</p> <p>Aquatic group (AG): 8</p> <p>Control group (CG): 11</p>
Interventions	<p>Pulmonary rehabilitation:</p> <p>Low-intensity water and floor exercises on COPD</p> <p>Duration: 8 weeks (3 times: Each session lasted 1 hour and 30 minutes)</p> <p>Usual care</p>
Outcomes	<p>Assessment:</p> <p>baseline and 8 weeks</p> <p>(6MWT), BODE Index, SGRQ</p>
Notes	Combined 2 intervention groups for analysis
Risk of bias	

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	The randomisation process was conducted by a researcher not involved in data collection (contact with study authors)
Allocation concealment (selection bias)	Low risk	Sealed envelopes (contact with study authors)
Blinding of participants and personnel (performance bias) All outcomes	High risk	Unable to blind participants because of the nature of the condition
Blinding of outcome assessment (detection bias) All outcomes	Low risk	All evaluations (initial and final) were performed by a single investigator, who did not know to which group participants were allocated
Incomplete outcome data (attrition bias) All outcomes	High risk	42 participants randomly assigned; losses: 10 Attrition: 24%
Selective reporting (reporting bias)	Low risk	It was reported that all said they would
Other bias	Low risk	None noted

Deering 2011

Methods	Study design: RCT; randomly assigned to 3 groups: controls, PR and acupuncture and PR Randomisation occurred with the use of a random numbers table
Participants	Setting: Dublin (identified via referral from the respiratory service) Inclusion criteria: <ul style="list-style-type: none"> • Diagnosis of COPD based on GOLD • Referred by a respiratory consultant or Outreach Team • MRC score of ≥ 3 • Ability to mobilise independently • Motivated to exercise independently Exclusion criteria: <ul style="list-style-type: none"> • Acute exacerbation within the past 4-6 weeks • Evidence of ischaemic heart disease • Uncontrolled hypertension • Insulin-dependent diabetes mellitus or musculoskeletal/neurological • Inability to exercise independently • Previous attendance at PR programme Participant status: Age (years \pm SD): RG: [PR only 67.7 \pm 5.3, PR + Acu 65.1 \pm 9.7]; CG: 68.6 \pm 5.5

	Gender (M/F): RG: [PR only 11/14, PR + Acu 8/8]; CG: 12/7 FEV ₁ % (pred ± SD): RG: [PR only 77.0 ±19 , PR + Acu 80.7 ± 24.2]; CG: 45.8 ± 18.3 Smokers, packs per year: RG: [PR only 51, PR + Acu 846.5]; CG: 46.2 Participants randomly assigned: 60 randomised (control 19, PR 25, 19 PR + Acu) Analysed: 14 control 11 PR	
Interventions	Pulmonary rehabilitation: out-patient programme (hospital-based PR) Aerobic, ULE, LLE, respiratory muscle training, Edu Duration: 7 weeks, 14 PR sessions Usual care: no specific intervention	
Outcomes	Assessment: Baseline, end of PR and 3-month follow-up St. George's Questionnaire Incremental shuttle walk test FEV ₁ , Pi Max Feree Living Physical Activity, EQ5D	
Notes	Only the PR group was reported on in the analysis	
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation occurred with use of a random numbers table
Allocation concealment (selection bias)	Unclear risk	No information available
Blinding of participants and personnel (performance bias) All outcomes	High risk	As a result of the nature of the intervention, it is not possible to blind participants or those delivering the programme
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Assessors and the medical team analysing the blood samples were blinded to the treatments received
Incomplete outcome data (attrition bias) All outcomes	High risk	Commenced: 44 in control and PR groups; assessed: 25 Attrition: 19 (42%)
Selective reporting (reporting bias)	Low risk	No protocol paper was registered, but all outcomes listed in the paper appear to have been reported

Other bias	Unclear risk	None identified
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Elci 2008

Methods	Study design: RCT; 2 groups Participants were randomly allocated to control or experimental groups with the use of number tables. Concealed until after allocation; once allocated, both participants and those delivering the intervention were aware of those in the intervention group	
Participants	Setting: <ul style="list-style-type: none">• Secondary care community hospital, Pulmonary Diseases Department, Turkey Inclusion criteria: <ul style="list-style-type: none">• Diagnosis of COPD• Absence of reversibility residence• Within the Malatya city boundary Exclusion criteria: <ul style="list-style-type: none">• Diagnosis of other respiratory disease such as tuberculosis or cancer• Inability to understand the pulmonary rehabilitation programme Participant status: Age (years \pm SD): RG: 59.67 \pm 8.6; CG: 58.08 \pm 11.45 Gender (M/F): RG: 33/6; CG: 33/6 FEV ₁ % (pred): RG: 47.7; CG: 46.28 FEV ₁ /FVC (\pm SD): RG: 55.46 \pm 8.79; CG: 55.10 \pm 7.17 Smokers %: RG: 33.3; CG: 20.5 Participants randomly assigned: 78 participants with COPD randomised: Analysed: 39 experimental group 39 control group	
Interventions	Pulmonary rehabilitation: combined home/community/out-patient Duration: 3 months; exercises twice a day for 10 minutes, 5 days a week, at home under the supervision of a relative All participants performed 24 sessions Aoribic, ULE, LLE, Edu Usual care: Control group received standard medical care	
Outcomes	Assessment: baseline,1 month, 3 months St. George's Questionnaire SF-36, HADS Hospital Anxiety and Depression, 6MWT, MMRC	
Notes		
Risk of bias		
Bias	Authors' judgement	Support for judgement

Elci 2008 (Continued)

Random sequence generation (selection bias)	Low risk	Randomly allocated to control or experimental groups with the use of number tables
Allocation concealment (selection bias)	Unclear risk	No information provided
Blinding of participants and personnel (performance bias) All outcomes	High risk	As a result of the nature of the intervention, participants had to be aware of their allocation
Blinding of outcome assessment (detection bias) All outcomes	Low risk	However, the nurse was blinded to the results of the SF-36, SGRQ, HADS and MMRC
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No account of attrition provided
Selective reporting (reporting bias)	Low risk	No protocol paper was registered, but all outcomes listed in the paper appear to have been reported
Other bias	High risk	Gender imbalance noted

Emery 1998

Methods	<p>Study design: RCT (3 groups: exercise, education and stress management (EXESM); education and stress management (control) Randomisation process: random numbers table Outcome assessments: blinded</p>
Participants	<p>Setting: out-patient Inclusion criteria:</p> <ul style="list-style-type: none"> • Stable COPD age > 50 years • Airflow obstruction demonstrated on spirometry • Clinical symptoms of COPD for longer than 6 months <p>Exclusion criteria:</p> <ul style="list-style-type: none"> • Significant cardiac disease or other diseases that might affect exercise tolerance or learning skills • Acute, reversible airway disease (asthma) without fixed airflow obstruction • Significant disabling disease such as tuberculosis, pulmonary • Fibrosis or cancer; unstable cardiac disorder during the previous 3 months • Medical conditions that limit participation in a regular exercise programme <p>Participant status: Age (years \pm SD): RG: 65 \pm 6; CG: 67 \pm 7 Gender (M/F): RG: 15/15; CG: 12/13 FEV₁ (\pmSD): RG: 1.29 L \pm 0.63; CG: 1.02 L \pm 0.37 Participants randomly assigned: Randomised: 79</p>

	Analysed: Rehab: 25 Control: 25	
Interventions	Pulmonary rehabilitation: 3 groups: floor group (FG), aquatic group (AG) and control group (out-patient) LLE, ULE, Edu, Psy Duration: 10 weeks (for 4 hours per day) Usual care: asked not to alter activities significantly during the 10-week study	
Outcomes	Assessment: baseline and after the 10-week intervention period ICET, SIP	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	From a random number schedule, printed on a piece of paper
Allocation concealment (selection bias)	Low risk	Study investigators unaware as to order of treatment group assignment (Cochrane Grade A)
Blinding of participants and personnel (performance bias) All outcomes	High risk	Concealed until after allocation; once allocated, both participants and those delivering the intervention were aware of those in the intervention group
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Technical staff conducting the assessments were not aware of group assignments
Incomplete outcome data (attrition bias) All outcomes	Low risk	Overall loss: 6 Attrition: 7.6%
Selective reporting (reporting bias)	Low risk	No protocol paper was registered, but all outcomes listed in the paper appear to have been reported
Other bias	Low risk	None noted

Methods	Study design: RCT (2 groups)	
Participants	Setting: out-patients and home patients recruited from Pulmonary Medicine Department in Goteborg, Sweden Inclusion criteria: <ul style="list-style-type: none">• Diagnosis of COPD• Age 47-75 years• FEV₁ < 50% (pred) after bronchodilator paO₂ of 8 kPa and stable condition Exclusion criteria: <ul style="list-style-type: none">• Disabling or severe disease other than COPD or the co-existence of other causes of impaired pulmonary function Participant status: Age (years ± SD): RG: 66 ± 5; CG: 67 ± 5 Gender (M/F): RG: 14/12; CG: 12/12 FEV ₁ % (pred): RG: 30.7; CG: 34.1 Smokers: RG: 6; CG: 4 Participants randomly assigned: Randomised: 55 Analysed: Rehab: 26 Control: 24	
Interventions	Pulmonary rehabilitation: out-patient and home based LLE, ULE, Edu, IMT Duration: 52 weeks (training at the physio department twice weekly for 6 weeks followed by once weekly for 6 weeks and every second week for 6 weeks, then monthly for the remainder of the year. Each session lasted 45 minutes Usual care: Control received usual out-patient care	
Outcomes	Assessment: baseline to 12 months 6-Minute WT, ICET SIP, SGRQ	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer random number tables
Allocation concealment (selection bias)	Low risk	Study investigators unaware as to order of treatment group assignment (Cochrane Grade A)
Blinding of participants and personnel (performance bias) All outcomes	High risk	Those receiving the programme had to be aware that they were receiving the intervention

Engström 1999 (Continued)

Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome assessments: blinded for HRQoL, not blinded for WT
Incomplete outcome data (attrition bias) All outcomes	Low risk	50 out of 55 completed (90.9%) Attrition rate: 9.1%
Selective reporting (reporting bias)	Low risk	No protocol paper was registered, but all outcomes listed in the paper appear to have been reported
Other bias	Low risk	None identified

Faager 2004

Methods	Study design: RCT (2 groups); 2 weeks after onset of oxygen therapy, 20 participants were randomly assigned to rehabilitation
Participants	<p>Setting: in-patient/home Department of Pulmonary Medicine of the Karolinska Hospital: over 2 years</p> <p>Inclusion criteria:</p> <ul style="list-style-type: none"> • Diagnosis of COPD • Established need for LTOT • Ability to move about with or without a walking frame • Willingness to participate in the study <p>Exclusion criteria:</p> <ul style="list-style-type: none"> • Symptomatic cardiac disease or neurological or orthopaedic mobility impairment <p>Participant status: Age (years \pm SD): RG: 72 \pm 9; CG: 70 \pm 8 Gender (M/F): RG: 3/7; CG: 3/7 FEV₁ % (pred \pm SD): RG: 26 \pm 7 ; CG: 28 \pm 6</p> <p>Participants randomly assigned: Randomised: 20 (RG: 10; CG: 10) Analysed: Rehab: 7 Control: 7</p>
Interventions	<p>Pulmonary rehabilitation: in-patient and home based Aerobic, ULE, LLE, Edu</p> <p>Duration: 8-Week programme with 1 training session a week; training took 90 to 120 minutes</p> <p>Usual care</p>
Outcomes	<p>Assessment: baseline and 8 weeks, 6 months CRQ, 6-Minute WT, spirometry, blood gas analyses, pulse oximetry, Hospital Anxiety and Depression Scale (HADS) Stanford Health</p>
Notes	

<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No clear statement on random sequence generation
Allocation concealment (selection bias)	Unclear risk	No detail re allocation concealment or how randomisation was done
Blinding of participants and personnel (performance bias) All outcomes	High risk	Both participants and those delivering the programme were aware of those included in the intervention group
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information provided
Incomplete outcome data (attrition bias) All outcomes	High risk	Commenced overall: 20; finished week 8: 14 Attrition: 30%
Selective reporting (reporting bias)	Low risk	No protocol paper was registered, but all outcomes listed in the paper appear to have been reported
Other bias	Low risk	None noted

Faulkner 2010

Methods	Study design: RCT (2 groups)
Participants	<p>Setting: recruited from primary care; 16 GP practices in Exeter</p> <p>Inclusion criteria:</p> <ul style="list-style-type: none"> • Clinical diagnosis of COPD, FEV₁/forced vital capacity (FVC) ratio \leq 70% • Smoking history > 10 pack-years • Symptoms considered to be inadequately controlled by short-acting bronchodilators • Willing and able to undertake a HEPA programme <p>Exclusion criteria:</p> <ul style="list-style-type: none"> • Body mass index (BMI) > 35 kg/m² • Recent respiratory tract infection • Oxygen desaturation (SaO₂) at rest < 90% • Prior participation in a PR programme • Serious co-morbid condition that would interfere with regular exercise training <p>Participant status: Age: not provided Gender (M/F): not provided</p>

	FEV ₁ % (pred): not provided Smokers: all current non-smokers Participants randomly assigned: Randomised: 20 (RG: 10; CG: 10) Analysed: Rehab:6 Control:8	
Interventions	Pulmonary rehabilitation: community (primary care setting) Exercise programme run in an exercise facility at a university Aerobic, ULE, LLE, Edu Duration: 8 weeks once-weekly 90-minute supervised exercise and education sessions delivered by a qualified exercise and healthcare practitioner Usual care: Control group received usual care. All were given tiotropium	
Outcomes	Assessment: baseline, 1 week post intervention CRQ, ISWT, lung information needs questionnaire (LINQ), HADS, 7-day physical activity recall questionnaire, physical self-perception profile (PSPP)	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation sequence, stratified for smoking status, computer generated by a statistician who was independent of the trial
Allocation concealment (selection bias)	Low risk	Group allocation was kept concealed by means of sealed envelopes, which were opened in sequence by the trial researcher following baseline assessment
Blinding of participants and personnel (performance bias) All outcomes	High risk	It was not possible to blind participants or GPs to group allocation
Blinding of outcome assessment (detection bias) All outcomes	High risk	Outcome assessors not blinded
Incomplete outcome data (attrition bias) All outcomes	High risk	20 randomly assigned; attrition: overall 6 (30%)
Selective reporting (reporting bias)	Low risk	All outcomes listed in the paper appear to have been reported

Other bias	Low risk	None noted
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Fernandez 2009

Methods	Study design: RCT (2 groups) performed in a 300-bed district hospital and involving patients with very severe COPD who received oxygen treatment
Participants	<p>Setting: Spanish study; 300-bed district hospital</p> <p>Inclusion criteria:</p> <ul style="list-style-type: none"> • Diagnosis of very severe COPD • Younger than 80 years of age • Stable COPD (2 months with no exacerbations) • Correct administration of pharmacological treatment • Home treatment with oxygen for at least 6 months <p>Exclusion criteria:</p> <ul style="list-style-type: none"> • Severe cardiovascular pathology, unstable angina or acute myocardial infarction, cerebrovascular accident • Physical or psychological disorder that impedes the practice of physical exercise <p>Participant status:</p> <p>Age (years \pm SD): RG: 66 \pm 8; CG: 70 \pm 5</p> <p>Gender (M/F): 1 woman, as the rest were men</p> <p>FEV₁ % (pred \pm SD): RG: 33 \pm 10; CG: 38 \pm 12</p> <p>FEV₁/FVC (\pm SD): RG: 42 \pm 10; CG: 42 \pm 11</p> <p>Participants randomly assigned:</p> <p>Randomised: 50 (RG: 30; CG: 20)</p> <p>Analysed:</p> <p>Rehab:27</p> <p>Control:14</p>
Interventions	<p>Pulmonary rehabilitation: home based</p> <p>Aerobic exercise, ULE, LLE, educational material, home physio visits</p> <p>Duration: received 2 one-hour sessions in the hospital. A minimum of 1 hour of exercise per day was indicated, for a minimum of 5 days per week</p> <p>Usual care</p>
Outcomes	<p>Assessment: baseline and Immediately post intervention (1 year)</p> <p>6MWT, SGRQ</p>
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not informed of process: only "randomly divided into 2 groups"
Allocation concealment (selection bias)	Unclear risk	Not informed

Fernandez 2009 (Continued)

Blinding of participants and personnel (performance bias) All outcomes	High risk	As a result of the nature of the intervention, unable to blind participants or those delivering the intervention
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not informed
Incomplete outcome data (attrition bias) All outcomes	Low risk	After 1 year, 41 participants completed (83.7%) Attrition: 16.3%
Selective reporting (reporting bias)	Low risk	No protocol paper was found, but all outcomes listed in the paper appear to have been reported
Other bias	High risk	All men; 1 woman excluded from analysis

Finnerty 2001

Methods	Study design: RCT (2 groups)
Participants	<p>Setting: recruited from an out-patient clinical at the Chester Hospital NHS Trust, UK</p> <p>Inclusion criteria:</p> <ul style="list-style-type: none"> • Long-standing airways disease, classified as COPD • Had therapy optimised • Given up smoking or prepared to make an active effort to stop smoking during the proposed programme <p>Exclusion criteria:</p> <ul style="list-style-type: none"> • Dementia or marked agitation or depression evident to investigators • Unstable medical condition, such as congestive cardiac failure, cor pulmonale, malignancy or cerebrovascular accident • Previously participated in a supervised respiratory rehabilitation programme <p>Participant status: Age (years \pm Sd): RG: 70.4 \pm 8.0; CG: 68.4 \pm 10.4 Gender (M/F): RG: 25/11; CG: 19/10 FEV₁ % (pred \pm SD): RG: 41.2 \pm 19.2; CG: 41.2 \pm 16.2 Smoking NO: RG: 2; CG: 6</p> <p>Participants randomly assigned: Randomised: 100 (27 did not attend initial assessment) Analysed: Rehab:36 Control: 29</p>
Interventions	<p>Pulmonary rehabilitation: 6-Week out-patient-based rehabilitation programme ULE, LLE, Edu</p> <p>Duration: 6-Week out-patient-based rehabilitation programme; 2 visits per week: 2-hour education visit and 1-hour exercise visit</p>

Finnerty 2001 (Continued)

	Usual care: Control group reviewed routinely as medical out-patients	
Outcomes	Assessment: baseline, 12 weeks and 24 weeks 6-Minute WT, SGRQ	
Notes	Jadad's score = 3	
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation was in blocks of 10, using random numbers
Allocation concealment (selection bias)	Low risk	Study investigators unaware as to order of treatment group assignment (Cochrane Grade A)
Blinding of participants and personnel (performance bias) All outcomes	High risk	As a result of the exercise programme, unable to blind allocation
Blinding of outcome assessment (detection bias) All outcomes	Low risk	"Both tests were supervised by a blinded observer who subsequently repeated these assessments"
Incomplete outcome data (attrition bias) All outcomes	High risk	100 randomly assigned; 55 completed (55%) Only 73 attended for initial assessment 45% attrition
Selective reporting (reporting bias)	Low risk	No protocol paper was found, but all outcomes listed in the paper appear to have been reported
Other bias	Low risk	None identified

Gohl 2006

Methods	Study design: RCT (2 groups)
Participants	<p>Setting: out-patient community, training in sports hall; Germany</p> <p>Inclusion criteria:</p> <ul style="list-style-type: none"> • Included participants suffered from medium to severe COPD • 50 to 75 years old <p>Exclusion criteria:</p> <ul style="list-style-type: none"> • Decompensated coronary heart disease, haemodynamically efficient cardiac arrhythmia or "Kartitiden," insufficiently adjusted arterial hypertension, global respiratory insufficiency, significant partial respiratory insufficiency (paO₂ < 50 mmHg and/or SaO₂ > 80% at rest), right heart overload due to pulmonary hypertension at

	rest (accelerative time > 100 m/s) <ul style="list-style-type: none">• Positive bronchodilation test showing an increase in FEV₁ > 15% exacerbated COPD• Severe obesity (BMI > 35)• Limited capacity on the bicycle ergometer Participant status: Age (years ± SD): RG: 62.5 ± 7; CG: 63.2 ± 8.5 Gender (M/F): RG: 6/4; CG: 7/2 FEV ₁ % (pred ± SD): RG: 53.4 ± 10.7; CG: 53.7 ± 5.8 Participants randomly assigned: Randomised: 34 (RG: 17; CG 17) Analysed: Rehab:10 Control: 9	
Interventions	Pulmonary rehabilitation: community, complex long-term training programme Aerobic exercise, ULE, LLE (escalating levels of activity over time) Duration: 12-month training programme Usual care: Control group did not receive therapy	
Outcomes	Assessment: Baseline and 12 months (end of intervention) 6MWT, St. George’s Questionnaire, SF-36, muscle force	
Notes		
<i>Risk of bias</i>		
Bias	Authors’ judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Assigned to training group or control group at random (chosen by lot)
Allocation concealment (selection bias)	Unclear risk	Not provided
Blinding of participants and personnel (performance bias) All outcomes	High risk	As a result of the nature of the intervention, it is not possible to blind participants or those delivering the intervention
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not provided
Incomplete outcome data (attrition bias) All outcomes	High risk	Commenced: 34; completed: 19; lost: 15 Attrition: 44%
Selective reporting (reporting bias)	Low risk	No protocol paper was found, but all outcomes listed in the paper appear to have been reported

Other bias	Low risk	None noted
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Goldstein 1994

Methods	Study design: RCT (2 groups) Randomisation process: random numbers table Outcome assessments: blinded	
Participants	Setting: in-patient/out-patient; Canada Inclusion criteria: <ul style="list-style-type: none">Severe stable COPD (forced expiratory volume in 1 second (FEV₁) < 40% predicted; FEV/forced vital capacity (FVC) < 0.7)Non-smoker for a minimum of 2 monthsDyspnoea in 3 or more activities of daily livingAbility to communicate in English. Exclusion criteria: <ul style="list-style-type: none">Participated in a supervised respiratory rehabilitation programme within the previous 2 yearsAssociated medical conditions that might limit exercise tolerance or cognitive functioning Participant status: Age (years ± SD): RG: 66 ± 7; CG: 65 ± 8 Gender (M/F): RG: 21/17; CG: 17/23 FEV ₁ % (pred ± SD): RG: 34.8 ±14.5; CG: 34.6 ± 11.8 FEV ₁ /FVC: RG: 36.8 ± 9.5; CG: 38.8 ± 12.4 Smoking packs (± SD): RG: 58 ± 24; CG: 51 ± 26 per year Participants randomly assigned: Randomised: 89 Analysed: Rehab: 38 Control: 40	
Interventions	Pulmonary rehabilitation: in-patient/home based Aerobics, LLE, ULE, BE, Edu, Psy Duration: 2 months of in-patient rehabilitation followed by 4 months of out-patient care Usual care: Control group received conventional care from general practitioner and respiratory specialist	
Outcomes	Assessment: baseline and 24 weeks 6-Minute WT, ICET, SSCET, CRQ, BDI/TDI	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement

Goldstein 1994 (Continued)

Random sequence generation (selection bias)	Low risk	Used random tables for allocation
Allocation concealment (selection bias)	Low risk	Study investigators unaware as to order of treatment group assignment (Cochrane Grade A)
Blinding of participants and personnel (performance bias) All outcomes	High risk	Both participants and those delivering the intervention were aware of the allocation of participants
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Investigator carrying out outcome assessments blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	89 randomised and 78 completed Attrition: 11 (12%)
Selective reporting (reporting bias)	Low risk	No protocol paper was found, but all outcomes listed in the paper appear to have been reported
Other bias	Low risk	None noted

Gomez 2006

Methods	Study design: RCT (3 groups); PR for 3 months and rehabilitation maintenance for 12 months (RHBM group). Second group received PR for 3 months only (RHB group) and the third was the control
Participants	<p>Setting: recruited by family physicians from 7 primary care practices in Palma de Mallorca, Spain</p> <p>Inclusion criteria:</p> <ul style="list-style-type: none"> • 35 to 74 years old • Moderate COPD according to GOLD criteria • Postbronchodilator results of FEV₁/FVC < 0.7, FEV₁ values between 50% and 80% • Smokers or non-smokers <p>Exclusion criteria:</p> <ul style="list-style-type: none"> • Any musculoskeletal condition that prevented exercising and walking test assessments • Terminal illness or other severe disease at the time of enrolment <p>Participant status: Age (years): RG (RHB: 64.1; RHBM: 64.9); CG: 63.4 Gender (M/F): RG: 39/9; CG: 19/4 FEV₁ % (pred): RG: 74 (Range 66.5-81.5); CG: 60.1 (Range 55.6-64.4) FEV₁/FVC: RG: 61.2; CG: 59.1</p> <p>Participants randomly assigned:</p>

	Randomised: 97 (33 RHB group and 32 RHBM; control 32) Analysed: Rehab:36 Control: 14	
Interventions	Pulmonary rehabilitation: community (primary care setting) Aerobic exercise, ULE, LLE, educational material Duration: 3 months; rehabilitation maintenance for 12 months Usual care: Group received routine care without rehabilitation	
Outcomes	Assessment: Baseline, 3 months and 12 months CRQ, pulmonary function tests, 6MWT	
Notes	Analyses completed on 3-month results for combined RHB and RHBM groups	
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Centrally administered, computer-generated block randomisation scheme using blocks of 6 with EPIDAT, stratified according to participating site
Allocation concealment (selection bias)	Low risk	See above
Blinding of participants and personnel (performance bias) All outcomes	High risk	As a result of the nature of the intervention, unable to blind participants and those delivering the intervention
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Health staff members involved in follow-up (a psychologist and a nurse) were blinded to participant assignment
Incomplete outcome data (attrition bias) All outcomes	High risk	Out of 97, only 50 at 3-month evaluation Attrition: 47 (48%)
Selective reporting (reporting bias)	Low risk	Trial registration (ISRCTN94514482); all outcomes stated in the study appear to have been measured
Other bias	Low risk	None noted

Methods	Study design: RCT (2 groups)
Participants	<p>Setting: out-patient: referred from an outpatient department in Leuven, Belgium</p> <p>Inclusion criteria:</p> <ul style="list-style-type: none"> • Younger than 75 years of age; forced expiratory volume in 1 second (FEV₁) less than 65% of predicted value • Stable clinical condition at inclusion <p>Exclusion criteria:</p> <ul style="list-style-type: none"> • Infection or COPD exacerbation in the previous 4 weeks • Severe medical problems, such as heart failure, myocardial infarction, cerebrovascular disease, cancer or orthopaedic disorders <p>Participant status:</p> <p>Age (years \pm SD): RG: 60 \pm 9; CG: 63 \pm 7 Gender (M/F): RG: 31/6; CG: 30/3 FEV₁ % (pred \pm SD): 41 \pm 16; RG: CG: 43 \pm 12</p> <p>Participants randomly assigned:</p> <p>Randomised: 100 Analysed: Rehab: 34 Control: 28</p>
Interventions	<p>Pulmonary rehabilitation: outpatient sessions; cycling, treadmill walking, stair climbing and peripheral muscle training LLE, ULE</p> <p>Duration: 24 weeks: 3 times a week in the first 3 months; during subsequent 3 months, training frequency was reduced to twice weekly. Each session had a duration of 1.5 hours</p> <p>Usual care: usual medical care</p>
Outcomes	<p>Assessment: baseline and at 6 months and 18 months</p> <p>6-Minute WT, ICET, CRQ</p> <p>Isometric quadriceps strength, inspiratory and expiratory muscle strength</p>
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation process: sealed envelopes
Allocation concealment (selection bias)	Low risk	Study investigators unaware as to order of treatment group assignment (Cochrane Grade A)
Blinding of participants and personnel (performance bias) All outcomes	High risk	Both participants and those delivering the intervention were aware of the allocation of participants

Gosselink 2000 (Continued)

Blinding of outcome assessment (detection bias) All outcomes	High risk	Outcome assessments: not blinded
Incomplete outcome data (attrition bias) All outcomes	High risk	Commenced: 100; 6 months: 62; remaining: 62% Attrition: 38%
Selective reporting (reporting bias)	Low risk	No protocol paper was found, but all outcomes listed in the paper appear to have been reported
Other bias	Low risk	None noted

Gottlieb 2011

Methods	Study design: RCT (2 groups) Single-centre, randomised, placebo-controlled, unblinded clinical trial
Participants	Setting: patients listed with 56 GPs in Copenhagen, Denmark Inclusion criteria: <ul style="list-style-type: none"> • Diagnosis of moderate COPD • Motivation for pulmonary rehabilitation Exclusion criteria: <ul style="list-style-type: none"> • Co-morbidity contraindicating rehabilitation • Participation in pulmonary rehabilitation within the past year • Cognitive disorders limiting ability to participate in physical training and educational sessions Participant status: Age (years, Range): RG: 74.1 (66-82); CG: 73.2 (67-88) Gender (M/F): RG: 7/15; CG: 7/13 FEV ₁ % (pred ± SD): RG: 64.27 ± 7.9; CG: 67.05 ± 8.8 FEV ₁ /FVC (± SD): RG: 0.54 ± 0.07; CG: 0.6 ± 0.1 Smokers: RG: 11; CG: 9 Participants randomly assigned: Randomised: 61 (RG: 35; CG: 26) Analysed: Rehab: 22 Control: 20
Interventions	Pulmonary rehabilitation: community Aerobic exercise, ULE, LLE, Edu, follow-up call Duration: 7 weeks; two 90-minute sessions a week Usual care: standard COPD care received from GP
Outcomes	Assessment: baseline and 6 months 6MWT, MRC, SGRQ
Notes	

<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation was performed using sealed opaque envelopes randomly assigned to participants
Allocation concealment (selection bias)	Low risk	
Blinding of participants and personnel (performance bias) All outcomes	High risk	Both participants and those delivering the intervention were aware of the allocation of participants
Blinding of outcome assessment (detection bias) All outcomes	High risk	Unblinded clinical trial
Incomplete outcome data (attrition bias) All outcomes	High risk	61 randomly assigned, 42 completed (68%) Attrition: 32%
Selective reporting (reporting bias)	Low risk	Study authors appear to have reported what they said they would at the beginning of the article
Other bias	Low risk	None identified

Griffiths 2000

Methods	Study design: RCT (2 groups)
Participants	<p>Setting: recruited from local hospitals and local general practices to participate; Wales Out-patient + Home-based follow-up</p> <p>Inclusion criteria:</p> <ul style="list-style-type: none"> • FEV₁ < 60% of predicted with < 20% reversibility • No change in symptoms or medication for 2 months <p>Exclusion criteria:</p> <ul style="list-style-type: none"> • Could not walk • Severe sensory or cognitive impairment or symptomatic ischaemic heart disease <p>Participant status: Age (years ± SD): RG: 68.2 ± 8.2; CG: 68.3 ± 8.1 Gender (M/F): RG: 57/36; CG: 54/37 FEV₁ % (pred ± SD): RG: 39.7 ± 16.2; CG: 39.4 ± 16.4 FEV₁ /FVC (± SD): RG: 0.49 ± 0.13; CG: 0.49 ± 0.13 Smoking, packs per year: RG: 43.5 (31.1); CG: 45.7 (21.9)</p> <p>Participants randomly assigned:</p>

	Randomised: 200 Analysed: Rehab: 93 Control: 91	
Interventions	Pulmonary rehabilitation: multi-disciplinary, out-patient/home based LLE, ULE, Edu, Psy, NS, SmC Duration: 6 weeks, 3 half-days per week; session 2 hours long; in addition encouraged to follow a home exercise routine Usual care: continued with usual out-patient or primary care follow-up	
Outcomes	Assessment: baseline and follow-up for 1 year Shuttle WT, CRQ, SF-36, SGRQ, HADS	
Notes	Jadad's score = 2	
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation process: sealed envelopes
Allocation concealment (selection bias)	Low risk	Study investigators unaware as to order of treatment group assignment (Cochrane Grade A)
Blinding of participants and personnel (performance bias) All outcomes	High risk	As a result of the nature of the intervention, it is not possible to blind participants or those delivering the intervention
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome assessments: blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	200 commenced; 180 completed Attrition: 10%
Selective reporting (reporting bias)	Low risk	No protocol paper was found, but all outcomes listed in the paper appear to have been reported
Other bias	Low risk	None noted

Methods	Study design: RCT (3 groups)	
Participants	Setting: patients from Ege University Hospital Turkey outpatient clinic admitted to the PR unit between January 2010 and November 2010 Inclusion criteria: <ul style="list-style-type: none">• Diagnosis of COPD• Evidence of nutritional depletion defined as meeting at least 1 of the following criteria (10):<ul style="list-style-type: none">◦ Body mass index (BMI/height squared) $\leq 21 \text{ kg/m}^2$, Fat Free Mass Index (FFM/height squared) $\leq 15 \text{ kg/m}^2$ for women or 16 kg/m^2 for men; or◦ BMI $\leq 25 \text{ kg/m}^2$ plus weight loss of at least 5% in 1 month, or at least 10% in 6 months, before admission Exclusion criteria: <ul style="list-style-type: none">• Disabling conditions (neuromuscular, malignant disorders, unstable cardiovascular disease, orthopaedic problems, severe pulmonary hypertension)• Unwilling to complete the programme• Suffering from acute exacerbation over the previous 4 weeks• Lack of motivation or poor compliance Participant status: Age (years \pm SD): RG: [PRNS: 64.0 ± 10.8 ; PR: 66.8 ± 9.6]; CG: 67.8 ± 6.6 Gender (M/F): RG: [PRNS 13/2; PR: 15/0]; CG: 16/0 FEV ₁ % (pred \pm SD): RG:[PRNS: 41.9 ± 10.8 ; PR: 41.9 ± 13.2]; CG: 39.3 ± 9.3 FEV ₁ /FVC (\pm SD): RG: [PRNS: 53.4 ± 15.8 ; PR: 49.0 ± 6.7]; CG: 46.7 ± 7.2 Participants randomly assigned: Randomised: 46 Analysed: Rehab: PRNS: 15; PR: 15 Control: 16	
Interventions	Pulmonary rehabilitation: out-patient programme (hospital based). Pulmonary rehabilitation and nutritional support (Pr Alone (PR) or PR and nutritional support (PRNS)) Aerobic exercise, ULE, LLE, educational material, nutritional support Duration: 8 weeks Usual care: usual medical standard care	
Outcomes	Assessment: baseline and following 8 weeks of PR MRC, 6MWT, ISWT, ESWT, SGRQ, HADS	
Notes	Reported results using combined group PR + PRNS	
Risk of bias		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Eligible patients were randomly assigned in a 1:1:1 ratio with the use of sealed envelopes
Allocation concealment (selection bias)	Low risk	As above

Blinding of participants and personnel (performance bias) All outcomes	High risk	As a result of the nature of the intervention, unable to blind participants or those delivering the intervention
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	No attrition reported
Selective reporting (reporting bias)	Low risk	No protocol paper was found, but all outcomes listed in the paper appear to have been reported
Other bias	High risk	All men; 15 in PR group, 15 in control. 2 women in PRNS

Güell 1995

Methods	Study design: RCT (2 groups) Randomisation process: random numbers table Outcome assessments: blinded
Participants	Setting: out-patient: secondary care respiratory clinic in Barcelona Inclusion criteria: <ul style="list-style-type: none"> • Participants older than 75 years • FEV₁ 70% of reference values, FEV₁/FVC 65%, PaO₂ 55 mmHg at rest • No indication for prescribing home oxygen therapy Exclusion criteria: <ul style="list-style-type: none"> • Experienced an exacerbation or hospitalised in the previous month • Clinically apparent heart disease or relevant bone or joint disease Participant status: Age (years): RG: 66 (7); CG: 65 (6) Gender (M/F): all men FEV ₁ % (pred): RG: 31 (12); CG: 39 (14) Participants randomly assigned: Randomised: 60 Analysed: Rehab: 29 Control: 27
Interventions	Pulmonary rehabilitation (out-patient and home based; 3 months of outpatient breathing retraining and chest physiotherapy; 3 months of daily supervised exercise) LLE, BE, PD Duration: 6 months (3 months of PR; participants were included in two 30-minute sessions each week (breathing retraining) combined with home exercise programme). Second 3-month period (exercise training): five 30-minute sessions weekly on a stationary cycle ergometer Usual care: Control group received standard care

Güell 1995 (Continued)

Outcomes	Assessment: baseline and 3, 6, 9, 12, 18 and 24 months 6MWT, ICET, CRQ	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Used random number tables; letter sent to LaCasse
Allocation concealment (selection bias)	High risk	No concealment
Blinding of participants and personnel (performance bias) All outcomes	High risk	Unable to blind both participants and those delivering the intervention because of the nature of the intervention
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Technicians who collected data for outcome measures at every visit, as explained below, were blinded to participants' allocation to PR or control groups
Incomplete outcome data (attrition bias) All outcomes	Low risk	All 60 participants completed 6 months of follow-up
Selective reporting (reporting bias)	Low risk	No protocol paper was found, but all outcomes listed in the paper appear to have been reported
Other bias	High risk	All men only

Güell 1998

Methods	Study design: RCT (2 groups)
Participants	<p>Setting: out-patient</p> <p>Inclusion criteria:</p> <ul style="list-style-type: none"> • Age \leq 75 years; FEV₁ < 70% of reference values; FEV₁/FVC ratio < 65%; Pao₂ > 55 mmHg at rest • No indications for home oxygen therapy • No exacerbation or hospitalisation in the previous 2 months <p>Exclusion criteria:</p> <ul style="list-style-type: none"> • Psychiatric disturbance • Heart disease • Relevant bone or joint disease <p>Participant status:</p>

	Age (years \pm SD): 68 \pm 8; CG: 66 \pm 8 Gender (M/F): RG: 16/2; CG: 17/0 FEV ₁ % (pred \pm SD): RG: 32% \pm 11; CG: 38% \pm 15 Participants randomly assigned: Randomised: 40 Analysed: Rehab: 18 Control: 17	
Interventions	Pulmonary rehabilitation: 2 months of chest physio and 2 months of muscle training LLE, IMT Duration: 8 weeks Usual care	
Outcomes	Assessment: baseline and post intervention (8 weeks) CRQ, 6MWT, dyspnoea, maximal workload	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random numbers table
Allocation concealment (selection bias)	High risk	Randomisation was not concealed, but the likelihood of bias introduced by unconcealed randomisation was reduced by recruitment of consecutive patients
Blinding of participants and personnel (performance bias) All outcomes	High risk	Unable to blind both participants and those delivering the intervention because of the nature of the intervention
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Technicians who collected data were blinded to participant allocation to the PRG or the CG, as were data analysts, until the analysis was deemed complete
Incomplete outcome data (attrition bias) All outcomes	Low risk	Commenced: 40; attrition: 5 (12%)
Selective reporting (reporting bias)	Low risk	No protocol paper was found, but all outcomes listed in the paper appear to have been reported
Other bias	Low risk	None noted

Hernandez 2000

Methods	Study design: RCT (2 groups) Randomisation process: random numbers table Outcome assessments: blinded
Participants	Setting: home-based; Seville, Spain Inclusion criteria: <ul style="list-style-type: none"> • COPD diagnosed in accordance with European Respiratory Society Consensus Statement • Stable phase of disease with optimal drug management Exclusion criteria: <ul style="list-style-type: none"> • Evidence of ischaemic heart disease, severe or uncontrolled systemic arterial hypertension, alterations in the thoracic cage • Neuromuscular disorders or intermittent claudication or osteoarticular lesions in the lower extremity that could affect normal ambulation • Acute exacerbation in the course of the programme excluded Participant status: Age (years \pm SD): RG: 64.3 \pm 8.3 ; CG: 63.1 \pm 6.9 Gender (M/F): RG: 20/0; CG: 17/0 FEV ₁ % (pred \pm SD): RG: 71.1 \pm 18.9; CG: 74.7 \pm 14.7 FEV ₁ /FVC (SD): RG: 47 \pm 9.9; CG: 42.3 \pm 12 Participants randomly assigned: Randomised: 60 Analysed: Rehab: 20 Control: 17
Interventions	Pulmonary rehabilitation: home rehabilitation programme; training intensity was determined individually LLE Duration: 12 weeks Usual care: Control group participants (standard medical treatment alone; also made visits to the hospital every 2 weeks for a clinical checkup and for supervision of treatment)
Outcomes	Assessment: baseline and 12 weeks ICET, Shuttle WT, CRQ, BDI/TDI
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random numbers table used
Allocation concealment (selection bias)	Unclear risk	No details provided
Blinding of participants and personnel (performance bias) All outcomes	High risk	Unable to blind both participants and those delivering the intervention because of the nature of the intervention

