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Original Research

Pulmonary rehabilitation for acute exacerbations of COPD: A systematic review

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ABSTRACT

Introduction and objectives: This systematic review summarized the evidence on the effects (benefits and harms) of pulmonary rehabilitation for individuals with acute exacerbations of chronic obstructive pulmonary disease (AECOPD).

Material and methods: We included randomized controlled trials comparing pulmonary rehabilitation to either active interventions or usual care regardless of setting. In March 2022, we searched MEDLINE, Scopus, CENTRAL, CINAHL and Web of Sciences, and trial registries. Record screening, data extraction and risk of bias assessment were undertaken by two reviewers. We assessed the certainty of the evidence using the GRADE approach.

Results: This systematic review included 18 studies (n = 1465), involving a combination of mixed settings (8 studies), inpatient settings (8 studies), and outpatient settings (2 studies). The studies were at high risk of performance, detection, and reporting biases. Compared to usual care, pulmonary rehabilitation probably improves AECOPD-related hospital readmissions (relative risk 0.56, 95% CI 0.36 to 0.86; moderate certainty evidence) and cardiovascular submaximal capacity (standardized mean difference 0.73, 95% CI 0.48 to 0.99; moderate certainty evidence). Low certainty evidence suggests that pulmonary rehabilitation may be beneficial on re-exacerbations, dyspnoea, and impact of disease. The evidence regarding the effects of pulmonary rehabilitation on health-related quality of life and mortality is very uncertain (very low certainty evidence).

Conclusion: Our results indicate that pulmonary rehabilitation may be an effective treatment option for individuals with AECOPD, irrespective of setting. Our certainty in this evidence base was limited due to small studies, heterogeneous rehabilitation programs, numerous methodological weaknesses, and a poor reporting of findings that were inconsistent with each other. Trialists should adhere to the latest reporting standards to strengthen this body of evidence.

Registration: The study protocol was registered in Open Science Framework (https://osf.io/amgbz/).

1. Introduction

Chronic obstructive pulmonary disease (COPD) is a serious respiratory illness and is currently the third leading cause of death worldwide. Approximately 80% of these deaths occur in low- and middle-income countries (LMIC) [1]. Patients with COPD may experience acute exacerbations of symptoms characterized by acute worsening of dyspnoea, cough, sputum production and purulence. These episodes are known as acute exacerbation of COPD (AECOPD) [2]. AECOPD can last for days or even weeks, it requires pharmacological treatment, and occasionally hospitalization [2,3]. AECOPD have clinical and economic consequences, including impairments in patient's quality of life, lung

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function, increased healthcare expenditure due to hospitalization related expenses, and sometimes death [2,3]. An integral and multidisciplinary management of an AECOPD is therefore a global public health priority, as stated by the World Health Organization (WHO) Global Action Plan for the Prevention and Control of Noncommunicable Diseases (NCDs) and the United Nations 2030 Agenda for Sustainable Development [1].

Pulmonary rehabilitation (PR) is defined as a non-pharmacological intervention that includes, but is not limited to, exercise training, education, and behavioural change. PR is designed to improve the physical and psychological condition of people with a chronic respiratory disease and to promote long-term adherence to health-enhancing behaviours [4]. While previous systematic reviews have suggested that PR may improve health-related quality of life (HRQoL), functional capacity, symptoms, and reduce hospitalization in people with AECOPD [5–8], the evidence base is limited by high risk of bias and low precision due to small study size.

In 2017, the joint European Respiratory Society (ERS) and American Thoracic Society (ATS) guideline on AECOPD management [8] made a conditional recommendation (very low certainty) against the initiation of PR during hospitalization and suggested starting PR no earlier than three weeks after hospital discharge. This recommendation was challenged by COPD specialists [9], who pointed out that ERS/ATS Task Force based their recommendations on a systematic review from 2009 [7], which had methodological limitations. The review's per-protocol analysis showed evidence of no difference between early PR and usual care and had inconsistencies in the assessment of the certainty of the evidence. The specialists argued that ERS/ATS Task Force should have made a strong recommendation in favour of starting PR in the first weeks after hospital discharge, without any conditional reservation.

The body of evidence on the effects of PR programs for COPD rehabilitation has grown steadily in recent years. The two most recent systematic reviews on PR for AECOPD have reported PR programs during hospitalization [10,11] or shortly after hospital discharge [10]. Of note is that more than 80% of all AECOPD are managed in outpatient settings (i.e., non-hospitalized) [12], and the need for studies in outpatients with AECOPD has been clearly stressed [6]. Earlier reviews have focused on maintenance programs for individuals with stable COPD [13] or reported multimodal programs with or without physical exercise [6]. The setting or PR program characteristics and the quality of these previous systematic reviews were important factors considered. Most of the existing reviews did not search for unpublished literature (i.e., clinical trial registries) or reported on stakeholders' engagement [6,10,14–17], and lack systematic assessments of the certainty of the evidence base [6,10,18]. An updated systematic review on PR for AECOPD, using robust methods, was therefore needed to inform clinical practice guidelines.

This review addressed the following question: what are the benefits and harms of PR interventions during an AECOPD? The findings of this systematic review informed the recommendations of the Colombian guidelines for the management of COPD [19]. Two systematic reviews have recently addressed similar research questions [6,10]; we broadened the literature searches, revised the studies included in these reviews, and assessed the certainty of the evidence.

2. Material and methods

This systematic review followed the Cochrane Handbook guidance and is reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) [20]. The full protocol was registered, and it is publicly available (https://osf.io/amgbz/). We present a summary of our methods in the following sections.

2.1. Eligibility criteria

We included RCTs of adults with an AECOPD, published between 2020 and 2022, that evaluated the effects of PR compared to usual care or any other active intervention. Our outcomes included: hospital readmissions, HRQoL, cardiovascular submaximal capacity, physical activity levels, mortality, dyspnoea, re-exacerbations, and impact of disease. Appendix 1 presents detailed eligibility criteria, outcome measurement tools and minimal clinically important difference (MCID) values we used for the outcome measures' interpretation. The guideline's panel prioritized the outcome measures included in this review and worked closely with the review team in the interpretation of the results (Appendix 1). We worked together with Dr Machado and included studies from her network meta-analysis [6] meeting our eligibility criteria.

2.2. Information sources

An information specialist developed the search strategy and ran the search in MEDLINE (Pubmed); Scopus; CENTRAL (Ovid); CINAHL (EBSCO); and Web of Sciences. We screened the included studies in Machado 2020 [6] NMA review against our eligibility criteria and limited our searches to studies published between 2020 and 2022. We applied no language restrictions. One review author (JM) searched for ongoing studies in the WHO ICTRP portal and ClinicalTrials.gov by using free search terms taken from the main search strategies (Appendix 2). The same author (JM) searched Google Scholar to capture additional grey literature resources (e.g., reports, dissertations, theses, and conference abstracts).

2.3. Selection process

We piloted the eligibility criteria in 10% of the anticipated total sample. Once we obtained high agreement (>70%) between pairs of reviewers, we used EPPI web tool [21] to individually screen citations. Pairs of reviewers screened titles and abstracts, and each relevant full-text article was independently reviewed against the eligibility criteria. In cases of disagreement, a third reviewer was available to resolve any discrepancies. To facilitate the review process, we employed machine learning functions such as priority screening. Please refer to our protocol for additional information.

2.4. Data collection

We utilized and supplemented data from Machado 2020 [6] and Du 2022 [18] for our analysis. This included the sample size and effect estimates for each study group along with corresponding dispersion measures.

Pairs of review authors extracted data independently and in duplicate using Excel forms created for this project. Any disagreements were resolved through discussion. Data extracted included: study ID, funding source, country and setting where the study took place, PICO components (population, intervention, comparison, and outcomes), PR interventions' details, and outcome measures. We extracted data for all follow-up periods reported. To present the PR interventions, we used the FITT –VP parameters [22,23], which included Frequency (how often is exercise done each week), Intensity (how hard is the exercise), Time (how long is the exercise duration), Type (what is the mode of exercise), Volume (what is the total amount of exercise), and Progression (how is the program advanced). We also assessed the reporting completeness of exercise interventions within the PR programs using the Consensus on Exercise Reporting Template (CERT) along with analysis by PR components [24].

2.5. Risk of bias assessment

Two reviewers assess studies' risk of bias independently using the Cochrane risk of bias version 1 tool [25]. We considered blinding separately for subjective and objective outcomes. Any financial and

non-financial conflicts of interest reported in the studies were collected as a separate category outside of RoB 1.0.

2.6. Data synthesis

We categorized the studies based on their PR components and the comparison group they evaluated. We pooled studies if two or more in the same comparison reporting the same outcome, were sufficiently homogeneous, and data direction permitted pooling. We arithmetically reversed scales when necessary. If post-intervention data were reported as median and interquartile range, we converted them to mean and SD by following the methods reported by Wan et al. [26]. When statistical pooling was not possible, we followed the Synthesis Without Meta analysis (SWiM) guideline to report the results narratively [27].

Assessment of heterogeneity and subgroup analysis: we began by verifying the accuracy of our data and visually inspecting forest plots to explore heterogeneity (e.g., checking the confidence intervals' overlap). To assess the presence of statistical heterogeneity, we used the Chi [2] test (with a threshold P value of <0.10) and quantified the heterogeneity using the I^2 statistic in accordance with the Cochrane Handbook [28]. If considerable heterogeneity was present ($I^2 > 70\%$), as suggested by Deeks et al. [28] we did not conduct any meta-analysis.

However, when there was less heterogeneity ($I^2 \leq 70\%$), one reviewer (JM) conducted a random effects meta-analysis using Review Manager 5.4.1 23 [29]. We calculated Risk Ratios (RRs) and their corresponding 95% confidence intervals (CIs) for dichotomous outcomes such as mortality, and either Mean Differences (MDs) or Standardized Mean Differences (SMDs) along with their 95% CIs for continuous outcomes.

Based on data availability, we determined the independent effects of different *PR components*.

- Exercise + education or behavioural change (Exe + E/BC)
- Exercise + education or behavioural change + psychological support (Exe + E/BC + Psycho)
- Exercise only (Exe)

Trustworthiness of all subgroup analyses was evaluated using the Credibility of Effect Modification Analyses (ICEMAN) instrument [29]. However, we found that subgroup analyses based on PR setting (home or centre-based PR) or supervision were deemed inadequate as of ICEMAN [29].

We report post-intervention and follow-up assessments data divided into five groups: 4–12 weeks, 24 weeks, 36 weeks, 48 weeks, and 96 weeks (reported by one study only). Each meta-analysis is reported by PR subgroups components, statistical heterogeneity, and the results of the sensitivity analysis.

Sensitivity analysis: we assessed the effects of both clinical and statistical heterogeneity on the pooled effect estimates by removing studies with high variability in the data (e.g., standard deviations exceeding mean scores) or studies with different therapeutic modalities in their PR programs (clinical heterogeneity) like Tai-Chi or yoga.

2.7. Certainty of the evidence

We followed the GRADE Working Group framework for gradings of evidence [30] and prepared *'Summary of findings, (SoF)'* tables for the eight outcomes prioritized by guideline members. In the SoF tables, we integrated analysis of certainty of the evidence and the interventions magnitude of effect. We used a partially contextualized approach to rate the certainty of the evidence [31,32], which means that for a point (or range) estimate of a single outcome we assessed our certainty that the true effects fell within the boundaries of a trivial, small, medium, or large effect. We used MCID thresholds (i.e., trivial to large) to determine these boundaries from a clinical perspective which are available in the literature. The GRADE approach considers the risk of bias and the body of literature to rate certainty into one of four levels.

- *High*: We are very confident that the true effect lies close to that of the estimate of the effect.
- *Moderate*: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
- *Low*: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.
- *Very Low*: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

We present the results of the comparison between PR and usual care in Table 2. The remaining SoF tables, are shown in the appendices.

3. Results

3.1. Search results

The databases search yielded 2989; we removed 146 duplicate records. We initiated priority screening to screen 2843 records at title and abstract. After screening 400 records, and only including one study (inclusion rate of 0.25%), we moved to single screening for the remaining 1336 records. We screened the full text of 110 documents. Seven studies met our eligibility criteria. We also assessed 42 studies from Machado 2020 [6], 13 studies from Du 2022 [34-45], and 25 references from other sources, and included 12 unique studies meeting our eligibility criteria [33–44]. In total, we identified 18 studies (Fig. 1), with three ongoing studies (Appendix 3) and 126 excluded studies (Appendix 4).

3.1.1. Characteristics of the included studies

We included 18 parallel RCTs conducted in 12 countries and published between 2010 and 2021 (median year 2016). Fifteen studies reported their research protocols, and 16 studies reported their funding sources. Appendix 5 provides additional characteristics of the included studies. The interventions for PR varied in their components, while the control groups were mostly described as usual care. Table 1 summarizes the studies characteristics.

3.1.2. Population

A total of 1465 participants (mean age 68 years) form the evidence base in this review [33–50]. The number of participants in the studies ranged from 26 [47] to 215 [34]. Seventeen studies reported participants' gender (mean percentage of females was 37%) [33–39,41–50]. Fifteen studies reported forced expiratory volume (FEV_1) with a mean percentage predicted FEV_1 of 43% (from 30% to 58%) [33–38,40–44,48–50]. The most common comorbidities (10 studies) were heart disease, diabetes, hypertension, respiratory disorders, anxiety, and depression [33,38,39,41–43,46–48,50]. Ethnicity was not reported in any of the studies.

The setting for eight studies (44%) was hospitals or clinics [34,36,40,41,43,44,46,48] while eight was mixed settings (i.e., hospital and home) [33,38,39,42,45,47,49,50] and two studies [35,37] were home-based PR program. Healthcare providers (e.g., physiotherapist and nurses) supervised the PR programs in 72% of the studies [34–36,38,39,41–45,47,48,50] (Appendix 5). Adherence reporting and monitoring procedures were poor and heterogeneous across studies (n = 6) with only three studies reporting adherence levels above 80% (Benzo 2016 [33], 85%; Borges 2014 [35], 95%; Liao 2021 [48], 87%).

