



# British Thoracic Society guideline on pulmonary rehabilitation in adults

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on behalf of the British Thoracic Society Standards of Care Committee

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## SUMMARY OF RECOMMENDATIONS

### The role of pulmonary rehabilitation

- Pulmonary rehabilitation should be offered to patients with chronic obstructive pulmonary disease (COPD) with a view to improving exercise capacity by a clinically important amount. (Grade A)
- Pulmonary rehabilitation should be offered to patients with COPD with a view to improving dyspnoea and health status by a clinically important amount. (Grade A)
- Different components within a pulmonary rehabilitation programme, such as resistance training, can influence quadriceps strength and this is addressed in the section 'Nature of training of these guidelines'. (✓)
- Pulmonary rehabilitation should be offered to patients with COPD with a view to improving psychological wellbeing. (Grade A)
- As a minimum, efficacy of pulmonary rehabilitation programmes needs to be regularly assessed by demonstrating clinically important improvements in exercise capacity, dyspnoea and health status. (Grade B)
- As part of regular assessment, patient satisfaction and feedback should be sought. (✓)

### Referral and assessment of patients for pulmonary rehabilitation

- The point of referral to pulmonary rehabilitation should be used as an opportunity to explore the patient's understanding of pulmonary rehabilitation, address concerns and to educate patients about the benefits of a pulmonary rehabilitation programme. (✓)
- Healthcare professionals making referrals to pulmonary rehabilitation should have basic knowledge about what a programme entails and effectiveness. A pulmonary rehabilitation programme should be presented by the referrer as a fundamental treatment for COPD rather than an optional extra. (✓)
- Initial assessment for pulmonary rehabilitation provides an opportunity to assess and refer for treatment of comorbidities prior to commencing. (✓)
- The setting of pulmonary rehabilitation, skill mix of the team and other comorbidities should always be considered in the risk assessment of patients entering a rehabilitation programme. (✓)

### Specific situations at assessment

#### Smoking

- Patients with COPD should be referred for pulmonary rehabilitation regardless of their smoking status. (Grade D)
- Patients referred to pulmonary rehabilitation should have their smoking status assessed and referral to smoking cessation services offered to smokers simultaneously. (✓)
- Pulmonary rehabilitation provides opportunities to offer smoking cessation advice. (✓)

#### Chronic respiratory failure

- Patients with COPD can be referred for pulmonary rehabilitation regardless of whether or not they have chronic respiratory failure. (Grade D)
- When considering the referral of patients with chronic respiratory failure, practitioners should reflect on the receiving setting and skill mix of the attending staff to provide safe pulmonary rehabilitation to these patients who have significant physiological impairment and potential for greater instability by the intended programme. (✓)

#### Cardiovascular disease comorbidity

- People with chronic respiratory disease should be referred to pulmonary rehabilitation irrespective of coexistent stable cardiovascular disease. (Grade D)
- A coexistent abdominal aortic aneurysm (AAA) <5.5 cm should not preclude referral to pulmonary rehabilitation and being included in moderate intensity aerobic exercise training, provided blood pressure is controlled. (Grade D)
- The referral process and/or the initial assessment for pulmonary rehabilitation offer an important opportunity to assess and optimise cardiovascular health and address risk factors for cardiovascular disease. (✓)
- In patients with COPD who have an AAA >5.5 cm, deemed not fit for surgery, pulmonary rehabilitation incorporating mild-moderate intensity aerobic exercise may be considered, but should not include resistance training. (✓)

#### Anxiety and depression

- Coexistent symptoms of anxiety and/or depression in patients with COPD should not preclude referral to pulmonary rehabilitation. (Grade D)

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- ▶ The referral process and the assessments for pulmonary rehabilitation offer important opportunities to detect and consider referral for ongoing support and management for depression. (✓)

#### MRC dyspnoea scale

- ▶ Patients with a Medical Research Council (MRC) Dyspnoea score of 3–5 who are functionally limited by breathlessness should be referred for outpatient pulmonary rehabilitation. (Grade A)
- ▶ Patients with a MRC dyspnoea score of 2 who are functionally limited by breathlessness should be referred for pulmonary rehabilitation. (Grade D)
- ▶ Patients with a MRC dyspnoea score of 5 who are house-bound should not routinely be offered supervised pulmonary rehabilitation within their home. (Grade B)
- ▶ Flexible and pragmatic approaches should be considered to facilitate exercise training in patients who have less severe COPD and who are less breathless. (✓)

#### Bronchodilator therapy

- ▶ Patients with COPD should be taking bronchodilator therapy in line with National Institute for Health and Clinical Excellence (NICE) COPD guidelines prior to referral to pulmonary rehabilitation. (Grade D)
- ▶ Pulmonary rehabilitation offers an opportunity to check and optimise inhaler technique. (✓)

#### Other considerations regarding referral to pulmonary rehabilitation

- ▶ Patients with unstable cardiac disease or locomotor difficulties that preclude exercise (eg, severe arthritis or severe peripheral vascular disease) should not be referred for pulmonary rehabilitation. (✓)
- ▶ Careful consideration should be given to patients who have significant cognitive or psychiatric impairment that would lead to an inability to follow simple commands in a group setting. (✓)
- ▶ In certain individual cases, facilitation of pulmonary rehabilitation may be aided by the support and attendance of a relative or carer. (✓)
- ▶ In case of doubt over the appropriateness of a patient for pulmonary rehabilitation, clinicians are advised to contact their local provider. (✓)

#### Structure of pulmonary rehabilitation

##### Frequency of supervised pulmonary rehabilitation sessions

- ▶ Pulmonary rehabilitation programmes should be a minimum of twice-weekly supervised sessions. (Grade D)
- ▶ In line with published pulmonary rehabilitation studies and the outcomes they demonstrate, a third session of prescribed exercise is recommended. This can be performed unsupervised. (✓)
- ▶ Encouragement of regular physical activity five times a week for 30 min each time is encouraged in line with standard healthy living advice. (✓)

##### Duration of pulmonary rehabilitation programmes

- ▶ Pulmonary rehabilitation programmes of 6–12 weeks are recommended. (Grade A)
- ▶ Pulmonary rehabilitation programmes including the attendance at a minimum of 12 supervised sessions are recommended, although individual patients can gain some benefit from fewer sessions. (Grade A)

- ▶ If training for less than 6 weeks is considered, this should be individualised and objective/subjective measures of benefit in place before patients graduate. For some individuals, reassessment at 4 weeks and graduation to independent gym training is a feasible possibility. (✓)

#### Rolling or cohort programmes

- ▶ Cohort or rolling programmes of pulmonary rehabilitation are both acceptable forms of delivery depending on local considerations. (Grade D)

#### Nature of training

- ▶ To ensure strength and endurance benefits in patients with COPD, a combination of progressive muscle resistance and aerobic training should be delivered during a pulmonary rehabilitation programme. (Grade B)
- ▶ Relevant expertise is required to deliver resistance training. (✓)
- ▶ Patients should be capable of continuing effective resistance training once supervised sessions have ended. The supervising rehabilitation therapist should ensure that patients are able and willing to continue with unsupervised resistance training. (✓)
- ▶ Prescribing of progressive strength exercise should be individualised for each patient, taking into consideration the initial health screening and any increase in risk from comorbidities. (✓)

#### Interval and continuous aerobic training

- ▶ Interval and continuous training can be applied safely and effectively within the context of pulmonary rehabilitation to patients with COPD. (Grade A)
- ▶ The choice of interval or continuous training will be down to the patient and/or therapist preference. (✓)
- ▶ In clinical practice, interval training may require a higher therapist to patient ratio to ensure adequate work rate and rest intervals are achieved compared with continuous training. (✓)

#### Goal setting in pulmonary rehabilitation

- ▶ Generic exercise training as opposed to individually targeted exercise training is recommended for pulmonary rehabilitation. (Grade D)
- ▶ While generic exercise training is recommended as opposed to an individually targeted exercise programme, the prescription of exercise is individualised to provide correct intensity. (✓)
- ▶ Besides the exercise elements of pulmonary rehabilitation, healthcare professionals commonly use goal setting to address specific hurdles. Given the personalised nature of this intervention to a patient's needs, evidence is difficult to quantify. (✓)
- ▶ The term 'goal setting' may require discussion with the patient. (✓)

#### Supervision in pulmonary rehabilitation

- ▶ A supervised pulmonary rehabilitation programme is recommended for patients with COPD. (Grade A)
- ▶ If considering a structured home-based rehabilitation programme for patients with COPD, the following important factors need careful consideration: mechanisms to offer remote support and/or supervision, provision of home exercise equipment and patient selection. (Grade B)
- ▶ There would be some benefit to increasing the options for pulmonary rehabilitation available to individuals with COPD, and increase the scope of the service. Geography may limit or stimulate options. (✓)

## Post-exacerbation pulmonary rehabilitation

Outcomes in post-exacerbation pulmonary rehabilitation

- ▶ Patients hospitalised for acute exacerbation of COPD should be offered pulmonary rehabilitation at hospital discharge to commence within 1 month of discharge. (Grade A)
- ▶ Providing post-exacerbation pulmonary rehabilitation alongside elective pulmonary rehabilitation courses can cause practical issues. Evaluation of innovative ways of delivering a combination of both modes of pulmonary rehabilitation in tandem would be useful. (√)

Completion of post-exacerbation pulmonary rehabilitation

- ▶ Clinical services providing post-exacerbation pulmonary rehabilitation commencing within 1 month of hospital discharge should carefully record uptake, adherence and completion rates. (Grade D)
- ▶ Patients who initially decline pulmonary rehabilitation commencing within 1 month of hospital discharge should be offered elective pulmonary rehabilitation. (Grade D)

## Adjuncts to pulmonary rehabilitation

Inspiratory muscle training and pulmonary rehabilitation

- ▶ Inspiratory muscle training (IMT) is not recommended as a routine adjunct to pulmonary rehabilitation. (Grade B)

Hormones and nutritional supplements and pulmonary rehabilitation

- ▶ No specific hormonal or nutritional supplement can currently be recommended as a routine adjunct to pulmonary rehabilitation. (Grade B)
- ▶ The optimal approaches for addressing malnutrition, sarcopenia or obesity in COPD are uncertain and this is a wider issue than this guideline covers. However, attendance at a pulmonary rehabilitation course presents an ideal opportunity to screen and educate patients on nutrition. (√)
- ▶ Patients with a body mass index (BMI) in the underweight or obese range should be considered for specific dietetic support. (√)

Non-invasive ventilation during pulmonary rehabilitation

- ▶ Long-term domiciliary non-invasive ventilation (NIV) should not be provided for the sole purpose of improving outcomes during pulmonary rehabilitation. (Grade D)
- ▶ Patients who already receive long-term domiciliary NIV for chronic respiratory failure should be offered the opportunity to exercise with NIV during pulmonary rehabilitation if acceptable and tolerable to the patient. (Grade D)

Supplemental oxygen in patients undergoing rehabilitation

- ▶ Supplemental oxygen should not be routinely used for all patients undergoing pulmonary rehabilitation. (Grade B)
- ▶ Supplemental oxygen during pulmonary rehabilitation should be offered to those who fulfil the assessment criteria for long-term or ambulatory oxygen unless there are compelling clinical reasons to use alternative criteria. (Grade D)
- ▶ Individuals who are prescribed oxygen but decline to use it during exercise should have this clearly documented in their notes. (√)
- ▶ Pulmonary rehabilitation provides an opportunity to assess the adequacy of the prescribed flow rate for patients already in receipt of long-term oxygen therapy (LTOT) or ambulatory oxygen. (√)

Supplemental heliox in patients undergoing rehabilitation

- ▶ Heliox should not be used as an adjunct to pulmonary rehabilitation unless there are comorbidities which require its administration. (Grade D)

Neuromuscular electrical stimulation and pulmonary rehabilitation

- ▶ If expertise in neuromuscular electrical stimulation (NMES) is available, selected patients (low BMI with evidence of quadriceps weakness) who are unable or unwilling to participate in pulmonary rehabilitation could be considered for NMES. (Grade D)

## Pulmonary rehabilitation in people with other chronic respiratory diseases

Non-cystic fibrosis bronchiectasis

- ▶ Patients with non-cystic fibrosis (CF) bronchiectasis who have breathlessness affecting their activities of daily living (ADL) should have access to and be considered for pulmonary rehabilitation. (Grade D)
- ▶ Unlike in patients with CF, in patients with COPD and non-CF bronchiectasis with multidrug-resistant organisms, for example *Pseudomonas aeruginosa*, there is no current evidence of cross infection. (√)

Interstitial lung diseases

- ▶ The benefits of exercise and the recommendation of incorporating exercise activities into a healthy lifestyle should be discussed with all patients with interstitial lung disease (ILD). Such discussion needs to be tailored to realistic achievability for that person's condition. (√)
- ▶ If healthcare professionals consider referring certain patients with stable ILD who are limited by breathlessness in ADL to pulmonary rehabilitation, they should discuss with the patient the likely benefits. (√)
- ▶ Patients with idiopathic pulmonary fibrosis (IPF) have a potential for significant desaturation during exercise related activities. (√)

Asthma

- ▶ The routine referral of patients with asthma to pulmonary rehabilitation is not recommended. (Grade D)
- ▶ The benefits of exercise and the recommendation of incorporating exercise activities into a healthy lifestyle should be discussed with all patients with asthma. (√)
- ▶ If healthcare professionals consider referring certain patients with stable asthma who are limited by breathlessness in ADL to pulmonary rehabilitation when on optimal therapy, they should discuss with the patient the likely benefits. (√)
- ▶ The British Thoracic Society (BTS)/Scottish Intercollegiate Guidelines Network (SIGN) asthma guideline draws attention to exercise-induced asthma and precautions to prevent this should be followed if appropriate. (√)

Other chronic respiratory diseases—in general

- ▶ Minimal clinically important different (MCID) changes and tools used to assess exercise capacity and quality of life for pulmonary rehabilitation in COPD are not necessarily transferable to other chronic respiratory diseases. While future research should address this, failure of rehabilitation should not be implied if failure to reach the COPD MCID for outcomes. (√)

- ▶ The educational element of pulmonary rehabilitation should be adapted for other chronic respiratory diseases if appropriate. (√)
- ▶ Practically, inclusion of patients with other chronic respiratory diseases into pulmonary rehabilitation will be alongside subjects with COPD. (√)
- ▶ General exercise should be encouraged for all patients with chronic respiratory disease. (√)

### Post pulmonary rehabilitation

#### Repeat pulmonary rehabilitation programmes

- ▶ Repeat pulmonary rehabilitation should be considered in patients who have completed a course of pulmonary rehabilitation more than 1 year previously. The likely benefits should be discussed and willing patients referred. (Grade B)
- ▶ Earlier repeat pulmonary rehabilitation should be considered in individuals with accelerated physiological decline or if additional benefits on a shorter timescale would be clinically valuable. (Grade D)
- ▶ It is unlikely that if the patient completed the pulmonary rehabilitation course originally and failed to gain a benefit, they would benefit a second time round, unless circumstances such as an exacerbation interrupted the initial programme. (√)

#### Maintenance

- ▶ All patients completing pulmonary rehabilitation should be encouraged to continue to exercise beyond the programme. (Grade A)
- ▶ Patients graduating from a pulmonary rehabilitation programme should be provided with opportunities for physical exercise beyond their rehabilitation programme. (√)

## INTRODUCTION

### Aim

Pulmonary rehabilitation has established itself as a key management strategy in people with chronic respiratory disease. The role of pulmonary rehabilitation has recently been highlighted in the Department of Health's 'An outcomes strategy for COPD and asthma in England'.<sup>1</sup> Since the BTS statement on pulmonary rehabilitation 2001, there has been a significant expansion in the literature for pulmonary rehabilitation.<sup>2</sup> This literature has contributed to our understanding of outcomes and markers of pulmonary rehabilitation, referral characteristics and patient selection, optimal programme structure, potential adjuncts to the main rehabilitation content, pulmonary rehabilitation in different settings such as following an exacerbation and maintaining the benefits of the programme after completion of the course. The UK model of pulmonary rehabilitation is not fully reflected in the American Thoracic Society/European Respiratory Society statement while other guidelines referring to pulmonary rehabilitation have either been disease or modality specific.<sup>3-5</sup> There is a need to provide a UK evidence-based guideline for pulmonary rehabilitation in adult patients with chronic respiratory disease in an outpatient setting.

For the purposes of the development of the guidelines, the Guideline Development Group (GDG) adopted the following working definition of pulmonary rehabilitation, broadly based on the NICE COPD guidelines: 'Pulmonary rehabilitation can be defined as an interdisciplinary programme of care for patients with chronic respiratory impairment that is individually tailored and designed to optimise each patient's physical and social performance and autonomy. Programmes comprise individualised exercise programmes and education'.<sup>3</sup>

### Target audience

The BTS pulmonary rehabilitation guideline is aimed primarily at practitioners within the UK. This includes doctors, nurses, physiotherapists, dieticians, occupational therapists and other healthcare professionals. It may be of relevance to other healthcare systems. It is intended to inform those conducting pulmonary rehabilitation and also those who manage patients with chronic respiratory disease who may be referred into a rehabilitation scheme.

### SCOPE

*Population:* people with chronic respiratory disease, focusing on COPD.

*Populations not covered:* children.

*Healthcare setting:* primary and secondary care.

*Topics:*

- The role of pulmonary rehabilitation.
- Referral and assessment.
- Structure of pulmonary rehabilitation including organisation and content.
- Post-exacerbation rehabilitation.
- Adjuncts to pulmonary rehabilitation.
- Other chronic respiratory diseases.
- Post pulmonary rehabilitation.

*Topics not covered:*

- Diagnosis and optimising COPD therapy otherwise.
- Peri-exacerbation inpatient exercise regimes.
- Elective inpatient pulmonary rehabilitation.\*
- Multidisciplinary care of cystic fibrosis.
- Pre-surgery and post-surgery pulmonary rehabilitation (including lung cancer).
- It was not possible to comprehensively cover all chronic respiratory diseases.
- Patient support groups.
- Healthcare costs/cost effectiveness.

\*While not covered specifically, occasionally inpatient pulmonary rehabilitation literature has been referred to in the absence of outpatient literature on a subject. This has been stated at the appropriate place.

The guideline refers to the NICE COPD guideline 2010, NICE commissioning guidelines, the BTS bronchiectasis guideline 2010 and the BTS/SIGN asthma guideline.<sup>3-8</sup> It does not overlap with details of other guidelines, such as smoking cessation, but clearly should dovetail.

### METHODOLOGY

This guideline is based on the best available evidence. The methodology used to write the guideline adheres strictly to the criteria as set by the AGREE collaboration, which is available online <http://www.agreetrust.org/resource-centre/agree-ii/>. The BTS Standards of Care Committee (SOCC) guideline production manual is available at [www.brit-thoracic.org.uk/guidelines.aspx](http://www.brit-thoracic.org.uk/guidelines.aspx)

### Clinical questions and literature search

Clinical questions were structured in the PICO (Patient, Intervention, Control, Outcome) format (web appendix 1) to define the scope of the guideline and inform the literature search.

Systematic electronic database searches were conducted to identify potentially relevant studies for inclusion in the guideline. For each topic area, the following databases were searched: Ovid MEDLINE (including MEDLINE In Process), Ovid EMBASE, and the Cochrane Library (including the Cochrane

Database of Systematic Reviews, the Database of Abstracts of Reviews of Effects) from 1980.

The searches were first run in August 2011 and updated in September 2012 (web appendix 2). Searches included a combination of indexed terms and free text terms and were limited to English language publications only. The initial search identified 2087 potential abstracts and the second search 173.

### Appraisal of literature

Appraisal was performed to be compliant with the AGREE collaboration. Four individuals (JDB, CEB, NJG and JHH) read the title and abstract of each article retrieved by the literature searches and decided whether the paper was definitely relevant, possibly relevant or not relevant to the project. Criteria formulated for categorising the abstracts into these three groups were:

- Whether the study addressed the clinical question.
- Whether the appropriate study type was used to produce the best evidence to answer the clinical question.
- Review articles were excluded.
- Abstract was in English.
- Abstracts were not rejected on the basis of the journal of publication, country in which the research was performed or published, or the date of publication.

The full paper was obtained for all relevant or possibly relevant abstracts and allocated to the relevant section(s) of the guideline.

The first screening process identified 472 of the initial 2087 reference abstracts to be definitely or possibly relevant to the guideline. Two guideline reviewers per section independently reviewed the abstracts to identify papers to be appraised for the guideline (appendix A). The two reviewers for each section then independently appraised each paper assigned to them using the SIGN critical appraisal checklists. The reliability of the evidence in each individual study was graded using the SIGN critical appraisal checklists and is shown in the evidence tables (++ , + or –). The body of evidence for each recommendation was summarised into evidence statements and graded using the SIGN grading system (see table 1). Disagreements were resolved by discussion with the section partner. The second literature search in September 2012 yielded 173 reference abstracts. Of these, 50 were identified as definitely or possibly relevant to the guideline. However, all of the

pertinent ones from this search had been identified by the GDG in the meantime and already incorporated.

### Considered judgement and grading of evidence

The GDG used the evidence tables to judge the body of evidence and grade recommendations for this guideline. Evidence tables, web appendices 3 and 4, are available online. When evidence was lacking to answer the formulated clinical questions, expert opinions were obtained through consensus. The following were considered in grading the recommendations:

- The available volume of the body of evidence.
- How applicable the obtained evidence was in making recommendations for the defined target audience of this guideline.
- Whether the evidence was generalisable to the target population for the guideline.
- Whether there was a clear consistency in the evidence obtained to support recommendations.
- What the implications of recommendations would be on clinical practice in terms of resources and skilled expertise.
- Cost effectiveness was not reviewed in detail as in-depth economic analysis of recommendations falls beyond the scope of this guideline.

Recommendations were graded from A to D as indicated by the strength of the evidence, as shown in table 2. In line with SIGN guidance, ‘minus’ evidence was considered in context, but in the absence of other ‘plus’ supporting evidence, it was discussed among the GDG regarding that point and any recommendation made was grade D. Important practical points lacking any research evidence, and not likely to be research evidence, were highlighted as ‘good practice points’. (✓)

### Drafting the guideline

The GDG corresponded regularly by email and meetings of the full group were held in March and June 2011, January, March, May and September 2012. A lay summary was written (appendix D). The BTS SOCC reviewed the draft guideline in November 2012. The draft guideline was presented and discussed at the Winter BTS meeting in December 2012 and a draft was subsequently available online in December 2012/January 2013 for public consultation. A draft guideline

**Table 1** Key to evidence statements

Grade	Evidence
1++	High-quality meta-analyses, systematic reviews of randomised controlled trials (RCTs), or RCTs with a very low risk of bias
1+	Well conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias
1–	Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias
2++	High-quality systematic reviews of case–control or cohort studies or high-quality case–control or cohort studies with a very low risk of confounding, bias or chance and a high probability that the relationship is causal
2+	Well conducted case–control or cohort studies with a low risk of confounding, bias or chance and a moderate probability that the relationship is causal
2–	Case–control or cohort studies with a high risk of confounding, bias or chance and a significant risk that the relationship is not causal
3	Non-analytic studies, for example, case reports, case series
4	Expert opinion

**Table 2** Grades of recommendations

Grade	Type of evidence
A	At least one meta-analysis, systematic review, or randomised controlled trial (RCT) rated as 1++ and directly applicable to the target population <i>or</i> A systematic review of RCTs or a body of evidence consisting principally of studies rated as 1+ directly applicable to the target population and demonstrating overall consistency of results
B	A body of evidence including studies rated as 2++ directly applicable to the target population and demonstrating overall consistency of results <i>or</i> Extrapolated evidence from studies rated as 1++ or 1+
C	A body of evidence including studies rated as 2+ directly applicable to the target population and demonstrating overall consistency of results <i>or</i> Extrapolated evidence from studies rated as 2++
D	Evidence level 3 or 4 <i>or</i> Extrapolated evidence from studies rated as 2+
✓	Important practical points for which there is no research evidence, nor is there likely to be any research evidence. The guideline committee wishes to emphasize these as Good Practice Points.

document was circulated to all the relevant stakeholders for consultation in December 2012/January 2013 (appendix B). The BTS SOCC re-reviewed the revised draft guideline in March 2013 and final SOCC approval was granted in April 2013.

The GDG members adhered to the BTS policy for the Declaration of Interests (available on BTS website or by contacting BTS Head Office). The BTS pulmonary rehabilitation guideline will be reviewed within the next 5 years.

## EVIDENCE

Chronic respiratory diseases are common worldwide, including in the UK, and are associated with significant morbidity and premature mortality. Such chronic respiratory diseases affect more than 10% of the population and include COPD, bronchiectasis, ILDs and asthma. They have significant impact on quality of life and physical functioning. Although primarily respiratory conditions with symptoms including dyspnoea, there are important contributing systemic consequences, including loss of skeletal muscle mass and function. The bulk of the pulmonary rehabilitation literature is based on COPD, where impairments including airflow obstruction, increased work of breathing, skeletal muscle dysfunction and deconditioning. Psychological wellbeing is also markedly affected by this chronic physical and social impairment, accompanied by the possibility of abrupt decline.

Pulmonary rehabilitation programmes have been developed to provide a framework for the delivery of individualised exercise programmes and disease-related educational sessions. This guideline describes the current state of the evidence on the effects of pulmonary rehabilitation in study settings. The document also provides recommendations on the practical aspects of delivering pulmonary rehabilitation. Such guidance would appear to be timely given national audit data suggesting marked variation in the services provided under the banner of 'pulmonary rehabilitation'. Referral criteria, course length, programme contributors, staff training and service evaluation differ markedly across the UK.<sup>9 10</sup>

### The role of pulmonary rehabilitation

One of the principle functions of pulmonary rehabilitation is to improve the symptoms of patients with chronic respiratory diseases. In the following section, the role of pulmonary rehabilitation in different outcome measures and markers is reviewed. The literature in this section is based on patients with COPD given that the core evidence for pulmonary rehabilitation is in patients with COPD. The section sets the scene as to why pulmonary rehabilitation should be considered as routine care.

Given the complex nature of the intervention, numerous outcome measures are used to capture the benefits. The conventional outcome measures include those reflecting a change in exercise capacity, quality of life, symptoms and levels of anxiety and depression. The field is continually widening, with other important patient-related outcome measures—for example, physical activity—being studied.

#### Exercise capacity

Change in exercise capacity following pulmonary rehabilitation has been subject to a Cochrane Review (updated 2009).<sup>11</sup> In this review a meta-analysis of the 13 trials in relation to maximal exercise capacity measured by a cycle ergometer test (268 patients received pulmonary rehabilitation, 243 received usual care) showed the weighted mean difference was 8.43 W. Other studies used other measures of maximal exercise capacity. In an adequately powered randomised controlled trial (RCT),

Griffiths *et al*<sup>12</sup> showed a between-group difference in incremental shuttle walk test (ISWT) scores of 75.9 m favouring the pulmonary rehabilitation group upon completion of the programme. Singh *et al*<sup>13</sup> reported the minimally clinical important improvement for ISWT of 47.5 m. The Cochrane review also described a treatment effect of 48 m favouring pulmonary rehabilitation in a meta-analysis of 16 trials (346 patients received pulmonary rehabilitation, 323 received usual care) that used the 6 min walk test (6MWT) to measure functional exercise capacity.<sup>14</sup> The minimally clinically important difference for the 6MWT in subjects with COPD is 54 m.<sup>15</sup> Different values have been published using alternative approaches.

#### Evidence statement

► Exercise capacity improves with pulmonary rehabilitation compared with usual care. (Evidence level 1++)

#### Recommendation

► Pulmonary rehabilitation should be offered to patients with COPD with a view to improving exercise capacity by a clinically important amount. (Grade A)

#### Dyspnoea and health status

In the same Cochrane review the effect of pulmonary rehabilitation on dyspnoea and health status were also reviewed.<sup>11</sup> This meta-analysis included Chronic Respiratory Questionnaire (CRQ) data showing an unequivocal reduction in dyspnoea following pulmonary rehabilitation. The other CRQ domains of fatigue, emotional function and patients' sense of control (mastery) were also shown to improve. In fact, the lower limits of all domains of the CRQ were found to exceed the MCID of 0.5 points, indicating that a significant clinical improvement in health status follow pulmonary rehabilitation.<sup>16</sup> The St Georges Respiratory Questionnaire (SGRQ) scores were also subject to a meta-analysis in the Cochrane review. This demonstrated that the weighted mean difference of the six trials reported exceeded the MCID of 4 for the total and domain scores.<sup>16</sup> Subsequently, other tools for health status such as the COPD assessment test (CAT) have been found to be responsive to pulmonary rehabilitation.<sup>17–19</sup>

#### Evidence statements

► Dyspnoea improves with pulmonary rehabilitation compared with usual care. (Evidence level 1++)

► Health status improves with pulmonary rehabilitation compared with usual care. (Evidence level 1++)

#### Recommendation

► Pulmonary rehabilitation should be offered to patients with COPD with a view to improving dyspnoea and health status by a clinically important amount. (Grade A)

#### Physical activity

There has been increasing interest in physical activity, as inactivity has been linked with reduced survival, poorer quality of life and increased healthcare utilisation.<sup>20–22</sup> A recent systematic review and meta-analysis of physical activity was unable to find any published RCT examining the effect of pulmonary rehabilitation compared with usual care.<sup>23</sup> They reviewed two randomised trials and five single-group interventional studies.<sup>24 25</sup> They concluded that current data suggest supervised exercise training may lead to a small but statistically significant effect on activity but the lack of a control limited interpretation. One of the randomised trials reported significant improvements in physical activity compared with a 'pre-control group' but patients in this group went on to receive a pulmonary rehabilitation intervention.<sup>25</sup> One of the single group studies reported no change at 3 months but improvement with 6 months of rehabilitation.<sup>26</sup> In summary, a consistent finding is a small increase in physical

activity following pulmonary rehabilitation, though its clinical significance is unknown.

#### Evidence statement

- ▶ Physical activity improves modestly with pulmonary rehabilitation. (Evidence level 2+)

#### Activities of daily living

Increased independence in ADL remains an important aim of pulmonary rehabilitation. However, the impact of pulmonary rehabilitation upon ADL has not yet been reported in a RCT. Measurement of physical activity with activity monitors provides a snapshot of the quantity of activity but does not provide information with regard to individual task completion. Self-reported measures of ADL have been shown to be reliable and sensitive to change following pulmonary rehabilitation programmes in the UK. These include the Canadian Occupational Performance Measure (COPM), London Chest ADL (LCADL) Scale, Manchester Respiratory ADL Scale and the Pulmonary Functional Status and Dyspnoea Questionnaire.<sup>27–30</sup> Prospective uncontrolled studies suggest that pulmonary rehabilitation does impact on ADL.<sup>25 31 32</sup> Sewell *et al*<sup>25</sup> compared an individualised exercise programme with a generic exercise programme and demonstrated statistically significant within-group improvements in COPM performance and satisfaction scores for both treatment groups. A further uncontrolled study has shown improvements in LCADL Scale scores.<sup>31</sup> A small study of 22 patients compared three measures of self-reported ADL and concluded that the LCADL and modified version of the pulmonary functional status and dyspnoea questionnaire (PFSDQ-M) were more responsive than the MRC scale.<sup>32</sup> However, the impact of pulmonary rehabilitation upon ADL has not been reported in a RCT comparing pulmonary rehabilitation with usual care.

#### Evidence statement

- ▶ Self-reported measures of ADL improve following pulmonary rehabilitation. (Evidence level 2+)

#### Muscle strength

Muscle strength, in particular the quadriceps, is an important systemic marker in COPD and weakness is associated with increased mortality and healthcare utilisation.<sup>33 34</sup> Interventions that can demonstrate improvements in strength are therefore desirable. It was decided to narrow the influence on pulmonary rehabilitation to quadriceps strength for this guideline, as this has been highlighted as an important muscle group in COPD.<sup>33</sup>

No RCTs of pulmonary rehabilitation that measured quadriceps strength were identified. As such, the GDG reviewed eight RCTs of exercise training versus control.<sup>35–42</sup> There were six studies composed solely of resistance training<sup>35 36 38 40–42</sup>; one study including a combination of aerobic and resistance training<sup>39</sup>; and one study including mobility training.<sup>37</sup> All studies incorporating resistance training demonstrated an increase in muscle strength. The seven positive studies demonstrated an increase of at least 16% (16.2%–37%) in quadriceps strength.

#### Evidence statement

- ▶ Quadriceps muscle strength is increased by exercise programmes incorporating resistance training compared with usual care. (Evidence level 1+)

#### Good practice point

- ▶ Different components within a pulmonary rehabilitation programme, such as resistance training, can influence quadriceps strength and this is addressed in the section 'Nature of training of these guidelines'. (√)

#### Psychological status

A meta-analysis of six RCTs concluded that pulmonary rehabilitation was more effective than standard care for the reduction of anxiety and depression.<sup>43</sup> Of the six trials in the review, one was methodologically weak and two were underpowered as outlined in the evidence table. However, the strongest data were from a large RCT comparing pulmonary rehabilitation (n=99) with usual care (n=101) completed by Griffiths *et al*,<sup>12</sup> who demonstrated a significant improvement in anxiety and depression as measured by the Hospital Anxiety and Depression Scale (HADS).