Hernandez 2000 (Continued)

Blinding of outcome assessment (detection bias) All outcomes	Low risk	Investigators were blinded (letter from study author)
Incomplete outcome data (attrition bias) All outcomes	High risk	60 randomly assigned; 37 completed (61.6%) Attrition: 38.3%
Selective reporting (reporting bias)	Low risk	It appears that all outcomes stated at the outset of the article were reported in the findings
Other bias	Low risk	Participants who were excluded because they did not meet the criteria appear to have been excluded after randomisation

Hoff 2007

Methods	Study design: RCT (2 groups)
Participants	<p>Setting: Norway</p> <p>Inclusion criteria:</p> <ul style="list-style-type: none"> • Clinical definition of COPD with $FEV_1/FVC < 70\%$ and $FEV_1 < 60\%$ predicted • Between 40 and 70 years of age <p>Exclusion criteria:</p> <ul style="list-style-type: none"> • History of cardiovascular disease, lung disease other than COPD, diabetes mellitus or other metabolic diseases, malignant disease, pregnancy • Corticosteroid use in the past 6 months • Respiratory tract infection within the past 4 weeks <p>Participant status: Age (years \pm SD): RG: 62.8 ± 1.4; CG: 60.6 ± 3.0 Gender (M/F): RG: 4/2; CG: 4/2 FEV_1/FVC (\pm SD): RG: 49.9 ± 4.6; CG: 45.2 ± 6.0</p> <p>Participants randomly assigned: Randomised: Analysed: 12 Rehab: 6 Control: 6</p>
Interventions	<p>Pulmonary rehabilitation: lab-based maximal strength training (seated horizontal leg press apparatus)</p> <p>LLE</p> <p>Duration: 8 weeks</p> <p>Usual care: Control group continued normal daily living with modest regular activity, as recommended by pulmonary physician</p>
Outcomes	<p>Assessment: baseline and week 8</p> <p>Incremental cycle ergometry</p>

Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information provided
Allocation concealment (selection bias)	Unclear risk	Insufficient information provided
Blinding of participants and personnel (performance bias) All outcomes	High risk	As a result of the nature of the intervention, unable to blind both participants and those delivering the intervention
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information provided
Incomplete outcome data (attrition bias) All outcomes	Low risk	All participants completed the study protocol with no adverse effects, and the MST group completed 100% of the planned training
Selective reporting (reporting bias)	Low risk	No protocol was identified. All outcomes identified in the methods section of the paper were reported in the results
Other bias	Low risk	None noted

Jones 1985

Methods	Study design: RCT (3 groups: exercise, resistive breathing, control)
Participants	<p>Setting: home based; recruited from a chest clinic in Dunedin, New Zealand</p> <p>Inclusion criteria:</p> <ul style="list-style-type: none"> • Fewer than 75 regular attendees at clinics • Severe irreversible airflow obstruction; FEV₁ < 1.2 and < 20% improvement after bronchodilator <p>Exclusion criteria:</p> <ul style="list-style-type: none"> • Angina pectoris, left and right heart failure, neuromuscular or skeletal disease that limited exercise <p>Participant status: Age (years ± SD): RG: 63.8 ± 6.09; CG: 62.7 ± 8.36 Gender (M/F): RG: 6/2; CG: 1/5 FEV₁ % (pred ± SD): RG: 0.78 ± 0.27; CG: 0.68 ± 0.12 Smoking: RG: 8; CG: 5</p> <p>Participants randomly assigned: Randomised: 30 (exercise 11, breathing 11, control 8)</p>

	Analysed: Rehab: exercise: 8, breathing: 7 Control: 6	
Interventions	Pulmonary rehabilitation: Simple physical exercises at home under the supervision of a physiotherapist and every 2 weeks in the gymnasium LLE, ULE Duration: 10 weeks Usual care: placebo respiratory device and usual care	
Outcomes	Assessment: baseline and 10 weeks 12-Minute WT, ICET, SSCET, daily diary, Lubin Affectometer	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation process: drawing lots
Allocation concealment (selection bias)	High risk	No concealment apparent
Blinding of participants and personnel (performance bias) All outcomes	High risk	As a result of the nature of the intervention, unable to blind both participants and those delivering the intervention
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome assessments: not blinded for ICET, blinded for the others
Incomplete outcome data (attrition bias) All outcomes	High risk	Commenced: 19; completed: 14 (73.7%) Attrition: 26.3%
Selective reporting (reporting bias)	Low risk	No protocol was identified. All outcomes identified in the methods section of the paper are reported in the results
Other bias	High risk	Control received a placebo respiratory device, which may have an impact

Methods	Study design: RCT (2 groups)	
Participants	Setting: Dept Chest Medicine in Izmir, Turkey Inclusion criteria: <ul style="list-style-type: none">• FEV₁ between 30% and 80% of predicted value• Clinical condition stable at the time of inclusion• No infections or COPD exacerbations in the preceding 4 weeks Exclusion criteria: <ul style="list-style-type: none">• Severe medical problems such as heart failure, recent myocardial infarction, cerebrovascular disease, orthopaedic problems and severe liver or kidney problems Participant status: Age (years ± SD): RG: 64.81 ± 9.4; CG: 67.21 ± 6.72 Gender (M/F): RG: 21/5; CG: 18/1 FEV ₁ %: RG: 55.50%; CG: 58% Participants randomly assigned: Randomised: 54 Analysed: Rehab: 26 Control: 19	
Interventions	Pulmonary rehabilitation: out-patient programme Aerobic exercise, ULE, LLE, breathing exercises, educational material Duration: 8 weeks Education component: 16 sessions of discussion (1 hour/wk) Exercise component: 3 times a week Usual care	
Outcomes	Assessment: baseline, week 8 and week 12 6MWT, SGRQ	
Notes	Week 8 data used for analysis	
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Participants were randomly assigned in a 1:1 ratio with the use of sealed envelopes
Allocation concealment (selection bias)	Low risk	
Blinding of participants and personnel (performance bias) All outcomes	High risk	As a result of the nature of the intervention, unable to blind both participants and those delivering the intervention
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not informed

Incomplete outcome data (attrition bias) All outcomes	Low risk	Commenced: 49; completed: 45 Attrition: 18.17%
Selective reporting (reporting bias)	Low risk	No protocol was identified. All outcomes identified in the methods section of the paper are reported in the results
Other bias	Low risk	Participants who were excluded because they did not meet the criteria appear to have been excluded after randomisation

Lake 1990

Methods	Study design: RCT (4 groups); participants were randomly assigned to a control group and to 3 actively trained groups
Participants	<p>Setting: intervention delivered in outpatient hospital setting; Perth, Western Australia</p> <p>Inclusion criteria:</p> <ul style="list-style-type: none"> • Severe COPD • Condition stable • Demonstrated minimal bronchodilator response • Receiving maximal medical treatment • Never been involved in an exercise programme <p>Exclusion criteria:</p> <ul style="list-style-type: none"> • Unstable cardiac disease; musculoskeletal disability preventing exercise; cor pulmonale; respiratory muscle fatigue (abdominal paradox) • Acute illness • Communication or transport difficulties <p>Participant status:</p> <p>Age (years \pm SD): RG: 66.3 \pm 6.8; CG: 65.7 \pm 3.5 Gender (M/F): RG: 6/1; CG: 4/3 FEV₁ % (pred \pm Sd): RG: 0.97 \pm 0.29; CG: 0.83 \pm 0.25</p> <p>Participants randomly assigned:</p> <p>Randomised: 28 Analysed: Rehab: 7 Control: 7</p>
Interventions	<p>Pulmonary rehabilitation: out-patient hospital based: 4 groups (combined exercise: 7; upper limb: 6; lower limb: 7; control)</p> <p>LLE or ULE or both</p> <p>Duration: 8 weeks (1 hour 3 times per week)</p> <p>Usual care</p>
Outcomes	<p>Assessment: baseline and immediately after the 8 weeks</p> <p>6MWT, ICET, IAET</p> <p>Bandura Scale of Well-being</p>

Lake 1990 (Continued)

Notes		
Risk of bias		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation process: randomisation chart
Allocation concealment (selection bias)	Unclear risk	No allocation concealment discussed
Blinding of participants and personnel (performance bias) All outcomes	High risk	As a result of the nature of the intervention, unable to blind participants and those delivering the intervention
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome assessments: blinded for ICET, not blinded for 6MWT
Incomplete outcome data (attrition bias) All outcomes	Low risk	Commenced: 28; finished: 26 (92.9%) Attrition: 7.1%
Selective reporting (reporting bias)	Low risk	No protocol was identified. All outcomes identified in the methods section of the paper were reported in the results
Other bias	Unclear risk	None noted

Lindsay 2005

Methods	Study design: RCT (2 groups)
Participants	<p>Setting: Lek Yuen Family Medicine Teaching Clinic, Hong Kong, and the Family Medicine Training Centre of the Prince of Wales Hospital</p> <p>Inclusion criteria:</p> <ul style="list-style-type: none"> • COPD: FEV₁ < 80% predicted and FEV₁/FVC ratio < 70% that does not change markedly over several months <p>Exclusion criteria:</p> <ul style="list-style-type: none"> • Could not walk; suffered from severe sensory or cognitive impairment, symptomatic ischaemic heart disease; or • Were on supplemental oxygen • Further exclusion criteria included glaucoma, prostate problems, pregnancy, breast-feeding, intolerance to ipratropium, bladder outlet problems and severe kidney problems, as these people would not be able to use tiotropium <p>Participant status:</p> <p>Age (years ± SD): RG: 69.5 ± 9.3; CG: 69.8 ± 10.3 Gender (M/F): RG: 20/5; CG: 18/7 FEV₁ % (pred ± SD): RG: 0.9 ± 0.3; CG: 0.8 ± 0.4</p>

	Current smoker: RG 3 (12%); CG: 7 (28) Participants randomly assigned: Randomised: 50 (25 each group) Analysed: Rehab: 21 Control: 20	
Interventions	Pulmonary rehabilitation: community (primary care setting) Aerobic exercise, ULE, LLE, educational material, home physio visits Duration: 6 weekly sessions of psychoeducation, each lasting for 2 hours Usual care: given tiotropium, which is considered standard usual care	
Outcomes	Assessment: baseline, start of PRP, end of PRP and 3 months 6MWD, spirometry, CRQ	
Notes	For analysis, used mean and standard deviation of all other studies, as did not provide SD	
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not provided
Allocation concealment (selection bias)	Unclear risk	Not provided
Blinding of participants and personnel (performance bias) All outcomes	High risk	As a result of the nature of the intervention, unable to blind participants and those delivering the intervention
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not provided
Incomplete outcome data (attrition bias) All outcomes	Low risk	50 randomly assigned; drop-out: 9 Attrition: 18%
Selective reporting (reporting bias)	Low risk	No protocol was identified. All outcomes identified in the methods section of the paper were reported in the results
Other bias	Low risk	None noted

Methods	Study design: RCT (3 groups) Single-blind	
Participants	Setting: conducted in Hong Kong, in the care of respiratory specialists of Jiangs Province Hospitals from October 2008 to October 2010 Inclusion criteria: COPD severity level at GOLD stages I and II Exclusion criteria: no serious co-morbidities (e.g. pulmonary tuberculosis, emphysema, congestive heart failure) Participant status: Age (years± SD):RG:[HQG: 61.82 ± 7.69; PRG: 61.34 ± 8.3]; CG: 62.2 ± 6.34 Gender (M/F): RG:[HQG: 78%/22%; RG: 72%/28%]; CG: 80%/20% FEV ₁ % (pred ± SD): [HQG: 74.43 ± 12.93; PRP: 75.31 ± 12.84;] FEV ₁ /FVC (± SD): RG[HQG: 60.73 ± 6.18; PRP: 61.27± 5.86]; control: 61.43 ± 6.17 Never smoked: HQG: 37.3%; PRP: 43.8%; control: 34.3% Participants randomly assigned: Randomised: 132 (PR: 36; Qiqong: 60; control: 36) Analysed: Rehab: 32 Control: 35	
Interventions	Pulmonary rehabilitation: combined in-patient and/or home/community/out-patient Aerobic exercise, ULE, LLE, peer support Duration: 6 months; then encouraged to participate in peer-led weekly walking and ball game activities thrice a week, 1 hour each time, for 6 months Usual care: received health education and was advised to continue exercising alone	
Outcomes	Assessment: baseline and 6 months 6MWD, Zhongshan COPD Questionnaire for QoL, immune cell factor, hospital admissions	
Notes	Used only exercise group for analysis	
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Participant allocation list was drawn on the basis of random order of the block ("H-H-H-P-P-C-C") for 20 times, until a list of 140 individuals in a specific order was obtained
Allocation concealment (selection bias)	Low risk	Not provided
Blinding of participants and personnel (performance bias) All outcomes	High risk	As a result of the nature of the intervention, participants and those delivering the programme could be randomly assigned

Blinding of outcome assessment (detection bias) All outcomes	Low risk	All outcome assessors were blinded to each participant's allocated group, as well as to the objectives of the study, to minimise bias
Incomplete outcome data (attrition bias) All outcomes	Low risk	Randomised: 132 (control: 36; PR: 36; Qigong: 60) 118 included in the final analysis (control: 35; PR: 32; Qigong: 51) So lost 14 overall (89%) participated; attrition: 11%
Selective reporting (reporting bias)	Low risk	No protocol was identified, but all results re stated outcomes seem to have been included
Other bias	Low risk	None noted

McGavin 1977

Methods	Study design: RCT (2 groups)
Participants	<p>Setting: home based; New Delhi, India</p> <p>Inclusion criteria:</p> <ul style="list-style-type: none"> • Younger than 70 years of age • Chronic bronchitis according to the criteria of the Medical Research Council <p>Exclusion criteria:</p> <ul style="list-style-type: none"> • Demonstrating reversibility post salbutamol • Taking corticosteroid medication • Patients with angina pectoris, intermittent claudication and disabling musculoskeletal disorders <p>Participant status: Age (years \pm SD): RG: 61.4 \pm 5.6, CG: 57.2 \pm 7.9 Gender (M/F): RG: 12/0; CG: 12/0 FEV₁ % (pred \pm SD): RG: 0.97 L \pm 0.33; CG: 1.15 L \pm 0.72 FEV₁ /FVC: RG:CG</p> <p>Participants randomly assigned: Randomised: 28 Analysed: Rehab: 12 Control: 12</p>
Interventions	<p>Pulmonary rehabilitation: home-based training programme consisting of graded stair-climbing exercises tailored to suit the ability of the individual LLE</p> <p>Duration: continuous, once a day, at least 5 days a week</p> <p>Usual care: Control group did not receive exercise instructions or an out-patient check at 2 weeks</p>

McGavin 1977 (Continued)

Outcomes	Assessment: baseline and mean 14 weeks control; mean 19 weeks intervention 12-Minute WT, ICET Interviews	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Used random numbers tables
Allocation concealment (selection bias)	Unclear risk	No information provided
Blinding of participants and personnel (performance bias) All outcomes	High risk	As a result of the nature of the intervention, participants and those delivering the programme could be randomly assigned
Blinding of outcome assessment (detection bias) All outcomes	High risk	Outcome assessments: not blinded (letter from study authors)
Incomplete outcome data (attrition bias) All outcomes	Low risk	28 started; 24 finished (85.7%) Attrition: 14.28%
Selective reporting (reporting bias)	Low risk	No protocol was identified, but all stated results re outcomes seem to have been included
Other bias	Low risk	None identified

McNamara 2013

Methods	Study design: RCT (3 groups, land based, water based, control)
Participants	Setting: patients referred to outpatient pulmonary rehabilitation at an Australian tertiary public hospital Inclusion criteria: <ul style="list-style-type: none"> • Diagnosis of COPD • In a stable phase • Presence of 1 or more physical co-morbidities (including musculoskeletal conditions affecting lumbar spine or lower limbs, 1 or more lower limb joint replacements restricting mobility and/or range of motion or peripheral vascular disease or neurological condition such as stroke or obesity with body mass index (BMI) > 32 kg/m²) Exclusion criteria: <ul style="list-style-type: none"> • Unstable cardiac disease

	<ul style="list-style-type: none">• Contraindications to water-based therapy such as uncontrollable incontinence or open wounds• Completed pulmonary rehabilitation in the past 12 months• Cognitive decline• Inability to understand oral and written English <p>Participant status: Age (years \pm SD): RG:[water: 72 \pm 10; land: 73 \pm 7]; CG: 70 \pm 9 Gender (M/F): RG: 15/23; CG: 7/8 FEV₁ % (pred \pm SD): RG: [WB: 60 \pm 10; LB: 62 \pm 15]; CG: 55 \pm 20 FEV₁ /FVC: RG: [WB: 59 \pm 9; LB: 58 \pm 9]; CG: 53 \pm 13 Current smokers: RG: [WB: 3; LB: 1]; CG: 2</p> <p>Participants randomly assigned: Randomised: 53 (control: 15; land based: 20; water based: 18) Analysed: Rehab: land based: 15; water based: 15 Control: 15</p>	
Interventions	<p>Pulmonary rehabilitation: out-patient programme: hospital gymnasium; participants walked at an intensity of 80% of the average 6MWT speed over ground or on a treadmill. Water-based exercise training group exercised in a hospital hydrotherapy pool Aerobic exercise, ULE, LLE</p> <p>Duration: 8 weeks; three 60-minute sessions a week of supervised exercise led by the same experienced physiotherapist</p> <p>Usual care: Control group participants received usual medical care and no exercise training. They were asked not to alter their exercise level over the study period</p>	
Outcomes	<p>Assessment: baseline and 8 weeks CRDQ, 6MWT, ISWT, ESWT</p>	
Notes	Please note: Combined intervention groups of land and water used for analysis	
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomly assigned by an investigator external to the study using a Web-based computer-generated sequence
Allocation concealment (selection bias)	Low risk	Concealed allocation achieved with the use of opaque envelopes
Blinding of participants and personnel (performance bias) All outcomes	High risk	As a result of the nature of the exercise interventions, it was not possible to blind therapists or participants to allocation

Blinding of outcome assessment (detection bias) All outcomes	Low risk	Assessor blinding
Incomplete outcome data (attrition bias) All outcomes	Low risk	Commenced: 53; analysed: 55 Attrition: 8 (15%)
Selective reporting (reporting bias)	Low risk	Registered on www.anzctr.org.au (AC-TRN0126000408583) Primary outcomes and all planned secondary outcomes appear to have been reported
Other bias	Low risk	None noted

Mehri 2007

Methods	Study design: RCT (2 groups)	
Participants	Setting: Iran Inclusion criteria: <ul style="list-style-type: none">• COPD as recommended in GOLD Exclusion criteria: Participant status: Age (years ± SD): RG: 52.1 ± 10.7; CG: 52.17 ± 11.6 Gender (M/F): RG: 11/9; CG: 7/11 FEV ₁ % (pred): RG:CG: not available FEV ₁ /FVC: RG:CG: not available Participants randomly assigned: Randomised: 38 (RG: 20, CG: 18) Analysed: Rehab: 20 Control: 18	
Interventions	Pulmonary rehabilitation: outpatient clinic, exercised on a treadmill Aerobic exercise, ULE, LLE Duration: 4 weeks, 2 times a week Usual care: Control group completed no treadmill exercise training	
Outcomes	Assessment: baseline and 4 weeks VO ₂ peak, based on the Rockport formula	
Notes		
Risk of bias		
Bias	Authors' judgement	Support for judgement

Mehri 2007 (Continued)

Random sequence generation (selection bias)	Unclear risk	No information provided
Allocation concealment (selection bias)	Unclear risk	No information provided
Blinding of participants and personnel (performance bias) All outcomes	High risk	As a result of the nature of the exercise interventions, it was not possible to blind therapists or participants to allocation
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information provided
Incomplete outcome data (attrition bias) All outcomes	Low risk	No attrition reported
Selective reporting (reporting bias)	Low risk	No protocol was identified, but all stated results re outcomes appear to have been included
Other bias	Low risk	None noted

Mendes De Oliveira 2010

Methods	<p>Study design: RCT (3 groups); outpatient group that performed all activities at the clinic, home-based group that performed activities at home and control group</p>
Participants	<p>Setting: private pulmonology clinic in Cascavel (southern Brazil)</p> <p>Inclusion criteria:</p> <ul style="list-style-type: none"> • COPD based on GOLD • Clinical stability in the 8 weeks before the study <p>Exclusion criteria:</p> <ul style="list-style-type: none"> • Hospitalisation; COPD instability • Presence of neuromuscular disease, associated respiratory disease, orthopaedic or neurological disease that affected gait • Recent impairment due to co-morbidities, such as myocardial infarction, heart failure, stroke or neoplasm; prior pneumonectomy or other thoracic surgery <p>Participant status: Age (years): RG: [home: 66.4; outpatients: 71.3]; CG: 70.8 Gender (M/F): RG:[home: 27/6; outpatients: 19/4]; CG: 19/10 FEV₁ % (pred): RG:[home 47.5 ; outpatient 51.5]; CG: 41.4</p> <p>Participants randomly assigned: Randomised: 117 Analysed: Rehab: home: 33; outpatient: 23 Control: 29</p>

Interventions	Pulmonary rehabilitation: outpatient clinic or home based Aerobic exercise, ULE, LLE, education Duration: 12 weeks, 3 times a week Usual care: Control group performed no PR	
Outcomes	Assessment: baseline and 12 weeks MRC, BODE Index, 6MWT	
Notes	Combined 2 intervention groups for the analysis	
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomly assigned electronically by a computer to 3 groups
Allocation concealment (selection bias)	Low risk	Not provided
Blinding of participants and personnel (performance bias) All outcomes	High risk	As a result of the nature of the intervention, unable to blind participants and those delivering intervention
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	2 duly trained healthcare professionals were responsible for the evaluations, which were performed by the same evaluators for all participants
Incomplete outcome data (attrition bias) All outcomes	High risk	Loss: 32; attrition: 27%
Selective reporting (reporting bias)	Low risk	No protocol was identified, but all stated results re outcomes appear to have been included
Other bias	Low risk	None noted

Nalbant 2011

Methods	Study design: RCT (2 groups)
Participants	Setting: nursing home residents in Turkey Inclusion criteria: <ul style="list-style-type: none"> • 60-85 years of age • Diagnosed with COPD Exclusion criteria:

	<ul style="list-style-type: none">● Systemic diseases affecting the respiratory system, requiring treatment● Arrhythmias and/or congestive heart failure, allergic rhinitis, atopy, with a history of malignancy● Continuous oxygen therapy● Acute COPD attacks in the period, steroid● Narcotic analgesics and chronic alcohol <p>Participant status: Age (years): RG: 73.5; CG: 68 Gender (M/F): RG: 11/3; CG: 13/2 FEV₁/FVC (Range): RG: 58.5 (48-65); CG: 57 (44-66) Participants randomly assigned: Randomised: 29 (RG: 14, CG: 15) Analysed: Rehab: 10 Control: 11</p>	
Interventions	<p>Pulmonary rehabilitation: Aerobic exercise, ULE, LLE, educational material Duration: 6 months, 3 days a week for 1.5 hours Usual care</p>	
Outcomes	<p>Assessment: baseline, 3 months and 6 months 6MWT, lower extremity strength test</p>	
Notes	Note: Only medians and ranges provided, so cannot be used in analysis	
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not provided
Allocation concealment (selection bias)	Unclear risk	Not provided
Blinding of participants and personnel (performance bias) All outcomes	High risk	As a result of the nature of the intervention, unable to blind participants and those providing intervention
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not provided
Incomplete outcome data (attrition bias) All outcomes	High risk	29 people were randomly assigned 21 completed; loss of 8 people Attrition: 28%

Selective reporting (reporting bias)	Low risk	No protocol was identified, but seems to have included all results re outcomes stated
Other bias	Low risk	None noted

O'Shea 2007

Methods	Study design: RCT (2 groups); single- blind randomised trial	
Participants	Setting: 4 sites including 3 regional health services and 1 large metropolitan hospital; Australia Inclusion criteria: <ul style="list-style-type: none">• Diagnosis of COPD Exclusion criteria: <ul style="list-style-type: none">• Respiratory condition other than COPD• Unstable medical conditions limiting performance of resistance exercise• PR in previous 12 months Participant status: Age (years ± SD): RG: 66.9 ± 7; CG: 68.4 ± 9.9 Gender (M/F): RG:CG FEV ₁ % (pred): RG: 49; CG: 52 FEV ₁ /FVC: RG: 50; CG: 49 Hx smoking per day: RG: 40; CG: 26.5 Participants randomly assigned: Randomised: 54 (27 to each group) Analysed: Rehab: 20 Control: 24	
Interventions	Pulmonary rehabilitation: outpatient clinic and home based: under the supervision of an experienced physiotherapist; progressive resistance exercise programme ULE, LLE Duration: 12 weeks: 1 session per week facilitated, 2 sessions performed independently at home Usual care: Control group received no intervention	
Outcomes	Assessment: baseline and 3 months and 6 months CRDQ, 6MWT, Timed Up and Go Test, Grocery Shelving Test, Patient-Specific Functional Scale, participation restrictions: London Handicap Scale, hand-held dynamometry	
Notes	Utilised data at 3 months for analysis	
Risk of bias		
Bias	Authors' judgement	Support for judgement

Random sequence generation (selection bias)	Low risk	Generated by member of the research team not involved in participant recruitment
Allocation concealment (selection bias)	Low risk	Concealed allocation
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants and those delivering the intervention were aware of which individuals were included in the intervention group
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Assessor blinding
Incomplete outcome data (attrition bias) All outcomes	Low risk	Commenced: 54; loss: 44 Attrition: 19%
Selective reporting (reporting bias)	Low risk	No protocol was identified, but all results re stated outcomes appear to have been included
Other bias	High risk	All male

Ozdemir 2010

Methods	Study design: RCT (2 groups): water based exercise (WE) and control
Participants	<p>Setting: Chest Diseases Outpatient Clinic between April 2006 and November 2006; Turkey</p> <p>Inclusion criteria:</p> <ul style="list-style-type: none"> • Moderate or severe COPD <p>Exclusion criteria:</p> <ul style="list-style-type: none"> • Without respiratory failure • Severe hypertension • Dizziness or fainting during exercise • Severe congestive heart failure that could not be controlled • Under treatment • Unstable coronary artery disease, terminal liver failure • Psychiatric instability, behavioural disorder • Suspected bronchial asthma • Ongoing infectious disease <p>Participant status: Age (years \pm SD): RG: 60.9 \pm 8.8; CG: 64.1 \pm 8.9 Gender (M/F): all male FEV₁ % (pred \pm SD): RG: 54.5 \pm 15.6; CG: 54.1 \pm 20.2 FEV₁/FVC (\pm SD) : RG: 56.0 \pm 10.5; CG: 54.6 \pm 9.1 Smoker: RG: 5 (20%); CG: 6 (24%)</p> <p>Participants randomly assigned:</p>

	Randomised: 50 (25 in each) Analysed: Rehab: 25 Control: 25	
Interventions	Pulmonary rehabilitation: out-patient; water-based exercise (WE) Aerobic exercise, ULE, LLE Duration: 4-Week water-based pulmonary rehabilitation for 35 minutes 3 times a week Usual care: received only medical therapy	
Outcomes	Assessment: baseline and 1 month Spirometry, 6MWT, CRDQ, HAD Scale, arterial blood gas examination	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	According to “tables of random numbers”
Allocation concealment (selection bias)	Unclear risk	No information provided
Blinding of participants and personnel (performance bias) All outcomes	High risk	As a result of the nature of the intervention, both participants and those delivering the intervention were aware of allocation
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information provided
Incomplete outcome data (attrition bias) All outcomes	Low risk	No attrition reported
Selective reporting (reporting bias)	High risk	No protocol was identified, but results for CRQ of rehabilitation group were not provided
Other bias	Low risk	None noted

Methods	Study design: RCT (2 groups)	
Participants	Setting: recruited from the pulmonary clinic at the University Hospital of Caracas Inclusion criteria: <ul style="list-style-type: none">• COPD diagnosed• Clinically stable• Receiving optimal medical therapy Exclusion criteria: <ul style="list-style-type: none">• Not clinically stable Participant status: Age (years ± SD): RG: 67 ± 5; CG: 62 ± 7 Gender (M/F): RG: 6/4; CG: 12/2 FEV ₁ % (pred ± SD): RG: 34 ± 11; CG: 30 ± 9 FEV ₁ /FVC (± SD): RG: 39 ± 7; CG: 30 ± 9 Participants randomly assigned: Randomised: 24 (PG: 10; CG: 14) Analysed: 24 Rehab: 10 Control: 14	
Interventions	Pulmonary rehabilitation: out-patient programme (hospital-based PR) Aerobic exercise, ULE, LLE Duration: 8-Week programme 3 days per week in groups of 2 or 3 Usual care: Control group received optimal care, as suggested by the American Thoracic Society	
Outcomes	Assessment: baseline and Immediately after PR (8 weeks) Spirometry, Beck Depression Inventory, State Trait Anxiety Inventory, MRC Scale, SGRQ	
Notes		
Risk of bias		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not informed
Allocation concealment (selection bias)	Unclear risk	Not informed
Blinding of participants and personnel (performance bias) All outcomes	High risk	As a result of the nature of the intervention, both participants and those delivering the intervention were aware of allocation
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not informed

Incomplete outcome data (attrition bias) All outcomes	Low risk	Commenced: 24 (control: 14; intervention: 10) No loss reported
Selective reporting (reporting bias)	High risk	No protocol was identified, but results for the rehabilitation group for CR were not provided
Other bias	Low risk	None noted

Petty 2006

Methods	Study design: RCT (3 groups): randomised tailored videotape, standard videotape, control
Participants	<p>Setting: physician referrals from private offices, the Denver office of Kaiser Permanente and the Denver Veterans Affairs Medical Center</p> <p>Inclusion criteria:</p> <ul style="list-style-type: none"> • Diagnosis of COPD, emphysema or chronic bronchitis; FEV₁ < 50% and predicted ratio FEV₁/FVC < 70% • Stable state <p>Exclusion criteria:</p> <ul style="list-style-type: none"> • Terminal condition such as late-stage lung cancer • Active involvement in a formal pulmonary rehabilitation programme <p>Participant status:</p> <p>Age (years ± SD): RG: [customised video: 68.8 ± 9.2; standard video: 68.4 ± 9.0]; CG: 66.8 ± 9.9</p> <p>Gender (M): RG:[customised video: 39 (54.2%); standard video: 41 (59.4%)]; CG: 40 (54.8%)</p> <p>Current smoker: RG:[customised video: 10 ± 14.3%]; standard video: 18 ± 26.5%]; CG: 22 ± 30.1%</p> <p>Participants randomly assigned:</p> <p>Randomised: 214 (customised video: 72; standard video: 69; control: 73)</p> <p>Analysed:</p> <p>Rehab: customised video: 52; standard video: 62</p> <p>Control: 61</p>
Interventions	<p>Pulmonary rehabilitation: home-based programme (in home): a tailored videotape (Group A) and a standard videotape (Group B)</p> <p>Aerobic exercise, ULE, LLE, educational material, home physio visits</p> <p>Duration: 8 weeks</p> <p>Usual care</p>
Outcomes	<p>Assessment:</p> <p>baseline and 8 weeks</p> <p>Fatigue Impact Scale (FIS), Seattle Obstructive Lung Questionnaire (SOLQ), SF-36, 6MWD</p>
Notes	Data could not be analysed, as full results were not available

<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomly assigned to 1 of 3 groups in a blocked fashion to achieve balance
Allocation concealment (selection bias)	Unclear risk	Not known
Blinding of participants and personnel (performance bias) All outcomes	High risk	As a result of the nature of the intervention, both participants and those delivering the intervention were aware of allocation
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Self-completion by participants
Incomplete outcome data (attrition bias) All outcomes	Low risk	Randomly assigned: 214; completed: 174 Attrition: 40 (19%)
Selective reporting (reporting bias)	High risk	No protocol was identified Results of the 6-minute walk test and SF-36 not presented
Other bias	Unclear risk	None noted

Reardon 1994

Methods	Study design: RCT (2 groups)
Participants	<p>Setting: out-patient; Connecticut</p> <p>Inclusion criteria:</p> <ul style="list-style-type: none"> • Clinical diagnosis of moderately severe to severe COPD • Significant exertional dyspnoea despite conventional medical therapy <p>Exclusion criteria:</p> <ul style="list-style-type: none"> • Significant associated medical problems that might interfere with ability to undergo OPR • Requiring continuous low-flow oxygen therapy <p>Participant status: Age (years): RG: 66.3; CG: 66.1 Gender (M/F): RG: 5/5; CG: 5/5 FEV₁ % (pred ± SD): RG: 35% ± 10; CG: 33% ± 15</p> <p>Participants randomly assigned: Randomised: 20 Analysed: Rehab: 10 Control: 10</p>

Reardon 1994 (Continued)

Interventions	Pulmonary rehabilitation: outpatient LLE, ULE, BE, Edu, Psy Duration: 6 weeks (12 three-hour sessions) Usual care: session with the OPR nurse clinician for optimisation of pulmonary therapy	
Outcomes	Assessment: baseline and 6 weeks ITT, BDI/TDI, 12MWD	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation process: random numbers table
Allocation concealment (selection bias)	Unclear risk	Not informed
Blinding of participants and personnel (performance bias) All outcomes	High risk	As a result of the nature of the intervention, both participants and those delivering the intervention were aware of allocation
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome assessments: blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	No participant loss after allocation
Selective reporting (reporting bias)	Low risk	No trial registration protocol was found at www.controlled-trials.com/mrct/ or www.who.int/trialsearch (searched for author names and parts of title of paper or intervention). However it would seem that all outcomes stated in the study were measured
Other bias	Low risk	None noted

Ringbaek 2000

Methods	Study design: RCT (2 groups) Randomisation process: sealed envelopes Outcome assessments: blinded
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Participants	Setting: delivered as an outpatient programme in Denmark Inclusion criteria: <ul style="list-style-type: none">• Stable COPD with FEV₁/FVC ratio 570%, FEV₁ > 0.6• Age < 75 years• Oxygen saturation without oxygen supply > 90% Exclusion criteria: <ul style="list-style-type: none">• In an exercise programme• Had another serious disease, such as cancer• Had home oxygen therapy• Were senile or suffered from a psychiatric disorder, or were dependent on walking equipment Participant status: Age (years ± SD): RG: 61.8 ± 6.8; CG: 64.6 ± 7.7 Gender (M/F): RG: 1/23; CG: 6/15 FEV ₁ % (pred ± SD): RG: 49.5 ± 17.4; CG: 44.3 ± 3.7 Current smoking: RG: 16; CG: 7 Participants randomly assigned: Randomised: 45 (RG: 24; control: 21) Analysed: Rehab: 17 Control: 19 (130 approached; 45 randomised)	
Interventions	Pulmonary rehabilitation: out-patient (hospital) Aerobic, LLE, ULE, education, nutritional support Duration: 8 weeks, 2 sessions a week of 2 hours Usual care: conventional community care	
Outcomes	Assessment: baseline and 8 weeks 6-Minute WT, SGRQ, Psychological General Well-being (PGWB), Borg Scale	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation process: sealed envelopes
Allocation concealment (selection bias)	Unclear risk	No information provided
Blinding of participants and personnel (performance bias) All outcomes	High risk	As a result of the nature of the intervention, both participants and those delivering the intervention were aware of allocation

Ringbaek 2000 (Continued)

Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome assessments: blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	Overall commenced: 45; finished: 36 (84.4%) Overall attrition: 7 (15.6%)
Selective reporting (reporting bias)	Low risk	No trial registration protocol was found at www.controlled-trials.com/mrct/ or www.who.int/trialsearch (searched for author names and parts of title of paper or intervention). However it would seem that all outcomes stated in the study were measured
Other bias	Low risk	None noted

Simpson 1992

Methods	Study design: RCT (2 groups), stratified
Participants	<p>Setting: out-patient</p> <p>Inclusion criteria:</p> <ul style="list-style-type: none"> • Clinically stable state, no recent infective exacerbation • Drug management considered to be optimal • FEV₁/VC < 0.7 • Body weight within 30% of predicted ideal body weight <p>Exclusion criteria:</p> <ul style="list-style-type: none"> • NOT clinically stable state • Recent infective exacerbation • Disorders likely to affect exercise and capacity to participate <p>Participant status: Age (years ± SD): RG: 73 ± 4.8; CG: 70 ± 5.7 Gender (M/F): RG: 5/9; CG: 10/4 FEV₁ % (pred ± SD): RG: 39.5 ± 18.96; CG: 39.2 ± 21.39 FEV₁/FVC: RG: 49.4 (12.95); CG: 47.8 (14.04)</p> <p>Participants randomly assigned: Randomised: 34 Analysed: Rehab: 14 Control: 14</p>
Interventions	<p>Pulmonary rehabilitation: Weight-lifting programme training was prescribed for upper and lower limb muscles; resistance was increased progressively LLE, ULE</p> <p>Duration: 8 weeks 3 times a week</p> <p>Usual care: Control group attended only for testing</p>

Simpson 1992 (Continued)

Outcomes	Assessment: baseline and 8 weeks 6MWT, ICET, SSCET, CRQ	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation process: coin toss
Allocation concealment (selection bias)	Unclear risk	No information provided
Blinding of participants and personnel (performance bias) All outcomes	High risk	As a result of the nature of the intervention, both participants and those delivering the intervention were aware of allocation
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome assessments: blinded for CRQ, not blinded for the others
Incomplete outcome data (attrition bias) All outcomes	Low risk	28/34 completed = 82.3% Attrition: 17.64%
Selective reporting (reporting bias)	Low risk	No trial registration protocol was found. However it would seem that all outcomes stated in the study were measured
Other bias	Low risk	None noted

Singh 2003

Methods	Study design: RCT (2 groups)
Participants	<p>Setting: home based, carried out by Department of Medicine, SMS Medical College and Hospital, Jaipur, India</p> <p>Inclusion criteria:</p> <ul style="list-style-type: none"> • Stable patients • Chronic bronchitis and/or emphysema with FEV₁/FVC ratio < 0.7 and FEV₁ • Less than 40% of predicted • Dyspnoea in 3 or more daily activities • Given up smoking for at least 2 months <p>Exclusion criteria:</p> <ul style="list-style-type: none"> • Involved in a pulmonary rehabilitation programme • Right ventricular failure, unstable ischaemic heart disease

	<ul style="list-style-type: none">● Oxygen saturation < 88% at rest● Musculoskeletal disease, acute exacerbation and pneumothorax <p>Participant status: Age (years ± SD): 59.3 ± 6.4 Gender (M/F): male 32 (80%), female 8 (20%) FEV₁ % (pred ± SD): RG: 28 ± 7.5; CG: 26 ± 7.1 FEV₁/FVC (±SD): RG: 44 ± 16; CG: 48 ± 10.4</p> <p>Participants randomly assigned: Randomised: 40 Analysed: Rehab: 20 Control: 20</p>	
Interventions	<p>Pulmonary rehabilitation: domiciliary pulmonary rehabilitation for 4 weeks; supervised weekly to ensure that participants were following the rehabilitation schedule properly and were taking regular treatment LLE, IMT</p> <p>Duration: 4 weeks 30 minutes twice a day</p> <p>Usual care: Control group participants were asked to continue their activities as usual</p>	
Outcomes	<p>Assessment: baseline and 4 weeks CRQ, 6MWT</p>	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation process: random numbers table
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	As a result of the nature of the intervention, both participants and those delivering the intervention were aware of allocation
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Outcome assessments: not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	No attrition
Selective reporting (reporting bias)	Low risk	All outcomes appearing in the controlled trial registry (clinicaltrials.gov) seem to have been reported on in the paper

Other bias	Low risk	None reported
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Sridhar 2008

Methods	Study design: RCT (2 groups)
Participants	<p>Setting: community and hospital care in West London</p> <p>Inclusion criteria:</p> <ul style="list-style-type: none"> Patients who had been discharged with a diagnosis of acute exacerbation of COPD as primary cause of admission <p>Exclusion criteria:</p> <ul style="list-style-type: none"> Significant comorbidity such as severe heart disease or cancer Any condition that would preclude participation in the physical therapy component <p>Participant status:</p> <p>Age (years \pm SD): RG: 69.9 \pm 9.6; CG: 69.68 \pm 10.4</p> <p>Gender (M/F): RG: 30/31; CG: 30/31</p> <p>FEV₁ % (pred \pm SD): RG: 42.9 \pm 15.5; CG: 48.9 \pm 18.69</p> <p>FEV₁/FVC: RG:CG</p> <p>Current smoker (Y/N): RG: 18/61; CG: 12/61</p> <p>Participants randomly assigned:</p> <p>Randomised: 122</p> <p>Analysed:</p> <p>Rehab: 47</p> <p>Control: 40</p>
Interventions	<p>Pulmonary rehabilitation: outpatient followed by home package</p> <p>Aerobic exercise, ULE, LLE, educational material, home physio visits</p> <p>Duration: 4 weeks, 2 attendances per week (1 hour of education, 1 hour of physical training)</p> <p>followed by 3 monthly home visits</p> <p>Usual care: Control group received usual care from primary care physician</p>
Outcomes	<p>Assessment:</p> <p>baseline and 6 months</p> <p>CRQ, hospital readmission rate</p>
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomly assigned with the use of random numbers to intervention or control group
Allocation concealment (selection bias)	Unclear risk	Not informed