3.1.3. Interventions: pulmonary rehabilitation programs

Eleven studies started the PR programs during hospitalization [34,36,39–41,45–47,49–51], three studies at discharge [33,37,44], and two studies started within 2 weeks of hospital discharge [35,43]. Two studies compared early PR vs late PR [38,42] with early PR initiated within 2 weeks of exacerbation [42] or discharge [38], and late PR initiated

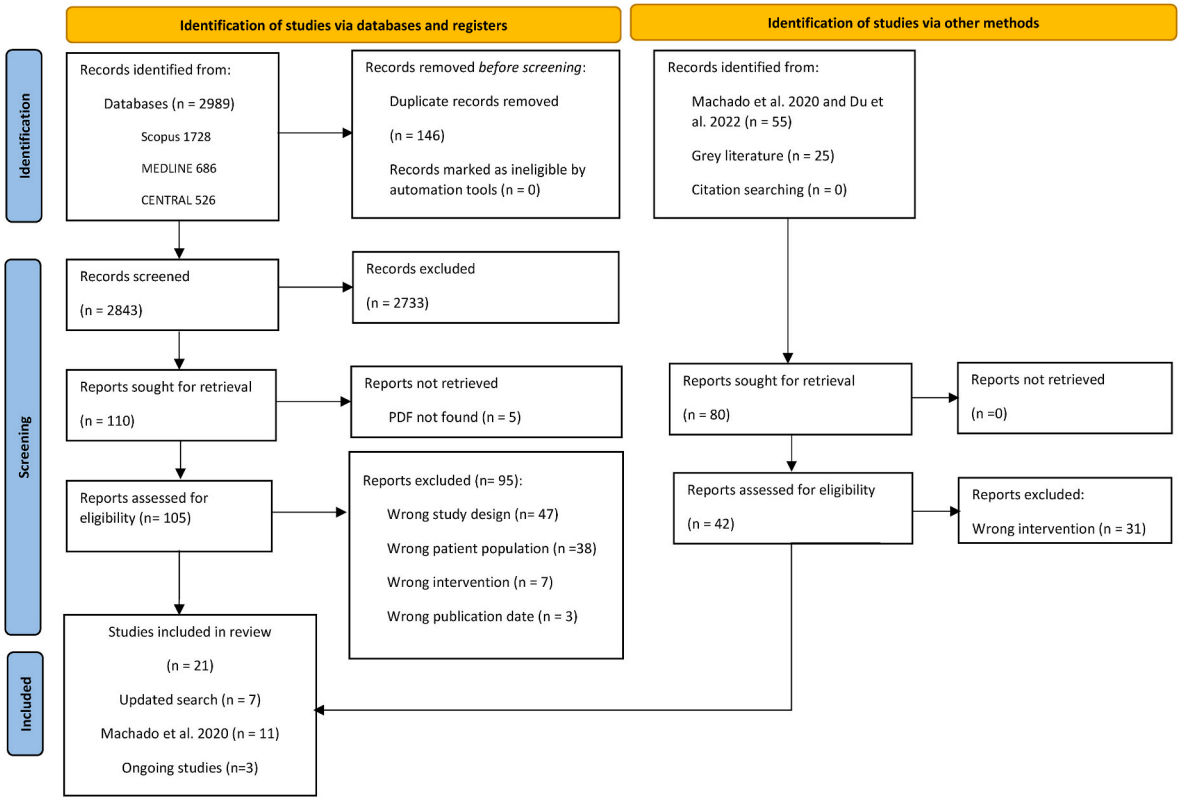

Fig. 1. PRISMA flow diagram for study selection.

either at 6 months after randomization or in a stable state [42], or at 2-month follow-up [38]. Ten studies provided the definition for the PR program [37–39,42,43,45–47,49,50]; PR lasted an average of six weeks (ranging from 4 days [39] to 12 weeks [35,42,50]).

PR components varied across studies including exercise-based rehabilitation, or multicomponent rehabilitation and motivational interviewing techniques. Exercise was prescribed together with chest physiotherapy (e.g., breathing exercises and airway clearance) [35,37–39,42,43,45–47,49,50]. We grouped the PR programs into the following groups.

1. **Exercise + education/behavioural change (Exe + E/BC) (n = 7)** [33,34,36,39–41,43] consisted of different exercise modes along with either educational or behavioural change interventions (e.g., aerobic exercises and dietary counselling).
2. **Exercise + education/behavioural change + psychological support (Exe + E/BC + Psycho) (n = 5)** [35,37,44,45,50] included exercise, educational or behavioural change approaches, and psychological support/psychotherapy (e.g., exercise, chest physiotherapy, and psychosocial support). Two studies used motivational interviewing techniques [37,44]; two studies used psychotherapy [45,50], and the remaining study included psychosocial support [35].
3. **Exercise only (Exe) (n = 4)** [46–49] different exercise modes, such as aerobic, stretching, or combined training of aerobic, resistance, and stretching.

The PR programs included different exercise modes, with 11 studies (61%) including more than one mode. Exercise modes were categorized as follows.

- Aerobic: two studies [41,46].
- Aerobic + flexibility: three studies [44,45,50].
- Aerobic + resistance: six studies [33,35,37,39,42,43].
- Aerobic + resistance + flexibility: two studies [36,48].
- Flexibility: one study [47].
- Resistance: four studies [34,38,40,49].

Subgroup analysis by exercise mode was not possible due to the limited number of studies.

3.1.3.1. Exercise interventions reporting. Across the 18 studies analysed (see Appendix 6), completeness of reporting [24] ranged from 0 to 100%. All studies reported on supervision and setting, while provider information was reported in 17 (94%) studies. The least reported items were exercise programs' adaptation (0%) and rules for starting level (1, 6%). Three CERT items, specifically provider (item 2) supervision (item 4) and exercise description (item 12) (e.g., sets, repetitions, duration, intensity) were reported in more than 80% of the PR programs. Further details, including an analysis by PR components, can be found in Appendix 6.

3.1.4. Control group

The included studies compared PR programs against usual care. In most cases, usual care involved following the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines, along with smoking cessation and healthy-living instructions [33,47]; respiratory therapy [41,43,50]; general counselling [37], and pharmacological treatment (e.g., bronchodilators, inhaled corticosteroids and antibiotics) [49]. Two Spanish studies had an active group in which participants received neuromuscular electrical stimulation protocols [40,48].

3.1.5. Outcomes

The most reported outcomes across studies were HRQoL (n = 13) and cardiovascular submaximal capacity (n = 13), followed by dyspnoea (n = 11). Seven studies documented hospital readmissions, and five studies reported mortality and re-exacerbations (Appendix 7).

Table 1
Characteristics of the included studies (n = 18).

Study ID Country and protocol	Population	Intervention and control	Outcomes
Benzo 2016 [33] United States NCT01058486	n = 215 (116 female) Exp: n = 108, age (yr) = 67.9 (SD 9.8) Con: n = 107, age (yr) = 68.1 (SD 9.2)	**Pulmonary rehabilitation**: Exe + E/BC FITT –VP: NR Exercise mode: A + R **Control**: Usual care	Hospital readmissions Physical activity levels Mortality Re-exacerbations
Borges 2014 [34] Brazil NCT01786928	n = 46 (16 female) Exp: n = 21, age (yr) = 64.1 (SD 12.5) Con: n = 25, age (yr) = 67.8 (SD 9.0)	**Pulmonary rehabilitation**: Exe + E/BC FITT –VP: 90 min x 3/wk x 1 wk; intensity 80% of 1RM Exercise mode: A + R **Control**: Usual care	HRQoL Cardiovascular submaximal capacity
Deepak 2014 [35] India Protocol NR	n = 60 (4 female) Exp: n = 30, age (yr) = 58.4 (SD 6.8) Con: n = 30, age (yr) = 59.4 (SD 6.7)	**Pulmonary rehabilitation**: Exe + E/BC + Psycho FITT –VP: 120 min x Frequency NR x 12 wks; intensity NR Exercise mode: A + R **Control**: Usual care	HRQoL Cardiovascular submaximal capacity Dyspnoea
He 2015 [36] China ChiCTR-TRC-13003068	n = 94 (64 female) Exp: n = 66, age (yr) = 69.2 (SD 1.53) Con: n = 28, age (yr) = 73.9 (SD 1.84)	**Pulmonary rehabilitation**: Exe + E/BC FITT –VP: 60 min x 2/day x until discharge; intensity 60% peak work rate and 3 to 5 on the Borg score. Exercise mode: A + R + F **Control**: Usual care	HRQoL Cardiovascular submaximal capacity Dyspnoea Impact of the disease
Johnson-Warrington 2016 [37] United Kingdom ISRCTN84599369	n = 78 (50 female) Exp: n = 39, age (yr) = 67.64 (SD 8.54) Con: n = 39, age (yr) = 68.33 (SD 7.73)	**Pulmonary rehabilitation**: Exe + E/BC + Psycho FITT –VP: 45 min x daily aerobic and 3/wks resistance x 10 wks; intensity NR Exercise mode: A + R **Control**: Usual care	Hospital readmissions HRQoL Cardiovascular submaximal capacity Mortality Dyspnoea
Khosravi 2020 [45] Iran IRCT20170618223320N5	n = 60 (17 female) Exp: n = 30, age (yr) = 70.25 (SD 7.5) Con: n = 30, age (yr) = 71.79 (SD 10.2)	**Pulmonary rehabilitation:** Exe + E/BC + Psycho FITT –VP: 30 min, x frequency NR x time NR; intensity NR Exercise mode: A + F **Control:** Usual care	Hospital readmissions
Kjaergaard 2020 [38] Denmark NCT02987439	n = 150 (87 female) Exp: n = 76, age (yr) = 72.7 (SD 9.4) Con: n = 74, age (yr) = 74.4 (SD 7.8)	**Pulmonary rehabilitation**: Early Exe + E/BC FITT –VP: 90 min x 2/wk x 7 wks; intensity 85% of VO2max Exercise mode: R **Control**: Late PR	Hospital readmissions Cardiovascular submaximal capacity Mortality Impact of disease
Knaut 2020 [46] Brazil U1111-1166-7480	n = 26 (15 female) Exp: n = 13, age (yr) = PR: 66.8 (SD9.49) Con: n = 13, age (yr) = CG: 69.3 (SD 13.5)	**Pulmonary rehabilitation**: Exe FITT –VP: 15 min x frequency NR x 4 wks; intensity NR Exercise mode: A **Control**: Usual care	HRQoL Cardiovascular submaximal capacity Dyspnoea
Liao 2015 [39] Taiwan NCT02329873	n = 62 (24 female) Exp: n = 31, age median (yr) = 68.0 (range 44.0–89.0) Con: n = 31, age median (yr) = 70.0 (range 52.0, 91.0)	**Pulmonary rehabilitation**: Exe + E/BC FITT –VP: 70 min, 2/day x 4 days; intensity NR Exercise mode: A + R **Control**: Usual care	Cardiovascular submaximal capacity Dyspnoea
Liao 2021 [47] China ChiCTR2000034530	n = 80 (17 female) Exp: n = 40, age (yr) = 61.83 (SD 6.63) Con: n = 40, age (yr) = 61.21 (SD 7.38)	**Pulmonary rehabilitation**: Exe FITT –VP: 60 min x 2/day x 12 wks; intensity 60–80% MHR Exercise mode: F **Control**: Usual care	HRQoL Cardiovascular submaximal capacity Dyspnoea Re-exacerbations
López-López 2019 [40] Spain NCT02515318	n = 66 (0 female) Exp: n = 22, age (yr) = 72.63 (SD 7.37) Con PT: n = 22, age (yr) = 71.20 (SD 11.53) Con: n = 22, age (yr) = 71.35 (SD 9.88)	**Pulmonary rehabilitation**: Exe + E/BC FITT –VP: duration NR x 1/day x 1 wk; intensity NR Exercise mode: R **Control**: Usual care	HRQoL Dyspnoea
López- López 2021 [48] Spain NCT04295655	n = 43 (4 female) Exp: n = 13, age (yr) = 74.92 (SD 7.07) Con FEG: n = 13, age (yr) = 75.80 (SD 8.61) Con: n = 17, age (yr) = 70.98 (SD 9.22)	**Pulmonary rehabilitation**: Exe FITT –VP: 60 min x 1/day x 9 days; intensity perceived dyspnoea and fatigue. Exercise mode: A + R + F **Control**: Usual care	HRQoL

(*continued on next page*)

Table 1 (*continued*)

Study ID Country and protocol	Population	Intervention and control	Outcomes
Lu 2020 [49] China ChiCTR–ION–16008854	n = 82 (0 female) Exp: n = 41, age (yr) = 67.4 (SD 7.1) Con: n = 41, age (yr) = 68.3 (SD 6.8)	**Pulmonary rehabilitation**: Exe FITT –VP: duration NR x 3/day x 8 wks Exercise mode: R **Control**: Usual care	Cardiovascular submaximal capacity Dyspnoea Impact of disease
Osadnik 2014 [41] Australia NCT01101282	n = 92 (32 female) Exp: n = 46, age (yr) = 69.5 SD (9.8) Con: n = 46, age (yr) = 67.8 (SD 11.6)	**Pulmonary rehabilitation**: Exe + E/BC + PEP FITT –VP: 50 min x 1/day x until discharge; intensity NR Exercise mode: A **Control**: Usual care	Hospital Readmission HRQoL Cardiovascular submaximal capacity Mortality Dyspnoea Re-exacerbations
Puhan 2012 [42] Switzerland Protocol NR	n = 36 (14 female) Exp: n = 19, age (yr) = 67.5 (SD 9.8) Con: n = 17, age (yr) = 66.5 (SD 6.2)	**Pulmonary rehabilitation**: Early Exe + E/BC FITT –VP: duration NR x frequency NR x 12 wks; intensity NR Exercise mode: A + R **Control**: Late PR	HRQoL Mortality Dyspnoea Re-exacerbations
Seymour 2010 [43] United Kingdom NCT00557115	n = 60 (32 female) Exp: n = 30, age (yr) = 67 (SD 10) Con: n = 30, age (yr) = 65 (SD 10)	**Pulmonary rehabilitation**: Exe + E/BC FITT –VP: 120 min x 2/wk x 8 wks; intensity NR Exercise mode: A + R **Control**: Usual care	Hospital readmission HRQoL Cardiovascular submaximal capacity Re-exacerbations
Song 2014 [44] Korea Protocol NR	n = 40 (13 female) Exp: n = 20, age (yr) = 66.6 (SD 11.1) Con: n = 20, age (yr) = 68.1 (SD 6.5)	**Pulmonary rehabilitation**: Exe + E/BC + Psycho FITT –VP: 120 min x frequency NR x 8 wks; intensity NR Exercise mode: A + F **Control**: Usual care	HRQoL Cardiovascular submaximal capacity
Zhang 2020 [50] China ChiCTR-TRC-14005108	n = 189 (44 female) Exp: n = 92, age (yr) = 65.53 (SD 6.64) Con: n = 97, age (yr) = 66.31 (SD 7.91)	**Pulmonary rehabilitation**: Exe + E/BC + Psycho FITT –VP: 55 min x 2/wk x 12 wks; intensity NR Exercise mode: A + F + Taichi **Control**: Usual care	Readmission (times) Readmission (days) Cardiovascular submaximal capacity Dyspnoea Impact of disease

A: aerobic. BC: behaviour change. Con: control. E: education. Exe: exercise. Exp: experimental or intervention group. FIIT: frequency, intensity, time, type of exercise. F: Flexibility. MHR: maximum heart rate. Min: minutes. NR: not reported. PEP: positive expiratory pressure. Psycho: psychotherapy. R: resistance. Ss: session(s). wk(s): week(s). Yr: years.

3.1.6. Risk of bias assessment

All included studies were assessed to be at high risk of bias (Fig. 2). Ten studies had an unclear risk of selection bias due to a lack of details on allocation concealment methods [33,35,36,39,43–47,49]. Due to the nature of exercise interventions, blinding of participants and personnel was not possible, resulting in all the studies being judged as having a high risk of performance bias. In addition, we judged the eight studies that used self-reported outcome measures to be at high risk of detection bias [33,35,36,38,42–44,46]. Despite registering their protocols *a priori*, most studies provided incomplete or contradictory information and were judged to be at high risk of selective outcome reporting [33,34,36–40,42,46,50,51]. Appendices 5 and 8 present further details on the risk of bias assessment.