#### Evidence statement

- ▶ Psychological status improves with pulmonary rehabilitation compared with usual care. (Evidence level 1+)

#### Recommendation

- ▶ Pulmonary rehabilitation should be offered to patients with COPD with a view to improving psychological wellbeing. (Grade A)

#### Nutritional status

Studies have shown variable results for weight change with pulmonary rehabilitation programmes. People presenting to pulmonary rehabilitation have differing body habitus and hence differing objectives of the multidisciplinary rehabilitation. This complicates looking for an overall change in weight in a group with pulmonary rehabilitation. Lan *et al*<sup>44</sup> showed an 0.8 kg weight increase following pulmonary rehabilitation in an underweight population. In normal weight patients, a similar gain of 0.6 kg following exercise training has been described.<sup>45</sup> However, in a trial examining the effect of nutritional supplementation, Steiner *et al*<sup>46</sup> showed weight loss of 0.6 kg in their placebo group following pulmonary rehabilitation. The magnitude of weight change in all these studies is of doubtful clinical significance. The effect of pulmonary rehabilitation on weight in the obese population is unknown. Recent retrospective data of a large pulmonary rehabilitation cohort has shown that baseline nutritional status (measured by BMI) has no effect on the efficacy of pulmonary rehabilitation in terms of exercise capacity or health status.<sup>47</sup>

#### Evidence statement

- ▶ Pulmonary rehabilitation has only a minor effect on body weight. Nutritional status at the start of rehabilitation does not affect outcomes such as exercise capacity or health status. (Evidence level 2–)

#### Self-efficacy

Self-efficacy describes the level of belief someone has in their ability to complete a chosen task or goal.<sup>48</sup> Self-efficacy for walking has been shown to be associated with adherence in pulmonary rehabilitation and is therefore an important outcome measure in pulmonary rehabilitation. To date there have not been any RCTs that measure the impact of pulmonary rehabilitation on self-efficacy compared with usual care. However, an early RCT compared pulmonary rehabilitation with education alone and demonstrated that self-efficacy improved in the intervention group.<sup>49</sup> Other prospective observational studies have also demonstrated that self-efficacy scores improve following pulmonary rehabilitation.<sup>31 50</sup> More recently, the PRAISE self-efficacy tool has been developed to measure levels of self-efficacy in relation to behaviours specific to pulmonary rehabilitation and has been shown to be reliable and sensitive to change following pulmonary rehabilitation in a prospective cohort study.<sup>51</sup>

**Evidence statement**

- ▶ Levels of self-efficacy improve following completion of pulmonary rehabilitation. (Evidence level 2++)

**Survival**

One RCT has explored the effect of pulmonary rehabilitation on survival in 119 people with COPD when stable.<sup>49</sup> The study was almost certainly underpowered to detect a mortality difference between the groups. In addition, the intervention and 'usual care' groups received education and the intervention group received monthly 'reinforcement' sessions for a year after completion of rehabilitation. Both groups had at least 6-monthly assessments by the research team for the following 6 years. Overall 6-year survival was 61% and there was no statistically significant difference between the intervention and control groups.

**Measuring pulmonary rehabilitation outcomes**

Although the benefits of pulmonary rehabilitation are shown in a variety of ways in this chapter, there are several key outcomes that should be the core part of any assessment of the individual and of the efficacy of the programme.

**Recommendation**

- ▶ As a minimum, efficacy of pulmonary rehabilitation programmes needs to be regularly assessed by demonstrating clinically important improvements in exercise capacity, dyspnoea and health status. (Grade B)

**Good practice point**

- ▶ As part of regular assessment, patient satisfaction and feedback should be sought. (✓)

**Referral and assessment of patients for pulmonary rehabilitation****Referral process**

There are certain aspects of the referral process to pulmonary rehabilitation that are recommended. Patients who are likely to benefit from pulmonary rehabilitation have their exercise capacity limited by breathlessness or muscle fatigue and may have difficulty understanding the rationale behind referral for exercise training. From qualitative studies, success and outcome of rehabilitation are positively influenced by the initial clinician interaction and detail provided about pulmonary rehabilitation.<sup>52–53</sup> Studies report that lack of understanding of the benefits of pulmonary rehabilitation may influence uptake.<sup>54–55</sup> In addition, addressing patients' concerns may improve uptake and completion.<sup>54</sup> A discussion should take place with the patient about their aims from pulmonary rehabilitation. This can be documented and may aid motivation.<sup>56</sup> Patient information and referral are covered in appendices C and E.

**Good practice points**

- ▶ The point of referral to pulmonary rehabilitation should be used as an opportunity to explore the patient's understanding of pulmonary rehabilitation, address concerns and to educate patients about the benefits of a pulmonary rehabilitation programme. (✓)
- ▶ Healthcare professionals making referrals to pulmonary rehabilitation should have basic knowledge about what a programme entails and effectiveness. A pulmonary rehabilitation programme should be presented by the referrer as a fundamental treatment for COPD rather than an optional extra. (✓)

**The period from referral to assessment**

Cognitive behavioural therapy (CBT) is an evidence-based psychological treatment focusing on thoughts, beliefs and attitudes,

how these impact on behaviour and dealing with problems and whether there are alternative ways. It was therefore considered whether CBT might improve the adherence to pulmonary rehabilitation if delivered immediately before the programme. In an uncontrolled study, the introduction of a group opt-in 1.5 h session which incorporated CBT techniques post referral was evaluated.<sup>57</sup> Compared with historical practice, fewer patients proceeded to the initial assessment but a similar proportion commenced pulmonary rehabilitation. There appeared to be less dropout for 'non-illness' reasons, such as transport difficulties or dislike of group activities.

**Evidence statement**

- ▶ Pre-pulmonary rehabilitation interventions using cognitive behavioural techniques may improve completion of pulmonary rehabilitation. (Evidence level 2–)

**Assessment**

Initial assessment for pulmonary rehabilitation should include a detailed description of the programme—for example, the requirement for exercise within a group setting. It should also confirm that there is no contraindication to rehabilitation. The initial assessment presents an opportunity to assess comorbidities and risk factors, for example, hypertension (see section 'Cardiovascular disease comorbidity') and consider referral for management to optimise benefit from the programme. Information on service specification of pulmonary rehabilitation is addressed in appendix F.

**Good practice points**

- ▶ Initial assessment for pulmonary rehabilitation provides an opportunity to assess and refer for treatment of comorbidities prior to commencing. (✓)
- ▶ The setting of pulmonary rehabilitation, skill mix of the team and other comorbidities should always be considered in the risk assessment of patients entering a rehabilitation programme. (✓)

**Specific situations at assessment**

In identifying suitable patients for pulmonary rehabilitation, there has been debate about the suitability and/or safety of pulmonary rehabilitation for patients with specific conditions, including:

- people who continue to smoke,
- people with chronic respiratory failure,
- people with coexistent cardiovascular disease,
- people with coexistent anxiety and/or depression,
- people with mild or most severe breathlessness.

Further, there has been discussion on the optimal pharmacological therapy for people with COPD commencing pulmonary rehabilitation.

**Smoking status**

There has been some debate as to whether current smoking should be an exclusion criterion for pulmonary rehabilitation.

A retrospective non-analytic study of 239 predominantly male patients with COPD showed that current smokers were less likely to attend at least two-thirds of training sessions while another uncontrolled study of 91 patients with COPD identified lower completion rates in current smokers.<sup>58–59</sup> However, in these studies a considerable proportion of current smokers attended and completed rehabilitation. There was no evidence that smokers failed to benefit to a similar degree as non-smokers. Pulmonary rehabilitation can provide an excellent opportunity to facilitate smoking cessation.<sup>60</sup>



**Evidence statement**

- ▶ Patients who currently smoke benefit from pulmonary rehabilitation. (Evidence level 3)

**Recommendation**

- ▶ Patients with COPD should be referred for pulmonary rehabilitation regardless of their smoking status. (Grade D)

**Good practice points**

- ▶ Patients referred to pulmonary rehabilitation should have their smoking status assessed and referral to smoking cessation services offered to smokers simultaneously. (✓)
- ▶ Pulmonary rehabilitation provides opportunities to offer smoking cessation advice. (✓)

**Chronic respiratory failure**

The issue of safety of pulmonary rehabilitation was considered in patients with chronic respiratory failure. Patients with chronic respiratory failure (defined as  $\text{PaO}_2 < 8\text{kPa}$ ,  $\text{PaCO}_2 > 6\text{kPa}$  or both) appear to gain similar benefit from pulmonary rehabilitation compared with patients without respiratory failure.<sup>61</sup> A prospective observational study of 1130 patients with severe COPD who underwent inpatient pulmonary rehabilitation showed that patients with and without chronic respiratory failure showed a similar response.<sup>61</sup> The GDG discussed this in light of the available studies and concluded that patients should not be excluded from pulmonary rehabilitation on this basis. Later sections of this guideline discuss the use of oxygen and non-invasive ventilation as an adjunct to pulmonary rehabilitation; see section on Adjuncts to pulmonary rehabilitation.

**Evidence statement**

- ▶ Patients with chronic respiratory failure gain as much benefit as those without chronic respiratory failure from pulmonary rehabilitation. (Evidence level 3)

**Recommendation**

- ▶ Patients with COPD can be referred for pulmonary rehabilitation regardless of whether or not they have chronic respiratory failure. (Grade D)

**Good practice point**

- ▶ When considering the referral of patients with chronic respiratory failure, practitioners should reflect on the receiving setting and skill mix of the attending staff to provide safe pulmonary rehabilitation to these patients who have significant physiological impairment and potential for greater instability by the intended programme. (✓)

**Cardiovascular disease comorbidity**

From a safety perspective it is logical that patients with unstable cardiovascular disease (eg, unstable angina, unstable arrhythmias) should not enter a rehabilitation programme until stabilised. Accordingly, all such patients are excluded from studies of pulmonary rehabilitation. However, patients should not be excluded from pulmonary rehabilitation on the basis of having stable cardiovascular disease and the initial assessment offers a potential opportunity to assess this aspect of their general health.

A retrospective observational study of 2962 patients with moderate to severe COPD completing pulmonary rehabilitation evaluated the impact of comorbidities, including cardiovascular comorbidity, on outcomes. Patients with a higher number of comorbidities, assessed using the Charlson index, were less likely to gain clinically significant improvement in walking distance and health-related quality of life but the level of comorbidity had no effect on improvement in breathlessness. Relating to cardiovascular comorbidities, their presence led to patients being less likely to show a significant improvement in

quality of life, equally likely to gain significant improvement in breathlessness and more likely to demonstrate an improvement in walking distance.<sup>62</sup> Further, the GDG considered that the standard MCID used for pulmonary rehabilitation may not be applicable in those with comorbidities—that is, patients may clinically improve by a noticeable amount at values less than the MCID traditionally used for a general rehabilitation population.

A prospective study from the same authors of 316 patients with moderate to severe COPD completing outpatient pulmonary rehabilitation showed no evidence that patients with cardiovascular comorbidity gained less benefit from pulmonary rehabilitation.<sup>63</sup> Furthermore there is emerging evidence that pulmonary rehabilitation may favourably benefit cardiovascular risk factors (eg, blood pressure).<sup>64 65</sup>

A further consideration is abdominal aortic aneurysm (AAA) and exercise. Indeed, AAAs are reported as more prevalent in patients with COPD than in the general population and are related to tobacco smoking and impaired lung function.<sup>66–69</sup> There was no literature exploring AAA's in patients with chronic respiratory disease and pulmonary rehabilitation. The guideline from the Society for Vascular Surgery (USA) documents that AAA rupture is not precipitated by moderate physical activity.<sup>70</sup> A small pilot reported relative safety of exercise in people who have AAAs but only studied people with 'small' AAA's (defined as 30–50 mm in diameter).<sup>71</sup> The GDG additionally sought vascular opinions, including that of the Vascular Society, UK, and concluded that in people with an AAA <5.5 cm with controlled blood pressure, a standard multidisciplinary pulmonary rehabilitation incorporating moderate intensity aerobic training should be considered safe.

An AAA >5.5 cm should usually lead to consideration for surgical intervention, although severity of COPD or other comorbidities may preclude surgery. The opinion of the Vascular Society UK was sought: there is no evidence that mild to moderate exercise is associated with an increased risk of rupture. This would include aerobic exercise, for example, walking or riding a bicycle at a steady pace without the need to become too uncomfortable. However, this would exclude exercise which is associated with a risk of transient blood pressure rise, such as lifting weights, press ups or sit ups. The GDG concluded that in subjects with COPD where surgery has been deemed inappropriate by a cardiac or vascular surgeon, pulmonary rehabilitation incorporating mild–moderate aerobic exercise can be considered.

**Evidence statements**

- ▶ Patients with chronic respiratory disease with coexistent stable cardiovascular disease benefit from pulmonary rehabilitation (Evidence level 3).
- ▶ Patients with aortic aneurysms <5.5 cm in diameter can perform moderate intensity aerobic exercise as part of pulmonary rehabilitation, provided blood pressure is controlled. (Evidence level 4)

**Recommendations**

- ▶ People with chronic respiratory disease should be referred to pulmonary rehabilitation irrespective of coexistent stable cardiovascular disease. (Grade D)
- ▶ A coexistent AAA <5.5 cm should not preclude referral to pulmonary rehabilitation and being included in moderate intensity aerobic exercise training, provided blood pressure is controlled. (Grade D)

**Good practice points**

- ▶ The referral process and/or the initial assessment for pulmonary rehabilitation offer an important opportunity to assess

and optimise cardiovascular health and address risk factors for cardiovascular disease. (✓)

- ▶ In patients with COPD who have an AAA >5.5 cm, deemed not fit for surgery, pulmonary rehabilitation incorporating mild–moderate intensity aerobic exercise may be considered, but should not include resistance training. (✓)

#### Anxiety and depression

It has been considered whether anxiety and depression should be addressed prior to pulmonary rehabilitation in case they affect adherence or willingness to adopt change. Harris *et al*<sup>54</sup> reported that patients who scored more highly for anxiety and depression were more likely to report breathlessness and fear exercise, irrespective of the MRC breathlessness score. However, we know that pulmonary rehabilitation conveys significant improvement in such parameters for those with mild to moderate depression who undergo rehabilitation.

A prospective non-analytic study of 81 patients with predominantly severe COPD showed no evidence that patients with higher levels of anxiety or depression (assessed using the HADS) obtain reduced benefit from pulmonary rehabilitation.<sup>72</sup> Indeed another observational study of 95 patients with COPD suggested that patients with a higher baseline level of anxiety gained greater benefit from exercise training.<sup>73</sup> A retrospective analysis of 518 patients entering pulmonary rehabilitation demonstrated a significant improvement in anxiety and depression according to the HADS score in those who had ‘presence’ or ‘probable’ anxiety or depression at baseline.<sup>74</sup> Baseline HADS score did not relate to completion or non-completion.

A systematic review of factors associated with completion of pulmonary rehabilitation indicated that patients with depression have a lower completion rate.<sup>75</sup> However, many do complete the programme and gain significant benefit.

#### Evidence statement

- ▶ People with symptoms of anxiety and/or depression benefit from pulmonary rehabilitation and should not be excluded from pulmonary rehabilitation. (Evidence level 3)

#### Recommendation

- ▶ Coexistent symptoms of anxiety and/or depression in patients with COPD should not preclude referral to pulmonary rehabilitation. (Grade D)

#### Good practice point

- ▶ The referral process and the assessments for pulmonary rehabilitation offer important opportunities to detect and consider referral for ongoing support and management for depression. (✓)

#### MRC dyspnoea grade

The traditional view of pulmonary rehabilitation has been to refer patients with an MRC breathless score of 3 or worse. The majority of outcome studies have included patients with COPD who had MRC scores of 3–5 and who attended outpatient programmes. There is overwhelming evidence of benefit from these studies incorporating hundreds of patients, albeit few of these studies stratified according to MRC grade.<sup>11 12</sup> However, in general, there has been a shift towards addressing COPD earlier in the natural history of the disease and debate has ensued as to whether pulmonary rehabilitation may be of benefit to those with MRC dyspnoea grade 2.

Two retrospective observational studies have shown that patients who have a MRC dyspnoea score of 2 obtain similar improvement in exercise capacity to patients with MRC scores of 3–5.<sup>76 77</sup> Both studies examined approximately 450 patients who completed outpatient pulmonary rehabilitation and in each

study more than 100 patients with MRC dyspnoea scores of 2 were included.

There is one single-centre, unblinded RCT of 61 patients with COPD who had moderate Global Initiative for Chronic Obstructive Lung Disease (GOLD) II airflow obstruction. Some of these patients had a MRC dyspnoea score of 2 but were not stratified by their MRC breathlessness. They were randomised to either pulmonary rehabilitation or usual care and the group completing pulmonary rehabilitation showed improvement in walking distance and quality of life.<sup>78</sup> In even milder airflow obstruction (symptomatic GOLD I), ventilatory responses with incremental cycling exercise show reduced exercise capacity compared with matched controls.<sup>64</sup> A flexible approach may be required to facilitate these patients completing exercise training.

There are conflicting results of pulmonary rehabilitation for those with MRC grade 5 breathlessness, depending on whether or not they are housebound. A well conducted, randomised, placebo-controlled trial of 60 patients with MRC breathless grade 5 who were housebound due to their breathlessness gained little benefit from supervised exercise training in their home.<sup>79</sup> In contrast, another large retrospective observational study which included 146 patients graded as MRC breathless grade 5, but who were able to attend and complete outpatient pulmonary rehabilitation, gained similar benefit to patients who had MRC scores of 3–4.<sup>76</sup> The location and nature of the programmes used in these studies and the level of functional limitation of recruited patients with MRC grade 5 may confound the outcomes.

#### Evidence statements

- ▶ Patients with chronic respiratory disease who are functionally limited because of dyspnoea benefit from pulmonary rehabilitation compared with usual care. (Evidence level 1++)
- ▶ People with COPD with a MRC dyspnoea score of 2 benefit from pulmonary rehabilitation. (Evidence level 3)
- ▶ Patients with COPD who have a MRC dyspnoea score of 5 who are able to attend an outpatient programme gain similar benefit from pulmonary rehabilitation as those with MRC dyspnoea 3–4. (Evidence level 3)

Patients with COPD who have a MRC dyspnoea score of 5 and are housebound are unlikely to gain significant improvement in walking distance, breathlessness and quality of life from supervised pulmonary rehabilitation delivered in their home. (Evidence level 1+)

#### Recommendations

- ▶ Patients with a MRC dyspnoea score of 3–5 who are functionally limited by breathlessness should be referred for outpatient pulmonary rehabilitation. (Grade A)
- ▶ Patients with a MRC dyspnoea score of 2 who are functionally limited by breathlessness should be referred for pulmonary rehabilitation. (Grade D)
- ▶ Patients with a MRC dyspnoea score of 5 who are housebound should not routinely be offered supervised pulmonary rehabilitation within their home. (Grade B)

#### Good practice point

- ▶ Flexible and pragmatic approaches should be considered to facilitate exercise training in patients who have less severe COPD and who are less breathless. (✓)

#### Bronchodilator therapy

The exercise component of pulmonary rehabilitation is beneficial, but the magnitude of benefit may be limited by modifiable factors. Bronchodilator drugs that reduce dyspnoea and dynamic hyperinflation may permit a greater amount of exercise and thus a greater gain from the rehabilitation programme. Two

RCTs have assessed the effect of tiotropium bromide (Spiriva, Boehringer) as an adjunct to pulmonary rehabilitation.<sup>80 81</sup> The generalisability of the findings of these trials is limited as they did not permit the use of long-acting  $\beta$  agonists or short-acting anti-cholinergics in any subject (thus any additional benefit in the treatment arm could be at least partially explained by treatment reduction in the placebo arm) and a large proportion of subjects took inhaled corticosteroids. In this context, both trials found the addition of tiotropium bromide to further improve dyspnoea, but only one found benefits in walk distance and quality of life. It should be noted that the larger showed pulmonary rehabilitation to be only modestly effective (6MWT improvement of around 10%) and there were no common tests of exercise capacity across the two trials. These studies did not set out to investigate whether there was a synergistic effect of commencing a COPD medication before pulmonary rehabilitation or whether the effects of the two interventions were simply additive. No trial has investigated any other standard COPD medication introduced specifically to attempt to increase the benefit gained from pulmonary rehabilitation.

#### Evidence statement

- ▶ The commencement of a regular inhaled long-acting muscarinic antagonist drug prior to pulmonary rehabilitation leads to greater improvement in breathlessness and greater improvement in walking distance and quality of life. It is uncertain whether these potential benefits are simply additive, how applicable they are to current standard practice, or what effect other COPD medications have as adjuncts. (Evidence level 1–)

#### Recommendation

- ▶ Patients with COPD should be taking bronchodilator therapy in line with NICE COPD guidelines prior to referral to pulmonary rehabilitation. (Grade D)

#### Good practice point

- ▶ Pulmonary rehabilitation offers an opportunity to check and optimise inhaler technique. (✓)

#### Other considerations regarding referral to pulmonary rehabilitation

The decision to refer may be influenced by other factors—for example, when it may be unsafe, inappropriate or impossible for patients to engage in pulmonary rehabilitation. Studies of pulmonary rehabilitation routinely include a number of standard clinical exclusion criteria resulting in such patients not being included in clinical trials. The main criteria include the presence of unstable cardiac disease, locomotor or neurological difficulties precluding exercise (eg, severe arthritis or peripheral vascular disease), patients in a terminal phase of their illness or the presence of significant cognitive or psychiatric impairment.<sup>12 82 83</sup>

#### Good practice points

- ▶ Patients with unstable cardiac disease or locomotor difficulties that preclude exercise (eg, severe arthritis or severe peripheral vascular disease) should not be referred for pulmonary rehabilitation. (✓)
- ▶ Careful consideration should be given to patients who have significant cognitive or psychiatric impairment that would lead to an inability to follow simple commands in a group setting. (✓)
- ▶ In certain individual cases, facilitation of pulmonary rehabilitation may be aided by the support and attendance of a relative or carer. (✓)
- ▶ In case of doubt over the appropriateness of a patient for pulmonary rehabilitation, clinicians are advised to contact their local provider. (✓)

## Structure of pulmonary rehabilitation

### Frequency of supervised pulmonary rehabilitation sessions

The frequency of supervised sessions during a course of pulmonary rehabilitation has not been clearly established. Traditionally in the UK, pulmonary rehabilitation takes place as an outpatient (either in a hospital or community setting) comprising a minimum of two supervised sessions per week. There is a large body of literature supporting the benefits of pulmonary rehabilitation and these have encompassed two supervised sessions and either a third supervised or formalised unsupervised pulmonary rehabilitation session.<sup>11 12</sup> In parallel with this, the general advice from the Department of Health recommends five sessions of 30 min of physical activity per week.<sup>84</sup>

A pilot feasibility study evaluating the effectiveness of a once weekly versus a twice weekly supervised programme and a randomised, parallel-group single-blind study experienced significant dropout rates, resulting in neither study being statistically powered.<sup>85 86</sup> The GDG noted that the improvement in walking distance with pulmonary rehabilitation in the once and twice weekly groups was minimal, raising concern about the programme in the parallel-group study.<sup>86</sup>

The optimum frequency of pulmonary rehabilitation is not known. There is insufficient evidence to demonstrate that once-weekly pulmonary rehabilitation is as effective as twice weekly in terms of improvement in exercise performance and health status. Most pulmonary rehabilitation studies showing benefit in the key outcome measures are based on at least two supervised pulmonary rehabilitation sessions a week.<sup>11 12</sup>

#### Recommendation

- ▶ Pulmonary rehabilitation programmes should be a minimum of twice-weekly supervised sessions. (Grade D)

#### Good practice points

- ▶ In line with published pulmonary rehabilitation studies and the outcomes they demonstrate, a third session of prescribed exercise is recommended. This can be performed unsupervised. (✓)
- ▶ Encouragement of regular physical activity five times a week for 30 min each time is encouraged in line with standard healthy living advice. (✓)

#### Duration of pulmonary rehabilitation programmes

The optimal pulmonary rehabilitation programme duration is unclear, with huge variation in the length of programme seen across Europe and the rest of the world. In the UK, for practical and economic reasons, programmes lasting longer than 6–8 weeks are not standard; however, there is some ongoing debate as to the efficacy of programmes lasting less than 6 weeks. Consequently we have examined the effect on exercise performance and health status of pulmonary rehabilitation lasting less than 6 weeks to programmes lasting 6–12 weeks. However, we have also commented on studies examining prolonged rehabilitation (greater than 12 weeks).

#### *Programmes shorter than 6 weeks compared with 6–12 weeks*

Two RCTs have been published comparing supervised training for 4 and 7 weeks from the same centre but with different subjects. Green *et al*<sup>87</sup> randomised 44 subjects to 4 weeks (8 supervised exercise sessions) or 7 weeks (14 sessions) of training and compared end of programme difference in health status and exercise capacity. The study power was based on health status (the primary outcome) and when compared with 4 weeks of training the group receiving 7 weeks of training showed significantly greater improvement in total CRQ score and the domains of dyspnoea, emotion and mastery. Exercise performance was a

secondary outcome and the study was not powered to find a difference in this measure. No significant difference in exercise performance was seen between the two groups.

Sewell *et al*<sup>88</sup> randomised patients to either 4 weeks or 7 weeks of supervised exercise. However, in contrast to Green *et al*, the 4-week group was directed to exercise unsupervised for weeks 5–7 and were then reassessed at the end of 7 weeks. The study was powered for equivalence and comparing the groups at 7 weeks and 6 months, there was no significant difference in incremental shuttle walk or health status.

The differences in study design and conflicting outcomes mean it is not possible to make a specific recommendation about programmes with a duration of less than 6 weeks. The study by Sewell *et al* shows that many individuals gained significant improvement in exercise performance and health status after 4 weeks but in this group the further assessment at 7 weeks may have influenced compliance with unsupervised exercise training during weeks 5–7.

Moreover, the overwhelming majority of pulmonary rehabilitation outcome studies are outpatient programmes of 6–12 weeks' duration. While the trials described in this section show that some subjects can gain benefit from programmes of <6 weeks' duration, this evidence base is not robust enough to recommend programmes of <6 weeks' duration are comparable to those lasting 6–12 weeks.

#### Studies of longer duration pulmonary rehabilitation

Three other RCTs examined pulmonary rehabilitation programme lengths in which at least one group completed rehabilitation lasting longer than 3 months, included in a systematic review.<sup>89–92</sup> Two of these studies assessed exercise performance as an outcome and demonstrated that the prolonged pulmonary rehabilitation (20 weeks vs 8 weeks and 18 months vs 3 months) significantly improved exercise performance with regard to 12 min walk test, 6MWT and stair climb, respectively.<sup>89 90</sup> All three studies measured health status or functional disability. Improvement in health status and function appeared to be greater in the groups undergoing prolonged rehabilitation.<sup>89–92</sup> One study highlighted a gender difference in response to health status improvements, with only men appearing to benefit greater in the long-term group compared with the short-term group.<sup>91</sup> We did not assess and analyse cost effectiveness in the guideline but consideration of a longer programme of >12 weeks would necessitate a full cost evaluation.

In summary, the optimum duration of a pulmonary rehabilitation programmes is not known. The majority of the programmes from which the evidence for pulmonary rehabilitation is based are at least 6 weeks long.<sup>11</sup> The RCTs studying shorter-duration programmes have conflicting results for health status and such programmes may be appropriate for specific subjects.<sup>87 88</sup>

#### Evidence statements

- ▶ Pulmonary rehabilitation of 6–12 weeks' duration has demonstrated significant benefits in exercise, dyspnoea and health status for patients with chronic respiratory disease compared with usual care. (Evidence level 1++)
- ▶ Pulmonary rehabilitation programmes with less than 6 weeks of supervised exercise can provide exercise and health status benefits for individuals with COPD. (Evidence level 1+)
- ▶ Benefits of pulmonary rehabilitation are even greater from programmes with a duration of more than 3 months, although the cost benefit would require further evaluation. (Evidence level 1+)

#### Recommendations

- ▶ Pulmonary rehabilitation programmes of 6–12 weeks are recommended. (Grade A)
- ▶ Pulmonary rehabilitation programmes including the attendance at a minimum of 12 supervised sessions are recommended, although individual patients can gain some benefit from fewer sessions. (Grade A)

#### Good practice point

- ▶ If training for less than 6 weeks is considered, this should be individualised and objective/subjective measures of benefit in place before patients graduate. For some individuals reassessment at 4 weeks and graduation to independent gym training is a feasible possibility. (√)

#### Rolling or cohort programmes

There is much debate regarding the comparative effectiveness of either a rolling or cohort-based rehabilitation programme. There is no high-quality evidence comparing the two formats. The GDG felt it was important to list the aspects of both types, which might be informative for those considering setting up a service; see appendix G.

#### Recommendation

- ▶ Cohort or rolling programmes of pulmonary rehabilitation are both acceptable forms of delivery depending on local considerations. (Grade D)

#### Education

The educational components of pulmonary rehabilitation are fundamentally integral to the format and success of the programme. Education comes into every aspect of pulmonary rehabilitation and in discrete educational sessions. Educational talks are discussed in more detail in appendix H.

The intention of the educational element is to support the lifestyle and behavioural change and assist self-management to promote decision making and self-efficacy. The educational and cultural backgrounds of the subjects and any physical (eg, impaired sight or hearing) and cognitive barriers need to be considered.

#### Nature of training

Lower limb weakness is common in patients with COPD and a poor prognostic indicator.<sup>33</sup> The standard training delivered for pulmonary rehabilitation is based around aerobic training, usually lower limb endurance training (commonly walking or cycling). The precise intensity for the endurance component has not yet been confirmed for individuals with chronic respiratory disease, although a target intensity of 60% of peak work rate is regarded as a minimum. The aim is to accumulate 30–60 min per session. For some individuals a single bout of 30 min is not achievable and shorter bouts should therefore be advised in order to accumulate 30 min. Progression should be observed in the longest achieved bout, aiming for 30 min of continuous activity.

We explored the evidence for additional resistance (strength) training, involving focused training of specific muscle groups with repetitive manoeuvres against heavy loads. Resistance training involves the major muscle groups, in particular the quadriceps muscles, and two to four sets should be completed, with each set comprising 10–15 repetitions. The weights chosen should be individualised and progressed once all sets can be completed with the selected weight. A minimum of 48 h between each session is advised.

The volume of evidence addressing this was low, with some methodological limitations in a number of trials. A systematic review encompassed several comparisons—combination approach,

resistance training alone and resistance training compared with another intervention.<sup>93</sup> Individual trials addressing the potential role of combined resistance compared with endurance training were reviewed. Of seven trials, four carried a high risk of bias.<sup>94–97</sup> There were three good-quality, albeit relatively small, randomised trials.<sup>98–100</sup> These trials did not demonstrate any significant additional benefits with the combined approach compared with endurance training alone regarding exercise tolerance as measured with field walking tests. There was an improvement in peripheral muscle strength; however this does not appear to translate into a demonstrable significant improvement in health-related quality of life. Functional outcome measures such as stair climbing were only assessed in the trials with a high risk of bias.<sup>95 96</sup>

One narrative review considering the longer term effects of resistance training has reported on three trials with inconsistent results.<sup>101</sup> Our patient representative acknowledged that patients often report it is harder to maintain progressive resistance exercise at an adequate intensity once supervision is no longer provided. It is of note that trials reviewed focused mainly on progressive resistance exercise delivered at an outpatient programme using weight-lifting exercise machinery. Lastly, the GDG considered that resistance training has other benefits, such as proven to reduce falls in older people in general. An in-depth review of these other benefits is outside the scope of the pulmonary rehabilitation guideline.<sup>102</sup>

#### Evidence statements

- ▶ Resistance training in combination with aerobic training leads to greater improvements in peripheral muscle strength than aerobic training alone. (Evidence level 1+)
- ▶ In patients with COPD, resistance training in combination with aerobic training does not lead to additional benefit to health-related quality of life, dyspnoea or exercise tolerance compared with aerobic training alone. (Evidence level 1+)

#### Recommendation

- ▶ To ensure strength and endurance benefits in patients with COPD, a combination of progressive muscle resistance and aerobic training should be delivered during a pulmonary rehabilitation programme. (Grade B)

#### Good practice points

- ▶ Relevant expertise is required to deliver resistance training. (√)
- ▶ Patients should be capable of continuing effective resistance training once supervised sessions have ended. The supervising rehabilitation therapist should ensure that patients are able and willing to continue with unsupervised resistance training. (√)
- ▶ Prescribing of progressive strength exercise should be individualised for each patient, taking into consideration the initial health screening and any increase in risk from comorbidities. (√)

#### Interval and continuous aerobic training

Interval training delivers short periods of high-intensity aerobic training interspersed with rest or low-intensity periods. The rationale is that it allows periods of work to be conducted at a higher intensity compared with aerobic training.

A Cochrane review directly considered this subject.<sup>103</sup> Zainuldin *et al* included RCTs comparing higher training intensity with lower training intensity or comparing continuous training with interval training in people with COPD. Studies that compared exercise training with no exercise training were excluded. Only RCTs were included and the review considered the following outcome measures:

- Maximal incremental cardiopulmonary exercise test: peak exercise intensity, peak oxygen consumption, peak minute ventilation and lactate threshold at isotime or isowork.
- Endurance cardiopulmonary exercise test (cycle or treadmill): exercise time.
- Functional exercise capacity: 6-min walk distance, incremental shuttle walk distance or endurance shuttle walk time (ESWT).
- Symptom scores, health-related quality of life and muscle strength.

Eleven studies were included in the meta-analysis (five being translations from foreign language). Of these, eight studies were specifically related to this subject, with three judged to be of low risk of randomisation bias. Studies had examined a diversity of training protocols, moderate to low sample sizes and potential selective reporting of outcomes. Furthermore, studies investigating interval versus continuous training in patients with COPD tended to compare training of equal work duration.

The results of the review conclude that interval training was not superior to continuous training for improving physiological outcomes, walking time or symptoms in people with moderate to severe COPD.

It must be noted that the training studies reported in the literature have all been completed on a cycle ergometer using a complex training programme and this may present challenges within the programme and pursuing this type of training regime at home and after graduation from rehabilitation.

#### Evidence statement

- ▶ Interval training and continuous training are equally effective modes of training in patients with COPD. (Evidence level 1++)

#### Recommendation

- ▶ Interval and continuous training can be applied safely and effectively within the context of pulmonary rehabilitation to patients with COPD. (Grade A)

#### Good practice points

- ▶ The choice of interval or continuous training will be down to the patient and/or therapist preference. (√)
- ▶ In clinical practice, interval training may require a higher therapist to patient ratio to ensure adequate work rate and rest intervals are achieved compared with continuous training. (√)

#### Goal setting in pulmonary rehabilitation

There has been discussion whether individualising the pulmonary rehabilitation programme to personal goals may improve outcomes of the programme. Individualised activity programmes have been investigated by a described RCT but trials of goal setting focusing on other aspects of pulmonary rehabilitation have not been reported.<sup>25</sup> Sewell *et al*<sup>25</sup> randomised 180 patients to either an individually targeted exercise programme or the control arm: a conventional general exercise programme. The ‘individually targeted exercise’ group chose ADL derived from completed COPM questionnaires—a questionnaire designed to detect changes in domestic function over time; whilst the general exercise programme group was made up of 10 standard exercises focusing on upper and lower limbs, and the trunk. The RCT demonstrated no significant difference between the goal-based therapies and standard treatment, although both groups improved similarly. The authors comment their intervention groups may have been too similar to the control with regard to exercises performed.<sup>25</sup>

Two other studies were considered in relation to this work but did not address the specific question of goal setting.<sup>104 105</sup> One aimed to gradually reduce dependency on centre-based group exercising in favour of increasing free living activity

levels<sup>104</sup>; while a small RCT explored different combinations of pulmonary rehabilitation—exercise training alone, exercise training plus activity training or exercise training plus lectures in 43 people.<sup>105</sup>

#### Evidence statement

- ▶ Individually targeted exercise programme in pulmonary rehabilitation does not offer any advantage over simple conventional general exercise training in patients with COPD. (Evidence level 1–)

#### Recommendation

- ▶ Generic exercise training as opposed to individually targeted exercise training is recommended for pulmonary rehabilitation. (Grade D)

#### Good practice points

- ▶ While generic exercise training is recommended as opposed to an individually targeted exercise programme, the prescription of exercise is individualised to provide correct intensity. (✓)
- ▶ Besides the exercise elements of pulmonary rehabilitation, healthcare professionals commonly use goal setting to address specific hurdles. Given the personalised nature of this intervention to a patient's needs, evidence is difficult to quantify. (✓)
- ▶ The term 'goal setting' may require discussion with the patient. (✓)

#### Supervision in pulmonary rehabilitation

The majority of the evidence for the role of pulmonary rehabilitation is based on supervised programmes. There is a limited evidence base describing unsupervised pulmonary rehabilitation. Most reported evidence is centred on home-based rehabilitation compared with a hospital-based supervised programme. However, caution is advised, given some of the home rehabilitation schemes included varying degrees of supervision or support.

