Optimizing pulmonary rehabilitation in chronic obstructive pulmonary disease – practical issues: A Canadian Thoracic Society Clinical Practice Guideline

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Pulmonary rehabilitation (PR) participation is the standard of care for patients with chronic obstructive pulmonary disease (COPD) who remain symptomatic despite bronchodilator therapies. However, there are questions about specific aspects of PR programming including optimal site of rehabilitation delivery, components of rehabilitation programming, duration of rehabilitation, target populations and timing of rehabilitation. The present document was compiled to specifically address these important clinical issues, using an evidence-based, systematic review process led by a representative interprofessional panel of experts.

The evidence reveals there are no differences in major patient-related outcomes of PR between nonhospital- (community or home sites) or hospital-based sites. There is strong support to recommend that COPD patients initiate PR within one month following an acute exacerbation due to benefits of improved dyspnea, exercise tolerance and health-related quality of life relative to usual care. Moreover, the benefits of PR are evident in both men and women, and in patients with moderate, severe and very severe COPD. The current review also suggests that longer PR programs, beyond six to eight weeks duration, be provided for COPD patients, and that while aerobic training is the foundation of PR, endurance and functional ability may be further improved with both aerobic and resistance training.

Key Words: *COPD; Chronic obstructive pulmonary disease; Management; Pulmonary rehabilitation*

L'optimisation de la réadaptation pulmonaire en cas de maladie pulmonaire obstructive chronique – des enjeux pratiques : Directives cliniques de la Société canadienne de thoracologie

La participation à une réadaptation pulmonaire (RP) est la norme de soins pour les patients ayant une maladie pulmonaire obstructive chronique (MPOC) qui demeure symptomatiques malgré une thérapie aux bronchodilatateurs. Cependant, des questions sont soulevées à l'égard d'aspects précis du programme de RP, y compris le lieu optimal d'exécution de la réadaptation, les éléments du programme de réadaptation, la durée de la réadaptation, les populations ciblées et le moment de la réadaptation. Le présent document a été compilé pour aborder précisément ces questions cliniques d'importance au moyen d'un processus d'analyse systématique probant dirigé par un groupe d'experts interprofessionnels représentatifs.

Les données probantes révèlent qu'il n'y a pas de différences dans les principales issues de la RP entre les patients en milieu non hospitalier (milieu communautaire ou à domicile) et hospitalier. Il est fortement préconisé de recommander que les patients ayant une MPOC amorcent la RP dans le mois suivant une exacerbation aiguë, en raison des avantages liés à l'amélioration de la dyspnée, à la tolérance à l'exercice et à la qualité de vie liée à la santé découlant des soins usuels. De plus, les bienfaits de la RP sont évidents tant chez les hommes que chez les femmes, de même que chez les patients ayant une MOPC modérée, grave ou très grave. L'analyse indique également d'offrir des programmes de RP plus longs, de plus de six à huit semaines, aux patients ayant un MPOC et que, même si l'entraînement aérobique est la base de la RP, l'endurance et la capacité fonctionnelle peuvent s'accroître grâce à un entraînement aérobique et musculaire.

Chronic obstructive pulmonary disease (COPD) is a respiratory disorder largely caused by smoking, and is characterized by progressive, partially reversible airway obstruction and lung hyperinflation, systemic manifestations, and increasing frequency and severity of exacerbations (1,2). Effective management of COPD includes both pharmacological and nonpharmacological therapies, which leads to improvement in meaningful patient-centred outcomes. Pulmonary rehabilitation (PR) is now the standard of care for individuals with COPD who remain symptomatic despite bronchodilator therapies (1,3). In addition to the significant benefits realized by the patient, it has recently become clear that PR also reduces health care resource use (4).

Despite recent evidence-based guidelines (3,5), practical clinical questions regarding many specific aspects of PR programming remain, including optimal site of rehabilitation delivery, components of rehabilitation programming, duration

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of rehabilitation, target populations and timing of rehabilitation. The present document was designed to specifically address these important clinical issues using an evidence-based, systematic review process led by a representative interprofessional panel of experts in the field.

TARGET POPULATION

The present clinical practice guideline applies to adult patients diagnosed with COPD.

TARGET USERS

The current document is intended for those involved in the coordination, design, delivery and evaluation of PR programs. They include university- and community-based respirologists, physiotherapists, exercise therapists, nurses, respiratory therapists, exercise physiologists, occupational therapists and health care administrators.

METHODOLOGY

Guideline development process

The Canadian Thoracic Society (CTS) Optimizing Pulmonary Rehabilitation in COPD Clinical Practice Guideline document was developed by an Expert Working Group panel of representative professionals involved in the coordination, design, delivery and evaluation of PR. The guideline was developed in accordance with the convention of the 23-item Appraisal of Guidelines for Research and Evaluation (AGREE II) instrument (6) – the current gold standard in appraising the reporting of clinical practice guidelines. The process was coordinated by the CTS Respiratory Guideline Committee and staff, with the assistance of a consultant librarian and methodology experts. The research questions are based on the Working Group's recognition of clinical care gaps and solicited needs of the target populations. Questions were constructed in accordance with the 'PICO' process, taking into consideration the Problem, Intervention, Comparison and Outcomes within each question, thus ensuring that an appropriate and answerable question was constructed. This process also enabled the development of a search strategy that outlined the types of studies, main topics and terms, inclusion and exclusion criteria considered in the search, as well as suitable databases for the search.

Literature search

Based on the criteria outlined within the search strategy for each of the research questions, various databases (MEDLINE, EMBASE, the Cochrane Library, the Canadian Medical Association InfoBase and the National Guideline Clearinghouse) were searched for pertinent literature published between 1990 and April 2009. In addition, supplementary references from articles and reviews identified by the Expert Working Group members were also scanned for additional citations.

Study selection criteria

Articles were selected for inclusion in the systematic review of the evidence if they reported data on the role of PR among adult individuals with COPD. Studies were required to report data on at least one of the following outcomes of interest: activity, exacerbations, health care use, quality of life or health status, and cost benefit or use.

Evidence synthesis

An initial review of abstracts informed the selection of full-text articles, with a minimum of two Working Group members assigned to each question. Data extraction tables were used to systematically extract evidence from included full-text articles, based on the predetermined inclusion and exclusion criteria supporting the research question. These tables were used to summarize and organize information such as study design, target population, interventions, outcomes, functional and clinical significance of findings, and for formulation of recommendations and supporting narrative text. Rejected full-text articles were also listed with reasons for their exclusion. Data extraction tables are available as online supplemental material (www.respiratoryguidelines.ca or www.pulsus.com). Narrative text of the key evidence and conclusions supporting the recommendations were completed before formulation of the recommendations.

Critical appraisal

The strengths and weaknesses of the evidence, along with the potential harms and benefits related to PR programs, were carefully considered in the generation of the recommendations. Although the majority of the evidence on this topic is comprised of small randomized trials or nonrandomized data, strong recommendations were provided when it was agreed through consensus that the majority of practitioners would choose similar recommendations if they were responsible for the development of similar guidance. This process was further strengthened by the circulation of the draft guideline to external experts who were given an opportunity to comment and help formulate the final recommendations before formal organizational approval and peer-review publication.

Recommendations

Decision regarding the strength of recommendations (Table 1) was achieved by a consensus process whereby Working Group members assigned to each of the research questions considered the strength of the evidence using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology (7). In addition, adverse effects, health benefits to patients, patient burden associated with adherence to the recommendations, cost effectiveness, extent to which the evidence answered the research question, and impact on morbidity, mortality and quality of life were considered (7,8) by the Expert Working Group members. Final consensus on the recommendations by the full committee was achieved via an open voting process. Extensive discussions were used to edit, correct and update the document.

Expert commentary and review

Expert reviewers identified by the Working Group and the Canadian Respiratory Guidelines Committee on the basis of their clinical and methodological expertise were invited to review the document. A draft of the clinical practice guidelines was circulated to the reviewers, feedback was gathered and relevant changes were incorporated into the document. Reviewers also used a short AGREE II (6) appraisal form to document their appraisal and further enhance the usability of the document.

It is anticipated that the present document, including the questions and content, will be regularly reviewed and updated to reflect the changing and growing bodies of evidence in this area.

TABLE 1
Strength of evidence and grading of recommendations

Quality of evidence	
Grade A	Well-designed randomized controlled trials with consistent and directly applicable results
Grade B	Randomized trials with limitations including inconsistent results or major methodological weaknesses
Grade C	Observational studies, and from generalization from randomized trials in one group of patients to a different group of patients
Strength of recommendation	
Grade 1	Strong recommendation, with desirable effects clearly outweighing undesirable effects (or vice versa)
Grade 2	Weak recommendation, with desirable effects closely balanced with undesirable effects

Adapted from references 3 and 7

TABLE 2
Literature search results informing recommendations

Section	Topic	Publications informing recommendations for practice, n (references)
I	Are nonhospital-based pulmonary rehabilitation programs as effective as hospital-based pulmonary rehabilitation programs in patients with COPD?	5 (11–15)
II	Does adding resistance training to aerobic training in pulmonary rehabilitation improve outcomes in individuals with COPD?	5 (17–21)
III	Does continuing pulmonary rehabilitation beyond the typical program length (ie, 6–8 weeks) improve outcomes in COPD patients compared with standard duration pulmonary rehabilitation?	6 (22–27)
IV	Are pulmonary rehabilitation programs as effective in patients with mild/moderate compared with patients with severe/very severe COPD?	5 (29–33)
V	Are pulmonary rehabilitation programs as effective in female compared with male COPD patients?	8 (24,25,36,41–45)
VI	Do patients who start pulmonary rehabilitation within one month of an AECOPD do better than patients who do not undergo pulmonary rehabilitation within one month of an AECOPD?	7 (51–57)

AE Acute exacerbation; COPD Chronic obstructive pulmonary disease

RESULTS

Literature search results

Table 2 summarizes the overall literature search results comprising the evidence base to inform the role of PR in patients with COPD. Results of the literature search are reported in each of the separate sections related to the questions of interest. Key recommendations and the supporting level of evidence were developed around each section and, where possible, barriers to implementation of recommendations were identified.

SECTION I

Question

Are nonhospital-based PR programs as effective as hospital-based PR programs in COPD?

Background

It is estimated that only 1.2% of the more than 750,000 Canadians suffering from COPD have access to PR programs (9). The capacity for increasing access to these programs may be hampered by various factors including cost, accessibility and patients' mobility limitations (10). Nonhospital-based programs presently account for only 7% of the total number of programs accessible by patients in Canada, but could be an alternative to hospital-based programs if effectiveness was assured (9,10).

Key evidence

The search strategy identified 453 citations, which were initially retrieved and reviewed for their relevance to the question. Of these citations, 423 were initially excluded, while a further 16 were excluded following more in-depth evaluation, thus, leaving 14 articles that were fully reviewed. Five articles met the criteria and were selected for data extraction and utilization, which included three randomized controlled trials, one noninferiority trial and one meta-analysis.

Strijbos et al (11) compared the effectiveness of nonhospital- and hospital-based programs on outcomes in moderate to severe COPD patients, and found no initial differences in the improvement in exercise tolerance or the reduction in dyspnea between rehabilitation sites. However, the reductions in dyspnea and improved exercise tolerance were maintained over the subsequent 18 months only in the nonhospital rehabilitation group. Elliott et al (12) compared the outcomes of three programs (group 1: three months of hospital followed by nine months of nonhospital rehabilitation; group 2: three months of hospital followed by nine months of community rehabilitation; and group 3: 12 months of community rehabilitation) and found that in patients with moderate to severe COPD, all three programs showed comparable reductions in dyspnea and improvements in health-related quality of life (HRQL). Only subjects in groups 1 and 2 increased 6 min walk test distance (6MWD), with no significant differences in the increase between these two groups. Güell et al (13) demonstrated similar improvements in 6MWD and dyspnea reduction between hospital and nonhospital rehabilitation groups in patients with severe to very severe COPD. The subjects also demonstrated similar increases in respiratory muscle and arm muscle strength. The hospital-based group increased their emotional domain on the Chronic Respiratory Questionnaire (CRQ) slightly more than the nonhospital-based group.