3.1.7. Effects of pulmonary rehabilitation on AECOPD

3.1.7.1. Hospital readmissions. Pooled data from five studies [33,37,43,45,50] (n = 590) showed that PR probably reduced the risk of AECOPD-related hospital readmissions by 44% at the end of intervention (RR 0.56, 95% CI 0.36 to 0.86; moderate certainty of evidence) (Fig. 3 and Table 2).

Similar evidence was found at 24 weeks follow up [33,45,50] (RR 0.63, 95% CI 0.47 to 0.84; n = 455; moderate certainty evidence). Low certainty evidence indicated that PR may reduce AECOPD-related hospital readmissions compared to usual care at 12-, 36-, 48-, and up to 96 weeks follow-up. More details are available in Fig. 4 and Appendix 9.

Regarding early PR vs late PR, Kjærgaard 2020 [38] found evidence of no effect between early and late PR in AECOPD-related hospital readmissions on a 12-month follow-up period and a sample of 131 participants (Hazard ratio (HR) 0.79, 95% CI 0.47 to 1.23; 131 participants). The authors used HR statistics which provides insight into the relative hazard of readmission between the two groups.

3.1.7.2. Health-related quality of life. Twelve studies measured this outcome. Benzo 2016 [34], reported an improvement in HRQoL compared to the control group at 6 and 12 months but was excluded from our pooled analysis due to a lack of effect estimates. The remaining 11 studies used different tools to measure participants' HRQoL, with six [33] using the SGRQ [52], three [35–37] using the CRQ [53], and the two [40,48] using the EQ-5D [54]. We multiplied SGRQ scores by −1 to adjust tool direction, so that higher scores mean improvement.

After adjusting the SGRQ scores to align with the other tools, our initial pooled analysis showed high statistical heterogeneity (I^2 = 89%). After removing Osadnik 2014 [42], Seymour 2010 [44], and Song 2014 [45], heterogeneity decreased to 26% and 0% across PR subgroups, but remained high for the overall pooled SMD (I^2 = 76%), leading us to choose not to present the pooled results. The pooled SMDs across groups ranged from 0.88 to 1.43, accompanied by high heterogeneity in the subgroup interaction test (I^2 = 89.9%) (very-low certainty of evidence) (Table 2).

Four studies [33,34,40,41] provided evidence of no effect of PR on HRQoL at 4–12 weeks (SMD 0.16, 95% CI -0.31 to 0.63; 4 studies; 70 participants), 24 weeks (SMD 0.06, 95% CI -1.11 to 1.22; 2 studies; 302 participants), or 48 weeks (SMD 0.79, 95% CI 0.51 to 1.07; 1 study; 214 participants) with very-low certainty of evidence (Appendix 9).

When comparing early PR vs late PR, Puhan's study [42] (n = 28) reported no difference between early and late PR in any of the various domains of the CRQ (dyspnoea, fatigue, emotional function, and mastery) at 6-, 12-, or 18- months follow-up.

3.1.7.3. Cardiovascular submaximal capacity. Eleven of the twelve studies that measured this outcome provided data for the meta-analysis. All studies used the 6-min walk test (6 MWD test), except for two studies [37] that used the Incremental Shuttle Walk Test (ISWT) [55]. One study was excluded due to the use of Tai Chi in the treatment group. Narrative

Table 2
Summary of findings table.

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	N° of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with usual care	Risk with pulmonary rehabilitation				
Hospital readmissions (COPD-related): 4–12 weeks, less is better	239 per 1000	**134 per 1000** (86–206)	**RR 0.56** (0.36–0.86)	590 (5 RCTs)	⨁⨁⨁◯ Moderate[a]	Moderate evidence suggests that PR probably reduces the risk of hospital readmissions by 44% relative to usual care.
Health-related quality of life (median 3 weeks): assessed with CRQ, SGRQ and EQ-5D, higher is better	Not estimable	SMD **0.78 SD higher** (0.35 higher to 1.22 higher)	Not estimable	416 (8 RCTs)	⨁◯◯◯ Very low[b,c]	When compared to usual care, PR results in a large HRQL increase. This evidence is very uncertain.
Cardiovascular submaximal Capacity (median 8 weeks): 6 MWT and ISWT, higher is better	Not estimable	SMD **0.73 higher** (0.48 higher to 0.99 higher)	Not estimable	495 (8 RCTs)	⨁⨁⨁◯Moderate[b]	Moderate evidence suggests that when compared to usual care, PR probably results in a large increase in cardiovascular submaximal capacity.
Physical activity levels (4 weeks): physical activity monitors	One study (Benzo 2016, n = 92) found no difference in any physical activity between the pulmonary rehabilitation and control arms at 4 weeks (effect estimates were not reported).		Not estimable	92 (1 RCT)	⨁◯◯◯ Very low[b,d]	Very uncertain evidence suggest that PR makes a difference in physical activity levels when compared to usual care.
Mortality (12 weeks)	83 per 1000	**12 per 1000** (1–228)	**RR 0.15** (0.01–2.74)	71 (1 RCT)	⨁◯◯◯ Very low[e,f]	The evidence is uncertain about the effect of PR on mortality compared to usual care.
Dyspnoea (median 8 weeks): mMRC (MCID 0.5) (0–4, lower is better	The mean dyspnoea: end of intervention was **2.4** points	MD **0.42 points lower** (0.57 lower to 0.27 lower)	–	586 (7 RCTs)	⨁⨁◯◯ Low[b]	When compared to usual care, PR may reduce dyspnoea by 0.42 points on the mMRC scale.
Re-exacerbations (12–48 weeks): admin data, lower is better	**0.9** number of re-exacerbations	MD **0.18 re-exacerbations lower** (0.22 lower to 0.14 lower)	–	372 (3 RCTs)	⨁⨁◯◯ Low[d,f]	Low certainty of evidence suggest that the mean number of re-exacerbations is 0.18 lower in the PR group compared to usual care.
Impact of disease (median 8 weeks): CAT test (8 items, 0 to 40, more impact) MCID 2	The mean impact of disease: end of intervention was **18** points	MD **3.94 points lower** (5.04 lower to 2.83 lower)	–	355 (3 RCTs)	⨁◯◯◯ Very low[a,d,g]	Pulmonary rehabilitation results in a large improvement in impact of disease compared to usual care. This evidence is very uncertain.

Population: individuals with an acute exacerbation of chronic pulmonary disease.
Setting: clinic/hospital (44%) and mixed (clinic/hospital and home, 44%).
Intervention: pulmonary rehabilitation (PR).
Comparison: usual care.
Timepoint: end of intervention.
***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CAT: COPD assessment test; **CI:** confidence interval; **COPD:** chronic obstructive pulmonary disease; **CRQ:** Chronic Respiratory Questionnaire; **HR:** hazard ratio; **HRQoL:** Health-related quality of life; **ISWT:** Incremental Shuttle Walk Test; **MCID:** Minimal clinically important difference; **MD:** mean difference; **mMRC:** Modified Medical Research Council Dyspnoea Scale; **RR:** risk ratio; **SGRQ:** St George's Respiratory Questionnaire; **SMD:** standardized mean difference; **6MWT:** Six Minute Walk Test.
GRADE Working Group grades of evidence.
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect. **Very low certainty:** we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.
Explanations.
a. Issues of selection and reporting biases.
b. Issues of selection, detection, attrition, and selective reporting biases.
c. High statistical heterogeneity (I^2 >80%).
d. Small sample size.
e. Wide confidence intervals and small sample size.
f. Issues of blinding and selective reporting biases.
g. High statistical heterogeneity (I^2 >60%).

results from Borges 2014 [34] (n = 19) suggested that PR resulted in an increase of 160 m (SD 61) in the intervention group when compared with the usual care group.

Initial analysis showed high heterogeneity (I^2 = 83%) but this was decreased to I^2 = 46% after exploring possible sources of statistical and clinical heterogeneity. Two studies were removed [50] because standard deviations exceeded mean scores. Pooled estimates showed large improvements in cardiovascular submaximal capacity for the PR group (SMD 0.73, 95% CI 0.48 to 0.99; 8 studies; 495 participants). The effects were consistent across PR subgroups as shown in Fig. 5. Moderate quality evidence indicated that PR probably increases cardiovascular submaximal capacity when compared to usual care at the end of intervention (Table 2).

Two studies [41,50] reported on the long-term effects of cardiovascular submaximal capacity. However, the studies were small, and their findings were inconsistent as shown in Fig. 6. Thus, we are uncertain about the effect of PR on cardiovascular submaximal capacity compared to usual care at 24-, 48-, and up to 96 weeks follow-up (Appendix 9).

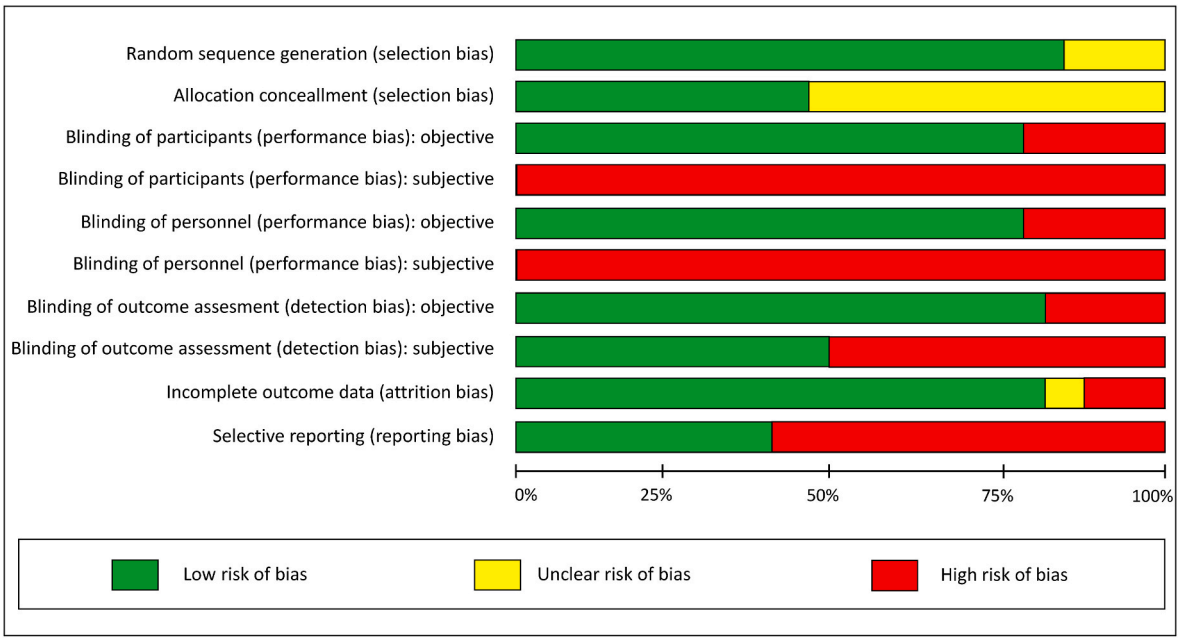

Fig. 2. Risk of bias for included studies.

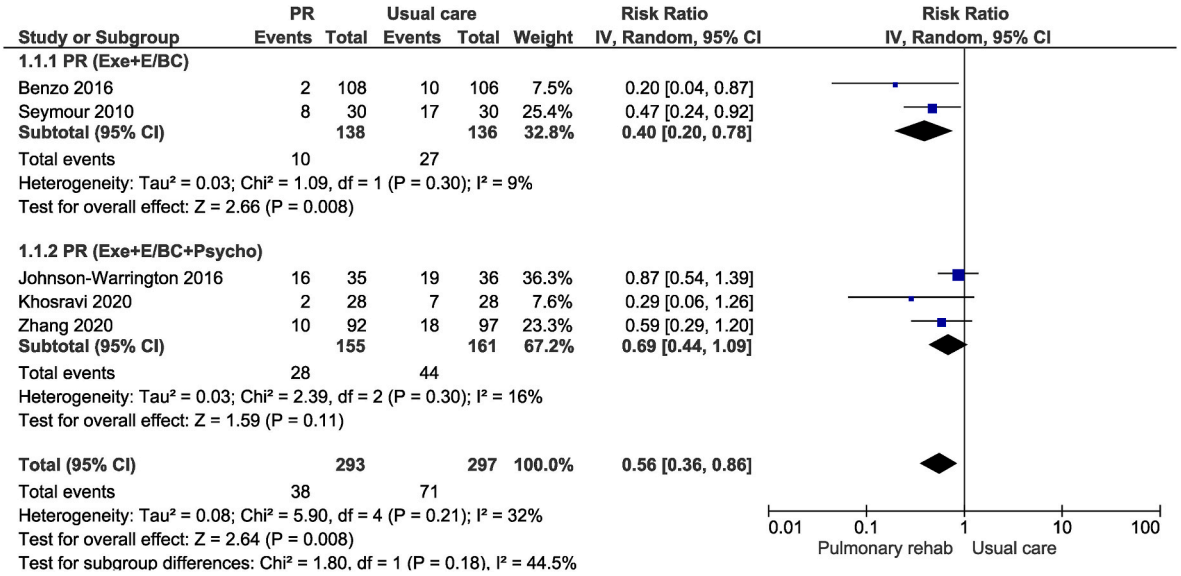

Fig. 3. Pulmonary rehabilitation compared to usual care for AECOPD-related hospital readmissions at end of intervention (4–12 weeks).

Early PR vs late PR evaluated by Kjærgaard 2020 [38] (n = 131) showed participants in early PR gained 33.9 m more than those in the late PR group at 2 months after the intervention. The outcome was measured by ISWT (MD 33.9 m, 95% CI 4.2 to 63.7). While 33.9 mts is a considerable gain, it fell short of the MICD of 47 m. However, the results were not sustained at 6 months after the intervention (MD 17.7 m, 95% CI −13.3 to 48.7).

3.1.7.4. Physical activity levels. Benzo 2016 [33] (n = 92) reported no difference between PR and usual care in any physical activity at any time point (very low certainty of the evidence). The study did not report any effect estimates (Table 2).

3.1.7.5. Mortality. Johnson-Warrington 2016 [37] (n = 71) reported evidence of no effect between PR and usual care on mortality at the end of the intervention (RR 0.15, 0.01 to 2.74) (Table 2). Similar findings were observed at 24- and 48-week follow up periods (Appendix 9). Thus, there is uncertainty regarding the effect of PR on mortality compared to usual care at any time points.

Regarding early PR vs late PR, two studies found no between groups difference. Kjærgaard 2020 [38] (n = 131) reported one-year cumulative mortality rate of 13% in the early PR group which did not differ from 10% in the late PR group (adjusted HR 1.04, 95% CI 0.36 to 3.01). Puhan 2012 [42] (n = 28) reported that two patients in each group died, but no further data were provided.

3.1.7.6. Dyspnoea. Ten studies measured this outcome at the end of the intervention. Of these, seven studies [35,36,41,46,47,49,50] used the mMRC scale, while two studies [39,40] used the modified Borg scale. The study by Johnson-Warrington 2016 [37] used the CRQ. We multiplied the scores of CRQ by −1, so that lower scores mean improvement. The results of the meta-analysis showed high heterogeneity (I^2 = 82%).