Blinding of participants and personnel (performance bias) All outcomes	High risk	As a result of the nature of the intervention, both participants and those delivering the intervention were aware of allocation
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Outcome assessments: not reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Commenced: 122; outcome data for 104 Attrition: 18 (15%)
Selective reporting (reporting bias)	Low risk	No trial registration protocol was found. However it would seem that all outcomes stated in the study were measured
Other bias	Unclear risk	None reported

Strijbos 1996

Methods	Study design: RCT (3 groups)
Participants	Setting: out-patient Inclusion criteria: Exclusion criteria: Participant status: Age (years \pm SD): RG: 61 \pm 6 ; CG: 63 \pm 5 Gender (M/F): RG: 14/1; CG: 12/3 FEV ₁ % (pred \pm SD): RG: 40.4 \pm 19.6; CG: 42.6 \pm 8.8 Participants randomly assigned: Randomised: 32 Analysed: Rehab: 15 Control: 15
Interventions	Pulmonary rehabilitation: hospital-based outpatient pulmonary rehabilitation programmes (HRPa) are compared with those of a 12-week home care rehabilitation programme (HCRP) LLE, BE, PD, Edu, Psy Duration: 12 weeks twice a week for 1-hour session Usual care: Control group received no rehabilitation therapy
Outcomes	Assessment: baseline, 3 months, 6 months, 12 months and 18 months 4-Minute WT, ICET, interviews
Notes	Utilised 3-month results for analysis

<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Lottery procedure used to determine which group participants allocated to
Allocation concealment (selection bias)	Unclear risk	No information related to allocation concealment provided
Blinding of participants and personnel (performance bias) All outcomes	High risk	As a result of the nature of the intervention, both participants and those delivering the intervention would be aware of allocation
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome assessments: blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	Started 50; finished 45; attrition at 3 months: 5 (10%)
Selective reporting (reporting bias)	Low risk	No trial registration protocol was found. However it would seem that all outcomes stated in the study were measured
Other bias	Low risk	None noted

Theander 2009

Methods	Study design: RCT (2 groups)
Participants	<p>Setting: pulmonary out-patient department in a central county district of Sweden</p> <p>Inclusion criteria:</p> <ul style="list-style-type: none"> • 75 years of age or younger • FEV₁ between 60% and 25% predicted after bronchodilatation <p>Exclusion criteria:</p> <ul style="list-style-type: none"> • Disabling or severe disease other than COPD • Impaired pulmonary function due to other disease • Long-term oxygen therapy • Alpha1-antitrypsin deficiency, cancer disease, untreated obstructive sleep apnoea syndrome, no COPD-related symptoms affecting activities of daily life <p>Participant status: Age (years): RG: 66; CG: 64 Gender (M/F): RG: 3/9; CG: 10/4 FEV₁ % (pred ± SD): RG: 35.1 ± 7.6; CG: 32.3 ± 9.5 Smokers: 3 in each group currently smoking</p> <p>Participants randomly assigned:</p>

	Randomised: 30 Analysed: Rehab: 12 Control: 14
Interventions	Pulmonary rehabilitation: out-patient programme (hospital based followed by home based), multi-disciplinary; comprising a physiotherapist, a dietician, an occupational therapist and a nurse. After 1 month, individualised home exercise added Aerobic exercise, ULE, LLE, breathing exercises, educational material, nutrition Duration: 12 weeks 2 days per week, 1 hour long Usual care: Control group received none of the multi-disciplinary rehabilitation programmes and no care from multi-disciplinary professionals
Outcomes	Assessment: baseline and 12 weeks 6MWD, SQRQ, hand grip strength and health perception, fatigue, functional limitations due to fatigue, functional performance and satisfaction
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation procedures were performed by an independent person from the research group, who took a random envelope from the prepared box with sealed envelopes
Allocation concealment (selection bias)	Low risk	For this purpose, we prepared 80 sealed opaque envelopes with assignment information
Blinding of participants and personnel (performance bias) All outcomes	High risk	As a result of the nature of the intervention, both participants and those delivering the intervention would be aware of allocation
Blinding of outcome assessment (detection bias) All outcomes	High risk	Data collection was performed by members of the rehabilitation group. Data collected were not blinded to the data collector
Incomplete outcome data (attrition bias) All outcomes	Low risk	26/30 complete data for analysis 4/30 lost to follow-up = 13.33%
Selective reporting (reporting bias)	Low risk	No trial registration protocol was found. However it would seem that all outcomes stated in the study were measured
Other bias	Low risk	None noted

Methods	Study design: RCT (2 groups)	
Participants	Setting: in-patient; France Inclusion criteria: <ul style="list-style-type: none">• Diagnosis of COPD• Obstruction not reversible• History smoking 30 packs/y on average Exclusion criteria: <ul style="list-style-type: none">• Heart failure• PaO₂ ≤ 60 mmHg or with hypercapnia• Current infection Participant status: Age (years ± SD): RG: 59.6 ± 2.75; CG: 58.2 ± 1.8 Gender (M/F): RG: 7/3; CG: 8/2 FEV ₁ /FVC: RG: 57.2; CG: 55.7 Participants randomly assigned: Randomised: 22 Analysed: Rehab: 10 Control: 10	
Interventions	Pulmonary rehabilitation: in-patient rehabilitation LLE, BE Duration: 8 weeks Usual care	
Outcomes	Assessment: baseline and 2 months ICET QoL: not measured	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation process: drawing lots Outcome assessments: not blinded
Allocation concealment (selection bias)	Unclear risk	No information related to allocation concealment provided
Blinding of participants and personnel (performance bias) All outcomes	High risk	As a result of the nature of the intervention, both participants and those delivering the intervention would be aware of allocation
Blinding of outcome assessment (detection bias) All outcomes	High risk	Outcome assessments: not blinded

Vallet 1994 (Continued)

Incomplete outcome data (attrition bias) All outcomes	Low risk	18/20 (90%) completed
Selective reporting (reporting bias)	Low risk	No trial registration protocol was found. However it would seem that all outcomes stated in the study were measured
Other bias	Low risk	None noted

Van Wetering 2010

Methods	Study design: RCT (2 groups)
Participants	<p>Setting:</p> <p>Inclusion criteria:</p> <ul style="list-style-type: none"> ● Impaired exercise capacity ● Stage 2 or 3 COPD ● Willing to participate in a community-based programme <p>Exclusion criteria:</p> <ol style="list-style-type: none"> 1. Prior rehabilitation 2. Serious co-morbidity that precluded exercise therapy 3. Lack of motivation to participate in the treatment programme <p>Participant status: Age (years \pm SD): RG: 65.9 \pm 8.8; CG: 67.2 \pm 8.9 Gender (M/F): 71% male in each group FEV₁ % (pred \pm SD): RG: 58 \pm 17; CG: 60 \pm 15 FEV₁/FVC: RG: 49 \pm 11; CG: 36.1 \pm 26.4 Current smokers (%): RG: 33%; CG: 24%</p> <p>Participants randomly assigned: Randomised: 199 Analysed: Rehab: 87 Control: 88</p>
Interventions	<p>Pulmonary rehabilitation: community (primary care setting) Standardised supervised rehabilitation phase and a 20-month active maintenance phase Aerobic exercise, ULE, LLE, educational material</p> <p>Duration: Initially 4-Month, followed by 20-month active maintenance phase (twice a day during 30 minutes)</p> <p>Usual care: received pharmacotherapy according to accepted guidelines</p>
Outcomes	<p>Assessment: baseline and 4 months (immediately after initial intervention) SGRQ, cycle endurance test (CET), 6MWD, muscle strength (handgrip force (HGF), isometric quadriceps peak torque (QPT), maximal inspiratory mouth pressure (Pimax)), 17 body composition (FFM)</p>

Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Care provided through a computerised procedure with concealed participant allocation
Allocation concealment (selection bias)	Low risk	Programme or usual care through a computerised procedure with concealed participant allocation
Blinding of participants and personnel (performance bias) All outcomes	High risk	As a result of the nature of the intervention, both participants and those delivering the intervention would be aware of allocation
Blinding of outcome assessment (detection bias) All outcomes	Low risk	All measurements were assessed single-blind
Incomplete outcome data (attrition bias) All outcomes	Low risk	Loss = 24 (12%) (intervention: 15 (4.7%); control: 9 (9.2%)) 88% completed, so 12% attrition
Selective reporting (reporting bias)	Low risk	From protocol paper (http://clinicaltrials.gov/ct2/show/NCT00840892), outcomes matched those in the protocol paper
Other bias	Low risk	None noted

Vijayan 2010

Methods	Study design: RCT (2 groups)
Participants	<p>Setting: India</p> <p>Inclusion criteria:</p> <ul style="list-style-type: none"> • Moderate to severe, as per GOLD guidelines. • 8 weeks on standard inhalational therapy • 4 weeks post exacerbation <p>Exclusion criteria:</p> <p>Participant status:</p> <p>Age (years): not provided</p> <p>Gender: not provided</p> <p>FEV₁ %: not provided</p> <p>FEV₁/FVC: not provided</p> <p>Participants randomly assigned:</p> <p>Randomised: 31 (15 control; 16 intervention)</p> <p>Analysed:</p>

	Rehab: 16 Control: 15	
Interventions	Pulmonary rehabilitation: not informed of venue Aerobic exercise, ULE, LLE Duration: 8 weeks (5 days a week for 90 minutes) Usual care: Both groups had medication adjusted for 8 weeks	
Outcomes	Assessment: baseline 6-Minute walk test (Only relevant test)	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No Information
Allocation concealment (selection bias)	Unclear risk	No details provided
Blinding of participants and personnel (performance bias) All outcomes	High risk	As a result of the nature of the intervention, both participants and those delivering the intervention would be aware of allocation
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No details provided
Incomplete outcome data (attrition bias) All outcomes	Low risk	No attrition reported
Selective reporting (reporting bias)	Unclear risk	Insufficient details provided
Other bias	High risk	Very superficial information available in relation to the study, precluding good quality assessment

Weiner 1992

Methods	Study design: RCT (3 groups): SIMT group received threshold inspiratory muscle trainer and exercise programme, exercise training group and control randomly matched to 3 groups according to the following criteria: age; FEV ₁ ; and FEV ₁ /FVC
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Participants	<p>Setting: out-patient; Isreal</p> <p>Inclusion criteria:</p> <ul style="list-style-type: none"> • Spirometric evidence of chronic airflow limitation that was not corrected by bronchodilator therapy <p>Exclusion criteria:</p> <p>Participant status:</p> <p>Age (years \pm SD): RG: 64.4 \pm 3; CG: 62.3 \pm 2.4</p> <p>Gender (M/F): RG: 6/6; CG: 5/7</p> <p>FEV₁ % (pred \pm SD): RG: 32.8 \pm 3; CG: 39.2 \pm 2.8</p> <p>Participants randomly assigned:</p> <p>Randomised: 24</p> <p>Analysed:</p> <p>Rehab: 12</p> <p>Control: 12</p>
Interventions	<p>Pulmonary rehabilitation: out-patient (hospital)</p> <p>Performed under the supervision of a physiotherapist</p> <p>LLE, ULE, IMT, BE</p> <p>Duration: 6 months, 3 times a week, each session consisting of 1 hour of training</p> <p>Usual care: no additional treatment</p>
Outcomes	<p>Assessment:</p> <p>baseline and 6 months</p> <p>12-Minute WT, ICET, SSCET</p> <p>QoL: not measured</p>
Notes	1 exercise only group used in the analysis

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation process: random numbers table
Allocation concealment (selection bias)	Unclear risk	No information related to allocation concealment provided
Blinding of participants and personnel (performance bias) All outcomes	High risk	As a result of the nature of the intervention, both participants and those delivering the intervention would be aware of allocation
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome assessments: blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up

Weiner 1992 (Continued)

Selective reporting (reporting bias)	High risk	No trial registration protocol was found. Results of SGRQ not available
Other bias	Low risk	None noted

Wen 2008

Methods	Study design: RCT (3 groups) High-intensity group Anaerobic threshold group Control group	
Participants	Setting: out-patient clinic in China Inclusion criteria: <ul style="list-style-type: none">• Diagnosis of COPD based on GOLD guidelines Exclusion criteria: <ul style="list-style-type: none">• Suffered from disability of lower extremity, serious cardiovascular disease (including unstable angina pectoris, uncontrolled congestive heart failure, acute myocardial infarction, uncontrolled hypertension, frequent premature atrial or ventricular contraction, severe pulmonary hypertension), postexercise syncope• Severe disorder of hepatic and renal function• Cognitive learning disability and mental illness Participant status: Age (years± SD): RG: [ATG: 67 ± 7; HIG: 68 ± 7]; CG: 66 ± 10 Gender (M/F): all male with exception of 1 FEV ₁ % (pred ± SD): RG:[ATG: 46 ± 10; HIG: 50 ± 14;] CG: 52 ± 14 Participants randomly assigned: Randomised: 41 (high-intensity group: 17; anaerobic threshold group: 15; control group: 9) Analysed: Rehab: High-intensity group: 17; anaerobic threshold group: 15 Control: 9	
Interventions	Pulmonary rehabilitation: bicycle exercise training Aerobic exercise, LLE Duration: 12 weeks, 2 days a week Usual care	
Outcomes	Assessment: baseline and 12 weeks SGRQ, Borg/Max Oxygen Intake	
Notes	No results available for the SGRQ	
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement

Random sequence generation (selection bias)	Unclear risk	No Information
Allocation concealment (selection bias)	Unclear risk	No details provided
Blinding of participants and personnel (performance bias) All outcomes	High risk	As a result of the nature of the intervention, both participants and those delivering the intervention would be aware of allocation
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No details provided
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	54 randomly assigned, 13 lost Attrition: 24%
Selective reporting (reporting bias)	Low risk	No trial registration protocol was found. However it would seem that all outcomes stated in the study were measured
Other bias	Low risk	None noted

Wijkstra 1994

Methods	Study design: RCT (2 groups), stratified
Participants	<p>Setting: home based</p> <p>Inclusion criteria:</p> <ul style="list-style-type: none"> • Clinically stable condition (no recent exacerbations) • Optimal drug management. • FEV₁ < 60% predicted; FEV₁/vital capacity (IVC) < 50%; after bronchodilator <p>Exclusion criteria:</p> <ul style="list-style-type: none"> • Evidence of ischaemic heart disease, intermittent claudication • Musculoskeletal disorders or other disabling diseases that could restrict the rehabilitation programme <p>Participant status:</p> <p>Age (years ± SD): RG: 64 ± 5; CG: 62 ± 5</p> <p>Gender (M/F): RG: 23/5; CG: 14/1</p> <p>FEV₁% (pred ± SD): RG: 44 ± 11; CG: 45 ± 9</p> <p>FEV₁/FVC (± SD): RG: 39 ± 8; CG: 36 ± 7</p> <p>Participants randomly assigned:</p> <p>Randomised: 45 (RG: 30; CG: 15)</p> <p>Analysed:</p> <p>Rehab: 28</p> <p>Control: 15</p>

Interventions	Pulmonary rehabilitation: out-patient clinic and home based: progressive physiotherapy programme LLE, ULE, IMT, BE, Edu, Psy, nurse home visited Duration: 12 weeks, twice a week In addition, participants had to practice twice a day for half an hour at home Usual care: Control group did not follow the above mentioned protocol	
Outcomes	Assessment: baseline and 12 weeks 6-Minute WT, ICET CRQ	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation process: stratified randomisation
Allocation concealment (selection bias)	Unclear risk	No details provided
Blinding of participants and personnel (performance bias) All outcomes	High risk	As a result of the nature of the intervention, both participants and those delivering the intervention would be aware of allocation
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	43/45 = 95.6% completed Attrition rate: 4.4%
Selective reporting (reporting bias)	Low risk	No trial registration protocol was found. However it would seem that all outcomes stated in the study were measured
Other bias	Low risk	None noted

Xie 2003

Methods	Study design: RCT (2 groups)
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Participants	Setting: home-based affiliated central hospital of Jilin Medical College, China Inclusion criteria: <ul style="list-style-type: none">• Diagnosing standard for chronic obstructive pulmonary disease established by the respiratory branch of the Chinese Medical Association Exclusion criteria: <ul style="list-style-type: none">• Ischaemic heart disease, severe uncontrolled hypertension, alteration in thoracic cage• Neuromuscular disorders or intermittent claudication or osteoarticular lesions in lower extremities that would affect mobilisation Participant status: Age (years± SD): RG: 54 ±6; CG: 54 ± 6 Gender (M/F): RG: 22/3; CG: 21/4 FEV ₁ % (pred ± SD): RG: 41.8 ± 15; CG: 40 ± 16.5 FEV ₁ /FVC(±SD): RG: 40.3 ± 9.3; CG: 42.3 ± 12.1 Participants randomly assigned: Randomised: 50 Analysed: Rehab: 25 Control: 25	
Interventions	Pulmonary rehabilitation: 1 home rehabilitation walking programme; training intensity was individually determined LLE Duration: 12 weeks, 6 days a week, duration of 1 hour Usual care: Control group participants (medical treatment alone) also made visits to the hospital every 2 weeks for clinical checkup	
Outcomes	Assessment: baseline and 12 weeks ICE, SWT, dyspnoea, lung function, blood gas	
Notes		
<i>Risk of bias</i>		
Bias	Authors’ judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation process: random numbers table
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	As a result of the nature of the intervention, both participants and those delivering the intervention would be aware of allocation
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Outcome assessments: not reported

Xie 2003 (Continued)

Incomplete outcome data (attrition bias) All outcomes	Low risk	No mention of attrition
Selective reporting (reporting bias)	Low risk	No trial registration protocol was found. However it would seem that all outcomes stated in the study were measured
Other bias	Low risk	None noted

6MWT: six-minute walk test; BDI/TDI: baseline dyspnoea index/transition dyspnoea index; BE: breathing exercises; CRQ: Chronic Respiratory Disease Questionnaire; Edu: education; IAET: incremental arm ergometer test; ICET: incremental cycle ergometer test; IMT: inspiratory muscle training; ITT: incremental treadmill test; LLE: lower limb exercise; NEADL: Nottingham Extended Activities of Daily Living scale; PD: postural drainage; POMS: profile of mood state; Psy: psychological support; QoL: quality of life; SGRQ: St. George's Respiratory Questionnaire; SIP: sickness impact profile; SSCET: steady-state cycle ergometer test; SSTT: steady-state treadmill test; ULE: upper limb exercise; WT: walk test; HADS: Hospital Anxiety Depression Scale.

Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
Akinci 2011	Not a randomised controlled trial
Ambrosino 1981	Experimental group did not receive exercise training
Ambrosino 2006	Control group does not receive 'usual care'
Amin 2011	Control group does not receive 'usual care'
Arnadottir 2001	Control group does not receive 'usual care'
Backer 2003	Control group does not receive 'usual care'
Bauldoff 1996	Control group does not receive 'usual care'
Bauldoff 2002	Wrong aim
Behnke 2002	No control group
Behnke 2002a	Control group does not receive 'usual care'
Behnke 2003	No control group
Bernard 1999	Control group does not receive 'usual care'

(Continued)

Berry 1996	Control group does not receive 'usual care'
Bjerre-Jepsen 1981	No physical exercise component
Bourbeau 2000	No physical exercise component
Bourjeily-Habr 2002	No physical exercise component
Breyer 2010	Control group does not receive 'usual care'
Brooks 2000	Control group does not receive 'usual care'
Böhning 1990	Wrong comparison
Cai 2003	No physical exercise component
Carrieri-Kohlman 96	Control group does not receive 'usual care'
Cegla 2002	No physical exercise component
Chen 2011	Control group does not receive 'usual care'
Ciric 2008	Not a randomised controlled trial
Clark 2000	FEV ₁ higher than 70% of predicted
Cockcroft 1985	Control group does not receive 'usual care'
Coppoolse 1999	Control group does not receive 'usual care'
Covey 2004	Not a randomised controlled trial (review article)
Cox 1993	Not a randomised controlled trial
de Blasio 2000	Not a randomised controlled trial (editorial)
de Lucas Ramos 1998	Experimental group does not receive exercise training
Dekhuijzen 1990	Control group does not receive 'usual care'
Dekhuijzen 1991	Control group does not receive 'usual care'
Demir-Deriven 2001	Control group does not receive 'usual care'
Demir-Deriven 2002	Wrong comparison (men compared with women)
Dewse 1998	Not a randomised controlled trial (review article)

(Continued)

Di Marzo 2000	No physical exercise component
Downes Vogel 2002	No physical exercise component
Dushianthan 2009	Not a randomised controlled trial (review article)
Egan 2012	Not a randomised controlled trial
Ellum 2002	Wrong comparison (effect of posture on dyspnoea)
Emtner 1998	Not COPD
Epstein 1997	Control group does not receive 'usual care'
Esteve 1996	Control group does not receive 'usual care'
Fan 2008	Control group does not receive 'usual care'
Foglio 2001	Control group does not receive 'usual care'
Gadoury 2005	Control group does not receive 'usual care'
Gale 2009	Not a randomised controlled trial
Garuti 2010	Not a randomised controlled trial (review article)
Gautier 1998	Control group does not receive 'usual care'
Gautier 2002	Control group does not receive 'usual care'
Ghanem 2010	Participants not clearly 4 weeks post exacerbation
Gimenez 2000	Control group does not receive 'usual care' Quasi-randomisation
Girodo 1992	Not COPD
Goldman 1997	FEV ₁ is higher than 70% predicted
Gormley 1993	Control group does not receive 'usual care'
Gosselink 1990	Control group does not receive 'usual care'
Green 1999	Control group does not receive 'usual care'
Griffiths 1996	Control group does not receive 'usual care'

(Continued)

Grosbois 1999	Control group does not receive 'usual care'
Gu 2011	No physical exercise component
Guell 2006	Control group does not receive 'usual care'
Harver 1989	Experimental group did not receive exercise training
Hawkins 1999	No physical exercise component
Hentschel 2002	Control group does not receive 'usual care'
Holland 2003	Control group does not receive 'usual care'
Hospes 2009	No physical exercise component
Houchen 2011	Control group does not receive 'usual care'
Innocenti 2000	Control group does not receive 'usual care'
Jensen 1983	No physical exercise component
Johnson 2000	Control group does not receive 'usual care'
Jungblut 2007	Not a randomised controlled trial
Kaplan 1990	Control group does not receive 'usual care'
Katsura 2000	Control group does not receive 'usual care'
Kurabayashi 1998	Experimental group does not receive exercise training
Kurabayashi 2000	Experimental group does not receive exercise training
Larson 1999	Control group does not receive 'usual care'
Lathlean 2008	Randomisation unclear
Laukandt 1998	Control group does not receive 'usual care'
Levine 1986	Wrong comparison
Lewczuk 1998	Not a randomised controlled trial
Li 2002	No physical exercise component
Liu 2002	Randomisation unclear

(Continued)

Lotshaw 2003	Control group does not receive 'usual care'
Ma 2002	Control group does not receive 'usual care'
Mador 2002	Healthy controls
Mador 2004	Control group does not receive 'usual care'
Make 2000	Non-randomised comparison
Martinez 1993	Control group does not receive 'usual care'
McKeogh 2012	Control group does not receive 'usual care'
Morgan 1999	Not a randomised controlled trial (review)
Moros Garcia 1996	Not randomised
Morris 2003	Control group does not receive 'usual care'
MTU 2003	Systematic review
Murphy 2004	Control group does not receive 'usual care'
Myers 2000	Enhancement strategy
Na 2005	Not a randomised controlled trial
Nasilowski 2011	Not a randomised controlled trial
Nava 1998	Unstable patients (wrong population)
Ndundu 2001	Case series
Neder 2002	Control group does not receive 'usual care'
Newall 2000	Control group does not receive 'usual care'
Nguyen 2005	Control group does not receive 'usual care'
Ninot 2011	Outcomes measured longer than 3 months after the end of the intervention
Nosworthy 1992	Control group does not receive 'usual care'
Nygren-Bonnier 2002	Control group does not receive 'usual care'
O'Hara 1987	Not a randomised controlled trial

(Continued)

Ortega 2002	Control group does not receive 'usual care'
Patessio 1994	Control group does not receive 'usual care'
Petersen 2008	Control group does not receive 'usual care'
Piantadosi 2000	No randomised comparison between PR and control group
Pison 2001	Not a randomised controlled trial (review article)
Pison 2008	Control group does not receive 'usual care'
Pitta 2004	Not a randomised controlled trial
Ponsioen 2010	Not a randomised controlled trial (review article)
Prince 1989	Control group does not receive 'usual care'
Probst 2003	Acute effect of walking aid on exercise capacity
Proshchaeu 2009	Control group does not receive 'usual care'
Puente 1996	2 types of training compared
Raschke 1990	Not randomised
Regiane Resqueti 2007	Control group does not receive 'usual care'
Reilly 2000	NETT trial does not meet entry criteria for the review
Riario-Sforza 2009	Randomisation unclear
Ries 1986	Control group does not receive 'usual care'
Ries 1988	Control group does not receive 'usual care'
Ries 1995	Control group does not receive 'usual care'
Roberts 1999	Control group does not receive 'usual care'
Rooyackers 1996	Control group does not receive 'usual care'
Rudkin 1997	Control group does not receive 'usual care'
Santiworakul 2009	Randomisation unclear
Sassi-Dambon 1995	Experimental group does not receive exercise training

(Continued)

Saunders 1965	No physical exercise component
Scherer 1998	Control group does not receive 'usual care'
Scorsone 2010	Control group does not receive 'usual care'
Semenyuk 2007	No physical exercise component
Serres 1997	Inadequate duration (shorter than 4 weeks)
Sewell 2005	Control group does not receive 'usual care'
Sinclair 1980	Not a randomised controlled trial
Sindhwani 2011	Not a randomised controlled trial
Sivori 1998	Control group does not receive 'usual care'
Solanes Garcia 2004	Randomisation unclear
Sparrow 1997	Control group does not receive 'usual care'
Spruit 2001	Control group does not receive 'usual care'
Steele 2008	Control group does not receive 'usual care'
Stellefson 2009	Not an exercise programme
Sudo 1997	Control group does not receive 'usual care'
Sugawara 2007	Control group does not receive 'usual care'
Sun 2003	No physical exercise component
Swerts 1990	Control group does not receive 'usual care'
Taylor 2012	Not an exercise programme
Toevs 1984	Control group does not receive 'usual care'
Troosters 1999	Not a randomised controlled trial (review article)
Tsang 2001	Control group does not receive 'usual care'
Ubaidullayev 1990	No physical exercise component
Vargas 1998	No physical exercise component

(Continued)

Vogiatzis 1999	Treatment allocation not randomised
Vogiatzis 2001	Control group does not receive 'usual care'
Vogiatzis 2002	Control group does not receive 'usual care'
Wadell 2005	Not a randomised controlled trial
Wadell 2013	Control group does not receive 'usual care'
Wanke 1994	Control group does not receive 'usual care'
Wedzicha 1998	Control group does not receive 'usual care'
Weiner 1992a	Not COPD
Wen 2004	Participants not clearly 4 weeks post exacerbation and length of intervention unclear
White 2002	Control group does not receive 'usual care'
Worth 1985	Not randomised
Xu 2010	Length of programme unclear
Yamanaka 2009	Not a randomised controlled trial
Yan 1996	Experimental group does not receive exercise training
Yosbauran 1996	Control group does not receive 'usual care'
Zanini 2002	Control group does not receive 'usual care'
Zhang 2008	No physical exercise component

COPD: chronic obstructive pulmonary disease; FEV₁: forced expiratory volume in one second; NETT: National Emphysema Treatment Trial; PR: pulmonary rehabilitation.

Characteristics of studies awaiting assessment *[ordered by study ID]*

Aksu 2006

Methods	3 groups
Participants	58 participants
Interventions	Pulmonary rehab: aerobic exercise group; aerobic exercise plus isotonic strengthening exercise group; control group with no exercise Duration: 3 times per week for 12 weeks Usual care: not known
Outcomes	Assessment: baseline and 12 weeks Exercise performance (measured by Bruce exercise tolerance test), 6MWT, dyspnoea scores, SGRQ, SF-36, BMI and pulmonary function
Notes	Not possible to establish contact with study authors

D'Amico 2010

Methods	Not known
Participants	RCT (2 groups)
Interventions	Pulmonary rehabilitation: indoor aerobic training Duration: 3 days per week, 60 minutes each time, for 6 months Usual care: not known
Outcomes	Spirometry, oxygen saturation, ambulatory blood pressure measurement, health-related quality of life (SF-12)
Notes	Not possible to establish contact with study authors

Meshcheryakova 2010

Methods	RCT (4 groups)
Participants	57 participants
Interventions	Pulmonary rehabilitation: physical training Duration: not known Usual care: standardised medication
Outcomes	6-Minute walk test, respiratory muscle strength, health-related quality of life (SF-36), lung function
Notes	Contact information: m'natalia1967@inbox.ru

Meshcheryakova 2012

Methods	RCT (3 groups)
Participants	45 participants
Interventions	Pulmonary rehabilitation: a physical exercise programme Duration: not known
Outcomes	BMI, pulmonary function, 6MWT, shortness of breath, health-related quality of life (SF-36), systemic inflammation blood indicators, blood testosterone, muscle power and depression
Notes	Contact information: m_natalia1967@inbox.ru

Ren 2011

Methods	RCT (3 groups)
Participants	89 patients with COPD, divided into groups according to severity of COPD
Interventions	Pulmonary rehabilitation: 2 different programmes used for 20 weeks Usual care: not known
Outcomes	Assessment: baseline and 20 weeks 6MWT, BODE Index, acute exacerbation frequency, Modified Medical Research Council Scale, BMI and pulmonary function (FEV ₁)
Notes	Not possible to establish contact with study authors

6MWT: six-minute walk test; BMI: body mass index; COPD: chronic obstructive pulmonary disease; FEV₁: forced expiratory volume in one second; RCT: randomised controlled trial; SF: Short Form; SGRQ: St. George's Respiratory Questionnaire.

Six studies were awaiting classification in the previous version of the review ([Corrado 1995](#); [Fernández 1998](#); [Shu 1998](#); [Tregonning 2000](#); [Ward 1999](#); [Wright 2002](#)). The current search yielded no related publications since 2006 to allow us to clarify the status of these studies.

Characteristics of ongoing studies [ordered by study ID]**Chang 2008**

Trial name or title	Pulmonary rehabilitation or self-management (PRSM) for chronic obstructive pulmonary disease (COPD)
Methods	RCT (3 groups) Individual randomisation, blinded outcome assessment, 3-monthly follow-up assessments across a 12-month period and concurrent economic evaluation
Participants	Target of 85 per group

Chang 2008 (Continued)

Interventions	Stanford Chronic Disease Self-Management programme vs multi-factorial pulmonary rehabilitation group vs usual care provided by a GP
Outcomes	Primary outcome measure is St. George's Respiratory Disease Questionnaire Secondary outcome measures are measured by Frenchay Activities Index, International Physical Activity Questionnaire, the Hospital Anxiety and Depression Scale, the COPD Self-Efficacy scale and 2 physiological measures (forced vital capacity in 1 second and an incremental shuttle walk) measured at baseline and at 3-monthly intervals across 12 months. Also, spirometry and incremental shuttle walk at baseline and at 3 months
Starting date	April 2008
Contact information	terrence.haines@monash.edu
Notes	Results not yet published

Gurgun 2011

Trial name or title	Efficacy of an Eight-Week Pulmonary Rehabilitation in COPD Patients: An Experience of a Single Center in Turkey
Methods	RCT (2 groups)
Participants	152 stable patients with COPD
Interventions	8-Week pulmonary rehabilitation programme vs usual care
Outcomes	Assessment: at 8 weeks Walking distance, perceived dyspnoea, health-related quality of life, anxiety and depression
Starting date	Not known
Contact information	ahev.gurgun@ege.edu.tr
Notes	Study still recruiting at the time of this review

Sathyapala 2008

Trial name or title	Comparison of Repetitive Magnetic Stimulation (rMS) and Exercise Versus No Active Treatment on Quadri-ceps Function in Chronic Obstructive Pulmonary Disease (COPD)
Methods	RCT (3 groups)
Participants	58

Sathyapala 2008 (Continued)

Interventions	Pulmonary rehabilitation: supervised 2-hour resistance and endurance exercise programme twice a week for 8 weeks Repetitive magnetic stimulation of the intramuscular branches of the femoral nerve for 3 hours twice a week for 8 weeks Usual care: no intervention
Outcomes	Assessment at 8 weeks Lung function, fat-free mass, quadriceps strength, locomotion time and movement intensity over a 2-day period
Starting date	2007
Contact information	m.polkey@imperial.ac.uk
Notes	Results not yet published

One ongoing study in the previous version of the review ([Whiteford 2004](#)) remains unpublished.

DATA AND ANALYSES

Comparison 1. Rehabilitation versus usual care

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 QoL - Change in CRQ (Fatigue)	19	1291	Mean Difference (IV, Random, 95% CI)	0.68 [0.45, 0.92]
2 QoL - Change in CRQ (Emotional Function)	19	1291	Mean Difference (IV, Random, 95% CI)	0.56 [0.34, 0.78]
3 QoL - Change in CRQ (Mastery)	19	1212	Mean Difference (IV, Random, 95% CI)	0.71 [0.47, 0.95]
4 QoL - Change in CRQ (Dyspnoea)	19	1283	Mean Difference (IV, Random, 95% CI)	0.79 [0.56, 1.03]
5 QoL - Change in SGRQ (Total)	19	1146	Mean Difference (IV, Random, 95% CI)	-6.89 [-9.26, -4.52]
6 QoL - Change in SGRQ (Symptoms)	19	1153	Mean Difference (IV, Random, 95% CI)	-5.09 [-7.69, -2.49]
7 QoL - Change in SGRQ (Impacts)	19	1149	Mean Difference (IV, Random, 95% CI)	-7.23 [-9.91, -4.55]
8 QoL - Change in SGRQ (Activity)	19	1148	Mean Difference (IV, Random, 95% CI)	-6.08 [-9.28, -2.88]
9 Maximal Exercise (Incremental shuttle walk test)	8	694	Mean Difference (IV, Random, 95% CI)	39.77 [22.38, 57.15]
10 Maximal Exercise Capacity (cycle ergometer)	16	779	Mean Difference (IV, Random, 95% CI)	6.77 [1.89, 11.65]
11 Functional Exercise Capacity (6MWT)	38	1879	Mean Difference (IV, Random, 95% CI)	43.93 [32.64, 55.21]

Comparison 2. Rehabilitation versus usual care (subgroup analysis hospital vs community)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 QoL - Change in CRQ (Fatigue)	19	1291	Mean Difference (IV, Random, 95% CI)	0.68 [0.45, 0.92]
1.1 QoL - Community CRQ (Fatigue)	9	648	Mean Difference (IV, Random, 95% CI)	0.44 [0.14, 0.75]
1.2 QoL - Hospital CRQ (Fatigue)	10	643	Mean Difference (IV, Random, 95% CI)	0.86 [0.58, 1.14]
2 QoL - Change in CRQ (Emotional Function)	19	1291	Mean Difference (IV, Random, 95% CI)	0.56 [0.34, 0.78]
2.1 QoL - Community (Emotional Function)	9	648	Mean Difference (IV, Random, 95% CI)	0.21 [0.04, 0.39]
2.2 QoL - Hospital CRQ (Emotional Function)	10	643	Mean Difference (IV, Random, 95% CI)	0.77 [0.51, 1.03]
3 QoL - Change in CRQ (Mastery)	19	1212	Mean Difference (IV, Random, 95% CI)	0.71 [0.47, 0.95]

3.1 QoL - Community CRQ (Mastery)	9	569	Mean Difference (IV, Random, 95% CI)	0.40 [0.12, 0.67]
3.2 QoL - Hospital CRQ (Mastery)	10	643	Mean Difference (IV, Random, 95% CI)	0.95 [0.70, 1.20]
4 QoL - Change in CRQ (Dyspnoea)	19	1283	Mean Difference (IV, Random, 95% CI)	0.82 [0.59, 1.05]
4.1 QoL - Community Based CRQ (Dyspnoea)	8	633	Mean Difference (IV, Random, 95% CI)	0.58 [0.34, 0.81]
4.2 QoL - Hospital Based CRQ (Dyspnoea)	11	650	Mean Difference (IV, Random, 95% CI)	0.99 [0.66, 1.32]
5 QoL - Change in SGRQ (Total)	19	1146	Mean Difference (IV, Random, 95% CI)	-6.89 [-9.26, -4.52]
5.1 QoL - Community in SGRQ (Total)	9	643	Mean Difference (IV, Random, 95% CI)	-8.15 [-12.16, -4.13]
5.2 QoL - Hospital SGRQ (Total)	10	503	Mean Difference (IV, Random, 95% CI)	-6.05 [-8.91, -3.20]
6 QoL - Change in SGRQ (Symptoms)	19	1153	Mean Difference (IV, Random, 95% CI)	-5.09 [-7.69, -2.49]
6.1 QoL - Community SGRQ (Symptoms)	9	649	Mean Difference (IV, Random, 95% CI)	-3.66 [-7.07, -0.24]
6.2 QoL - Hospital SGRQ (Symptoms)	10	504	Mean Difference (IV, Random, 95% CI)	-6.91 [-10.51, -3.30]
7 QoL - Change in SGRQ (Impacts)	19	1149	Mean Difference (IV, Random, 95% CI)	-7.23 [-9.91, -4.55]
7.1 QoL - Community SGRQ (Impacts)	9	646	Mean Difference (IV, Random, 95% CI)	-8.17 [-10.00, -4.34]
7.2 QoL - Hospital SGRQ (Impacts)	10	503	Mean Difference (IV, Random, 95% CI)	-6.21 [-10.33, -2.09]
8 QoL - Change in SGRQ (Activity)	19	1148	Mean Difference (IV, Random, 95% CI)	-6.08 [-9.28, -2.88]
8.1 QoL - Community SGRQ (Activity)	9	645	Mean Difference (IV, Random, 95% CI)	-7.82 [-13.37, -2.28]
8.2 QoL - Hospital SGRQ (Activity)	10	503	Mean Difference (IV, Random, 95% CI)	-4.58 [-8.16, 1.00]

Comparison 3. Rehabilitation versus usual care (subgroup analysis exercise only vs exercise and other)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 QoL - Change in CRQ (Fatigue)	19	1291	Mean Difference (IV, Random, 95% CI)	0.68 [0.45, 0.92]
1.1 QoL - Exercise Only CRQ (Fatigue)	10	480	Mean Difference (IV, Random, 95% CI)	0.73 [0.54, 0.92]
1.2 QoL - Exercise + Other CRQ (Fatigue)	9	811	Mean Difference (IV, Random, 95% CI)	0.61 [0.18, 1.03]
2 QoL - Change in CRQ (Emotional Function)	19	1291	Mean Difference (IV, Random, 95% CI)	0.56 [0.34, 0.78]
2.1 QoL - Exercise Only CRQ (Emotional Function)	10	480	Mean Difference (IV, Random, 95% CI)	0.51 [0.31, 0.71]