Maltais et al (14) reported the results of a multicentre, randomized, noninferiority trial in which 252 patients with moderate to very severe COPD were randomly assigned to either an outpatient hospital- or home-based eight-week rehabilitation program. In this study, the reductions in dyspnea were significant and not different between groups, and were maintained after 12 months. In addition, 6MWD improved only slightly in the outpatient hospital-based group; however, cycling endurance time increased significantly and similarly in both groups. These benefits were similarly maintained in both rehabilitation interventions at one year.

Conclusions

The findings from the three randomized trials confirm that functional outcomes were similar between nonhospital- and hospital-based programs. These conclusions were corroborated by Oh and Seo (15) in a 2007 meta-analysis examining the effectiveness of PR programs. The analysis demonstrated that the pooled effect sizes for exercise tolerance from 19 studies were not different, regardless of whether rehabilitation occurred at home or in hospital.

In summary, outcomes including HRQL, exercise tolerance and reductions in dyspnea did not differ according to the site of PR. It is highly recommended that patients with COPD have access to either hospital- or nonhospital- (home or community) based PR programs.

QUESTION #1

Are nonhospital-based PR programs as effective as hospital-based PR programs in patients with COPD?

The following recommendation is based on evidence from four studies, one meta-analysis and consensus of the CTS COPD expert panel.

RECOMMENDATION #1

There are no differences in major patient-related outcomes of PR between nonhospital- (community or home sites) or hospital-based sites. It is strongly recommended that all COPD patients have access to PR programs regardless of program site. (GRADE: 1A)

SECTION II

Question

Does adding resistance training (RT) to aerobic training (AT) in PR improve outcomes in patients with COPD?

Background

More than one decade previously, an American Thoracic Society (ATS) statement noted that peripheral muscle weakness was associated with exercise limitation in patients with COPD (16). The ATS's guidelines stated that strength training was a rational component of a PR program. More recently, the ATS/European Respiratory Society Statement on Pulmonary Rehabilitation (5) noted that individually tailored endurance training (aerobic exercise such as walking or cycling) was the cornerstone of PR. The authors also added that RT (strength training using progressive resistance techniques with free or machine weights, elastic resistance, or lifting the body against gravity to increase the ability to exert or resist a force) appears to be worthwhile because it has the potential to improve muscle mass and strength, and may cause less dyspnea than AT. The benefit of combining aerobic with resistance training (AT+RT) in healthy individuals remains controversial. This subject has not been systematically reviewed in patients with COPD.

Key evidence

A total of 527 abstracts were initially identified by the search process, of which 26 were selected for complete review. Five studies fully met the criteria and were selected for data extraction and utilization.

All exercise training programs were offered on an outpatient basis, and varied from eight to 13 weeks in duration with sessions two (17,18) or three (19-21) times per week. All AT used 20 min to 40 min of lower extremity exercise. Three studies (17,18,20) used treadmill or cycle ergometer training, while the other studies (19-21) used cycle ergometer training only. AT intensity was prescribed as a percentage of maximum workload from a graded exercise test, peak heart rate on the 6 min walk test (17) or in terms of perceived exertion (18). All RT programs included upper and lower extremity exercise and used variable resistance machines for weight training. These included universal gym apparatus (17,18,21) and equipment that used hydraulic resistance (19,20). Three studies (19-21) used a one repetition maximum, while the others (17,18) used the number of repetitions completed to prescribe and progress exercise intensity.

There were greater improvements in lower and upper extremity strength following AT+RT compared with AT alone. There was a nonsignificant tendency for greater improvements in functional tasks for the upper (reach test or arm raise: P=0.16) and lower extremities (sit to stand: P=0.10). Changes in exercise capacity were comparable for both training groups, although the change in 6MWD tended to be higher for AT+RT, and the maximum work rate for the cycle ergometer test tended to be higher for the AT group. No post-training between group differences were found for HRQL as measured by the CRQ.

This systematic review suggests that AT+RT is more effective than AT alone in improving endurance and functional ability. However, the training volume in four of the five studies was greater in the AT+RT group. The study by Ortega et al (21) demonstrated that using one-half the volume of the aerobic component and one-half the volume of the strengthening component resulted in similar improvements in endurance, dyspnea and quality of life when compared with either AT alone or strength training alone. Therefore, training volume more than or in addition to RT may be the primary stimulus for the improvements noted in the AT+RT groups. AT+RT resulted in better performance on functional tests (17,18). The superiority of AT+RT may also have been influenced by the fact that only one study specified how AT was progressed over the training period (20). Lack of progression would have limited improvements in endurance. In contrast, progression of RT occurred in all studies.

Conclusions

The evidence supports RT performed in conjunction with aerobic exercise. The benefits of exercise are specific to the metabolic and recruitment demands placed on muscle. AT is required to improve cardiovascular and muscular endurance; thus, it should not be excluded from PR programming – but serve as its foundation. Given the specificity of training, exercise must be individually tailored to maximize benefits and to minimize any possible risks to the cardiovascular and musculoskeletal systems.

QUESTION #2

Does adding RT to an AT protocol in PR improve outcomes in individuals with COPD?

The following recommendation is based on evidence from five studies and consensus of the CTS COPD expert panel.

RECOMMENDATION #2
AT+RT is more effective than AT alone in improving endurance and functional ability. While AT is the foundation of PR, it is recommended that both AT and RT be prescribed to COPD patients. (GRADE: 2B)

SECTION III

Question
Does continuing PR beyond the typical program length (ie, six to eight weeks) improve outcomes in COPD patients compared with standard duration PR?

Background
The length of PR varies in programs across Canada (9). Studies have examined the effect of program duration as short as four weeks (22) and as long as 18 months (23). The length of the program may have important implications on accessibility and adherence to exercise (24), as well as on the effectiveness and duration of benefits.

Key evidence
The search strategy identified 209 citations, of which 178 were excluded after review. Of the remaining 31 articles, six studies with 707 participants met the inclusion criteria.

One large study – The Reconditioning Exercise and COPD Trial (REACT) – examined the effect of a three-month versus an 18-month supervised PR program in individuals with COPD (23,25,26). The 18-month exercise program resulted in greater improvements in self-reported disability and physical function than the three-month program (23), but provided little added benefit for cognitive function (26). Foy et al (25) reported on the above program and noted greater benefit for the longer duration program in men compared with women. However, a longer program may also negatively impact attendance. A retrospective review (24) recently reported that a longer PR program was an independent risk factor for lower attendance.

Although not directly addressing the research question, two studies (22,27) conducted by the same group of researchers compared a four-week PR program to a program of seven weeks duration, both using twice-weekly exercise. One study (27) demonstrated that the longer program resulted in a greater benefit in health status, while the other study (22) found the shorter and longer programs to be equivalent.

Studies specifically examining maintenance protocols after rehabilitation did not directly address the question and were, therefore, not included. A Cochrane review (28) on this topic is registered, but not yet complete.

Conclusion
The results of this review provided evidence of greater benefits of a longer program (18 months) compared with a shorter program (three months), although the results may be moderated by a number of factors including sex.

QUESTION #3
Does continuing PR beyond the typical program length (ie, six to eight weeks) improve outcomes in COPD patients compared with a standard duration PR?

The following recommendation is based on limited evidence from six studies and consensus of the CTS COPD expert panel.

RECOMMENDATION #3
It is recommended that longer PR programs, beyond six to eight weeks duration, be provided for COPD patients. (GRADE: 2B)

SECTION IV

Question
Are PR programs as effective in patients with mild to moderate COPD compared with patients with severe to very severe COPD?

Background
The effectiveness of PR on subgroups of COPD patients (eg, mild versus severe), remains unclear for two primary reasons. First, few studies have implemented identical PR programs among various COPD subgroups and, second, many patients may not recognize early COPD or consider it disabling enough to necessitate or consider PR.

Key evidence
The search strategy identified 534 citations, of which 489 were excluded after review. Of the remaining 45 articles, three met the inclusion criteria and two others were identified after review of the full-text article reference lists. A total of five studies with 427 participants satisfied the inclusion criteria.

Four studies were open-label observational studies that prospectively enrolled participants with COPD into inpatient (29) or outpatient PR programs (30-32). Another study (33) randomly assigned participants to endurance training plus strength training and calisthenics (treatment arm) versus strength training and calisthenics alone (control arm), but provided data according to the severity of airflow limitation for the treatment arm only. Program length varied from two to 12 weeks, with sessions two to six times per week. Four programs combined strength training with endurance exercise (29,30,32,33), and one used endurance training alone (31). In one study (29), PR was administered following an acute exacerbation of COPD (AECOPD). The definition of disease severity varied among the studies, and a cut-off for forced expiratory volume in 1 s (FEV_1) per cent predicted of either 40% or 50% predicted was used to differentiate mild to moderate from severe to very severe COPD.

All five studies demonstrated improvements in peak work rate (31-33) or 6MWD (29,30,32) independent of COPD severity. There were clinically meaningful improvements in 6MWD (34) for all participants irrespective of disease severity, although these improvements were not statistically significant in all studies. Two studies (29,32) reported improvements in Borg dyspnea and fatigue ratings among all groups studied.

Improved quality of life was reported in three studies with similar improvements in St George's Respiratory Questionnaire scores regardless of disease severity (29,32), and similar improvements in the CRQ-Dyspnea and CRQ-Fatigue scores regardless of disease severity (30). There were improvements in CRQ-Mastery scores in the severe group only, and no change in CRQ-Emotional function scores in any group. None of the studies reported the impact of rehabilitation on activity level, exacerbation rates, health care use, cost effectiveness or patient burden.

These results are similar to those of a meta-analysis (35) of PR that assessed effectiveness according to disease severity

from the patients' Medical Research Council (MRC) dyspnea grade. Only randomized controlled trials evaluating PR versus no rehabilitation were included. There were similar improvements in 6MWD and CRQ-Dyspnea scores when studies were pooled according to disease severity.

Three studies evaluated the effect of PR according to the MRC dyspnea grade (1) at baseline. Two observational studies (36,37) found that the benefit was similar regardless of baseline MRC grade. However, a randomized controlled trial (38) that was stratified according to MRC dyspnea grade found that participants with severe dyspnea (MRC grade 5) did not benefit in exercise capacity or quality of life, whereas those with less dyspnea (MRC grade 3 or 4) showed improvements in both. Baseline FEV_1 per cent predicted was similar in both groups despite differing MRC dyspnea scores.

Conclusions

PR results in improvements in exercise capacity, dyspnea and quality of life in patients with moderate, severe and very severe COPD. Presently, there are insufficient data to make a recommendation regarding patients with mild COPD. It is uncertain whether prescribing PR to all patients regardless of disease severity is cost effective.

QUESTION #4

Are PR programs as effective in patients with mild to moderate COPD compared with patients with severe to very severe COPD?

The following recommendation is based on evidence from five studies and consensus of the CTS COPD expert panel.

RECOMMENDATION #4

It is strongly recommended that patients with moderate, severe and very severe COPD participate in PR. (GRADE: 1C)

Currently, there are insufficient data to make a recommendation regarding patients with mild COPD.

SECTION V

Question

Are PR programs as effective in female compared with male COPD patients?

Background

Women now contribute significantly to the prevalence and disease burden of COPD, yet a meta-analysis of PR outcomes completed by Lacasse et al (39) in 1996, found only four studies that investigated an equal number of men and women, with only 22% of the total reported population in the analysis being women. The question of whether rehabilitation programs are as effective in women compared with men has also been recently addressed in the cardiovascular setting (40).

Key evidence

The search strategy identified 111 citations, of which 84 were excluded after initial review. Of the remaining 27 articles, a total of eight studies with 1671 participants satisfied the inclusion criteria. One study was a randomized controlled trial, two were case-controlled trials and five were observational trials. Two other papers were identified after review of the full-text article reference lists: one was a review article exploring women and COPD, and the other was an observational analysis of women entering PR.

Quality of life is uniformly improved with PR for both men and women. The only significant sex difference reported was that men had ongoing quality of life benefits in a maintenance PR program of 18 months compared with no further documented benefit for women beyond a program lasting three months (25). This was not due to nonadherence with the program or the magnitude of exercise training. Another study (41) examining outcomes after intensive inpatient PR showed a trend for more men to display a significant improvement in HRQL than women; however, this difference did not reach significance.