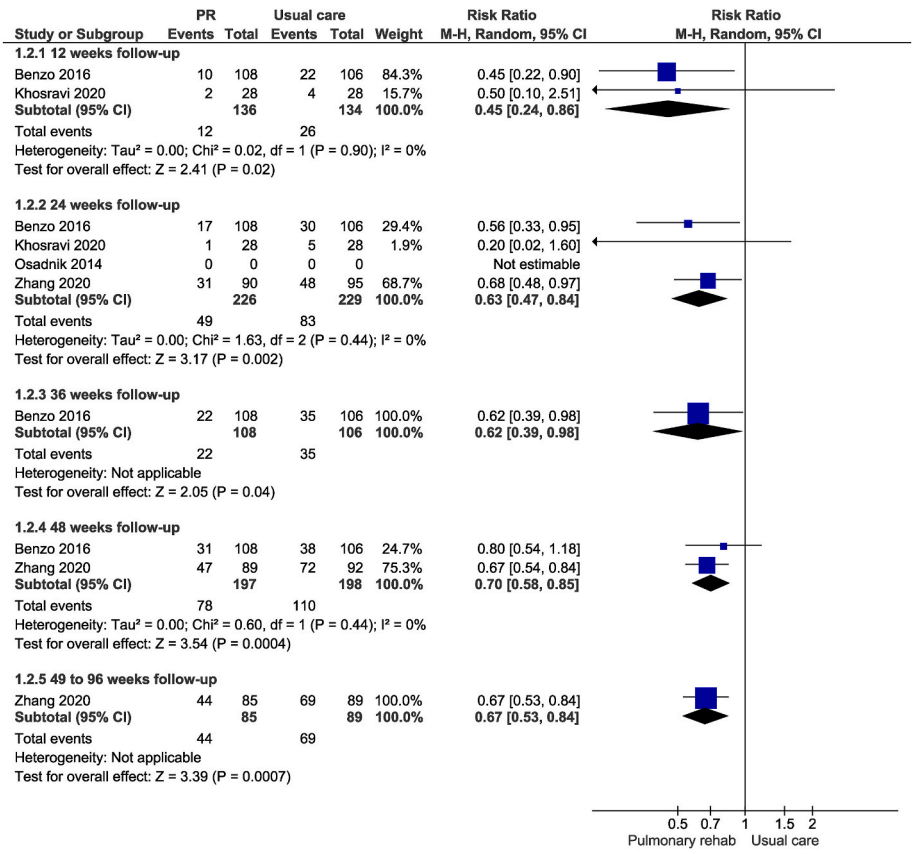

Fig. 4. Pulmonary rehabilitation compared to usual care for AECOPD-related hospital readmissions (follow-up 12–96 weeks).

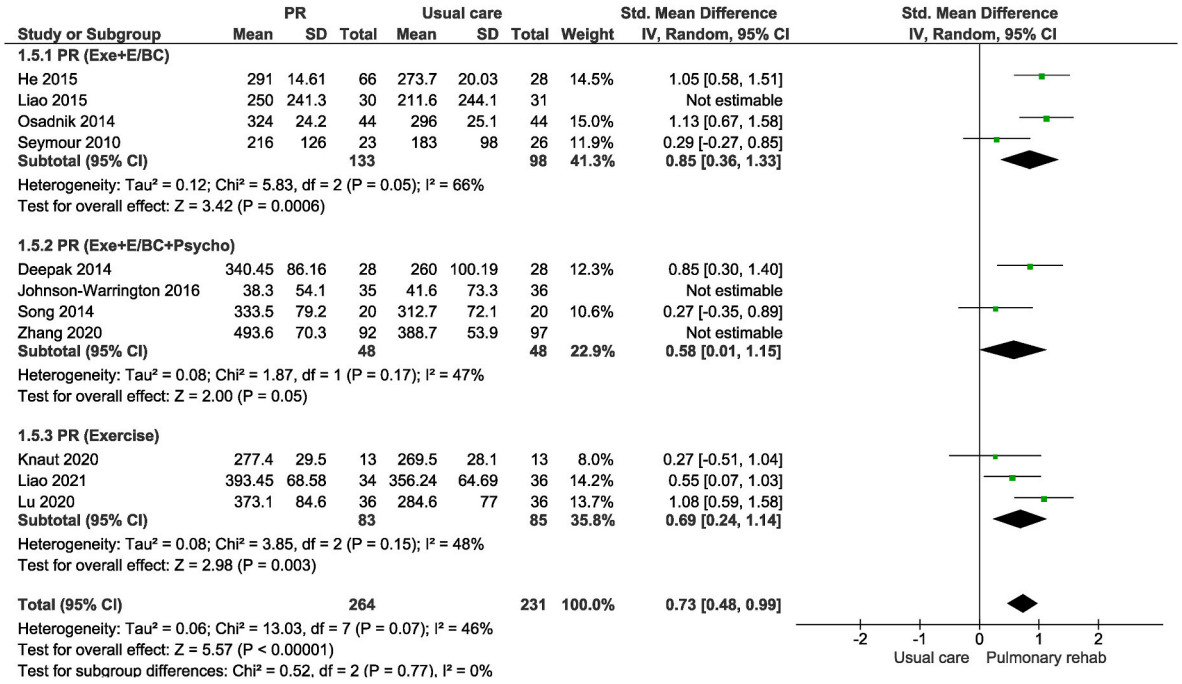

Fig. 5. Sensitivity analysis of the effects of pulmonary rehabilitation compared to usual care on cardiovascular submaximal capacity at end of intervention (median 8 weeks).

In the sensitivity analysis, we removed studies not using the mMRC scale [37,39,40], which reduced heterogeneity to $I^2 = 58\%$ (MD -0.42, 95% CI -0.57 to −0.27: 7 studies, 586 participants) as shown in Fig. 7. Low certainty evidence suggests that when compared to usual care, PR may slightly reduce dyspnoea (Table 2).

Data on long-term effects were provided by three studies [40,41,50]. Results suggest that there is evidence of no effect at 12–24 weeks; pooled effect is not reported due to high heterogeneity ($I^2 = 99\%$). Zhang 2020

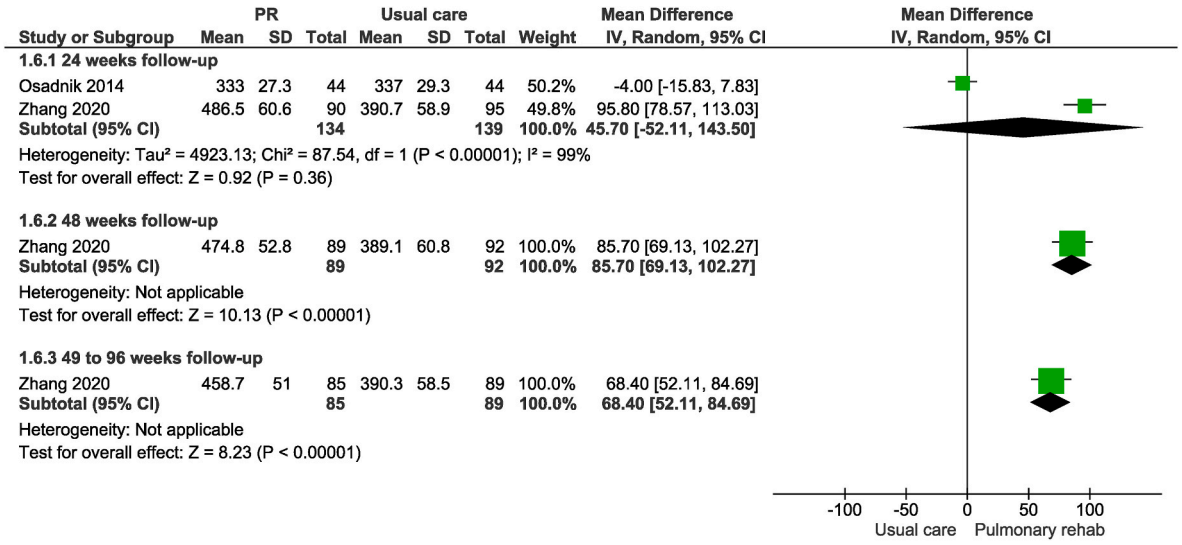

Fig. 6. Effects of pulmonary rehabilitation compared to usual care on cardiovascular submaximal capacity at long-term.

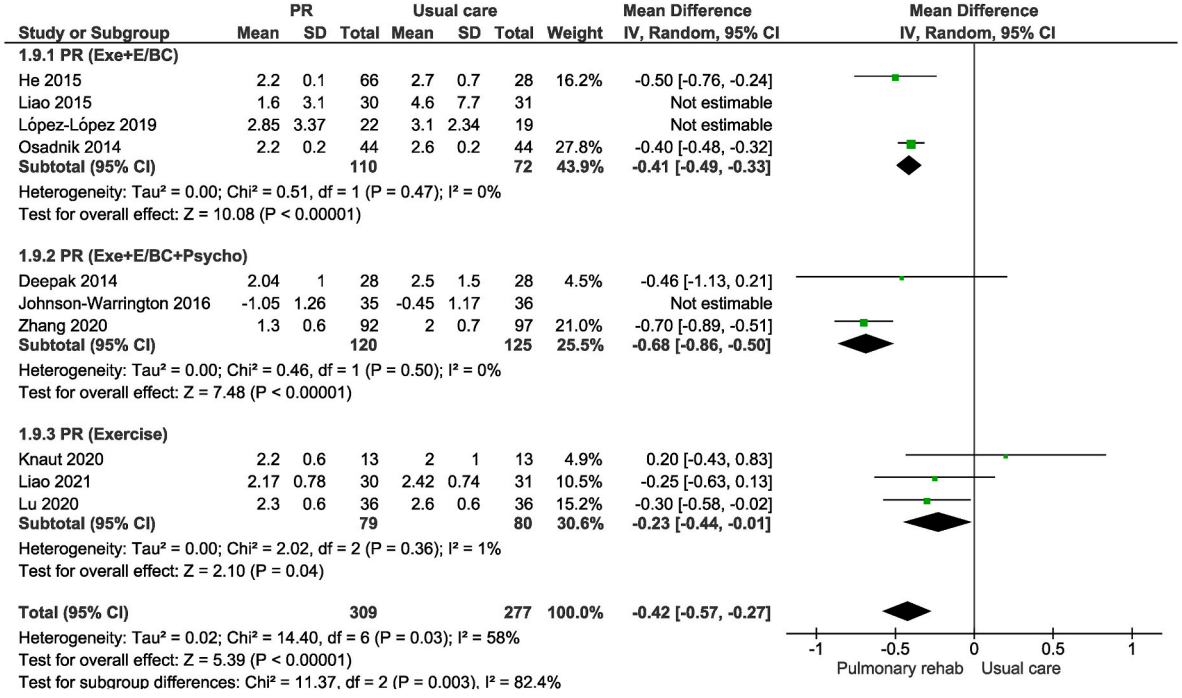

Fig. 7. Sensitivity analysis of the effects of pulmonary rehabilitation compared to usual care on dyspnoea at end of intervention (median 8 weeks).

[50] (n = 181) reported less dyspnoea symptoms in the PR group compared to usual care at 48- and 49-to-96-week follow-up. The evidence of the effect is uncertain due to high heterogeneity and inconsistent findings. Fig. 8 and Appendix 9 provide further details.

In the early PR vs late PR comparison reported by Puhan 2012 [42] (n = 28) dyspnoea was assessed using the self-reported MRC dyspnoea scale. Participants in the early PR group reported less dyspnoea than those in late PR at the end of intervention (6-months) (MD 0.83, 95% CI 0.10 to 1.57). These gains were not sustained at 12- and 18-month follow-up (MD at 18 months 0.27, 95% CI –0.45 to 1.00, 12 months data not shown).

3.1.7.7. Re-exacerbations. Four studies [33,41,43,47] reported the mean number of re-exacerbations, except for Osadnik 2014 [41] which reported the median number of re-exacerbations and interquartile range. The converted mean and SD from Osadnik 2014 [41] were considerably wide. The meta-analysis' results showed that PR was more effective than usual care at 12- to 48-week follow-up in reducing the mean number of re-exacerbations (MD –0.18, 95% CI –0.22 to –0.14; 372 participants; I^2 = 0%) (Fig. 9). Of note, Liao 2021 [47] (n = 70), which used exercise-only PR contributed to 99% of this effect estimate. In addition, narrative findings from Seymour 2010 [43] (n = 60) suggested a lower mean number of re-exacerbations per participant in the PR group than in the usual care group (0.27 vs 1.1, $p < 0.01$) with no SDs nor CIs reported. Overall, low quality evidence suggests that PR may slightly reduce the number of re-exacerbations compared to usual care at 12- to 48-week follow-up (Table 2) (see Fig. 10).

Regarding early PR vs late PR, Puhan 2012 [42] reported no difference between early and late PR in re-exacerbations over the 18-month follow-up (RR 0.96, 95% CI 0.84 to 1.94; n = 28).

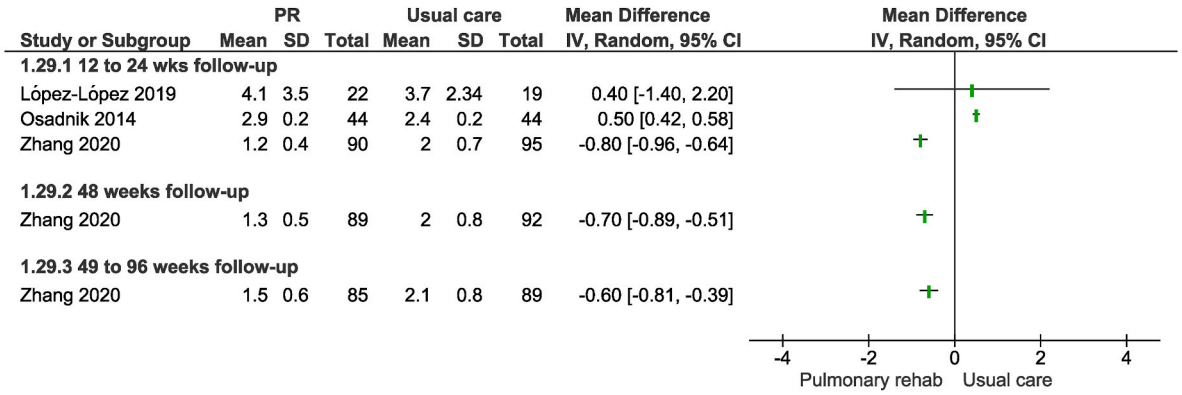

Fig. 8. Long-term effects of pulmonary rehabilitation compared to usual care on dyspnoea.