2.2 QoL - Exercise + Other CRQ (Emotional Function)	9	811	Mean Difference (IV, Random, 95% CI)	0.58 [0.16, 1.00]
3 QoL - Change in CRQ (Mastery)	19	1212	Mean Difference (IV, Random, 95% CI)	0.71 [0.47, 0.95]
3.1 QoL - Exercise Only CRQ (Mastery)	10	480	Mean Difference (IV, Random, 95% CI)	0.66 [0.44, 0.88]
3.2 QoL - Exercise + Other CRQ (Mastery)	9	732	Mean Difference (IV, Random, 95% CI)	0.74 [0.31, 1.18]
4 QoL - Change in CRQ (Dyspnoea)	19	1283	Mean Difference (IV, Random, 95% CI)	0.79 [0.56, 1.03]
4.1 QoL - Exercise Only CRQ (Dyspnoea)	10	474	Mean Difference (IV, Random, 95% CI)	0.83 [0.56, 1.09]
4.2 QoL - Exercise + Other CRQ (Dyspnoea)	9	809	Mean Difference (IV, Random, 95% CI)	0.74 [0.35, 1.13]
5 QoL - Change in SGRQ (Total)	19	1146	Mean Difference (IV, Random, 95% CI)	-6.89 [-9.26, -4.52]
5.1 QoL Exercise Only SGRQ (Total)	5	230	Mean Difference (IV, Random, 95% CI)	-7.87 [-16.72, 0.98]
5.2 QoL Exercise + Other SGRQ (Total)	14	916	Mean Difference (IV, Random, 95% CI)	-6.76 [-9.19, -4.34]
6 QoL - Change in SGRQ (Symptoms)	19	1153	Mean Difference (IV, Random, 95% CI)	-5.09 [-7.69, -2.49]
6.1 QoL - Exercise Only SGRQ (Symptoms)	5	230	Mean Difference (IV, Random, 95% CI)	-7.38 [-12.33, -2.44]
6.2 QoL - Exercise + Other SGRQ (Symptoms)	14	923	Mean Difference (IV, Random, 95% CI)	-4.38 [-7.62, -1.15]
7 QoL - Change in SGRQ (Impacts)	19	1149	Mean Difference (IV, Random, 95% CI)	-7.23 [-9.91, -4.55]
7.1 QoL - Exercise Only SGRQ (Impacts)	5	230	Mean Difference (IV, Random, 95% CI)	-6.11 [-12.60, 0.38]
7.2 QoL - Exercise + Other SGRQ (Impacts)	14	919	Mean Difference (IV, Random, 95% CI)	-7.61 [-10.64, -4.57]
8 QoL - Change in SGRQ (Activity)	19	1148	Mean Difference (IV, Random, 95% CI)	-6.08 [-9.28, -2.88]
8.1 QoL - Exercise Only SGRQ (Activity)	5	230	Mean Difference (IV, Random, 95% CI)	-9.33 [-21.66, 2.99]
8.2 QoL - Exercise + Other SGRQ (Activity)	14	918	Mean Difference (IV, Random, 95% CI)	-5.79 [-8.95, -2.64]

Comparison 4. Rehabilitation versus usual care (sensitivity analysis by allocation concealment and incomplete outcome)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 QoL - Change in CRQ (Dyspnoea)	5	384	Mean Difference (IV, Random, 95% CI)	0.99 [0.64, 1.34]
1.1 QoL - Low Risk CRQ (Dyspnoea)	5	384	Mean Difference (IV, Random, 95% CI)	0.99 [0.64, 1.34]

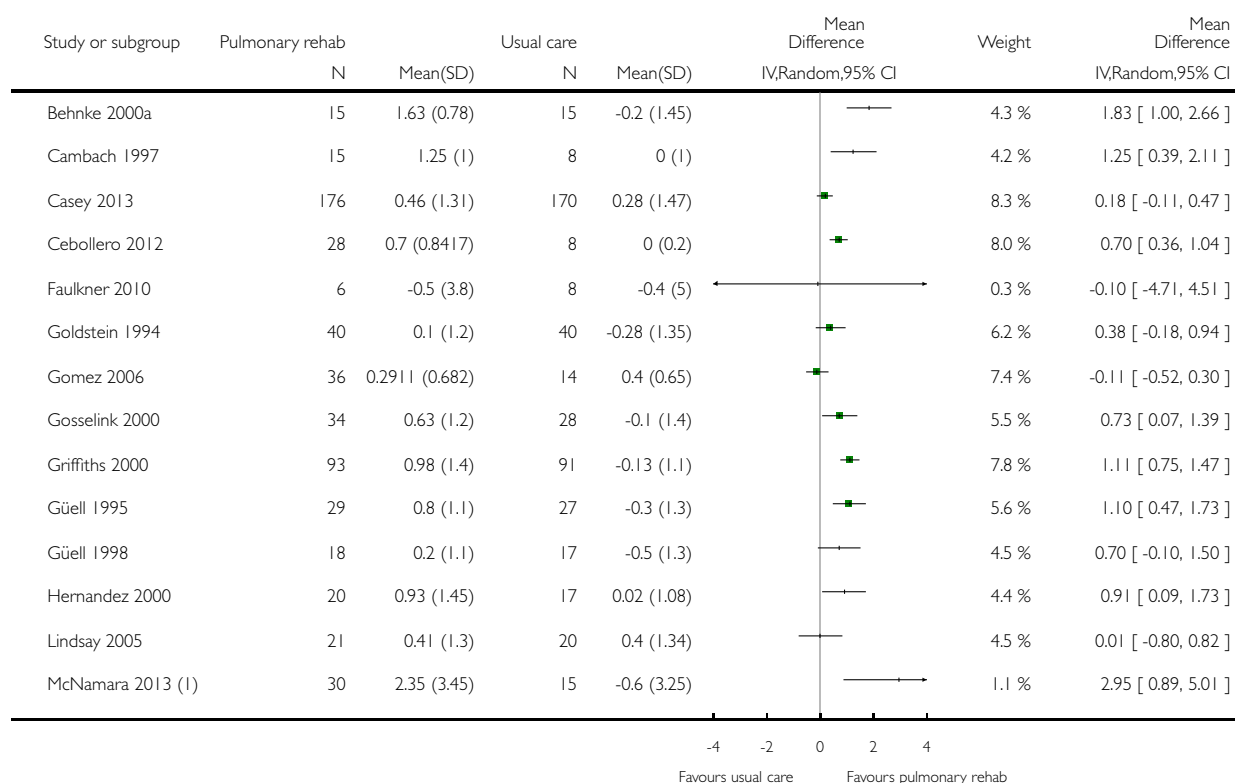
2 QoL - Change in CRQ (Emotional Function)	5	386	Mean Difference (IV, Random, 95% CI)	0.60 [0.09, 1.11]
2.1 QoL - Low Risk (Emotional Function)	5	386	Mean Difference (IV, Random, 95% CI)	0.60 [0.09, 1.11]
3 QoL - Low Risk CRQ (Fatigue)	5	386	Mean Difference (IV, Random, 95% CI)	0.90 [0.41, 1.39]
4 QoL - Low Risk CRQ (Mastery)	5	386	Mean Difference (IV, Random, 95% CI)	0.77 [0.28, 1.26]
5 QoL - Low Risk SGRQ (Total)	7	572	Mean Difference (IV, Random, 95% CI)	-5.15 [-7.95, -2.36]
6 QoL - Low Risk SGRQ (Symptoms)	7	572	Mean Difference (IV, Random, 95% CI)	-4.12 [-8.45, 0.21]
7 QoL - Low Risk SGRQ (Impacts)	7	572	Mean Difference (IV, Random, 95% CI)	-5.92 [-10.01, -1.82]
8 QoL - Low Risk SGRQ (Activity)	7	572	Mean Difference (IV, Random, 95% CI)	-5.33 [-8.10, -2.57]

Analysis 1.1. Comparison 1 Rehabilitation versus usual care, Outcome 1 QoL - Change in CRQ (Fatigue).

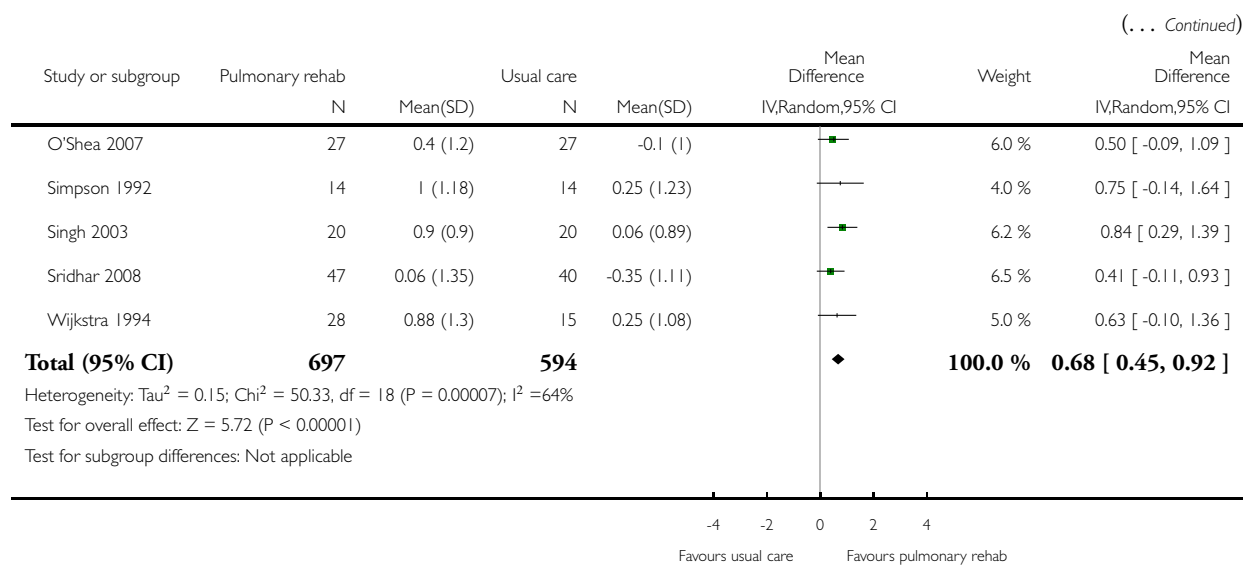
Review: Pulmonary rehabilitation for chronic obstructive pulmonary disease

Comparison: 1 Rehabilitation versus usual care

Outcome: 1 QoL - Change in CRQ (Fatigue)



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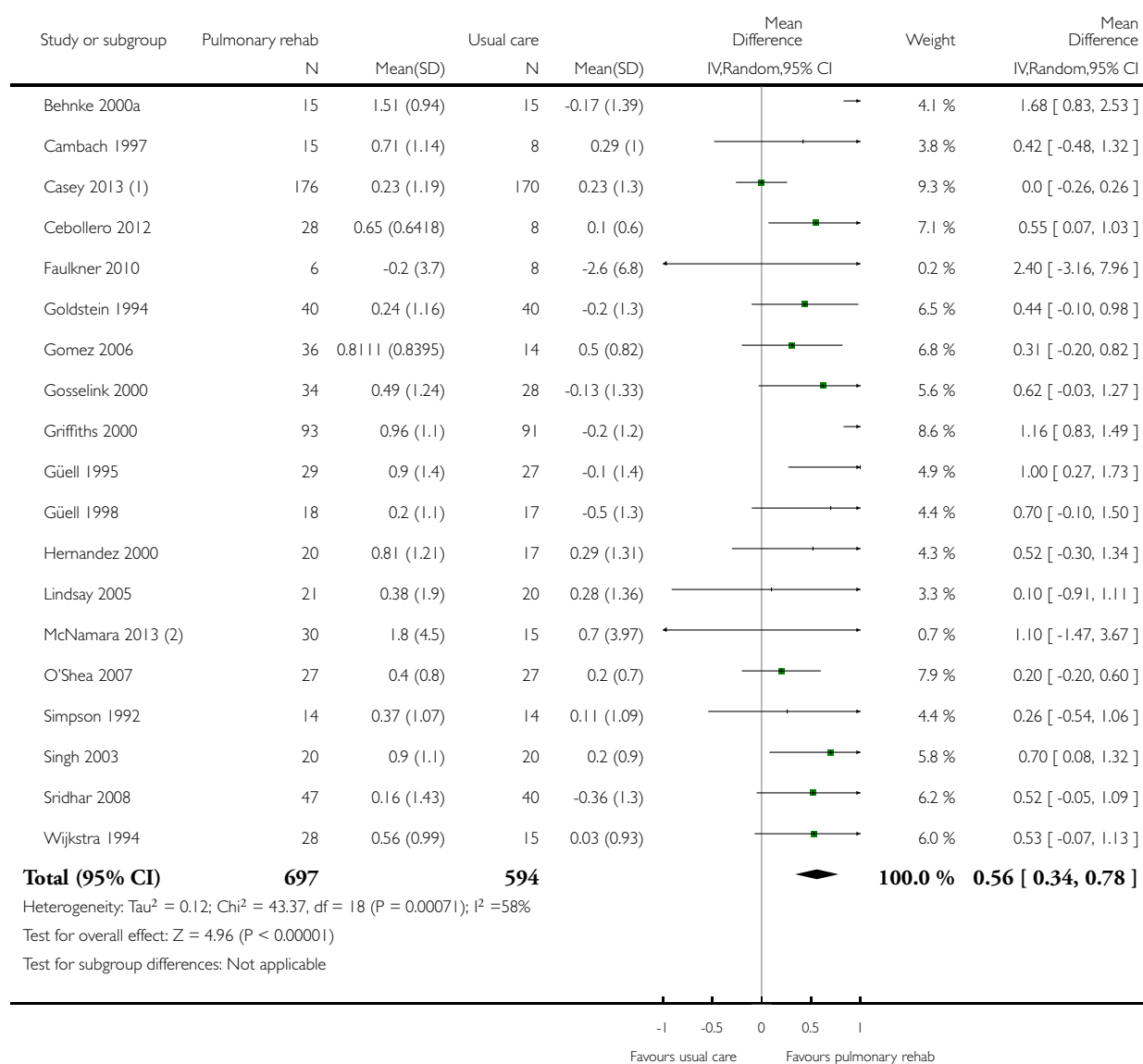
(1) Mcnamara 2012: Used combined mean and SD for the two Intervention groups land (based/ water based). Calculated SD of the change from CI

Analysis 1.2. Comparison 1 Rehabilitation versus usual care, Outcome 2 QoL - Change in CRQ (Emotional Function).

Review: Pulmonary rehabilitation for chronic obstructive pulmonary disease

Comparison: 1 Rehabilitation versus usual care

Outcome: 2 QoL - Change in CRQ (Emotional Function)



(1) adjusted sample size to account for use of cluster samples in Casey

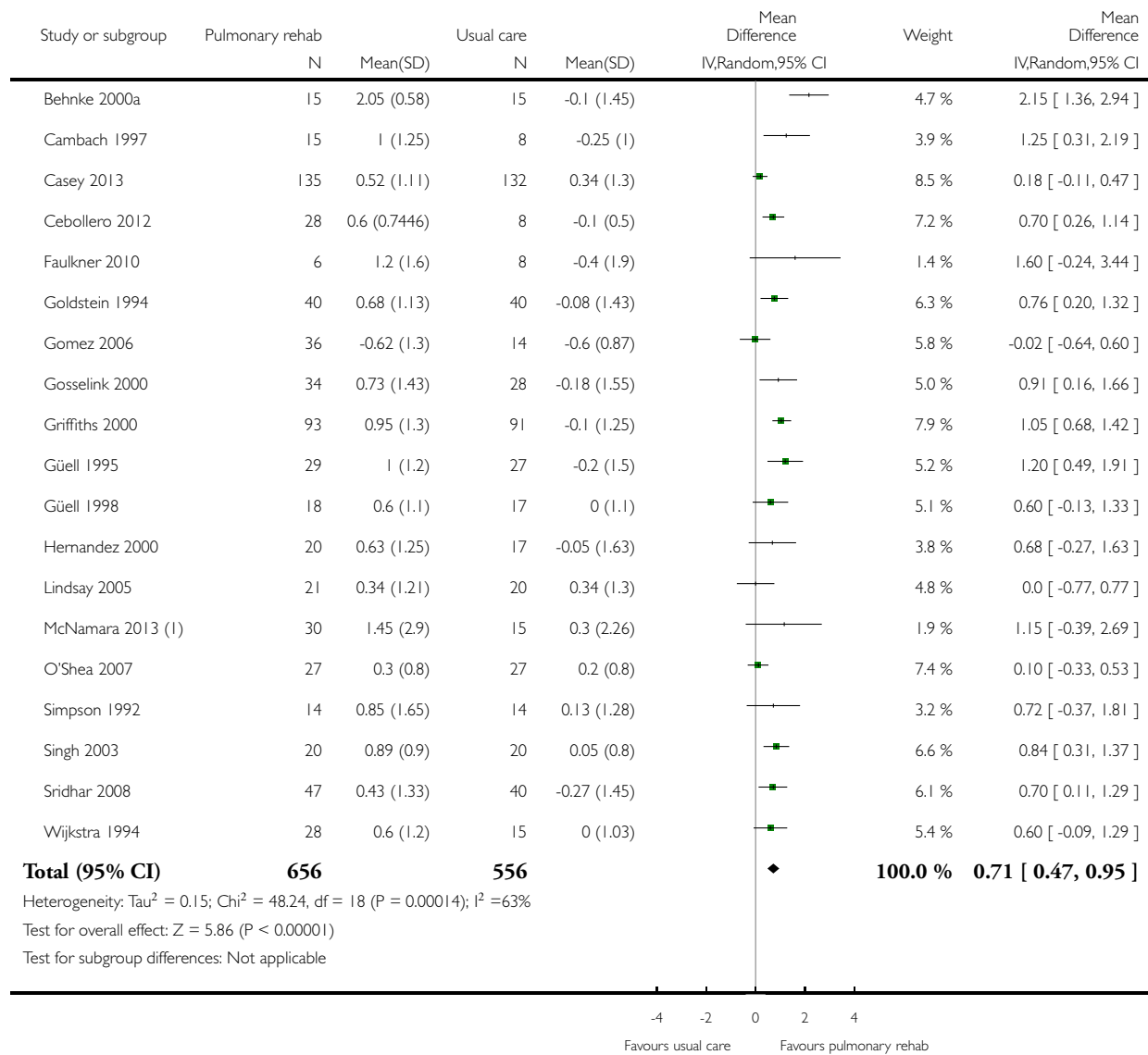
(2) McNamara 2012: Used combined mean and SD for the two Intervention groups land (based/ water based). Calculated SD of the change from CI

Analysis 1.3. Comparison 1 Rehabilitation versus usual care, Outcome 3 QoL - Change in CRQ (Mastery).

Review: Pulmonary rehabilitation for chronic obstructive pulmonary disease

Comparison: 1 Rehabilitation versus usual care

Outcome: 3 QoL - Change in CRQ (Mastery)



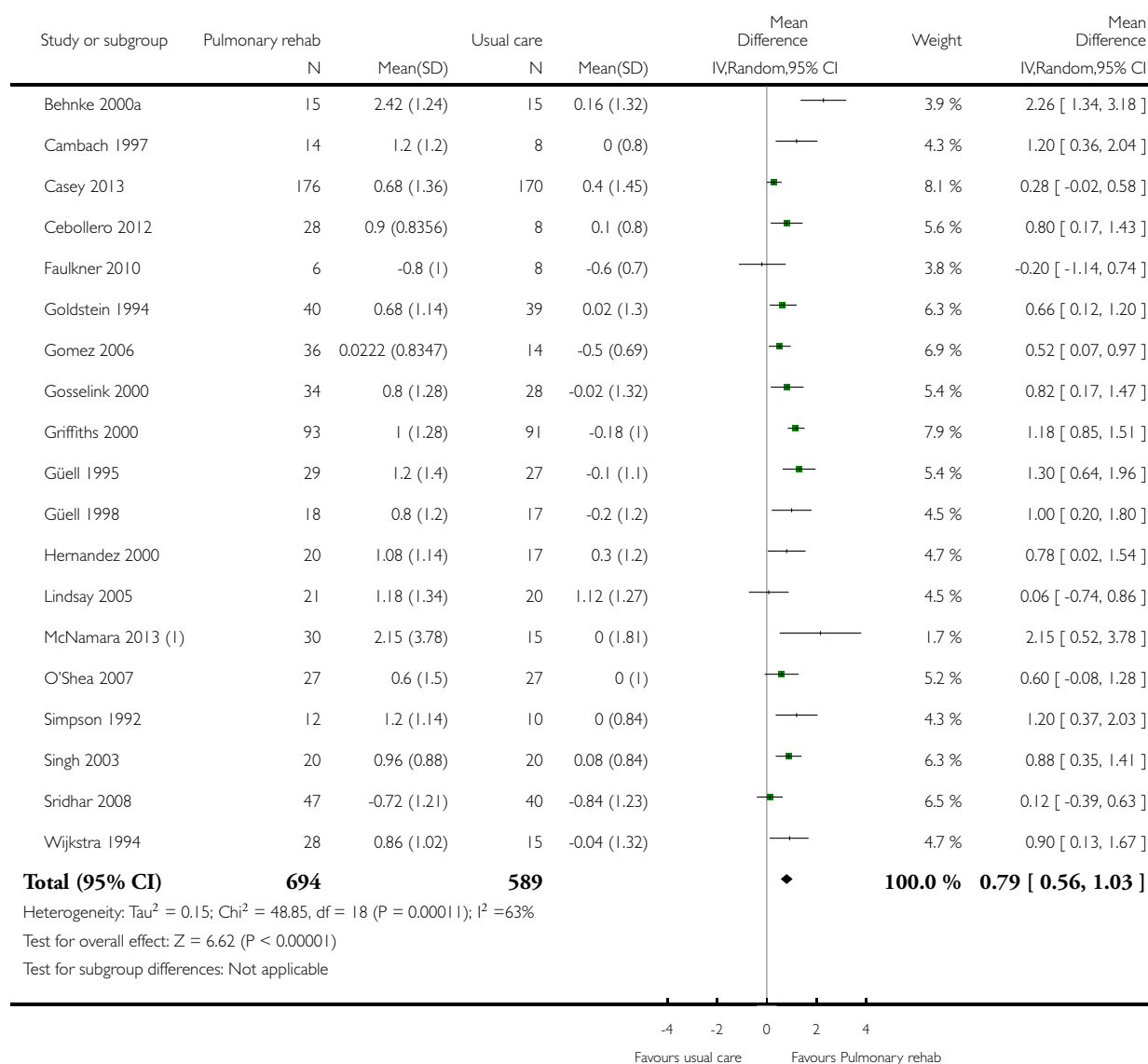
(1) McNamara 2012: Used combined mean and SD for the two Intervention groups land (based/ water based). Calculated SD of the change from CI

Analysis 1.4. Comparison 1 Rehabilitation versus usual care, Outcome 4 QoL - Change in CRQ (Dyspnoea).

Review: Pulmonary rehabilitation for chronic obstructive pulmonary disease

Comparison: 1 Rehabilitation versus usual care

Outcome: 4 QoL - Change in CRQ (Dyspnoea)



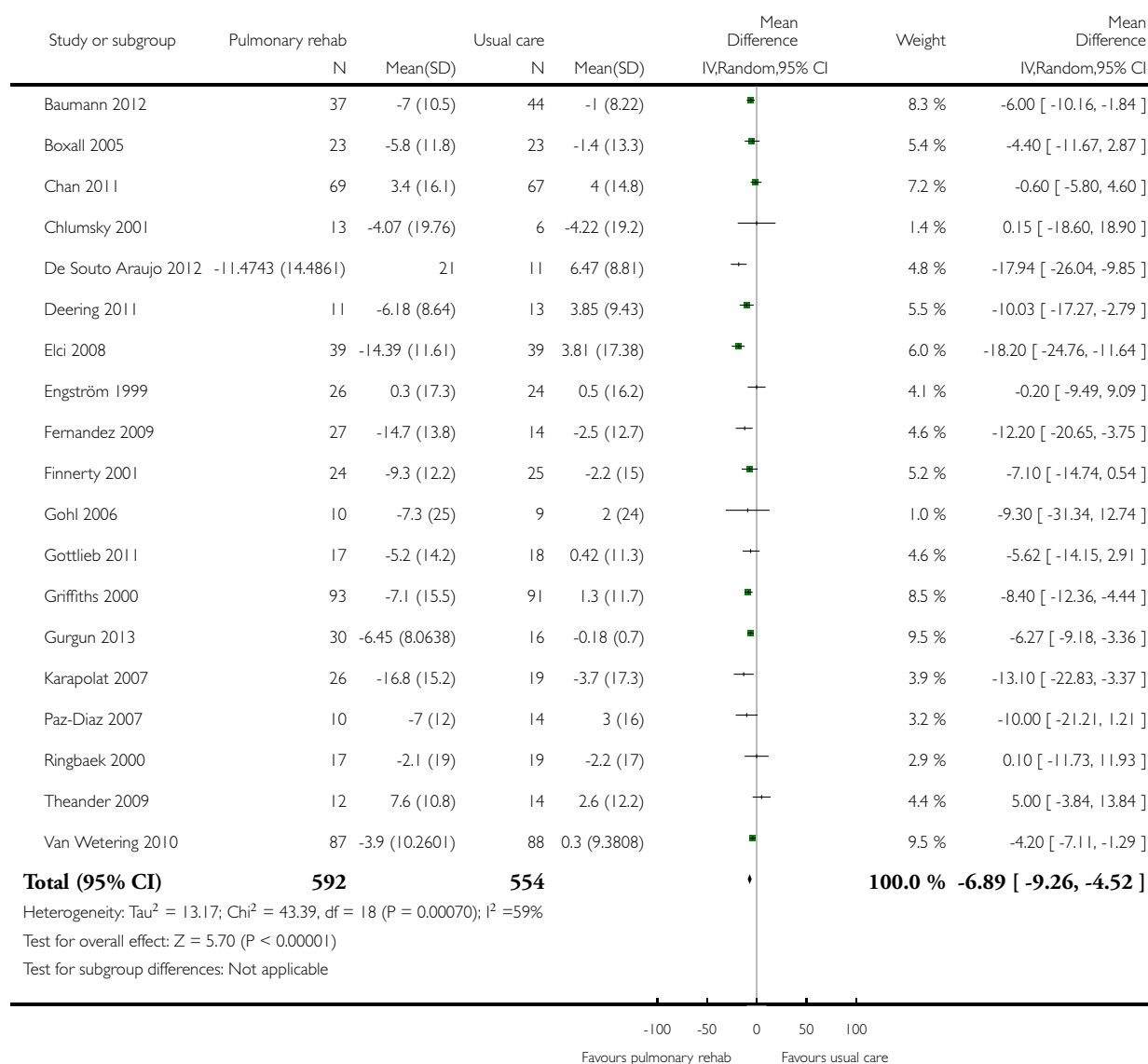
(1) McNamara 2012: Used combined mean and SD for the two Intervention groups land (based/ water based). Calculated SD of the change from CI

Analysis 1.5. Comparison 1 Rehabilitation versus usual care, Outcome 5 QoL - Change in SGRQ (Total).

Review: Pulmonary rehabilitation for chronic obstructive pulmonary disease

Comparison: 1 Rehabilitation versus usual care

Outcome: 5 QoL - Change in SGRQ (Total)

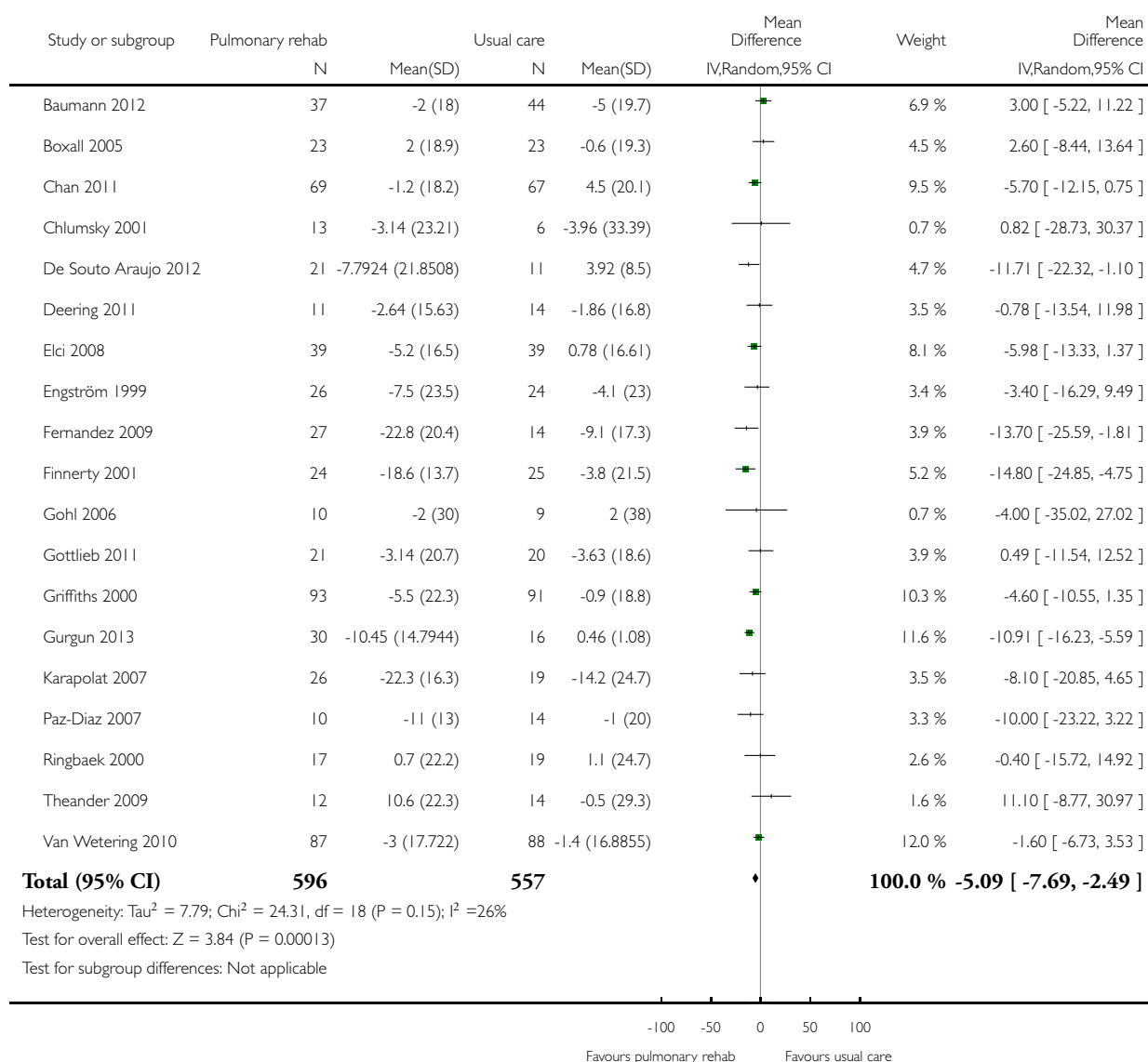


Analysis 1.6. Comparison 1 Rehabilitation versus usual care, Outcome 6 QoL - Change in SGRQ (Symptoms).

Review: Pulmonary rehabilitation for chronic obstructive pulmonary disease

Comparison: 1 Rehabilitation versus usual care

Outcome: 6 QoL - Change in SGRQ (Symptoms)

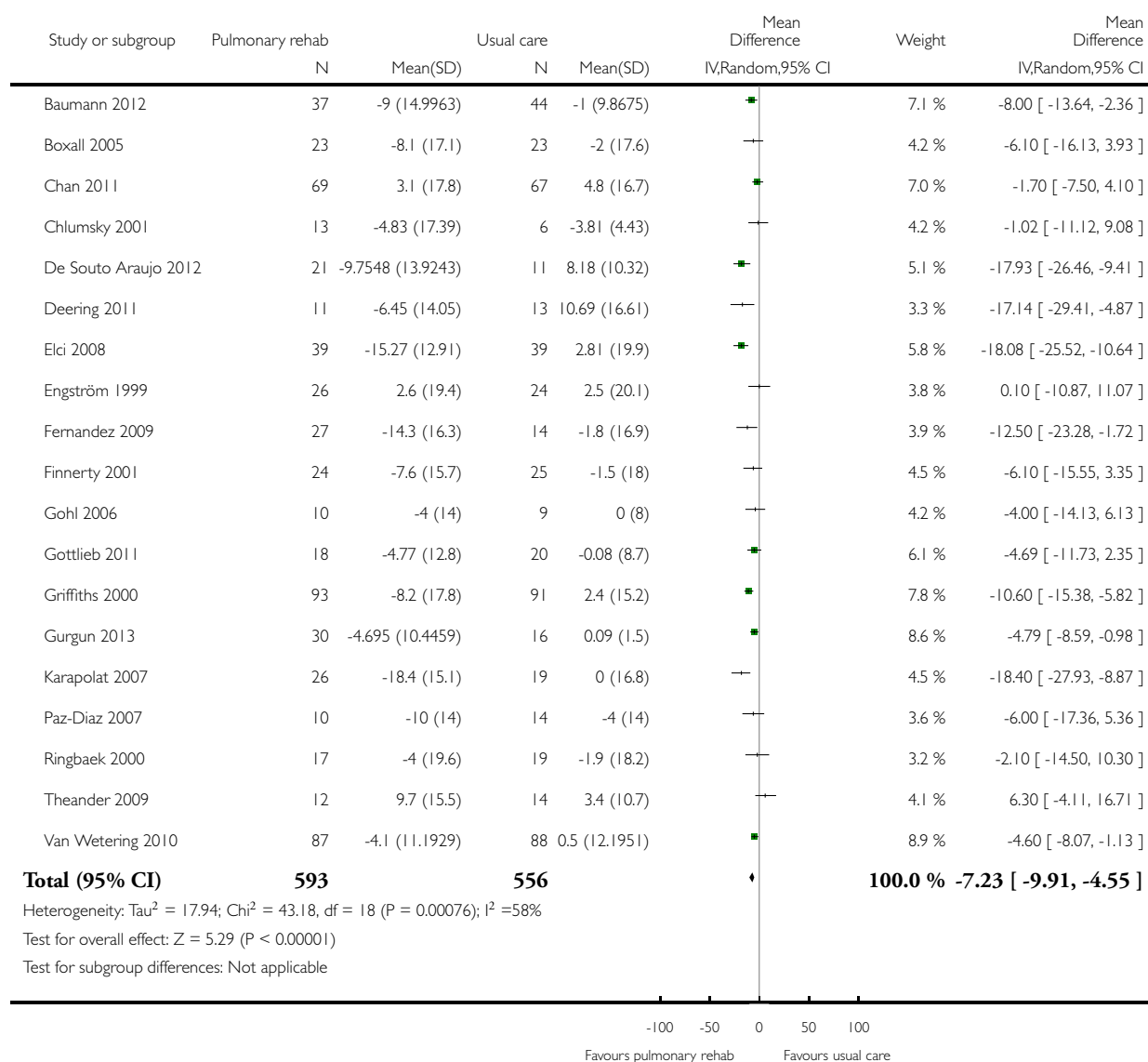


Analysis 1.7. Comparison 1 Rehabilitation versus usual care, Outcome 7 QoL - Change in SGRQ (Impacts).

Review: Pulmonary rehabilitation for chronic obstructive pulmonary disease

Comparison: 1 Rehabilitation versus usual care

Outcome: 7 QoL - Change in SGRQ (Impacts)

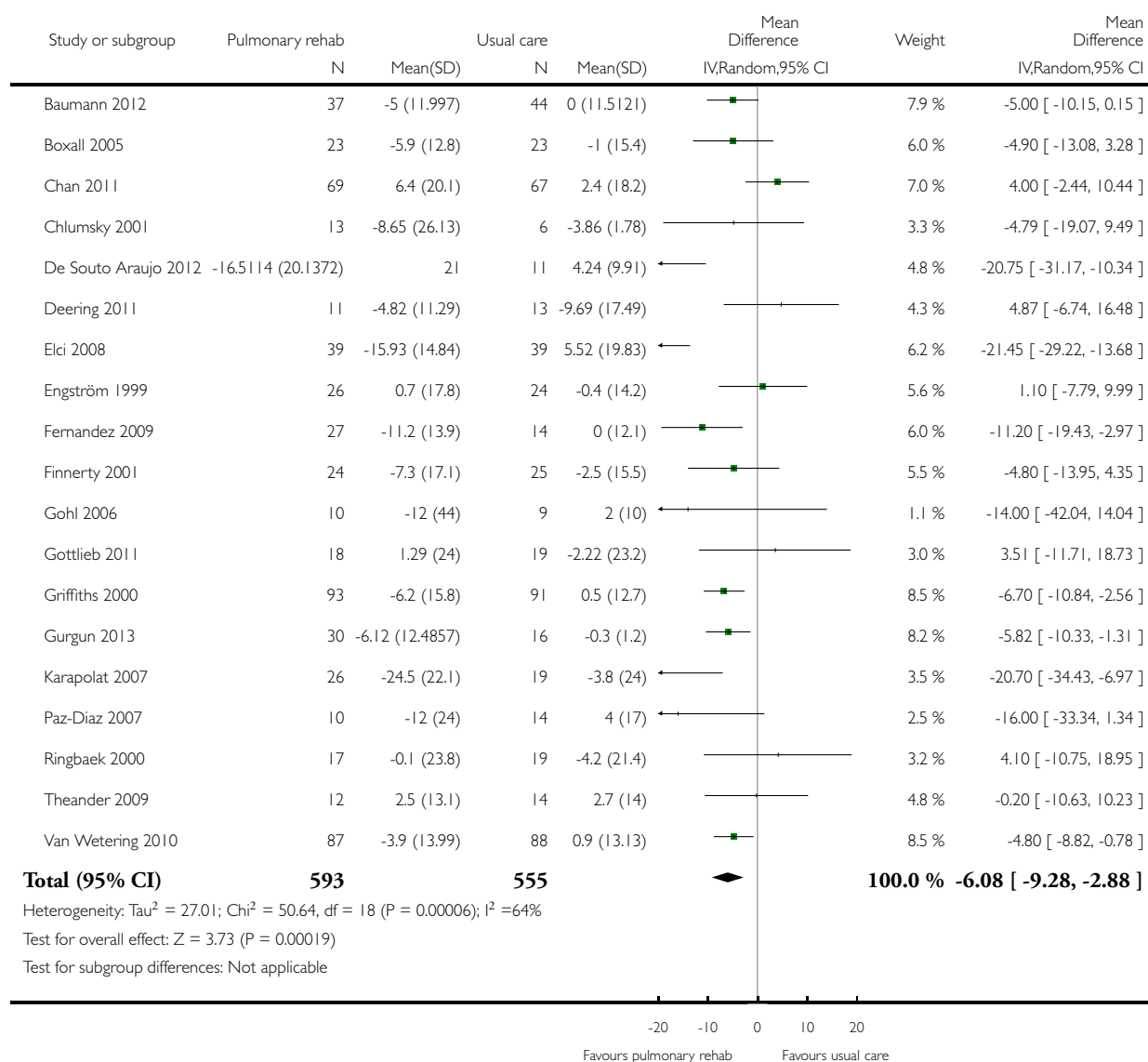


Analysis 1.8. Comparison 1 Rehabilitation versus usual care, Outcome 8 QoL - Change in SGRQ (Activity).

Review: Pulmonary rehabilitation for chronic obstructive pulmonary disease

Comparison: 1 Rehabilitation versus usual care

Outcome: 8 QoL - Change in SGRQ (Activity)

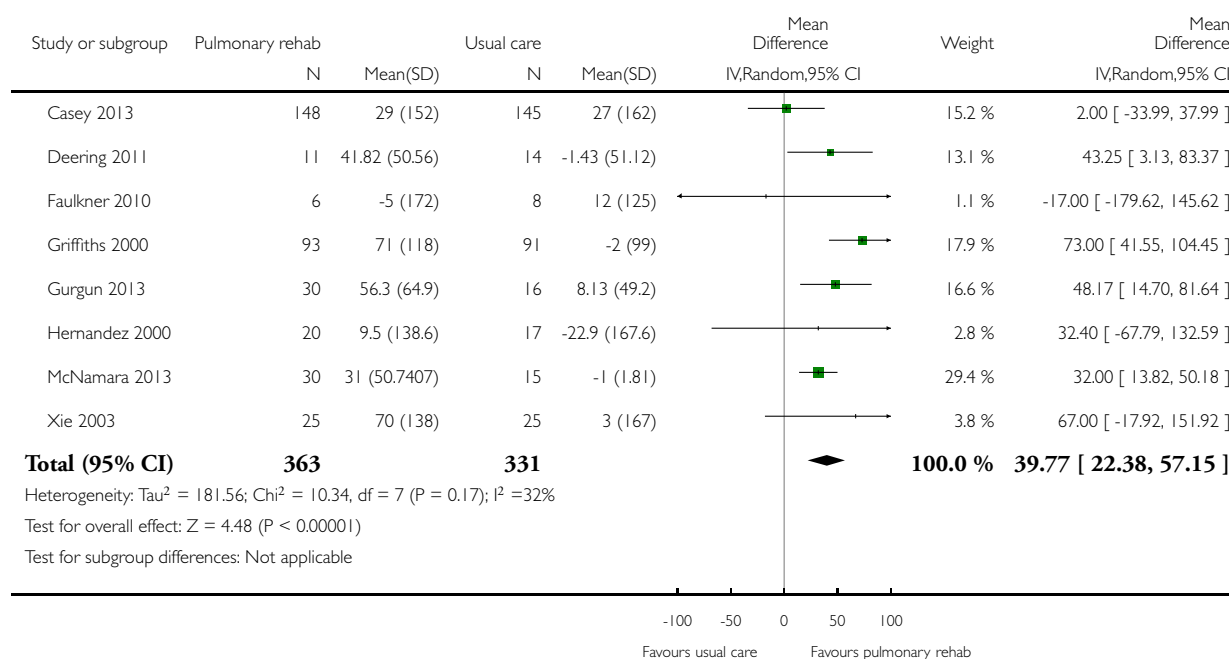


Analysis 1.9. Comparison 1 Rehabilitation versus usual care, Outcome 9 Maximal Exercise (Incremental shuttle walk test).