Studies were reviewed if they randomised rehabilitation participants to a home rehabilitation programme or a supervised programme. Studies comparing home-based rehabilitation with a control group were excluded. All studies reported exercise performance and quality of life as important outcomes. Only one 'home' study was conducted in the UK.<sup>106</sup> The largest study (n=252) comparing home rehabilitation with conventional rehabilitation was conducted in Canada, where the structure of the hospital-based rehabilitation is similar to that offered in the UK.<sup>107</sup> It was powered for non-inferiority. In this study the home exercise training was preceded with 4 weeks of educational sessions at hospital outpatients and then an exercise bike was provided in the home. Exercise was not supervised but was initiated by an exercise specialist in the patient's own home and weekly phone calls were made. Changes in cycle endurance time were similar between and within group, while changes in the 6MWT were minimal (gain of 8–11 m) in both groups, but not different between the groups. A similar approach was adopted by Guell *et al*,<sup>108</sup> with group education before allocating exercise training to either home or hospital; again there were no important differences between the groups after 9 weeks in this small RCT but this was unlikely to be powered for equivalence. Two studies adopted a broadly similar approach to that delivered in the UK; one over 8 weeks and one over 12 weeks.<sup>109 110</sup> Puente-Maestu *et al*<sup>109</sup> showed differences in the physiological response to the two environments but performance was similar. Both groups had structured exercise regimes to follow. While not supervised exercise, there was a weekly hospital visit to record and encourage compliance with the home programme. A further 12-week home-based rehabilitation incorporated supervised exercise in the hospital and the

home pulmonary rehabilitation setting.<sup>111</sup> The UK-based study compared brief advice with hospital-based pulmonary rehabilitation with a greater improvement observed in the hospital-based group in terms of exercise performance, although benefit in health-related quality of life was similar (though both small improvements) between groups.<sup>106</sup>

The approaches across studies are not consistent and methodological quality is variable. Furthermore, overall the population recruited seems similar at baseline to those routinely recruited to a studied pulmonary rehabilitation programme. All studies recruited patients with moderate to severe COPD with a moderate degree of disability. However, the exercise capacity at baseline seems to be higher than that reported in UK studies, reflecting the selection bias of this trial; that is, recruiting patients who are more able to accommodate a home-based training programme. The largest study provided personal exercise bicycle equipment for the participants to use at home. The education component of rehabilitation was delivered prior to engaging in the unsupervised exercise; this ranged from a 1:1 contact to a 4-week group programme of education.<sup>106 112</sup>

These trials may allow the scope of pulmonary rehabilitation to be increased in the UK. However, the educational needs of the individual need attention; mechanisms to offer remote supervision, provision of home exercise equipment and patient selection are important factors that need careful consideration.

Telehealth is an innovative consideration of delivering health services to patients with COPD. In the context of pulmonary rehabilitation, technology has the potential to be used as an adjunct to rehabilitation or even provide a 'rehabilitative' service to individuals in isolated areas or with transport difficulties. To date there have been few reports integrating technology into the rehabilitation service.

There are reports of using simple pedometers as adjuncts to rehabilitation or telephone counselling as an alternative approach to improve exercise performance, but there are limited data on using technology in the form of e-health, mobile 'smart' phones or telemedicine.<sup>113 114</sup> One notable exception showed benefits of mobile phone technology incorporating downloaded music with a tempo to match walking speed and global positioning system to monitor. However, the benefits seen were compared with a no-intervention group.<sup>115</sup>

#### Evidence statements

- ▶ The reported exercise and health status benefits of pulmonary rehabilitation have been based predominantly on supervised pulmonary rehabilitation programmes. (Evidence level 1++)
- ▶ Home-based pulmonary rehabilitation can lead to similar improvements in walking distance compared with supervised hospital pulmonary programmes; however, the educational needs, supervision, patient selection and provision of exercise equipment need to be considered. (Evidence level 1+)
- ▶ Brief advice is inferior to low-intensity group pulmonary rehabilitation. (Evidence level 1–)

#### Recommendations

- ▶ A supervised pulmonary rehabilitation programme is recommended for patients with COPD. (Grade A)
- ▶ If considering a structured home-based rehabilitation programme for selected patients with COPD, the following important factors need careful consideration: mechanisms to offer remote support and/or supervision, provision of home exercise equipment and patient selection. (Grade B)

#### Good practice point

- ▶ There would be some benefit to increasing the options for pulmonary rehabilitation available to individuals with COPD,

and increase the scope of the service. Geography may limit or stimulate options. (√)

### Post-exacerbation pulmonary rehabilitation

The evidence presented thus far has focused on pulmonary rehabilitation delivered to patients who are clinically stable—elective pulmonary rehabilitation. Exacerbations of COPD are associated with worsening symptoms and health-related quality of life that may persist for several months, and increased mortality and healthcare use. Exercise capacity and physical activity levels are impaired during and after an exacerbation, contributing to skeletal muscle dysfunction, particularly of the lower limbs. Clinical studies have therefore explored whether pulmonary rehabilitation delivered in the few weeks following an acute exacerbation of COPD has a role compared with usual post-exacerbation care. This post-exacerbation pulmonary rehabilitation is often termed ‘early’ pulmonary rehabilitation if commencing within 1 month of hospital discharge for an exacerbation.

#### Outcomes in post-exacerbation pulmonary rehabilitation

A recent Cochrane review aimed to assess the effects of ‘early’ pulmonary rehabilitation within 3 weeks after COPD exacerbations (the majority requiring hospitalisation or hospital at home services) on future hospital admissions (primary outcome) and other patient-important outcomes (mortality, health-related quality of life and exercise capacity).<sup>116</sup> Nine trials involving 432 patients were identified which compared ‘early’ pulmonary rehabilitation with conventional community care. Pulmonary rehabilitation significantly reduced hospital admissions with a number needed to treat of 4. However, as healthcare utilisation was only assessed over the short to medium duration of the study, it is unclear whether the reduction in hospital admissions was a result of the programme or increased contact with the study team. Pulmonary rehabilitation also reduced mortality, although the effect of the intervention may have been overestimated due to the small number of events. Nevertheless, no study reported any excess adverse events with the intervention.

There were also statistically and clinically significant improvements in health-related quality of life. Significant improvements (in excess of the recognised minimally important differences) were also seen in exercise capacity (6MWT and ISWT). The longer term benefits in exercise capacity and quality of life are not known.

A further RCT by Ko *et al*<sup>117</sup>, published after the Cochrane review, was also considered. This trial recruited 60 subjects and compared early post-exacerbation pulmonary rehabilitation within 2–3 weeks of hospital discharge with usual care. Although health-related quality of life was improved at 3 months and 6 months, no differences were seen by 12 months. Furthermore, although there was a trend towards fewer admissions in the first 3 months in the early pulmonary rehabilitation group, this waned with time. However, the study cohort was probably not medically optimised.

To date, only one study has compared ‘early’ post-exacerbation pulmonary rehabilitation with ‘late’ post-exacerbation pulmonary rehabilitation (delivered 6 months after exacerbation) with an 18-month follow-up.<sup>118</sup> No significant differences were seen in health-related quality of life or exacerbation rates between the groups. However, due to recruitment issues this study was underpowered.

#### Evidence statements

- ▶ Pulmonary rehabilitation delivered within 1 month of hospital discharge for acute exacerbation of COPD is not

associated with adverse effects or excess mortality compared with usual care. (Evidence level 1+)

- ▶ Participation in pulmonary rehabilitation delivered within 1 month of hospital discharge for acute exacerbation of COPD reduces short-term risk of future hospital admission compared with usual care. (Evidence level 1+)
- ▶ Pulmonary rehabilitation delivered within 1 month of hospital discharge for acute exacerbation of COPD improves short-term health-related quality of life compared with usual care. (Evidence level 1+)
- ▶ Pulmonary rehabilitation delivered within 1 month of hospital discharge for acute exacerbation of COPD improves short-term exercise capacity compared with usual care. (Evidence level 1+)

#### Recommendation

- ▶ Patients hospitalised for acute exacerbation of COPD should be offered pulmonary rehabilitation at hospital discharge to commence within 1 month of discharge. (Grade A)

#### Good practice point

- ▶ Providing post-exacerbation pulmonary rehabilitation alongside elective pulmonary rehabilitation courses can cause practical issues. Evaluation of innovative ways of delivering a combination of both modes of pulmonary rehabilitation in tandem would be useful. (√)

#### Completion of post-exacerbation pulmonary rehabilitation

It is well recognised that a proportion of patients fail to adhere to or complete elective pulmonary rehabilitation. Given that patients are physically and psychologically vulnerable in the early post-hospital discharge period, and that infective exacerbations often cluster, the GDG considered whether completion rates of ‘early’ post-exacerbation pulmonary rehabilitation (commenced within 1 month of hospital discharge) might be lower than with providing elective pulmonary rehabilitation to the same patients post hospital admission for an exacerbation but when the patient becomes more stable.<sup>119</sup>

There were no studies that directly addressed this issue. From 12 potential abstracts; nine compared early post-exacerbation pulmonary rehabilitation with usual care; one was a review paper and the ‘early’ intervention in one study was more than 4 weeks after exacerbation. Only one study was reviewed in full.<sup>118</sup> This compared ‘early’ (within 2 weeks of exacerbation) with ‘late’ pulmonary rehabilitation delivered 6 months after exacerbation. However, a proportion of exacerbations in this study did not necessitate hospitalisation. The study was also significantly underpowered due to recruitment problems and there were high numbers of dropouts and deviations from planned intervention. Furthermore, the intervention delivered was a mixture of inpatient and outpatient pulmonary rehabilitation which was inconsistent in both groups.

We further examined the individual RCTs considered in the Cochrane review that compared early post-exacerbation pulmonary rehabilitation shortly after hospital discharge with usual care.<sup>116</sup> ‘Completion rate’ data were often completion of the research study rather than completion for pulmonary rehabilitation. Only four studies reported any data on the attendance at pulmonary rehabilitation. Man *et al*<sup>120</sup> reported 67% of the intervention group attending more than 50% of pulmonary rehabilitation sessions, while in the cohort of Seymour *et al*<sup>121</sup>, 77% attended more than 50% of pulmonary rehabilitation sessions. Ko *et al*<sup>117</sup> reported that 73% of the intervention group attended at least 70% of sessions while only 40% attended more than 75% of sessions in the study of Eaton *et al*,<sup>122</sup> despite the investigators providing free door-to-door transport.

The GDG considered these data to be in line with published figures of elective pulmonary rehabilitation. There was insufficient evidence to suggest that attendance was lower with pulmonary rehabilitation started within 1 month of hospital discharge compared with elective pulmonary rehabilitation.

However, it should be noted that these patients are highly selected (consenting to participate in a RCT). Studies have suggested poor recruitment for the early post-exacerbation trials, and by extension, poor uptake (acceptance of the referral and commencing the course) for early post-exacerbation pulmonary rehabilitation. Seymour *et al*<sup>121</sup> only managed to recruit 60 patients from three hospitals over a 3-year period. In other studies, less than 50% of patients eligible for the study consented.<sup>117 122</sup> This raises questions as to whether the benefits of pulmonary rehabilitation shortly after hospital discharge can be generalised to unselected patients.

#### Recommendations

- ▶ Clinical services providing post-exacerbation pulmonary rehabilitation commencing within 1 month of hospital discharge should carefully record uptake, adherence and completion rates. (Grade D)
- ▶ Patients who initially decline pulmonary rehabilitation commencing within 1 month of hospital discharge should be offered elective pulmonary rehabilitation. (Grade D)

#### Adjuncts to pulmonary rehabilitation

This section reviews the available evidence for or against additional interventions (adjuncts) to standard multidisciplinary pulmonary rehabilitation. To qualify, the study had to consider the additional intervention delivered in parallel as part of pulmonary rehabilitation. Some of the proposed interventions may or may not have an evidence base for use in chronic respiratory disease in their own right and this was beyond the scope of the pulmonary rehabilitation guideline. The adjuncts were assessed according to patient-centred outcome measures, including walking distance, health status and dyspnoea. In many areas, the studies were of modest size which limits the strength of the evidence. Further, often the adjunct was explored in an unselected group of pulmonary rehabilitation candidates. We therefore do not rule out future research showing potential merit of certain adjuncts in select subgroups. Further, combinations of adjuncts remain relatively unexplored field.<sup>123</sup> The following adjuncts are explored in turn: inspiratory muscle training (IMT); hormones and nutritional supplements; non-invasive ventilation (NIV); oxygen; heliox and neuromuscular electrical stimulation (NMES).

#### IMT and pulmonary rehabilitation

The exercise capacity of patients with COPD is usually limited by dyspnoea.<sup>124</sup> An intervention that reduced dyspnoea could therefore potentially permit greater exercise and increase the benefits seen with pulmonary rehabilitation programmes. IMT attempts to improve respiratory muscle strength and endurance through two types of training. Inspiratory resistive training uses devices that permit inhalation against resistance at a certain threshold. With normocapnic hyperpnoea the individual is required to achieve supranormal target ventilation while PaCO<sub>2</sub> is kept constant. IMT may improve dyspnoea by favourably altering the ratio between the current inspiratory pressure generated and the maximal inspiratory pressure (PI/PI<sub>max</sub>)<sup>125–127</sup> and by reducing compromising dynamic hyperinflation<sup>128 129</sup> through a reduction in inspiratory time.<sup>130</sup>

Normocapnic hyperpnoea involves exercising the inspiratory muscles using periods of rapid breathing and deep inhalation of a controlled gas mix to ensure circulating

normocapnoea. It is therefore more akin to endurance training, but appears to have relevant potential beneficial effects.<sup>131</sup> Its use as an adjunct to pulmonary rehabilitation has been examined in one small quasi-randomised study where it resulted in greater respiratory muscle endurance and PI<sub>max</sub>, but had no effect on exercise outcome or quality of life.<sup>132</sup>

Threshold load training is delivered using small handheld devices that allow flow only when inspiratory pressure reaches a preset but adjustable level. It can therefore deliver strength and endurance type training. It appears safe and well tolerated in individuals with a variety of diagnoses, including COPD.<sup>133</sup> A pilot study in 36 patients with COPD found that use of IMT in addition to an exercise programme led to greater improvement in walk test distance than those who undertook exercise alone,<sup>134</sup> although a subsequent RCT in 25 patients with COPD found no such benefit.<sup>135</sup> Similarly, another pilot study in 42 patients found IMT led to greater improvement in cardiopulmonary exercise test parameters after an exercise programme.<sup>136</sup> These study findings appear at considerable risk of bias given their limitations in key areas (see evidence tables). These findings were not subsequently replicated in two RCTs assessing IMT as an adjunct to exercise programmes, with low risk of bias.<sup>135 137</sup>

Given the lack of consistency and the considerable limitations of the studies considered, IMT is not recommended as a routine adjunct to pulmonary rehabilitation. After assessment a respiratory physiotherapist may feel this is an appropriate adjunct for individual patients. However, post hoc subgroup analysis of the available studies did not identify a specific type of patient most likely to respond to IMT, so it cannot presently be recommended more broadly.

#### Evidence statement

- ▶ IMT using threshold loading devices or normocapnic hyperpnoea does not appear to augment the beneficial effects of general exercise training in patients with COPD. (Evidence level 1+)

#### Recommendation

- ▶ IMT is not recommended as a routine adjunct to pulmonary rehabilitation. (Grade B)

#### Hormones and nutritional supplements and pulmonary rehabilitation

Although the exercise component of pulmonary rehabilitation is beneficial, the degree of benefit may be limited by modifiable factors in many patients with COPD. Therefore, there has been research interest in maximising the effects of pulmonary rehabilitation by attempting to address nutritional constraints and the general catabolic state in COPD.

COPD is a catabolic state and individuals are at risk of becoming underweight, which is a poor prognostic feature.<sup>138</sup> Subclinical nutritional deficiencies may also exist that could constrain the benefits of pulmonary rehabilitation.<sup>139</sup> Supplementation of calories may therefore allow anabolism during pulmonary rehabilitation programmes and specific supplements may promote improvements in muscle efficiency and strength. The use of a standard supplement drink containing protein, fat and carbohydrate has been evaluated in a well described RCT and an inpatient trial with historical controls.<sup>46 140</sup> Both studies report additional weight gain of around 1 kg in those receiving supplements but no robust differences in strength or endurance measures.

Several small trials have evaluated specific nutritional supplements, but limitations in study design and lack of replication limit the inference that can be made regarding the efficacy of supplementation with L-carnitine,<sup>141</sup> amino acids<sup>142 143</sup> or



polyunsaturated fatty acids.<sup>144</sup> Creatine supplementation has been studied more widely, though not using the same dose: one trial found significant improvements in limb strength and endurance,<sup>145</sup> but this finding was not replicated in a subsequent study or a larger well conducted RCT.<sup>146 147</sup> All three studies concurred on the lack of benefit in walk test performance. Despite a lack of evidence supporting any specific nutritional intervention in pulmonary rehabilitation to date, it should be acknowledged that a referral to pulmonary rehabilitation provides an ideal opportunity for anthropometrical and nutritional assessment to take place, thus providing an opportunity to identify individuals at greatest risk of malnutrition, enabling a referral to specialised dietetic primary or secondary care services.

Anabolic steroids have been used to augment the effects of training in healthy individuals and for cachexia in chronic diseases.<sup>148</sup> Their use has been considered as to whether it may therefore augment the gains seen with pulmonary rehabilitation, potentially to a greater extent than in the healthy population due to the general catabolic state in COPD. The effects of testosterone and nandrolone have been explored in randomised placebo controlled clinical trials (in men only).<sup>35 149</sup> Both of these studies found that anabolic steroids increased fat-free mass. There was no clinically significant improvement in measures of exercise capacity, though maximal leg strength improved with testosterone.

The aforementioned studies have focused on single interventions, but it may be argued that applying concurrent complementary interventions is a more logical approach. Nutritional supplementation, anabolic steroids and pulmonary rehabilitation appear to confer some benefit over controls when used together.<sup>150</sup> However, this multifaceted approach has not been tested against a course of standard pulmonary rehabilitation and as such it is difficult to draw firm conclusions for usual practice.

#### Evidence statements

- ▶ Additional general nutritional supplementation does not significantly improve measures of exercise performance beyond the gains seen with pulmonary rehabilitation. (Evidence level 1+)
- ▶ Creatine supplementation does not augment the gains in exercise capacity resulting from pulmonary rehabilitation. (Evidence level 1+)
- ▶ Anabolic steroids do not substantially augment the exercise capacity gains achieved with pulmonary rehabilitation but produce small improvements in fat free mass and some measures of muscle strength. (Evidence level 1+)

#### Recommendation

- ▶ No specific hormonal or nutritional supplement can currently be recommended as a routine adjunct to pulmonary rehabilitation. (Grade B)

#### Good practice points

- ▶ The optimal approaches for addressing malnutrition, sarcopenia or obesity in COPD are uncertain and this is a wider issue than this guideline covers. However, attendance at a pulmonary rehabilitation course presents an ideal opportunity to screen and educate patients on nutrition. (✓)
- ▶ Patients with a BMI in the underweight or obese range should be considered for specific dietetic support. (✓)

#### NIV during pulmonary rehabilitation

Given the integration of NIV to the care of some patients with ventilatory failure in COPD, there has been discussion as to whether the use of the NIV during the exercise of pulmonary rehabilitation might improve walking distance and dyspnoea. The GDG were aware of studies that addressed the effects of

concurrent domiciliary NIV with pulmonary rehabilitation,<sup>151–153</sup> and others, including a systematic review,<sup>154</sup> that examined the acute effects of NIV on exercise capacity rather than as part of a pulmonary rehabilitation/exercise training programme.

There were seven small RCTs which compared assisted ventilation during pulmonary rehabilitation with exercise training alone in patients with COPD. The presence of type II respiratory failure was not necessary for inclusion and the available data suggested that for the most part there was no resting hypercapnia. One study was not reviewed as mild patients were recruited and type II respiratory failure was specifically excluded.<sup>155</sup> Of the remaining studies,<sup>156–161</sup> all suggested some improvement in exercise performance with NIV either directly or indirectly (eg, lactate levels), but none showed clinically significant improvements in walk distance compared with pulmonary rehabilitation alone. In general, the studies had small numbers, were often unblinded and the randomisation process was unclear. Furthermore, these studies were performed in the laboratory setting with supervised training rather than in the real life outpatient pulmonary rehabilitation setting. Little information was given about patient tolerability/preference and health economic data were lacking.

There was consensus from the GDG that patients with stable type II respiratory failure should not be excluded from pulmonary rehabilitation referral (see section Referral and assessment) of patients for pulmonary rehabilitation – Assessment). Furthermore, it is acceptable for patients established on domiciliary NIV to exercise with NIV during pulmonary rehabilitation if acceptable and tolerable to the patient.

#### Evidence statement

- ▶ There is not a role for the routine use of assisted ventilation during pulmonary rehabilitation in patients who have type II respiratory failure who are not already on domiciliary NIV. (Evidence level 1–)

#### Recommendations

- ▶ Long-term domiciliary NIV should not be provided for the sole purpose of improving outcomes during pulmonary rehabilitation. (Grade D)
- ▶ Patients who already receive long-term domiciliary NIV for chronic respiratory failure should be offered the opportunity to exercise with NIV during pulmonary rehabilitation if acceptable and tolerable to the patient. (Grade D)

#### Supplemental oxygen in patients undergoing rehabilitation

Individuals with COPD are limited by their breathlessness,<sup>128</sup> and in contrast to healthy individuals, their exertions are predominantly curtailed by limitation of ventilation and oxygenation rather than reaching their maximum heart rate.<sup>162</sup> As supplemental oxygen can increase exercise capacity acutely in those with severe COPD,<sup>163</sup> it is possible that such supplementation could increase the amount of training that patients with COPD could undertake. Simply being able to undertake a greater amount of training was postulated to augment the benefits from pulmonary rehabilitation. In addition, alleviation of a degree of pulmonary limitation was proposed to allow greater cardiac and muscular stress and thus have further beneficial effects on stroke volume and oxygen extraction.

In light of the above, trials investigating the use of supplemental oxygen with pulmonary rehabilitation have tended to recruit patients with more severe COPD indicated by a variety of criteria: spirometry,<sup>164</sup> desaturation on exercise,<sup>165</sup> both<sup>166</sup> or by fulfilling criteria for ambulatory oxygen.<sup>167</sup> The one trial that was more inclusive still reported a mean forced expiratory volume in 1 s in the total study populations of less than 50%

predicted.<sup>168</sup> The heterogeneity of baseline performance in these papers highlights the difficulty in using a single parameter to assess the severity of COPD. All of these trials were small and only one was double blinded and placebo controlled.<sup>164</sup> This study by Emtner *et al* reported an improvement in health-related quality of life (Short Form 36) and in respiratory rate at isotime (the only trial to study effort independent isotime measurements) but not in other parameters such as dyspnoea, peak work or Chronic Respiratory Disease Questionnaire. These findings are consistent with the lack of additional benefit in walk test distance and short questionnaires seen in other studies.<sup>165 166 168</sup> A randomised trial considered only individuals who were hypoxaemic on exertion and had improved saturations with supplemental oxygen. This trial reports a very large additional benefit in ESWT,<sup>167</sup> though no commensurate additional gains in quality of life or breathlessness. The GDG felt the study carried a significant risk of bias that influenced its findings. Therefore its results require replication before they can be widely applied.

It would seem to be of limited benefit to combine these study results in a formal meta-analysis given the variation in inclusion criteria, interventions, rehabilitation/training programmes and assessment methods.

Overall, there is no clear evidence supporting the routine use of supplementary oxygen for all patients to augment the benefits of pulmonary rehabilitation. Supplemental oxygen may be of benefit in selected individuals, but there is currently little information to inform this choice, especially given the intra-individual variability of oxygen saturations on exercise on a day-to-day basis. No clinical measures have been demonstrated to robustly predict those individuals with COPD who may gain additional benefit (in terms of exercise or quality of life parameters) from supplemental oxygen during pulmonary rehabilitation. Likewise, no parameters have been shown to assess the risk of hypoxia-related harm during rehabilitation or predict who may avoid this with the administration of supplemental oxygen.

The BTS guidance on ambulatory oxygen prescription therefore appears to be a reasonable criterion to apply for patients attending pulmonary rehabilitation in this regard, although previous guidance has always recommended assessing for ambulatory oxygen on completion of pulmonary rehabilitation and hence does not directly address the rehabilitation period itself. At the time of the BTS pulmonary rehabilitation guideline publication, the BTS domiciliary oxygen guideline is being prepared. Pulmonary rehabilitation also provides an opportunity to assess the adequacy of the prescribed flow rate for patients already in receipt of LTOT or ambulatory oxygen.

Profound desaturation on exercise has the potential to lead to end-organ impairment and compromise the benefits of exercise. The trials discussed above largely did not permit saturations to fall below 90% but it is unclear if this threshold is of special significance. No trial reported adverse events during exercise that could have been attributed to hypoxia, and the experience of the guideline group was that this was representative of the apparent safety of pulmonary rehabilitation programmes. Until further evidence is available, the level of exercise-induced hypoxia that is acceptable will depend on clinical judgement in individual cases, and practitioners will have their own thresholds that will prompt further investigation for occult comorbidity or perhaps influence decisions on the nature of the programme instituted. These decisions may be more difficult in patients with lung fibrosis who tend to desaturate more readily on exercise but often with lesser symptomatic awareness. No trials reported adverse events related to oxygen toxicity.

## Evidence statements

- ▶ Individuals with COPD who desaturate on exercise may benefit from the use of oxygen during pulmonary rehabilitation and show improved exercise capacity. It is unclear whether patients with other chronic respiratory diseases who desaturate gain the same benefit. (Evidence level 2+)
- ▶ Supplemental oxygen during pulmonary rehabilitation is safe in individuals with moderate to severe COPD. (Evidence level 1+)

## Recommendations

- ▶ Supplemental oxygen should not be routinely used for all patients undergoing pulmonary rehabilitation. (Grade B)
- ▶ Supplemental oxygen during pulmonary rehabilitation should be offered to those who fulfil the assessment criteria for long-term or ambulatory oxygen unless there are compelling clinical reasons to use alternative criteria. (Grade D)

## Good practice points

- ▶ Individuals who are prescribed oxygen but decline to use it during exercise should have this clearly documented in their notes. (✓)
- ▶ Pulmonary rehabilitation provides an opportunity to assess the adequacy of the prescribed flow rate for patients already in receipt of LTOT or ambulatory oxygen. (✓)

## Supplemental heliox in patients undergoing rehabilitation

Heliox is a mixture of helium and oxygen. Most often a mixture of 21% oxygen and 79% helium is used, but up to 40% oxygen has been studied. It has a similar viscosity to air but a significantly lower density. This means it is more likely to be laminar rather than turbulent flow in a given airway, which generates less resistance and can reduce the work of breathing. The administration of heliox has therefore been used for the treatment of large airway obstruction and vocal cord dysfunction, but it is of uncertain benefit in acute obstructive airways disease (potentially because the lower gas density exacerbates small airway collapse).<sup>169 170</sup> As heliox reduces the work of breathing, it may permit greater exercise capacity in more stable patients with COPD, and as described above potentially increases the benefit from pulmonary rehabilitation.

Two studies have evaluated this intervention. The studies did not find additional benefits in their heliox arm when heliox (60% helium) was compared with supplemental oxygen,<sup>171</sup> or heliox (79% helium) was compared with bi-level pressure support NIV<sup>156</sup> or pulmonary rehabilitation alone.<sup>156</sup> These trials were small and the study groups were heterogeneous in baseline function and response to rehabilitation. Hence, a small but meaningful additional beneficial effect of heliox cannot be discounted, but this is unlikely to be cost effective.

## Evidence statement

- ▶ Heliox does not appear to augment the benefits of pulmonary rehabilitation. (Evidence level 1–)

## Recommendation

- ▶ Heliox should not be used as an adjunct to pulmonary rehabilitation unless there are comorbidities which require its administration. (Grade D)

## NMES and pulmonary rehabilitation

Despite the unequivocal benefits of whole body exercise training in stable disease, such intervention may be difficult to deliver in patients with severe ventilatory limitation during acute exacerbations or those with severe muscle wasting. Non-volitional techniques, such as NMES, which are independent of these factors, have been proposed as alternative therapeutic modalities.

The GDG were aware of several randomised studies and systematic reviews that addressed the effects of NMES in COPD.<sup>172–173</sup> However, only two studies examined the adjuvant use of NMES with exercise training.<sup>174–175</sup> One of these studies recruited inpatients receiving mechanical ventilation which was beyond the scope of these guidelines<sup>175</sup>; hence only one study was reviewed in detail.

In a RCT, 17 highly selected patients with COPD (low BMI, quadriceps weakness, severe limitation in cycle ergometry, recent exacerbation requiring hospitalisation or intensive care) received either 4 weeks of quadriceps NMES (four 30-min sessions per week) with usual rehabilitation or usual rehabilitation alone.<sup>174</sup> The usual rehabilitation included active limb mobilisations with or without aerobic exercise and an educational component. Large improvements were seen in quadriceps maximum voluntary contraction after NMES plus usual rehabilitation compared with usual rehabilitation alone. Furthermore, there was a more significant reduction in breathlessness. Both groups significantly improved 6 min walk distance, but there was no between-group difference. Caution needs to be applied when interpreting the results. The patient group was highly selected and may not be typical of the general outpatient pulmonary rehabilitation population in the UK. The randomisation procedure was not described, there was no sham NMES and the tester was not blinded. Although patients seemed to tolerate NMES, it was not clear whether the NMES was set up by the therapist or the patient themselves. This is potentially important given that staff time is the major contributor to pulmonary rehabilitation costs.

There have been several small, single-centre studies supporting the benefits of NMES in improving quadriceps strength and exercise capacity, particularly in patients with more severe COPD or in the post-exacerbation setting.<sup>174–176–180</sup>

#### Evidence statement

- ▶ There is no role for the routine use of NMES as an adjunct to pulmonary rehabilitation in patients with COPD, based on current literature. (Evidence level 1–)

#### Recommendation

- ▶ If expertise in NMES is available, selected patients (low BMI with evidence of quadriceps weakness) who are unable or unwilling to participate in pulmonary rehabilitation could be considered for NMES. (Grade D)

### Pulmonary rehabilitation in people with other chronic respiratory diseases

The vast majority of evidence for pulmonary rehabilitation stems from patients with COPD. Yet there are many patients with other chronic respiratory disease who experience similar symptoms and are functionally limited. It is reasonable to imply that the same mechanisms of deconditioning and lack of confidence are likely to apply to all chronic diseases which have dyspnoea as the core symptom. Few trials have considered the effect of pulmonary rehabilitation, compared with usual care, in populations other than COPD, making it difficult to comprehensively address. We have addressed through a series of structured PICO questions non-CF bronchiectasis, ILD and stable asthma, but recognise that the discussion could encompass a much wider field of conditions and is not meant to bias opinion against those not covered. Further, in general, we recognise that establishing robust evidence in certain conditions for or against the role of a pulmonary rehabilitation programme specifically may not be feasible given the short life expectancy.

### Non-CF bronchiectasis

A small RCT of subjects with non-CF bronchiectasis compared pulmonary rehabilitation, pulmonary rehabilitation with IMT and a control group; n=32 in total.<sup>181</sup> Both pulmonary rehabilitation groups showed significant improvements in walking distance using ISWT and endurance exercise compared with the control group. There was a significant improvement in quality of life in the pulmonary rehabilitation plus IMT group but not in the pulmonary rehabilitation group alone compared with the controls, although the study was not powered for this outcome. The GDG additionally considered the evidence in the BTS bronchiectasis guideline (2010) and the bronchiectasis quality standards state that all patients with bronchiectasis should have access to and be considered for referral for pulmonary rehabilitation.<sup>6–182–183</sup>

#### Evidence statements

- ▶ Patients with non-CF bronchiectasis benefit from pulmonary rehabilitation in terms of exercise capacity compared with usual care. (Evidence level 1–)
- ▶ Patients with non-CF bronchiectasis benefit from pulmonary rehabilitation in terms of quality of life compared with usual care. (Evidence level 1–)

#### Recommendation

- ▶ Patients with non-CF bronchiectasis who have breathlessness affecting their ADL should have access to and be considered for pulmonary rehabilitation. (Grade D)

#### Good practice point

- ▶ Unlike in patients with CF, in patients with COPD and non-CF bronchiectasis with multidrug-resistant organisms, for example *P aeruginosa*, there is no current evidence of cross infection. (√)

### Interstitial lung diseases

ILDs represent a broad diagnosis and the presentation and prognosis vary according to the specific diagnosis, which makes considering the impact of pulmonary rehabilitation complicated if they are considered as a whole. More specifically idiopathic pulmonary fibrosis (IPF) is often associated with progressive clinical and physiological deterioration over 6–12 months and patients with IPF often show marked desaturation during exercise. Importantly, we have focused on ILD as opposed to the breadth of all restrictive lung diseases, such as chest wall disease and other extra-thoracic causes.