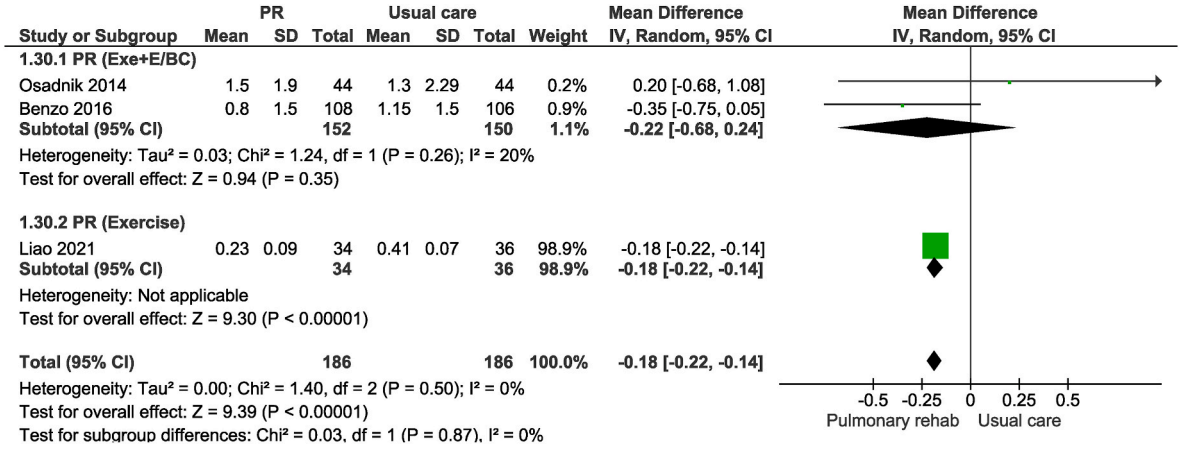

Fig. 9. Effects of pulmonary rehabilitation compared to usual care on re-exacerbations (12–48 weeks).

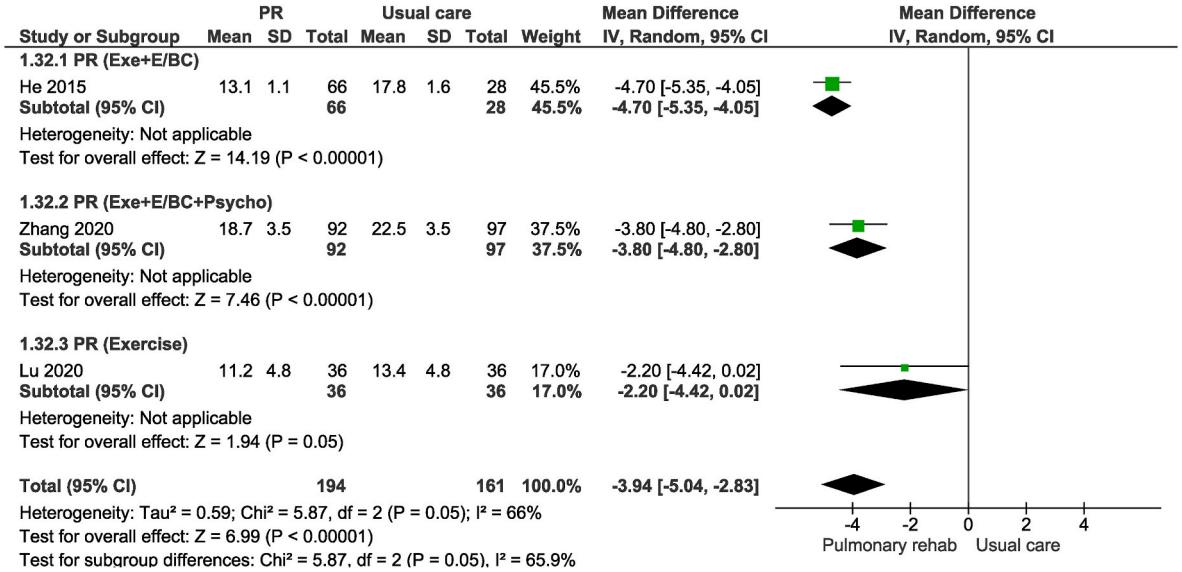

Fig. 10. Effects of pulmonary rehabilitation compared to usual care on impact of disease at end of intervention (median 8 weeks).

3.1.7.8. Impact of disease. The pooled data from three studies showed that PR reduced the impact of AECOPD on participants' daily life by 3.94 points compared to usual care (MD –3.94, 95% CI -5.04 to −2.83; 355 participants) [36,49,50] at the end of intervention. However, the evidence regarding the effect of PR on the overall impact of disease compared to usual care at the end of the intervention period is uncertain (Table 2). Low quality evidence indicates that PR may result in large reductions in the impact of the disease (between four to five points) at follow up periods of 12-, 48- and up to 96-weeks (Fig. 11 and Appendix 9).

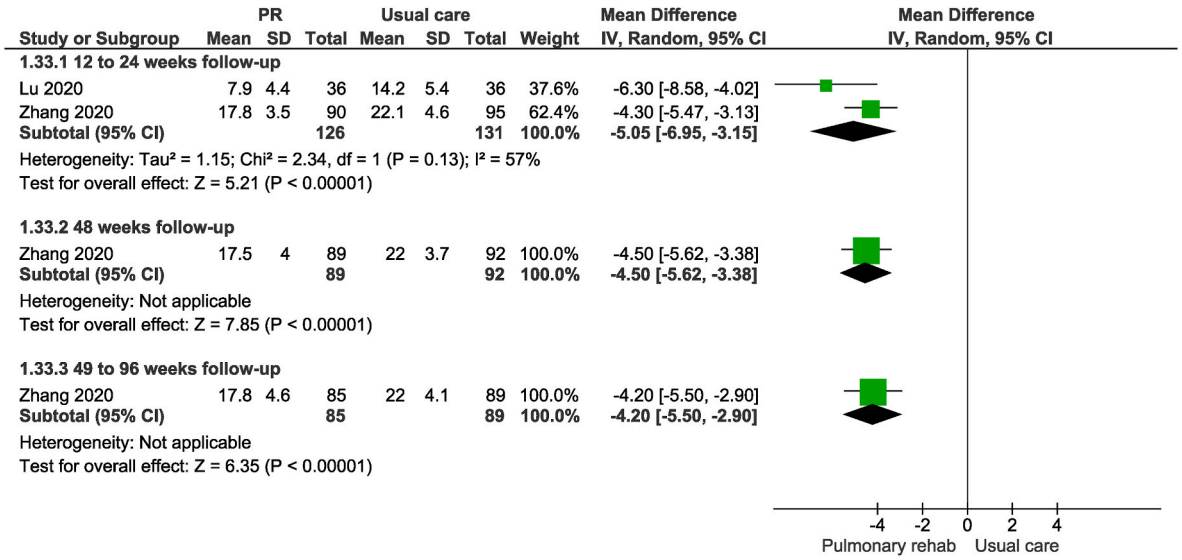

Fig. 11. Effects of pulmonary rehabilitation compared to usual care on impact of disease at long-term (12–96 weeks).

Regarding early PR vs late PR, Kjærgaard 2020 [38] (n = 131) found no between-group differences at either two months (MD −1.4, 95% CI −3.4 to 0.6) or six months follow-up (MD −1.4, 95% CI −3.5 to 0.6).

4. Discussion

4.1. Summary of main results

Evidence from 18 RCTs showed that PR can provide benefits for individuals with AECOPD, especially in terms of reducing hospital readmissions and improving cardiovascular submaximal capacity. However, due to high clinical or statistical heterogeneity in the studies, the effects of PR on HRQoL, dyspnoea, physical activity levels, mortality, re-exacerbations, and impact of disease's outcomes were less conclusive. Our findings suggest that PR may have a greater impact on disease outcomes in the long-term rather than in the short-term. The two studies that evaluated early versus late PR programs provided evidence of no between group differences for most outcomes.

4.2. Overall completeness and applicability

The evidence base on the benefits and harms of PR for individuals with AECOPD is heterogeneous and its applicability to a typical patient in a clinical setting merit careful consideration. Most PR programs reviewed included mixed components and lasted around six weeks; they included chest physiotherapy, supervised exercise, and educational interventions delivered at home or rehabilitation centres. However, the sample sizes were small, and the studies were conducted in different countries with varying PR components and usual care. Additionally, the PR programs reporting was poor, making it difficult to assess adaptations made to the original intervention, progression rules, and adverse events. To improve reporting, trialists should adhere to international reporting guidelines like CERT [24] and CONSORT [56]. Some outcomes, such as physical activity levels and mortality had limited evidence, preventing us from conducting planned subgroup analyses. Standardized outcome measurement tools are needed. Three small ongoing studies were identified (Appendix 3). We anticipate they will not change our conclusions significantly.

4.3. Certainty of the evidence

Our trust in the evidence ranged from very low to moderate. We downgraded the evidence because of several limitations in the risk of bias assessment, such as the lack of allocation concealment and participant/provider blinding, as well as uncertainty around selective reporting. Additionally, the number of trial participants was very low, confidence intervals were wide, and heterogeneity was high.

5. Strengths and limitations

We adhered to the latest methodological standards and used GRADE approach to assess the certainty of evidence. We provided SoF tables and contextualized them around MICD, as suggested by recent guidance from the GRADE working group [31]. In addition, we summarized the intervention reporting completeness and provided subgroup analysis by rehabilitation components. These, we hope, will enhance the review's usability for healthcare providers, guideline developers and decision makers. To the best of our knowledge, this review was partially assisted by artificial intelligence (AI), which is proved to be trustworthy and continuous to gain acceptability among reviewers [57,58].

We limited our eligibility criteria to individuals with AECOPD and a specific definition of PR, which leaves out studies including individuals with stable COPD or maintenance PR programs. Other reviews [6,17,18] have covered these areas. We did not include any telemonitoring/telemedicine type interventions as we are aware of a Cochrane protocol which will have a similar PICO [59]. We then decided to leave telemonitoring/telemedicine intervention to the Cochrane group. The Cochrane protocol population does not include AECOPD but individuals with COPD.

5.1. Agreements and disagreements with other studies or reviews

Our review showed positive effects of PR on cardiovascular submaximal capacity and COPD-related hospital readmissions (moderate certainty evidence), while the evidence on dysponea, HRQoL, and mortality remains uncertain. Previous reviews [16,18,60] have also confirmed the limited evidence for PR's effects on dyspnoea (e.g., high risk of bias and heterogeneous findings across studies). Contrary to our findings of very-low certainty, some reviews [6,10,11,16,18,60] have reported positive effects of PR on HRQoL. We found low certainty evidence for PR effects on impact of disease; this coincides with the evidence of no effect on the CAT test reported by a previous systematic review focusing on inpatient PR programs [11]. Lastly, our review is the first to explore the effects of PR on physical activity levels and therefore we cannot make comparisons with other reviews.

In summary, despite the considerable heterogeneity and

methodological flaws in the current body of evidence, our findings suggest that PR should be considered in the management of AECOPD irrespective of the setting. To advance the field, trialists should adhere to the latest standards of conduct and reporting fostering a more cohesive, precise, and reliable understanding of PR's role for AECOPD.

Additional information

Support

Sources: This review was conducted to inform one recommendation in the Update of the Colombian Guideline for the prevention, diagnosis, and management of Chronic Obstructive Pulmonary Disease in adults [19]. Prospective registration in the Guidelines International Network (GIN) database is available at: https://guidelines.ebmportal.com/guidelines-international-network?search=COPD&type=search.

Sponsor: The systematic review was funded by ASONEUMOCITO (In Spanish, La Asociación Colombiana de Neumología y Cirugía de Toráx).

Role of sponsor or funder: ASONEUMOCITO had no influence on the development of this review. Panel members from the institution participated in the outcome prioritization process. Funders had no role in study design, data collection and analysis, decision to publish, or preparation of this manuscript.

6. Availability of data and other materials

The templates for data collection, the extracted data and the data used for all of the analyses are available from the main author upon reasonable request.

Ethical disclosures

Support

Sources: This review was conducted to inform one recommendation in the Update of the Colombian Guideline for the prevention, diagnosis, and management of Chronic Obstructive Pulmonary Disease in adults [12]. Prospective registration in the Guidelines International Network (GIN) database is available at: https://guidelines.ebmportal.com/guidelines-international-network?search=COPD&type=search.

Sponsor: The systematic review was funded by ASONEUMOCITO (In Spanish, La Asociación Colombiana de Neumología y Cirugía de Toráx).

Role of sponsor or funder: ASONEUMOCITO had no influence on the development of this review. Panel members from the institution participated in the outcome prioritization process. Funders had no role in study design, data collection and analysis, decision to publish, or preparation of this manuscript.

CRediT authorship contribution statement

Jose F. Meneses-Echavez: designed the study with important advice from guideline panel members, Sebastián Castaño Duque and did the literature search, did the study selection, data, extraction, and risk of bias assessment, conducted the final, Formal analysis, with advice from JB, assessed the certainty of the evidence, drafted the manuscript, and all others contributed to the interpretation of results and the final manuscript. **Nathaly Chavez Guapo:** did the study selection, data, extraction, and risk of bias assessment. **Andrés Felipe Loaiza-Betancur:** designed the study with important advice from guideline panel members, did the study selection, data, extraction, and risk of bias assessment. **Ana Machado:** did the study selection, data, extraction, and risk of bias assessment, All authors read and approved the final manuscript for publication. **Julia Bidonde:** designed the study with important advice from guideline panel members, assessed the certainty of the evidence.

Declaration of competing interest

None

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Appendix 1. Eligibility criteria

Population: Adults with an AECOPD, which was defined as episodes of acute worsening of respiratory symptoms that result in additional therapy. Worsening may present as sputum colour changes or an increase in dyspnoea and leading to a change in medication, happening within three weeks from the deterioration (onset) of symptoms or two weeks after discharge [8,61]. We included studies conducted during hospitalization as well as after discharge.

Intervention: Overall, PR may include (but is not limited to) aerobic exercise training or resistance training for upper and lower limbs at least twice a week, executed at 60%–70% of the maximum load determined by one repetition maximum test, and in most cases accompanied by either health education or dietary counselling. We considered for inclusion any form of aerobic or resistance training regardless of frequency, duration, or intensity. Our research protocol presents all definitions according to exercise modes used in this review.

Comparison: No PR, usual care, and any other active intervention (e.g., the comparison between two forms of pulmonary rehabilitation or versus another behavioural change approach).

Outcomes

We mapped out recent guidelines and presented a broad list of outcomes to panel members in January 2022. By following the GRADE approach [62], panel members rated the importance of the outcomes for decision-making on a 9-point scale: 1 to 3 as limited or no importance; 4 to 6 as important, but not critical; and 7 to 9 as critical. This information is available from the first author upon request.

Hospital readmissions, as reported by trialists. We extracted the number or percentage of participants who required hospital readmission, or the hospitalization rate, or both. We registered exacerbation-related admissions. Hospital readmissions are measured with administrative data.