Review: Pulmonary rehabilitation for chronic obstructive pulmonary disease

Comparison: 1 Rehabilitation versus usual care

Outcome: 9 Maximal Exercise (Incremental shuttle walk test)

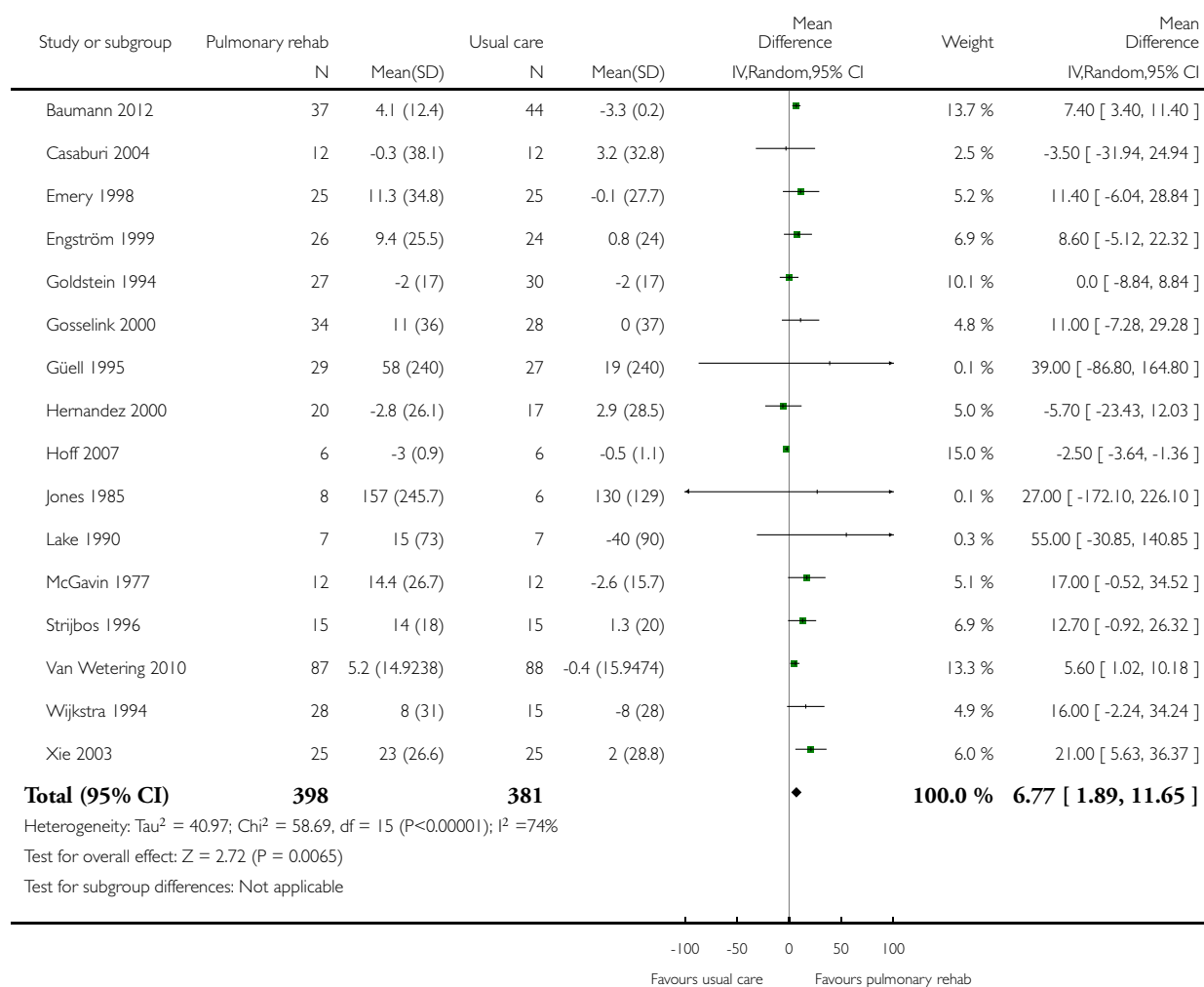


Analysis 1.10. Comparison 1 Rehabilitation versus usual care, Outcome 10 Maximal Exercise Capacity (cycle ergometer).

Review: Pulmonary rehabilitation for chronic obstructive pulmonary disease

Comparison: 1 Rehabilitation versus usual care

Outcome: 10 Maximal Exercise Capacity (cycle ergometer)

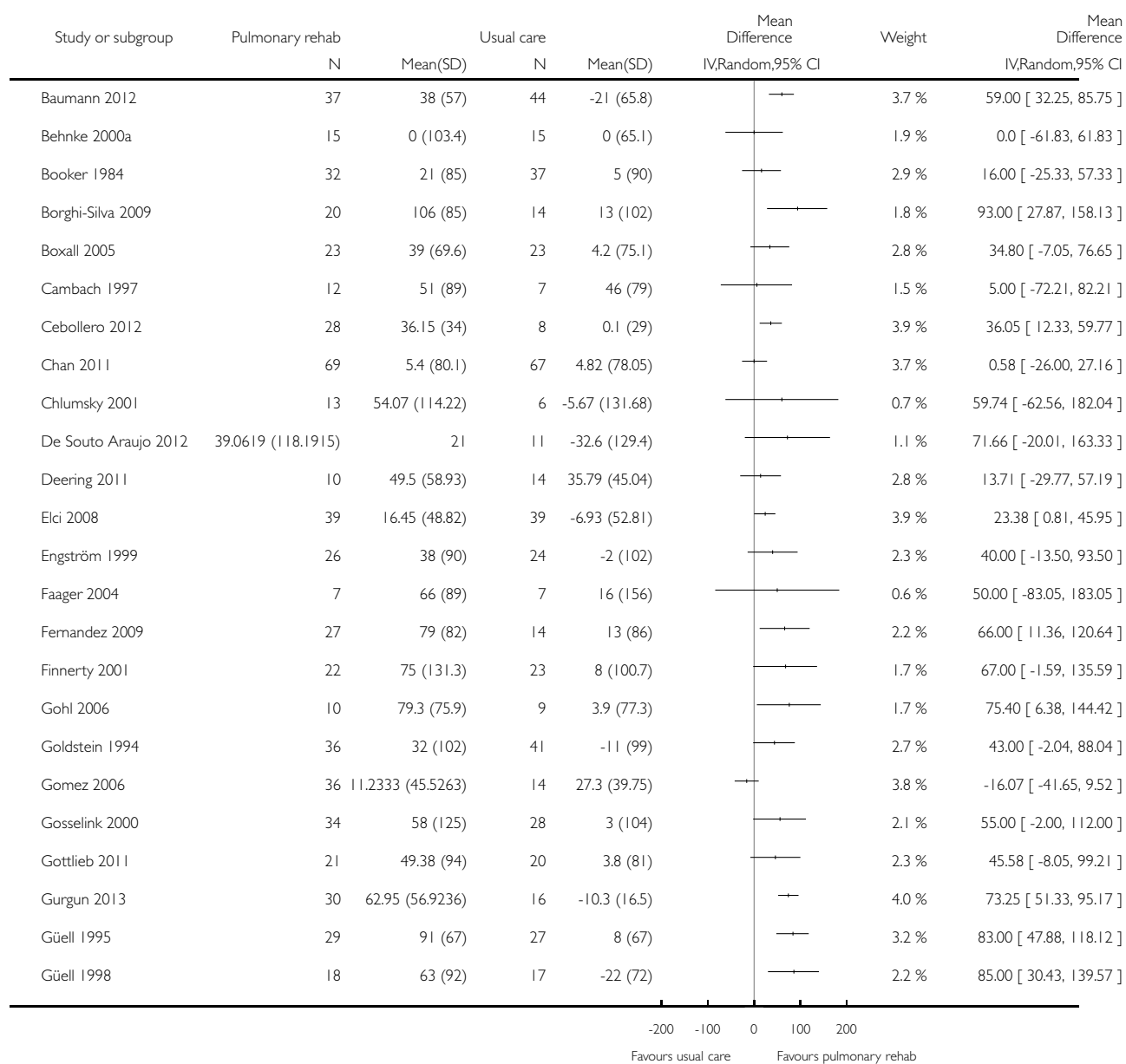


Analysis 1.11. Comparison 1 Rehabilitation versus usual care, Outcome 11 Functional Exercise Capacity (6MWT)).

Review: Pulmonary rehabilitation for chronic obstructive pulmonary disease

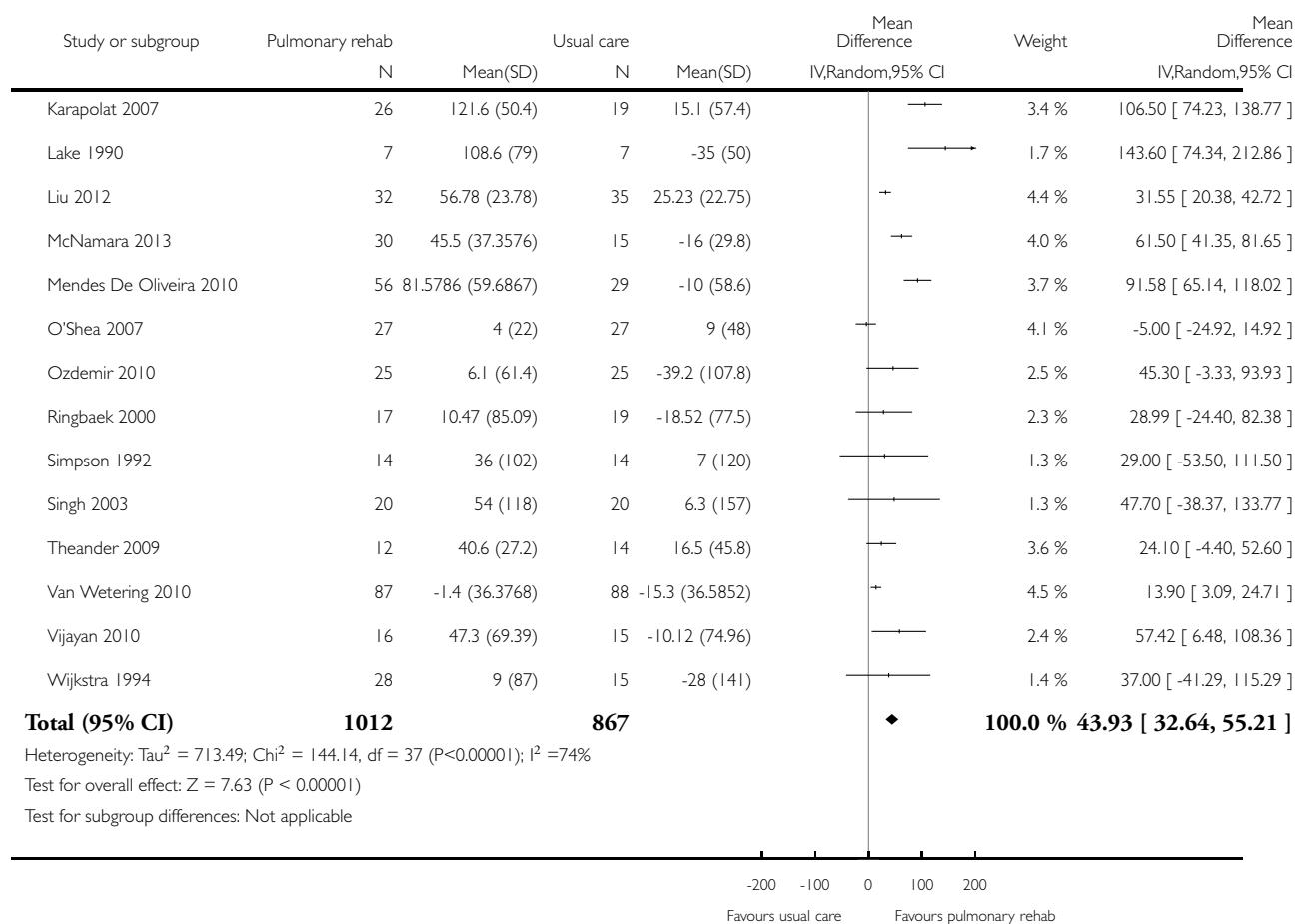
Comparison: 1 Rehabilitation versus usual care

Outcome: 11 Functional Exercise Capacity (6MWT)



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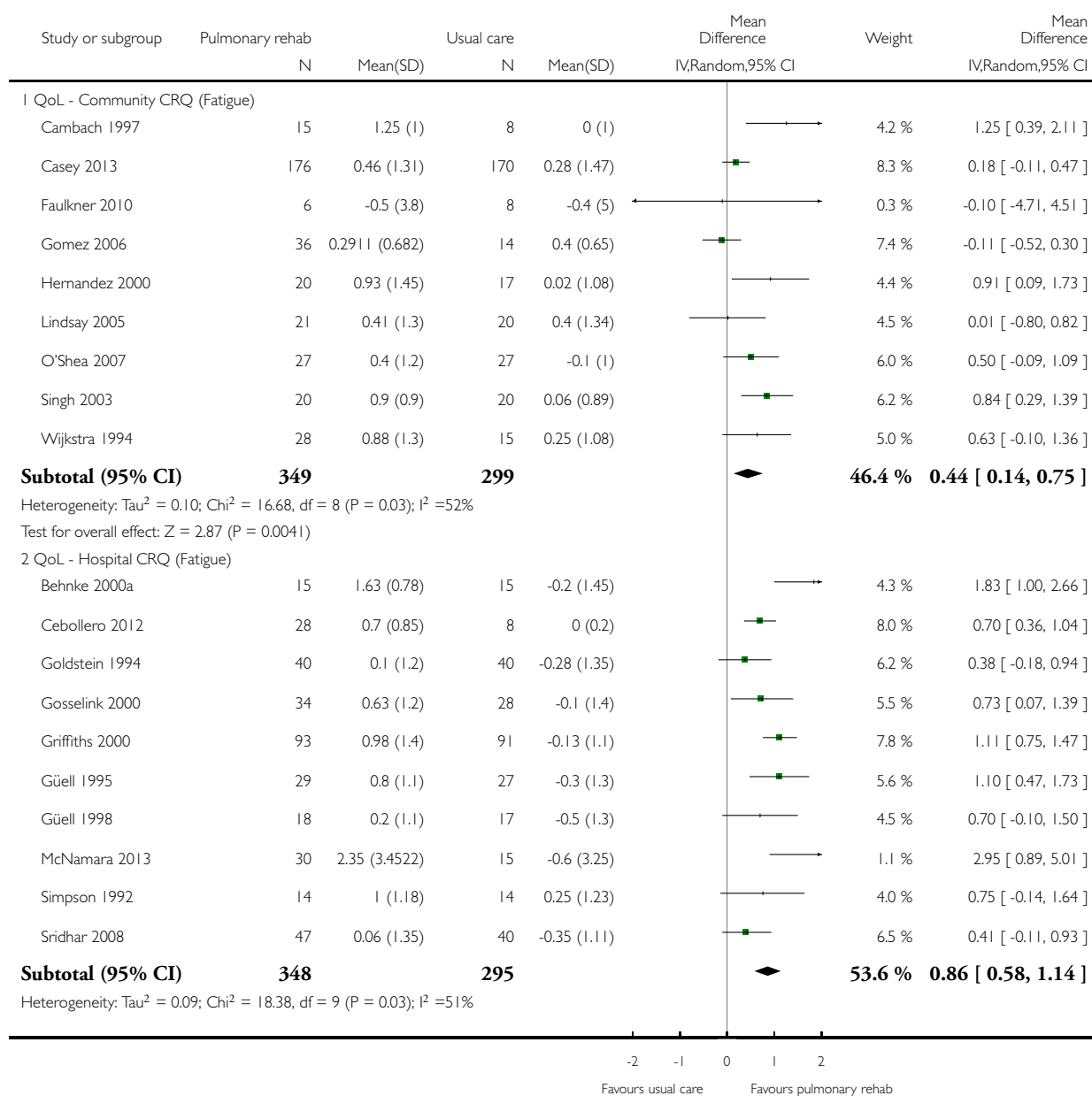


Analysis 2.1. Comparison 2 Rehabilitation versus usual care (subgroup analysis hospital vs community), Outcome 1 QoL - Change in CRQ (Fatigue).

Review: Pulmonary rehabilitation for chronic obstructive pulmonary disease

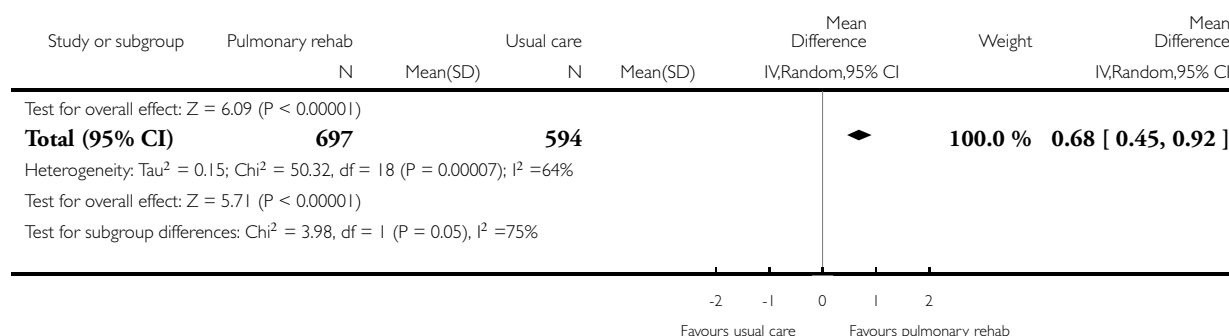
Comparison: 2 Rehabilitation versus usual care (subgroup analysis hospital vs community)

Outcome: 1 QoL - Change in CRQ (Fatigue)



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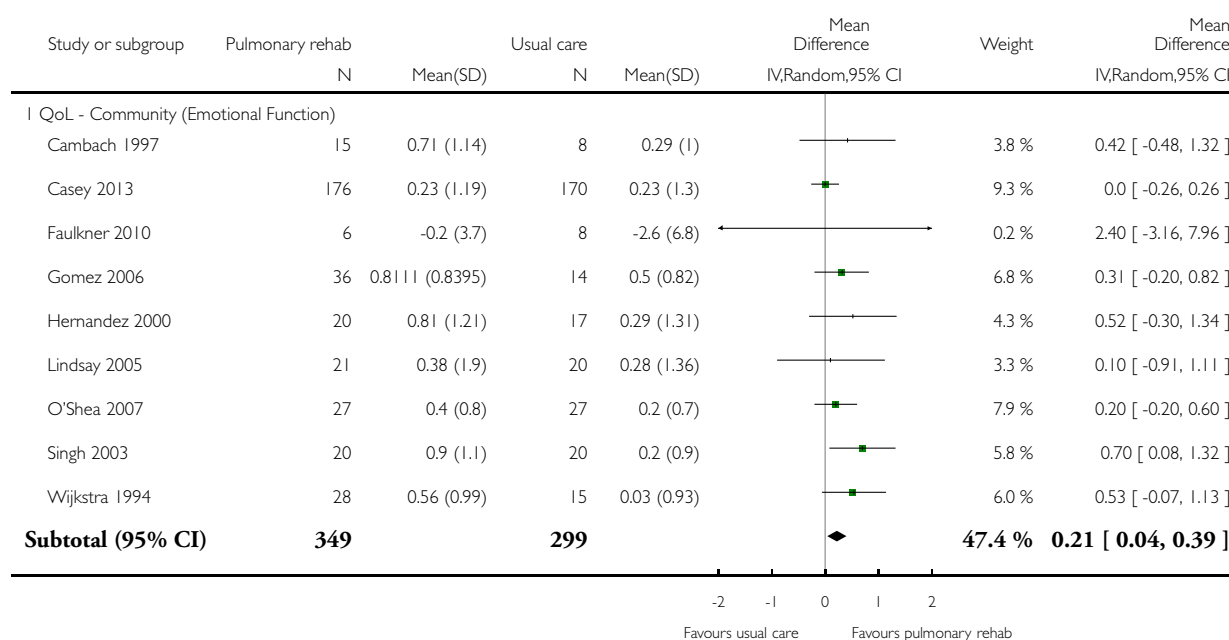


Analysis 2.2. Comparison 2 Rehabilitation versus usual care (subgroup analysis hospital vs community), Outcome 2 QoL - Change in CRQ (Emotional Function).

Review: Pulmonary rehabilitation for chronic obstructive pulmonary disease

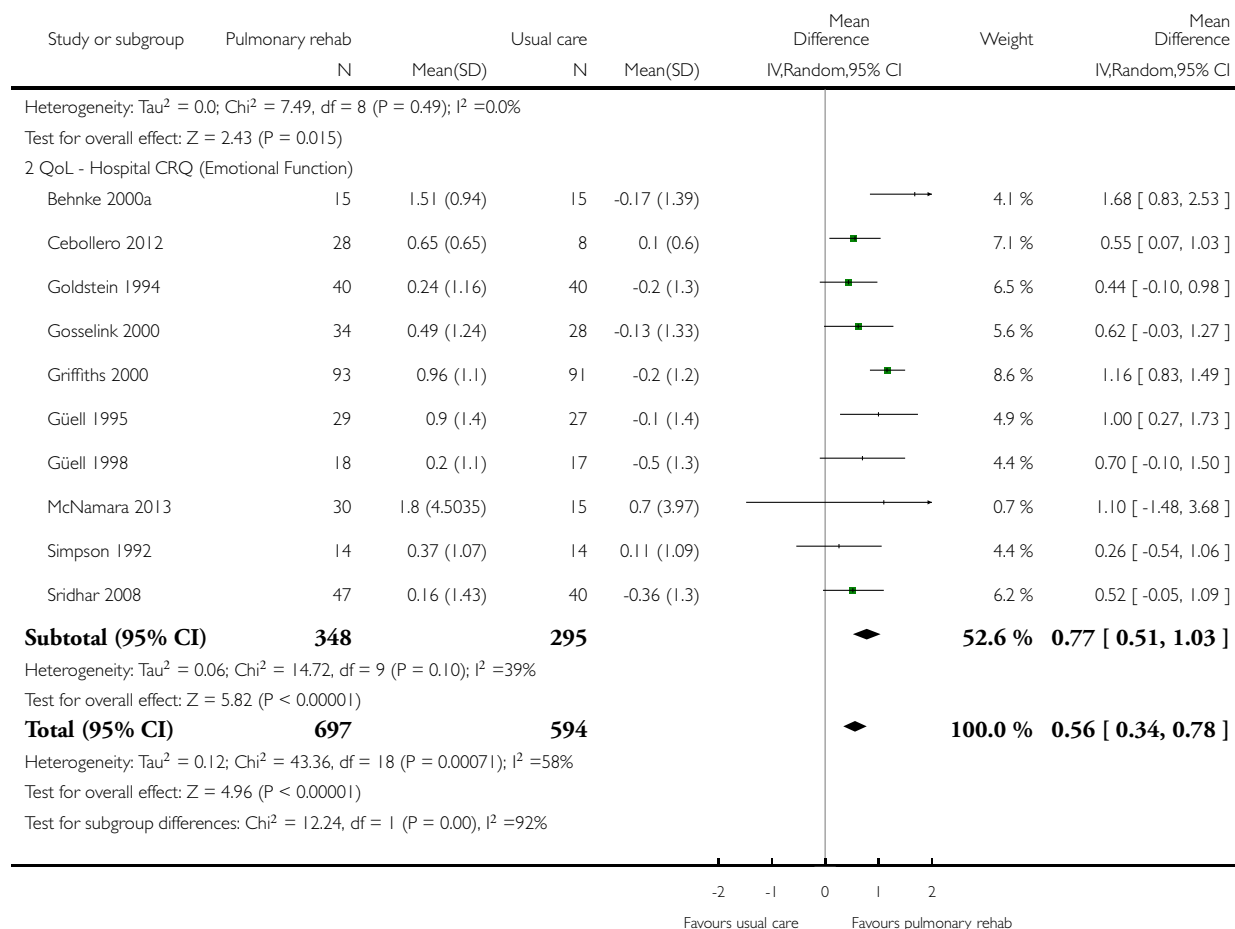
Comparison: 2 Rehabilitation versus usual care (subgroup analysis hospital vs community)

Outcome: 2 QoL - Change in CRQ (Emotional Function)



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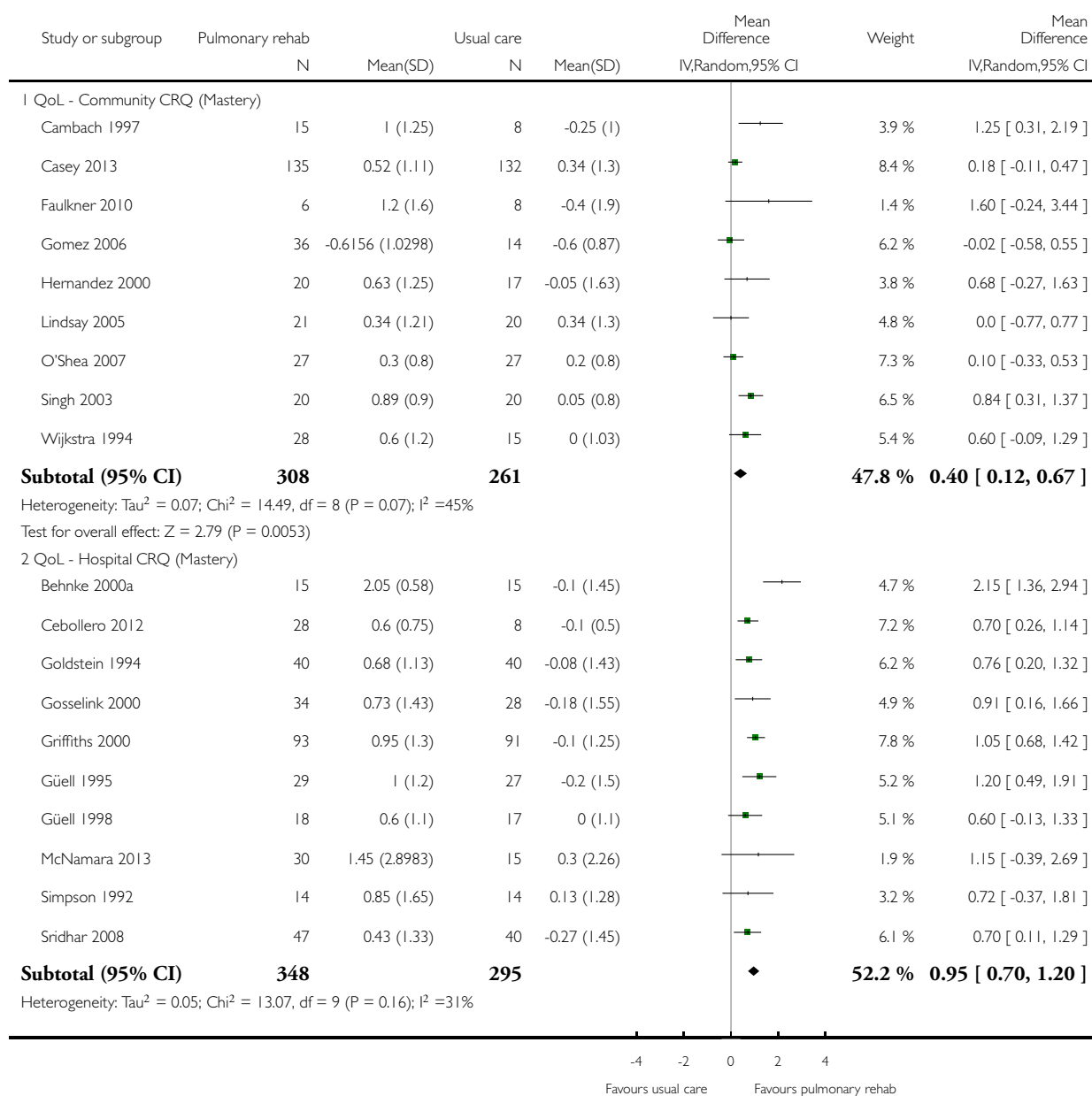


Analysis 2.3. Comparison 2 Rehabilitation versus usual care (subgroup analysis hospital vs community), Outcome 3 QoL - Change in CRQ (Mastery).

Review: Pulmonary rehabilitation for chronic obstructive pulmonary disease

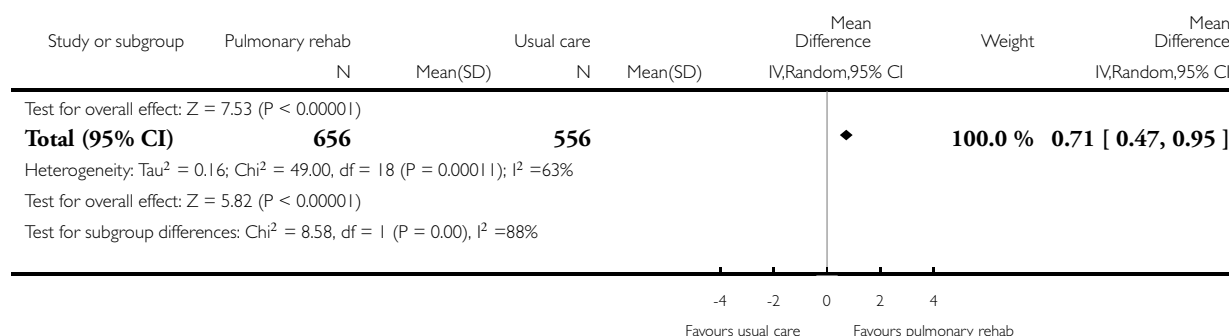
Comparison: 2 Rehabilitation versus usual care (subgroup analysis hospital vs community)

Outcome: 3 QoL - Change in CRQ (Mastery)



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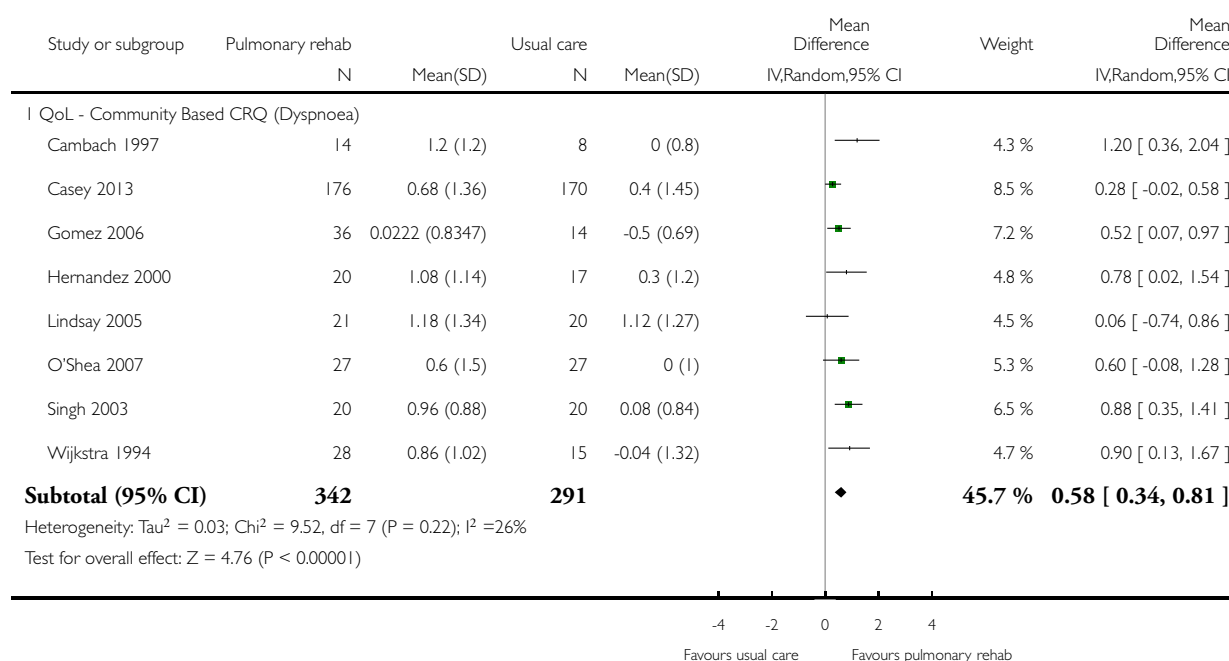


Analysis 2.4. Comparison 2 Rehabilitation versus usual care (subgroup analysis hospital vs community), Outcome 4 QoL - Change in CRQ (Dyspnoea).

Review: Pulmonary rehabilitation for chronic obstructive pulmonary disease

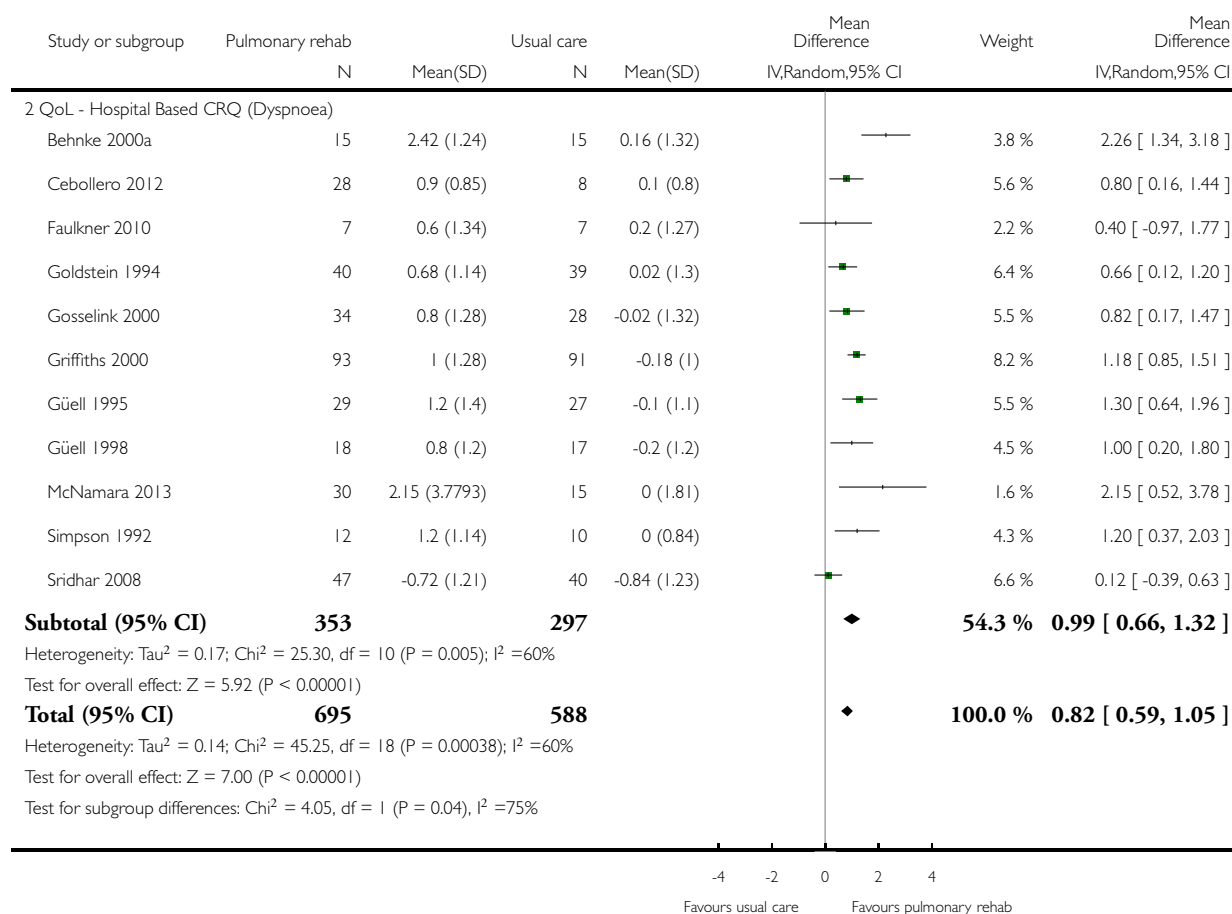
Comparison: 2 Rehabilitation versus usual care (subgroup analysis hospital vs community)

Outcome: 4 QoL - Change in CRQ (Dyspnoea)



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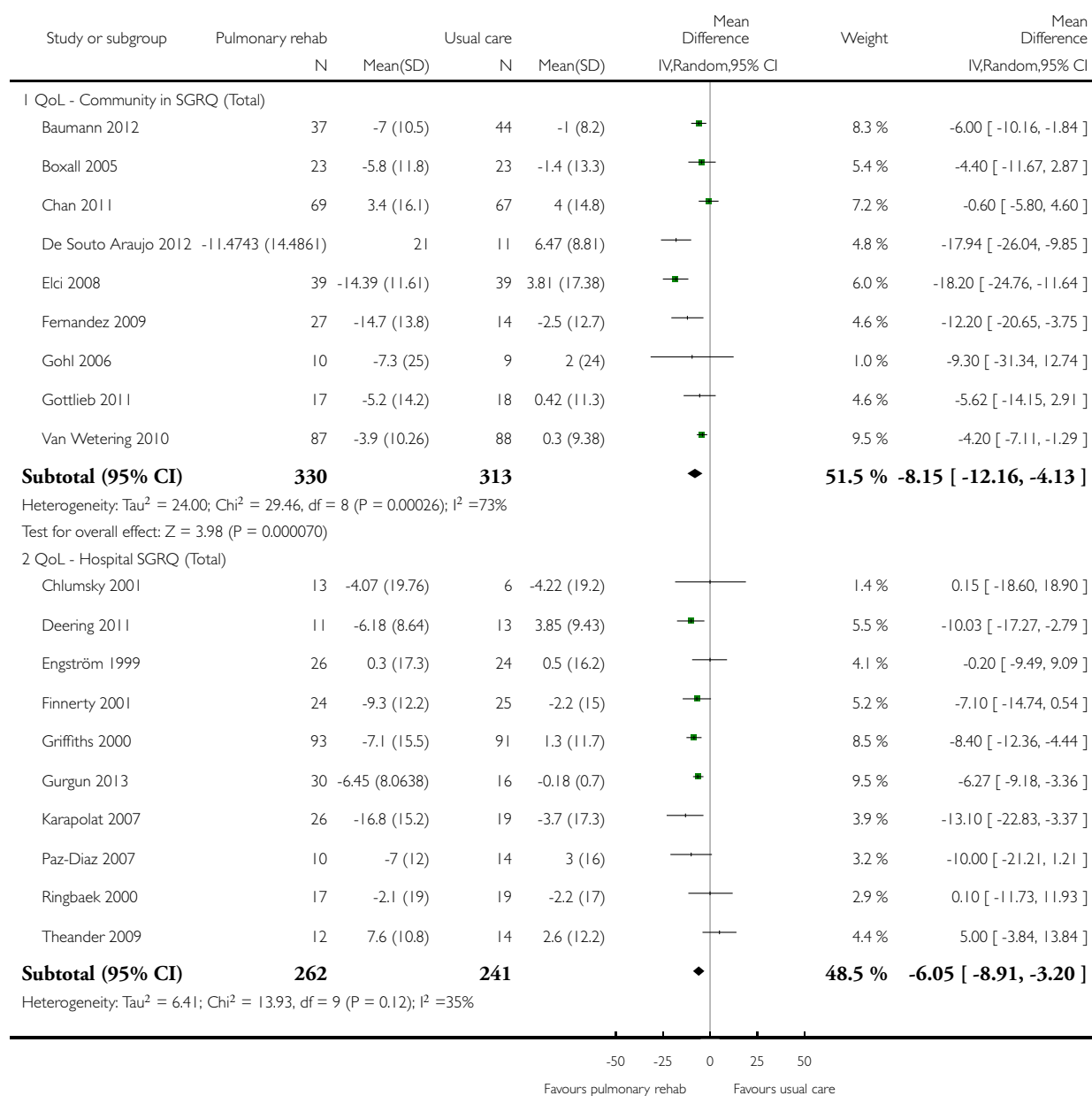


Analysis 2.5. Comparison 2 Rehabilitation versus usual care (subgroup analysis hospital vs community), Outcome 5 QoL - Change in SGRQ (Total).