A RCT from Japan included 30 patients with IPF randomised to pulmonary rehabilitation or a control arm. The study showed improvements in walking distance on a 6MWT and in quality of life using the SGRQ, but not in dyspnoea rating.<sup>184</sup>

Forty-four patients with ILD, including 25 with IPF, were studied before and after an 8-week pulmonary rehabilitation programme and 6 months later in an uncontrolled study.<sup>185</sup> There was improvement in 6 min walking distance with pulmonary rehabilitation in the IPF (mean 21 m improvement) and other ILD group (mean 43 m), with 40% of the IPF group and 52% of the other ILD group reaching a minimally important difference of 34 m at rehabilitation completion. Similarly, dyspnoea improved in both groups. There was marked variability in response between individuals.<sup>185</sup>

Holland *et al*<sup>185</sup> suggested that patients with IPF have greater improvements in functional exercise capacity when pulmonary rehabilitation is delivered early in the course of disease. Patients with other ILDs achieve significant gains in exercise capacity regardless of disease severity and are more likely than those with IPF to achieve sustained improvements in dyspnoea.<sup>185</sup>

The GDG were aware of a further well conducted exercise-based RCT in 57 patients with ILD (60% with IPF). This was not pulmonary rehabilitation and discussion ensued as to whether it should be included, given the paucity of literature otherwise. This study demonstrated modest improvements in functional exercise tolerance, dyspnoea and quality of life compared with telephone support.<sup>186</sup> Importantly it was safe and feasible. There were four deaths (two per arm) during the study period, highlighting that patients with ILD can be critically ill. The effects of the exercise training were lost at the 6-month follow-up but this cannot be assumed post pulmonary rehabilitation. The GDG also considered that lack of any sustained benefit at 6 months may be due to underlying disease progression.

The GDG recognised the wide individual variation in the course of the conditions comprising ILD. This may make pulmonary rehabilitation a consideration for some. However, for others, a formalised pulmonary rehabilitation programme would be futile and management should focus on other palliative measures.

#### Evidence statements

- ▶ Patients with ILD benefit from pulmonary rehabilitation with improvements in exercise and quality of life. (Evidence level 1–)
- ▶ Patients with ILD benefit from exercise training with improvements in exercise and quality of life compared with telephone support. (Evidence level 1+)
- ▶ The benefits of pulmonary rehabilitation in patients with ILD are not sustained at 6 months. (Evidence level 3)
- ▶ The benefits of an exercise training programme in patients with ILD are not sustained at 6 months. (Evidence level 1+)

#### Good practice points

- ▶ The benefits of exercise and the recommendation of incorporating exercise activities into a healthy lifestyle should be discussed with all patients with ILD. Such discussion needs to be tailored to realistic achievability for that person's condition. (√)
- ▶ If healthcare professionals consider referring certain patients with stable ILD who are limited by breathlessness in ADL to pulmonary rehabilitation, they should discuss with the patient regarding the likely benefits. (√)
- ▶ Patients with IPF have a potential for significant desaturation during exercise-related activities. (√)

#### Asthma

One RCT studying patients with asthma and COPD (divided into diagnostic groups a posteriori) showed improvements in exercise tolerance and quality of life in those who completed a 12-week programme of pulmonary rehabilitation. However, the study findings are limited by a lack of power calculation in methodology and likely underpowered for the subgroup analysis. Compared with usual care, patients with asthma showed improvements in exercise tolerance, quality of life and a dyspnoea score.<sup>187</sup>

While not pulmonary rehabilitation, there is a Cochrane review supporting physical training in subjects with asthma, although the majority of the small population studies were conducted in children and did not focus on symptomatic subjects. It is therefore of little relevance here. The conclusions of the review acknowledged the diversity of the intervention type, duration, subjects and outcome measures of the studies.<sup>188</sup>

Standard asthma management should be managed according to the BTS/SIGN asthma guideline and the reader is drawn to the recommendation that physical training should be seen as part of a general approach to improving a healthy lifestyle following a Cochrane review.<sup>8 189</sup> The BTS/SIGN asthma guideline

raises standard precautions regarding observation for exercise-induced asthma if appropriate.

The GDG accepted that there is often overlap in asthma and COPD diagnoses and that many patients diagnosed with asthma have fixed airflow limitation and present with symptoms of persisting breathlessness and exercise intolerance in a similar manner to COPD. These patients are likely to benefit from pulmonary rehabilitation.

#### Recommendation

- ▶ The routine referral of patients with asthma to pulmonary rehabilitation is not recommended. (Grade D)

#### Good practice points

- ▶ The benefits of exercise and the recommendation of incorporating exercise activities into a healthy lifestyle should be discussed with all patients with asthma. (√)
- ▶ If healthcare professionals consider referring certain patients with stable asthma who are limited by breathlessness in ADL to pulmonary rehabilitation when on optimal therapy, they should discuss with the patient the likely benefits. (√)
- ▶ The BTS/SIGN asthma guideline draws attention to exercise-induced asthma and precautions to prevent this should be followed if appropriate. (√)

#### Other chronic respiratory diseases—in general

##### Good practice points

- ▶ MCID changes and tools used to assess exercise capacity and quality of life for pulmonary rehabilitation in COPD are not necessarily transferable to other chronic respiratory diseases. While future research should address this, failure of rehabilitation should not be implied if failure to reach the COPD MCID for outcomes. (√)
- ▶ The educational element of pulmonary rehabilitation should be adapted for other chronic respiratory diseases if appropriate. (√)
- ▶ Practically, inclusion of patients with other chronic respiratory diseases into pulmonary rehabilitation will be alongside subjects with COPD. (√)
- ▶ General exercise should be encouraged for all patients with chronic respiratory disease. (√)

#### Post pulmonary rehabilitation

##### Repeat pulmonary rehabilitation programmes

The clinical conditions for which pulmonary rehabilitation is routinely offered result in progressive loss of function over time. It is therefore likely that any benefits arising from an initial programme of pulmonary rehabilitation will decay toward baseline function. There is the potential that a further course of pulmonary rehabilitation at a distant time point may provide further benefit.

Several RCTs and observational studies in which pulmonary rehabilitation is compared with standard care or education alone have followed participants for a protracted period. All studies have found that the initial beneficial effects diminish over time. However, those completing pulmonary rehabilitation courses have significantly greater quality of life, exercise capacity and fewer days in hospital than those in the control groups in the year after the intervention.<sup>12 190 191</sup> The benefits appear to persist to some degree at 18 months,<sup>39</sup> but there are conflicting data on whether a meaningful difference in exercise capacity persists at 2 years.<sup>192 193</sup>

Repeating pulmonary rehabilitation in those whose condition has deteriorated over time after their initial programme leads to improvements in quality of life and exercise capacity that have been reported to be similar in magnitude to those seen with the first intervention in retrospective reviews and two likely

underpowered RCTs.<sup>192 194–196</sup> A third session is again of short-term benefit.<sup>194</sup> In those completing pulmonary rehabilitation in the NETT study, patients who had completed pulmonary rehabilitation previously (n=777) did not gain as much improvement in terms of exercise and quality of life on repeat as those for which it was their first programme (n=441), although they did improve.<sup>197</sup>

The timing of a repeat course of pulmonary rehabilitation would appear to be influenced by the aim of the intervention. As noted above, the great majority of the initial benefit is lost by 24 months, and two RCTs of routinely repeated pulmonary rehabilitation at a lesser interval have shown no major additional benefit from an intervening extra session in terms of exercise capacity at the end of the study.<sup>194 195</sup> However, earlier repeat courses do lead to short-term benefits in exercise capacity and quality of life, which may be important in specific circumstances (eg, preoperatively). Additionally, in these studies the frequency of exacerbations appears lower in those who received additional courses,<sup>194</sup> with fewer days spent in hospital.<sup>195</sup> Although these findings are based on a small number of events, it raises the possibility that there is a subgroup of patients who are prone to frequent exacerbation who may benefit from early repeat pulmonary rehabilitation. A single small study followed patients after an initial course of pulmonary rehabilitation and randomised those who had an exacerbation during follow-up to either a further rehabilitation course or standard care.<sup>198</sup> This study found no benefit in its major endpoints, although the occurrence of further exacerbations during follow-up makes it difficult to interpret the results.

Two small studies have sought baseline factors associated with a sustained response to pulmonary rehabilitation: a higher initial PaCO<sub>2</sub> was independently (positively) associated with a maintained initial improvement in quality of life, and a low baseline quality of life with a poor response.<sup>199 200</sup> Neither of these studies provides sufficient evidence for the creation of a predictive tool.

#### Evidence statements

- ▶ The benefits from pulmonary rehabilitation persist to some degree for at least 1 year. (Evidence level 2+)
- ▶ Repeating pulmonary rehabilitation after a period of 1 year provides benefits in exercise capacity and quality of life. (Evidence level 4)

#### Recommendations

- ▶ Repeat pulmonary rehabilitation should be considered in patients who have completed a course of pulmonary rehabilitation more than 1 year previously. The likely benefits should be discussed and willing patients referred. (Grade B)
- ▶ Earlier repeat pulmonary rehabilitation should be considered in individuals with accelerated physiological decline or if additional benefits on a shorter timescale would be clinically valuable. (Grade D)

#### Good practice point

- ▶ It is unlikely that if the patient completed the pulmonary rehabilitation course originally and failed to gain a benefit, they would benefit a second time round; unless circumstances such as an exacerbation interrupted the initial programme. (√)

#### Maintenance

Studies evaluating post-pulmonary rehabilitation maintenance exercise demonstrated a range of strategies in terms of exercise type, level of supervision, duration and frequency of maintenance programme. No consensus emerged from the literature about the definition of post-pulmonary rehabilitation exercise maintenance, making it difficult in some cases to distinguish

between a ‘maintenance’ programme and extension of the initial pulmonary rehabilitation programme.

A small number of RCTs investigated the benefit of maintenance compared with no clear strategy post rehabilitation. Three studies describe the value of a structured maintenance approach after a standard out-patient course of rehabilitation.<sup>201–203</sup> One UK-based study examined the value of telephone follow-up.<sup>204</sup> One small RCT (n=20) described the value of an unsupervised home programme compared with no advice at all, which would essentially reflect best usual care; it would be unusual to graduate from a rehabilitation programme with no advice at all.<sup>205</sup> The studies that described maintenance strategies chose different approaches over differing lengths of time. Brooks *et al*<sup>201</sup> described a monthly supervised exercise session with telephone support in the interim. Measurements were taken at 3-monthly intervals up to 12 months and no benefit was observed in either exercise tolerance or quality of life compared with the control group for this approach. Ries *et al*<sup>202</sup> described a large study (n=172), again offering 12 months of maintenance, comprising weekly telephone contact and monthly exercise sessions. Patients were followed up for 24 months. During the intervention period, there were benefits observed in exercise capacity but not in quality of life. Between 12 and 24 months there was no support provided and the difference between the groups narrowed and was not significant. A more intense maintenance programme was provided by Ringbaek *et al*<sup>203</sup> with weekly sessions for 6 months after a 7-week outpatient programme, fortnightly sessions for a second 6 months and no supervision for a final 6 months. At 18 months there was no difference between the two groups. Again, however, examining the ‘maintenance’ group over the first 12 months, some advantages were observed, largely associated with a decline in performance in the control group, and maintenance of benefit acquired as a consequence of the initial rehabilitation phase with the intervention group. The study by Waterhouse *et al*,<sup>204</sup> a UK-based study, looked at a telephone support system only. After completing a RCT of community versus hospital-based rehabilitation, participants were randomised to either telephone maintenance or usual care. There was no discernible benefit associated with this strategy at any time point up to 18 months post graduation from rehabilitation.

There have been a couple of studies exploring maintenance after alternative forms of delivering the initial rehabilitation. Wijkstra *et al*<sup>206 207</sup> explored two maintenance strategies after a 3-month course of home-based rehabilitation; the study also recruited a control group. The intervention group was divided to receive either weekly exercise supervised by a physical therapist or monthly sessions for a further 15 months. The study was underpowered (n=11 and n=12 respectively) but demonstrated an advantage of both maintenance strategies in quality of life and physical performance. The quality of life was significantly improved in the group receiving the monthly support compared with the control group. The 6MWT distance was maintained during the 18-month period in the maintenance groups, while the control group declined. This was not different between groups but there was a significant within-group decline observed in the control group. More recently, there has been an examination of a maintenance programme after an initial inpatient programme.<sup>208</sup> The maintenance approach was coordinated with a health community network that included self-help organisations. In total, the maintenance group received 96 sessions supervised by a healthcare professional over a 12-month period (exercise and psychosocial support). This study ‘consecutively allocated’ individuals (assume not randomised) to this package of care (n=14) or standard care (n=26). Although a small study, the

data suggested important benefits in exercise capacity and quality of life. Interestingly there was also a reduction in hospital days for respiratory illness. This form of maintenance was probably not dissimilar to many rehabilitation programmes offered in the UK.

#### Evidence statement

- ▶ Continuation of supervised exercise training beyond pulmonary rehabilitation protects the patient from a decline in exercise capacity compared with a control group. (Evidence level 1–)

#### Recommendation

- ▶ All patients completing pulmonary rehabilitation should be encouraged to continue to exercise beyond the programme. (Grade A)

#### Good practice point

- ▶ Patients graduating from a pulmonary rehabilitation programme should be provided with opportunities for physical exercise beyond their rehabilitation programme. (✓)

### SUMMARY OF RESEARCH RECOMMENDATIONS

- ▶ To develop validated easy-to-use, sensitive outcome tools that extend the range to incorporate assessment of pulmonary rehabilitation on extra-pulmonary manifestations, such as daily physical activity, skeletal muscle dysfunction, osteoporosis and cardiovascular risk, which are of prognostic significance in COPD.
- ▶ To understand whether pulmonary rehabilitation may preserve health with the aim of reducing long-term disability and dependence in those with milder chronic respiratory disease and how best this rehabilitation is delivered.
- ▶ Poor uptake and adherence remain significant barriers to effective pulmonary rehabilitation. There is a need for robust, well designed trials to explore techniques in the pre and peri pulmonary rehabilitation period that might improve uptake and adherence. This is also pertinent to post-exacerbation pulmonary rehabilitation.
- ▶ Personalisation of pulmonary rehabilitation:
  - To identify clinical phenotypes that may respond differently to pulmonary rehabilitation.
  - Objective tests of patient competency during pulmonary rehabilitation can help personalise and optimise the programme structure at an individual level.
  - Individualising the relative proportions of resistance and aerobic training during pulmonary rehabilitation according to clinical phenotype or skeletal muscle structure/function has yet to be studied.
- ▶ The relative sustainability and duration of benefits of resistance and aerobic training is required.
- ▶ The optimal structure of pulmonary rehabilitation remains unknown. More robust studies are required to determine quality, cost effectiveness and greater choice of delivery. To improve accessibility to pulmonary rehabilitation, such research may include technologies.
- ▶ In comparison to exercise training, there has been considerably less work on the educational element of pulmonary rehabilitation.
- ▶ An unanswered question is whether there is value in delaying post-hospitalisation pulmonary rehabilitation (ie, comparing elective vs early pulmonary rehabilitation following hospitalisation for exacerbation of COPD).
- ▶ Robust research to explore further the role of nutritional supplementation and hormones as adjuncts to pulmonary rehabilitation. This should include:
  - specific clinical phenotypes and/or using alternative regimens for anabolic steroids;
- while some nutritional supplements have been rigorously researched, several studies have been small or used multiple endpoints; similarly, there are opportunities to consider alternative nutritional supplements in combination with pulmonary rehabilitation;
- several muscle anabolic and anti-cachexia drugs are in development and well designed studies are required to test whether these have value as an adjunct to pulmonary rehabilitation and which clinical phenotypes are most likely to benefit.
- ▶ The wider value of ambulatory oxygen, outside of pulmonary rehabilitation, remains contentious. Further study on the optimal threshold for the use of ambulatory oxygen would be welcome as would clarification regarding whether there is potential harm from hypoxia-related or exercise-related systemic inflammation and oxidative stress.
- ▶ Other adjuncts such as NIV in routinely supporting exercise training in the context of a pulmonary rehabilitation programme are required. This is particularly pertinent in patients with chronic respiratory failure. Further, high-quality studies of NMES as an adjunct are required, including the clinical phenotype most likely to benefit.
- ▶ Robust research to optimise pulmonary rehabilitation to produce meaningful and sustainable behaviour change is of particular importance, such as leading to improvement in physical activity.
- ▶ Patients with chronic respiratory diseases other than COPD are increasingly referred to pulmonary rehabilitation. Knowledge gained from patients with COPD has been extrapolated to patients with other chronic respiratory disease and there is a dearth of studies examining specific non-COPD populations. Unanswered questions in people with chronic respiratory disease that require further research include:
  - the appropriateness of outcome measures originally designed in COPD populations for use in other chronic respiratory diseases;
  - the responsiveness of disease-specific outcome measures, particularly health status questionnaires;
  - the effect on healthcare resource usage and health economic benefits of pulmonary rehabilitation;
  - the optimal length and duration of pulmonary rehabilitation;
  - the duration of benefits of pulmonary rehabilitation, including rapidly progressive conditions such as IPF.
  - the relative merits of different components of training (eg, resistance vs aerobic; upper limb vs lower limb);
  - the effects, if any, of individualised goal setting;
  - the value of individualising the education component of PR according to disease;
  - the optimal timing of pulmonary rehabilitation and whether there is value in providing post-hospitalisation pulmonary rehabilitation in exacerbations of other chronic respiratory disease;
  - the impact of exacerbation frequency on pulmonary rehabilitation compliance and response in conditions associated with frequent exacerbations such as bronchiectasis.
- ▶ Repeating pulmonary rehabilitation programmes seems logical given the natural decline in function and health status following the course, but requires further study to elucidate the optimal frequency and the manner of delivery.
- ▶ More studies are needed to determine effective delivery models for maintenance exercise following a pulmonary rehabilitation programme. This might include the use of telehealth technologies.

## AUDIT

An audit of pulmonary rehabilitation will be offered as part of the 2013-2016 National COPD Audit Programme (England and Wales) which has been commissioned by the Healthcare Quality Improvement Partnership (HQIP) on behalf of the Department of Health. It is part of the National Clinical Audit and Patient Outcomes Programme.

## CONCLUSIONS

This is an evidenced-based guideline for pulmonary rehabilitation. Its focus is on delivering a quality pulmonary rehabilitation programme for appropriate patients with chronic respiratory disease and to this end it includes sections on many aspects: outcomes, referral, content and design, timing, adjuncts, other chronic respiratory disease and the post-pulmonary rehabilitation period. However, in compiling the guideline, we recognise that it could not encompass all the important questions pertaining to pulmonary rehabilitation. We *a priori* opted not to evaluate healthcare utilisation costs.

This is a rapidly progressive research field and the guideline will be reviewed in the next 5 years.

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## APPENDIX A: COMMITTEE MEMBERS

A full list of the GDG members and the contributors to each section of the guideline is given below, along with individual members representing other organisations.

	Sections
Dr Elaine Bevan-Smith	Referral, elements, post exacerbation, post rehabilitation
Dr John Blakey	Adjuncts, post rehabilitation, lay summary
Dr Charlotte Bolton	Chair
Mr Patrick Crowe	Patient representative, lay summary
Dr Sarah Elkin	Post rehabilitation
Dr Rachel Garrod	Elements, non-COPD rehabilitation
Dr Neil Greening	Outcomes, adjuncts
Ms Karen Heslop	Referral, elements, post rehabilitation, non-COPD rehabilitation
Dr James Hull	Referral
Dr Will Man	Post exacerbation, adjuncts, research recommendations
Professor Mike Morgan, representing the Royal College of Physicians, London	Programme characteristics, adjuncts
Mr David Proud	Programme characteristics, elements, adjuncts
Professor Mike Roberts	Outcomes, adjuncts
Dr Louise Sewell, representing the College of Occupational Therapists	Outcomes, programme characteristics
Professor Sally Singh	Programme characteristics, elements, post rehabilitation
Dr Paul Walker	Referral, programme characteristics
Ms Sandy Walmsley, representing the Primary Care Respiratory Society, UK	Programme characteristics, outcomes

A full list of the GDG declarations of interest can be found on the British Thoracic Society website or by contacting the British Thoracic Society Head Office.

## APPENDIX B: LIST OF STAKEHOLDERS

- ▶ Association of Chartered Physiotherapists in Respiratory Care
- ▶ Association of Respiratory Nurse Specialists
- ▶ British Geriatrics Society
- ▶ British Lung Foundation
- ▶ College of Occupational Therapists
- ▶ Primary Care Respiratory Society, UK
- ▶ Royal College of Physicians London

- ▶ Royal College of Physicians and Surgeons of Glasgow
- ▶ The Thoracic Society of Australia and New Zealand

## APPENDIX C: PATIENT INFORMATION

More information on pulmonary rehabilitation patient leaflets is available from [http://www.improvement.nhs.uk/documents/BLF/PR\\_BK22\\_2012\\_v1.pdf](http://www.improvement.nhs.uk/documents/BLF/PR_BK22_2012_v1.pdf) or from the British Lung Foundation.

Some centres opt to formulate their own personalised leaflets discussing venues, timings and how patients can be referred. In addition, contact information for the rehabilitation team can be incorporated.

## APPENDIX D: LAY SUMMARY

### INTRODUCTION

#### Pulmonary rehabilitation

Long-term chest problems that interfere with daily life, such as chronic obstructive pulmonary disease (COPD), are common. They are a major cause of suffering, and also a considerable expense to the NHS as they lead to a large number of hospital admissions.

Pulmonary rehabilitation is a programme of exercise and education for people with long-term chest problems. Many studies have shown that pulmonary rehabilitation improves measurements of health and wellbeing, such as the distance an individual can walk or their likelihood of needing to go to hospital.

#### Why a guideline is needed

It is not clear how to get the most from a pulmonary rehabilitation programme. Basic questions such as who should start on the programme and how long a programme should last are still sources of discussion. Because of this uncertainty, there is a need to come to conclusions on best practice and set standards.

The British Thoracic Society produced its first statement on pulmonary rehabilitation in 2001. Since then, a large number of relevant studies have been published. A more detailed guideline has therefore been produced.

#### Who is the guideline for?

This guideline will mainly be of use for healthcare professionals who are involved in the care of people with long-term chest problems. It will also be useful for those who are involved in planning and funding services.

#### How the guideline was developed

This guideline was produced following a standard method. The first step was to gather a group who are involved in pulmonary rehabilitation programmes, including doctors, nurses, physiotherapists, an occupational therapist, a dietician and a patient

representative. The details of this Guideline Development Group are given in appendix A.

This group produced a long list of important questions in a standard format. An independent centre then undertook a detailed search and found a very large number of publications that might help answer the questions. These publications were reviewed in a standard manner in detail by at least two people. The whole group discussed the evidence around each question. Further comments were sought from other healthcare professionals, experts in developing guidelines, and patient groups.

### Evidence

Throughout the main guideline document, the type of study providing information is indicated by a number. The strength of the evidence supporting each recommendation is shown by a letter (A=highest). Detailed information on each publication is included in the web appendix.

## RECOMMENDATIONS

### Outcomes

Currently pulmonary rehabilitation services do not collect the same information on people attending courses.

We recommend that services make assessments before and after rehabilitation. These assessments should measure the distance an individual can walk, their degree of breathlessness, their overall health status, their ability to do everyday tasks, and psychological aspects, such as anxiety.

### Referral

There has been discussion around who should be considered for pulmonary rehabilitation. For example, some people have been thought to be too well or too ill to gain benefit. However, we found that people with severe chest problems and those with more mild breathlessness may benefit from pulmonary rehabilitation. Similarly, there is no evidence that current smokers or people with depression will not benefit.

People with unstable heart problems or with very severe muscle or joint problems have other priorities and pulmonary rehabilitation should be deferred.

People who are referred should receive accurate information about the planned pulmonary rehabilitation programme and the likely benefits. There should be an opportunity for discussion of the referral.

People who are referred for pulmonary rehabilitation should have their treatment for their chest condition reviewed at the time of referral. They will often have other conditions so the referral process provides an opportunity to identify problems such as malnourishment, depression, smoking and high blood pressure.

### Programme characteristics

A variety of pulmonary rehabilitation programmes are provided in the UK. Most involve a programme lasting at least 6 weeks. This approach is supported by the available research.

Pulmonary rehabilitation programmes should include at least two supervised sessions per week. Less frequent contact may be less beneficial. Participants should be assisted and encouraged to do further exercise at home.

Programmes should include a variety of training types to provide benefits in strength and exercise capacity. There is no clear support for any particular format of this varied training.

Providing rehabilitation at home seems to be feasible, either in person or supported with internet video calls. Presently it is not possible to say who could take part in such programmes and still gain the same benefits as they would have had from standard pulmonary rehabilitation.

### Rehabilitation after exacerbations

A rapid worsening in breathlessness and cough, along with a decline in measurements of lung capacity or oxygen levels, is referred to as an exacerbation of COPD. These distressing events may lead to admission to hospital.

Taking part in pulmonary rehabilitation soon after discharge gets people back to their usual level more quickly than they otherwise would. It also reduces the risk of coming back into hospital in the short term, and makes people feel better. We therefore recommend pulmonary rehabilitation for everyone admitted with an exacerbation of COPD. We also recommend that the providers of rehabilitation record the proportion of people who attend and complete these courses.

### Aids to pulmonary rehabilitation

Several studies have investigated whether the benefits of pulmonary rehabilitation can be increased by adding something to the programme.

The guideline group examined trials of devices that train the breathing muscles, hormone and nutritional supplements, helium-containing gas mixtures and electrical muscle stimulators. These measures appear safe, but adding them to rehabilitation does not lead to greater benefit in walking distance or breathlessness so they are not routinely recommended.

People with long-term chest conditions may have oxygen or a ventilator at home. These treatments should not be started just for pulmonary rehabilitation.

### Pulmonary rehabilitation for other conditions

Almost all studies investigating pulmonary rehabilitation have included people with COPD. However, many people are limited by other long-term chest problems. The guideline group suggests that anyone in this situation has the opportunity to discuss referral for pulmonary rehabilitation.

### After rehabilitation

The improvements following pulmonary rehabilitation fade over time. We reviewed studies investigating whether maintenance sessions or repeat programmes were of benefit.

Generally, a repeat programme of pulmonary rehabilitation is of benefit if the last completed programme was more than 1 year ago. A shorter interval should be considered if there is a reason for rapid decline (such as an admission) or a need to be in the best possible condition (such as before a major operation).

All individuals who complete a course of pulmonary rehabilitation should be encouraged to continue to exercise.

## APPENDIX E: ESSENTIAL INFORMATION REQUIRED ON A REFERRAL FORM TO PULMONARY REHABILITATION

- ▶ Name, date of birth, contact details.
- ▶ Known communication/language barriers.
- ▶ Respiratory diagnosis:
  - spirometry for those with COPD;
  - height, weight, BP, oxygen saturations at rest are desirable.
- ▶ Medical Research Council breathlessness score.
- ▶ Smoking status.
- ▶ Therapies:
  - current list of medication;
  - use of oxygen:
    - ▷ long-term oxygen therapy, short-burst oxygen therapy, ambulatory;
    - ▷ oxygen saturations;
  - use of domiciliary NIV.
- ▶ Significant and relevant comorbidities:
  - that may need consideration by provider before acceptance, in line with section ‘Referral and assessment of patients for pulmonary rehabilitation’;

- that may need to be considered in risk assessment, in line with section ‘Referral and assessment of patients for pulmonary rehabilitation’.
- ▶ Transport needs—if applicable to that rehabilitation provider: the referrer should have discussed with the patient about the referral and discussed the likely benefit of partaking.

## APPENDIX F: SERVICE SPECIFICATION

Staffing is addressed in the Department of Health Service Specification for pulmonary rehabilitation: <http://www.dh.gov.uk/health/2012/08/copd-toolkit><sup>209</sup>

It highlights a multidisciplinary staff with sufficient competencies and experience; administration support; sufficient cover for annual leave, sickness leave and maternity leave. Staff should have regular updates and training.

The Service Specification also provides useful and practical advice on equipment and risk assessment.

## APPENDIX G: CHARACTERISTICS OF ROLLING AND COHORT PULMONARY REHABILITATION PROGRAMMES

	Rolling	Cohort
Nature of programme	Continuing cycle of sessions, with patients joining when there is a space and leaving after completing a programme of sessions	All patients start and finish the programme at the same time
Waiting list	<ul style="list-style-type: none"> <li>▶ May enter the programme when a space occurs (eg, from a dropout) so may curtail waiting list and could be more efficient</li> <li>▶ Permits a fast-track facility for entry of post-rehabilitation subjects</li> <li>▶ Potentially allows better capacity</li> </ul>	As an accumulative number of patients wait to start a cohort programme, the waiting list is distorted
Rehabilitation delivered at different locations by same team	Not suitable This is only suitable if the programme always runs at the same venue	Suitable
Education programme	The order of educational talks for the individual is governed by the point of entry	Can ‘flow’ in a logical order
Group dynamics	A new patient may be the sole new participant which may potentially be beneficial or a challenge	Patients all start together; permits group learning of lifestyle challenges
Assessments	Requires the ability to perform pre and post assessments in parallel to the course	Dedicated assessment slots can be programmed for all subjects pre and post rehabilitation
Duration of programme	Permits opportunity for early graduation to the gym and/or lengthening programme if required	Fixed length for each programme

## APPENDIX H: SUGGESTED EDUCATIONAL TALKS TO ENCOMPASS IN THE PULMONARY REHABILITATION PROGRAMME

- ▶ Anatomy, physiology, pathology—in health and in chronic respiratory disease.
- ▶ Medication (including oxygen therapy).
- ▶ Smoking cessation.
- ▶ Dyspnoea/symptom management.
- ▶ Chest clearance techniques.
- ▶ Energy conservation/pacing.
- ▶ Patient support groups.
- ▶ Nutritional advice.
- ▶ Managing travel.
- ▶ Benefits system and welfare rights.
- ▶ Advance directives.
- ▶ Anxiety management and relaxation.
- ▶ Goal setting and rewards.
- ▶ Relaxation.
- ▶ Confidence, self-efficacy and self-management.
- ▶ Identifying and changing beliefs about exercise and health-related behaviours.
- ▶ Loving relationships/sexuality.
- ▶ Exacerbation management (including coping with setbacks and relapses).
- ▶ The benefits of physical exercise.
- ▶ Opportunities to exercise after pulmonary rehabilitation.

The talks should be delivered by members of the pulmonary rehabilitation staff with the opportunity to address questions. Inviting a former pulmonary rehabilitation graduate or member of a local Breathe Easy group should be considered. Supplementing the talks with written educational information is advised.

Patient satisfaction surveys and questionnaires containing disease-specific information (eg, for the Lung Information Needs Questionnaire or the Bristol Chronic Obstructive Pulmonary Disease Knowledge questionnaire) ensure quality of the educational aspects.<sup>210 211</sup>

Supplemental practical information is provided by the service specification for pulmonary rehabilitation at <http://www.dh.gov.uk/health/2012/08/copd-toolkit><sup>209</sup>

## **BTS Guideline on Pulmonary Rehabilitation in adults**

### **Web appendix 1: Clinical Questions**

- **Do patients with COPD who continue to smoke get similar benefit and have similar completion rates from pulmonary rehabilitation compared with ex-smokers? Should they be referred?**
- **Do patients with COPD with chronic respiratory failure get similar benefit from pulmonary rehabilitation compared with those who do not have chronic respiratory failure and is it safe? Should they be referred?**
- **Do patients with COPD with co-existent cardiovascular disease get similar benefit from pulmonary rehabilitation compared with those who do not have cardiovascular disease and is it safe? Should they be referred?**
- **Do patients with COPD with co-existent anxiety and depression get similar benefit from pulmonary rehabilitation compared with those who are not anxious or depressed? Should they be referred?**
- **Do patients with COPD who are MRC grade 2 breathless get similar benefit from pulmonary rehabilitation compared with those with greater breathlessness? Should they be referred?**
- **Do patients with COPD who are MRC grade 5 breathless get similar benefit from pulmonary rehabilitation compared with those with MRC grade 3-4? Should they be referred?**
- **Role of pharmacological agents at referral to pulmonary rehabilitation.**
- **Is once weekly supervised pulmonary rehabilitation as effective at improving exercise performance and health status in patients with chronic respiratory disease when compared with a twice (or thrice) weekly supervised programme?**

- Are pulmonary rehabilitation programmes that are less than 6 weeks in duration equally effective at improving exercise performance and health status in patients with chronic respiratory disease when compared with programmes that are longer or equal to 6 weeks in duration?
- Are rolling programmes of pulmonary rehabilitation equally effective as stand-alone programmes for patients with chronic respiratory disease?
- Are Pulmonary rehabilitation programmes that include resistance training and aerobic training more effective at improving exercise performance in patients with chronic respiratory disease when compared with aerobic training alone.
- Are Pulmonary rehabilitation programmes that include interval training more effective at improving exercise performance in patients with chronic respiratory disease when compared with continuous aerobic training?
- Do pulmonary rehabilitation programmes that include personal goal setting achieve greater improvements in functioning when compared with programmes that do not include personal goal setting?
- In patients with COPD does face to face twice-weekly supervision of pulmonary rehabilitation lead to greater improvements in walk test distance and dyspnoea scores than supervision provided by internet support /manual etc ?
- Does Pulmonary Rehabilitation within one month of discharge improve outcomes in COPD patients hospitalised for acute exacerbations of COPD compared with usual care?
- What is the completion rate of Pulmonary Rehabilitation within one month of hospital discharge in unselected patients compared with elective pulmonary rehabilitation?



- Does a cognitive-behavioural component delivered before commencing rehabilitation improve compliance (adherence / completion) of pulmonary rehabilitation?
- What is the impact of a pulmonary rehabilitation programme on the exercise, physical activity, muscle strength, health status, psychological state, and nutritional status of participants compared with usual care without pulmonary rehabilitation?
- What is the impact of a pulmonary rehabilitation programme on survival of participants compared with usual care without pulmonary rehabilitation?
- In patients with COPD does inspiratory muscle training plus pulmonary rehabilitation lead to greater improvements in exercise tolerance and dyspnoea scores than pulmonary rehabilitation alone?
- In patients with COPD does therapy with hormones / drug / nutraceuticals plus pulmonary rehabilitation lead to greater improvements in walk test distance and dyspnoea scores than pulmonary rehabilitation alone?
- In patients with COPD does non-invasive ventilation (NIV) DURING exercise of pulmonary rehabilitation lead to greater improvements in walk test distance and dyspnoea scores than pulmonary rehabilitation alone in those with type II respiratory failure?
- In patients with COPD does neuromuscular electrical stimulation (NMES) plus pulmonary rehabilitation lead to greater improvements in walk test distance and dyspnoea scores than pulmonary rehabilitation alone?
- In patients with COPD and exercise desaturation does the acute administration of medical gases DURING the exercise component of pulmonary rehabilitation lead to

**greater improvements in walk test distance and dyspnoea scores than pulmonary rehabilitation in room air?**

- **Should pulmonary rehabilitation be repeated? If so, when?**
- **Should maintenance “exercise” be offered following their first pulmonary rehabilitation**
- **Does pulmonary rehabilitation lead to improvement in exercise capacity, health status, breathlessness in adult patients with non-CF bronchiectasis compared with patients with non-CF bronchiectasis that do not undergo rehabilitation?**
- **Does pulmonary rehabilitation lead to improvement in exercise capacity, health status, breathlessness in adult patients with interstitial lung disease compared with patients with interstitial lung disease that do not undergo rehabilitation?**
- **Does pulmonary rehabilitation lead to improvement in exercise capacity, health status, breathlessness in adult patients with asthma compared with patients with asthma that do not undergo rehabilitation?**

## **b) Web appendix: Literature Search details**

Sources to be searched for the guidelines;

Cochrane Database of Systematic Reviews (CDSR)  
Database of Abstracts of Reviews of Effects (DARE)  
MEDLINE  
EMBASE

Dates searched: 1980 onwards

All study types

English language only

Four search strategies used- COPD, bronchiectasis, restrictive lung disease, and asthma.