Four of six studies that objectively assessed exercise capacity using the 6MWD or 12 min walk test distance reported similar improvements for both men and women (36,42-44). One study demonstrated that men had a statistically greater improvement in 6MWD than women; however, values were not adjusted as per cent predicted and did not attain a minimal clinically important difference (41). Another study (45) found that women had a greater loss in 12 min walk distance than men following PR, which was not explained by the initial pre-PR assessment.

Symptoms of dyspnea in women were improved as much as men during and after PR. In fact, three studies (25,43,44) showed a significantly greater improvement in dyspnea scores with PR in women than in men. Furthermore, sex did not seem to predict PR attendance (24).

The interesting issue raised from this review relates to potential sex differences in disease manifestations, although this was not a primary objective of this review. One study (42) found no difference in self-reported variables, such as health status or quality of life between men and women, despite women having a higher FEV_1 per cent predicted and 6MWD per cent predicted. Another study (43) revealed that although women were younger and had less smoking exposure and better lung function, the clinical severity of COPD and mortality was similar in men and women. A cohort study comparing men with women entering a pulmonary clinic and matched for FEV_1 (response to PR was not assessed), showed women were younger and had less smoking exposure, but worse quality of life, higher dyspnea scores and more exacerbations of COPD (46).

Conclusions

There is limited information available regarding the impact of sex on the response to PR. Clinical studies that have compared the responses of women with that of men, or studies that have provided a subanalysis that considers sex, suggest the benefits of PR are realized by both women and men.

QUESTION #5

Are PR programs as effective in female compared with male COPD patients?

The following recommendation is based on evidence from eight studies and consensus of the CTS COPD expert panel.

RECOMMENDATION #5

The benefits of PR are realized by both women and men. It is strongly recommended that both women and men be referred for PR. (GRADE: 1C)

SECTION VI

Question

Do patients who undergo PR within one month of an AECOPD do better than patients who do not undergo PR within one month of an AECOPD?

Background

AECOPD represent a significant burden to the patient and the health care system. According to the Canadian Institute for Health Information, COPD accounts for the highest rate of hospital admissions among major chronic illnesses in Canada (47). The average cost for a 10-day admission for COPD in 2008 was $10,000 (48). Eighteen per cent of patients with AECOPD were readmitted to hospital once in the year following their exacerbation, while 14% were readmitted twice during that time frame (47). Moreover, AECOPD contributes to disease progression and are associated with a decline in quality of life and premature death (49). Because an AECOPD can be a distressing event for COPD patients, the time immediately following an AECOPD may represent an ideal opportunity for rehabilitation to facilitate lifestyle change (50); however, the effectiveness of PR immediately after AECOPD has yet to be rigorously evaluated.

Key evidence

The search strategy identified 220 citations that were initially retrieved and reviewed for relevance to the question. Sixteen articles were selected for full-text review, with four articles satisfying the inclusion criteria and their data extracted after review. Data were also extracted from an additional three articles not identified in the initial search. In total, six prospective, randomized controlled trials that enrolled 317 participants and studied PR within one month of an AECOPD, as well as one meta-analysis, were included.

PR consisted of AT with or without strength training. Walking was the most common aerobic exercise. Some programs began at the inpatient stage (51-54) and used daily exercise sessions. In one study (54), the majority of patients were mechanically ventilated at the beginning of PR. Outpatient interventions ranged from daily to twice per week and program duration varied greatly, from eight weeks to 18 months. All studies were single-centre trials with modest sample sizes (n=26 to n=84).

Compared with usual care, PR within one month of an AECOPD was found to improve exercise capacity (51-56), dyspnea (51-53,55) and quality of life (51,52,54-56). Four studies (52,54,55,57) examined health care use, two studies (52,55) reported reduced hospital readmission rates in the PR group when compared with usual care, while one study (56) demonstrated a trend toward reduction (P=0.06). A recent Cochrane review (58) found a significant reduction in the odds of hospital readmission (OR 0.13; 95% CI 0.04 to 0.35) and death between PR and usual care groups (OR 0.29; 95% CI 0.10 to 0.84). Two trials (51,55) explicitly examined adverse events with PR, with none noted. These results were consistent with a recent randomized controlled trial (59), which demonstrated that early mobilization of critically ill patients was well tolerated and resulted in better functional outcome compared with patients who did not exercise. Seymour et al (60) also recently found that postexacerbation PR in COPD patients significantly reduced re-exacerbation events requiring hospital attendance or admission.

Conclusions

PR initiated within one month of an AECOPD is safe and improves exercise capacity, dyspnea and HRQL compared with usual care. It appears to decrease mortality and is associated with decreased health care costs.

PR performed immediately following an AECOPD improves health outcomes compared with usual care. The long-term benefits of early postexacerbation rehabilitation versus later conventional rehabilitation of stable COPD patients have not been studied. There is no evidence that PR performed within one month following an AECOPD increases the risk of adverse events.

QUESTION #6

Do patients who undergo PR within one month of an AECOPD do better than patients who do not undergo PR within one month of an AECOPD?

The following recommendations are based on evidence from six studies, one meta-analysis and consensus of the CTS COPD expert panel.

RECOMMENDATION #6

It is strongly recommended that COPD patients undergo PR within one month following an AECOPD due to evidence supporting improved dyspnea, exercise tolerance and HRQL compared with usual care. (GRADE: 1B)

PR within one month following AECOPD is also recommended due to evidence supporting reduced hospital admissions and mortality compared with usual care. (GRADE: 2C)

DISCUSSION

The present clinical practice guideline addresses a number of clinically meaningful issues using an evidence-based, systematic review process led by a representative interprofessional panel of experts in the field. The evidence from the reviews, and the experience and guidance afforded by the Expert Working Group members, enabled the formulation of practical answers, direction and guidance for the various professionals involved in the coordination, design, delivery and evaluation of PR programs (Table 3).

However, the process also clearly identified many gaps in our understanding that are deserving of further study and attention. These include gaps relating to optimal maintenance programming and maintaining the benefits of rehabilitation, the intensity of exercise training, incremental benefits of various program components, the value of exercise and activity outside the PR setting, the contributions and effects of anxiety and depression or other patient-specific factors in this setting, various adjunct techniques to maximize the training afforded by PR, and barriers to participation and adherence to PR.

Access to PR and adherence to participation remain two of the most significant challenges in this field. Only a very small proportion of patients with COPD have access to PR programs (9). Acknowledging the important benefits of the intervention (3-5,61) and appreciating that PR is now the standard of care for patients who remain symptomatic despite appropriate bronchodilator therapies (1), there is an immediate urgency for these obstacles to be addressed and to be removed. It is not acceptable for health care providers, patients or health care systems to accept the current status quo – the benefits cannot be ignored.

TABLE 3
Summary of evidence-based recommendations

Recommendation	Summary	Strength of recommendation/ quality of evidence
1	There are no differences in major patient-related outcomes of pulmonary rehabilitation between nonhospital- (community or home sites) or hospital-based sites. It is strongly recommended that all COPD patients have access to pulmonary rehabilitation programs regardless of program site	GRADE 1A
2	Aerobic and resistance training offered together is better than aerobic training alone in improving endurance and functional ability. While aerobic training is the foundation of pulmonary rehabilitation, it is recommended that both aerobic and resistance training be prescribed to COPD patients	GRADE 2B
3	It is recommended that longer pulmonary rehabilitation programs, beyond six to eight weeks duration, be provided for COPD patients	GRADE 2B
4	It is strongly recommended that patients with moderate, severe and very severe COPD participate in pulmonary rehabilitation	GRADE 1C
5	The benefits of pulmonary rehabilitation are realized by both women and men. It is strongly recommended that both women and men be referred for pulmonary rehabilitation	GRADE 1C
6	It is strongly recommended that COPD patients undergo pulmonary rehabilitation within one month following an AECOPD due to evidence supporting improved dyspnea, exercise tolerance and health-related quality of life compared with usual care	GRADE 1B
	Pulmonary rehabilitation within one month following an AECOPD is also recommended due to evidence supporting reduced hospital admissions and mortality compared with usual care	GRADE 2C

AE Acute exacerbation; COPD Chronic obstructive pulmonary disease

Similarly, we must better understand issues concerning adherence to participation in PR programs. Patients and health care systems can not realize the benefits of PR with infrequent or short-lived participation. Patients must advance their attitudes and behaviours, and accept PR as an integral component of their management. However, changes in more than patient adherence are necessary for this to be successful. Barriers to participation in PR and the burdens of therapy must also be acknowledged and minimized (62). Health care professionals and health care systems involved in the care of patients must support and enable patients to participate in PR. A collective effort by health care professionals is required for patients, families and health care systems to fully realize the many substantive benefits of PR in COPD.

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Included Studies

[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
1	Strijbos JH, 1996	2	0		1	1	0	2	Mod-severe COPD	Standard CAD/MSK	1	Hosp outpatient 1 / home care 2 / UC 3	Decreased Dyspnea in 1 & 2 vs. 3. Reduction maintained in 2	Bike and walk improved 1 & 2 vs. 3. Maintained in 2	Not measured	No standardized tool but felt "better" in 1 & 2 vs. 3	Not measured	Not measured	Not measured		Not described	45	61 yrs	38 M, 7 F	Not mentioned		Not reported	HRQL not standardized	N/A	Benefits in 1 & 2 maintained in 2
2	Elliot M, 2004	2	0		1	1	1	Not specified	Mod-severe COPD	Standard CAD/MSK/SaO2 <85%. Or cognitive problems, communication difficulties, recent respiratory infections	2	Hosp/Home 1, Hosp/Community 2, Community/community 3: three groups received education and exercise program (2x / 5hrs/term)	CRQ Dyspnea dimension: improved in 1,2 and 3	6MWD improved in 1 and 2 but not 3	Not measured	Improved in 1,2 and 3	Not measured	Not measured	Not measured		Not described	43	68 yrs	23M/20F	Not mentioned		Not reported	RDW not described, Exercise prescription not adequately describe	N/A	Community based exercise programs do not improve 6MWD, improve only domains of mastery and Dyspnea on the CRQ, long-term participation is poor.
3	Goel PMR, 2007	2	0		1	1	0	1	Severe to very severe COPD, 50-75 yrs, stable condition, free of exacerbation in the last 4 weeks	Standard CAD/MSK, significant reversibility in obstruction, hypoxemia, diagnosis of asthma	0	Hosp training 1/home training 2	CRQ Dyspnea dimension: improved in 1 and 2	Pimax and Pemax improved in 1 and 2 arm strength improved in 1 and 2, 6MWD improved in 1 and 2	Not measured	Improved in 1, only Dyspnea in 2	Not measured	Not measured	Not measured		Sealed envelopes, testing blinded	57	66 yrs	0	Not mentioned		Not reported	Exercise regimen different between 1 and 2, walking treated as leg muscle training, small groups; only men	N/A	Benefits between 1 and 2 similar (to exercise tolerance, HRQOL (emotional domain only)) improvement greater in 1
4	Maltais, 2008	5 (randomized non-inferiority trial)	0		1	0	1	2	GOLD II - IV	Standard CAD/MSK, asthma, terminal disease, psychologic	0	Hosp training 1/home training 2	CRQ Dyspnea dimension: improved in 1 and 2 (statistically and clinically significant), maintained in 1 and 2 at 12 months (only clinical sig in 2 at 12 months)	6MWD improved in 1 only, not maintained, cycling endurance time improved in 1 and 2 and maintained in both	Not measured	Improved in 1 and 2, maintained in both except fatigue only maintained in 2	Not measured	Not measured	Not measured		Computer generated permuted block scheme, stratified by sex and trial site	252	66 yrs	140M/112F	Not mentioned		885 adverse events (similar between 1 and 2) including: 101 hosp, 53 CV and 2 deaths	Primarily cycling exercise which resulted in smaller exercise capacity improvements in walk distance than usual	N/A	2 is not inferior to 1 in Dyspnea, health status and exercise capacity
6	Oh, 2007	5 (meta-analysis)	1		N/A	N/A	0	Local university	COPD - Not specified	Not specified		Hosp training 1/home or home and hosp 2	Not reported	Pooled effect sizes significant but no difference between them for 1 and 2	Not measured	Not measured	Not measured	Not measured	Not measured		N/A	19 studies	63.8 yrs pooled	N/A	N/A		N/A	N/A	N/A	Site does not have an impact on changes in exercise capacity