Review: Pulmonary rehabilitation for chronic obstructive pulmonary disease

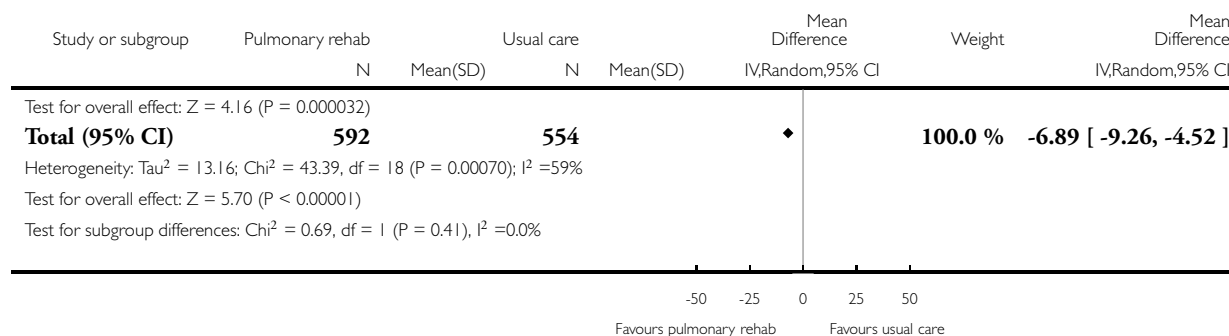
Comparison: 2 Rehabilitation versus usual care (subgroup analysis hospital vs community)

Outcome: 5 QoL - Change in SGRQ (Total)



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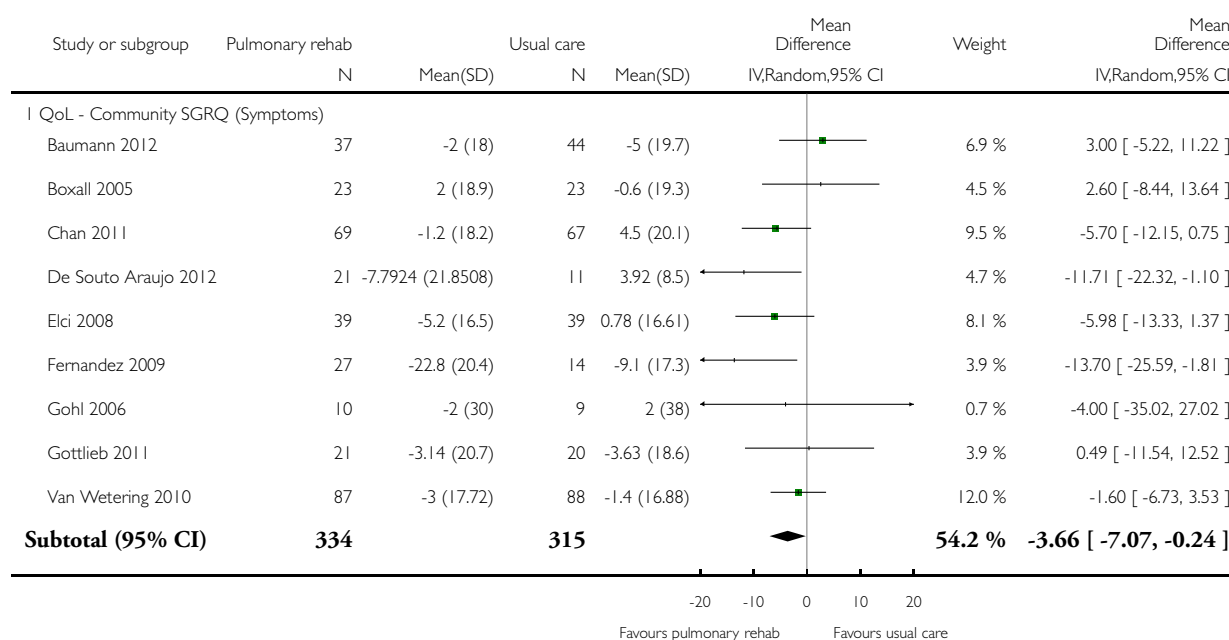


Analysis 2.6. Comparison 2 Rehabilitation versus usual care (subgroup analysis hospital vs community), Outcome 6 QoL - Change in SGRQ (Symptoms).

Review: Pulmonary rehabilitation for chronic obstructive pulmonary disease

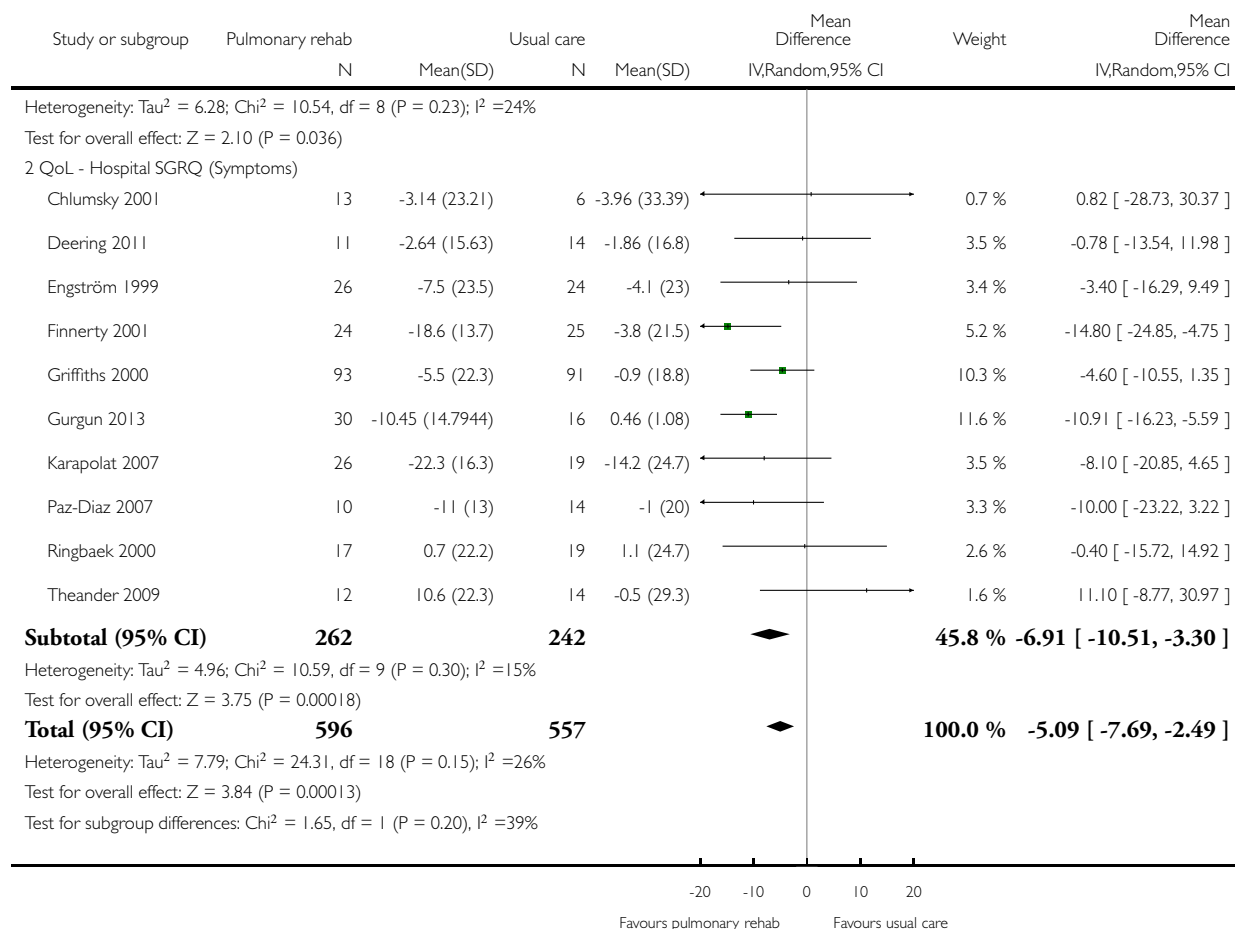
Comparison: 2 Rehabilitation versus usual care (subgroup analysis hospital vs community)

Outcome: 6 QoL - Change in SGRQ (Symptoms)



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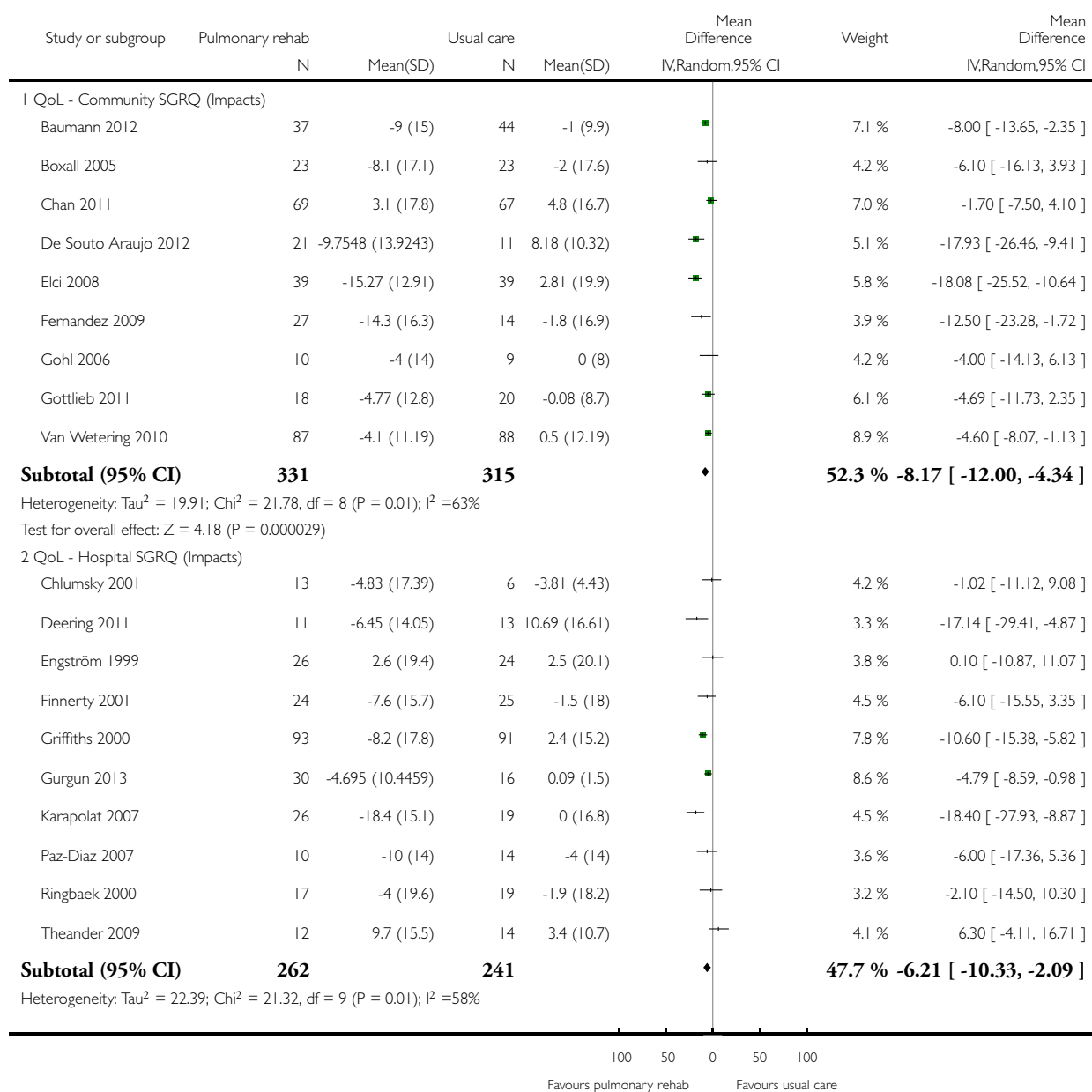


Analysis 2.7. Comparison 2 Rehabilitation versus usual care (subgroup analysis hospital vs community), Outcome 7 QoL - Change in SGRQ (Impacts).

Review: Pulmonary rehabilitation for chronic obstructive pulmonary disease

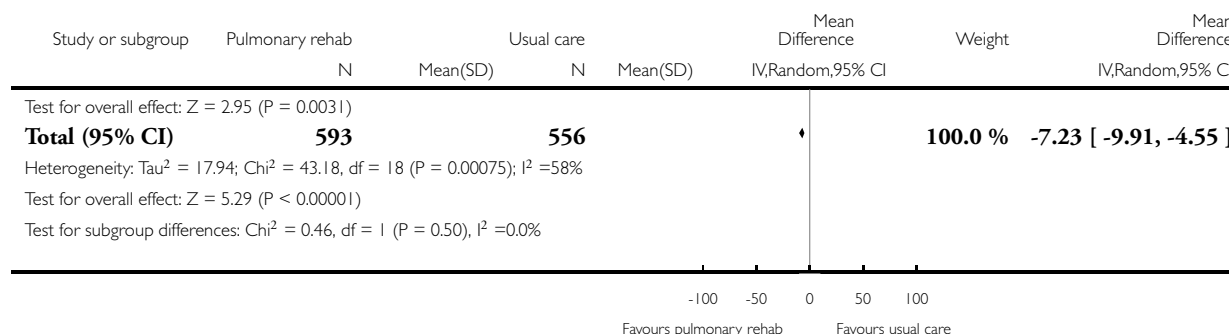
Comparison: 2 Rehabilitation versus usual care (subgroup analysis hospital vs community)

Outcome: 7 QoL - Change in SGRQ (Impacts)



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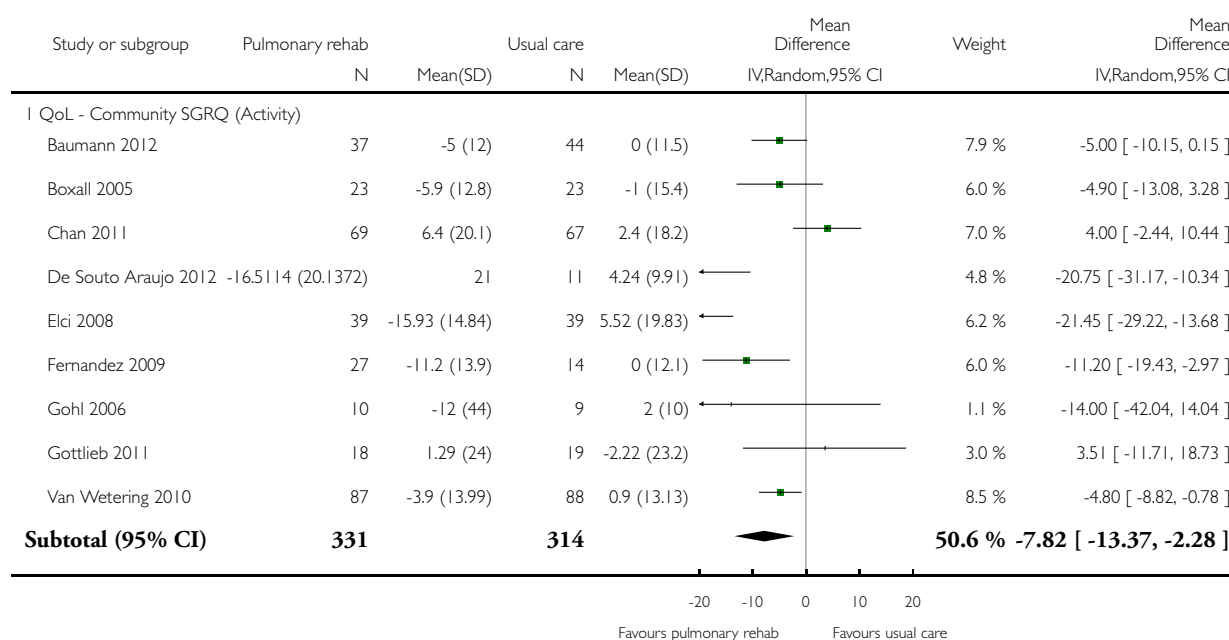


Analysis 2.8. Comparison 2 Rehabilitation versus usual care (subgroup analysis hospital vs community), Outcome 8 QoL - Change in SGRQ (Activity).

Review: Pulmonary rehabilitation for chronic obstructive pulmonary disease

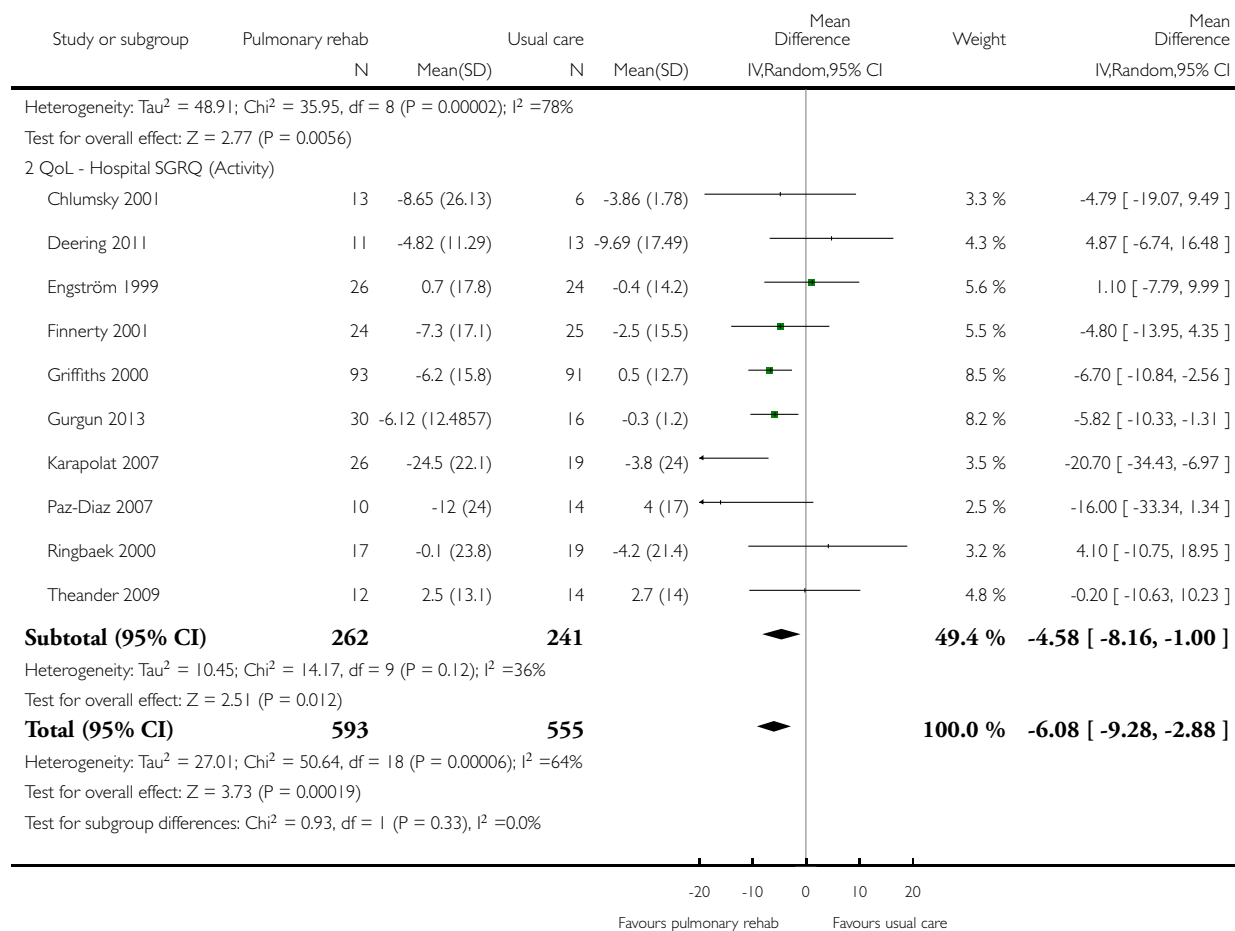
Comparison: 2 Rehabilitation versus usual care (subgroup analysis hospital vs community)

Outcome: 8 QoL - Change in SGRQ (Activity)



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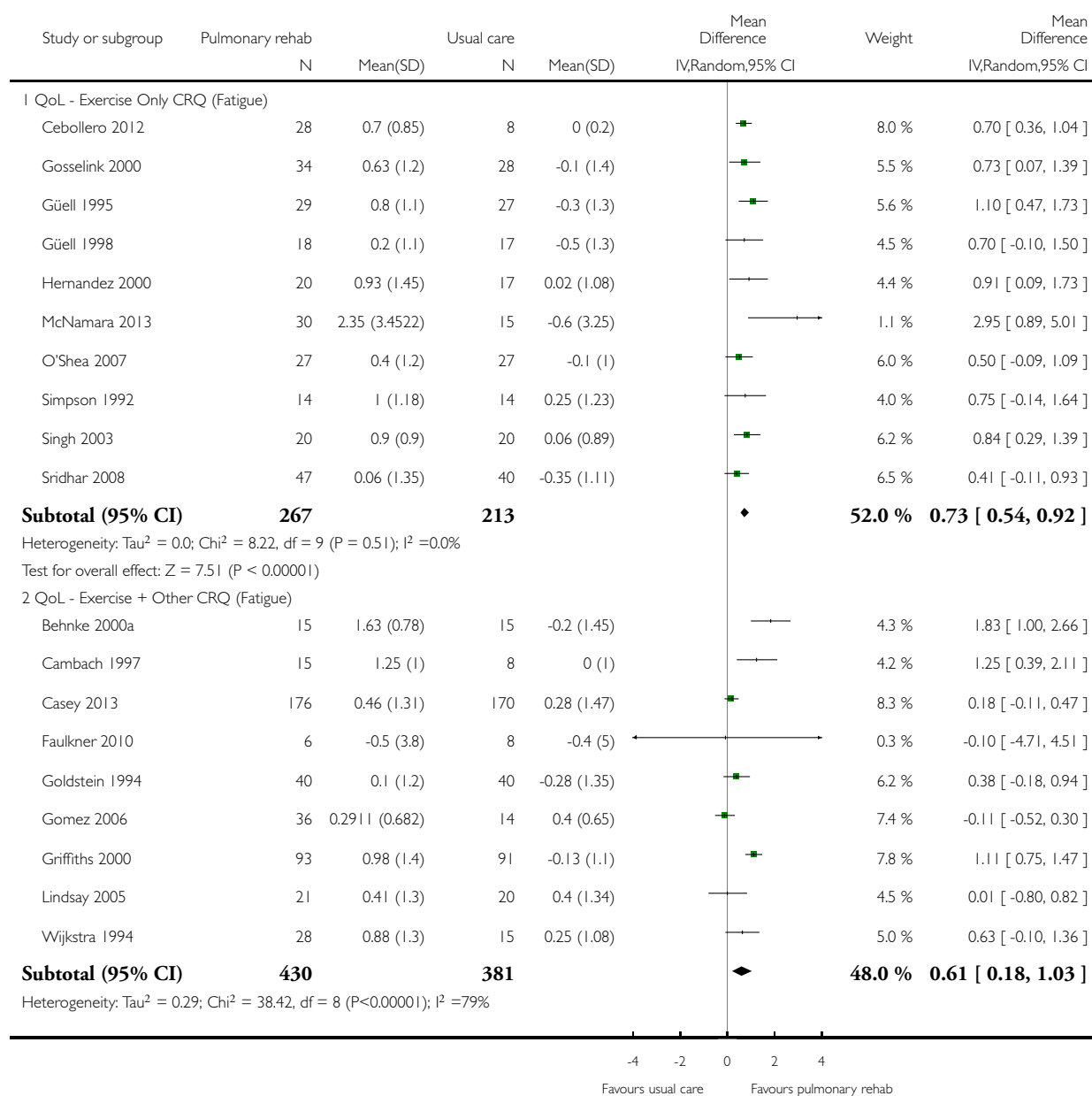


Analysis 3.1. Comparison 3 Rehabilitation versus usual care (subgroup analysis exercise only vs exercise and other), Outcome 1 QoL - Change in CRQ (Fatigue).

Review: Pulmonary rehabilitation for chronic obstructive pulmonary disease

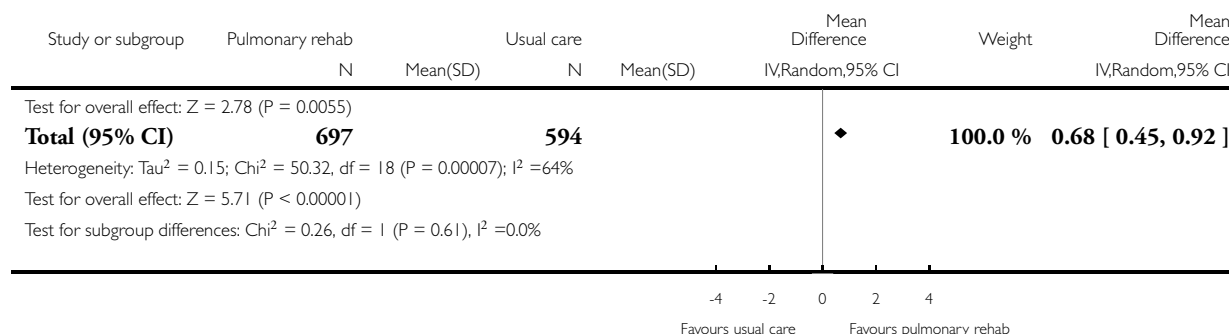
Comparison: 3 Rehabilitation versus usual care (subgroup analysis exercise only vs exercise and other)

Outcome: 1 QoL - Change in CRQ (Fatigue)



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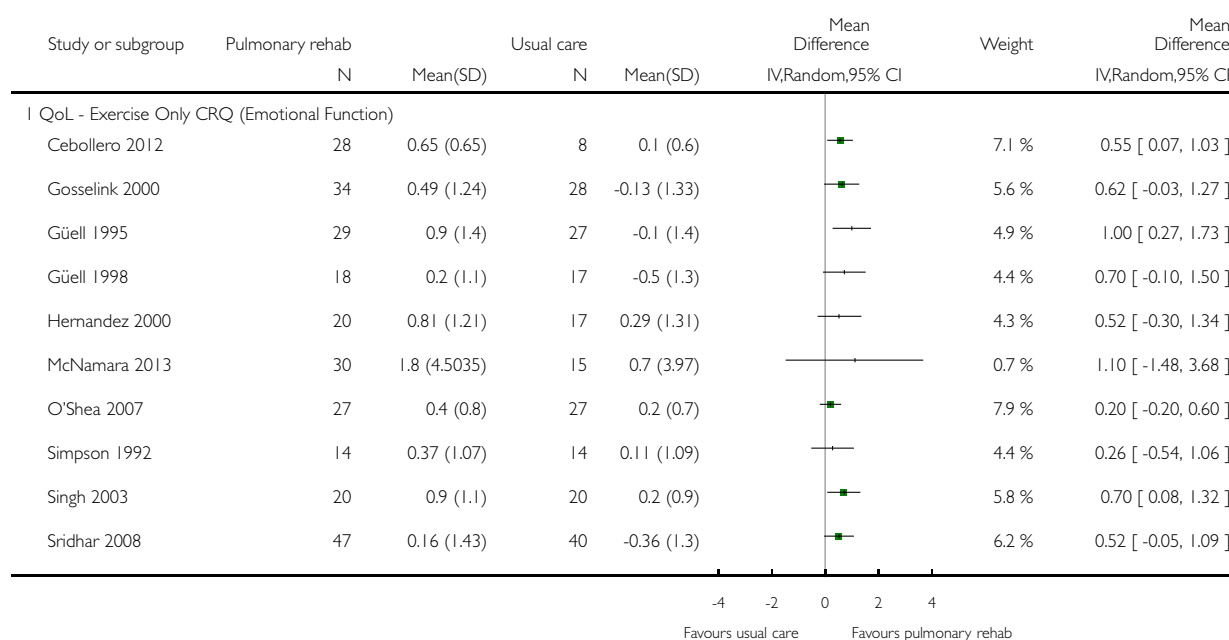


Analysis 3.2. Comparison 3 Rehabilitation versus usual care (subgroup analysis exercise only vs exercise and other), Outcome 2 QoL - Change in CRQ (Emotional Function).

Review: Pulmonary rehabilitation for chronic obstructive pulmonary disease

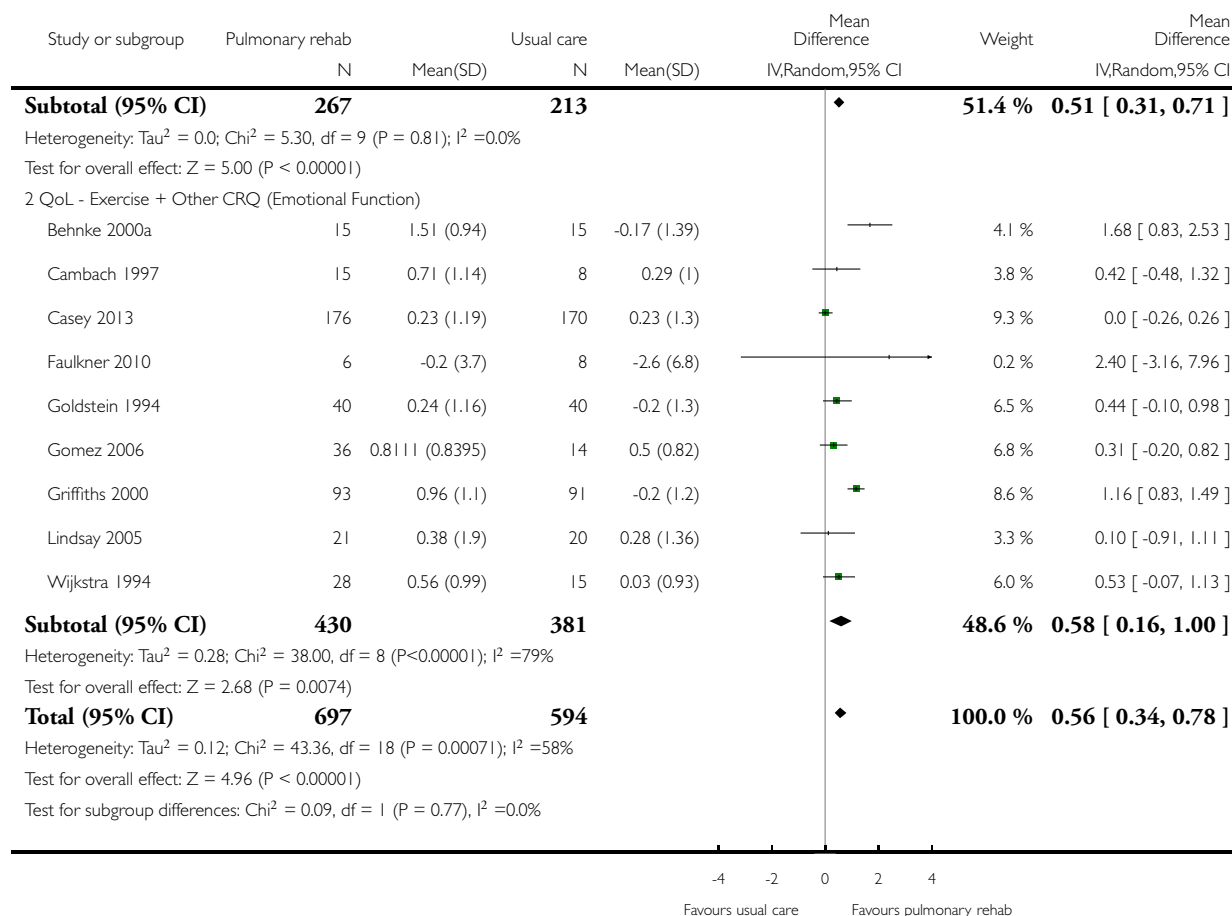
Comparison: 3 Rehabilitation versus usual care (subgroup analysis exercise only vs exercise and other)

Outcome: 2 QoL - Change in CRQ (Emotional Function)



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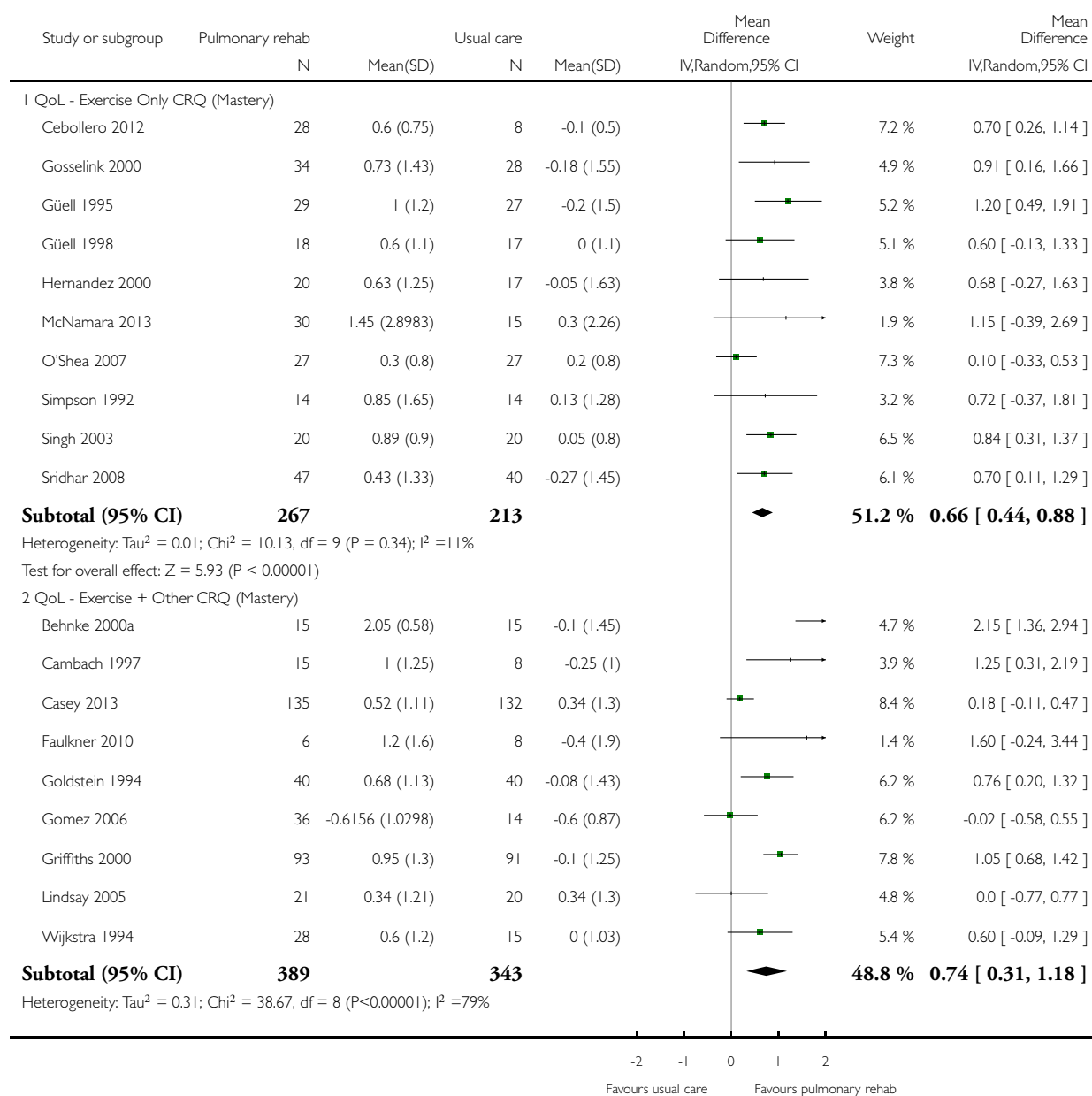


Analysis 3.3. Comparison 3 Rehabilitation versus usual care (subgroup analysis exercise only vs exercise and other), Outcome 3 QoL - Change in CRQ (Mastery).

Review: Pulmonary rehabilitation for chronic obstructive pulmonary disease

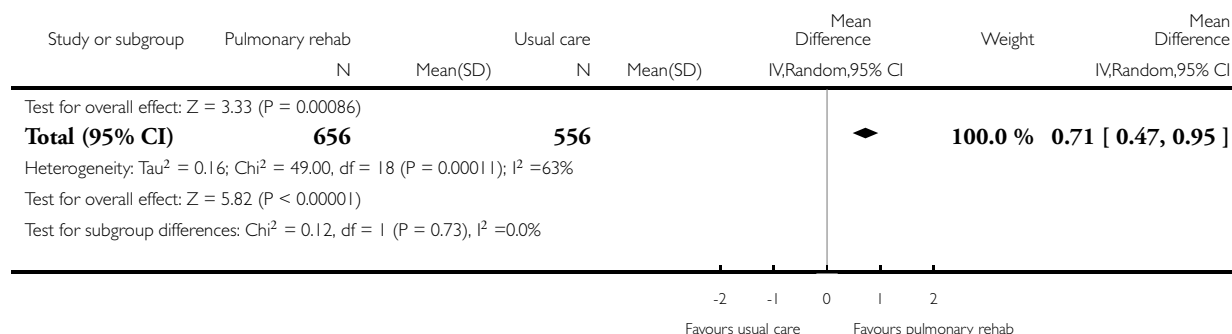
Comparison: 3 Rehabilitation versus usual care (subgroup analysis exercise only vs exercise and other)

Outcome: 3 QoL - Change in CRQ (Mastery)



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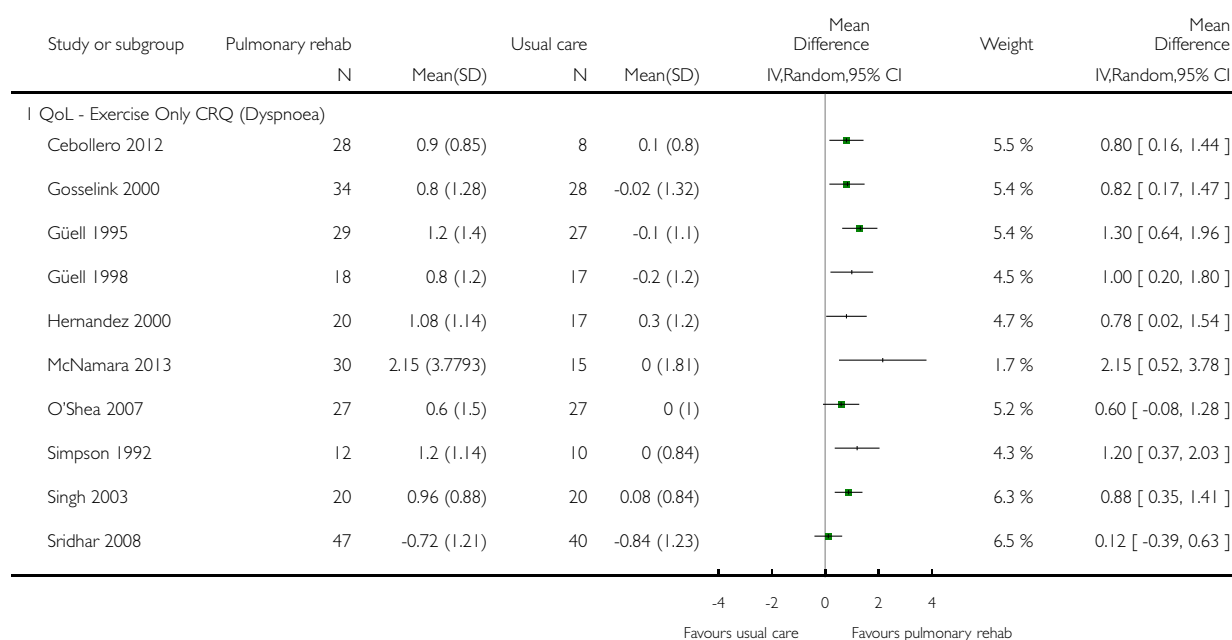


Analysis 3.4. Comparison 3 Rehabilitation versus usual care (subgroup analysis exercise only vs exercise and other), Outcome 4 QoL - Change in CRQ (Dyspnoea).