### **1.COPD search**

#### **Cochrane Library (includes CDSR and DARE)**

<http://www.thecochranelibrary.com>

Searched online 05/08/11

#1 MeSH descriptor Pulmonary Disease, Chronic Obstructive explode all trees 1669

#2 (COPD or "chronic obstructive pulmonary disease" or "pulmonary disease, chronic obstructive"):ti,ab 6357

#3 ("chronic obstructive airway\* disease" or "chronic airflow limitation"):ti,ab 132

#4 ("chronic obstructive lung disease" or "lung disease, chronic obstructive"):ti,ab 786

#5 (#1 OR #2 OR #3 OR #4) 7042

#6 (pulmonary near/3 rehabilitat\*):ti,ab 453

#7 (#5 AND #6) 365

#8 MeSH descriptor Pulmonary Disease, Chronic Obstructive, this term only with qualifier: RH 235

#9 (#7 OR #8) 481

#10 (#7 OR #8), from 1980 to 2011 30

Of 30 results 9 were from Cochrane Database of Systematic Reviews (CDSR) and 21 from Database of Reviews of Effects (DARE).

#### **MEDLINE**

Searched 05/08/11 via OVID interface

Ovid MEDLINE(R) <1948 to July Week 4 2011>

1 exp Pulmonary Disease, Chronic Obstructive/ (16419)

2 (COPD or "chronic obstructive pulmonary disease" or "pulmonary disease, chronic obstructive").ti,ab. (25628)

3 ("chronic obstructive airway\$ disease" or "chronic airflow limitation").ti,ab. (915)

- 4 ("chronic obstructive lung disease" or "lung disease, chronic obstructive").ti,ab. (2494)
- 5 1 or 2 or 3 or 4 (31618)
- 6 (pulmonary adj3 rehabilitat\$).ti,ab. (1507)
- 7 5 and 6 (1023)
- 8 \*Pulmonary Disease, Chronic Obstructive/rh [Rehabilitation] (735)
- 9 7 or 8 (1343)
- 10 limit 9 to (english language and yr="1980 - 2011") (1127)

## EMBASE

Searched 05/08/11 via OVID interface

Embase <1980 to 2011 Week 30>

- 1 exp chronic obstructive lung disease/ (51618)
- 2 (COPD or "chronic obstructive pulmonary disease" or "pulmonary disease, chronic obstructive").ti,ab. (32905)
- 3 ("chronic obstructive airway\$ disease" or "chronic airflow limitation").ti,ab. (1116)
- 4 ("chronic obstructive lung disease" or "lung disease, chronic obstructive").ti,ab. (2956)
- 5 1 or 2 or 3 or 4 (57587)
- 6 (pulmonary adj3 rehabilitat\$).ti,ab. (2037)
- 7 5 and 6 (1508)
- 8 \*chronic obstructive lung disease/rh [Rehabilitation] (1886)
- 9 7 or 8 (2581)
- 10 limit 9 to (english language and yr="1980 - 2011") (1931)

## Results

Database	Results	After deduplication	Custom 4 field
Cochrane Database of Systematic Reviews	9	9	main search Cochrane Database of Systematic Reviews 05/08/11
Database of Abstracts of Reviews of Effects	21	21	main search DARE (non-Cochrane systematic reviews) 05/08/11
MEDLINE	1343	1085	main search Medline 05/08/11
EMBASE	1931	972	main search Embase 05/08/11

<b>Total</b>	<b>3304</b>	<b>2087</b>	
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2087 results saved to Endnote X3 library bts pulmonary rehab.enl

## 2. Bronchiectasis search

### Cochrane Library (includes CDSR and DARE)

<http://www.thecochranelibrary.com>

Searched online 11/08/11

#1 (pulmonary near/3 rehabilitat\*):ti,ab 453

#2 MeSH descriptor Bronchiectasis explode all trees 124

#3 bronchiectasis:ti,ab 240

#4 "kartagener syndrome":ti,ab 0

#5 (#2 OR #3 OR #4) 275

#6 (#1 AND #5), from 1980 to 2011 7

Of 7 results in entire Cochrane Library 1 was from Cochrane Database of Systematic Reviews (CDSR) and none from Database of Reviews of Effects (DARE).

### MEDLINE

Searched 11/08/11 via OVID interface

Ovid MEDLINE(R) <1948 to August Week 1 2011>

1 (pulmonary adj3 rehabilitat\$).ti,ab. (1510)

2 exp Bronchiectasis/ (6778)

3 bronchiectasis.ti,ab. (5128)

4 "kartagener syndrome".ti,ab. (170)

5 2 or 3 or 4 (8706)

6 1 and 5 (17)

7 limit 6 to (english language and yr="1980 - 2011") (13)

### EMBASE

Searched 11/08/11 via OVID interface

Embase <1980 to 2011 Week 31>

1 (pulmonary adj3 rehabilitat\$).ti,ab. (2039)

2 exp Bronchiectasis/ (10031)

3 bronchiectasis.ti,ab. (6097)

4 "kartagener syndrome".ti,ab. (198)

5 2 or 3 or 4 (11405)

6 1 and 5 (37)

7 limit 6 to (english language and yr="1980 - 2011") (30)

## Results

Database	Results	After deduplication	Custom 4 field
Cochrane Database of Systematic Reviews	1	1	Q9 bronchiectasis CDSR 12/08/11
Database of Abstracts of Reviews of Effects	0	0	
MEDLINE	13	12	Q9 bronchiectasis medline 12/08/11
EMBASE	30	16	Q9 bronchiectasis embase 12/08/11
<b>Total</b>	<b>44</b>	<b>29</b>	

29 results saved to Endnote X3 library bts pulmonary rehab.enl were not deduplicated against the results of the COPD, restrictive lung disease or asthma searches.

### 3. Restrictive lung disease search

#### Cochrane Library (includes CDSR and DARE)

<http://www.thecochranelibrary.com>

Searched online 11/08/11

#1 (pulmonary near/3 rehabilitat\*):ti,ab 453

#2 MeSH descriptor Idiopathic Interstitial Pneumonias explode all trees 13

#3 "idiopathic pulmonary fibrosis":ti,ab 127

#4 "Idiopathic interstitial pneumonia":ti,ab 7

#5 MeSH descriptor Sarcoidosis explode all trees 105

#6 sarcoidosis:ti,ab 168

#7 MeSH descriptor Pulmonary Eosinophilia explode all trees 23

#8 "Eosinophilic pneumonia":ti,ab 1

#9 MeSH descriptor Lymphangiomyomatosis explode all trees 4

#10 lymphangiomyomatosis\*:ti,ab 4

#11 MeSH descriptor Histiocytosis, Langerhans-Cell explode all trees 10

#12 "pulmonary Langerhans cell histiocytosis":ti,ab 1

#13 MeSH descriptor Pulmonary Alveolar Proteinosis explode all trees 2

#14 "pulmonary alveolar proteinosis":ti,ab 3

#15 (#2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14) 350

#16 (#1 AND #15), from 1980 to 2011 7

Of 7 results in entire Cochrane Library none were from Cochrane Database of Systematic Reviews (CDSR) or from Database of Reviews of Effects (DARE).

### **MEDLINE**

Searched 11/08/11 via OVID interface

Ovid MEDLINE(R) <1948 to August Week 1 2011>

- 1 (pulmonary adj3 rehabilitat\$).ti,ab. (1510)
- 2 exp Idiopathic Interstitial Pneumonias/ (1240)
- 3 "idiopathic pulmonary fibros\$".ti,ab. (2749)
- 4 "Idiopathic interstitial pneumonia\$".ti,ab. (617)
- 5 exp Sarcoidosis/ (19537)
- 6 sarcoidosis.ti,ab. (16735)
- 7 exp Pulmonary Eosinophilia/ (2141)
- 8 "Eosinophilic pneumonia\$".ti,ab. (796)
- 9 exp Lymphangioliomyomatosis/ (712)
- 10 lymphangioliomyomatosis\$.ti,ab. (832)
- 11 exp Histiocytosis, Langerhans-Cell/ (6349)
- 12 "pulmonary Langerhans\$ cell histiocytosis\$".ti,ab. (159)
- 13 exp Pulmonary Alveolar Proteinosis/ (1181)
- 14 "pulmonary alveolar proteinosis\$".ti,ab. (921)
- 15 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 (35891)
- 16 1 and 15 (16)
- 17 limit 16 to (english language and yr="1980 - 2011") (11)

### **EMBASE**

Searched 11/08/11 via OVID interface

Embase <1980 to 2011 Week 31>

- 1 (pulmonary adj3 rehabilitat\$).ti,ab. (2039)
- 2 exp interstitial pneumonia/ (7074)
- 3 "idiopathic pulmonary fibros\$".ti,ab. (3350)
- 4 "Idiopathic interstitial pneumonia\$".ti,ab. (768)
- 5 exp Sarcoidosis/ (22878)
- 6 sarcoidosis.ti,ab. (18865)
- 7 exp Loeffler pneumonia/ (2462)
- 8 "Eosinophilic pneumonia\$".ti,ab. (977)
- 9 exp lymphangioliomyomatosis/ (1022)

- 10 lymphangioliomyomatosis\$.ti,ab. (980)
- 11 exp histiocytosis X/ (4354)
- 12 "pulmonary Langerhans\$ cell histiocytosis\$.ti,ab. (195)
- 13 exp lung alveolus proteinosis/ (1503)
- 14 "pulmonary alveolar proteinosis\$.ti,ab. (998)
- 15 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 (44441)
- 16 1 and 15 (24)
- 17 limit 16 to (english language and yr="1980 - 2011") (18)

**Results**

Database	Results	After deduplication	Custom 4 field
Cochrane Database of Systematic Reviews	0	0	
Database of Abstracts of Reviews of Effects	0	0	
MEDLINE	11	11	Q9 restrictive lung disease medline 12/08/11
EMBASE	18	8	Q9 restrictive lung disease embase 12/08/11
<b>Total</b>	<b>29</b>	<b>19</b>	

19 results saved to Endnote X3 library bts pulmonary rehab.enl were not deduplicated against the results of the COPD, bronchiectasis or asthma searches.

**4. Asthma search**

**Cochrane Library (includes CDSR and DARE)**

<http://www.thecochranelibrary.com>

Searched online 11/08/11

#1 (pulmonary near/3 rehabilitat\*):ti,ab 453

#2 MeSH descriptor Asthma explode all trees 8569

#3 asthma\*:ti,ab 17864



#4 (#2 OR #3) 18448

#5 (#1 AND #4), from 1980 to 2011 14

Of 14 results in entire Cochrane Library none were from Cochrane Database of Systematic Reviews (CDSR) and 1 was from Database of Reviews of Effects (DARE).

### MEDLINE

Searched 11/08/11 via OVID interface

Ovid MEDLINE(R) <1948 to August Week 1 2011>

- 1 (pulmonary adj3 rehabilitat\$.ti,ab. (1510)
- 2 exp Asthma/ (96007)
- 3 asthma\$.ti,ab. (101127)
- 4 2 or 3 (118985)
- 5 1 and 4 (73)
- 6 limit 5 to (english language and yr="1980 - 2011") (49)

### EMBASE

Searched 11/08/11 via OVID interface

Embase <1980 to 2011 Week 31>

- 1 (pulmonary adj3 rehabilitat\$.ti,ab. (2039)
- 2 exp Asthma/ (147677)
- 3 asthma\$.ti,ab. (124740)
- 4 2 or 3 (165715)
- 5 1 and 4 (122)
- 6 limit 5 to (english language and yr="1980 - 2011") (89)

### Results

Database	Results	After deduplication	Custom 4 field
Cochrane Database of Systematic Reviews	0	0	
Database of Abstracts of Reviews of Effects	1	1	Q9 asthma DARE 12/08/11
MEDLINE	49	47	Q9 asthma medline 12/08/11
EMBASE	89	44	Q9 asthma embase

			12/08/11
<b>Total</b>	<b>139</b>	<b>92</b>	

92 results saved to Endnote X3 library bts pulmonary rehab.enl were not deduplicated against the results of the COPD, bronchiectasis or restrictive lung disease searches.



## **BTS Guideline on Pulmonary Rehabilitation in adults**

### **Web appendix 3: Evidence tables**

The evidence tables can be found as an online appendix at the British Thoracic Society website. See separate document. Abbreviations for the evidence tables are listed in web appendix 4.

**Title: The British Thoracic Society Guideline on Pulmonary Rehabilitation in Adults**

**Short Title: BTS Pulmonary Rehabilitation Guideline**

### **Web Appendix 3 - EVIDENCE TABLES**

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**iii) Web appendix: Evidence tables**

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Ambrosino N, Foglio K, Balzano G, <i>et. al</i> ; Tiotropium Multicentric Italian Study Group. Int J Chron Obstruct Pulmon Dis. 2008; 3(4):771-80.	RCT	1-	234	234 (196 male) patients with COPD – FEV1 1.1(0.4)L; 41(13)% predicted randomised to tiotropium or placebo before pulmonary rehabilitation. 87 tiotropium and 90 placebo patients completed study	Tiotropium  All subjects had 8 week outpatient pulmonary rehabilitation (3 exercise sessions/week).	Placebo	12 weeks after pulmonary rehabilitation	Comparison of group response tiotropium vs. placebo. Outcome measures exercise capacity (6MWT), dyspnoea (TDI) and HRQOL (SGRQ)	Both groups improved 6MWD after pulmonary rehabilitation (27m tiotropium vs. 33m placebo) but no difference between the groups at end of pulmonary rehabilitation or 12 weeks post-pulmonary rehabilitation. Both groups improved TDI after pulmonary rehabilitation (3.6 tiotropium vs. 2.3 placebo) with larger increase in tiotropium (p<0.001). both groups improved SGRQ after pulmonary rehabilitation (-8.1 tiotropium vs. -6.1 placebo) maintained after 12 week follow-up but no difference between groups at either time point	Boehringer Ingelheim and Pfizer Pharmaceuticals (Italy)

Comments: Patients with COPD improve walking distance, dyspnoea and HRQOL with pulmonary rehabilitation. Tiotropium enhances improvement in breathlessness but not walking distance or HRQOL. The randomisation process is unclear (and exact “1:1” raises concern). There is no mention of allocation concealment or blinding methods. The difference in medication use at trial entry meant far more of the placebo arm had medication stopped (ICS/anticholinergics). An ITT analysis is reported in the methods but not undertaken – analysis is neither ITT nor per-protocol and numbers vary by analysis.

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Arnold R, Ranchor AV, Koëter GH, <i>et</i>	Cohort	2-	39	COPD, age 40-80, FEV1<70%, no	Pulmonary rehabilitation	Pre and post	mean duration 20	Rand 36 health survey, Cantril's	Improvements in overall quality of	Not stated

*al. Changes in personal control as a predictor of quality of life after pulmonary rehabilitation. Patient Education and Counselling. 2006; 61: 99–108.*

Comments:

**Bibliographic citation**  
 Baldi S, Aquilani R, Pinna GD, *et al.* Fat-free mass change after nutritional rehabilitation in weight losing COPD: role of insulin, C-reactive protein and tissue hypoxia. *Int J Chron Obstruct Pulmon Dis.* 2010; 5: 29-39.

psychiatric illness in previous year

weeks

ladder, Mastery scale of Pearlin and Schooler, Self-efficacy scale of Sullivan et al

life and self-efficacy. No change in mastery, symptoms of COPD

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Baldi S, Aquilani R, Pinna GD, <i>et al.</i> Fat-free mass change after nutritional rehabilitation in weight losing COPD: role of insulin, C-reactive protein and tissue hypoxia. <i>Int J Chron Obstruct Pulmon Dis.</i> 2010; 5: 29-39.	RCT	1-	28 subjects; Intervention group; 14 (13 analysed) Control group; 14 (13 analysed)	COPD diagnosis, >5% weight loss in previous 6 months, clinically stable	4 grams of essential amino acid (EAA) solution x 2 / day with an initial 4 week inpatient and then 8 week outpatient pulmonary rehabilitation programme.	4 week inpatient and then 8 week outpatient pulmonary rehabilitation programme	12 weeks.	Body weight, FFM Change in FFM in contrast to fasting insulin plasma levels, (CRP) and oxygen extraction tension.	Body weight; EAA group average increase of 3.8kg +/- 2.6kg (p 0.0002) and – 0.1kg +/- 1.1kg (p 0.81) in Control group. FFM; EAA group average increase of 1.5kg +/- 2.6kg (p 0.05) and –0.1kg +/- 2.3kg in Control group (p 0.94). In EAA group FFM significantly related to fasting insulin (r2 = 0.68, p <0.0005), CRP (r2 = 0.46, p <0.01) and oxygen extraction tension (r2 = 0.46, p <0.01).	Not stated

Comments: No details of randomising process. No details of compliance regarding home based pulmonary rehabilitation programme. Results not ITT.

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Bernard S, Whitton F, Leblanc P, <i>et al.</i> Aerobic and strength training in patients with COPD. <i>Am J Resp Crit Care</i>	RT Reviewed in O'Shea systematic review	1+	45 (36 completed)	Mod – severe COPD	12 week Combination of aerobic training and strength training X 3 sessions per week.	12 week aerobic training alone	12 weeks	Peripheral muscle strength and composition, 6MWD, HRQOL	Small non-significant trend towards improvement in walking distance. Sig increase in muscle strength.	Supported in part by the Fonds de la Recherche en Santé du Québec and by la Fondation J. D. Bégin, Université



Med. 1999; 159(3):  
896 – 901.

No improvement  
in HRQOL

Laval.

Comments: No concealment of treatment allocation

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Berry MJ, Rejeski WJ, Miller ME, <i>et al.</i> A lifestyle activity intervention in patients with chronic obstructive pulmonary disease. <i>Respiratory Medicine.</i> 2010; 104: 829-839.	RCT (single blinded)	1-	176 randomised:  intervention group= 87 control group= 89.	FEV1/FVC ≤70%, FEV1 ≥20% pred. Reported difficulty in performing at least one of several daily activities (listed in paper) due to dyspnoea. Number of exclusions including severe CV disease, no active treatment for cancer, not participated in a pulmonary rehabilitation or exercise programme in the previous 3 months	Lifestyle activity programme (LAP).	Traditional exercise treatment (TET)	12 months	<b>Primary outcome;</b> Moderate physical activity (kcal / week). <b>Secondary outcomes;</b> Physical function (6 MWT, stair climb time, Short physical performance battery (SPPB), Self-reported disability, Health related QOL (CRDQ, CESD, SF-36). Exercise capacity via VO2 peak and total time during graded exercise test on treadmill.	No significant 'between group' differences seen at 12 month follow up.	Supported grants HL 53755, AG 21332 and M01 RR07122 from the National Institutes of Health

Comments: Well written although appears to have lost power. Single blinded. Results not ITT. Study patients pre assessed prior to randomisation to select most motivated to complete self-monitoring over 12 months.

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Berry MJ, Adair NE, Sevensky KS <i>et al.</i> Inspiratory Muscle Training and Whole Body Reconditioning in chronic obstructive pulmonary disease. <i>Am J Respir Crit Care Med.</i> 1996; 153:1812-6	RCT	1+	25 total: 8 IMT & GER, 9 GER, 8 flexibility exercise and sham IMT	Mild to moderate COPD by usual definitions	GER: individualised strength and aerobic exercise plan thrice weekly over 12 weeks; IMT: threshold trainer at increasing % to 80% P <sub>Imax</sub>	Flexibility exercises, breathing exercises, IMT at 15% P <sub>Imax</sub>	End of intervention	Pimax; CPEX outcomes; 12 MWT; dyspnoea score	12 MWT increases of 400 ft in both active arms. No change in dyspnoea scores or CPEX parameters.	Charity

Comments: 2 drop-outs from this small study, similar baseline characteristics. Blinding described but not randomisation process. Analyses strategy appropriate.

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Borg-Silva A,	RCT	1-	16 patients (10 male);	Stable COPD,	2g oral L-	Saline solution	6 weeks	Nutritional status,	Blood lactate,	L-carnitine partly

**Baldissera V, Sampaio LMM, et al. L-Carnitine as an ergogenic aid for patients with chronic obstructive pulmonary disease submitted to whole-body and respiratory muscle training programs. Brazilian Journal of Medical and Biological Research. 2006; 39: 465-474.**

8 in intervention group  
8 in control group.

FEV1 <50% / FVC <70% predicted and clinical history consistent with COPD

carnitine daily

“similar in colour, shape and taste” to L-carnitine. (Dose not specified).

exercise tolerance on a treadmill and 6MWD, blood lactate, heart rate, blood pressure, respiratory muscle strength.

blood pressure, oxygen saturation, heart rate at identical exercise levels lower in intervention group post training (p <0.05) Increases in PImax sig greater in intervention group v control (40+/- 14 vs. 14 +/- 5 cm H2O p<0.05). Increases in 6MWD sig improved in intervention group v control (87 +/- 30 vs. 34 +/- 29m p<0.05). Blood lactate concentration was sig lower in intervention group v control (1.6 +/- 0.7 vs. 2.3 +/- 0.7 Mm/L, p<0.05)

supplied by Sinto-farma as a donation and additional Sintofarma L-carnitine supplies funded by FAPESP (No. 00/00311-6)

**Comments: Randomising process poorly detailed, study workers not blinded, risk of recall bias when using diet history recall. Anthropometric measurements (Tricep skin fold (TSF) and mid-arm circumference (MAC)) carried out although not stated if same worker completed all measurements.**

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Borghi-Silva A, Mendes RG, Toledo AC, et al. Adjuncts to physical training of patients with severe COPD: Oxygen or noninvasive ventilation? Respiratory Care. 2010; 55(7):885-94.	RCT	1-	28 randomised; 24 completed	GOLD 3 or 4 COPD	Supplemental oxygen via NS to keep SpO2>90% plus pulmonary rehabilitation for 6 weeks	Bi-level pressure support NIV (at maximum pressures tolerated) plus pulmonary rehabilitation for 6 weeks	End of pulmonary rehabilitation	6MWT; SGRQ; CPEX; knee extension power /endurance	74m additional increase (mean) in 6MWT; no difference in leg power, SGRQ, or VO2max.	Not stated
<b>Comments: The study was small and not blinded.</b>										
Bibliographic	Study	Ev lev	Number patients	Patient	Intervention	Comparison	Length of	Outcome measures	Effect size	Source of funding

<b>citation</b>	<b>type</b>			<b>characteristics</b>		<b>follow up</b>				
<b>Broekhuizen R, Wouters EFM, Creutzberg EC, et al. Polyunsaturated fatty acids improve exercise capacity in chronic obstructive pulmonary disease. Thorax. 2005; 60: 376-382.</b>	RCT double blinded	1-	Total; 102 Intervention; 51 (38 completed) Placebo; 51(42 completed)	Clinically stable GOLD stage II-IV	Polyunsaturated fatty acids PUFA's; Dose 9 g / day (containing 1.04g EPA & DHA)	Placebo; 9g daily containing 80% palm oil and 20% sunflower oil, iso-calorific as PUFA intervention arm	8 weeks	Body composition, Functional capacity; (Lung function, Incremental cycle ergometry test, submaximal cycle test, isokinetic quadriceps strength) Inflammatory markers; CRP, (IL)-6, TNF.	Comparison of intervention vs. placebo; Peak load of incremental exercise test increased in PUFA group more than placebo; (mean diff +9.7W, p=0.009). PUFA group; Greater duration of constant work rate (mean diff +4.3 minutes, p 0.023)	Supported by Numico Research BV

**Comments: No details of randomisation process. High drop-out rate of 25% in intervention group. Results not ITT.**

<b>Bibliographic citation</b>	<b>Study type</b>	<b>Ev lev</b>	<b>Number patients</b>	<b>Patient characteristics</b>	<b>Intervention</b>	<b>Comparison</b>	<b>Length of follow up</b>	<b>Outcome measures</b>	<b>Effect size</b>	<b>Source of funding</b>
<b>Broekhuizen R, Creutzberg EC, Weling-Scheepers CA et al. Optimizing oral nutritional drink supplementation in patients with chronic obstructive pulmonary disease. British Journal of Nutrition. 2005; 93: 965-971.</b>	Non-RCT	2-	39 subjects (group A; n=19 Group B; n=20)	Stable COPD, admitted consecutively to inpatient pulmonary rehabilitation unit and requiring nutritional support + at least one of following: BMI equal to or below 21 kg/m2 FFMI equal to or below 16 (men)/ 15 (women) kg/m2 BMI equal to or below 25 kg/m2 & weight loss equal to or over 5% in 1 month or equal to or above 10% in 6 months prior to admission to pulmonary	Group A; x 3 125 ml cartons Respifor supplement drinks daily (2380kJ, 20% energy from protein, 60% from carbohydrate, 20% from fat)	X 3 200 ml cartons supplement drinks daily (3350 kJ, 22.3% energy from protein, 59.7% from carbohydrate, 18% from fat)	8 weeks	Body composition (weight, FFM, fat mass (FM)) Lung function (FEV1) Exercise capacity (incremental bicycle ergometry test) Health status (SGRQ)	Between group results; Group A gained more weight than group B (3.3kg vs. 2.0 kg respectively; p 0.019)	Nutritional supplements provided by Numico Research BV

rehabilitation  
centre.

**Comments:** Study carried out between years 1995-97 (group B), 2000-2002 (Group A) not detailed if hospital menu changed across this time period. Body composition obtained via bioelectrical impedance indicating a possible source of bias (no details of protocol used to minimise bias during measurements). No indication if trial was blinded. Study does not indicate amount of supplements consumed/ not consumed over 8 weeks.

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Brooks D, Krip B, Mangovski-Alzamora S, Goldstein RS. The effect of post rehabilitation programmes among individuals with chronic obstructive pulmonary disease. Eur Resp J. 2002; 20(1):20-9.	RCT	1-	Total 109 patients, 50 in intervention group and 59 in control group. Completers = 18 in intervention group and 23 in control group	Severe stable COPD <40%. Completion of pulmonary rehab programme Non-Smoker 49-85 years Exclusions – co morbidities impacting on exercise tolerance or cognitive functioning, non-compliance, non English speaking, NIV, living too far away.	Enhanced 12 m follow up, patients attended 2 hour monthly support sessions, supervised exercise and group discussion. Between these sessions patients had phone call from physiotherapist to discuss programme adherence and any concerns.	Conventional follow up had therapist contact every 3 months for 12 months where they were asked standardized questions re their illness and hospitalization s. Individuals encouraged to continue or resume exercise programmes and identify concerns to therapist	3,6,9 ,and 12 months	6MWD CRDQ SGRQ	No difference between either group after 1 year. Walking distances improved in study group at 6 months but went back to the same after 12 months.	Not stated

**Comments:** The authors conclude that all patients who completed a pulmonary rehabilitation programme had deteriorated by 12 months in terms of exercise tolerance and HRQOL. Poor post programme compliance appeared to be a factor which was not improved by an enhanced contact with Health Care Professionals. As there is no agreed definition of pulmonary rehabilitation maintenance, we need to establish the dose response of maintenance. Monthly group sessions in this study had limited effectiveness. Large drop out in both groups after 6 months. Conventional group received monthly visits at home.

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Cambach W, Chadwick-Straver RV, Wagenaar RC, et al. The effects of a community-based pulmonary rehabilitation programme on exercise tolerance and quality of life: a randomised control trial. Eur Resp J. 1997;	RCT cross over study	1 -	99 patients from 8 practices. 43 of the 66 who completed were asthmatic	Pulmonary rehabilitation conducted in local physiotherapy practices in Netherlands.	Pulmonary rehabilitation including drug treatment	Drug treatment alone.	3 & 6 months	Incremental cycle ergometer test; submaximal cycle ergometer test; 6MWT; CRDQ	6MWD in asthma group alone: Pulmonary rehabilitation-Control (n=18) change in 6MWD at 3 months 63 (89)m Control – pulmonary rehabilitation n= 17 8 (63)m	National Health Insurance Council. Glaxo provided peak flow meters

10:104-113.

Comments: Small numbers of asthma patients entered into study. Of 99 patients with asthma and COPD 66 completed. Patients were seen in small groups of 3 or 4 which may not be that representative of UK programmes and the rehabilitation was delivered for 90 minutes over a 3 month period, again not reflective of UK programmes. COPD patients in the pulmonary rehabilitation – Control arm showed little benefit compared with COPD patients in the control- pulmonary rehabilitation arm suggesting there may be problems with the programme itself, however differences for the asthma group were substantive in benefit of rehab. Randomisation was carried out within individual practices using block randomisation and sealed envelopes leading to possible randomisation bias due to localities. Diagnosis as to whether COPD or asthma made a posteriori. No power calculation.

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Carone M, Patessio A, Ambrosino N, et al. Efficacy of pulmonary rehabilitation in chronic respiratory failure (CRF) due to chronic obstructive pulmonary disease (COPD) : The Maugeri Study. <i>Resp Med.</i> 2007; 101 (12):2447-2453.	Cohort	3	1130	855 male and 192 female patients with COPD. 720 did not have CRF and 327 had CRF (defined as a PaO <sub>2</sub> <8kPa, PaCO <sub>2</sub> >6kPa or both). Mean FEV1 47% in non-CRF group and 39% in CRF.	All subjects	Subjects completed “tailored” inpatient pulmonary rehabilitation exercising 5 x/week	NA	Comparison of group response based on presence or absence of chronic respiratory failure. Outcome measures (6MWD), breathlessness (MRC score and TDI) and quality of life (SGRQ)	No significant difference in main outcomes when CRF and non-CRF patients are compared. 6MWD improvement 48(4) m CRF vs. 48(3) m non-CRF. MRC improvement 0.85(0.06) CRF vs. 0.73(0.03) non-CRF. TDI improvement 9.7(0.15) CRF vs. 3.8(0.1) non-CRF. SGRQ improvement 8.3(1.5) CRF vs. 10.1(0.6) non-CRF	Italian Ministry of Health

Comments: COPD patients with CRF gained similar benefits from a not clearly defined pulmonary rehabilitation programme compared with patients without CRF

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Carr S J, Hill K, Brooks D, Goldstein RS. Pulmonary rehabilitation after acute exacerbation of chronic obstructive pulmonary disease in patients who previously completed a pulmonary rehabilitation	RCT	1-	33 (28 completed)	COPD patients who had undergone pulmonary rehabilitation. Followed-up and randomised if exacerbation occurred.	3 week pulmonary rehab course	Usual care	7 weeks post second pulmonary rehabilitation course	CRDQ; 6MWT	No difference in per protocol analysis. Exclusion of those with further exacerbation suggested small improvement in dyspnoea (no change in 6MWD).	Not stated

program. J  
 Cardiopulm Rehab  
 Prev. 2009;  
 29(5):318-24.  
 Comments:

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Casaburi R, Kukafka D, Cooper CB. <i>et al.</i> Improvement in exercise tolerance with the combination of tiotropium and pulmonary rehabilitation in patients with COPD. Chest. 2005; 127 (3): 809-817.	RCT	1-	126	Patients with COPD – 57% male, FEV1 0.88(0.36) L; 34(12) % predicted – randomised to pulmonary rehabilitation with or without tiotropium. 47 tiotropium and 44 control subjects completed study	All subjects	8 week outpatient pulmonary rehabilitation with 3 supervised exercise sessions/week. Randomised to tiotropium or placebo which was taken 5 weeks before, during and 12 weeks after pulmonary rehabilitation	12 weeks	Comparison of group response based on taking tiotropium or placebo. Outcome measures endurance exercise time (minutes) on self-limited constant load treadmill test set to 80% of peak achieved on incremental treadmill test, dyspnoea (TDI) and HRQOL (SGRQ)	Tiotropium patients endurance exercise time increased 5.35 minutes greater than placebo at end of pulmonary rehabilitation and 6.6 minutes greater than placebo at 12 weeks post-pulmonary rehabilitation (both p<0.05). TDI scores not significantly different at end of pulmonary rehabilitation but 1.67 greater improvement with tiotropium compared with placebo at 12 weeks post-pulmonary rehabilitation (p<0.05). SGRQ score 4 point greater improvement tiotropium vs. placebo at end of pulmonary rehabilitation and 12 weeks post-	Boehringer Ingelheim and Pfizer Pharmaceuticals

pulmonary rehabilitation but not significantly different

Comments: The addition of tiotropium to other bronchodilator therapy before, during and after pulmonary rehabilitation leads to greater improvement in exercise capacity after pulmonary rehabilitation and greater improvement in exercise capacity and dyspnoea 12 weeks post-pulmonary rehabilitation. Randomisation, allocation concealment, and blinding are not adequately reported. One caution (acknowledged by the authors) is that they use parametric statistics for skewed censored data – the one analysis they include using a non-parametric approach reduced the number of significant findings. However, the results are consistent across measures and the effect size is large.