Excluded Studies

Bibliographic Citation 1st Author, Year	Reason for Exclusion
ACCP/AACVPR_1997	Not Relevant
Aizawa, 2007	No information. Rejected for analysis purposes (opinion based on literature review only)
Alexander JL_2008	Not Relevant
Barakat S_2008	Not Relevant
Battaglia E_2009	Not Relevant
Bauldoff GS_1996	Not Relevant
Bauldoff GS_2002	Not Relevant
Bauldoff GS_2005	Not Relevant
Behnke M_2000	Not Relevant
Behnke M_2003	Not Relevant
Belza B_2005	Not Relevant
Bestall JC_2003	Not Relevant
Borel JC_2004	Not Relevant
Boxall AM_2005	Not Relevant
Cambach W_1997	Not Relevant
Carrieri-Kohlman V_1996	Not Relevant
Carrieri-Kohlman V_2005	Not Relevant
Clark CJ_1996	Not Relevant
Debigare R_2004	Not Relevant
Donesky-Cuenco D_2007	Not Relevant
du M, Taube K_2009	Not Relevant
Engstrom CP_1999	Not Relevant
Finnerty JP_2001	Not Relevant
Garrod R_2000	Not Relevant
Grosbois JM_1999	Not Relevant
Hernandez MT_2000	Not Relevant
Kongsgaard M_2004	Not Relevant
Koppers RJ_2006	Not Relevant
Lacasse Y_2006	Not Relevant
Lacasse Y_2007	Not Relevant
Lake FR_1990	Not Relevant
Larson JL_1999	Not Relevant
Mahler DA_1998	Not Relevant
Maltais F_2005	Not Relevant
Man WD_2004	Not Relevant
Moore J_2009	Not Relevant
Murphy N_2005	Not Relevant
Nici L_2006	Not Relevant
O'Donnell DE_2003	Not Relevant
O'Donnell DE_2004	Not Relevant
Oh EG_2003	Not Relevant
O'Shea SD_2007	Not Relevant
Ouksel H_2004	Not Relevant
Puente-Maestu L_2000 Mar	Not Relevant
Reardon J_1994	Not Relevant
Ries AL_2008	Not Relevant
Ries, 2005	Pre NETT trial - supervised sessions only
Ringbaek T_2008	Not Relevant
Rochester, 2000	No information. Rejected for analysis purposes (opinion based on literature review only)
Schoo AM_1997	Not Relevant
Shahin B_2008	Not Relevant
Societe (French) 2005 Nov	Not Relevant
Societe (French) 2005 Sep	Not Relevant
Spencer J_2007	Not Relevant
Steele BG_2008	Not Relevant
Stulbarg MS_2002	Not Relevant
Ward JA_2002	Not Relevant
Wijkstra PJ_1995	Not Relevant
Wijkstra PJ_1996	Not Relevant

Included Studies

#	Bibliographic Citation 1st Author, Year	Study Design 1 0=Obsrv, 1=Case CS 2=RCT	Study Design 2 0=Prosp, 1=Retro, 2=NA	Open Label 0=No not blinded 1=Yes	Consecutive 0=No, cherry picked 1=Yes	Informed Consent 0=No 1=Yes	Ethics Approval 0=No 1=Yes	Funding Source 0=Public, 1=Gov, 2=NGO, 3=Healthcare	Eligibility Criteria Inclusion Criteria	Exclusion Criteria	Health Care Setting 0=Multicenter, 1=Multicounty, 2=Urban, 3=Rural, 4=Other	Intervention AT = Aerobic only or aerobic plus sham RT= Aerobic plus resistance	Outcome(s) – Bold Primary Outcomes 1. Reduction in Dyspnea	2. Improved exercise capacity	3. Improved activity	4. Improved QoL/health status	5. Decreased exacerbations	6. Decreased health care utilization	7. Cost-effectiveness	Other	Randomization Method	Participant Characteristics N	Age	Gender (M/F)	Race 0=C, 1=B, 2=Other	Other	Side Effects	Limits	Reproducibility	Authors Conclusion
1	Phillips, 2006	2	0	0	0 Participants were switched between groups based on symptoms	1	0	Not reported	COPD, Referral to PR because of worsening status. FEV1<60%. **recent hospital admissions.**	No specific		**Aerobic**=RPE<13 (3 METS) x 20-40min; cycle, arm ergometer, TM intensity U/C RT x 8 exercise or recumbent stepper **Resistance**= 50% 1RM Chest & Leg Press; Biceps, Triceps, Lats to 10 reps then progress; **13 wk** **Progression** poorly described	Not measured	**1RM chest & leg press**	Senior Fitness Test - Includes: 6MWT (ft), Mod lift & reach (# reps), chair stand (#reps), scratch test (in), TUG (sec), Arm curl (# reps)	Not measured	Not measured	Not measured	Not measured		Not described	19 - problems to changes to group assignment	ET=70±2; RT=71±1 SEs not SDs reported	ET=8/1; RT=6/4	Not reported		One participant in RT group developed low back pain in week 2.	1RM was not reliable; some subjects may have been recovering from AECOPD; changes in group assignment during the study Small number of subjects	Poor = Exercise prescription vague; See limits	Single set of low intensity strength exercise produces improvement in strength **and functional fitness.** Results comparable to studies that used multiple sets
2	Panton, 2004	3	0	0	0	0	0	Not reported	None - COPD without recent infection	CV or NM conditions that preclude strength testing and training		**Aerobic**=30 min chair aerobics + 30 min TM/Bike etc @ 50-70%HRR; 2x/wk; No Progression **Resistance**= 3 sets of 10-12 reps → 3 sets of 8 reps x 12 exercise; Not based on 1RM; Progress when achieve sets and reps **12 wk** intervention	Borg's Dyspnea scale did not change	**1RM chest press &leg extension** (N) **Hand grip** (N) **12MWT** (m)	ADL test (8 standardized tests)	Not measured	Not measured	Not measured	Not measured	Body Comp (DEXA) Cholesterol PFT	**NOT RANDOMIZED**	ET=8 RT=9	ET=63±8; RT=61±7	ET=2/6; RT=6/3		BMI=30-	None related to study intervention(s)	3 subjects too large for DEXA RT more males All subjects had been ET x 2 years - suggests aerobic capacity plateaued + no change in 12MWD RT intensity = 32-64%, below threshold Small number of subjects	Fair "chair aerobics" = 50% of ET Lack of precision in RT	RT is well tolerated and improves function in COPD who participating in ET
3	Mador, 2004	2	0	0	1	1	1	Not reported	Dx COPD clinical course, Irreversible PFT, Nonsmoking x 3 mo, participate PR	None stated	2	**Aerobic**=20 min bike @50% Wmax, when Dyspnea <5 ↑ W by 10%; 15 min TM when Dyspnea <5 ↑ speed or grade **Resistance**=1 set, 10 reps @ 60%1RM, progress to 3 sets, then ↑ 5 lb. (Hams, quads, lats, pecs) **3x/wk, 8 wk**	CRQ Dyspnea Yes both groups showed pre-post improvement	**GXT cycle** **Constant W cycle** **6MWT** **Peak Force** on hydraulic resistance Quad fatigue - Mag Stim (potentiated and unpotentiated) pre-post change but not between groups	6MWD showed pre-post change for both groups but not between group differences.	CRQ - sig improvement in 2 or 3 of 4 domains	Not measured	Not measured	Not measured	Spirometry Lung volume MIP	By PR group with sealed envelop	CT 13 RT=11	CT 68±2; RT=74±2(sig older) SE rather than SD reported	All male - VA	Not reported	BMI ET27.6+.4 RT27.5+.2	None related to study intervention(s)	RT just at threshold for strength increase (60% 1RM) No info re: extent of progression over the 8 wk training period Small number of subjects	Good all subjects completed 24 sessions	Aerobic plus Resistance (RT) training improved strength moreso than AT but did not translate into greater improved endurance than AT
4	Ortega, 2002	2	0	0	0, Yes but process not described	0, Not stated	0, Not stated	Not reported	COPD, irreversible PFT	None stated	2	**Aerobic**=40 min cycle @ 70%Wmax **Resistance**=5 ex @70-85% 1RM, 4-6 reps x 4 sets (multi gym) **Combined**= 20 min aerobic + 2 sets resistance **Control** group **3d/wk, 12 wk**	BDI yes, Dyspnea domain of CRQ improved for both groups but no diff between groups	**1RM** (Lats, pects, triceps, deltoid, quads, hams) **GXT cycle** (VO2 & Wmax) **Constant WL** cycle @70% Wmax (min) **ISWT** (distance)	No significant change in shuttle for pre-post changes or between group differences.	CRQ 2 of 4 domains in CRQ improved for both groups but no diff between groups	Not measured	Not measured	Not measured	Both groups improved strength and RT improvement was greater than AT improvement	Not described	ET=16 RT=17 Comb=14 Control 18	ET=66±8 RT=66±6 Comb=60±9	ET=14/2 RT=14/3 Comb=13/1		ET	None related to study intervention(s)		Very good	Resistance training is well tolerated and superior to endurance training for improving strength, ET better vs. RT to improve endurance. Combo is the optimal training strategy.
5	Bernard, 1999	2	0	0	1	1	1	1 - FRSQ	COPD, irreversible bronchial obstruction	Stable at time of entry; CV or NM conditions that preclude strength testing and training	2	**Aerobic**= 30 min bike @80% Wmax plus 45 mins of breathing and relaxation exercises **or** **Aerobic plus Resistance** 45 min 4 ex (pect, lats, glut, quads), wk 1&2=60%1RM, 10 reps, 2 sets→80%1RM 10 reps, 3 sets, when complete 10 reps progress *(not specify how)* **3x/wk, 12 wk**	CRQ Dyspnea Yes both groups showed pre-post improvement	**1RM** - kg (Lats, pects, quads, gluts) **GXT cycle** (VO2, Wmax, Ve, La) **6MWT** (m) Yes both groups showed pre-post improvement	6MWD	CRQ Yes both groups showed pre-post improvement in most dimensions of CRQ	Not measured	Not measured	Not measured	CSA thigh (CT) Improved in AT–RT group	Not described coin toss p. 897 second paragraph last sentence	ET=15 of 19 completed RT= 21 of 26 completed	ET=67±9 RT=64±7	ET=11/4 RT=17/4		**BMI** ET=25+4 RT=27+5	Clearly stated none related to study intervention(s)	Unequal group size. Authors suggest type II error with respect to peak ex work Used 6MWT to assess endurance but trained on bike (specificity principle); RT group had a higher baseline exercise tolerance.	Very good Although hydraulic resistance is more difficult to replicate	Addition of RT to ET was safe and well tolerated in people with severe COPD and associated with greater improvement in strength and muscle mass vs. ET alone. More study needed to clarify improvement in needed to improve ex tolerance and HQOL.