Health-related quality of life (HRQoL). There is not a widely accepted definition of HRQoL for COPD [63]. We used the following definition: "how well a person functions in their life and his or her perceived wellbeing in physical, mental, and social domains of health" [64]. Functioning refers to an individual's ability to carry out some pre-defined activities, while well-being refers to an individual's subjective feelings. HRQoL can be measured via disease-specific questionnaires (e.g., St George's Respiratory Questionnaire, SGRQ or Chronic Respiratory Disease Questionnaire,

CRQ) or generic health questionnaires (e.g., 36-item Short Form, EQ-5D, or Euro-QoL).
Establishing the minimal clinically important difference (MCID) for HRQoL measures is challenging. However, empirical data indicates that a mean change in the SGRQ scores of 4 units is associated with slightly efficacious treatment, 8 units for moderately efficacious change and 12 units for very efficacious treatment [65,66]. In addition, we interpreted an increase of 0.5 points in CRQ as MICD [67].
Cardiovascular submaximal capacity, or VO_2max, defined as the maximum amount of oxygen that a subject can use per unit of time and body weight [68]. This can be measured by field exercise tests (e.g., 6-minute walk distance test, 6MWD, shuttle walk tests) or laboratory exercise tests (e.g., cardiopulmonary exercise test). Thirty meters were interpreted as a MICD for the 6MWD in people with an AECOPD [69].
Physical activity levels (PAL), is defined as the total energy used over 24 hours divided by basal metabolic rate over (in the same) 24 hours [70]. PAL can be measured via monitor movement (e.g., accelerometer or pedometer), number of steps/days, or study specific questionnaire/survey (e.g., Global Physical Activity Questionnaire – GPAQ or International Physical Activity Questionnaire – IPAQ). We found no MCID for this outcome.
Mortality, reported as number and/or percentage of patients that died following an AECOPD.
Dyspnoea, as defined by the American Thoracic Society as "a subjective experience of breathing discomfort that consists of qualitatively distinct sensations that vary in intensity this experience derives from interactions among multiple physiological, psychological, social, and environmental factors, and may induce secondary physiological and behavioural responses" [71]. Dyspnoea can be measured by validated instruments (e.g., modified Medical Research Council dyspnoea questionnaire (mMRC), modified Borg scale, or the New York Heart Association functional grade). A reduction of 0.5 points of the mMRC is considered as a MCID [72].
Re-exacerbations, measured as the number or % of participants that re-exacerbate or the time to first moderate or severe exacerbation.
Impact of disease, defined as the impact of COPD symptoms on participants' daily life, and how this evolves over time [73]. This outcome is traditionally measured by validated patient-reported instruments assessing the impact of COPD on health status, such as the COPD Assessment Test (CAT) [73]. The CAT is used to assess disease progression, decline in functional status, and gauge effectiveness of PR programs. CAT scores (scores 0 to 5, higher scores indicate higher impact) have been shown to correlate with mortality [74] as well as patient-reported symptom improvement [75]. The difference of two points is considered clinically important [72].

We set no restrictions on setting/country where the primary studies are conducted.

Appendix 2. Search strategy (English-Spanish)

Característica	Reporte	
Tipo de búsqueda	Actualización	
Base de datos	MEDLINE	
Plataforma	PubMed	
Fecha de búsqueda	04-03-2022	
Rango de fecha de búsqueda	01-01-2020 hasta 04-03-2022	
Restricciones de lenguaje	Ninguna	
Otros límites	RCT	
Estrategia de búsqueda	1. "Lung Diseases, Obstructive" [Mesh]	226,063
	2. "Pulmonary Disease, Chronic Obstructive" [Mesh]	62,305
	3. Emphysema*	38,186
	4. (chronic* n3 bronchiti*)	37
	5. (obstruct* n3 (pulmonary or lung* or airway* or airflow* or bronch* or respirat*))	840
	6. (COPD or AECOPD or AECB)	98,517
	7. (acute n5 exacerbat* n5 COPD)	11
	8. (acute n5 exacerbati* n5 chronic n5 obstruct* n5 pulmonary n5 disease*)	12
	9. #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8	270,442
	10. "Physical Therapy Modalities" [Mesh]	168,962
	11. "Physical Fitness" [Mesh]	34,413
	12. "Physical Endurance" [Mesh]	36,115
	13. "Exercise Therapy" [Mesh]	58,599
	14. "Physical Exertion" [Mesh]	57,211
	15. "Exercise Test" [Mesh]	68,996
	16. "Exercise" [Mesh]	226,928
	17. ((pulmonary [Title/Abstract] OR respiratory [Title/Abstract]) n3 rehabilitation*)	73
	18. ((pulmonary [Title/Abstract] OR respiratory [Title/Abstract]) n3 therap*)	1822
	19. Exercis*[Title/Abstract]	335,092
	20. (physical* n3 (activit*[Title/Abstract] OR train*[Title/Abstract] OR fitness*[Title/Abstract] OR therap*[Title/Abstract]))	1762
	21. Interval train*[Title/Abstract]	3696
	22. "Breathing Exercises" [Mesh]	4009
	23. ((resistance [Title/Abstract] OR aerobic*[Title/Abstract] OR balance [Title/Abstract] OR flexibility [Title/Abstract] OR strength [Title/Abstract] OR stretch [Title/Abstract]) n3 train*)	260
	24. #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23	630,953
	25. #9 AND #24	16,663
	26. ((randomized controlled trial [pt]) OR (controlled clinical trial [pt]) OR (randomized [tiab] OR randomized [tiab]) OR (placebo [tiab]) OR (drug therapy [sh]) OR (randomly [tiab]) OR (trial [tiab]) OR (groups [tiab])) NOT (animals [mh] NOT humans [mh])	4,682,504
	27. #25 AND #26	6593
	28. ("2020/01/01" [Date - Publication]: "3000" [Date - Publication])	3,421,236
	29. #27 AND #28	686

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Característica	Reporte
Referencias identificadas	686

Característica	Reporte
Tipo de búsqueda	Actualización
Base de datos	SCOPUS
Plataforma	SCOPUS
Fecha de búsqueda	05-03-2022
Rango de fecha de búsqueda	2020 al 2022
Restricciones de lenguaje	Ninguna
Otros límites	Ninguna
Estrategia de búsqueda	ALL (((“acute exacerbation of chronic obstructive pulmonary disease” OR “AECOPD” OR “acute exacerbation of COPD” OR “exacerbation of COPD”) AND (“inpatient” OR “outpatient” OR “community” OR “community-base” OR “primary care” OR “home” OR “domiciliary”) AND (“pulmonary rehabilitation” OR “respiratory rehabilitation” OR “physiotherapy” OR “physical therapy” OR “respiratory physiotherapy” OR “respiratory physical therapy” OR “exercise” OR “exercise training” OR “breathing exercise” OR “breathing technique” OR “airway clearance” OR “walking” OR “aerobic training” OR “resistance training” OR “balance training” OR “flexibility training” OR “stretch training” OR “strength training” OR “education” OR “psychoeducation” OR “psychosocial support”)))
Referencias identificadas	1728

Característica	Reporte
Tipo de búsqueda	Actualización
Base de datos	Web of Science
Plataforma	Web of Science
Fecha de búsqueda	05-03-2022
Rango de fecha de búsqueda	2020 al 2022
Restricciones de lenguaje	Ninguna
Otros límites	Ninguna
Estrategia de búsqueda	((TS= (“acute exacerbation of chronic obstructive pulmonary disease” OR “AECOPD” OR “acute exacerbation of COPD” OR “exacerbation of COPD")) AND (TS=(“inpatient” OR “outpatient” OR “community” OR “community-base” OR “primary care” OR “home” OR “domiciliary”)) AND (TS=(“pulmonary rehabilitation” OR “respiratory rehabilitation” OR “physiotherapy” OR “physical therapy” OR “respiratory physiotherapy” OR “respiratory physical therapy” OR “exercise” OR “exercise training” OR “breathing exercise” OR “breathing technique” OR “airway clearance” OR “walking” OR “aerobic training” OR “resistance training” OR “balance training” OR “flexibility training” OR “stretch training” OR “strength training” OR “education” OR “psychoeducation” OR “psychosocial support”)))
Referencias identificadas	25

Característica	Reporte
Tipo de búsqueda	Actualización
Base de datos	CINAHL
Plataforma	EBSCO
Fecha de búsqueda	05-03-2022
Rango de fecha de búsqueda	January 01, 2020 al March 31, 2022
Restricciones de lenguaje	Ninguna
Otros límites	Ninguna
Estrategia de búsqueda	(“acute exacerbation of chronic obstructive pulmonary disease” OR “AECOPD” OR “acute exacerbation of COPD” OR “exacerbation of COPD”) AND (“pulmonary rehabilitation” OR “respiratory rehabilitation” OR “physiotherapy” OR “physical therapy” OR “respiratory physiotherapy” OR “respiratory physical therapy” OR “exercise” OR “exercise training” OR “breathing exercise” OR “breathing technique” OR “airway clearance” OR “walking” OR “aerobic training” OR “resistance training” OR “balance training” OR “flexibility training” OR “stretch training” OR “strength training” OR “education” OR “psychoeducation” OR “psychosocial support”)
Referencias identificadas	24

Característica	Reporte
Tipo de búsqueda	Actualización
Base de datos	CENTRAL
Plataforma	OVID
Fecha de búsqueda	05-03-2022
Rango de fecha de búsqueda	2020 al 2022
Restricciones de lenguaje	Ninguna
Otros límites	RCT
Estrategia de búsqueda	1. Lung Diseases, Obstructive/(3094) 2. Exp Pulmonary Disease, Chronic Obstructive/(6146) 3. Emphysema$.tw. (1416) 4. (chronic$ adj3 bronchiti$).tw. (1911) 5. (obstruct$ adj3 (pulmonary or lung$ or airway$ or airflow$ or bronch$ or respirat$)).tw. (17,582) 6. (COPD or AECOPD or AECB).tw. (18,260) 7. (acute adj5 exacerbati$ adj5 chronic adj5 obstruct$ adj5 pulmonary adj5 disease$).tw. (836)

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Característica	Reporte
	8. (acute adj5 exacerbat$ adj5 COPD).tw. (1167) 9. Or/1–8 (28,269) 10. Physical Therapy Modalities/(4028) 11. Exp Physical Fitness/(3010) 12. Exp Physical endurance/(6327) 13. Exp Exercise Therapy/(15,499) 14. Physical Exertion/(3969) 15. Exp Exercise Test/(8684) 16. Exp Exercise/(27,003) 17. ((pulmonary or respiratory) adj3 rehabilitation$).ti,ab. (2471) 18. ((pulmonary or respiratory) adj3 therap$).ti,ab. (2958) 19. Exercis$.ti,ab. (103,672) 20. (physical$ adj3 (activit$ or train$ or fitness$ or therap$)).ti,ab. (48,369) 21. Interval train$.ti,ab. (2690) 22. Exp Breathing Exercises/(950) 23. ((resistance or aerobic$ or balance or flexibility or strength or stretch) adj3 train$).ti,ab. (18,464) 24. Or/10–23 (150,576) 25. 9 and 24 (6308) 26. (controlled clinical trial or randomized controlled trial).pt. (634,024) 27. (randomized or randomized).ab,ti. (901,412) 28. Placebo.ab,ti. (333,127) 29. Randomly.ab,ti. (287,797) 30. Trial.ab,ti. (686,036) 31. Groups.ab,ti. (534,954) 32. Or/26–31 (1,464,108) 33. Animals/(10,884) 34. Humans/(635,447) 35. 33 not (33 and 34) (3) 36. 32 not 35 (1,464,107) 37. 25 and 36 (4840) 38. Limit 37 to yr = 2020–2022 (526)
Referencias identificadas	526

Appendix 3. Ongoing studies

ChiCTR2000030129 (2020)

Trial name or title	Clinical therapeutic effect of high flow oxygen inhalation (HFNC) combined with respiratory rehabilitation on patients with acute attack of COPD: a multicenter prospective randomized controlled clinical study
Objective	To observe the overall effect of high flow oxygen inhalation (HFNC) combined with respiratory rehabilitation on patients with COPD, including clinical symptoms, exercise ability, quality of life and psychological state.
Methods	Design: parallel randomized controlled trial (four groups)
Participants	Inclusion: Patients with acute exacerbation of COPD are also diagnosed according to the guideline, classification, and stage; aged 40–80 years; received standard bronchodilator drugs; non-participation in other lung rehabilitation studies or other influential studies. Exclusion: Patients with chronic cough caused by tuberculosis, fungus, tumour, irritant gas, allergy, etc; patients with other respiratory diseases that can cause asthma or dyspnoea; pregnant or lactating women, allergic to this drug; patients with severe primary diseases such as cardiovascular, liver, kidney and hematopoietic system, diabetes and mental illness; those with severe centre of gravity dysfunction; patients receiving medication for other diseases; patients with observational factors affecting curative effect; failure to follow prescribed medication, inability to determine efficacy or incomplete information, etc. Those who influence efficacy or safety judgment.
Interventions	Group 1: HFNC (n = 50) Group 2: HFNC and pulmonary rehabilitation (n = 50) Group 3: Pulmonary rehabilitation (n = 50) Group 4: Conventional therapy (n = 50)
Outcomes	Pulmonary function The COPD Assessment Test (CAT) The Modified Medical Research Council (mMRC) Dyspnoea Scale The Saint George's Respiratory Questionnaire (SGRQ) Six Minute Walk Test (6 MWT) The Symptom Assessment Scale (SAS) The Symptom Distress Scale (SDS) Clinical symptoms
Starting date	Start date: 2020-04-01 Completion date: not reported
Contact information	Correspondence: Li Shanqun Tel: +86 19121803647 E-mail: lsq18616880856@163.com Zhongshan Hospital Affiliated Fudan University Shanghai, China
Notes	Status: Not yet recruiting ChiCTR2000030129: http://www.chictr.org.cn/showprojen.aspx?proj=49766

ChiCTR2000040246 (2020)

Trial name or title	Long term effect of early pulmonary rehabilitation on elderly patients with acute exacerbation of Chronic obstructive pulmonary disease: a randomized controlled study
Objective	To observe the long-term effect of pulmonary rehabilitation combined with Chinese and Western medicine in the early stage of acute exacerbation of chronic obstructive pulmonary disease (AECOPD) in the elderly
Methods	Design: parallel randomized controlled trial (two groups)
Participants	Inclusion: Aged ≥ 65 years old; according to the diagnostic criteria of AECOPD (2018 gold guidelines), and FEV1 < 80%; diagnostic criteria of COPD: chronic cough, expectoration, dyspnoea, smoking history ≥ 10 pack years, FEV1/FVC <0.70 after using bronchodilator; acute exacerbation: cough, expectoration (increased sputum volume or purulent sputum) and dyspnoea. Exclusion: There were serious or unstable complications (acute heart failure, acute renal failure, malignant tumour); patients who cannot perform pulmonary rehabilitation (such as unconsciousness, long-term bed rest, recent acute cerebrovascular disease, etc.); unable to provide relevant information; patients who do not sign informed consent
Interventions	Group 1: Pulmonary rehabilitation (n = 46) Group 2: Routine treatment (n = 46)
Outcomes	Rehospitalization for AECOPD within three months
Starting date	Start date: 2020-07-01 Completion date: not reported
Contact information	Correspondence: Lu Wang Tel: +86 15801630624 E-mail: luwnag8503@163.com Beijing Geriatric Hospital Beijing, China
Notes	Status: Not yet recruiting ChiCTR2000040246 https://studiesearch.who.int/Trial2.aspx?TrialID=ChiCTR2000040246

Cox (2021)