Review: Pulmonary rehabilitation for chronic obstructive pulmonary disease

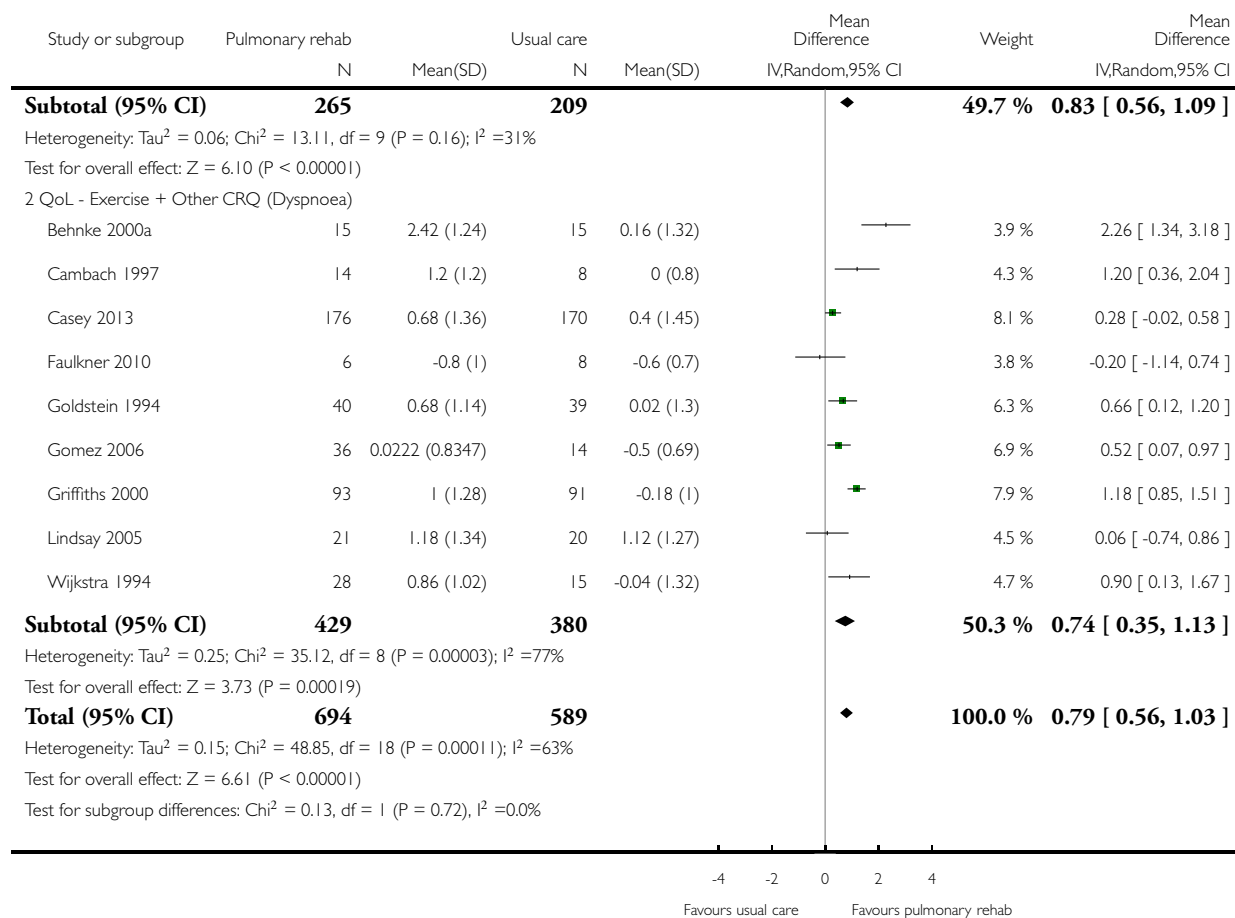
Comparison: 3 Rehabilitation versus usual care (subgroup analysis exercise only vs exercise and other)

Outcome: 4 QoL - Change in CRQ (Dyspnoea)



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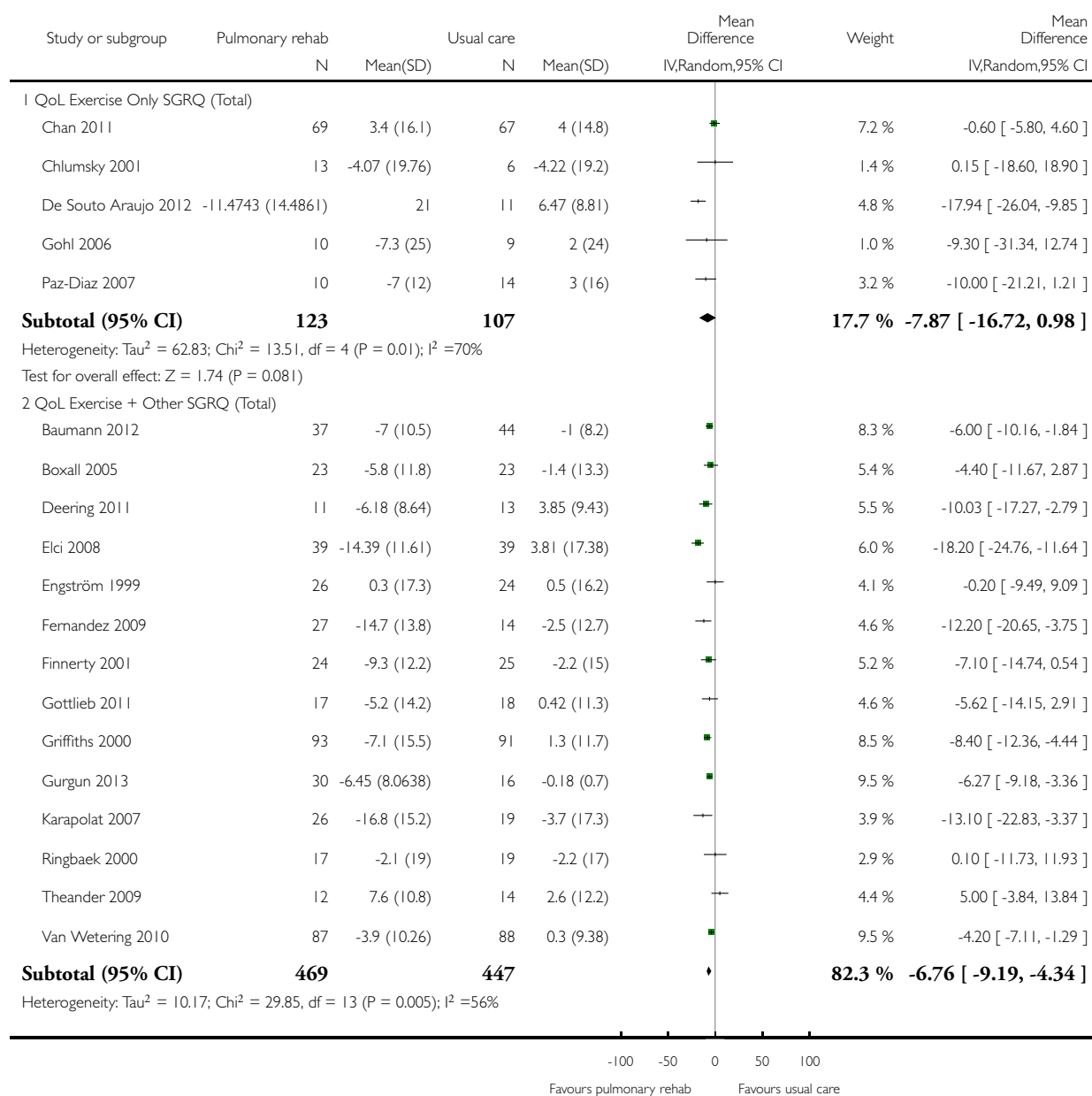


Analysis 3.5. Comparison 3 Rehabilitation versus usual care (subgroup analysis exercise only vs exercise and other), Outcome 5 QoL - Change in SGRQ (Total).

Review: Pulmonary rehabilitation for chronic obstructive pulmonary disease

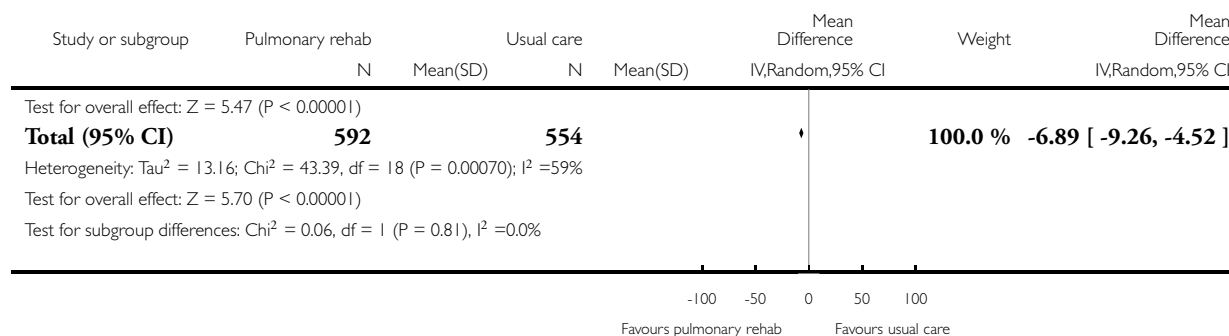
Comparison: 3 Rehabilitation versus usual care (subgroup analysis exercise only vs exercise and other)

Outcome: 5 QoL - Change in SGRQ (Total)



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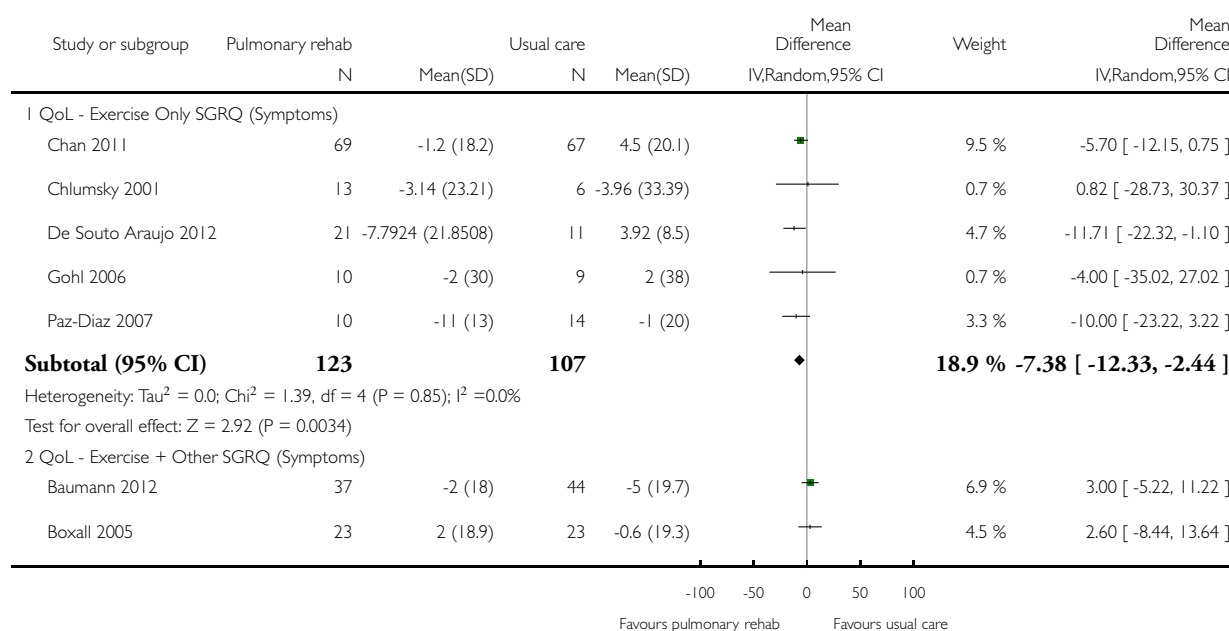


Analysis 3.6. Comparison 3 Rehabilitation versus usual care (subgroup analysis exercise only vs exercise and other), Outcome 6 QoL - Change in SGRQ (Symptoms).

Review: Pulmonary rehabilitation for chronic obstructive pulmonary disease

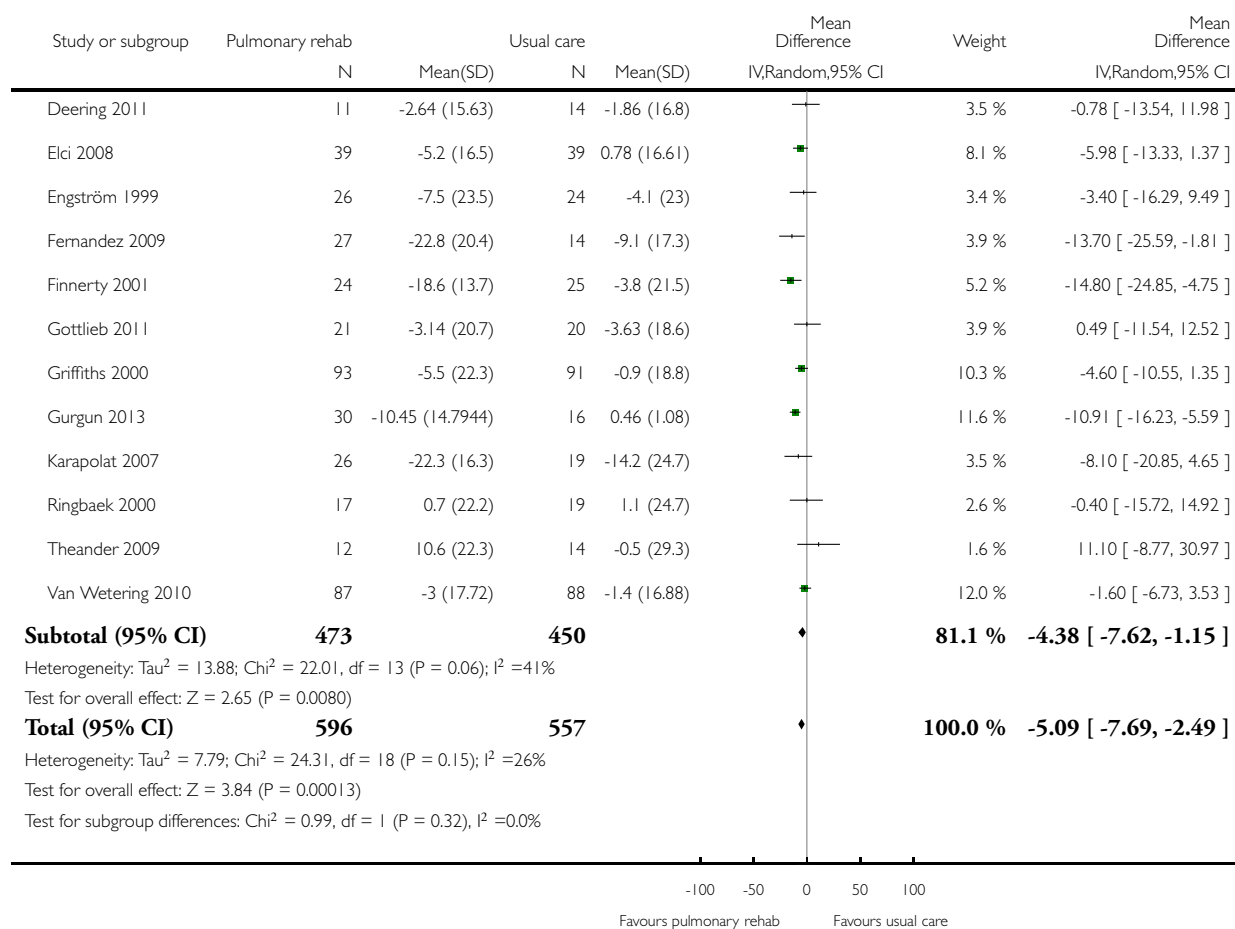
Comparison: 3 Rehabilitation versus usual care (subgroup analysis exercise only vs exercise and other)

Outcome: 6 QoL - Change in SGRQ (Symptoms)



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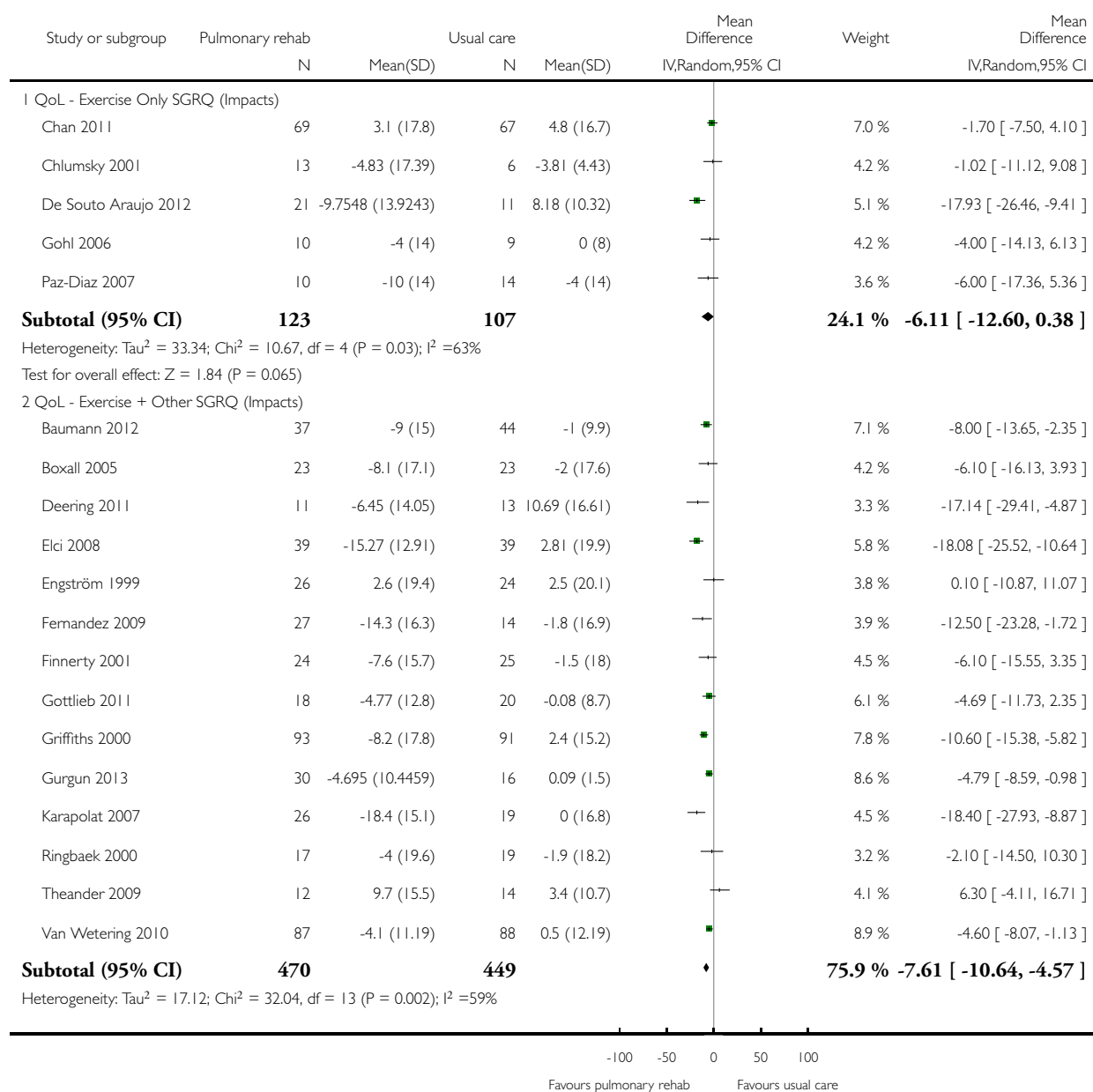


Analysis 3.7. Comparison 3 Rehabilitation versus usual care (subgroup analysis exercise only vs exercise and other), Outcome 7 QoL - Change in SGRQ (Impacts).

Review: Pulmonary rehabilitation for chronic obstructive pulmonary disease

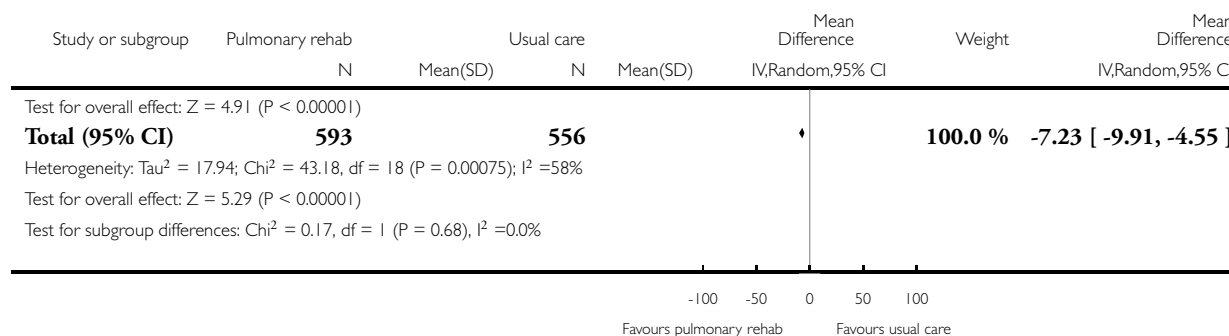
Comparison: 3 Rehabilitation versus usual care (subgroup analysis exercise only vs exercise and other)

Outcome: 7 QoL - Change in SGRQ (Impacts)



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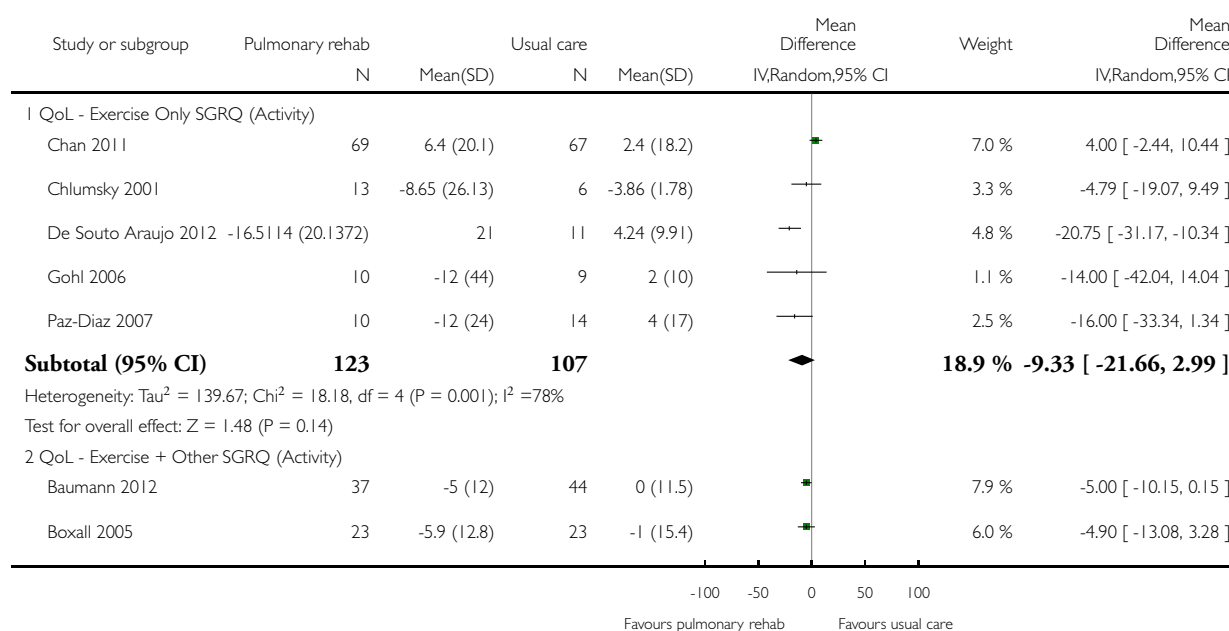


Analysis 3.8. Comparison 3 Rehabilitation versus usual care (subgroup analysis exercise only vs exercise and other), Outcome 8 QoL - Change in SGRQ (Activity).

Review: Pulmonary rehabilitation for chronic obstructive pulmonary disease

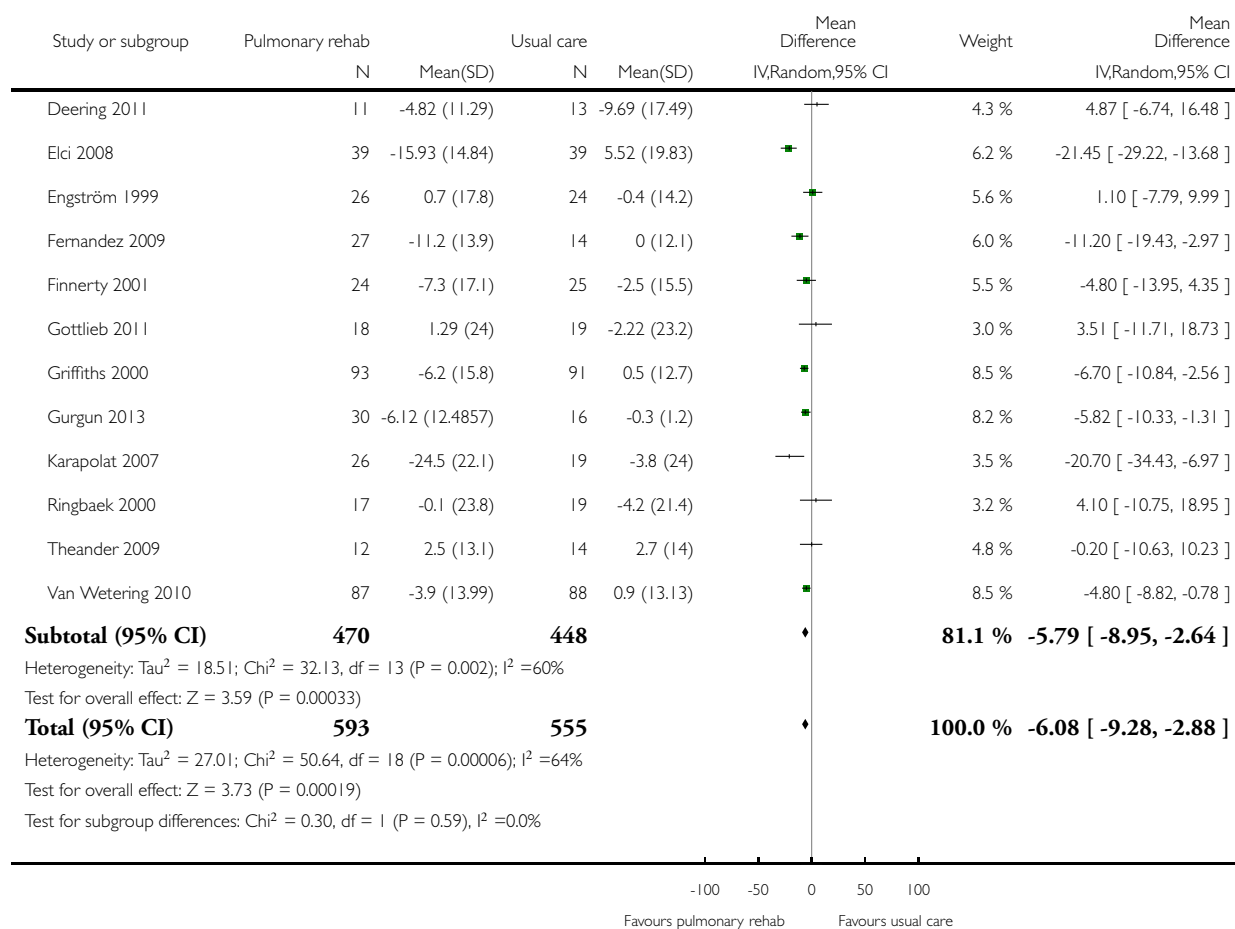
Comparison: 3 Rehabilitation versus usual care (subgroup analysis exercise only vs exercise and other)

Outcome: 8 QoL - Change in SGRQ (Activity)



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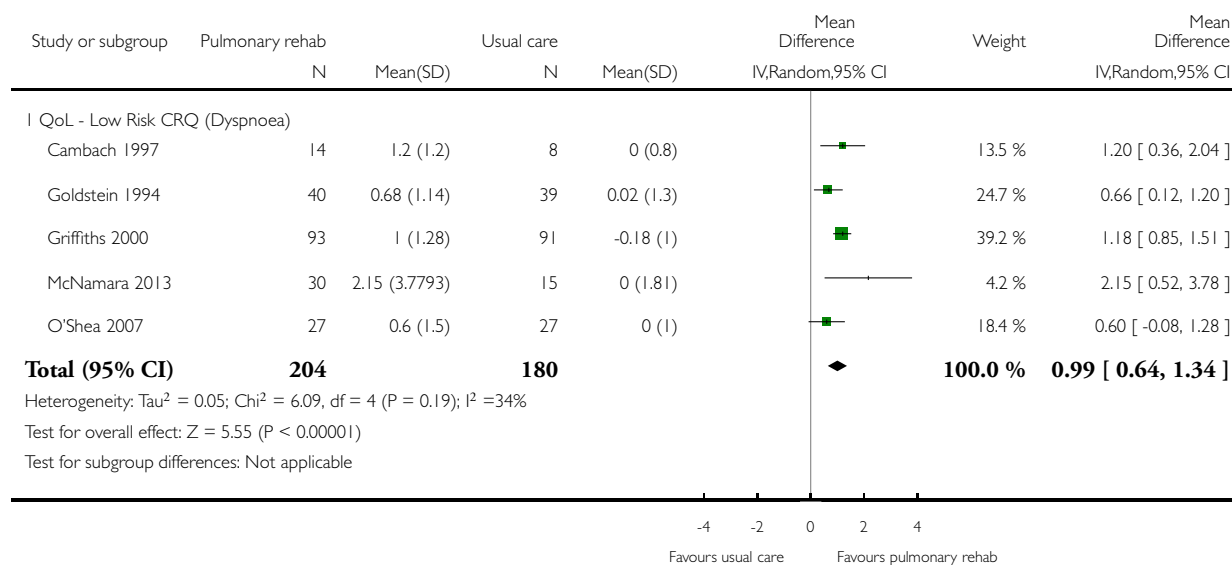


Analysis 4.1. Comparison 4 Rehabilitation versus usual care (sensitivity analysis by allocation concealment and incomplete outcome), Outcome 1 QoL - Change in CRQ (Dyspnoea).

Review: Pulmonary rehabilitation for chronic obstructive pulmonary disease

Comparison: 4 Rehabilitation versus usual care (sensitivity analysis by allocation concealment and incomplete outcome)

Outcome: 1 QoL - Change in CRQ (Dyspnoea)

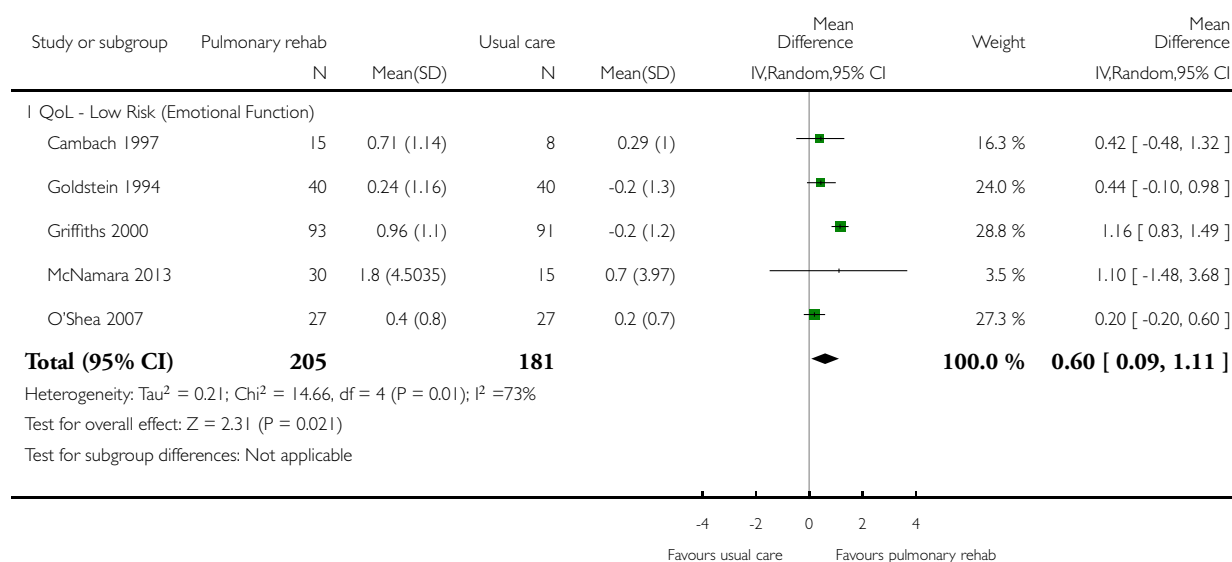


Analysis 4.2. Comparison 4 Rehabilitation versus usual care (sensitivity analysis by allocation concealment and incomplete outcome), Outcome 2 QoL - Change in CRQ (Emotional Function).

Review: Pulmonary rehabilitation for chronic obstructive pulmonary disease

Comparison: 4 Rehabilitation versus usual care (sensitivity analysis by allocation concealment and incomplete outcome)

Outcome: 2 QoL - Change in CRQ (Emotional Function)

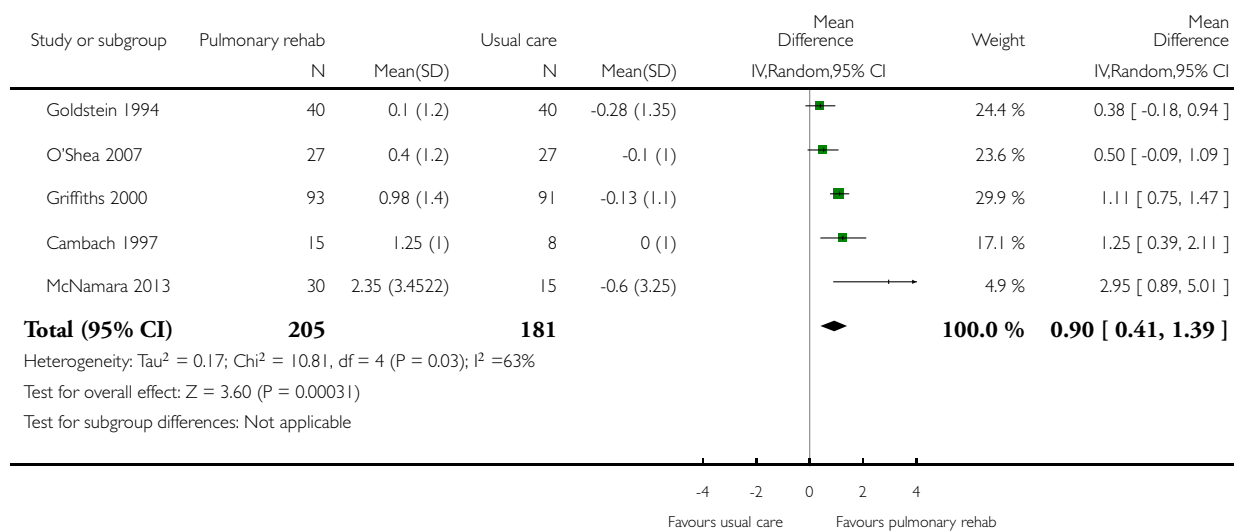


Analysis 4.3. Comparison 4 Rehabilitation versus usual care (sensitivity analysis by allocation concealment and incomplete outcome), Outcome 3 QoL - Low Risk CRQ (Fatigue).

Review: Pulmonary rehabilitation for chronic obstructive pulmonary disease

Comparison: 4 Rehabilitation versus usual care (sensitivity analysis by allocation concealment and incomplete outcome)

Outcome: 3 QoL - Low Risk CRQ (Fatigue)

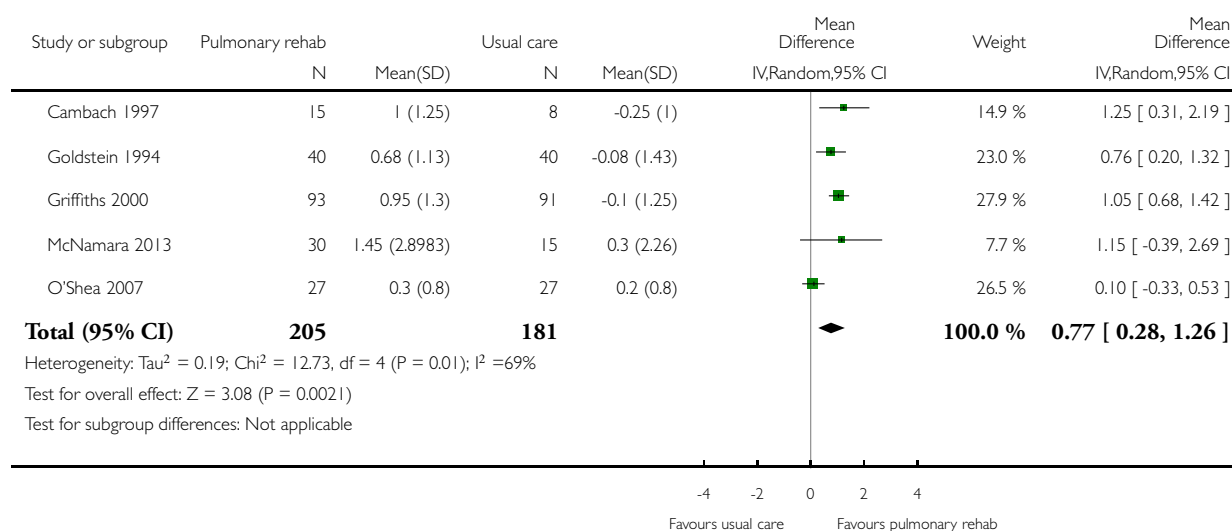


Analysis 4.4. Comparison 4 Rehabilitation versus usual care (sensitivity analysis by allocation concealment and incomplete outcome), Outcome 4 QoL - Low Risk CRQ (Mastery).

Review: Pulmonary rehabilitation for chronic obstructive pulmonary disease

Comparison: 4 Rehabilitation versus usual care (sensitivity analysis by allocation concealment and incomplete outcome)

Outcome: 4 QoL - Low Risk CRQ (Mastery)

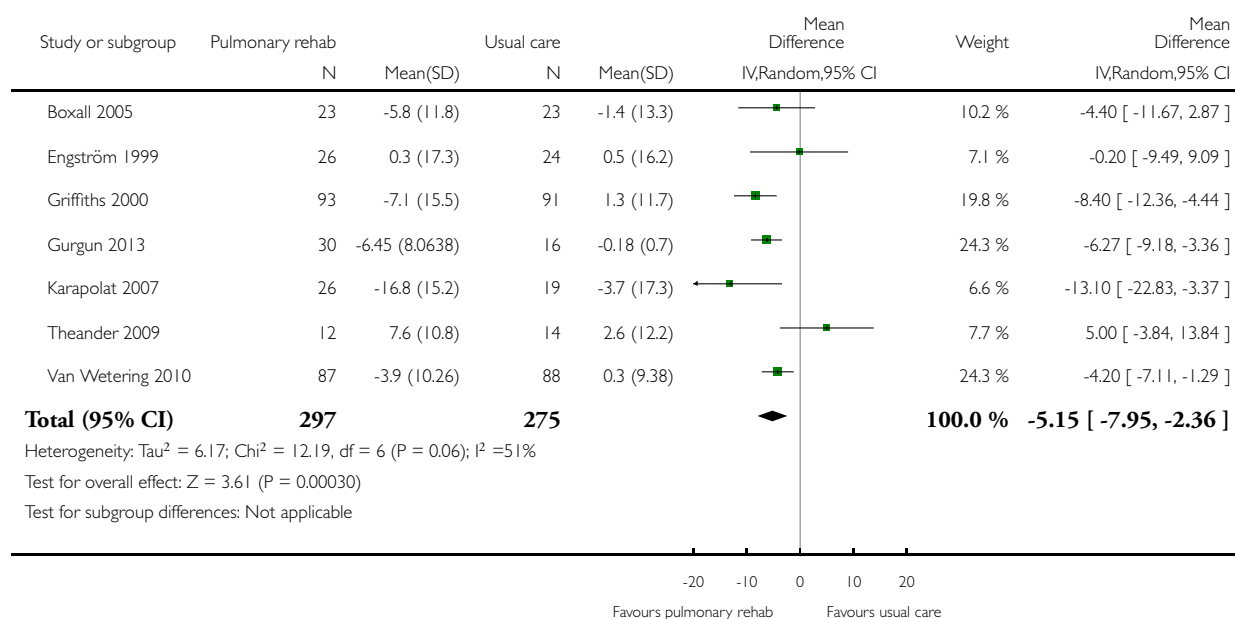


Analysis 4.5. Comparison 4 Rehabilitation versus usual care (sensitivity analysis by allocation concealment and incomplete outcome), Outcome 5 QoL - Low Risk SGRQ (Total).