Abbreviations: ET = aerobic training only; RT = aerobic plus resistive training

Excluded Studies

Bibliographic Citation 1st Author, Year	Reason for Exclusion
Arnardottir RH_2006	Not Relevant
Arnardottir RH_2007	Not Relevant
Chavannes N_2002	Not Relevant
Gimenez M_2000	Not Relevant
Maltais F_1997	Not Relevant
Marrara KT_2008	Not Relevant
Martinez FJ_1993	Not Relevant
McCarren B_2000	Not Relevant
Nakamura Y_2008	Not Relevant
Normandin EA_2002	Not Relevant
O'Donnell DE_1998 May	Not Relevant
Paciocco G_2004	Not Relevant
Ringbaek TJ_2000	Not Relevant
Rooyackers JM_2003	Not Relevant
Skumlien S_2008	Not Relevant
Spencer LM_2007	Not Relevant
Spruit MA_2005	Not Relevant
Troosters T_2000	Not Relevant
Varga J_ 2007	Not Relevant
Vogiatzis I_2001	Not Relevant
Vogiatzis I_2005	Not Relevant

Included Studies

#	Reference (1st author, Year)	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	Eligibility Criteria: Inclusion Criteria	Exclusion Criteria	Design and Dosage	Follow-up	[illegible]	Baseline Data	[illegible]	Pt Characteristics: N	Age	Gender	[illegible]	Other	Clinical Results	Functional Results	Other Important Results	Side Effects	Comments
1	Berry et al., JCPR, 2003	2	0	1 Single-blinded (blinding of outcome assessors)	1	1	1	Completed a 3 months supervised, center-based exercise program; attended at least 60% of exercise sessions before randomization and agreed to continue regardless of allocation AND (1) had an expiratory airflow limitation that was not reversible with bronchodilator inhalation such that the ratio of the one second forced expiratory volume (FEV1) to the forced vital capacity (FVC) was less than or equal to 70% and the FEV1 was greater than or equal to 20% of predicted; (2) reported difficulty in performing at least one of the following activities as a result of dyspnea: walking a city block, grocery shopping, doing household chores, lifting objects chest height or higher, walking up stairs, and getting out of a chair; (3) were free of severe cardiovascular and peripheral vascular disease; (4) were not undergoing active treatment for cancer; (5) were free of uncontrolled diabetes or hypertension; (6) had not actively participated in a pulmonary or exercise rehabilitation program during the previous 6 months; (7) had no plans to move from the area within the next 15 months; (8) were willing to accept random assignment to either one of the intervention arms.	None stated; see inclusion criteria	After 3 months PR program, randomized to either to short term (ST) or long term (LT) group. Thos in LT continue to exercise 15 months in centre-based program	Before 3 months PR (time 0); following the 3 months intervention (time 3); and 18 months from start of study				140 randomized with 70 in each arm; 66 completed trial in ST and 62 in LT	66.9 (65.5-68.3) in ST versus 68.4 (67-69.8) in LT	39/31 (men/women) in ST versus 39/31 (men/women) in LT	Not reported		LT reported 12% less disability than ST, walked 9% farther during 6MWT, climbed steps 11% faster and completed an overhead task 8% faster.	An 18 month exercise program results in greater improvements in self-reported disability and physical function in COPD compared to 3 months only.		None	Fits research question very well
2	Emery and Berry, Medicine and Science in Sports and Exercise, 2001	2	0	1 Probably single-blinded since from REACT trial	1	1	1	FEV1/FVC less than or equal to 70% and FEV1 was greater or equally than 20% of predicted value- irreversible with mode- difficulty ADL activities because of SOB and not participating in regular exercise or PR in last 6 months	Active treatment for another major illness, inability to perform exercise, consumption of more than 2 drinks per day and living away from centre	After 3 months PR program, randomized to either to short term (ST) or long term (LT) group. Those in LT continue to exercise 15 months in centre-based program	Before 3 months PR (time 0); following the 3 months intervention (time 3); and 18 months from start of study.				Initially 40 volunteers at baseline, 29 tested at 3 months and 15 tested at 18 months.	66.45 (7.64)	18/11 (M/F)	Not reported		After three months of exercise, cognitive function and walk distance improved- At 18 months, cognitive performance not different between the two groups, but walk distance improved significantly for the long-term group, but not for the short-term group.- Improvement in cognition predicted by decrease in VE.	3 months may be sufficient for the gains in cognition	Exercise did not have impact on depression - however patients were not depressed	None	This is the same trial as Berry trial just added the cognitive measures
3	Sabit et al., Respiratory Medicine, 2008	0	1	1	1	0 (retrospective)	1	Enrolled in outpatient rehabilitation, attended at least one session (reference 5 for inclusion criteria)		No intervention, just retrospective analysis on who benefits and which factors at baseline predict poor attendance	Baseline and end of program		(1) age; (2) gender; (3) diagnosis (COPD or other); (4) body mass index (BMI); (5)% predicted forced expiratory volume in 1 s (FEV1); (6) Medical Research Council (MRC) Dyspnea score; (7) St. George's Respiratory Questionnaire (SGRQ) total score; (8) number of COPD exacerbations requiring hospital admission in the preceding 12 months; (9) self-reported smoking status; (10) presence of major co-morbidities, classified as cardiovascular, neurological or musculoskeletal conditions; (11) distance (in miles) between home and PRP (calculated using zip/post codes); (12) average length of journey reported by patients and (13) long (18 week) or short (6 week) PRP.	Attendance	243 patients (238 in analysis)	66.5 (8.7)	146 males	Mostly white		Attending a long PR (p<0.05) were independent risk factors for low attendance			None	Retrospective review that shows that duration of rehab negatively impact attendance but not designed to answer the question.
4	Foy et al., Chest 2001	2	0	1	1	1	1	Disability associated with SOB or diagnosis of CB and/or emphysema, ambulatory, 55-90 years, FEV1/FVC <70% and FEV1>20% predicted and not actively engaged in exercise program	Concurrent history of other serious illness	After 3 months PR program, randomized to either to short term (ST) or long term (LT) group. Thos in LT continue to exercise 15 months in centre-based program	Before 3 months PR (time 0); following the 3 months intervention (time 3); and 18 months from start of study				140 randomized with 70 in each arm; 56 completed trial in ST and 62 in LT	66.9 (5.93) in ST versus 68.4 (5.96) in LT	39/31 (men/women) in ST versus 39/31 (men/women) in LT	Not reported		Men in the LT group reported significantly more favorable scores than men in the ST group for dyspnea, fatigue, emotional function and mastery. No difference at 18 months for women for any of the subscales.	An 18 month exercise program results in greater improvements in self-reported disability and physical function in COPD compared to 3 months only.	18 months had little added benefits for women but added benefits for men	None	Fits research question very well; same trial as Berry et al 2003

Excluded Studies

Bibliographic Citation	Reason for Exclusion
1st Author, Year	
Behnke et al. Monaldi Arch Chest Dis, 2003	Does not meet the C of PICO
	Comparison group received no exercise/rehab
Lacasse et al., Swiss Med Wkly, 2004	Does not answer our question. Editorial review; no original data.
Kerstjens and Hacken , BMJ Clinical Evidence, 2008	Does not address our question. Systematic review on COPD treatment.
Pitta et al., Chest 2008,	Does not meet the C of PICO
	No comparison group; longitudinal study looking at the effects of PR after 3 months and 6 months in same group.
Salman et al., J Gen Intern Med 2003	Metanalysis on effectives of rehabilitation. Can we still use their findings? They showed that the effect of rehab in severe patients was only significant if program lasted 6 months or longer. However, not sure that meets the C of the PICO question.
Goldstein et al., Chest 1997	Does not meet the C or I of PICO
	Compared cost-effectiveness of 6 months of rehab versus usual care (no rehab)
Heppner et al., JCPR 2006	Does not meet the C of PICO. Maintenance study instead of duration study
	Comparison group received no exercise/rehab
Trooster et al., 2000	Does not meet the C or I of PICO
	Did not mesure the effect of extending the program to 6 months + the comparison group received no exercise
Steinsbek and Lokmundal, 2009	Does not meet the C or I of PICO
	Did not measure the effect of extending the program to 2 years + no comparison group
California Pulmonary Rehabilitation Collaborative Group, JCPR, 2004	Does not meet the C or I of PICO
	Extended the follow-up, but not the intervention + no comparison group (longitudinal study)
Guell et al., Chest, 2000	Does not meet the C of PICO
	Comparison group received no exercise/rehab
Hernandez et al, Chest 2000	Does not meet the C or I of PICO
	Compared standard-length rehab program to no exercise/rehab
Cox et al., Lung, 1999	Does not meet the C or I of PICO
	Comparison group received no exercise/rehab + intervention group received standard-length rehab
Engstrom et al., Scand J Rehab Med, 1999	Does not meet the C or I of PICO
	Comparison group received no exercise/rehab + did not measure the effect of extending the rehab program to 12 months
Abramson et al., MJA, 2006	Unrelated (review article on management of COPD)
Elliott et al., Respirology, 2004	Compared setting rather than duration. Data from long term maintenance not analyzed because of drop out
Spencer et al. BMC Pulmonary Medicine, 2007	Only a protocol- no data
Romagnoli et al., Respiration , 2006	This examines repeating PR at 6 and 12 months, not prolonging the PR.
Puente- Maestu et al., Lung, 2003	Does not meet the C of PICO
	Compared supervised PR plus maintenance to non supervise PR + maintenance
Carrieri et al., 2005	Does not meet C or I
	3 interventions: 1) dyspnea self management with home exercise program(DM); 2)DM + 4 supervised treadmill exercise every other week for 2 months; 3) DM + 24 supervised treadmill exercise sessions 3x/week over 2 months- so more about volume rather than duration.
Brooks et al., Eur Respir J, 2002	Does not meet the C of PICO. Maintenance study instead of duration study
Moullec et al., Respiratory Med, 2008	Does not meet the C of PICO. Maintenance study instead of duration study
Ries et al., Am J Respir Crit Care Med., 2003	Does not meet the C of PICO. Maintenance study instead of duration study
Rossi et al., Chest 2005	Does not meet the the C of the PICO.
Clini et al., Chest 2001	This study did not isolate program duration (different setting, different volumes)
Green et al., Thorax 2001	Relates to effect of a shortened program

Included Studies

#	1st Author, Year	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	Eligibility Criteria: Inclusion Criteria	Eligibility Criteria: Exclusion Criteria
1	Arnardottir, 2006 (ref 17)	2	0	1	1	1	1	1	Ex-smoker or current smoker, an FEV1/FVC ratio <0.7 after bronchodilation, a smoking history of more than 10 years and forced expiratory volume in 1 s (FEV1) <80% of predicted value were included	Other diseases that could interfere with training (e.g. ischemic cardiac disease, musculo-skeletal problems) and an increase of FEV1>20% following inhalation of a bronchodilator
2	Clini, 2002 (ref 100)	0	2	1	1	1	1	Not specified	Male, ex-smoker, clinically stable	Atopy
3	Garuti, 2003 (ref 184)	0	0	1	1	1	1	Not specified	COPD patients admitted rehab following acute exacerbation, history of smoking current non-smokers, no steroids, stable condition, stable inhaled therapy PLUS MRC > 2, FEV1 < 80%, FEV1/FVC < 0.7, PO2 > 60 mmHg, motivated	Unstable medical condition, severe LV dysfunction, resting hypoxemia, cancer or inability to cooperate, inability to perform most activities of daily living
4	Berry, 1999 (not included in original search)	0	0	1	1	1	1	1	FEV/FVC < 0.7, FEV1 > 20%, at least one ADL causing dyspnea, able to walk for 8 min, willingness to participate, no active exercise program or PR in the past 6 months, absence of comorbid illness that would not allow exercise	Not specified
5	Vogiatzis 1999 (not included in original search)	0	0	1	1	1	1	1	FEV1/FVC < 0.65, FEV1 < 70%, nonsmoking for at least 2 months, optimized medical therapy, no exercise limiting cardiac or neuromuscular disease, clinically and physiologically stable	Exacerbation within the past 2 months