Trial name or title	Home-based pulmonary rehabilitation early after hospitalization in COPD (early HomeBase): protocol for a randomized controlled trial
Objective	To compare hospital readmission rates, clinical outcomes and costs between people with COPD who undertake a home-based programme of pulmonary rehabilitation commenced early (within two weeks) of hospital discharge with usual care.
Methods	Design: parallel, multisite, randomized controlled trial (two groups)
Participants	Inclusion: Diagnosis of COPD; admitted to hospital for an exacerbation of COPD; age ≥40 years; able to read and speak English. Exclusion: Life expectancy <6 months; comorbidities that preclude exercise training (may include, but are not limited to, neurological or musculoskeletal impairment; acute unstable cardiac disease).
Interventions	Group 1: Home-based pulmonary rehabilitation commenced early after hospitalization (early HomeBase) (n = 66) Group 2: Usual care and a weekly phone call for attention control (n = 66)
Outcomes	Readmission to hospital (Primary outcome) Secondary outcomes Exercise capacity (1-min sit-to-stand, 1STS) Self-efficacy (Pulmonary Rehabilitation Adapted Index of Self Efficacy, PRAISE) Dyspnoea: The Modified Medical Research Council (mMRC) Dyspnoea Scale Anxiety/Depression (Hospital Anxiety and Depression Scale, HADS) Health-related QoL (Chronic Respiratory Disease Questionnaire, CRDQ and EQ-5D-5L) Physical activity (Accelerometry)
Starting date	Start date: January 2020 Completion date: December 2023
Contact information	Correspondence: Narelle S Cox Tel: +61 3 9903 0134 E-mail: Narelle.Cox@monash.edu Monash University, Level 6, The Alfred Centre 99 Commercial Road Melbourne, Australia
Notes	Status: Recruiting The trial was registered prospectively at www.anzctr.org.au (ACTRN 12619001122145) on August 12, 2019, including details of trial sites. Publication: https://bmjopenrespres.bmj.com/content/8/1/e001107

Appendix 4. Studies excluded at full-text screening

Wrong publication date and companions (n = 3)	
Buscemi (2020)	Efficacy of osteopathic treatment in patients with stable moderate-to-severe chronic obstructive pulmonary disease: A randomized controlled pilot study
Lopez-Lopez (2020)	Results on health-related quality of life and functionality of a patient-centred self-management program in hospitalized COPD: a randomized control trial
Lopez-Lopez (2021)	Randomized feasibility study of twice a day functional electrostimulation in patients with severe chronic obstructive pulmonary disease hospitalized for acute exacerbation
Wrong patient population (n = 38)	
Barker (2020)	The Effects of a Video Intervention on Posthospitalization Pulmonary Rehabilitation Uptake. A Randomized Controlled Trial
Bonnevie (2020)	Mid-term effects of pulmonary rehabilitation on cognitive function in people with severe chronic obstructive pulmonary disease
Butler (2020)	Randomized controlled trial of community-based, post-rehabilitation exercise in COPD
Candemir (2021)	Maintenance of pulmonary rehabilitation benefits in patients with COPD: is a structured 5-year follow-up program helpful?
ChiCTR2100052230 (2021)	Effect of exercise training on moderate and severe COPD: a randomized controlled clinical trial
Daynes (2021)	Randomized controlled trial to investigate the use of high-frequency airway oscillations as training to improve dyspnoea (TIDe) in COPD.
Galdiz (2021)	Telerehabilitation Programme as a Maintenance Strategy for COPD Patients: A 12-Month Randomized Clinical Trial

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Haukeland-Parker (2021)	Pulmonary rehabilitation to improve physical capacity, dyspnoea, and quality of life following pulmonary embolism (the PeRehab study): study protocol for a two-centre randomized controlled trial
Huang (2021)	Effect of internet-based self-management on pulmonary function rehabilitation and living quality in patients with chronic obstructive pulmonary disease
Kohlbrenner (2021)	A few more steps lead to improvements in endothelial function in severe and very severe COPD
Kaasgaard (2020)	Sing-a-Limg: group singing as training modality in pulmonary rehabilitation for patients with Chronic Obstructive Pulmonary Disease (COPD): a multicentre, cluster-randomized, non-inferiority-controlled trial
Lee (2022)	The effect of lung-conduction exercise in chronic obstructive pulmonary disease Randomized, assessor-blind, multicentre pilot trial
Macdonald (2022)	Chronotropic index during 6-min walk and acute respiratory events in COPDGene
Marques (2020)	A randomized controlled trial of respiratory physiotherapy in lower respiratory tract infections
NCT04711057 (2021)	CENTR (AR): lungs Moving
Provencher (2020)	Supporting at-risk older adults transitioning from hospital to home: Who benefits from an evidence-based patient-centred discharge planning intervention? Post-hoc analysis from a randomized trial
Rehman (2020)	Effect of passive stretching of respiratory muscles on chest expansion and 6-min walk distance in COPD patients
Rodríguez-Blanco (2021)	Breathing exercises versus strength exercises through telerehabilitation in coronavirus disease 2019 patients in the acute phase: A randomized controlled trial
Sandelowsky (2020)	Patient outcomes following GPs' educations about COPD: a cluster randomized controlled trial
Selzler (2021)	Evaluation of an enhanced pulmonary rehabilitation program: A randomized controlled trial
Shah (2020)	The impact of a structured multi-disciplinary early mobilization program on clinical outcomes in hospitalized patients with pneumonia and acute exacerbations of chronic obstructive pulmonary disease
Shahpasand (2021)	The effect of local heat therapy on fatigue among patients with chronic obstructive pulmonary disease: A randomized controlled clinical trial
Spielmanns (2020)	Impact of a smartphone application (KAIA COPD app) in combination with Activity Monitoring as a maintenance prOgram following PUlmonary Rehabilitation in COPD: The protocol for the AMOPUR Study, an international, multicenter, parallel group, randomized, controlled study
To (2020)	An information-motivation-behavioural-based model and adherence to inhalation therapy and other health outcomes in patients with chronic obstructive pulmonary disease: A pilot randomized controlled trial
Tomruk (2020)	Effects of thoracic kinesio taping on pulmonary functions, respiratory muscle strength and functional capacity in patients with chronic obstructive pulmonary disease: A randomized controlled trial
Tülüce (2021)	The Effect of Education and Motivational Interviewing on COPD Management and Outcome Parameters in COPD Patients.
Vitacca (2021)	Patients recovering from exacerbations of COPD with and without hospitalization need: could ICF score be an additional pulmonary rehabilitation outcome?
Wageck (2020)	The impact of COPD exacerbations in the year following pulmonary rehabilitation: Secondary analysis of a randomized controlled trial
Wen (2020)	Effect of a rehabilitation garden on rehabilitation efficacy in elderly patients with chronic obstructive pulmonary disease
Willard-Grace (2020)	Lay health coaching to increase appropriate inhaler use in COPD: A randomized controlled trial
Wong (2021)	Cost-effectiveness of a preventive self-care health management program for community-dwelling older adults: A randomized controlled trial
Yeh (2020)	BEAM study (Breathing, Education, Awareness, Movement): a randomized controlled feasibility trial of tai chi exercise in patients with COPD
Yohannes (2021)	Long-Term Benefits of Pulmonary Rehabilitation in Patients With COPD: A 2-Year Follow-Up Study
Yu (2020)	The research of Tuna Huichun Gong on pulmonary function, exercise tolerance, and quality of life in patients with chronic obstructive pulmonary disease based on the concept of early pulmonary rehabilitation
Zhang (2020)	Clinical efficiency of acupoint embedding on chronic obstructive pulmonary disease complicated with anxiety/depression: A randomized controlled study
Zhang (2020)	[Clinical effect of nutritional and psychological intervention combined with pulmonary rehabilitation exercise on patients with chronic obstructive pulmonary disease].
Zhu (2021)	An analysis of the dynamic changes in the self-efficacy and quality of life of elderly patients with chronic obstructive pulmonary disease following community-based rehabilitation
Wrong intervention (n = 7)	
Bitos (2021)	Effect of High-Flow Oxygen on Exercise Performance in COPD Patients. Randomized Trial
Granados-Santiago (2020)	Shared decision-making and patient engagement program during acute exacerbation of COPD hospitalization: A randomized control trial.
Hill (2020)	Effect of Using a Wheeled Walker on Physical Activity and Sedentary Time in People with Chronic Obstructive Pulmonary Disease: A Randomized Cross-Over Trial
Ko (2021)	Effect of short-course exercise training on the frequency of exacerbations and physical activity in patients with COPD: A randomized controlled trial
Ko (2021)	Effect of Short-Course Exercise Training on the Frequency of Exacerbations and Physical Activity in Patients With COPD: a Randomized Controlled Trial
Kütmeç (2021)	The effect of back massage on physiological parameters, dyspnoea, and anxiety in patients with chronic obstructive pulmonary disease in the intensive care unit: A randomized clinical trial
Rassouli (2021)	Telehealth mitigates COPD disease progression compared to standard of care: a randomized controlled crossover trial
Wrong study design (n = 47)	
Al Chikhanie (2021)	Trajectories of COPD patients' response to repeated pulmonary rehabilitation programs: Response to repeated COPD rehabilitation
Amin (2021)	Managing hospitalized patients with a COPD exacerbation: the role of hospitalists and the multidisciplinary team
Andrianopoulos (2021)	Benefits of pulmonary rehabilitation in COPD patients with mild cognitive impairment – A pilot study
Bamonti (2021)	Predictors of Outpatient Pulmonary Rehabilitation Uptake, Adherence, Completion, and Treatment Response Among Male U.S. Veterans with Chronic Obstructive Pulmonary Disease
Barker (2021)	Integrating home-based exercise training with a hospital at home service for patients hospitalized with acute exacerbations of COPD: Developing the model using accelerated experience-based Co-design
Beauchamp (2021)	Feasibility of a 6-Month Home-Based Fall Prevention Exercise Program in Older Adults with COPD.
Blackstock (2021)	Using telemedicine to provide education for the symptomatic patient with chronic respiratory disease
Bonnevie (2020)	Mid-term effects of pulmonary rehabilitation on cognitive function in people with severe chronic obstructive pulmonary disease
Borg (2021)	Free diving-inspired breathing techniques for COPD patients: A pilot study
Campos-Juanatey (2020)	Assessment of the impact of pulmonary rehabilitation on sexual activity in patients with chronic obstructive pulmonary disease
Candemir (2021)	Maintenance of pulmonary rehabilitation benefits in patients with COPD: is a structured 5-year follow-up program helpful?
Criner (2022)	Feasibility of Using Daily Home High-Flow Nasal Therapy in COPD Patients Following a Recent COPD Hospitalization
Deng (2021)	A home-based pulmonary rehabilitation mHealth system to enhance the exercise capacity of patients with COPD: development and evaluation
France (2021)	Cognitive function following pulmonary rehabilitation and post-discharge recovery from exacerbation in people with COPD
Giusti (2022)	The Effects of an Acceptance and Commitment-Informed Interdisciplinary Rehabilitation Program for Chronic Airway Diseases on Health Status and Psychological Symptoms
Grosbois (2022)	Physical and affective components of dyspnoea are improved by pulmonary rehabilitation in COPD
Herkert (2021)	Home-based exercise program for patients with combined advanced chronic cardiac and pulmonary diseases: Exploratory study
Hurley (2020)	A feasibility pragmatic clinical trial of a primary care network exercise and education program for people with COPD
Ilić (2020)	The influence of pulmonary rehabilitation on the exacerbations of chronic obstructive pulmonary disease in Serbia
JIN (2020)	Study progress on safety of exercise intervention in patients at acute exacerbation of chronic obstructive pulmonary disease.

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Júnior (2020)	Influence of pulmonary rehabilitation in patients with COPD exacerbator phenotype
Keerthiga (2020)	Comparison of sitting calisthenics vs respiratory muscle stretch gymnastics to desensitize dyspnoea in moderate COPD patients
Kelly (2021)	Cognitive behavioural approaches for managing dyspnoea in people with chronic obstructive pulmonary disease (COPD)
Kowalczyk (2021)	A checklist-based method for improving COPD care for the elderly in general practice: study protocol for a cluster randomized controlled trial using electronic health records
Kurpatov (2020)	Assessment of the respiratory muscle's strength at patients with chronic obstructive pulmonary disease with various forms of comorbidity
Lee (2020)	Efficacy of unsupervised home-based pulmonary rehabilitation for patients with chronic obstructive pulmonary disease
Li (2020)	Nonadherence in home-based pulmonary rehabilitation program for COPD patients
Lindenauer (2020)	Association between Initiation of Pulmonary Rehabilitation after Hospitalization for COPD and 1-Year Survival among Medicare Beneficiaries
Macdonald (2022)	Chronotropic index during 6-min walk and acute respiratory events in COPD Gene
Machado (2020)	Effects of a community-based pulmonary rehabilitation programme during acute exacerbations of chronic obstructive pulmonary disease – A quasi-experimental pilot study
Machado (2021)	Extra-pulmonary manifestations of COPD and the role of pulmonary rehabilitation: a symptom-centred approach
McNaughton (2020)	Taking charge: A proposed psychological intervention to improve pulmonary rehabilitation outcomes for people with COPD
Meys (2020)	Impact of mild-to-moderate exacerbations on outcomes of neuromuscular electrical stimulation (NMES) in patients with COPD
Myers (2021)	Pulmonary rehabilitation and readmission rates for medicare beneficiaries with acute exacerbation of chronic obstructive pulmonary disease
Nici (2021)	Pulmonary rehabilitation after a chronic obstructive pulmonary disease exacerbation: Impact on readmission risk in a real-world setting
Park (2021)	Effects of a cognitive rehabilitation programme on cognitive function, self-management and quality of life in patients with chronic obstructive pulmonary disease
Polastri (2020)	Physiotherapeutic regimen in patients with chronic obstructive pulmonary disease: From the intensive care unit to home-based rehabilitation
Prasungriyo (2021)	Effect of pharmacy counselling on readmissions in patients with acute exacerbations of COPD: A randomized controlled trial
Ramon (2020)	Efficacy of a physical activity coaching programme after hospitalization for a COPD exacerbation
Reis (2021)	long-term pulmonary rehabilitation progressively reduces hospitalizations and mortality in patients with severe COPD: a 5-year follow-up
Rutkowski (2021)	Monitoring physical activity with a wearable sensor in patients with COPD during in-hospital pulmonary rehabilitation program: A pilot study
Shimoda (2021)	In-hospital pulmonary rehabilitation after completion of primary respiratory disease treatment improves physical activity and ADL performance: A prospective intervention study
Souto-miranda (2022)	Functional Status Following Pulmonary Rehabilitation: Responders and Non-Responders
Tsutsui (2021)	Pulmonary rehabilitation in a post-covid-19 world: Telerehabilitation as a new standard in patients with COPD
Vitacca (2021)	Patients recovering from exacerbations of COPD with and without hospitalization need: could ICF score be an additional pulmonary rehabilitation outcome?
Yuanhao (2021)	Application of the bedside sitting respiratory training in patients with acute exacerbation of chronic obstructive pulmonary disease complicated with respiratory failure
Zhang (2022)	Effect of pulmonary rehabilitation in patients with chronic obstructive pulmonary disease: a systematic review and meta-analysis of randomized controlled studies
Full text not available	
Arvind (2022)	Home-Based Pulmonary Rehabilitation of COPD Individuals Using the Wearable Respeck Monitor
Frei (2021)	Effectiveness of a long-term home-based exercise training program using minimal equipment vs. usual care in COPD patients: the HOMEX-1 RCT
Hajizadeh (2020)	Referral to telehealth delivered pulmonary rehabilitation (TelePR) versus standard pulmonary rehabilitation (SPR) in Hispanic and African patients hospitalized for COPD Exacerbations: results of a randomized controlled trial
Medina-Mirapeix (2022)	Prognostic value of the five-repetition sit-to-stand test for mortality in people with chronic obstructive pulmonary disease
Tian (2021)	Home-Based Integrated Telemedical Intervention System for Management of Chronic Obstructive Pulmonary Disease in Guangdong, China: development and Cluster Randomized Controlled Study