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Casaburi R, Bhasin S, Cosentino L, <i>et al.</i> Effects of Testosterone and Resistance Training in Men with Chronic Obstructive Pulmonary Disease. <i>Am J Respir Crit Care Med.</i> 2004; 170 (8):870-8.	RCT	1+	53 (all men) (47 completed) (11 testosterone + training, 12 testosterone alone 12 placebo + training, 12 placebo alone	Age 55 to 80 years, FEV1 of 60% predicted or less, and FEV1 to vital capacity ratio of 60% or less. serum testosterone was 400 ng/dl or less. Exclusion criteria significant cardiovascular or orthopaedic impairments, body weight of less than 75% or more than 130% of ideal, symptomatic benign prostatic hypertrophy, prostate cancer history, serum prostate specific antigen of more than 4 µg/L, or haemoglobin of more than 16 g/dl.	Strength training and/or testosterone supplementation (100mg IM)	Resistance training, Resistance training + testosterone, placebo, Testosterone	10 weeks	Strength, muscle mass, exercise endurance, blood markers, lung function	Lean body mass; Testosterone alone increased 2.2kg (p<0.001) Testosterone + training increased 3.3kg (p<0.001) Maximum leg press strength; Testosterone alone increase 17.2%, Placebo + training increase 17.4%, Testosterone + training 26.8% (p<0.001)	California Tobacco-Related Disease Research Programme, grant number 6RT-036, the resources of the General Clinical Research Centre, grant M01-RR00425 of the National Center for Research Resources, and the BioTechnology General Corporation (Iselin, NJ)
Comments: Men only										
Cindy Ng LW, Mackney J, Jenkins S, Hill K. Does	Systematic review and	2++	Randomised trials n=201, Single arm intervention n=266.	COPD, Original paper in English, Minimum 4	Exercise training	N/A	6 weeks to 6 months	Physical activity in absolute values (e.g. steps, activity count)	Statistically significant, but clinically small	None

exercise training change physical activity in people with COPD? A systematic review and meta-analysis. *Chronic Respiratory Disease*. 2012; 9:17-26.

meta-analysis (cohort studies, case-control studies)

weeks exercise therapy, used physical activity monitor.

increase in physical activity (Effect size 0.12)

<b>Bibliographic citation</b>	<b>Study type</b>	<b>Ev lev</b>	<b>Number patients</b>	<b>Patient characteristics</b>	<b>Intervention</b>	<b>Comparison</b>	<b>Length of follow up</b>	<b>Outcome measures</b>	<b>Effect size</b>	<b>Source of funding</b>
Clark CJ, Cochrane L, Mackay E. Low intensity peripheral muscle conditioning improves exercise tolerance and breathlessness in COPD. <i>Eur Respir J</i> . 1996; 9(12):2590-6. Comments: Training programme likely insufficient	RCT	1-	10 (sub-group of 48 patients)	COPD. 58 years old, FEV1 67% predicted	The Hairmyres home exercise programme	Usual care	12 weeks	Peripheral muscle endurance, peripheral muscle strength, whole body endurance, aerobic capacity	No effect	Not stated
Clark CJ, Cochrane LM, Mackay E, Paton B. Skeletal muscle strength and endurance in patients with mild COPD and the effects of weight training. <i>Eur Respir J</i> . 2000; 15(1):92-7. Comments:	RCT	1+	43	49 years, FEV1 77%	10 x 8 reps of 70% maximum. All major muscle groups	Control group	12 weeks	Isokinetic muscle strength. Endurance walk. Isotonic muscle strength (1RM)	Increase in isotonic strength (quadriceps 7.6 Kg), increase in isokinetic strength. Increase in endurance walk test.	Not stated
Costes F, Agresti A, Court-Fortune I, et al. Noninvasive ventilation during exercise training improves exercise tolerance in	RCT	1-	7 controls 7 intervention	COPD FEV1 31.5% predicted mean age 63 years	NIV during pulmonary rehabilitation programme	Unassisted training programme	before and after pulmonary rehabilitation programme	Exercise capacity at steady state in incremental test NIV increased exercise tolerance, reduced dyspnoea, and prevented exercise-	Improvement in peak VO2 18% vs. 2% p<0.05 ns change in constant work load duration and in lactate levels	Not stated



patients with COPD. Journal of Cardiopulmonary rehabilitation. 2003;23:307-313.

Comments: Pilot, un blinded study, very small numbers.

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Coventry PA, Hind D. Comprehensive pulmonary rehabilitation for anxiety and depression in adults with chronic obstructive pulmonary disease: Systematic review and meta-analysis Journal of Psychosomatic Research. 2007; 63:551–565.	Systematic review and meta-analysis	1+	269	Clinically stable, age >18, 80% patients at least with moderate to severe COPD	Comprehensive pulmonary rehabilitation	Usual care	10 weeks to 1 year	CES-D depression, SCL-90 R, STAI state anxiety, HADS	-0.33 SMD for anxiety, -0.58 SMD for depression	Medical Research Council Special Training Fellowship in Health Services Research

Comments:

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Creutzberg EC, Wouters EF, Mostert R, <i>et al.</i> A role for anabolic steroids in the rehabilitation of patients with COPD? A double blind placebo controlled randomised trial. Chest. 2003;124:1733-42.	RCT	1+	63 (63 male) 33 intervention (19 maintenance low dose oral glucocorticosteroids), 30 placebo (12 maintenance low dose glucocorticosteroids)	Consecutively admitted to pulmonary rehabilitation, COPD, inpatients FEV1 <70% with an increase in FEV1 of <10% after inhalation of a B2-agonist. Clinically stable	50 mg Nandrolone deconoate (ND) in 1 mL arachis oil IM injection day 1, 15, 29, 43	1 mL arachis oil	8 weeks	Body composition, Muscle function, exercise performance, Health status, erythropoietic parameters	Fat free mass (mean); ND +1.7kg, placebo +0.3kg (p=0.015). Intracellular mass (mean); ND +1.8 kg placebo -0.5 kg (p=0.002) Patients receiving low-dose oral glucocorticosteroids; Max inspiratory muscle strength; ND +6.0 cm H2O v -2.18 cm H2O (p=0.046) Peak workload; ND 20.47W v placebo 4.8W (p=0.023)	Supported by NV Organon

induced oxygen desaturation both before and after training

Comments: Good detail of randomised process.

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Crisafulli E, Costi S, Luppi F, <i>et al.</i> Role of comorbidities in a cohort with COPD undergoing pulmonary rehabilitation. <i>Thorax.</i> 2008; 63:487-492.	Cohort	3	2962	2150 male and 812 female patients with COPD (FEV1 49(15)% predicted. Co-morbidity defined using the Charlson index. Groups were divided into Charlson score 0, 1, 2 and >2. Heart disease defined by the presence or absence of CHF and/or IHD	All subjects	A minimum of 15 inpatient or outpatient pulmonary rehabilitation sessions	NA	Comparison of group response based on level of co-morbidity. 51% had Charlson score of 0, 38% had a Charlson score of 1, 11% had a Charlson score of 2 and 2% had a Charlson score of >2. Outcome measures exercise capacity (6MWD), breathlessness (MRC score) and quality of life (SGRQ)	Using multiple logistic regression analysis patients with a higher Charlson index were less likely to gain a 54 m improvement in 6MWD (OR 0.72 (0.54-0.98), p<0.03) and gain a 4 point improvement in SGRQ (OR 0.51(0.38-0.68), p<0.001). Patients with heart disease were more likely to improve 6MWD (OR 2.36 (1.85-3.01), p<0.001) but less likely to improve SGRQ (OR 0.67 (0.55-0.83, p<0.001)	Not stated

Comments: The vast majority of COPD patients with or without co-morbidity or heart disease gain significant improvement in 6MWD, MRC score and SGRQ after pulmonary rehabilitation. However, the presence of more co-morbidity is associated with a modest reduction in 6MWD and SGRQ but not MRC score improvement. Heart disease is associated with a greater 6MWD improvement but poorer SGRQ improvement

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Crisafulli E, Gorgone P, Vagaggini B, <i>et al.</i> Effect of standard rehabilitation in COPD outpatients with comorbidities. <i>Eur Resp J.</i> 2010; 36 (5):1042-1048.	Cohort	3	316	235 male and 81 female patients with COPD (FEV1 50(14)% predicted. Co-morbidity defined using the Charlson index. Groups were divided into Charlson score 0, 1, 2+. Heart disease defined by the presence	All subjects	8 week pulmonary rehabilitation with 3 hour+ session x 3/week. Minimum 21 sessions attended	NA	Comparison of the proportion of patients gaining a 54 m improvement in 6MWD, a 1 point improvement in MRC score and a 4 point improvement in SGRQ. Groups divided according to Charlson score of 0 (38%), 1 (34%) and 2+ (28%) and heart disease – 21% had	Using multiple logistic regression analysis co-morbidity and heart disease was not related to improvement in 6MWD and SGRQ after pulmonary rehabilitation. Fewer (61%) of patients with 0 co-morbidity achieved a 1 point	Not stated

or absence of  
CHF and/or IHD

heart disease

improvement in  
MRC score  
compared to  
patients with 1  
(84%) and 2+  
(70%) co-  
morbidity. Heart  
disease was  
unrelated to MRC  
improvement

**Comments: Patients with more co-morbidities and heart disease are at least as likely to gain improvement in walking distance, breathlessness and quality of life after pulmonary rehabilitation.**

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Deacon S, Vincent EE, Greenhaff PL <i>et al.</i> Randomized Controlled Trial of Dietary Creatine as an Adjunct Therapy to Physical Training in Chronic Obstructive Pulmonary Disease. <i>Am J Respir Crit Care Med.</i> 2008; 178:233–239.	RCT	1+	80	"COPD patients" - no spirometric or history criteria - undergoing pulmonary rehabilitation	Loaded for 5 days with 22 g Creatine daily in four divided doses, followed by maintenance dose during PR of 3.76 g Creatine daily	Loading of 24g lactose daily in divided doses followed by a maintenance of 4g lactose daily	8 weeks (end of pulmonary rehabilitation )	ISWT, ESWT, FFM, muscle strength, CRDQ, muscle creatine	No significant differences seen	Charity: British Lung Foundation

**Comments: A well conducted study. Claims of a definitive answer are tempered by the low power of the study (powered to detect a doubling of the effect of pulmonary rehabilitation).**

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
de Blok BMJ, de Greef MHG, ten Hacken NHT, <i>et al.</i> The effects of a lifestyle physical activity counselling program with feedback of a pedometer during pulmonary rehabilitation in patients with COPD: A pilot study. <i>Patient Education and</i>	RCT	1-	21 enrolled. 16 completed (per protocol analysis)	Diagnosis of COPD, age 40-85. Literate in Dutch	Lifestyle physical activity counselling programme with pedometer+ pulmonary rehabilitation	Regular pulmonary rehabilitation programme	9 weeks	Daily physical activity (Primary). Physical fitness, HRQOL, ADLs, Depression, Self-efficacy (secondary)	No statistically significant difference between groups. . Control group increased by 19%, Intervention group by 69%)	Not stated

Counselling. 2006; 61: 48–55.

Comments:

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Dourado VZ, Tanni SE, Antunes LCO, <i>et al.</i> Effect of three exercise programs on patients with chronic obstructive pulmonary disease. Brazilian Journal of Medical and Biological Research. 2009; 42: 263-271.	Randomised to 3 different treatment groups	1-	47	COPD. Acute exacerbation excluded and co-morbidity i.e. cardio vascular disease excluded.	Strength training	Strength training (ST) vs. general low intensity training (LGT) vs. combination training (CT)	12 weeks	6MWD, AQ20, FEV1, BMI, FFM, SGRQ. Muscle strength, functional fitness	In the ST and CT groups, an additional improvement in 1-RM values was shown (P < 0.05) compared to the LGT group (ST = 10 ± 6 to 57 ± 36 kg; CT = 6 ± 2 to 38 ± 16 kg; LGT = 1 ± 2 to 16 ± 12 kg). The addition of strength training to low intensity general training increased muscle strength; however, it produced no additional improvement in walking endurance, dyspnoea or quality of life	Not stated

Comments:

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
du Moulin M, Taube K, Wegscheider K, <i>et al.</i> Home-based exercise training as maintenance after outpatient pulmonary rehabilitation. Respiration. 2009; 77:139-145.	RCT	1-	20 patients recruited. 8 completers.	Only patients not planning to attend other forms of maintenance were included. Moderate COPD – FEV1 50 – 80% Exclusions – significant co-morbidity	Individualised training plan – to walk 125% of last 6MWD 3 x days or combined into 1 walk a day. Home based setting. Telephone contact 4 weekly for motivation.	Control groups no instruction re physical activity.	Baseline (completion of pulmonary rehabilitation programme), 3 and 6 months	Primary outcome 6MWD. Secondary endpoints – HRQOL (CRDQ), lung function (FEV1).	Significantly better 6MWD (p= 0.033), CRDQ scores (p= 0.027) and FEV1 (p= 0.007) in intervention group	Not stated

Comments: The authors conclude that their maintenance strategy had a significant effect on health outcomes in patients with moderate COPD. The initial out-patient pulmonary rehabilitation programme was only 3 weeks. The authors argue that short, intensive programmes are effective and commonplace in the German healthcare system. Outcomes were only measured up to 6 months, so we are not able to see the longer term effect of the intervention. The authors acknowledge the very small study sample and report that recruitment was difficult. The study was insufficiently powered, with only 10 patients in each arm. There was a very high dropout percentage of 60% in each arm. The authors suggest that as results were analysed using ITT, the effect size may have been larger. Only patients with moderate COPD not planning to attend other maintenance programmes were included, so results are only generalisable to a sub-group of patients graduating from a pulmonary rehabilitation programme. The authors report that maintenance groups are readily available to graduates of their programme, so it is possible that this group was less motivated than a cross section of all patients completing pulmonary rehabilitation. The control group may, therefore have been more likely to decline faster than a cross section, as they may not be motivated to continue with an active lifestyle per se. The reported improvements in 6MWD and CRDQ in the intervention group are below the level of clinical relevance. Despite these limitations, the unsupervised home exercise appears to, at the least; maintain the effects of a pulmonary rehabilitation.

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Dyer F, Callaghan J, Cheema K, Bott J. Ambulatory oxygen improves the effectiveness of pulmonary rehabilitation in selected patients with Chronic Obstructive Pulmonary Disease. Chronic Respiratory Disease. 2012; 9 (2):83-91.	RCT	1-	55 randomised, 47 completed.	“patients with COPD” not using home oxygen meeting criteria for ambulatory oxygen	Pulmonary rehabilitation sessions twice weekly for 7 weeks with supplemental oxygen 2-6 litres.	Pulmonary rehabilitation only (no placebo)	End of pulmonary rehabilitation	ESWT; HADS; CRDQ	Major improvements in ESWT – O2 group improved almost 1 km through pulmonary rehabilitation. Additional benefit of 0.5 km versus room air group. No change in CRDQ or HADS	Charity

Comments: Small study (underpowered for clinically expected difference and sample size calculation not inflated for expected drop-outs). Randomisation process is described but only the walk test assessor was blinded (not participants/other authors/statistical analysis). No placebo was used for the standard care group, though they were assessed using an oxygen cylinder in the final walk test.

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Emtner M, Porszasz J, Burns M, et al Benefits of Supplemental Oxygen in Exercise Training in Nonhypoxemic Chronic Obstructive Pulmonary Disease Patients. Am J Respir Crit Care Med. 2003; 168:1034–1042.	RCT	1+	29	COPD with FEV1<50%. Not hypoxaemic at rest.	7 week pulmonary rehabilitation programme; 3 l/min oxygen during exercise	7 week pulmonary rehabilitation programme; 3 l/min air during exercise	End of pulmonary rehabilitation	CPEX (incremental and constant tests in air and with 30% O2); ABG; lung volumes & transfer capacity; CRDQ; SF-36	10% additional reduction in respiratory rate at isotime; four SF-36 sections showed improvement with oxygen versus one with air. No additional improvement in the great majority of parameters measured	Charity

Comments: Largely a well conducted/described study. The discussion and abstract perhaps overstate the additional benefit of supplemental oxygen seen in the study.

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Evans RA, Singh SJ, Collier R, <i>et al.</i> Pulmonary Rehabilitation is successful for COPD irrespective of MRC dyspnoea grade. <i>Resp Med.</i> 2009; 103 (7):1070-1075.	Cohort	3	450	55% male patients with COPD (FEV1 40(18)% predicted; 1.0(0.5)L of who 395 (85%) completed pulmonary rehabilitation. MRC2 = 15%, MRC3 = 25%, MRC4 = 27% and MRC5 = 32%	All subjects	7 weeks outpatient PR – 2 week supervised sessions and daily home exercise	NA	Comparison of group response based on MRC2 vs. MRC3, 4 or 5. Outcome measure exercise capacity (ISWT)	No significant difference in change in exercise capacity in MRC2 vs. MRC3, 4 and 5. Median (IQR) improvement 66(50-83)m in MRC2 vs. 63(50-75)m MRC3 vs. 59(49-70)m MRC4 vs. 54(43-64) MRC5	Not stated

Comments: After completion of pulmonary rehabilitation patients with baseline MRC2 dyspnoea gain similar improvement in walking distance and breathlessness as MRC3, 4 and 5 patients

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Faager G, Söderland K, Skold CM, <i>et al.</i> Creatine supplementation and physical training in patients with COPD: A double blind, placebo-controlled study. <i>International Journal of COPD.</i> 2006; 1(4): 445–453.	RCT	1-	23	COPD by BTS criteria	Oral creatine. Creatine dose was 0.3 g/kg body weight/day during seven days and then 0.07 g/kg body weight/day during the remaining 7 weeks	Oral glucose powder - dose not described	8 weeks	ESWT, FEV1, muscle strength (grip and knee extensor)	No significant differences seen	Not stated

Comments: A small study reduced further in power by some outcomes having been assessed only in a subset. Randomisation and blinding not adequately described.

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Fernandez AM, Pascual J, Ferrando C, <i>et al.</i> Home-based pulmonary rehabilitation in very severe COPD: is it safe and useful? <i>Journal of</i>	RCT	1-	42 (Intervention=27, control=15)	GOLD 4 COPD, on LTOT, no severe CVS co-morbidity, <80 years, Clinically stable for 2/12	2 initial hospital sessions, then 5/week home based unsupervised exercise, twice a month visits for first 2 months.	Control group (though received education)	1 year	Pulmonary function tests, 6MWT, SGRQ	Significant improvement in 6MWT, SGRQ at one year in rehab group	Not stated

**Cardiopulmonary Rehabilitation & Prevention. 2009; 29(5):325-31**

Adherence defined as one hour per day 5/week >80% of the time.

**Comments: Long period of rehab. Good results in very severe cohort. Low drop-out/mortality and excellent adherence in such a severe group.**

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
<b>Foglio K, Bianchi L, Ambrosino N. Is it really useful to repeat outpatient pulmonary rehabilitation programs in patients with chronic airway obstruction? A 2-year controlled study. Chest. 2001; 119(6):1696-704.</b>	RCT	1-	61 randomised, 36 completed	26 patients with COPD by ATS criteria, 35 with asthma. All underwent 8 week pulmonary rehabilitation programme at baseline	Pulmonary rehabilitation at one year and two years	Pulmonary rehabilitation at two years	2 years (up to end of pulmonary rehabilitation session)	Lung function and volumes; ABG; CPEX; 6MWD; BDI &TDI; SGRQ; exacerbations (steroid course); admissions	Short term gains seen in symptoms, QOL, and exercise capacity with each rehab session but no additive effect from the additional session. The only exception was the reduction in exacerbations seen (all 19 of those in the control group had at least one exacerbation whereas 8/17 in the active arm did not.	Not stated

**Comments: Randomisation process unclear. Though blinding is reported, it appears insufficient as the patients were free to disclose the information to the technicians and those undertaking medical care, trial visits, and analyses were not blinded. Small initial sample with large proportion of drop-outs.**

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
<b>Franssen FME, Broekhuizen R, Janssen PP, et al. Effects of Whole-Body Exercise Training on Body Composition and Functional Capacity in Normal-Weight Patients With COPD. Chest. 2004; 12:2021-8.</b>	Cohort	2+	50	COPD. FEV1 <70% predicted. BMI >21 and FFM >15 (women)/>16 men	Inpatient pulmonary rehabilitation	n/a	8 weeks	Weight, FFM, exercise capacity, quadriceps strength	Weight increased by 0.6Kg. 35% increase in peak work rate and 17% increase in VO2	Not stated

**Comments:**

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Fuld J, Kilduff LP, Neder JA, <i>et al.</i> Creatine supplementation during pulmonary rehabilitation in chronic obstructive pulmonary disease Thorax. 2005; 60:531–537.	RCT	1-	38	"Moderate to severe COPD"	5.7 g creatine monohydrate, equivalent to 5 g creatine and 35 g glucose per dose	glucose polymer only (40.7 g per dose)	12 weeks	FEV1, MIP, Weight, Fat free mass, upper and lower limb strengths, exercise test, shuttle walk test, SGRQ	No difference in exercise test results. Lower limb strength and endurance notably better than placebo (improvements over baseline of >15%); Handgrip endurance increased significantly but less markedly (8.0% increase in repetitions vs. 2.2%). Fat free mass improved by around 1 kg compared to placebo.	Wellcome Trust

**Comments:** There were several drop-outs with little explanation. The confidence intervals for "significantly different" endpoints overlap raising concern over the clarity of the analysis description. There are far more endpoints analysed than patients completing the trial raising the possibility of chance findings.

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Garcia-Aymerich J, Lange P, Benet M <i>et al.</i> Regular physical activity reduces hospital admission and mortality in chronic obstructive pulmonary disease: a population based cohort study. Thorax. 2006; 61:772–778.	Cohort	2+	2386	Obstructive spirometry (FEV1/FVC <70%)	n/a	n/a	Mean F/u 12 years	physical activity, hospital admissions	n/a	Danish Heart Foundation, Generalitat de Catalunya

**Comments:**

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Garrod R, Paul EA, Wedzicha JA.	RCT	1-	25 randomised; 22 completed	"severe stable COPD" ;	6 weeks pulmonary	6 weeks pulmonary	End of pulmonary	Spirometry; ISWT; HAD; CRDQ; ADL	1.5 unit fall in Borg score; others	Not stated



Supplemental oxygen during pulmonary rehabilitation in patients with COPD with exercise hypoxaemia. *Thorax*. 2000; 55(7):539-43.

FEV1<40%; less than 15% reversibility to salbutamol; all desaturated on exercise to <90%

rehabilitation with supplemental oxygen (4l/min)

rehabilitation with compressed air (4l/min)

rehabilitation

questionnaire

no difference

Comments: The study was underpowered to provide any degree of certainty that the intervention was ineffective. No record of effect of oxygen on training undertaken. Investigators were not blinded raising the possibility of bias.

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Garrod R, Paul EA, Wedzicha JA. An evaluation of the reliability and sensitivity of the London Chest Activity of Daily Living Scale (LCADL). <i>Respiratory medicine</i> . 2002; 96:725-730.	Cohort	2+	59	Stable, severe COPD. In pulmonary rehabilitation programme	n/a	LCADL pre and post pulmonary rehabilitation	4 weeks	LCADL	Statistically significant reduction in LCADL score following pulmonary rehabilitation (-5.91 of total score)	Not stated
Garrod R, Marshall J, Jones F. Self-efficacy measurement and goal attainment after pulmonary rehabilitation. <i>International Journal of COPD</i> . 2008; 3:791-6.	Cohort	2+	74 enrolled. Outcomes on 48 patients	Known COPD undergoing pulmonary rehabilitation	n/a	COPD self-efficacy scale (CSES) pre and post pulmonary rehabilitation	7 weeks	Chronic Obstructive Pulmonary Disease Self-Efficacy scale (CSES) (Primary). 6MWD, Health status, Quads strength, depression, breathlessness during ALD (secondary)	mean change (95% CI) in CSES scores = 0.27 (0.04-0.51): Significant correlations of CSES with 6MWD (r=0.37 p<0.01)LCADL (r=-0.33 p<0.01, SGRQ (r=-0.51 p<0.001)	The Health Foundation
Gottlieb V, Lyngsø AM, Nybo B, et al. Pulmonary	RCT	1-	61	61 subjects aged 65+ years with moderate COPD	All subjects	7 week PR – 2 supervised exercise	18 months	Comparison of group response pulmonary rehabilitation vs.	Pulmonary rehabilitation subjects had	Not stated

Rehabilitation for Moderate COPD (Gold 2)-Does It Have An Effect? Journal of COPD. 2011; 8 (5):380-386.

(GOLD 2) of who 42 completed the trial (22/35 pulmonary rehabilitation and 20/26) usual care. 28/42 completing subjects female. FEV1 was 64(8)% predicted; 1.43(0.32)L PR vs. 67(9)% predicted; 1.57(0.41)L control

sessions/week

control. Outcomes exercise capacity (6MWD), HRQOL (SGRQ) and dyspnoea (Borg at end of 6MWT)

greater increase in 6MWD (46m) vs. control (4m). No difference in peak Borg between groups. SGRQ improved but magnitude unclear - 6.4(11.3) in text but 5.2 in table; however, not significant though no improvement in control. Benefit gained lost by 18 months follow-up

Comments: Patients with moderate COPD (GOLD 2 – FEV1 50-80% predicted) improve walking distance with pulmonary rehabilitation compared to controls but lose benefit by 18 months

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Graves J, Sandrey V, Graves T, Smith DL. Effectiveness of a group opt-in session on uptake and graduation rates for pulmonary Rehabilitation. Chron Resp Dis. 2010; 7(3):159-64.	Cohort	2-	200 patients in control group, 400 in historical intervention group	Patients referred to pulmonary rehabilitation programme. Patients had own transport	Group opt-in session, 1 ½ hours, using CBT and information giving.	Conventional care – no opt-in session (historical)	To end of pulmonary rehabilitation programme (8 weeks)	DNA, graduation from pulmonary rehabilitation programme, reasons for drop out.	Reduction in drop out due to non-illness reasons (p=0.001)	Not stated

Comments: The authors conclude that the intervention has increased the overall efficiency of the pulmonary rehabilitation programme and they are able to treat more patients without increasing staffing. This intervention is interesting and there was a clear reduction in drop out following its' introduction. The study design raises a high possibility of confounding, with staff being more aware of the need to prevent drop out this may have affected post-intervention programme delivery. Therefore this study cannot be more highly rated as a source of evidence. The study report did not indicate that this potential confounder had been considered during analysis. The positive outcome obtained following introduction of this intervention cannot be confidently attributed to the intervention alone.

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Green RH, Singh SJ, Williams J, Morgan MDL. A randomised controlled trial of four weeks versus seven weeks of pulmonary rehabilitation in	RCT	1+	44 ( 4 weeks=23, 7 weeks =21)	Diagnosed with COPD (FEV1 <80%, ratio FEV1/FVC <70%) and consistent symptoms	Pulmonary rehabilitation duration 4 weeks v 7 weeks.	4 weeks pulmonary rehabilitation	4 week group measured at 0 and 4 weeks. 7 week group measured at 0 and 7 weeks.	ISWT, Treadmill Endurance Test, CRDQ	Mean difference between groups: ISWT - 16.9 metres (p=0.415) CRDQ dyspnoea - 0.8 (p=0.021), mastery - 0.84(p=0.027), , emotion -0.89	Not stated

(p=0.003),

chronic obstructive pulmonary disease. *Thorax*. 2001; 56: 143-145.

Comments:

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Greening NJ, Evans RA, Williams JEA, <i>et al</i> . Does body mass index influence the outcomes of a walking-based pulmonary rehabilitation programme in COPD? <i>Chronic Respiratory Disease</i> . May 2012; 9: 99-106.	Cohort	2+	601	COPD. GOLD II-IV	Pulmonary rehabilitation	Across different BMI	6 weeks	ISWT, ESWT, CRDQ	Similar across all groups	NIHR CLAHRC LNR

Comments:

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Griffiths TL, Burr ML, Campbell IA <i>et al</i> . Results at 1 year of outpatient multidisciplinary pulmonary rehabilitation: a randomised controlled trial. <i>Lancet</i> . 2000; 355: 362-368.	RCT	1++	200	COPD, FEV1 <60% predicted (<20% reversibility), Clinically stable for 2 months	Pulmonary rehabilitation	Control group	1 year	Walking capacity, SF-36, HADS, SGRQ, health care utilisation	Reduction in number of hospital days. Increased walking capacity and health status	Wales Office of Research and development.

Comments:

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Grosbois JM, Lamblin C, Lemaire B, <i>et al</i> . Long-term benefits of exercise maintenance after outpatient rehabilitation program in	Prospective non randomised trial	2-	71 patients allocated to 4 groups. Group A 18, group B 18, Group C 18 and group D 17. 58 patients completed study.	Moderate to severe COPD. Dyspnoea on exertion limiting ADL's, FEV1<70%, stable with optimal drug management, no	Group A – twice a week supervised maintenance exercise, group B – once a week supervised maintenance	Group D no maintenance exercise	18 months	FEV1, exercise capacity, dyspnoea.	Significant post rehabilitation deterioration in FEV1 in control group, but maintained in intervention groups. Significant	Not stated

patients with chronic obstructive pulmonary disease. J Cardiopulm Rehab. 1999; 19(4): 216-225.

IHD or muscular skeletal disorder. exercise, group C, unsupervised home exercise.

difference in exercise capacity at 18 months in favour of intervention groups. No differences in dyspnoea at any point between groups.

**Comments: Non – randomised – patients self-selected groups. Definite benefits of maintenance compared to no maintenance, No difference between unsupervised and supervised maintenance. Daily home exercise appears to maintain workload as does weekly exercise session. The authors conclude that there were definite benefits of exercise maintenance after outpatient pulmonary rehabilitation. There are limitations within the methodology increasing the risk of selection bias and the study has poor statistical power so can only be coded -.**

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Guell MR, de Lucas P, Gáldiz JB, <i>et al.</i> Home vs. hospital-based pulmonary rehabilitation for patients with chronic obstructive pulmonary disease: A Spanish multicenter trial. Archivos de Bronconeumologia . 2008; 44(10): 512-518.	RCT	1-	51 patient, 28 hospital, 23 home	Moderate to severe (stable) COPD	Exercise and education	2 education sessions and 4 supervised exercise sessions over 2 weeks and then randomised to home or hospital based exercise	6 months	6MWT, CRDQ	Both intervention groups improved at 9 weeks and 6 months. 6MWT at 9 weeks, difference = 8.69m (p=0.61), at 6 months difference = 6.55m (p=0.73). CRDQ (D) 9 weeks difference =0.21 (p=0.33), at 6 months difference =0.13 (p=0.65)	Not stated

**Comments: small study-, no power calculation described, probably underpowered, outcome assessment blinded**

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Guell R. Resqueti V, PT, Sanganis M, <i>et al.</i> Impact of pulmonary rehabilitation on psychosocial morbidity in patients with severe COPD. Chest. 2006; 129(4): 899-904.	RCT	1-	Pulmonary rehabilitation = 18, control group = 17	COPD aged <75 years, FEV1<70% predicted, no home oxygen, no exacerbations in past 2 months	Non-psychologically based 16 week pulmonary rehabilitation programme	Usual care	16 weeks	6MWD, Milton Behavioural Health Inventory, revised Symptom Checklist (SCL-90-R), CRDQ	6MWD Control = - 22 pulmonary rehabilitation = +63 CRDQ change in scores Dyspnoea: control group -0.2, pulmonary rehabilitation +0.8 Fatigue: control group -0.5,	SEPAR

pulmonary rehabilitation +0.2  
Emotion: control group -0.4, pulmonary rehabilitation +0.3  
Mastery: control group 0, pulmonary rehabilitation +0.6

**Comments:**

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
<b>Harris M, Smith BJ, and Veale AJ, et al. Providing reviews of evidence to COPD patients: Controlled prospective 12 month trial . Chronic Resp Dis. 2009; 6 (3):165-173.</b>	Controlled before and after design.  (Not randomised).	2-	249 included at baseline, intervention arm 125, control arm 124. Pulmonary rehabilitation was explored as a subgroup. Numbers unknown. Completed to 12 months intervention 100, control, 101	Mod to severe COPD, able to read English. Exclusions, dementia, lung cancer or unstable illness.	Patients were given a manual of evidence (summary of Cochrane reviews) for COPD interventions. The manual contained 'cues' and tips for questions to discuss with the doctor.	Patients who were given a conventional pamphlet containing information re COPD	12 months	Enrolment in pulmonary rehabilitation Plus rates of influenza vaccination, rate of bone densitometry testing  Secondary measures – CRDQ mastery, knowledge of COPD, Communication with usual doctor; satisfaction with disease related information, anxiety.	Enrolment in rehabilitation showed sig change for most socio-disadvantaged group	The Australian commonwealth Dept. of Health and Ageing. TQEH research foundation.

**Comments:** The authors conclude that providing research evidence to patients with COPD did not lead to an improved application of that evidence, although patients reported they found it useful. There appears to be a significantly higher uptake in pulmonary rehabilitation uptake in the intervention group, but only in the higher socioeconomic disadvantaged group. Pulmonary rehabilitation uptake was one of 3 self-management applications that were addressed in this study and numbers of patients in this subgroup are not reported. It is therefore difficult to apply the findings to the guideline question, however the study adds to the body of evidence supporting the hypothesis that pre-rehabilitation interventions may increase uptake. Differences in groups at baseline – 19 patients in intervention group (compared to 3 in control group) had previously attended pulmonary rehabilitation. Socioeconomic disadvantage appeared to be a modifier.

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
<b>Hawkins P, Johnson LC, Nikolettou D, et al Proportional assist ventilation as an aid to exercise training in severe COPD. Thorax. 2002; 57:853-9.</b>	RCT	1-	10 intervention and 9 controls	COPD severe FEV1 mean 27% predicted -all men bar 2 in the control group who were women. PaCO2 mean 5.8 kPa at baseline so not type II failure.	Proportional assist ventilation via BiPAP mean first volume assist at 12.7 cms H2O exercise cycle ergometer three times a week for 6 weeks for 30	Unassisted	Tested two days before start of programme and on two days in the week after the programme completed	Spirometry lactate peak heart rate peak work rate training intensity as weight/work peak all as change from baseline	The ventilation assist group had a statistically significant increased weight/wpeak at 6 weeks (CI 3.2-27.1) p=0.016) as did work rate after training in the	British Lung Foundation and Respiroics who also provided the ventilators

minutes a session with progressive increase of work rate over the time course of the programme

assist group 18.5% increase p=0.005 and lactate at same work rate was significantly less (reduced by 30% p=0.002) compared to baseline

Comments: Small unblinded study

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Heppner PS, Morgan C, Kaplan RM, Ries AL. Regular walking and long-term maintenance of outcomes after pulmonary rehabilitation. Journal of Cardiopulmonary Rehab. 2006; 26(1): 44-53.	RCT	1-	164 patients randomised to 2 groups	107 patients had mod – severe COPD, 16 had either restrictive lung disease or mixture of restrictive and obstructive Mean FEV1 = 47%	12 months maintenance programme. Weekly telephone calls and monthly supervised sessions	12 months standard care – referral back to health care provider, documented homecare programme and monthly alumni meetings	24 months	Walking frequency HRQOL Dyspnoea 6MWD Self-efficacy for walking Hospital in patient days emergency room visits FEV1	44% of maintenance group were found to be regular walkers, 38% of control group. Therefore data was pooled from those groups in order to focus on regularity of walking. At 12 months, regular walkers had sig better HRQOL than irregular walkers (p=0.01) Post rehabilitation decline in dyspnoea occurred less in regular walking group than irregular walking group (p= 0.01) No differences in rate of decline in 6MWD between groups. Regular walkers maintained post rehabilitation self-efficacy compared	Not stated

to irregular  
walkers (p=0.01)

Comments: The subjects from the original study and control groups were pooled. Regular walking was associated with long term maintenance of the functional benefits of a pulmonary rehabilitation programme. Regular walkers had better HRQOL, less impairments from dyspnoea and better self-efficacy for walking. Monthly supervised reinforcement sessions made no difference to whether patients became regular walkers or not. This study gives limited information but does suggest that regular walking may be a protective factor for the loss of benefits following pulmonary rehabilitation. The study was originally designed to explore the effects of maintenance on outcomes. The data about walking was observed at completion of the study. This raises the possibility of confounders.