#	1st Author, Year	Health Care Setting	Intervention	1. Reduction in Dyspnea	2. [illegible]	3. [illegible]	4. [illegible]	5. [illegible]	6. [illegible]	7. [illegible]	Other
1	Arnardottir, 2006 (ref 17)	2	8 weeks of rehab: Group A - endurance two times per week, resistance training and calisthenics once a week; Group B - resistance training and calisthenics twice per week. Hypoxemic patients (SaO2<90%) were permitted to use supplemental oxygen	X	Increased peak watts in both groups; Moderate 75 to 80 W; Severe 58 to 68 W (Taken from Fig 3)	X	X	X	X	X	X
2	Clini, 2002 (ref 100)	2	3 x 3-hr sessions per week x 8-10 weeks resistance and aerobic exercise	Reduced Borg dyspnea in Mild (7.7 to 6.0); Moderate (6.4 to 5.5); Severe (8.9 to 8.1)	MILD: increased peak watts (91 to 107 watts); 6MWD statistically unchanged (483 to 502 m); MODERATE: increased peak watts (82 to 94); 6MWD statistically unchanged (473 to 503); SEVERE: increased peak watts (68 to 75 watts); statistically unchanged 6MWD (380 to 324 m)	X	Improved SGRQ in Mild (38 to 31); Moderate (39 to 33); Severe (48 to 43)	X	X	X	Reduced Borg leg fatigue in Mild (7.5 to 6.1); Moderate (7.7 to 6.2); Severe (7.9 to 8.7)
3	Garuti, 2003 (ref 184)	2	Inpatient 12 sessions (6 times per week for 3 hours per session); strength, balance, endurance, walking, ROM	Reduced Borg dyspnea in Mild/Moderate (4.9 to 2.4); Severe (5.3 to 3.0); Very Severe (5.6 to 3.5)	Increased 6 MWD in Mild/Moderate (361 to 429m); Severe (326 to 404 m); Very Severe (272 to 357m)	X	Improved SGRQ in Mild/Moderate (53 to 48); Severe (53 to 44); Very Severe (60 to 53). No stat. Sig change in 'impact' or 'activity' domain but 'symptom' domain improved. Improved HAD-anxiety in Mild/Moderate (9.1 to 7.7); Severe (9.0 to 7.2); Very Severe (9.1 to 8.7). Improved HAD-depression in Mild/Moderate (9.4 to 8.2); Severe (9.1 to 8.2); Very Severe (9.0 to 7.4)	X	X	X	Reduced Borg leg fatigue in Mild/Moderate (5.5 to 3.6); Severe (8.0 to 4.3); Very Severe (6.4 to 4.8)
4	Berry, 1999 (not included in original search)	2	3x/week strength, walking, stretching for 12 weeks	X	Increased 6 MWD in Mild/Moderate (500 to 561); Severe (447 to 519); Very Severe (458 to 485)	X	Improved CRQ-dyspnea in Mild/Moderate (3.9 to 4.6); Severe (4.1 to 4.6); Very Severe (3.9 to 4.3). Improved CRQ-fatigue in Mild/Moderate (4.4 to 4.9); Severe (4.1 to 4.6); Very Severe (3.9 to 4.5). Improved CRQ-emotional function in Mild/Moderate (5.3 to 5.4); no difference in Severe and Very Severe. Improved CRQ-mastery in Mild/Moderate (6.0 to 6.2); Severe (5.8 to 6); no difference in Very Severe	X	X	X	Magnitude of improvement in CRQ are small and may not be clinically meaningful
5	Vogiatzis 1999 (not included in original search)	2	Cycling & walking 3x/week for 1 hour x 12 weeks. Intensity adjusted over the program.		Increased peak watts in Mild/Moderate (89 to 105) and Severe (63 to 76)	X	X	X	X	X	X

#	1st Author, Year	Randomization Method	Participant Characteristics: N	Age	Gender	[illegible]	Other	[illegible]	Limits	[illegible]	Authors Conclusion
1	Arnardottir, 2006 (ref 17)	Stratified randomized blocks of four	Group A (n=20), Group B (n=22)	Group A = 65+/-2, Group B = 68 +/-2	Group A (F=10), Group B (F=11)	NA	Group A Moderate (FEV1 40-59%) n=7, Severe (FEV1 < 40%) n=13	Not reported	Only report data according to severity for Group A and peak work rate (W)	NA	"Severity of illness did not affect exercise response"
2	Clini, 2002 (ref 100)	NA	Mild (n=15), Mod (n=15), Severe (n=17)	Mild 59(5) years, Mod 67(7), Severe 68(8)	0	NA	Mild (n=15) FEV1 73(6)%, Mod (n=15) 58(6)%, Severe (n=17) 35(5)%. Based on ERS FEV1/severity guidelines; 7/17 severe used supplementary oxygen and had cor pulmonale	Not reported	Observational study	NA	"Peak work significantly increased by 17, 15 and 10% in mild, moderate and severe patients respectively, whereas the increase in 6 MWD was not significant." "The lowest increase in peak watts was due to 7 patients (severe group) with cor pulmonale"
3	Garuti, 2003 (ref 184)	NA	Mild/Moderate (n=48); Severe (n=53); Very Severe (n=48)	Mild/Moderate (70 +/- 7), Severe (68 +/-8), Very Severe (69 +/- 7)	Mild/Moderate (30M, 18F), Severe (33M, 20F), Very Severe (31M; 17F)	NA	Group 1 (Gold stage 2a [FEV1 50-80%(Mild/Moderate)]: mean FEV1 63(9)% Group 2 (stage 2b [FEV1 30-50%(Severe)]: 42(6)%), Group 3 (stage 3 (FEV1 < 30%(Very Severe)]: 25(7)%)	Not reported	Observation study. No control group. Continued medical treatment/convalescence may have contributed to improvements	NA	COPD patients of different severity may benefit from in patient pulmonary rehabilitation(12 sessions over 14 days) in terms of physical performance and health-related quality of life following an acute exacerbation
4	Berry, 1999 (not included in original search)	NA	Mild/Moderate (n=99), Severe (n=36), Very Severe (n=16)	Mild/Moderate 67.4(6.1) years, Severe 68.3(6.2), Very Severe 66.1(5.6)	Mild/Moderate (54M, 45F); Severe (22M, 14F), Very Severe (10M, 6F)	NA	Mild/Moderate FEV1 > 50%, Severe 35-50%, Very Severe < 35%	Not reported	Observational study. Unequal sample sizes per group	NA	"The results of this investigation show that all patients with COPD, despite the severity of the disease"
5	Vogiatzis 1999 (not included in original search)	NA	Mild/Moderate (n=32), Severe (n=28)	Training Group = 64+/8	Not reported for severity groups	NA	Mild/Moderate FEV1 >40; Severe FEV1 < 40	Not reported	Observational study, limited data for disease severity reported	NA	"Training benefits are unrelated to and independent of underlying airflow limitation, comparable benefits were observed for patients with % predicted FEV1 < 40% and for those whose FEV1 exceeded this threshold"