Review: Pulmonary rehabilitation for chronic obstructive pulmonary disease

Comparison: 4 Rehabilitation versus usual care (sensitivity analysis by allocation concealment and incomplete outcome)

Outcome: 5 QoL - Low Risk SGRQ (Total)

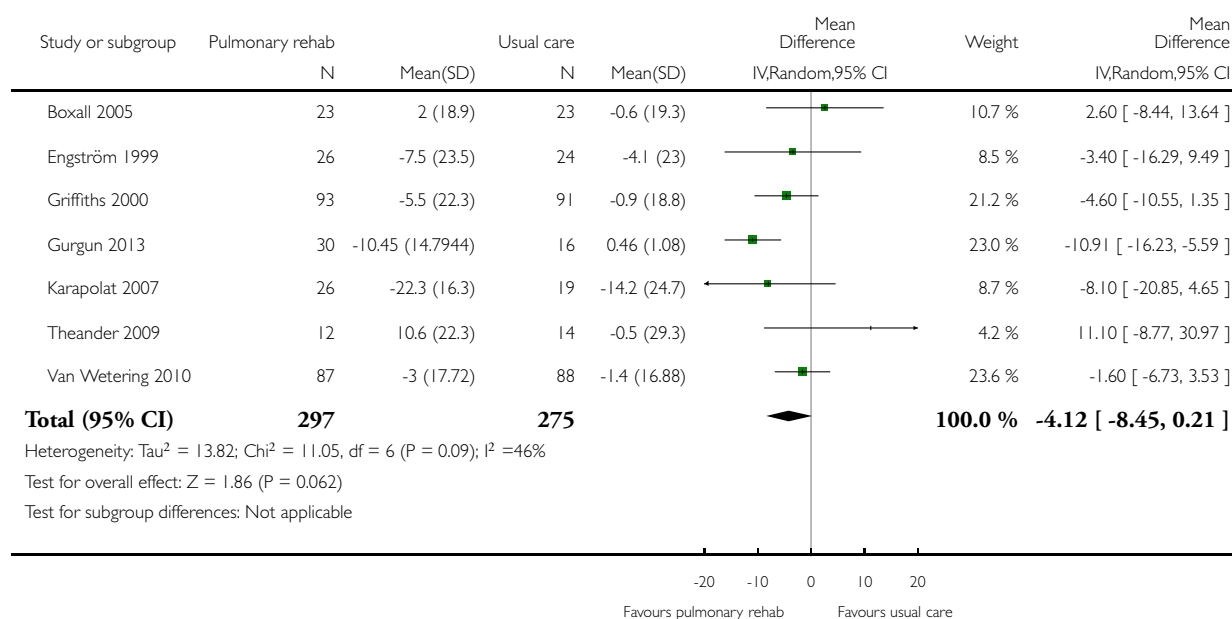


Analysis 4.6. Comparison 4 Rehabilitation versus usual care (sensitivity analysis by allocation concealment and incomplete outcome), Outcome 6 QoL - Low Risk SGRQ (Symptoms).

Review: Pulmonary rehabilitation for chronic obstructive pulmonary disease

Comparison: 4 Rehabilitation versus usual care (sensitivity analysis by allocation concealment and incomplete outcome)

Outcome: 6 QoL - Low Risk SGRQ (Symptoms)

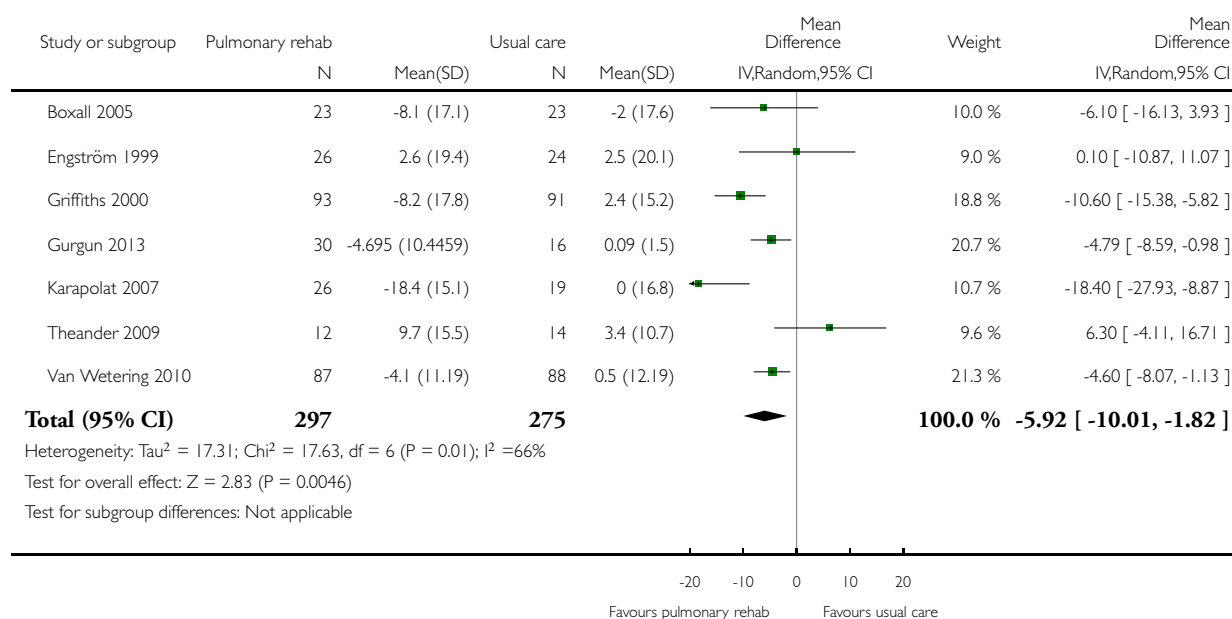


Analysis 4.7. Comparison 4 Rehabilitation versus usual care (sensitivity analysis by allocation concealment and incomplete outcome), Outcome 7 QoL - Low Risk SGRQ (Impacts).

Review: Pulmonary rehabilitation for chronic obstructive pulmonary disease

Comparison: 4 Rehabilitation versus usual care (sensitivity analysis by allocation concealment and incomplete outcome)

Outcome: 7 QoL - Low Risk SGRQ (Impacts)

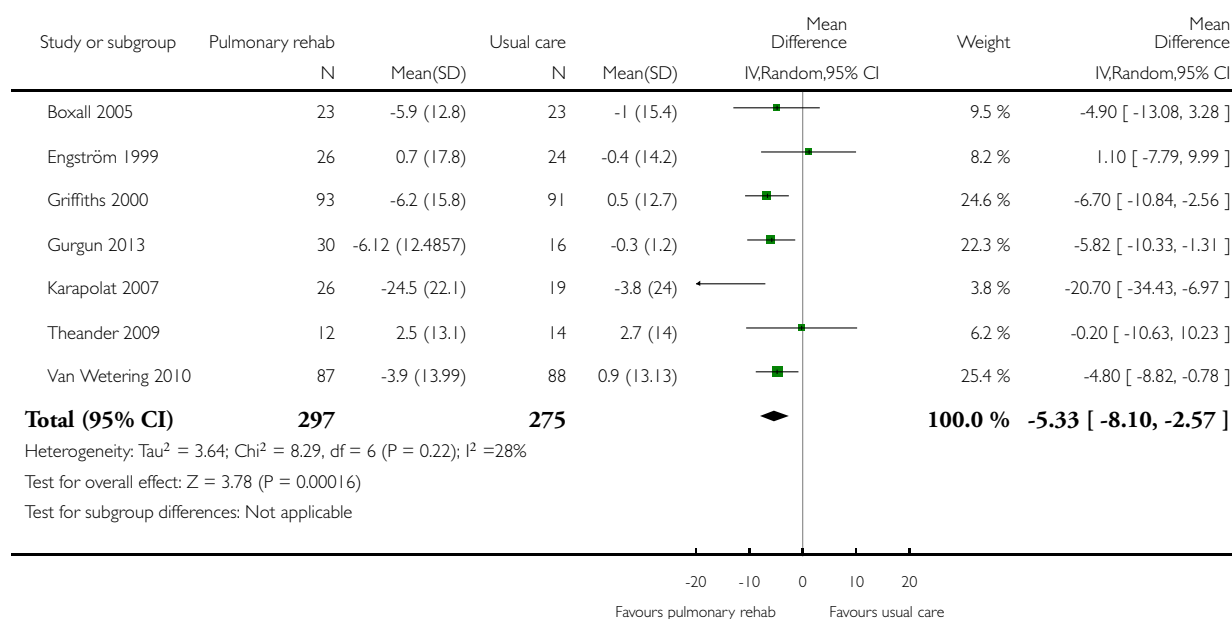


Analysis 4.8. Comparison 4 Rehabilitation versus usual care (sensitivity analysis by allocation concealment and incomplete outcome), Outcome 8 QoL - Low Risk SGRQ (Activity).

Review: Pulmonary rehabilitation for chronic obstructive pulmonary disease

Comparison: 4 Rehabilitation versus usual care (sensitivity analysis by allocation concealment and incomplete outcome)

Outcome: 8 QoL - Low Risk SGRQ (Activity)



ADDITIONAL TABLES

Table 1. Publication bias: results of Egger and Begg-Mazumdar Kendall's tests

CRQ Fatigue	Bias indicators Begg-Mazumdar: Kendall's tau = 0.22807; P value 0.1863 Egger: bias = 1.61189 (95% CI = -0.194745 to 3.418525); P value 0.077
CRQ Emotional	Bias indicators Begg-Mazumdar: Kendall's tau = 0.204678; P value 0.2378 Egger: bias = 0.997332 (95% CI = -0.618039 to 2.612702); P value 0.2101
CRQ Mastery	Bias indicators Begg-Mazumdar: Kendall's tau = 0.146199; P value 0.4063 Egger: bias = 1.531134 (95% CI = -0.268167 to 3.330434); P value 0.0904

Table 1. Publication bias: results of Egger and Begg-Mazumdar Kendall's tests (Continued)

CRQ Dyspnoea (see Figure 4 for funnel plot)	Bias indicators Begg-Mazumdar: Kendall's tau = 0.274854; P value 0.1082 Egger: bias = 1.275427 (95% CI = -0.761574 to 3.312427); P value 0.204
SGRQ Total (see Figure 5 for funnel plot)	Bias indicators Begg-Mazumdar: Kendall's tau = -0.052632; P value 0.73 Egger: bias = -0.459813 (95% CI = -2.086751 to 1.167125); P value 0.5588
SGRQ Symptoms	Bias indicators Begg-Mazumdar: Kendall's tau = 0.017544; P value 0.945 Egger: bias = 0.076734 (95% CI = -1.241745 to 1.395213); P value 0.9037
SQRQ Activity	Bias indicators Begg-Mazumdar: Kendall's tau = -0.052632; P value 0.73 Egger: bias = -0.336937 (95% CI = -2.10096 to 1.427086); P value 0.692
6MWT	Bias indicators Begg-Mazumdar: Kendall's tau = 0.16074; P value 0.1601 Egger: bias = 1.24304 (95% CI = 0.183967 to 2.302131); P value 0.0227
Incremental Shuttle Walk Test	Bias indicators Begg-Mazumdar: Kendall's tau = 0.0776906; P value 0.846 Egger: bias = -0.21 2523 (95% CI = -2.7776 to 2.351859); P value 0.846
Cycle Ergometer	Bias indicators Begg-Mazumdar: Kendall's tau = -0.2666667; P value 0.139 Egger: bias = 1.57164 (95% CI = 0.6053 to 2.337984); P value 0.0036

Table 2. Baseline characteristics

Study	Re-hab sam- ple size	Male	Female	Mean age (SD)	FEV ₁ (SD)	Con- trol sam- ple size	Male	Female	Mean (SD)	age	FEV ₁ (SD)
Barakat 2008	35	na	na	63.7	41.9	36	na	na	65.9		43.3
Baumann 2012	37	na	na	65	45	44	na	na	63		47
Behnke 2000a	23	12	3	64.0 (1)	34.1 (7.4)	23	11	4	68.0 (2.2)		37.5 (6.6)
Bend- strup 1997	27	7	9	64 (3)	1.02 L/ min (0.06)	20	7	9	65 (2)		1.04 L/min (0.07)

Table 2. Baseline characteristics (Continued)

Booker 1984	32	na	na	66 (8)	0.85 L (0.29)	37	na	na	65 (7)	0.97 L (0.37)
Borghi-Silva 2009	20	13	7	67 (10)	33 (9)	14	12	8	67(10)	35 (11)
Boxall 2005	23	11	12	77.6 (7.6)	40.5 (15.9)	23	15	8	75.8 (8.1)	37.7 (15.0)
Busch 1988	7	5	2	65 (16)	26% (9)	7	6	1	66 (16)	27% (11)
Cambach 1997	15	7	8	62 (5)	59% (16)	8	6	2	62 (9)	60% (23)
Casaburi 2004	12	12	0	69 (10)	36% (9)	12	12	0	68 (9)	39% (12)
Casey 2013	178	117	61	68.8 (10.2)	57.6 (14.3)	172	106	66	68.4 (10.3)	59.7 (13.8)
Cebollero 2012	28	28	0	68 (7)	47.8 (5)	8	8	0	69(5)	38.7 (5)
Chan 2011	69	61	8	73.6 (7.5)	91 (0.39)	67	58	9	73.6 (7.4)	89 (0.39)
Chlumsky 2001	13	12	1	63 (11)	43% (21)	6	5	1	65 (13)	51% (17)
Clark 1996	32	na	na	58 (8)	1.72 L (0.83)	16	na	na	55 (8)	1.44 L (0.59)
Cochrane 2006	74	32	42	na	na	50	18	32	na	na
Cockcroft 1981	18	18	0	61 (5)	1.53 L (0.70)	16	16	0	60 (5)	1.32 L (0.44)
De Souto Araujo 2012	21	12	9	59	39.2 (11.4) /43.9 (10.3)	11	8	3	71.1	45.1 (12.6)
Deering 2011	25	11	14	67.7 (5.3)	77.0 (19)	19	8	8	68.6 (5.5)	45.8 (18.3)

Table 2. Baseline characteristics *(Continued)*

Elci 2008	39	33	6	59.67 (8.6)	47.7	39	33	6	58.08 (11.45)	46.28
Emery 1998	25	15	14	65 (6)	1.29 L (0.63)	25	12	13	67 (7)	1.02 L (0.37)
Engström 1999	26	14	12	66 (5)	31% (11)	24	12	12	67 (5)	34% (10)
Faager 2004	10	3	7	72 (9)	26 (7)	10	3	7	70 (8)	28 (6)
Faulkner 2010	10	na	na	na	na	10	na	na	na	na
Fernandez 2009	30	29	1	66 (8)	33 (10)	20	20	0	70 (5)	38 (12)
Finnerty 2001	36	25	11	70 (8)	41% (19)	29	19	10	68 (10)	41% (16)
Gohl 2006	17	6	4	62.5 (7)	53.4 (10.7)	17	7	2	53.7 (5.8)	63.2 (8.5)
Goldstein 1994	38	21	17	66 (7)	35% (15)	40	17	23	65 (8)	35% (12)
Gosselink 2000	37	31	6	60 (9)	41% (16)	33	30	3	63 (7)	43% (12)
Gottlieb 2011	35	7	15	74.1 (66-82)	64.27 (7.9)	26	7	13	73.2 (67-88)	67.05 (8.8)
Griffiths 2000	93	57	37	68 (8)	40% (16)	91	54	37	68 (8)	39% (16)
Gurgun 2013	30	28	28	64.0 (10.8)	41.9 (10.8)	16	15	1	67.8 (6.6)	39.3 (9.3)
Güell 1995	30	30	30	64 (7)	31% (12)	30	30	0	66 (6)	39% (14)
Güell 1998	18	16	2	68 (8)	32% (11)	17	17	0	66 (8)	38% (15)
Hernandez 2000	20	20	0	64 (8)	71.1 (18.9)	17	17	0	63 (7)	74.7 (14.7)

Table 2. Baseline characteristics (Continued)

Hoff 2007	6	4	2	62.8 (1.4)	49.9 (4.6)	6	4	2	60.6 (3.0)	45.2 (6.0)
Jones 1985	8	6	2	64 (6)	0.78 L (0.27)	6	1	5	63 (8)	0.68 L (0.12)
Karapolat 2007	26	21	5	64.81 (9.4)	55.50%	19	18	1	67.21 (6.72)	58%
Lake 1990	7	6	1	66.3 (6.8)	0.83 L (0.25)	7	4	3	65.7 (3.5)	0.97 L (0.29)
Lindsay 2005	25	20	5	69.5 (9.3)	0.9 L (0.3)	25	18	7	69.8 (10.3)	0.8 L (0.4)
Liu 2012	36	26	10	61.34 (8.3)	61.27 (5.86)	36	29	7	62.2 (6.34)	61.43 (6.17)
McGavin 1977	12	12	0	61 (6)	0.97 L (0.33)	12	12	0	57 (8)	1.15 L (0.72)
McNa-mara 2013	38	18	15	72 (10)	60 (10)	15	8	7	70 (9)	55 (20)
Mehri 2007	20	11	9	52.1 (10.7)	na	18	7	11	52.17 (11.6)	na
Mendes De Oliveira 2010	56	46	10	66.4/71.3	47.5/ 51.5	29	19	10	70.8	41.4
Nalbant 2011	14	11	3	73.5	58.5 (48-65)	15	13	2	68	57 (44-66)
O'Shea 2007	27	na	na	66.9 (7)	49	27	na	na	68.4 (9.9)	52
Ozdemir 2010	25	25	0	60.9 (8.8)	54.5 (15.6)	25	25	0	64.1 (8.9)	54.1 (20.2)
Paz-Diaz 2007	10	6	4	67 (5)	34 (11)	14	12	2	62 (7)	30 (9)
Petty 2006	149	80	69	68.8 (9.2)	na	73	40	33	66.8 (9.9)	na

Table 2. Baseline characteristics *(Continued)*

Reardon 1994	10	5	5	66 (8)	35% (10)	10	5	5	66 (7)	33% (15)
Ringbaek 2000	24	1	23	62 (7)	50% (17)	21	6	15	65 (8)	44% (14)
Gomez 2006	64	39	9	64.1/64.9	74 (66.5- 81.5)	33	19	4	63.4	60.1 (55.6- 64.4)
Simpson 1992	14	5	9	73 (5)	40% (19)	14	10	4	70 (6)	39% (21)
Singh 2003	20	na	na	na	28 (7.5)	20	na	na	na	26 (7.1)
Sridhar 2008	61	30	31	69.9 (9.6)	42.9 (15. 5)	61	30	31	69.68 (10.4)	48.9 (18.69)
Strijbos 1996	15	14	1	61 (6)	40% (20)	15	12	3	63 (5)	43% (9)
Theander 2009	15	3	9	66	35.1 (7.6)	15	10	4	64	32.3 (9.5)
Valler 1994	10	7	3	60 (9)	57.2	10	8	2	58 (6)	55.7
Van Wetering 2010	102	72	30	65.9 (8.8)	58 (17)	97	69	28	67.2 (8.9)	60 (15)
Vijayan 2010	16	na	na	na	na	15	na	na	na	na
Weiner 1992	12	6	6	67 (9)	32.8 (3)	12	5	7	61 (9)	39.2 (2.8)
Wen 2008	32	31	1	67 (7)/68 (7)	46 (10)/50 (14)	9	9	0	66(10)	52 (14)
Wijkstra 1994	28	23	5	64 (5)	44% (11)	15	14	1	62 (5)	45% (9)
Xie 2003	25	22	3	54 (6)	42% (16)	25	21	4	54 (6)	40% (17)

na: not available.

Table 3. Study design

Study	Follow-up	Duration (weeks)	Setting	Programme type
Barakat 2008	14 weeks	14	Outpatient	Exercise + other
Baumann 2012	6 months	8	Community	Exercise + other
Behnke 2000a	3, 6 months	24	Inpatient	Exercise + other
Bendstrup 1997	12, 24 weeks	12	Outpatient	Exercise
Booker 1984	3, 6, 12 months	9	Home	Exercise + other
Borghi-Silva 2009	6 weeks	6	Outpatient	Exercise
Boxall 2005	12 weeks	12	Home	Exercise + other
Busch 1988	18 weeks	18	Home	Exercise
Cambach 1997	3 months	12	Community	Exercise + other
Casaburi 2004	10 weeks	10	Outpatient	Exercise + other
Casey 2013	12 weeks	8	Community	Exercise + other
Cebollero 2012	12 weeks	12	Outpatient	Exercise
Chan 2011	3 months	12	Community	Exercise
Chlumsky 2001	8 weeks	8	Outpatient	Exercise
Clark 1996	12 weeks	12	Home	Exercise
Cochrane 2006	6 weeks, 6 months, 12 months	6	Outpatient	Exercise + other
Cockcroft 1981	2, 6 months	6	Outpatient	Exercise
De Souto Araujo 2012	8 weeks	8	Community	Exercise
Deering 2011	8 weeks	7	Outpatient	Exercise + other
Elci 2008	1, 3 months	12	Community /Home	Exercise + other
Emery 1998	10 weeks	10	Outpatient	Exercise + other

Table 3. Study design (Continued)

Engström 1999	12 months	52	Outpatient /Home	Exercise + other
Faager 2004	8 weeks, 6 months	8	Inpatient /Home	Exercise + other
Faulkner 2010	week 9	8	Community	Exercise + other
Fernandez 2009	1 year	52	Home	Exercise + other
Finnerty 2001	12, 24 weeks	6	Outpatient	Exercise + other
Gohl 2006	12 months	52	Community	Exercise
Goldstein 1994	24 weeks	8	Inpatient	Exercise + other
Gosselink 2000	6, 18 months	24	Outpatient	Exercise
Gottlieb 2011	6 months	7	Community	Exercise + other
Griffiths 2000	1 year	6	Outpatients /Home	Exercise + other
Gomez 2006	3, 6 months	12	Community	Exercise + other
Güell 1995	3, 6, 9, 12, 18, 24 months	12	Outpatient /Home	Exercise
Güell 1998	8 weeks	8	Outpatient	Exercise
Gurgun 2013	8 weeks, 6 months	8	Outpatient	Exercise + other
Hernandez 2000	12 weeks	12	Home	Exercise
Hoff 2007	8 weeks	8	Outpatient	Exercise
Jones 1985	10 weeks	10	Home	Exercise
Karapolat 2007	8, 12 weeks	8	Outpatient	Exercise + other
Lake 1990	8 weeks	8	Outpatient	Exercise
Lindsay 2005	6 weeks, 3 months	6	Community	Exercise + other
Liu 2012	6 months	24	Inpatient /Home	Exercise
McGavin 1977	14 weeks	≥12	Home	Exercise

Table 3. Study design (Continued)

McNamara 2013	8 weeks	8	Outpatient	Exercise
Mehri 2007	4 weeks	4	Outpatient	Exercise
Mendes De Oliveira 2010	12 weeks	12	Outpatient /Home	Exercise + other
Nalbant 2011	3, 6 months	24	Nursing home	Exercise + other
O'Shea 2007	3, 6 months	12	Outpatient /Home	Exercise
Ozdemir 2010	1 month	4	Outpatient	Exercise
Paz-Diaz 2007	8 weeks	8	Outpatient	Exercise
Petty 2006	8 weeks	8	Home	Exercise + other
Reardon 1994	6 weeks	6	Outpatient	Exercise + other
Ringbaek 2000	8 weeks	8	Outpatient	Exercise + other
Simpson 1992	8 weeks	8	Outpatient	Exercise
Singh 2003	4 weeks	4	Home	Exercise
Sridhar 2008	6 months	6	Outpatients /Home	Exercise + other
Strijbos 1996	3, 6, 12, 18 months	12	Outpatient	Exercise + other
Theander 2009	12 weeks	12	Outpatient /Home	Exercise + other
Vallet 1994	8 weeks	8	Inpatient	Exercise
Van Wetering 2010	4 months	12	Community	Exercise + other
Vijayan 2010	Unclear	6	Unclear	Exercise
Weiner 1992	6 months	24	Outpatient	Exercise
Wen 2008	12 weeks	12	Outpatient	Exercise
Wijkstra 1994	12 weeks	12	Outpatient /Home	Exercise + other

Table 3. Study design (Continued)

Xie 2003	12 weeks	12	Home	Exercise
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Table 4. Summary of subgroup analysis

Pulmonary rehabilitation versus usual care. Subgroup: community versus hospital-delivered programme					
Outcome	Subscale	Subgroups	Heterogeneity	MD [95% CI]	Test for subgroup differences
CRQ	Fatigue	Community	Tau ² = 0.10; I ² = 52%	0.44 [0.14, 0.75]	Chi ² = 3.98, df = 1 (P value 0.05), I ² = 74.9%
		Hospital	Tau ² = 0.09; I ² = 51%	0.86 [0.58, 1.14]	
CRQ	Emotional Function	Community	Tau ² = 0.00; I ² = 0%	0.21 [0.04, 0.39]	Chi ² = 12.24, df = 1 (P value 0.0005), I ² = 91.8%
		Hospital	Tau ² = 0.06; I ² = 39%	0.77 [0.51, 1.03]	
CRQ	Mastery	Community	Tau ² = 0.07; I ² = 45%	0.40 [0.12, 0.67]	Chi ² = 8.58, df = 1 (P value 0.003), I ² = 88.3%
		Hospital	Tau ² = 0.05; I ² = 31%	0.95 [0.70, 1.20]	
CRQ	Dyspnoea	Community	Tau ² = 0.03; I ² = 26%	0.58 [0.34, 0.81]	Chi ² = 4.05, df = 1 (P value 0.04), I ² = 75.3%
		Hospital	Tau ² = 0.17; I ² = 60%	0.99 [0.66, 1.32]	
SGRQ	Total	Community	Tau ² = 24.00; I ² = 73%	-8.15 [-12.16, -4.13]	Chi ² = 0.69, df = 1 (P value 0.41), I ² = 0%
		Hospital	Tau ² = 6.41; I ² = 35%	-6.05 [-8.91, -3.20]	
SGRQ	Symptoms	Community	Tau ² = 6.28; I ² = 24%	-3.66 [-7.07, -0.24]	Chi ² = 1.65, df = 1 (P value 0.20), I ² = 39.2%
		Hospital	Tau ² = 4.96; I ² = 15%	-6.91 [-10.51, -3.30]	
SGRQ	Impact	Community	Tau ² = 19.91; I ² = 63%	-8.17 [-12.00, -4.34]	Chi ² = 0.46, df = 1 (P value 0.50), I ² = 0%
		Hospital	Tau ² = 22.39; I ² = 58%	-6.21 [-10.33, -2.09]	
SGRQ	Activity	Community	Tau ² = 48.91; I ² = 78%	-7.82 [-13.37, -2.28]	Chi ² = 0.93, df = 1 (P value 0.33), I ² = 0%
		Hospital	Tau ² = 10.45; I ² = 36%	-4.58 [-8.16, -1.00]	
Pulmonary rehabilitation versus usual care. Subgroup: exercise only programme versus exercise plus additional elements in programme					

Table 4. Summary of subgroup analysis (Continued)

Outcome	Subscale	Subgroups	Heterogeneity	MD [95% CI]	Test for subgroup differences
CRQ	Fatigue	Exercise only	$\text{Tau}^2 = 0.00$; $I^2 = 0\%$	0.73 [0.54, 0.92]	$\text{Chi}^2 = 0.26$, $\text{df} = 1$ (P value 0.61), $I^2 = 0\%$
		Exercise + other	$\text{Tau}^2 = 0.29$; $I^2 = 79\%$	0.61 [0.18, 1.03]	
CRQ	Emotional Function	Exercise only	$\text{Tau}^2 = 0.00$; $I^2 = 0\%$	0.51 [0.31, 0.71]	$\text{Chi}^2 = 0.09$, $\text{df} = 1$ (P value 0.77), $I^2 = 0\%$
		Exercise + other	$\text{Tau}^2 = 0.28$; $I^2 = 79\%$	0.58 [0.16, 1.00]	
CRQ	Mastery	Exercise only	$\text{Tau}^2 = 0.01$; $I^2 = 11\%$	0.66 [0.44, 0.88]	$\text{Chi}^2 = 0.12$, $\text{df} = 1$ (P value 0.73), $I^2 = 0\%$
		Exercise + other	$\text{Tau}^2 = 0.31$; $I^2 = 79\%$	0.74 [0.31, 1.18]	
CRQ	Dyspnoea	Exercise only	$\text{Tau}^2 = 0.06$; $I^2 = 31\%$	0.83 [0.56, 1.10]	$\text{Chi}^2 = 0.13$, $\text{df} = 1$ (P value 0.72), $I^2 = 0\%$
		Exercise + other	$\text{Tau}^2 = 0.25$; $I^2 = 77\%$	0.74 [0.35, 1.13]	
SGRQ	Total	Exercise only	$\text{Tau}^2 = 62.83$; $I^2 = 70\%$	-7.87 [-16.72, 0.98]	$\text{Chi}^2 = 0.06$, $\text{df} = 1$ (P value 0.81), $I^2 = 0\%$
		Exercise + other	$\text{Tau}^2 = 10.17$; $I^2 = 56\%$	-6.76 [-9.19, -4.34]	
SGRQ	Symptoms	Exercise only	$\text{Tau}^2 = 0.00$; $I^2 = 0\%$	-7.38 [-12.33, -2.44]	$\text{Chi}^2 = 0.99$, $\text{df} = 1$ (P value 0.32), $I^2 = 0\%$
		Exercise + other	$\text{Tau}^2 = 13.88$; $I^2 = 41\%$	-4.38 [-7.62, -1.15]	
SGRQ	Impact	Exercise only	$\text{Tau}^2 = 33.34$; $I^2 = 63\%$	-6.11 [-12.60, 0.38]	$\text{Chi}^2 = 0.17$, $\text{df} = 1$ (P value 0.68), $I^2 = 0\%$
		Exercise + other	$\text{Tau}^2 = 17.12$; $I^2 = 59\%$	-7.61 [-10.64, -4.57]	
SGRQ	Activity	Exercise only	$\text{Tau}^2 = 139.67$; $I^2 = 78\%$	-9.33 [-21.66, 2.99]	$\text{Chi}^2 = 0.30$, $\text{df} = 1$ (P value 0.59), $I^2 = 0\%$
		Exercise + other	$\text{Tau}^2 = 18.51$; $I^2 = 60\%$	-5.79 [-8.95, -2.64]	

CRQ: Chronic Respiratory Disease Questionnaire; MD: mean difference; SGRQ: St. George's Respiratory Questionnaire.

APPENDICES

Appendix 1. Archive of previous search methods and results

Search strategy used for review versions published up to 2004

We searched all records in the Cochrane Airways Group Register coded as 'COPD' for original articles published in any language using the following strategy: rehabilitat* or fitness* or exercis* or physical* or train*

In the first version of this review (Lacasse 1996), 522 publications were retrieved from the computerised search. The review authors reduced this list to 68 potentially eligible papers (quadratic weighted Kappa 0.53, 95% CI 0.45 to 0.61) that were assessed in detail. From this study list, 47 were excluded as the result of wrong population studies (n = 4), intervention not meeting the definition of rehabilitation (n = 7), control group not receiving conventional community care (n = 29), trials not randomised (n = 7). Both primary review authors agreed to include 17 papers in the meta-analysis (quadratic Kappa 0.89, 95% CI 0.65 to 1.00). Six of the 14 RCTs included in the original meta-analysis (Lacasse 1996) were not uncovered by this literature search. Therefore, a total of 23 randomised controlled trials were included. This represents an addition of nine RCTs to the meta-analysis published in 1996 (Lacasse 1996). We contacted the authors of these trials for any additional information required; response rate was 91% (21/23).

An updated search for the review was undertaken in October 2004, which identified an additional 998 references. These were filtered to a list of 139 references, which were considered in the update of the review. Of these, 93 studies failed to meet the inclusion criteria. The original version of the review as previously indicated had included 23 trials. From the updated search (2004), eight additional RCTs (represented by 17 references) met the inclusion criteria of the review (Behnke 2000a; Boxall 2005; Casaburi 2004; Chlumsky 2001; Finnerty 2001; Güell 1998; Singh 2003; Xie 2003). Six papers were awaiting assessment (Corrado 1995: published as conference abstract; Fernández 1998: paper not available; Shu 1998: published as conference abstract; Tregonning 2000: published as conference abstract; Ward 1999: published as conference abstract; Wright 2002: unclear study methods). One trial was ongoing (Whiteford 2004). As an outcome of the update in 2004, a total of 31 RCTs (represented by 65 references) contributed to the meta-analysis.

Appendix 2. 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 Respiriology (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 3. Search strategy to identify relevant trials from the CAGR

#1 MeSH DESCRIPTOR Pulmonary Disease, Chronic Obstructive Explode All

#2 MeSH DESCRIPTOR Bronchitis, Chronic

#3 (obstruct*) near3 (pulmonary or lung* or airway* or airflow* or bronch* or respirat*)

#4 COPD:MISC1

#5 (COPD OR COAD OR COBD):TI,AB,KW

#6 #1 OR #2 OR #3 OR #4 OR #5

#7 MeSH DESCRIPTOR Rehabilitation

#8 MeSH DESCRIPTOR Respiratory Therapy

#9 rehabilitat*

#10 fitness*

#11 exercis*

#12 train*

#13 #7 or #8 or #9 or #10 or #11 or #12

#14 #6 and #13

[Note: in search line #4, MISC1 denotes the field in which the reference has been coded for condition, in this case, COPD]

Appendix 4. Exclusion criteria used to sort and categorise references

Exclusion criteria
Less than 90% of participants have a diagnosis of COPD
Not a programme, or programme does NOT contain any exercise component
Has an exercise component but is NOT aerobically demanding
Programme of less than 4 weeks' duration
Control received more than conventional care
Includes ventilated patients (hospital ventilated)
Within 4 weeks post exacerbation
This citation linked to main study paper already being screened
Duplicate citation (identical to a citation previously included)
The intervention is a medication

Appendix 5. Eligibility classification allocated to studies

Classification	Action
Excluded	Study excluded
Important article but not to be included in review	Study excluded
Included but needs translation	Study included and proceeds to next stage
Included	Study included and proceeds to next stage
More information needed before inclusion decision	Awaiting additional information before study proceeds

Appendix 6. Risk of bias domains and judgements

Sequence generation (possible selection bias)

A detailed description of the methods used to generate the allocation sequence was developed for each study to facilitate an assessment of whether it should produce comparable groups.

Risk of bias for sequence generation was graded based on the following:

- low risk (any truly random process, e.g. random number table; computer random number generator);
- high risk (any non-random process, e.g. odd or even date of birth; hospital or clinic record number); or
- unclear risk.

Allocation concealment (possible selection bias)

A description of the methods used to conceal the allocation sequence for each study was presented, and this determined whether the intervention allocation might have been anticipated in advance of, or during, recruitment, or changed after assignment.

Risk of bias associated with allocation concealment was graded as follows:

- low risk (e.g. telephone or central randomisation; consecutively numbered sealed opaque envelopes);
- high risk (open random allocation; unsealed or non-opaque envelopes, alternation; date of birth); or
- unclear risk.

Blinding of participants and personnel (possible performance bias)

The nature of the interventions involved in pulmonary rehabilitation would make it highly unlikely or impossible to blind participants or personnel delivering the interventions.

However, it would be possible to blind outcome assessors. Therefore, we assessed the risk of bias for blinding of outcome assessors as:

- high risk;
- low risk; or
- unclear risk.

Blinding of outcome assessment (checking for possible detection bias)

We will describe for each included study the methods used, if any, to blind outcome assessors from knowledge of which intervention participants received. We will assess the risk of bias for blinding of outcome assessment as:

- low risk;
- high risk; or

- unclear risk.

Incomplete outcome data (possible attrition bias associated with withdrawals, drop-outs, deviations from original protocol)

A description of completeness of data for each outcome at all stages of the study was presented. This included examining attrition and exclusions from the analysis. Each study was examined to identify whether attrition and exclusions were reported (comparing the numbers presented at each stage with the total number of randomised participants). The studies were also examined for rationale and justifications explaining any attrition or exclusions. In instances where enough information could be identified or was obtained from the trial authors, we re-included missing data in the analyses. We assessed the risk of bias for completeness of data as follows:

- low risk (20% or less missing data);
- high risk (more than 20% missing data); or
- unclear risk.

Selective reporting bias

Studies were examined for selective outcome reporting bias by cross-checking that all outcomes identified in the methods section of the results publication were reported in the results section of the trial publication(s).

The risk of bias for selective reporting was graded as follows:

- high risk (where not all of the study's prespecified outcomes had been reported; one or more reported primary outcomes were not prespecified; outcomes of interest were reported incompletely and so cannot be used; study failed to include results of a key outcome that would have been expected to have been reported);
- low risk (where it was clear that all of the study's prespecified outcomes and all expected outcomes of interest to the review have been reported); or
- unclear risk.

Other sources of bias (bias due to problems not covered by the items above)

If the review authors believed that any other possible sources of bias were matters of concern, these were recorded.

The level at which studies were seen to be free of other problems that could put them at risk of bias was graded as:

- low risk;
- high risk; or
- unclear risk.

Overall risk of bias

An overall judgement was made in relation to whether studies were at high risk of bias, according to the criteria given in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011) and identified above. The magnitude of the overall bias, along with the degree to which the bias was likely to have impacted the findings, was assessed for each study using the following grades:

- low risk;
- high risk; or
- unclear risk.

WHAT'S NEW

Last assessed as up-to-date: 26 March 2014.

Date	Event	Description
21 April 2015	Amended	Typo in CI for functional exercise capacity in results corrected

HISTORY

Protocol first published: Issue 1, 1998

Review first published: Issue 1, 2003

Date	Event	Description
26 March 2014	New citation required and conclusions have changed	New author team Abstract, plain language summary and results redrafted. Inclusion criteria modified and outcomes defined. Methods brought up to date, including use of current Cochrane risk of bias tool. Summary of findings table added Conclusions strengthened through the addition of 35 new studies, and recommendations for future research modified Only assessments completed up to and within 3 months of completion of the intervention included in the analysis Studies that commenced within 4 weeks of an acute exacerbation of COPD excluded, as a separate systematic review examined the effects of pulmonary rehabilitation following exacerbations of chronic obstructive pulmonary disease (Puhan 2011) Additional subgroup analysis undertaken
26 March 2014	New search has been performed	New literature search run
20 August 2008	Amended	Converted to new review format
16 June 2006	New citation required and conclusions have changed	Substantive amendments made

CONTRIBUTIONS OF AUTHORS

BMC and DC selected trials.

BMC, DC, EM and KM extracted data.

BMC, DC, EM, DD and KM assessed the methodological quality of trials.

BMC was responsible for handling data in RevMan.

BMC and DD designed the meta-analysis.

BMC and DD completed the clinical interpretation of results.

YL provided support and guidance throughout the update and critically reviewed the final manuscript.

DECLARATIONS OF INTEREST

The review authors DC, BMC, KM and DD were involved in the PRINCE study conducted by [Casey 2013](#), a cluster-randomised trial that was included in this review. The risk of bias table for this study was therefore completed by two independent review authors, who were not involved in this trial but were experienced in conducting Cochrane systematic reviews. These were the review authors EM and Miriam Brennan, Lecturer at the School of Nursing & Midwifery, NUI Galway.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

In this current update, the following changes were made from the previous version.

- We made the following changes to the inclusion and exclusion criteria.
 - We excluded randomised controlled trials that focused on participants:
 - ◊ who were ventilated; or
 - ◊ who had an acute exacerbation within four weeks before commencement of the intervention
 - We excluded interventions for which the physical activity component was considered to not be aerobically demanding (such as respiratory muscle training, breathing exercises, Tai Chi and yoga). The degree of aerobic demand was assessed for each individual intervention by examining the detailed description of the intervention in identified studies. We also excluded programmes of less than four weeks' duration.
- We clarified what was considered usual care.

INDEX TERMS

Medical Subject Headings (MeSH)

*Exercise Tolerance; *Health Status; *Quality of Life; Dyspnea [rehabilitation]; Pulmonary Disease, Chronic Obstructive [psychology; *rehabilitation]; Randomized Controlled Trials as Topic

MeSH check words

Female; Humans; Male