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Hoff J, Tjønnna AE, Steinshamn S, <i>et al.</i> Maximal strength training of the legs in COPD: a therapy for mechanical inefficiency. <i>J. Med Sci Sports Exerc.</i> 2007; 39(2):220-6.	RCT	1+	12	COPD (GOLD guidelines), age 40-70, FEV1 <60%. Metabolic disease, cardiovascular disease, steroid use in last 6 months.	8 weeks resistance training	Control	8 weeks	Pulmonary function tests, haemoglobin, lactate, 1RM strength, rate of force development (70% 1RM), mechanical efficiency	36 Kg 1RM increase, 1957 N/s increase dynamic rate of force development, 332 N increase in static peak force, no increase in dynamic peak force.	Norwegian Research Council

Comments:

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Holland A, Hill CJ, Conron M, <i>et al.</i> Short-term improvement in exercise capacity and symptoms following exercise training in interstitial lung disease. <i>Thorax.</i> 2008; 63: 549-554.	RCT	1+  (but only exercise)	57 patients with ILD (34 IPF)	Patients attending hospital with ILD	8 weeks of supervised exercise training	Weekly telephone support	26 weeks	Functional exercise capacity, maximal exercise capacity, quality of life and dyspnoea.	6MWD increased (mean difference to control 35m, 95% CI 6 to 64 m). A significant reduction in MRC (0.7 points, 95% CI 0.1 to 1.3); dyspnoea improved (p=0.04) and fatigue (p<0.01) on CRDQ. Exercise training reduced heart rate at maximum isowork load (p=0.01). After 6 months no differences between the training and control group for any outcome	Victoria Tuberculosis and Lung Association.

variable.

**Comments: Small numbers. Exercise training improves exercise capacity and symptoms in patients with ILD, but these benefits are not sustained 6 months following intervention.**

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Johnson JE, Gavin DJ, Adams-Dramiga S. Effects of training with heliox and noninvasive positive pressure ventilation on exercise ability in patients with severe COPD. Chest. 2002; 122(2):464-72.	RCT	1-	39 enrolled. 32 completed	COPD with FEV1<50% predicted	6 weeks pulmonary rehabilitation with supplemental Heliox (79% helium, 21% oxygen), or supplemental bi-level pressure support NIV (8-12 / 2)	6 weeks pulmonary rehabilitation	End of pulmonary rehabilitation	Treadmill test;	No effect with Heliox. NIV increased exercise time and workload acutely. NIV during training increased %change in unassisted exercise time (89.6+/-57.7 versus 37+/-33%; p=0.016) but not workload compared with unassisted training.	Not stated

**Comments: Not double-blind; Underpowered to see clinically meaningful improvements; very low NIV pressures used. More dropped out in NIV group. No information about randomisation process.**

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Kayahan B, Karapolat H, Atyntoprak E, et al. <i>et al.</i> Psychological outcomes of an outpatient pulmonary rehabilitation program in patients with chronic obstructive pulmonary disease. Respiratory Medicine. 2006; 100(6): 1050-7.	Cohort study	2-	26 pulmonary rehabilitation 19 control	COPD aged 50-75yrs, COPD, smoked >20yrs, no exacerbations in past 8 weeks	8 week pulmonary rehabilitation programme	usual care - not described	8 weeks	HAM - A (anxiety measure) HAM - D (depression measure), dyspnoea VAS, 6MWD, SGRQ	HAM -A (anxiety measure) pulmonary rehabilitation = - 3.04, control = + 0.82 p=0.042 (between group); 6MWD pulmonary rehabilitation = +121.54m, control = + 15.12m p<0.05; SGRQ pulmonary rehabilitation = - 16.79, control = - 3.65 p<0.05	Not stated

**Comments:**

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Ko FW, Dai DL, Ngai J, <i>et al</i>	RCT	1+	30 in each arm,	Patients admitted to hospital with	Pulmonary rehabilitation	Usual care to include	1 year following	6MWD MRC	No statistical differences	Hong Kong lung foundation grant.



Effect of early pulmonary rehabilitation on health care utilization and health status in patients hospitalised with acute exacerbations of COPD. *Respirology*. 2011; 16: 617-624.

acute exacerbation COPD. FEV1/FVC ratio <70%, FEV1<70%, Over 40 years. Exclusions: major joint problems and severe angina, or who had attended pulmonary rehabilitation in preceding year.

programme group 3 times a week for 8 weeks

instruction to patient to do home walking

discharge

Borg SGRQ CPE acute exacerbation COPD Hospitalisations A and E visits

between groups in any parameter. SGRQ was statistically better in the pulmonary rehabilitation group (p=0.04). Trend towards fewer admissions in first 3 months in pulmonary rehabilitation programme group but this diminished over time.

Respiratory research fund Chinese university of Hong Kong

Comments: Conclusions – better HRQOL in pulmonary rehabilitation programme up to 6 months without reduction in healthcare utilization at 1 year. Patients not medically optimised prior to pulmonary rehabilitation.

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Kongsgaard M, Backer V, Jørgensen K <i>et al</i> . Heavy resistance training increases muscle size, strength and physical function in elderly male COPD-patients—a pilot study. <i>Respiratory Medicine</i> . 2004; 98 (10):1000-1007.	RCT	1-	18	COPD, Age 65-80, non lower limb fracture in previous 6 months, dependence on more than one walking devise, male	4 sets of 8 reps at 80% 1RM	Control (breathing exercises)	12 weeks	Isometric and isokinectic strength, 5RM strength, lung function, ADLs, Gait climbing time	37% increase in 5RM quads strength	Not stated

Comments: Male only. Per protocol analysis

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Kovelis D, Zabatiero J, Oldenberg N, <i>et al</i> . Responsiveness of three instruments to assess self-reported functional status in patients with COPD. <i>Journal of COPD</i> . 2011; 8:334-	Prospective cohort study	2-	22	Confirmed diagnosis of COPD according to GOLD, stable disease, no other comorbidities that would impair ADL	12 week training programme of 1 hour sessions attending 3 times per week.	None	12 weeks	PFSDQ-M, LCADL, MRC scale, SRGQ, 6 MWD	PFSDQ-M: Dyspnoea 0.26, Fatigue 0.16, change in ADL 0.33 LCADL: self-care = 0.6, domestic 0.26, Activity= 0.61, leisure = 0.61, total= 0.45: MR= 0.36	Grant from National Council for Scientific and Technological Development, Brazil

9.										
Comments:										
Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Kubo H, Honda N, Tsuji F, <i>et al.</i> Effects of dietary supplements on the Fischer ratio before and after pulmonary rehabilitation. Asia Pac J Clin Nutr. 2006 15;(4): 551-55.	Intervention trial	2-	8 (7 male) Arm 1; 4 male Arm 2; 3 male	COPD (Emphysema) Stable	4 grams protein (Branched chain amino acids) contained in 200ml liquid supplement drink +pulmonary rehabilitation (1 session per week for 8 weeks)	Pulmonary rehabilitation alone (as intervention)	8 weeks	6 MWD, QOL (CRDQ), Fischer ratio, Serum albumin	Results only provided in graphical format. No numerical data provided.	Not stated
Comments: Not randomised or blinded. Very small. No statistical analysis details. Diet self-reported therefore increasing variability, no data regarding compliance with home exercise, no measure of lean tissue.										
Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Lan CC, Yang MC, Lee CH, <i>et al.</i> Pulmonary rehabilitation improves exercise capacity and quality of life in underweight patients with chronic obstructive pulmonary disease. Respiriology. 2011; 16: 276-83.	Controlled trial (non-randomised)	1-	44	COPD, stable for 3 months.	Pulmonary rehabilitation	Underweight versus non-underweight	12 weeks	Weight (secondary). CPE (primary), SGRQ.	Underweight group increased weight by 0.8kg. Significant improvements in peak VO2. No significant difference in peak workload between groups.	Not stated
Comments:										
Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Lacasse Y, Goldstein R, Lasserson TJ, <i>et al.</i> Pulmonary rehabilitation for chronic obstructive pulmonary disease. Cochrane Database of Systematic	Systematic review and meta-analysis	1++	CRDQ n=618, SGRQ n=384, 6MWD n=669	Clinical diagnosis of COPD, >90% had COPD, FEV1 <70% predicted	Comprehensive pulmonary rehabilitation	Usual care	6 weeks to one year	CRDQ, SGRQ, 6MWD	Improvements in CRDQ (range from 0.76- 1.06), SGRQ (range from 4.68-6.27), 6MWD 48m	None

Reviews. 2006.  
DOI:  
10.1002/14651858.  
CD003793.pub2.

Comments:

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Larson JL, Covey MK, Wirtz SE, <i>et al.</i> Cycle Ergometer and Inspiratory Muscle Training in chronic obstructive pulmonary disease. <i>Am J Respir Crit Care Med.</i> 1999; 160:500-507.	RCT	1-	53 total: 13 IMT; 14 CET; 14 CET &IMT; 12 health education	Moderate to severe COPD by usual definitions	[4 months of] IMT: threshold loading device with incremental resistance to 60% Pimax; CET: 5 days a week on bike, tailor programme	Health education (general and related to COPD)	End of intervention	Pimax; CPEX outcomes; submaximal ET outcomes; respiratory muscle endurance; dyspnoea score	No clear difference in VO2; no difference in CRDQ; improvement in Rating of Perceived Breathlessness and Rating of Perceived Leg Fatigue of 20% versus no CET	National Institute of Nursing Research, National Institutes of Health, RO1-NR01428.

Comments: Randomisation and blinding not described. Analyses appear to be against baseline. No clear primary outcome and no adjustment for multiple testing

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Liddell F, Webber J. Pulmonary rehabilitation for chronic obstructive pulmonary disease: a pilot study evaluating a once weekly versus twice weekly supervised programme. <i>Physiotherapy.</i> 2010; 96:68-74.	Pilot study	3	30 patients with COPD	COPD patients on waiting list for pulmonary rehabilitation.	Once weekly pulmonary rehabilitation for 8 weeks	Twice weekly pulmonary rehabilitation for 8 weeks	Not stated	ISWT, ESWT, SGRQ	Significantly underpowered.  ITT median (IQR) ISWT: once weekly: 60 (0 - 70)m; twice weekly 50 (0-60)m	Not stated

Comments: Pilot feasibility study enrolling 36 patients, 6 excluded at commencement of study and only 20 patients completed study. Limitations due to small numbers. Recommended further research to demonstrate whether once weekly pulmonary rehabilitation is as effective as twice weekly.

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Lindsay, M, Lee A, Poon P, <i>et al.</i> Does pulmonary rehabilitation give additional benefit over tiotropium therapy in primary	RCT	1-	50	COPD patients (FEV1 <80% predicted and FEV1/FVC ratio < 70%)	18mcg tiotropium +6 weeks pulmonary rehabilitation programme	18mcg tiotropium	3 months	FEV1, 6MWD, VAS, CRDQ	6MWD – Pulmonary rehabilitation- +22.98 metres, control- +30.8 m; (NS) CRDQ dyspnoea	Chinese University of Hong Kong

care management of chronic obstructive pulmonary disease? Randomized controlled clinical trial in Hong Kong Chinese. *Journal of Clinical Pharmacy & Therapeutics*. 2005; 30(6): 567-73.

Pulmonary rehabilitation- +1.18 Control +1.12 (NS); CRDQ fatigue Pulmonary rehabilitation- +0.38, control +0.28 (NS); CRDQ emotional Pulmonary rehabilitation - +0.38 control 0.28 (NS); CRDQ mastery Pulmonary rehabilitation - +0.34, control +0.34 (NS)

**Comments:**

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Mador MJ, Deniz O, Aggarwal A, <i>et al</i> Effect of Respiratory Muscle Endurance Training in Patients with COPD Undergoing Pulmonary Rehabilitation. <i>Chest</i> . 2005; 128:1216-1224.	RCT	1-	29 total: 15 combined 14 pulmonary rehabilitation alone	Description of COPD but no threshold for inclusion given	8 weeks. Standard pulmonary rehabilitation programme plus normocapnoeic hyperpnoea	Standard pulmonary rehabilitation programme including endurance training	End of intervention	CRDQ; CPEX outcomes; respiratory muscle endurance/Pimax	Improvement with IMT greater for respiratory muscle endurance (20%) and Pimax (10%)	Swiss National Science Foundation

Comments: Per protocol analyses only (9 drop-outs). Randomisation and blinding not described, classes of 3-5 not individuals randomised.

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Man WD, Grant A, Hogg L, <i>et al</i> . Pulmonary rehabilitation in patients with MRC Dyspnoea scale 2. <i>Thorax</i> . 2011; 66:263 doi:10.1136/thx.	Cohort	3	442	45% male patients with COPD who completed pulmonary rehabilitation. 126 patients MRC2 vs. 316 patients MRC3-4. MRC2 58% pred. Vs.	All subjects	8 week pulmonary rehabilitation- 2 supervised and 1 unsupervised session/week	NA	Comparison of group response based on MRC2 vs. MRC3-4. Outcome measures exercise capacity (ISWT), dyspnoea	No significant difference outcomes MRC2 vs. MRC3-4. Mean ISWT improvement 83(7)m MRC2 vs.	National Institute for Lung Research UK

2010.136085.

MRC3-4 54%

(CRDQ-D) and anxiety/depression (HAD)

68(5)m MRC3-4. CRDQ-D improvement 0.75(0.11) MRC2 vs. 0.75(0.07) MRC3-4. Similar median HAD-A and HAD-D improvement

Comments: Patients with baseline MRC2 dyspnoea gain similar improvement in walking distance and breathlessness as MRC3-4 patients

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Maltais F, Bourbeau J, Shapiro S, <i>et al.</i> Effects of home-based pulmonary rehabilitation in patients with chronic obstructive pulmonary disease: A randomized trial. <i>Annals of Internal Medicine.</i> 2008; 149(12): p. 869-878.	RCT	1+	Baseline = 252 Outpatient 126 Home 126	Moderate to severe (stable) COPD	Exercise	Outpatient vs. home based programme. Centre based education - followed by randomisation to either home or hospital exercise	1 year	CRDQ, SGRQ, spirometry, 6MWT, incremental cycle test	Non-inferiority study - Primary outcome between group difference at 3 months 0.05(-0.21 to 0.29) p=0.74	Canadian Institute of health Research & Respiratory Health Network of the Fonds de la Recherche en sante de Quebec

Comments: Designed and powered as a non-inferiority study but outcomes not blinded, therefore increased risk of bias

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Mendes De Oliveira JC, Filho FS, Sampaio LM, <i>et al.</i> Outpatient vs. home-based pulmonary rehabilitation in COPD: A randomized controlled trial. <i>Multidisciplinary Respiratory Medicine,</i> 2010; 5(6): 401-408.	RCT	1-	117 patients: 42 home rehabilitation, 46 outpatient, 29 control,	Moderate to severe (stable) COPD	Exercise	Exercise at home or hospital (all received education prior to randomisation)	12 weeks	6 minute walking test and BODE	No significant difference between intervention groups for 6MWT(p=0.44) &, BODE (p=0.90)	Brazilian fostering agencies Fundação de Amparo a Pesquisa do Estado de São Paulo. Conselho Nacional de Desenvolvimento Científico e Tecnológico.

Comments: Poorly described power calculation, not blind outcome assessment, no assessment of HRQOL

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
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<b>Moullec G, Ninot G, Varray A, et al.</b> An innovative maintenance follow-up programme after a first in patient pulmonary rehabilitation. <i>Respiratory Medicine</i> . 2008; 102:556-566.	Controlled trial	1-(but not randomised)	40; 27 completed	Moderate to severe COPD  Exclusions: LTOT or significant medical / psychiatric disorders	Maintenance: exercise (3.5h/week) health education (2h/month), psychosocial support (1h/month)	Letter outlining standard recommended care post rehabilitation	1 year	Primary: 6MWD  Secondary included QOL, maximal exercise test, physical activity, attendance	Change in ISWT: 75.8 (32-119.6)m favouring maintenance QOL (SGRQ: Symptoms): -18.5 (-30.9, -6.2)	Fond d'Aide à la Qualité des Soins de Ville (FAQSV) of the Union Régionale des Caisses d'Assurance Maladie (URCAM). Agence Régionale de l'Hospitalisation (ARH) of the region Languedoc-Roussillon in France
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Comments: No comment re blinding or randomisation. Consecutive assignment not random allocation. Small, underpowered study. Outcomes well described. The intense maintenance strategy appears to offer significant benefit. In the UK, this might be considered to be year-long rehabilitation. However it demonstrates that with continued supervision of exercise benefits are maintained and improved upon after the initial in-patient phase of rehabilitation.

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
<b>Newall C, Stockley RA, Hill SL.</b> Exercise training and respiratory muscle training in patients with bronchiectasis. <i>Thorax</i> . 2005; 60: 943-948.	RCT	1-	32 randomised to 3 groups 2 patients dropped out during the training programme from each training group, a further 2 in each training group dropped out during the follow up. 6 in total.	Patients with bronchiectasis confirmed by high resolution computed tomography.  Excluded if COPD too	Pulmonary rehabilitation plus inspiratory muscle training (12 patients - 9 at follow-up)	Pulmonary rehabilitation with sham IMT (11, 8 at follow-up) & a control group (no intervention - 9)	3 months	Lung function, respiratory muscle strength, ISWT, maximal incremental treadmill test, submaximal exercise test, SGRQ, sputum volume	Changes in ISWT in both pulmonary rehabilitation groups at 3 months 96.7 (59.6 to 133.7) m in pulmonary rehabilitation plus sham IMT. 124.5 (63.2 to 185.9)m in pulmonary rehabilitation IMT no change in control 11.0 (216.9 to 38.9) 0.002 Changes statistically significant between both pulmonary rehabilitation groups and control not between pulmonary	Not stated

rehabilitation  
groups

Comments: Table 1 is misleading- says baseline characteristics of 32 who completed, results indicate only 27 patients completed (17 in total in both pulmonary rehabilitation groups). Compared to control pulmonary rehabilitation was effective at improving exercise tolerance in bronchiectasis. Randomisation computer generated. No discussion of blinding. Study underpowered to detect additional effects of IMT on the pulmonary rehabilitation.

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Ninot G, Moullec G, Picot MC, <i>et al.</i> Cost-saving effect of supervised exercise associated to COPD self-management education program. <i>Respiratory Medicine</i> , 2011; 105(3): 377-85.	RCT	1-	38	61-65 years old, principally male (84%), FEV1 % pred = 55%, 6MWT= 397 (usual care), 450 (intervention), SGRQ= 41-44	4 weeks pulmonary rehabilitation (cycle exercise + self-management education)	Usual care	12 months	6MWT, SGRQ, Voorrips score, Cycle workload, Nottingham health profile, healthcare utilisation	Significant increase in 6MWT, SGRQ symptom domain, Voorrips score	Hospital

Comments: Some statistical question remains. Outcomes at one year. No post pulmonary rehabilitation measures done.

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Nishiyama O, Kondoh Y, Kimura T, <i>et al.</i> Effects of pulmonary rehabilitation in patients with idiopathic pulmonary fibrosis. <i>Respirology</i> . 2008; 13 (3):394-399.	RCT	1-	30 patients Randomised to 15 in each group. 2 dropped out from pulmonary rehabilitation group. 28 patients completed study	Patients with IPF attending outpatient clinic= aged >50 - <75 Exclusion of other causes of interstitial lung disease	Pulmonary rehabilitation - 10 week	Control 15 patients competed	10 weeks	Pulmonary function, blood gases, 6MWT, dyspnoea, SGRQ	Difference in change between groups for 6MWD 46.3 (8.3-84.4)m Change in total SGRQ score between groups - 6.1 (-11.7-0.5)	Grant-in-Aid for interstitial lung diseases from the Japanese Ministry of Health, Labor andWelfare.

Comments: Randomisation made using sealed envelopes, no mention of blinding of assessor, small sample size 13 in rehab group completed, 15 in control group. No discussion of sample size a priori and small sample size likely to overestimate treatment effect. Difference in change between groups was significant at p<0.01 but confidence intervals wide and not encompassing MCID. No description of what the control group received.

Patients with only relatively mild impairments entered and short term evaluation only. Non exercise element of pulmonary rehabilitation poorly described.

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Norweg AM, Whiteson J, Malgady R <i>et al.</i> The Effectiveness of Different Combinations of Pulmonary Rehabilitation	RCT	1-	43: Exercise training plus activity training (ETAT) = 18 Exercise training plus lecture series (ETLS) = 10 Exercise training alone (ETA) = 15	Patients referred to an outpatient pulmonary rehabilitation programme	ETAT	1. ETA. 2. ETLS.	Up to 24 weeks	Chronic Respiratory Disease Questionnaire; COPD Efficacy Scale; Pulmonary Functional	ETAT; less dyspnoea (p≤0.04) fatigue (p≤0.01) increased activity involvement (p≤0.02) & total functional status (p≤0.02) in short	New York State Occupational Therapy Association Grant.

Program  
Components. A  
Randomised  
Controlled Trial.  
Chest. 2005; 128:  
663-672.

Status and  
Dyspnoea  
Questionnaire  
(PFSDQ).  
6MWD  
term only for  
older patients.  
ETAT; achieved  
higher gains in  
QOL (p=0.04) by  
week 24. ETLs;  
sig worse  
emotional  
function &  
functional status  
in older patients  
(p<0.03)

Comments: Confidence in findings low due to several factors suggesting a high risk of bias; Low numbers, lacked power, Authors acknowledge patients predominantly highly educated. Main author not blinded to group assignment. Significant baseline differences (age). Results not analysed as ITT.

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
O'Neill B, McKevitt AM, Bradley J, et al. A comparison of twice weekly versus once weekly supervision during pulmonary rehabilitation in Chronic Obstructive Pulmonary Disease. Arch Phys Med Rehabil. 2007; 88:167-172.	Randomised control parallel group study	2-	91. 66 completed	COPD patients recruited from pulmonary rehabilitation outpatient clinic	Once weekly supervised pulmonary rehabilitation sessions for 6 weeks (and 2 unsupervised)	Twice weekly supervised pulmonary rehabilitation sessions for 6 weeks (and 1 unsupervised)	6 months	Included ISWT, ESWT, CRDQ,	Mean (95% CI) difference in changes between groups ISWT 13.5m (-10, 37m)  ESWT 72s (-96, 241s); CRDQ 2.54 (-3, 8)	Not stated

Comments: Randomised study comparing once weekly with twice weekly supervised sessions of pulmonary rehabilitation. No difference in outcomes and minimal improvement in both arms, any beneficial effects of pulmonary rehabilitation had diminished by 6 month follow up. Limitations of study include high dropout meant that study was not powered and as such the number of patients completing the programme may have been too low to demonstrate a difference between two groups. Not powered originally for equivalence. Blinded assessor for outcomes.

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
O'Shea F, Taylor J, Paratz D. Progressive Resistance Exercise Improves Muscle Strength and May Improve Elements of Performance of Daily Activities for People With COPD A Systematic	Systematic review	1++	18 controlled trials included (5 relating specifically to PICO) n= 679	Severe COPD participants mean FEV1 % predicted 45.9% and mean age 63.7	Resisted training	Endurance and resisted training programmes compared with resisted training only	miscellaneous	Muscle strength, ADL	Meta-analysis found large sizes for increases in leg press strength (Mw change, 16.2%; 0.96; 95% CI, 0.26 to 1.66 [p 0.006]; Q 7.74 [p	The authors have reported to the ACCP that no significant conflicts of interest exist with any companies/organizations whose products or services may be



Review  
 Simone D. Chest  
 2009; 136(5):1269-  
 1283.

0.11])20,21,25,29, 34; whereas, small s favouring progressive resistance exercise were shown for latissimus dorsi strength (Mw change, 18.3%; 0.43; 95% CI, 0.07 to 0.8 [p 0.02]; Q 3.09 [p 0.37]).22,28,31,33 No difference in biceps strength (Mw change, 18%; 0.23; 95% CI, 0.25 to 0.71 [p 0.34]; Q 0.05 [p 0.82]) was demonstrated after progressive resistance exercise when compared with no intervention or aerobic training. Concurrent progressive resistance exercise and aerobic training compared with aerobic training alone ( 0.19; 95% CI, 0.30 to 0.69 [p 0.44]; Q 8.4 [p 0.76]). discussed in this article.

Comments: Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
O'Shea, S., Taylor N, Paratz J. A predominantly	RCT	1-	54	COPD, No pulmonary rehabilitation in	Home based resistance programme	Versus usual care	24 weeks	Strength (hand held dynamometer).	Increased strength by 3.8 kg at 12 weeks.	Equipment grant: Thermaband

home based progressive resistance exercise program increases knee extensor strength in the short term in people with chronic obstructive pulmonary disease. A randomised controlled trial. *Aus J of Physiotherapy*. 2007; 53: 229-237.

previous 12 months, unstable disease preventing resistance training

using rubber resistance bands

Knee extensor, hip abductor, Shoulder horizontal flexor, Shoulder flexor.

Not maintained by 24 weeks

Comments: Only 15 subjects in training group completed training completely (per protocol).

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Ortega F, Toral, J, Cejudo, P. <i>et al</i> . Comparison of effects of strength and endurance training in patients with chronic obstructive pulmonary disease. <i>Am J Respir Crit Care Med</i> . 2002; 166: 669-674.	RCT	1-	72 patients entered study, 7 dropped out.	COPD irreversible obstruction.	Training programme 3 alternate days a week for 12 weeks	Endurance training alone, vs. strength training alone, vs. combined endurance and strength vs. control.	12 weeks	SWT, FEV1, breathlessness, HRQOL	At 12 weeks post training, all exercise groups showed sig increases in endurance testing compared to baseline. Endurance group improvements were sig higher than in strength group alone. Combined group acquired most benefits of each intervention	Supported by grants from Fondo de Investigaciones Sanitarias (FIS 97/0472) and Consejería de Salud, Junta de Andalucía (96/67), Spain

Notes: The data is based on small sample sizes which limits generalisation. Authors conclude there may be type 2 error. Post programme improvement in SWT only statistically significant in strength group which raises concern re the efficacy of the programme itself.

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Panton LB, Golden	Reviewed	1-	17	COPD, no	Combined	Aerobic	12 weeks	Muscle strength,	Small non-	Tennessee

**J, Broeder CE, et al.** in O'Shea systematic review. Controlled trial (not randomised)  
**The effects of resistance training on functional outcomes in patients with COPD.** Eur J Appl Physiol. 2004; 91:443-9.

evidence of recent acute exacerbation. No contradictory comorbidities

resistance / aerobic programme

programme only

12 MWD ADL's

significant trend towards improved walking distance but no improvement in walking distance for control group.

university grant

**Comments: No improvement in 12 minute walking test in control group. Most of the subjects had been attending the programme for at least 2 years prior to the study. High risk of bias.**

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
<b>Paz-Diaz, H. Montes de oca M, Lopez JM, Celli BR.</b> Pulmonary rehabilitation improves depression, anxiety, dyspnoea and health status in patients with COPD. American Journal of Physical Medicine & Rehabilitation, 2007; 86(1):30-6.	RCT	1-	Pulmonary rehabilitation = 10, control = 14	Severe COPD	A 2 month pulmonary rehabilitation programme attending 3 days per week in groups of 2 -3. No mention of education programme.	Usual care - visited physician every 3 weeks.	2 months	Beck depression inventory, STAI, MRC, SGRQ	Beck Depression Inventory pulmonary rehabilitation = -8 control = -2; pulmonary rehabilitation change p<0.01; SGRQ pulmonary rehabilitation = -8 control = +3 PR change p<0.01; STAI trait pulmonary rehabilitation = -16 control = +2 pulmonary rehabilitation change p=0.06	Not stated

**Comments:**

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
<b>Petersen MAW, Mittendorfer B, Magkos F, et al.</b> Physical activity counteracts increased whole-body protein breakdown in chronic obstructive pulmonary disease	Case-control study	2+	19 (pulmonary rehabilitation= 9, Control=10)	COPD, >20 pack years, MRC III-V	7 week pulmonary rehabilitation programme. Controls received education	Control group (though received education)	7 weeks	ISWT, SGRQ, systemic inflammatory markers, Leucine concentration	Improved exercise performance in terms of ISWT, though not health status or calculated VO2 max. There was a decrease in protein	Centre - Danish National Research Foundation (# 02-512-55). Study - The Danish Lung Association, the Danish Medical Research Council (# 22-01-009), the

patients.  
 Scandinavian  
 Journal of Medicine  
 & Science in Sports.  
 2008; 18(5):557-64.

breakdown  
 following  
 training.  
 Commission of the  
 European  
 Communities, the  
 US  
 National Institutes  
 of Health grants  
 AR 49869, DK  
 56341,  
 grants from the  
 University of  
 Copenhagen, the  
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 Hospital  
 Corporation, the  
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 Celinder, and the  
 Foundation of  
 Managing  
 Director Jacob  
 Madsen & Spouse  
 Olga Madsen

Comments: Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Phillips WT, Benton MJ, Wagner CL, Riley C. The effect of single set resistance training on strength and functional fitness in pulmonary rehabilitation patients. Journal of Cardiopulmonary Rehabilitation. 2006; 26:5 330-337.	Randomised trial. Reviewed in O'Shea systematic review	1-	20	Pulmonary rehabilitation patients	Endurance programme combined with resistance training	Endurance based 8 week programme	8 weeks	Function	Significant improvement in muscle strength and functional ability	
Comments Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Puente-Maestu L, Sáenz ML, Sáenz P, et	RCT	1-	49 patients	Moderate to severe (stable)	Exercise	Hospital (treadmill)vs.	8 weeks	CRDQ, incremental and	Both groups improved.	Not stated

*al.* Comparison of effects of supervised versus self-monitored training programmes in patients with chronic obstructive pulmonary disease. Eur Respir J. 2000 Mar;15(3):517-25.

COPD

home (pedometer based)

endurance cycle test.

CRDQ not different between groups

Comments: No power calculation, probably underpowered, outcome assessment not blinded, explored physiological response in detail.

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Puhan MA , Gimeno-Santos E, Scharplatz M, <i>et al.</i> Pulmonary rehabilitation following exacerbations of chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews. 2011; DOI: 10.1002/14651858.005305.pub3.	Cochrane Review	1++	Nine trials involving 432 patients (Hospital readmission 250, mortality 110, HRQOL 259 , exercise capacity 428	>90% of the patients had COPD Post- in or out patient care following acute exacerbation.	Any in-patient or out-patient pulmonary rehabilitation programme, including at least physical exercise. Programmes commenced either immediately after initiation of acute exacerbation treatment or up to 3 weeks afterwards.	Conventional community care following acute exacerbation COPD.	Admission to hospital: ranged 3 to 18 months, mean 25 weeks. Mortality range 3 to 48 months, mean 107 weeks.	Hospital admissions HRQOL acute exacerbation rates Outpatient visits Length of readmissions Mortality Exercise capacity Withdrawals Adverse effects Costs	Early pulmonary rehabilitation sig reduced hospital admissions (pooled odds ratio 0.22 [95% CI 0.08 to 0.58] with a number needed to treat (NNT) of 4 [95% CI 3 to 8], over 25 weeks. Pulmonary rehabilitation reduced mortality (OR 0.28; 95% CI 0.10 to 0.84), NNT 6 [95% CI 5 to 30] over 107 weeks). Sig difference in HRQOL, 6MWD and SWT favours pulmonary rehab.	1 salary funded by Helmut Horten foundation Switzerland

Comments: Authors state that effect size may be overestimated as study samples small, however with such large effect size, unlikely that can be attributed to bias only. Patients may be more willing to change behaviour

after acute exacerbation. Possibility of interruption to pulmonary rehabilitation if patients re-exacerbate. Authors suggest methodologically sound and large studies. Also analyses of cost effectiveness.

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Puhan MA, Spaar A, Frey M, <i>et al.</i> Early versus Late Pulmonary Rehabilitation in Chronic Obstructive Pulmonary Disease Patients with Acute Exacerbations: A Randomized Trial. <i>Respiration.</i> 2012; 83:499-506.	RCT	1-	36 (19 intervention; 17 control)	COPD patients treated for exacerbation; GOLD II-IV; Age 40+; at least 2 exacerbations in the last 2 years; INPATIENT or OUTPATIENT care for acute exacerbation	"Early Pulmonary rehabilitation" within 2 weeks	"Late pulmonary rehabilitation" 6 months after randomisation	18 months	Exacerbation rate, health related quality of life, mortality	No statistically significant differences between groups.	The Swiss Lung League, the Lung Leagues of the cantons of Aargau, Grisons, Lucerne, Nidwalden, Solothurn, Thurgau, Valais, Vaud and Zurich, the Klinik Barmelweid, the 4 clinics of Crans-Montana (Quadrimed), the Höhenkliniken of Zurich, Astra Zeneca Switzerland.

Comments: Underpowered due to problems with recruitment; high numbers of dropout and deviations from planned programme; mixture of in-patient and outpatient pulmonary rehabilitation; not all patients had hospitalised exacerbations.

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Reuveny R, Ben-Dov I, Gaides M, Reichert N. Ventilatory support during training improves training benefit in severe COPD. <i>Israeli Medical Association Journal.</i> 2005; 7:151-155.	RCT	1-	9 intervention 10 controls	COPD severe FEV1 32% pred. Only 2 women. Baseline ABG not given but ETCO2 post exercise was low normal so very unlikely to have type II failure.	BiPAP during training using a treadmill 45 minutes twice a week, to maintain constant workload, for 2 months in total	No assistance	1 week before and at the end of training	VO2 max training speed anaerobic threshold exercise lactate level exercise ventilation	Intervention group had improvements compared to the control group training speed increased by 94% vs. 41% p<0.005, increased in VO2 max 23% compared to baseline p<0.005 whilst no change in peak lactate.	Israel Lung Foundation

End tidal CO2 was lower 38 mmHg vs. 40 in the controls p<0.05.