Excluded Studies

#	Reference 1st author, Year	Title	Citation	Level of Review	Reason for Exclusion	Comments
8	Alexander 2008	The effect of strength training on functional fitness with chronic lung disease enrolled in pulmonary rehabilitation	Alexander JL, Phillips WT, Wagner CL. The effect of strength training on functional fitness in older patients with chronic lung disease enrolled in pulmonary rehabilitation. Rehabilitation Nursing 2008 May;33(3):91-7.	2	No comparison	
13	Ambrosino 2008	Developing concepts in the pulmonary rehabilitation of COPD	Ambrosino N, Casaburi R, Ford G, Goldstein R, Morgan MD, Rudolf M, et al. Developing concepts in the pulmonary rehabilitation of COPD. [Review] [58 refs]. Respiratory Medicine 2008 Jun;102 Suppl 1:S17-S26.	2	Review article	
18	Arnardottir 2007	Interval training compared with continuous training in patients with COPD	Arnardottir RH, Boman G, Larsson K, Hedenstrom H, Emtner M. Interval training compared with continuous training in patients with COPD. Respiratory Medicine 2007 Jun;101(6):1196-204.	2	No comparison	Stratified randomization (FEV1 > or < 40% but no results reported)
20	Babb 1997	The relationship between maximal expiratory flow and increases in maximal exercise capacity with exercise training	Babb TG, Long KA, Rodarte JR. The relationship between maximal expiratory flow and increases of maximal exercise capacity with exercise training. American Journal of Respiratory and Critical Care Medicine 1997;156(1):Date.	2	No comparison	Mild patients only
23	Barakat 2008	Outpatient pulmonary rehabilitation in patients with chronic obstructive pulmonary disease	Barakat S, Michele G, George P, Nicole V, Guy A. Outpatient pulmonary rehabilitation in patients with chronic obstructive pulmonary disease. International Journal of Copd 2008;3(1):155-62.	2	No comparison	Severe COPD only
30	Battaglia 2009	Rationale of the combined use of inspiratory and expiratory devices in improving maximal inspiratory pressure and maximal expiratory pressure of patients with chronic obstructive pulmonary disease	Battaglia E, Fulgenzi A, Ferrero ME. Rationale of the combined use of inspiratory and expiratory devices in improving maximal inspiratory pressure and maximal expiratory pressure of patients with chronic obstructive pulmonary disease. Archives of Physical Medicine & Rehabilitation 2009 Jun;90(6):913-8.	2	No data	Included GOLD I-IV and reports better outcome in I & II compared to III & IV in discussion
45	Berry 2003	A randomized controlled trial comparing long-term and short-term exercise in patients with chronic obstructive pulmonary disease	Berry MJ, Rejeski WJ, Adair NE, Ettinger WHJ, Zaccaro DJ, Sevick MA. A randomized, controlled trial comparing long-term and short-term exercise in patients with chronic obstructive pulmonary disease. Journal of Cardiopulmonary Rehabilitation 2003 Jan;23(1):60-8.	2	No comparison	Mean FEV1 ~ 60%
46	Bianchi 2002	Lack of additional effect of adjunct of assisted ventilation to pulmonary rehabilitation in mild COPD patients	Bianchi L, Foglio K, Porta R, Baiardi R, Vitacca M, Ambrosino N. Lack of additional effect of adjunct of assisted ventilation to pulmonary rehabilitation in mild COPD patients. Respiratory Medicine 2002 May;96(5):359-67.	2	No comparison	
53	Borghi-Silva 2006	L-carnitine as an ergogenic aid for patients with chronic obstructive pulmonary disease submitted to whole body and respiratory muscle training programs	Borghi-Silva A, Baldissera V, Sampaio LM, Pires-DiLorenzo VA, Jamami M, Demonte A, 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 & Biological Research 2006 Apr;39(4):465-74.	2	No comparison	
75	Carrieri-Kohlman 2005	Impact of brief or extended exercise training program on the benefit of a dyspnea self-management program in COPD	Carrieri-Kohlman V, Nguyen HQ, Donesky-Cuenco D, mir-Devinen S, Neuhaus J, Stulbarg MS. Impact of brief or extended exercise training on the benefit of a dyspnea self-management program in COPD.[see comment]. Journal of Cardiopulmonary Rehabilitation 2005 Sep;25(5):275-84.	2	No comparison	
76	Carter 2003	Peak physiologic responses to arm and leg ergometry in male and female patients with airflow obstruction	Carter R, Holiday DB, Stocks J, Tiep B. Peak physiologic responses to arm and leg ergometry in male and female patients with airflow obstruction. Chest 2003 Aug;124(2):511-8.	2	No intervention	
78	Casaburi 1991	Reductions in exercise lactic acidosis and ventilation as a result of exercise training in patients with obstructive lung disease	Casaburi RPZDW. Reductions in exercise lactic acidosis and ventilation as a result of exercise training in patients with obstructive lung disease. American Review Respiratory Diseases 1991;143(1):9-18.	2	No comparison	
91	Chavannes 2002	Effects of physical activity in mild to moderate COPD: a systematic review	Chavannes N, Vollenberg JJ, van S, Wouters EF. Effects of physical activity in mild to moderate COPD: a systematic review.[see comment]. [Review] [30 refs]. British Journal of General Practice 2002 Jul;52(480):574-8.	2	Systematic review	Summarizes RCTs in patients with mild to moderate COPD and RR
92	Chee 2008	Treatment of mild chronic obstructive pulmonary disease	Chee A, Sin DD. Treatment of mild chronic obstructive pulmonary disease. [Review] [72 refs]. International Journal of Copd 2008;3(4):563-73.	2	Review article	References for RR in mild COPD
97	Clark 2000	Skeletal muscle strength and endurance in patients with mild COPD and the effects of weight training	Clark CJ, Cochrane LM, Mackay E, Paton B. Skeletal muscle strength and endurance in patients with mild COPD and the effects of weight training.[erratum appears in Eur Respir J 2000 Apr;15(4):816]. European Respiratory Journal 2000 Jan;15(1):92-7.	2	No comparison	Mild COPD only
99	Clini 2001	Effect of pulmonary rehabilitation on exhaled nitric oxide in patients with chronic obstructive pulmonary disease	Clini E, Bianchi L, Foglio K, Porta R, Vitacca M, Ambrosino N. Effect of pulmonary rehabilitation on exhaled nitric oxide in patients with chronic obstructive pulmonary disease. Thorax 2001 Jul;56(7):519-23.	2	No comparison	Mild to moderate COPD only
108	Cote 2005	Pulmonary rehabilitation and the BODE index in COPD	Cote CG, Celli BR. Pulmonary rehabilitation and the BODE index in COPD.[see comment]. European Respiratory Journal 2005 Oct;26(4):630-6.	2	No comparison	
115	Cox 1993	A pulmonary rehabilitation program for patients with asthma and mild chronic obstructive pulmonary diseases (COPD)	Cox NJ, Hendricks JC, Binkhorst RA, van H. A pulmonary rehabilitation program for patients with asthma and mild chronic obstructive pulmonary diseases (COPD). Lung 1993;171(4):235-44.	2	No comparison	
142	Dourado 2006	Relationship of upper-limb and thoracic muscle strength to 6-min walk distance in COPD patients	Dourado VZ, Antunes LC, Tanni SE, de P, Padovani CR, Godoy I. Relationship of upper-limb and thoracic muscle strength to 6-min walk distance in COPD patients. Chest 2006 Mar;129(3):551-7.	2	No intervention	
158	Evans 2009	Pulmonary rehabilitation is successful for COPD irrespective of MRC dyspnoea grade	Evans RA, Singh SJ, Collier R, Williams JE, Morgan MDL. Pulmonary rehabilitation is successful for COPD irrespective of MRC dyspnoea grade. Respiratory Medicine 2009;103(7):Date.	2	No data	Discussion reports improvement in all patients regardless of GOLD stage
167	Franssen 2004	Effects of whole-body exercise training on body composition and functional capacity in normal-weight patients with COPD	Franssen FM, Broekhuizen R, Janssen PP, Wouters EF, Schols AM. Effects of whole-body exercise training on body composition and functional capacity in normal-weight patients with COPD. Chest 2004 Jun;125(6):2021-8.	2	No comparison	
177	Garcia-Aymerich 2007	Regular physical activity modifies smoking-related lung function decline and reduces risk of chronic obstructive pulmonary disease: a population-based cohort study	Garcia-Aymerich J, Lange P, Benet M, Schnohr P, Anto JM. Regular physical activity modifies smoking-related lung function decline and reduces risk of chronic obstructive pulmonary disease: a population-based cohort study.[see comment]. American Journal of Respiratory & Critical Care Medicine 2001 Mar 7;175(5):458-63.	2	No comparison	Observational study eval decline in FEV1 depending upon level of PA (no decline in mild patients [discussion only])
180	Garrod 1997	The quantification of physical training as part of pulmonary rehabilitation on the daily life and well-being in patients with severe and moderate COPD	Garrod R. The quantification of physical training as part of pulmonary rehabilitation on the daily life and well-being in patients with severe and moderate COPD. European Respiratory Journal - Supplement 1997;10(Suppl 25):86.	2	No comparison	ERS Abstract
181	Garrod 1997	Randomised controlled trial of hospital out-patient pulmonary rehabilitation in moderate COPD: early effects	Garrod R, Bestall JC, Garnham R, Paul EA, Jones PW, Wedzicha JA. Randomised controlled trial of hospital out-patient pulmonary rehabilitation in moderate COPD: Early effects. Physiotherapy 1997;83(7):Date.	2	No comparison	
183	Garrod 2007	The relationship between inflammatory markers and disability in chronic obstructive pulmonary disease (COPD)	Garrod R, Marshall J, Barley E, Fredericks S, Hagan G. The relationship between inflammatory markers and disability in chronic obstructive pulmonary disease (COPD). Primary Care Respiratory Journal 2007 Aug;16(4):236-40.	2	No intervention	
187	Gerardi 2001	Non-pulmonary factors affective survival in patients completing pulmonary rehabilitation	Gerardi D, ZuWallack R. Non-pulmonary factors affecting survival in patients completing pulmonary rehabilitation. [Review] [29 refs]. Monaldi Archives for Chest Disease 2001 Aug;56(4):331-5.	2	No intervention	
214	Haave 2007	Improvements in exercise capacity during a 4-weeks pulmonary rehabilitation program for COPD patients do not correspond with improvements in self-reported health status or quality of life	Haave E, Hyland ME, Engvik H. Improvements in exercise capacity during a 4-weeks pulmonary rehabilitation program for COPD patients do not correspond with improvements in self-reported health status or quality of life. International Journal of Copd 2007;2(3):355-9.	2	No comparison	
235	Izumizaki 2008	Effects of inspiratory muscle thixotropy on the 6-min walk distance in COPD	Izumizaki M, Satake M, Takahashi H, Sugawara K, Shioya T, Homma I. Effects of inspiratory muscle thixotropy on the 6-min walk distance in COPD. Respiratory Medicine 2008 Jul;102(7):970-7.	2	Not respiratory rehabilitation	
248	Karapolat 2007	Do the benefits gained using a short-term pulmonary rehabilitation program remain in COPD patients after participation?	Karapolat H, Atasever A, Atamaz F, Kirazli Y, Elmas F, Erdinc E. Do the benefits gained using a short-term pulmonary rehabilitation program remain in COPD patients after participation? Lung 2007 Jul;185(4):221-5.	2	No data	Discussion reports no difference in outcome according to FEV1
250	Kayahan 2006	Psychological outcomes of an outpatient pulmonary rehabilitation program in patients with chronic obstructive pulmonary disease	Kayahan B, Karapolat H, Atyntoprak E, Atasever A, Ozturk O. Psychological outcomes of an outpatient pulmonary rehabilitation program in patients with chronic obstructive pulmonary disease. Respiratory Medicine 2006;100(6):Date.	2	No comparison	All GOLD stages included but no assessment
253	Ketelaars 1997	Long-term outcome of pulmonary rehabilitation in patients with COPD	Ketelaars CA, bu-Saad HH, Schlosser MA, Mostert R, Wouters EF. Long-term outcome of pulmonary rehabilitation in patients with COPD.[see comment]. Chest 1997 Aug;112(2):363-9.	2	No comparison	Discussion reports that rate of decline in benefit not associated with FEV1
263	Lacasse 1999	Overviews of respiratory rehabilitation in chronic obstructive pulmonary disease	Lacasse Y, Goldstein RS. Overviews of respiratory rehabilitation in chronic obstructive pulmonary disease. [Review] [33 refs]. Monaldi Archives for Chest Disease 1999 Apr;54(2):163-7.	2	Review article	
279	Lizak 2008	Female and male chronic obstructive pulmonary disease patients with severe dyspnea do not profit less from pulmonary rehabilitation	Lizak MK, Singh S, Lubina S, Zembala M. Female and male chronic obstructive pulmonary disease patients with severe dyspnea do not profit less from pulmonary rehabilitation. Polskie Archiwum Medycyny Wewnetrznej 2008 Jul;118(7-8):413-8.	2	No comparison	Stratified according to MRC grade not FEV1/severity
292	Maltais 1997	Intensity of training and physiologic adaptation in patients with chronic obstructive pulmonary disease	Maltais F, LeBlanc P, Jobin J, Berube C, Bruneau J, Carrier L, et al. Intensity of training and physiologic adaptation in patients with chronic obstructive pulmonary disease. American Journal of Respiratory & Critical Care Medicine 1997 Feb;155(2):555-61.	2	Not a prespecified outcome	Outcome = training intensity
323	Morgan 1999	The prediction of benefit from pulmonary rehabilitation: setting, training intensity and the effect of selection by disability	Morgan MD. The prediction of benefit from pulmonary rehabilitation: setting, training intensity and the effect of selection by disability. [Review] [26 refs]. Thorax 1999 Aug;54 Suppl 2:S3-S7.	2	Review article	
328	Nakamura 2008	Effects of aerobic training and recreational activities in patients with chronic obstructive pulmonary disease	Nakamura Y, Tanaka K, Shigematsu R, Nakagaichi M, Inoue M, Homma T. Effects of aerobic training and recreational activities in patients with chronic obstructive pulmonary disease. International Journal of Rehabilitation Research 2008 Dec;31(4):275-83.	2	No comparison	
408	Ries 1995	Effects of pulmonary rehabilitation on physiologic and psychosocial outcomes in patients with chronic obstructive pulmonary disease	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 Jun 1;122(11):823-32.	2	No data	Reports no difference according to FEV1 but no group comparison
415	Ringbaek 2000	Rehabilitation of patients with chronic obstructive pulmonary disease. Exercise twice a week is not sufficient!	Ringbaek TJ, Broendum E, Hemmingsen L, Lybeck K, Nielsen D, Andersen C, et al. Rehabilitation of patients with chronic obstructive pulmonary disease. Exercise twice a week is not sufficient! Respiratory Medicine 2000 Feb;94(2):150-4.	2	No comparison	
419	Rossi 2005	Length and clinical effectiveness of pulmonary rehabilitation in outpatients with chronic airway obstruction	Rossi G, Florini F, Romagnoli M, Bellantone T, Lucic S, Lugli D, et al. Length and clinical effectiveness of pulmonary rehabilitation in outpatients with chronic airway obstruction. Chest 2005 Jan;127(1):105-9.	2	No comparison	
423	Salman 2003	Rehabilitation for patients with chronic obstructive pulmonary disease: meta-analysis of randomized controlled trials	Salman GF, Mosier MC, Beasley BW, Calkins DR. Rehabilitation for patients with chronic obstructive pulmonary disease: meta-analysis of randomized controlled trials.[see comment]. Journal of General Internal Medicine 2003 Mar;18(3):213-21.	2	Systematic review	Provides effect sizes for RR according to severity
440	Singh 2005	Physiotherapy in stable COPD	Singh S. Physiotherapy in stable COPD. Chronic Respiratory Disease 2005;2(2):Date.	2	Editorial	
443	Skumlien 2007	Four weeks' intensive rehabilitation generates significant health effects in COPD patients	Skumlien S, Skogedal EA, Bjortuft O, Ryg MS. Four weeks' intensive rehabilitation generates significant health effects in COPD patients.[see comment]. Chronic Respiratory Disease 2007;4(1):5-13.	2	No comparison	
469	Tay 2007	A systematic review: Effects of inspiratory muscle training on the exercise tolerance (using the 6 minute walk test) of stage II-III COPD patients	Tay YL, Chieng JR, Tan ML, Tan WQ, Zeng QZ, Kong LY. A systematic review: Effects of inspiratory muscle training on the exercise tolerance (using the 6 minute walk test) of stage II-III COPD patients. Physiotherapy Singapore 2007;10(1):Date.	2	Systematic review	No comparison & not respiratory rehabilitation
487	Vallet 1994	Value of individualized rehabilitation at the ventilatory threshold level in moderately severe chronic obstructive pulmonary disease	Vallet G, Varray A, Fontaine JL, Prefaut C. Interest of individualized training program at the ventilatory threshold in mild to moderate COPD patients. [French]. Revue des Maladies Respiratoires 1994;11(5):Date.	2	No comparison	
509	Wedzicha 1998	Randomized controlled trial of pulmonary rehabilitation in severe chronic obstructive pulmonary disease patients, stratified with the MRC dyspnoea scale	Wedzicha JA, Bestall JC, Garrod R, Garnham R, Paul EA, Jones PW. Randomized controlled trial of pulmonary rehabilitation in severe chronic obstructive pulmonary disease patients, stratified with the MRC dyspnoea scale. European Respiratory Journal 1998 Aug;12(2):363-9.	2	No comparison	Stratified according to MRC grade not FEV1/severity

Included studies

Excluded Studies

Bibliographic Citation 1st Author, Year	Reason for Exclusion
Berry MJ_2003	Not Relevant
Clini E_2001	Not Relevant
Gadoury MA_2005	Not Relevant
Garcia-Aymerich J_2006	Not Relevant
Grodner S_1996	Not Relevant
Heppner PS_2006	Not Relevant
Kayahan B_2006	Not Relevant
Leung ACSC_2006	Not Relevant
Low G_2006	Not Relevant
Maltais F_2008	Not Relevant
O'Donnell DE_2007	Not Relevant
Puhan MA_2008	Not Relevant
Rajendran AJ_1998	Not Relevant
Ries AL_2003	Not Relevant
Schols AM_1998	Not Relevant
Skumlien S_2007	Not Relevant
Slinde F_2005	Not Relevant
Spruit MA_2005	Not Relevant
Theander K_2009	Not Relevant
Varkey AB_2004	Not Relevant
Wilson DH_2004	Not Relevant

Included Studies

#	Bibliographic Citation: 1st Author, Year	Study Design/Score 1	Study Design/Score 2	Open Label	Completion	Informed Consent	Ethics Approved	Funding Source	Eligibility Criteria: Inclusion Criteria	Eligibility Criteria: Exclusion Criteria	Health Care Setting	Intervention	Outcome(s): 1. Reduction in Dyspnea	2. Improved exercise capacity	3. Improved ADL	4. Improved Quality of life	5. Decreased exacerbations	6. Decreased health care utilization	7. Cost-effectiveness	Other	Randomization Method	Participant Characteristics: N	Age	Gender	Race	Other	Side Effects	Limits	Generalizability	Authors Conclusion
1	Lalon, 2009	2	0	N/A	1	1	1	2	AECOPD, COPD (ATS/ERS); dyspnea with ADL; able to complete HRQL	Comorbidities and/or cognitive dysfunction preventing participation in PR;	2	PR vs UC following AECOPD, PR – Input → Output x 3 mo; **Input PR** – walking, U + L/E strength exercise; min of 30 min/day **Output** – 1hr/day, 2x/wk; exercise not defined	No significant between group difference in BORG during 6MWT No significant between group difference in mMRC No significant between group difference in CRQ dyspnea	Both groups clinically significantly increase 6MWD; No significant between group difference 6MWD	N/A	Significantly better CRQ Fatigue, SF-36 Physical Component and HADS anxiety in PR group at 3 months. No change UC	N/A	No between group difference in readmissions (trend toward improvement in PR). No between group difference in unscheduled visits to A&E Data from hospital & doctor records and reconciled with patient diaries.	N/A	No significant between group difference in BODE index.	Computer generated with allocation concealed until intervention assigned	At completion: UC=45 PR=39	UC: 70±10 PR: 70±9	UC (f): 42% PR(f): 45%	Not reported	Charlson Index of co-morbidity: 3.1 FEV1: UC= 35% PR=36%	State no adverse effects of PR	Underpowered: needed 80/group to detect a "significant" decrease in readmission rate with an alpha=0.5 and 80% power Exercise intervention poorly defined Acceptable adherence (75% attendance) in only 40% of PR subjects AECOPD not defined	Poor	Early PR is safe and feasible. Positive but no significant changes in their study; could be enhanced by larger number of subjects.
2	Behnke, 2000	2	0	N/A	Not reported	1	1	Not industry	4-7 days post-AECOPD	Unstable cardiac disease, decomp cor pulmonale, diseases that prevented participation in exercise program	2 + home setting, urban	Random allocation to PR or UC group. UC=no structure program PR=Hospital → Home-based Walking Program **Hospital** 0-11 days: walk 6x/day based on daily 6MWD **Home** 11d-6 mo. walking 125% of best 6MWD in Hosp **Follow-up**: diaries; biweekly visits x 3 mo; weekly phone call 3-6 mo; monthly hospital-based assessments 1,2,3,6 months	6MWT significant between group difference in BORG CRQ-dyspnea significant between group difference at 3 mo (6.4 units) and at 6 mo (11.4 units) BDI/TDI significant between group difference at day 11, months 3, 6	6MWT: significant improvement at day 10 through to 6 months in PR group, no change in UC	N/A	CRQ Only PR group improved; significant between group difference at 3 & 6 months in all but emotion	N/A	N/A	N/A	Change in 6MWD correlate with change TDI, CRQ; TDI with CRQ; change FEV1 with CRQ, TDI, 6MWD	Not identified	UC 15 PR=15	UC: 68±2.2 PR=64±1.9	UC (0) 11 PR(0)=12	Not reported	Meds not different between group throughout study	Not specifically assessed	Small numbers, didn't define AECOPD	High	Significant improvements in exercise performance. CRQ could occur after recovery from AECOPD and maintained after d/c when supported by a home-based walking program.
3	Behnke, 2003	2	0	N/A	Not reported	1	1	Not industry	4-7 days post-AECOPD	Unstable cardiac disease, decomp cor pulmonale, diseases that prevented participation in exercise program	3 + home setting, urban	As per Behnke et al 2000 **6-18 mo**: 15 min walk/day @125% 6MWD at d/c. Apparently this was progressed (change in 6MWD) during the weekly home visit BUT home visits ended at the end of 3 months. There is a heading for "Assessments during hospital visits" but doesn't present timeline.	BORG significantly better in PR group from 3 to 18 months CRQ (dyspnea) significantly better in PR group through 18 months; TDI significant between group difference: [PR 4.4, UC [illegible]]	6MWD significantly better in PR from 11 days through 18months 5self-paced TM test	N/A	CRQ (all subscales) significant between group difference: [difference in total score ~ 40 units]	Disease-related hospital admission between group difference = 0.05	Hospital admission significant between group difference B2 inhaler use significant between group difference	N/A		Not identified	UC=12 PR=14	UC=69±6.9 PR=64±7.5	UC (0)=9 PR(0)=11	Not reported	FEV1: UC=37.5±6.9 PR=34.8±7.1 BMI: UC=23.3±3.1 PR=24.5±4.1	Not specifically assessed	Small numbers NB. Defined exacerbation and exacerbation related admission in this study	Poor. Difficult to understand how exercise was progressed. It is unlikely that distance remained 125% of d/c walk distance for 18 months and still resulted in significant increases in walk distance.	Home-based walking training over 18 months reduced the number of hospital admissions and the use of B2-agonists in patients with severe COPD. "It seems unlikely that the initial exacerbation has significantly affected the outcome of the long-term training, since lung function and exercise parameters were stable from hospital discharge over 18 months". Authors believe that it is the exercise compliance, associated with the initial training program, that kept the training group superior.
4	Kirsten, 1998	2	0	N/A	Not reported	0	0	Not industry	6-8 days post-AECOPD	Unstable cardiac disease, decomp cor pulmonale, diseases that prevented participation in exercise program	2	Random allocation to PR or UC group. UC=no structure program PR=Hospital → Home-based Walking Program Hospital 0-11 days: walk 6x/day based on daily 6MWT	TDI significant between group difference BORG during 6MWT significant between group difference	Both increased 6MWD, greater increase in PR No significant between group difference in absolute difference	N/A	N/A	N/A	N/A	N/A	Physiology during exercise significant between group difference in: VE, VO2/kg, VO2/HR	Not identified	UC=14 PR=15	UC=65.6±12 PR=62.3±9	UC (0)=14 PR(0)=12	Not reported		Not specifically assessed	Small numbers, no ethical approval or informed consent, tapered steroids during trial-continued recovery; didn't define AECOPD	Good	Exercise training significantly improves exercise capacity in patients with severe COPD following AECOPD
5	Man, 2004	2	0	N/A	1	0	0	Not industry	Inpatient with primary Dx of AECOPD	Comorbidity that limited exercise training; No PR in the year preceding AECOPD	2	Admit to hospital with AECOPD, allocate to UC or PR within 10 day admission PR: 2 classes/wk x 8wk; 2hr/class, aerobic & resistance exercise + education; Home Exercise Program (30 min/day)	CRQ (Dyspnea) difference better in PR vs. UC at 3 months (5.5 units with 95% CI (2-9))	ISWT significant between group difference		SF-36, CRQ, SGRQ (impact & total) significant better in PR group vs. UC at 3 months	Significantly less Accident & Emergency visits over 3 months in PR group vs. UC	Significantly less Accident & Emergency visits over 3 months in PR group vs. UC			Randomization number generator for first patient into study, minimization method for rest	UC 21 PR 21	UC [illegible] PR [illegible]	UC (0) 8 PR(0) 9	Not reported	FEV1 UC 37% PR=42%	State no adverse effects of PR	Low: AECOPD not defined, Ex not well described. AECOPD not defined	[illegible] ex not well defined	Early PR post-AECOPD is feasible and safe and leads to clinically significant improvement in ex cap and health status at 3 months. It may reduce health utilization but small numbers limited the power of the study.
6	Murphy, 2005	2	0	N/A	1	1	1	Not identified	COPD (FEV1<60%), post-AECOPD (defined) Apparently all were admitted to hospital for Rx of AECOPD	CHF, Pneumonia, Pneumo, PE, PE, arrhythmia	Home-based training in Ireland (maybe 2 or 3)	Baseline assessment 1 day pre-d/c → allocation to UC or PR UC not defined **PR** **Supervised Home Exercise**: 2x/wk, 30-40 min; **Unsupervised exercise** on other days: monitored with diary (data not reported in results) **Exercise**=Stair Stepping, Sit-to-Stand, Theraband U/E exercise	BORG no significant between group difference during ISWT Both groups improve Borg and MRC No significant between group difference MRC	PR had significant improvement in ISWT, no change UC 3MST significant between group difference no significant between group difference MVIC quads or hand grip; no improvement in either group	N/A	EQ-5D & EQ-Thermometer Both groups improved SGRQtot. Greater improvement in SGRQ in PR vs. UC	No significant between group difference in exacerbations; trend to fewer in PR (p=0.06)	N/A	N/A		1:1 ratio using blinded sealed envelopes randomization following baseline assessment	UC=13 PR=13	UC=65±11 PR=67±10	UC (0)=7 PR(0)=10	Not reported		Not specifically addressed. Accounted for drop out, which did not include adverse events.	Small sample size and no power analysis Exercise program not well defined No information on home exercise activity. Time to start program (post-hospital d/c not defined Can't reproduce resistance intensity with theraband	Poor because exercise poorly defined	Exercise post-AECOPD is safe and well-tolerated. It improved exercise capacity, reduced dyspnea during ADL and improved QOL. Trend to reducing subsequent AECOPD at 3 months post-initial exacerbation. Small number a problem.
7	Nava, 1998	2	0	N/A	1	1	1	State no commercial party had a direct financial interest	COPD (ATS) Clinically stable (defined) following admission to RICU for acute RF. Ventilated (invasive or noninvasive).	Systemic neuro, severe orthopedic disease or CV instability or severe arrhythmias	2	Enroll in study 3-5 days post-admission to RICU Randomize to Standard Care (UC) + progressive ambulation or Comprehensive Care (PR) = 4 Step Program: 2 sessions/day, 30-45 min/session. All patients Steps 1&2. Step 1: bed exercise, posture, DB&C if necessary, approximately 24 hr post-admit to RICU. Step 2: progressive amb. Step 3: IMT (10 min bid, 30%MIP), L/E exercise (cycle x 20 min)+25 steps 5x/day Step 4: TM bid, 3x/wk, 70%max GXT	Significant between group difference in decreased in dyspnea (VAS) during 6MWT	PR only had significant increase 6MWT	N/A	N/A	N/A	LOS no significant between group difference	N/A	MIP significant between group difference HR response during 6MWT significant improved in PR only	Computer generated	UC=20 PR=60 Uneven group numbers for ethical reasons	UC=67±9 PR=65±6	UC (0)=13 PR(0)=38	Not reported	PR: PaCO2=60, FEV1= 31%, FVC=71% UC: PaCO2=56, FEV1=33%, FVC=74%	Not addressed specifically.	Different number of subjects in 2 groups with few in control group	Good - better than usual description of activity in each step.	People with COPD following acute RF, most of whom were ventilated showed greater improvements in function in response to early PR (exercise tolerance and dyspnea) compared to similar patients who received standard therapy.

Excluded Studies

#	Bibliographic Citation	Reason for Exclusion
	1st Author, Year	
1	Cao Z_2006	Not relevant
2	Carr SJ_2007	Not relevant
3	Clini E_2009	Not relevant
4	Donaldson GC_2001	Not relevant
5	Garrod R_1997 - No abstract	Not relevant
6	Garuti G_2003	Not relevant
7	Glassman SJ_1998	Not relevant
8	Pasqua F_2009	Not relevant
9	Puhan MA_2007	Not relevant
10	Riario-Sforza GG_2005	Not relevant
11	Vincent HK_2002	Not relevant
12	Vivodtzev I_2006	Not relevant