**Comments:**

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Riario-Sforza G.G, Incorvaia C, Paterniti F, <i>et al.</i> Effects of pulmonary rehabilitation on exercise capacity in patients with COPD: a number needed to treat study. Intern J of Chronic Obstruct Pul Dis. 2009; 4: 315-9.	Case-control study	2-	284 (Rehab=222, Control=62)	COPD, attending a pulmonary rehabilitation programme.	6 week pulmonary rehabilitation programme	Control group	6 weeks	6MWT	NNT=2 for GOLD II-IV, NNT=8 for GOLD I (per protocol analysis)	Not stated

**Comments:**

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Ries AL, Kaplan RM, Limberg TM, Prewitt LM. Effects of pulmonary rehabilitation on physiologic and psychosocial outcomes in patients with chronic obstructive pulmonary disease. Annals of Internal Medicine. 1995; 122:823-833.	RCT	2+	119 patients in total randomised 57 to the intervention group	Mild to severe COPD 32 women no other serious medical conditions at time of enrolment ex-smokers or smokers committed to quitting age 61.5 vs. 63.6 (control) mean FEV1 1.2 litres no % predicted given ratio 42%.	8 weeks pulmonary rehabilitation programme 12 x 4 hour sessions including education exercise psychosocial support and specific respiratory care education followed by monthly refresher for one year	8 weeks education only programme 4 x 2 hour video sessions	6 years	Survival pulmonary function tests; maximal exercise tolerance, self-efficacy; Quality of well-being; CES-D; university of California SOB Q Health Care utilisation	Survival: 67% rehab vs. 56% control p=0.32 Rehab produced significantly greater improvements in exercise endurance; maximum exercise tolerance; symptoms of perceived breathlessness and muscle	NHLBI

Comments:										
Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Ries RM, Kaplan R, Myers R, Prewitt LM. Maintenance after pulmonary rehabilitation in chronic lung disease: a Randomized trial. Am J Respir Crit Care Med. 2003; 15; 167(6):880-888.	RCT	1+	172 were randomised to experimental group (87) or control (85) 148 completed 12 month follow up, 131 completed 24 month follow up	Chronic lung disease	Maintenance intervention consisting of weekly telephone calls and monthly supervised reinforcement sessions for 12 months	Standard care control group referral back to usual healthcare provider. Invited to regular monthly alumni meetings.	6, 12 and 24 months following rehab	Pulmonary function Exercise tolerance Dyspnoea HRQOL Healthcare use	fatigue; reported SOB with activities and self-efficacy for walking (latter - rehab improved 1.4 (3.1); control 0.1 (2.9), p≤0.05  Modest effect in experimental group. During intervention year, sig better maintained exercise tolerance, health status and hospital days in experimental group. After 24 months, both groups had returned to levels of ET and HRQOL slightly above pre-rehabilitation levels. In 2 <sup>nd</sup> year healthcare utilization significantly lower in experimental group. No difference in survival.	Not stated



Comments: Authors concluded that a maintenance programme of phone calls plus monthly contact had modest effect on health benefits but did not prevent regression of benefits after intervention. It may be the intervention that was not effective enough. Health care utilization dropped.

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Ringbaek T, Brøndum E, Martínez G <i>et al.</i> Long-term effects of 1-year maintenance training on physical functioning and health status in patients with chronic obstructive pulmonary disease: A randomized controlled study. <i>J Cardiopulm Rehab and Prevention</i> 2010; 30: 47-52.	RCT	1-	96 patients in total – intervention n=55, control n=41.	Stable COPD FEV1<80% predicted, ration <70% predicted. Motivated. Completion of 7 week pulmonary rehabilitation programme.  Exclusions – significant co morbidities	Instructed to continue unsupervised training at home plus weekly supervised training sessions 1 <sup>st</sup> 6 months, fortnightly for 2 <sup>nd</sup> 6 months.	Instructed to continue unsupervised training at home	3,6,12, and 18 months	Primary outcome – ESWT and SGRQ. Secondary outcomes – hospitalization, admission rates, length of stay, adherence to training, attendance.	Authors report sig improved walking time, but no report of effect size. No sig differences in SGRQ at any time. No difference in hospitalization.	Not stated

Comments: The results appear unclear. Unclear how many patients completed the study. High percentage of drop out – authors state comparable but higher in control group which may affect results. Decline in SGRQ in both groups after 6 months. No difference between groups to first hospitalization. Improved ESWT which disappeared when intervention stopped.

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Romagnoli M, Dell'Orso D, Lorenzi C, <i>et al.</i> Repeated pulmonary rehabilitation in severe and disabled COPD patients. <i>Respiration</i> . 2006;73(6):769-76.	RCT	1-	35 randomised, 29 completed	COPD by GOLD standard; FEV1<50% predicted; MRC at least 3; all completed an initial 18 week pulmonary rehabilitation programme	Further pulmonary rehabilitation programmes at 6 and 12 months	Further pulmonary rehabilitation programmes at 12 months	12 months in total	Full lung function including MIP; ABG; 6MWD; Dyspnoea and fatigue at peak effort (modified Borg); SGRQ; hospital admissions	The additional rehab session reduced SGRQ symptom sub-score but did not affect the other outcomes tested	Not stated

Comments: Randomisation and blinding not well described. Per-protocol analyses only. Large number of analyses (multiple end-points, time points, and comparisons) using parametric statistics for data that is bounded and not normally distributed.

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Rooyackers JM, Dekhuijzen PN, Van Herwaarden CL, Folgering HT. Training with	RCT	1-	24 randomised.	COPD by ATS criteria. Hypoxic on exercise.	10 weeks pulmonary rehabilitation with 4l /min oxygen via nasal cannulae	10 weeks pulmonary rehabilitation (no placebo)	End of pulmonary rehabilitation	CPEX (incremental and constant); Lung volumes and transfer factor; 6MWD; stair-	No additional benefit of supplemental oxygen	Charity: Netherlands Asthma Foundation (90.22).

supplemental oxygen in patients with COPD and hypoxaemia at peak exercise. *European Resp Journal*. 1997; 10(6):1278-84.

climbing; peripheral muscle endurance; CRDQ

Comments: Not blinded; randomisation process not described; no placebo gas; study underpowered for clinically meaningful gains; analysis of bounded data as if normally distributed

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Sabit R, Griffiths TL, Watkins AJ, <i>et al</i> . Predictors of poor attendance at an outpatient pulmonary rehabilitation programme. <i>Respir Med</i> . 2008; 102 (6): 819-824.	Qualitative	3	239	159 male, 80 female patients with COPD (FEV1 40(15)% predicted)	All subjects	Subjects completed either 6 or 18 week outpatient pulmonary rehabilitation. Sessions x 3/week for up to 2 hours	NA	Attendance rate	A higher attendance rate was seen in non-smokers. 17.7% smokers attended at least 2 out of 3 pulmonary rehabilitation sessions while 56.5% attended fewer than 2 out of 3 sessions (p<0.01). Using multiple regression analysis smoking status contributed to attendance.	Welsh office R&D (WORD)

Comments: Current smoking contributes to lower attendance at pulmonary rehabilitation sessions

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Scorsone D, Bartolini S, Saporiti R, <i>et al</i> . Does a low-density gas mixture or oxygen supplementation improve exercise training in COPD? <i>CHEST</i> . 2010 Nov; 138(5):1133-9.	RCT	1-	30	History of COPD with airflow obstruction (not otherwise clarified)	Thrice weekly for 8 weeks supervised exercise programme plus 40% supplemental oxygen or heliox (60/40)	Thrice weekly for 8 weeks supervised exercise programme	End of programme	CPEX (incremental and constant load); lung volumes & transfer factor.	No additional benefit	Government

Comments: The study appears to be at low risk of bias as described. However, the small size of the trial (10 patients per arm) is insufficient to exclude a clinically meaningful benefit from the active interventions studied given the inter-individual variation.

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Sewell L, Singh SJ, Williams JEA, <i>et al.</i> (2006) How long should outpatient pulmonary rehabilitation be? A randomised controlled trial of 4 weeks versus 7 weeks. <i>Thorax</i> . 2006; 61: 767-771. Comments:	RCT	1+	100 (control 4 weeks = 50, pulmonary rehabilitation 7 weeks= 50)	COPD	Pulmonary rehabilitation duration 4 weeks supervised +3 weeks unsupervised v 7 weeks supervised		Outcomes measured at 0, 4 (in 4 week group only), 7 weeks and finally 6 months.	ISWT, ESWT, CRDQ, BPQ	ESWT diff between groups =124.6 seconds (p=0.024)	Funded by a Trevor Clay grant from the British Lung Foundation

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Sewell L; Singh S; Williams JEA, <i>et al.</i> Can individualised rehabilitation improve functional independence in elderly patients with COPD? <i>CHEST</i> . 2005. 128. 1194-1200.	RCT	1-	180	Patients with COPD referred to pulmonary rehabilitation assessment clinic	ITEP – Individually targeted exercise programme	GEP- conventional general exercise programme	Baseline, 7 weeks pulmonary rehabilitation then after pulmonary rehabilitation intervention.	Physical activity monitors; Canadian Occupational Performance Measure; ISWT; Chronic Respiratory questionnaire - self reported.	Both ITEP & GEP made significant improvements within group in all outcomes however no significant 'Between group' differences were observed in any outcome.	Trent Regional Research Scheme

Comments: Pragmatic study however lost power in GEP arm due to higher than expected drop outs. Results not ITT.

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Simpson K, Killian K, McCartney N, <i>et al.</i> Randomised controlled trial of weightlifting exercise in patients with chronic airflow limitation. <i>Thorax</i> . 1992; 47:70-75. Comments: Difference in baseline gender (corrected with % predicted values)	RCT	1-	34 (28 completed)	COPD. 73 years old. FEV1 39% predicted.	10 repetitions resistance training, progressing from 50% to 85% max. Maximum redone every 6 sessions.	Control	8 weeks	Strength	61N increase in quads strength (25%)	Medical Research Council of Canada

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Skumlien, S, Skogedal EA, Bjørtuft φ, <i>et al.</i> Four weeks' intensive rehabilitation generates significant health effects in COPD patients. <i>Chronic Respiratory Disease.</i> 2007; 4(1): 5-13.	Cohort study	2+	Pulmonary rehabilitation= 40, control = 20	COPD patients living within 6 hours of travel from clinic.	4 week in patient pulmonary rehabilitation programme.	Usual care - control patients on pulmonary rehabilitation waiting list	Pulmonary rehabilitation subjects – 4 weeks Control subjects – assessed 4 months prior to start of pulmonary rehabilitation then at start of pulmonary rehabilitation programme	Work rate peak, SGRQ, 6MWD, TET	Work rate peak, watts pulmonary rehabilitation +26 Control +7 p <0.05; 6MWD pulmonary rehabilitation +14 (n=33) Control +-5 NS; SGRQ (total scores) pulmonary rehabilitation - 66 (n=33) Control -0.5	Not stated

**Comments:**

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Stav D, Raz M, Shpirer I. Three years of pulmonary rehabilitation: inhibit the decline in airflow obstruction, improves exercise endurance time, and body-mass index, in chronic obstructive pulmonary disease. <i>BMC Pulmonary Medicine.</i> 2009; 9:26.	Controlled trial	2+	80 (40 in each group)	COPD, On LABA or ICS/LABA, <70 years, FEV1 30-60% predicted, stable 2 months prior to recruitment	3 years, twice weekly supervised exercise + unsupervised, psychologist as needed	Control group	3 years	Cycle incremental, cycle endurance, FEV1, BMI	75ml difference in FEV1 in 3 years. Improved and sustained exercise performance. BMI remained stable in rehab group (reduced in control group)	Tel Aviv Lung Association

**Comments:** Long period of rehab. Small clinical difference in FEV1

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Steiner MC, Barton R, Singh SJ, Morgan	RCT	1+	85 (60 completed)	At least moderate COPD by BTS	125 ml supplement drink:	Non-nutritive	8 weeks	ISWT, ESWT, handgrip, quads	No difference in exercise	University Hospitals Leicester

**MDL. Nutritional enhancement of exercise performance in chronic obstructive pulmonary disease: a randomised Controlled trial. Thorax. 2003; 58:745–751.**

criteria excluded if BMI >30 or diabetic

570 kcal daily in the following macronutrient composition: carbohydrate 60%, fat 20%, protein 20%.

Both had pulmonary rehabilitation.

visually identical placebo  
  
Pulmonary rehabilitation.

strength, weight, FFM,

capacity, supplement group gained weight (0.63kg). Control group lost weight (0.58Kg), p=0.004

and Nutricia, Zoetermeer, The Netherlands.

**Comments: Only 60 patients completed the study so the findings should not be interpreted as definitive**

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
<b>Srijbos JH, Postma D, van Altna R, et al. A comparison between an outpatient hospital-based pulmonary rehabilitation program and a home-care pulmonary rehabilitation program in patients with COPD. A follow-up of 18 months. CHEST. 1996; 109(2):366-72.</b>	RCT	1-	50 patients 18 hospital, 17 home care 15 control	Moderate to severe (stable) COPD	Exercise and education	Hospital vs. home vs. control	18 months	Spirometry, cycle test, Borg, 4 min walk distance (primary outcome not identified)	Both intervention groups improved in exercise test (w max) at 3 months. Home group maintained benefit at 12 and 18 months (p<0.05)	Not stated

**Comments: Small study-underpowered, outcome assessment not blinded.**

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
<b>Toledo A, Borghi-Silva A, Malosá Sampaio LM, et al. The impact of non-invasive ventilation during the physical training in patients with moderate-to-severe chronic obstructive pulmonary disease (COPD). Clinics.</b>	RCT	1-	18	COPD patients; FEV<60% predicted; clinically stable for 6 months	Bi-level ventilation (IPAP 10-15cmH2O; EPAP 4-6cmH2O). Training programme: 12 weeks, 30 minutes three times a week, treadmill walking 70% maximum speed	Unassisted training programme	Before and after training	Incremental treadmill walk, blood lactate, respiratory muscle strength, isotime Borg, isotime oxygen saturations	Both groups showed improvements in walk distance, respiratory muscle strength and peripheral oxygen saturation, and a reduction in Borg dyspnoea	Not stated

2007;62(2):113-20.

scores. Blood lactate significantly decreased and VO2 significantly increased in NIV group. Only change in blood lactate stated to be significantly different between groups.

**Comments: No information about randomisation process. Patients and investigators not blinded. Underpowered/small numbers. Statistical testing for difference between groups not mentioned for all outcomes.**

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Trappenburg JC, Troosters T, Spruit MA, <i>et al.</i> Psychosocial conditions do not affect short-term outcome of multidisciplinary rehabilitation in chronic obstructive pulmonary disease. Arch Phys Med Rehabil 2005 86(9):1788-92	Cohort	3	81	Patients with COPD (FEV1 40(15)% predicted	All subjects	12 week outpatient rehabilitation with 2 hour sessions, 3 / week	NA	Change in psychological metrics (HAD, PAIS-SR), social support / interactions (SSL-N), QAL (CRDQ, HRQOL) functional capacity (6MWT, Max aerobic capacity)	Significant improvements in functional exercise capacity, HRQOL, functional status, depression and anxiety observed. Baseline psychological measures did not relate to change in functional capacity.	University Grant

**Comments: Outcome from this prolonged pulmonary rehabilitation programme was independent of baseline psychological and socioeconomic status. Study limitations include study selection bias.**

Bibliographic citation	Study type	Ev level	Number patients	Patient characteristics	Intervention	Comparison	Length of Follow-up	Outcome measures	Effect Size	Source of Funding
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<b>Troosters T, Gosselink R, Decramer M. Short and long term effects of outpatient rehabilitation in patients with chronic obstructive pulmonary disease. Am J Med. 2000; 109:207-212.</b>	RCT	1-	100 enrolled, 62 analysed	COPD, FEV1 <65% predicted, <75 years, clinical stable	Exercise training, concurrent aerobic and resistance training for 6 months	<b>Control</b>	<b>18 months</b>	Isometric strength, maximal exercise performance, quality of life, health economic, functional 51entilat performance	18Nm increase in quads strength at 6 months, 15Nm at 18 months	Fonds voor Wetenschappelijk Onderzoek-Vlaanderen, Levenslijn grant
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Comments: Per protocol analysis (only 62% included)

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
<b>van 't Hul A, Gosselink R, Hollander P, et al. Training with inspiratory pressure support in patients with severe COPD. European Respiratory Journal. 2006; 27 (1): 65-72.</b>	RCT	1-	37 randomised; 29 completed	COPD patients; 40-75 years; FEV<60% predicted; 51entilator limitation to exercise capacity; resting PaO2>8kPa	Inspiratory pressure Support 10 (IPS10) cmH2O (training: 8 week cycling programme, 45 minutes three times a week).	Sham Inspiratory pressure Support 5 cmH2O (training: 8 week cycling programme, 45 minutes three times a week).	Pre and post training	ISW, SGRQ, Constant Load cycle endurance (75% of Wpeak)	Significantly higher training intensity in IPS10 group; change in ISW statistically significantly higher in IPS10 group (31+/-21m versus 13+/-31m); change in cycling endurance significantly higher in IPS10 group (7.4+/-5.4 versus 3.9+/-6.0 minutes); no change in SGRQ	Dutch Asthma Foundation

Comments: Improvement in ISW unlikely to be clinically significant. Underpowered. No measurement of breathlessness. SGRQ unchanged. Apart from cycling, no other component generally seen in outpatient programme provided. However investigator made measurements blinded and patients used sham ventilator.

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Vincent E, Sewell L, Wagg K, <i>et al.</i> , <b>Measuring a change in self-efficacy following pulmonary rehabilitation: an evaluation of the PRAISE tool.</b> CHEST. 2011; 140: 1534-9.	Detailed a reliability study and a prospective observational uncontrolled cohort study	2+	29 patients analysed for reliability study and 225 patients recruited to sensitivity study	Clinically stable COPD attending pulmonary rehabilitation	7 week pulmonary rehabilitation programme attending 2 times per week	None	7 weeks	PRAISE score, MRC, ISWT	Change in PRAISE after pulmonary rehabilitation = 3.59, mean change in ISWT= 83.44 metres.	British Lung Foundation Project grant
Comments:										
Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Vivodtzev I, Pépin JL, Vottero G, <i>et al.</i> <b>Improvement in quadriceps strength and dyspnoea in daily tasks after 1 month of electrical stimulation in severely deconditioned and malnourished COPD.</b> Chest. 2006; 129(6):1540-1548.	RCT	1- (very select population)	17	Severe COPD, FEV1 <50%, BMI <22, QMVC <50%, Endurance bike <5 minutes at 20W, Recent hospital stay requiring 1/12 inpatient rehab, Clinically stable	Usual rehabilitation + NMES	Usual rehabilitation	4 weeks	Quality of life (MRF 28), 6MWT, quadriceps strength, muscle composition (n=11)	Improvement in quadriceps strength, No difference in walking (possibly underpowered), Improvement in dyspnoea in daily tasks domain of MRF 28	Grants from the Association pour le Traitement, la Re'éducation et la Re'adaptation des Insuffisants Respiratoires (ATRIR), "Bourse Andre' Dion," Nyons, France
Comments:										
Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding



<p>Vonbank K, Strasser B, Mondrzyk J <i>et al.</i> Strength training increases maximum working capacity in patients with COPD--randomized clinical trial comparing three training modalities.</p> <p>Respiratory Medicine (2012) 106(4), 557-563.</p>	RCT	1+	43 randomised 36 completed	Stable COPD mean FEV1% 55 mean age 60 years	Progressive strength training (ST) 2 x week 12 weeks	vs. endurance training (ET) and vs. combined strength and endurance (CT)	12 week training period	Cardiopulmonary exercise testing, FEV1, muscle strength, QOL	Muscle strength (leg press, bench press and bench pull) improved in all three training groups with a significant higher improvement in the ST ( mean (SD) 39.3 (27.7)%, 20.9 (19.8)%, 20.3 (10.3)% and the CT (43.3 (40.2)%, 18.1 (12.4)%, 21.6 (26.6%) compared to the ET alone 20.4 (32.3)%, 6.4 (16.3)%, 12.1 (15.5)%. no diff between groups for other outcomes	Austrian national research fund	
Comments	Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
<p>Wadell K, Henriksson-Larsen K, Lundgren R. Physical training with and without oxygen in patients with chronic obstructive pulmonary disease and exercise-induced hypoxaemia. Journal of Rehabilitation Medicine.</p>	RCT	1-	22 randomised, 20 completed	COPD by ERS criteria	8 weeks of thrice weekly exercise with oxygen 5l/min via nasal cannulae	8 weeks of thrice weekly exercise	End of exercise programme	6MWT; distance walked in training; venous pCO2; serum lactate; oxygen saturation; Borg	No difference	Charity and industry	

2001;33(5):200-205.

Comments: Single blind study. The small heterogeneous sample experienced a large training effect hence the study was underpowered to detect additional effects of oxygen supplementation

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Wanke T, Formanek D, Lahrman H, <i>et al.</i> Effects of Combined Inspiratory Muscle Training and Cycle Ergometer Training on Exercise Performance in Patients with COPD. European Respiratory Journal. 1994; 7:2205-2211.	RCT	1-	42 total: 21 IMT & CET and 21 CET alone	COPD by usual definition (all severities)	8 weeks. CET: 4 x week tailored exercise on cycle ergometer, IMT: extensive resistance training and endurance training using individualised threshold device	CET only. No sham, no peripheral muscle training	End of intervention	Inspiratory pressures, CPEX parameters	Multiple significant results with IMT versus CET: 15-20% greater increase in inspiratory pressures. 10% greater VO2max/Wmax /Vtmax	Austrian National Bank

Comments: 18 of initial 60 dropped out but reasons not well covered and differential rate not given. Randomisation process not covered. Study not blinded. Most analyses are given versus baseline.

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Waterhouse JC, Walters SJ, Oluboyede Y, Lawson RA <i>et al.</i> A randomised 2 x 2 trial of community versus hospital pulmonary rehabilitation for chronic obstructive pulmonary disease followed by telephone or conventional follow up. Health Technol Assess 2010; 14(6).	RCT	1++	240 4 groups	COPD diagnosis based on GOLD criteria MRC 3 or worse Clinically stable  Exclusion: inability to understand educational talks, prognosis of 2 years or less; LTOT or significant desaturation; musculoskeletal problems precluding exercise training; no access to phone; unstable / uncontrolled cardiac disease	4 arms; Community pulmonary rehabilitation plus phone call follow up; Community pulmonary rehabilitation no phone call follow up; Hospital pulmonary rehabilitation plus phone call follow up; hospital pulmonary rehabilitation no phone call follow up.  Here: phone call maintenance	No phone call maintenance	18 months	ESWT, SF-6D	ESWT 56.9 (-25.2, 139)m, p=0.174  SF-6D 0.02 (0.04, 0.00), p=0.09	HTA

Comments: Well-designed study exploring the value of community vs. hospital based rehabilitation. Second phase of study evaluated benefit of telephone call, no benefits identified in any outcomes.

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
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<b>Wedzicha JA, Bestall JC, Garrod R, et al. Randomised controlled trial of pulmonary rehabilitation in severe chronic obstructive disease patients, stratified with MRC dyspnoea scale. European Respiratory Journal. 1998; 12 (2):363-369.</b>	RCT	1+	126	Patients with COPD stratified into MRC 3-4 (n=66) and MRC 5 (n=60). Approximately half of overall group male. MRC 3-4 patients FEV1 approximately 0.98L; 37% predicted. MRC 5 patients FEV1 approximately 0.82L; 37% predicted. Each group (MRC 3-4 and MRC 5) randomised to exercise and education or education only	All subjects	8 week pulmonary rehabilitation – 2 supervised exercise and education sessions/week (exercise group) vs. 2 education sessions/week (control). Outpatient exercise for MRC 3-4 and home exercise MRC 5	End of pulmonary rehabilitation	Comparison of group response exercise (pulmonary rehabilitation and education) vs. control (education) in patients who completed. MRC 3-4: 29 completed exercise vs. 27 control. MRC 5: 26 completed exercise vs. 28 control. Outcome measures exercise capacity (ISWT), HRQOL (SGRQ and CRDQ)	MRC 3-4 patients improved ISWT 88m with exercise significantly more than - 16m control. Also significant improvement CRDQ 14 exercise vs. 6 control. No difference SGRQ between groups. MRC 5 subjects showed no significant improvement ISWT, CRDQ or SGRQ in either exercise or control groups	UK NHS Research and Development programme
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**Comments: Patients who are severely dyspnoeic and housebound with breathlessness (MRC 5) fail to gain benefit from 8 week home exercise programme whereas patients with moderate dyspnoea (MRC 3-4) improve exercise capacity and 1 measure of health related quality of life after outpatient pulmonary rehabilitation.**

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
<b>Weiner P, Azgad Y, Ganam R. Inspiratory muscle training combined with general exercise reconditioning in patients with COPD. Chest. 1992; 102:1351-56.</b>	RCT	1-	36 total: 12 IMT & general exercise reconditioning; 12 general exercise reconditioning; 12 nil	"Chronic airflow limitation"	6 months. IMT: threshold device increased toward 80% Pimax, frequency of use unclear; General exercise reconditioning: cycling then rowing then weights, frequency unclear. Sham IMT was used in general exercise	"No intervention" group did not have sham IMT or other contact. ?standard care	End of intervention	Pimax; respiratory muscle endurance; 12 MWT	200m mean increase in GENERAL EXERCISE RECONDITIONING and IMT group, no change in other groups	Not stated.

reconditioning group.

Comments: Not truly randomly assigned - a matching process is described. Control group poorly described.

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
White RJ, Rudkin S, Harrison S, <i>et al.</i> Pulmonary rehabilitation compared with brief advice given for severe chronic obstructive pulmonary disease. <i>Journal of Cardiopulmonary Rehabilitation.</i> 2002; 22(5): 338-44.	RCT	1+	103 patients	Moderate to severe (stable) COPD	Exercise	Hospital based pulmonary rehabilitation home vs. brief intervention	3 months	CRDQ & ISWT	Both intervention groups improved at 3 months. CRDQ (D) weeks difference =0.4 (p>0.05)) ISWT difference = 34.1m (p<0.05).	Funding Academic Institution (Frenchay Respiratory Fund)

Comments: Power calculation assumed superiority, probably underpowered, outcome assessment blinded.

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Wijkstra PJ, Ten Vergent EM, van Altena R, <i>et al.</i> Long term benefits of rehabilitation at home on quality of life and exercise tolerance in patients with chronic obstructive pulmonary disease. <i>Thorax.</i> 1995; 50:824-828.	Pilot RCT	1-	45. 33 completed. 3 arms	Diagnosed COPD. FEV1 <60% predicted; post bronchodilator FEV1/IVC < 50%	Maintenance strategies post rehabilitation	Control (no intervention including no original rehabilitation)	18 months	QOL: CRDQ	Mean difference not described.	Nederlands Astma Fonds (89.29) and the Foundation Astmabestrijding.

Comment: The authors concluded that after a 3 month course of rehabilitation benefits were observed in the groups that had either weekly or monthly supervised rehabilitation sessions.

The sample size for each of the three groups was very small (n=11,12 & 13 for each of the three groups weekly, monthly and control respectively). Not blinded, mean differences between groups not described.

6MWT compared to baseline and not between groups. Assume same study as Wijkstra 1996.

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Wijkstra P J, van der Mark TW, Kraan J, <i>et al.</i> Long term effects of home rehabilitation	Pilot RCT	1-	45. 33 completed. 3 arms	Confirmed diagnosis of COPD	Maintenance 1/week; 1/ month following intensive pulmonary	Control arm who had no initial pulmonary rehabilitation	18 months	Wmax; lung function, 6MWD and inspiratory muscles.	Mean difference not described for WMax. Stated to not be	Nederlands Astma Fonds and Foundation Astmabestrijding

on physical performance in chronic obstructive pulmonary disease. Am. J. Resp. Crit. Care. Med. 1996; 153:1234-41.

rehabilitation n

significantly different between groups.

**Comments:** The authors concluded that after a 3 month course of pulmonary rehabilitation benefits were observed in the groups that had either weekly or monthly supervised pulmonary rehabilitation sessions. The sample size for each of the three groups was very small (n=11,12 & 13 for each of the three groups weekly, monthly and control respectively). No power calculation reported. Blinding not documented.

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Withers NJ, Rudkin ST, White RJ. Anxiety and Depression in Severe Chronic Obstructive Pulmonary Disease: The Effects of Pulmonary Rehabilitation. J Cardiopulm Rehabil. 1999; 19(6):362-365.	Cohort	3	95	62 male and 33 female patients with COPD (FEV1 0.8(0.31)L). Anxiety and depression defined using the Hospital Anxiety and Depression Questionnaire with scores of 10+ indication a high level of anxiety and depression	All subjects	6 week outpatient pulmonary rehabilitation with 3 hour sessions 2x/week	NA	Comparison of improvement in ISWT in patients with/without high level of anxiety and depression.	Similar improvement in ISWD in patients with (30m) and without (25m) high depression score. Greater improvement in ISWD in patients with (50m) vs. without (20m) high anxiety score (p<0.05)	Not stated

**Comments:** COPD patients with high HAD anxiety and depression scores gain similar or greater improvement in walking distance compared to patients with normal scores

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Young P, Dewse M, Fergusson W, Kolbe J. Respiratory rehabilitation in chronic obstructive pulmonary disease: predictors of nonadherence. Eur Respir J 1999 13: 855-859.	Qualitative	3	91	50-55% male patients with COPD (FEV1 34(13)% predicted, mean FEV1 0.9L)	All subjects	Subjects completed 4 week pulmonary rehabilitation programme	NA	Completion rate defined as those referred to pulmonary rehabilitation who agreed to attend and completed the 4 week programme	A lower proportion of non-smokers (8%) completed the programme than non-smokers (28%, p<0.02). Current smokers had odds of 0.3 (0.1-0.9) of pulmonary rehabilitation completion	Not stated

**Comments:** Completion rate was good in both groups but fewer current smokers completed pulmonary rehabilitation programme

Bibliographic citation	Study type	Ev lev	Number patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding
Zainuldin R, Mackey MG, Alison JA. Optimal intensity and type of leg exercise training for people with chronic obstructive pulmonary disease (Review). The Cochrane Collaboration. 2011; Issue 9(11).	Meta-analysis	1++	Eight included studies were analysed (367 participants)	COPD patients defined by FEV1/FVC ratio < 0.7	Continuous exercise training	Interval training	12 sessions or more	Primary outcomes were at peak exercise (peak work rate, peak oxygen consumption, peak minute ventilation and lactate threshold), at isowork or isotime, endurance time on a constant work rate test and functional exercise capacity (six-minute walk distance).	When comparing continuous and interval training, there were no significant differences in any of the primary outcomes, except for oxygen consumption at isotime (MD 0.08; 95% CI 0.01 to 0.16) but the treatment effect was not considered clinically important.	Cochrane airways collaboration- unfunded

Comments:

# Title: The British Thoracic Society Guideline on Pulmonary Rehabilitation in Adults

## Short Title: BTS Pulmonary Rehabilitation Guideline

### Web Appendix 4 - ABBREVIATIONS FOR EVIDENCE TABLES

6MWT	6 minute walk test
6MWD	6 minute walk distance
12MWD	12 minute walk distance
12MWT	12 minute walk test
ABG	Arterial blood gases
ADL	Activities of daily living
AQ20	Airways questionnaire 20
ATS	American Thoracic Society
BDI	Baseline dyspnoea index
BiPAP	Bilevel positive airway pressure
BMI	Body mass index
BPQ	Breathing problems questionnaire
BTS	British Thoracic Society
CBT	Cognitive behavioural therapy
CES-D	Centre for epidemiologic studies depression scale
CET	Cycle ergometry training
CHF	Chronic heart failure
COPD	Chronic obstructive pulmonary disease
CPE	Cardiopulmonary exercise
CPEX	Cardiopulmonary exercise testing
CRDQ	Chronic respiratory disease questionnaire
CRF	Chronic respiratory failure
CRP	C reactive protein
CSES-D	Center for Epidemiologic Studies Depression Scale
CSES	COPD self efficacy scale
CT	Combined training
DHA	Docosahexaenoic acid
DNA	Did not attend
EAA	Essential amino acids
EPA	Eicosapentaenoic acid
EPAP	Expiratory pressure levels
ERS	European Respiratory Society
ESWT	Endurance shuttle walk test
ET	Endurance training
ETCO <sub>2</sub>	End tidal CO <sub>2</sub>
ETA	Exercise training alone
ETLS	Exercise training plus lecture series
ETAT	Exercise training plus activity training
FEV <sub>1</sub>	Forced expiratory volume in 1 second
FFM	Fat free mass
FFMI	Fat free mass index
FM	Fat mass
FVC	Forced vital capacity
GEP	Generalised exercise programme
GER	General exercise reconditioning
GOLD	Global initiative for chronic obstructive lung disease
HADS	Hospital anxiety and depression score

HAM-A	Hamilton anxiety rating scale
HAM-D	Hamilton depression rating scale
HRCT	High resolution computed tomography
HRQOL	Health related quality of life
ICS	Inhaled corticosteroids
IHD	Ischaemic heart disease
ILD	Interstitial lung disease
IL6	Inter leukin 6
IM	Intermuscular
IMT	Inspiratory muscle training
IPAP	Inspiratory pressure levels
IPF	Idiopathic pulmonary fibrosis
IPS10	Inspiratory pressure support 10
IQR	Interquartile range
ISWT	Incremental shuttle walk test
ITEP	Individually targeted exercise programme
ITT	Intention to treat
IVC	Inspiratory vital capacity
LABA	Long acting beta agonist
LAP	Lifestyle activity programme
LCADL	London chest activity of daily living scale
LGT	Low intensity general training group
LTOT	Long term oxygen therapy
MIP	Maximum inspiratory pressure
MRC	Medical research council scale
Mw	Weighed mean
MRF28	Maugeri respiratory failure questionnaire
ND	Nandrolone decanoate
NIV	Non invasive ventilation
NIVS	Noninvasive ventilator support
NMES	Neuromuscular electrical stimulation
NNT	Number needed to treat
NS	Non significant
O <sub>2</sub>	Oxygen
PAIS-SR	Psychosocial adjustment to illness scale-self report
PaCO <sub>2</sub>	Partical pressure of carbon dioxide
PaO <sub>2</sub>	Partial pressure of oxygen
PFSDQ	Pulmonary functional status and dsypnoea questionnaire
PeMax	Maximal expiratory mouth pressure
PiMAX	Maximal inspiratory mouth pressure
PRAISE	Pulmonary rehabilitation adapted index of self efficacy
PUFA	Polyunsaturated fatty acid
RM	Repitition maximum test
MVC	Maximal voluntary contraction
QOL	Quality of life
RCT	Randomised controlled trial
SCL-90R	Symptom checklist 90R
SF-36	Short form 36
SGRQ	St Georges respiratory questionnaire
SMD	Standardised mean difference
SOB	Shortness of breath
SpO <sub>2</sub>	Saturation of peripheral oxygen
SPPB	Short physical performance battery
ST	Strength training group



STAI	State trait anxiety inventory
SWT	Shuttle walk test
TDI	Transition dyspnoea index
TET	Traditional exercise training
TNF	Tumour necrosis factor
VAS	Visual analogue scale
VO <sub>2</sub> max	Maximal oxygen consumption