Appendix 5. Characteristics of the included studies

Benzo 2016	
Study characteristics	
Methods	**Study design:** RCT, parallel Country: United States of America **Duration:** 10 weeks
Participants	215 participants PR n = 106, control n = 108 (withdraw after randomization 1) Female: PR 57%, control 52% Age (mean, SD): PR 67.9 (9.8), control 68.1 (9.2) FEV% mean: PR 40.5, control 40.3 **Other characteristics:** Hospitalization in the past 12 months: PR 57%, control 60% **Inclusion criteria:** patients admitted for a COPD exacerbation, older than 40 years, current or past cigarette smoking history of more than 10 pack-years, ability to speak English, and access to a telephone **Exclusion criteria:** any medical conditions that would impair their ability to participate in the study or to provide informed consent or if they were receiving hospice care
Interventions	**PR components:** exercise + education/behaviour change **Exercise mode:** aerobic, resistance training (strengthening) Timing: at hospital discharge Frequency: NR Intensity: NR Duration: NR Length: NR Supervision: mixed/partially Adherence: 85% Provider: nurse or respiratory therapist Setting: hospital and home

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Benzo 2016		
Study characteristics		
Control	**Usual care:** participants received therapeutic care in accordance with the Global Initiative for Chronic Obstructive Lung Disease (GOLD) and were also referred for conventional pulmonary rehabilitation	
Outcomes	**Hospital readmissions:** 1, 3, 6, 9, and 12 months **HRQoL:** CRQ, physical (dyspnoea and fatigue) and emotional domains 6 and 12 months **Physical activity levels:** 6 and 12 months **Mortality:** 12 months **Re-exacerbations:** 12 months	
Attrition	Reasons for not completing the intervention were: death during the study period (n = 3), unable to contact (n = 6) and refusal to complete the scheduled calls (n = 7)	
Notes	**Funding:** NHLBI grant R01 HL09468 from the national institutes of health **Another identifier:** NCT01058486	
Risk of bias		
Bias	**Author's judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low	Randomization was achieved using a computer-generated simple binomial randomization program, stratified by centre
Allocation concealment (selection bias)	Unclear	No further information provided
Blinding of participants (performance bias): Objective outcomes (i.e., FEV1)	Low	No further information is provided, but assumed that these outcomes cannot be influenced by participants
Blinding of participants (performance bias): Subjective outcomes (i.e., HRQoL)	High	No further information is provided, but the outcome is likely to be influenced by participants
Blinding of personnel (performance bias): Objective outcomes (i.e., FEV1)	Low	No further information is provided, but assumed that these outcomes cannot be influenced by personnel
Blinding of personnel (performance bias): Subjective outcomes (i.e., HRQoL)	High	No further information is provided, but the outcome is likely to be influenced by personnel
Blinding of outcome assessment (detection bias): Objective outcomes (i.e., FEV1)	Low	No further information is provided, but assumed that these outcomes cannot be influenced by outcome assessors
Blinding of outcome assessment (detection bias): Subjective outcomes (i.e., HRQoL)	High	No further information is provided, but the outcome is likely to be influenced by outcome assessor
Incomplete outcome data (attrition bias)	Low	There was a similar rate of attrition in both treatment groups. Intention-to-treat analysis was performed and reported
Selective reporting (reporting bias)	High	Self-efficacy for physical activity and disease management, and active energy expenditure were secondary outcome measures planned in the registered protocol but not reported in the full text publication

Borges 2014	
Study characteristics	
Methods	**Study design:** RCT, parallel Country: Brazil **Duration:** 1 week
Participants	46 participants PR n = 21, control n = 25 Female %: PR 47%, control 29% Age (mean, SD): PR 64.1 (12.5), control 67.8 (9.0) FEV% mean: PR 41.7, control 39.1 **Other characteristics:** smoking, pack-years (mean, SD): PR 48.7 (19.3), control 50.8 (20.4); number of hospitalizations in the past year PR 9, control 5 **Inclusion criteria:** COPD (FEV in 1 s/forced vital capacity <70%) exacerbation characterized by an increase in sputum or cough or worsening of dyspnoea; no hospitalization in the last 30 days; aged between 40 and 85 years; absence of musculoskeletal or neurologic conditions that might affect exercise performance; no participation in a rehabilitation program in the last 6 months; and absence of any other pulmonary diseases. **Exclusion criteria:** patients transferred to the intensive care unit (ICU) before the second day of hospitalization; patients exhibiting changes in mental status; worsening of hypoxemia (arterial oxygen pressure <40 mmHg at room air) and/or respiratory acidosis (hydrogen ion concentration <7.25); hospitalization time <5 days; or inability to complete any of the evaluations.
Interventions	**PR components:** exercise + education/behaviour change **Exercise mode:** resistance training (strengthening) and whole-body resistance training program Timing: third day of hospitalization Frequency: 1 session/day Intensity: 80% of 1RM Duration: 90 min Length: minimum 3 sessions (one week) Supervision: yes Adherence: 95% Provider: physiotherapist Setting: hospital
Control	**Usual care:** normative daily care, including chest physiotherapy to remove bronchial secretions, non-invasive ventilation if needed, and verbal instructions to carry on with their normative daily physical activities
Outcomes	**HRQoL:** Saint George's Respiratory Questionnaire, symptom, activity, impact and total domains at discharge and 1 month after discharge **Cardiovascular submaximal capacity:** 6 MWD (m), during hospitalization
Attrition	Lost follow up PR: n = 6 (reason: transferred to ICU after day 2 (n = 3): early discharge <5 days (n = 2); hospital readmission with less than 30 days (n = 1). Control: lost follow-up: n = 11 (Reason: transferred to ICU after day 2 (n = 3);

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Borges 2014		
Study characteristics		
	early discharge <5 days (n = 4); died less than 30 days after discharge (n = 2); not attended the hospital after 30 days (n = 2)	
Notes	**Funding:** Sao Paulo research foundation (grant no. 2007/51-354-7) and Brazilian scientific foundation (grant no. 305987/2010–0) **Another identifier:** NCT01786928	
Risk of bias		
Bias	**Author's judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low	Randomization was achieved using a computer-generated process
Allocation concealment (selection bias)	Low	Allocation was concealed in sealed opaque envelopes
Blinding of participants (performance bias): Objective outcomes (i.e., FEV1)	Low	No further information is provided, but assumed that these outcomes cannot be influenced by participants
Blinding of participants (performance bias): Subjective outcomes (i.e., HRQoL)	High	No further information is provided, but the outcome is likely to be influenced by participants
Blinding of personnel (performance bias): Objective outcomes (i.e., FEV1)	Low	No further information is provided, but assumed that these outcomes cannot be influenced by personnel
Blinding of personnel (performance bias): Subjective outcomes (i.e., HRQoL)	High	No further information is provided, but the outcome is likely to be influenced by personnel
Blinding of outcome assessment (detection bias): Objective outcomes (i.e., FEV1)	Low	Outcome assessment performed by a blinded assessor
Blinding of outcome assessment (detection bias): Subjective outcomes (i.e., HRQoL)	Low	Outcome assessment performed by a blinded assessor
Incomplete outcome data (attrition bias)	Low	There was a similar rate of attrition in both treatment groups
Selective reporting (reporting bias)	High	Exercise capacity, health-related quality of life, systemic inflammatory levels and blood gas analysis are outcomes reported that were not planned in the registered protocol

Deepak 2014	
Study characteristics	
Methods	**Study design:** RCT, parallel Country: India **Duration:** 12 weeks
Participants	60 participants PR n = 30, control n = 30 Female %: 7% in both groups Age (mean, SD): PR 58.4 (6.8), control 59.4 (6.7) FEV% mean: PR 53.3, control 46.7 **Other characteristics:** Pack-years mean: PR 43.1, control 33.9 **Inclusion criteria:** consecutive patients who were admitted with an AECOPD and were discharged from the hospital **Exclusion criteria:** severely ill patients who were unable to walk, or patients with unstable cardiovascular disease (unstable angina or recent acute myocardial infarction), had cognitive impairment, disabling arthritis, and severe neurological disease
Interventions	**PR components:** education/behaviour change + patient assessment + exercise + chest physiotherapy + nutrition and psychosocial support **Exercise mode:** aerobic exercise, resistance training (strengthening) Timing: within 2 weeks of hospital discharge Frequency: NR Intensity: NR Duration: 120 min Length: 12 weeks Supervision: yes Adherence: NR Provider: physiotherapist and doctor Setting: home
Control	**Usual care:** conventional treatment without pulmonary rehabilitation
Outcomes	**HRQoL:** Saint George's Respiratory Questionnaire, symptom, activity, impact and total domains 3 months **Cardiovascular submaximal capacity:** Saint George's Respiratory Questionnaire 3 months **Dyspnoea:** mMRC 3 months
Attrition	NR
Notes	**Funding:** not reported **Another identifier:** protocol registration not reported
Risk of bias	
Bias	**Author's judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low	Randomization was achieved using a computer-generated process
Allocation concealment (selection bias)	Unclear	No further information provided

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Deepak 2014		
Study characteristics		
Blinding of participants (performance bias): Objective outcomes (i.e., FEV1)	Low	No further information is provided, but assumed that these outcomes cannot be influenced by participants
Blinding of participants (performance bias): Subjective outcomes (i.e., HRQoL)	High	No further information is provided, but the outcome is likely to be influenced by participants
Blinding of personnel (performance bias): Objective outcomes (i.e., FEV1)	Low	No further information is provided, but assumed that these outcomes cannot be influenced by personnel
Blinding of personnel (performance bias): Subjective outcomes (i.e., HRQoL)	High	No further information is provided, but the outcome is likely to be influenced by personnel
Blinding of outcome assessment (detection bias): Objective outcomes (i.e., FEV1)	Low	No further information is provided, but assumed that these outcomes cannot be influenced by outcome assessor
Blinding of outcome assessment (detection bias): Subjective outcomes (i.e., HRQoL)	High	No further information is provided, but the outcome is likely to be influenced by outcome assessor
Incomplete outcome data (attrition bias)	High	Higher proportion of missing data in the control group and reasons not specified
Selective reporting (reporting bias)	Low risk of bias	The study protocol is not available but it is clear that the published reports include all expected outcomes, including those that were pre-specified in methods.

He 2015	
Study characteristics	
Methods	**Study design:** RCT, parallel Country: China **Duration:** 9 days
Participants	101 participants PR n = 66, control n = 28 (withdrawn after randomization 7) Female %: PR 9.1%, control 17.9% Age (mean, SD): PR 69.2 (1.53), control 73.9 (1.84) FEV% mean: PR 38, control 39 **Other characteristics:** Brinkman index (mean, SD): PR 851 (85.03), control 783 (107.65) **Inclusion criteria:** patients admitted due to AECOPD, if they reported a limitation in daily activities due to dyspnoea on exertion, as categorized using the Modified Medical Research Council (mMRC) dyspnoea grade >0 **Exclusion criteria:** patients with some condition like, uncontrolled heart failure, sever lower limb arthritis, and symptomatic peripheral vascular disease, which may affect the outcome of dyspnoea or exercise tolerance; severe orthopaedic or neurological disorders limiting exercise performance; unstable cardiac disease; and inability to understand or complete questionnaires
Interventions	**PR components:** exercise + education/behaviour change + relaxation + breathing retraining **Exercise mode:** aerobic exercise, resistance training (strengthening), stretching Timing: second day of hospitalization Frequency: 2 sessions/day Intensity: between 3 and 5 on the Borg breathlessness score, 60% of the peak work rate achieved in the 6-min walk test at baseline Duration: 60 min Length: until discharge (9 days) Supervision: yes Adherence: NR Provider: physiotherapist Setting: hospital
Control	**Usual care:** NR
Outcomes	**HRQoL:** Chronic Respiratory Questionnaire at discharge **Cardiovascular submaximal capacity:** 6 MWD (m) at discharge **Dyspnoea:** mMRC at discharge **Impact of the disease:** COPD assessment test (CAT) at discharge
Attrition	7 withdraw after randomizations
Notes	**Funding:** national natural science foundation of China (81,200,044) and Shanghai Pujiang program (12PJ1407800) and research fund for the doctoral program of higher education of China (20,120,072,120,070) **Another identifier:** ChiCTR-TRC-13003068

Risk of bias		
Bias	**Author's judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low	Randomization was achieved using a computer-generated process
Allocation concealment (selection bias)	Unclear	No further information provided
Blinding of participants (performance bias): Objective outcomes (i.e., FEV1)	Low	No further information is provided, but assumed that these outcomes cannot be influenced by participants
Blinding of participants (performance bias): Subjective outcomes (i.e., HRQoL)	High	Participants were not blinded
Blinding of personnel (performance bias): Objective outcomes (i.e., FEV1)	Low	No further information is provided, but assumed that these outcomes cannot be influenced by personnel
Blinding of personnel (performance bias): Subjective outcomes (i.e., HRQoL)	High	Personnel were not blinded
Blinding of outcome assessment (detection bias): Objective outcomes (i.e., FEV1)	Low	No further information is provided, but assumed that these outcomes cannot be influenced by outcome assessors

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He 2015		
Study characteristics		
Blinding of outcome assessment (detection bias): Subjective outcomes (i.e., HRQoL)	High	Outcome assessors were not blinded
Incomplete outcome data (attrition bias)	Low	There was a similar rate of attrition in both treatment groups
Selective reporting (reporting bias)	High	Differences between the pre-specified outcomes in the registered protocol and the outcomes reported in the study
Johnson-Warrington 2016		
Study characteristics		
Methods	**Study design**: RCT, parallel Country: United Kingdom **Duration:** 10 weeks	
Participants	78 participants PR n = 39, control n = 39 Female%: PR 61.54%, control 66.67% Age (mean, SD): PR 67.64 (8.54), control 68.33 (7.73) FEV% mean: PR: 40.47, control 42.45 **Other characteristics:** Pack-years (mean, SD): PR 52.39 (34.32), control 48.33 (29.02) **Inclusion criteria:** established diagnosis of AECOPD and grade 2–5 dyspnoea according to the Medical Research Council **Exclusion criteria:** unable to safely participate in unsupervised exercise (i.e., due to psychiatric, locomotive, cardiac, or neurological impairments); involved in other research; unable to read English; had previously received SPACE for COPD or completed PR within the previous 6 months; had four or more admissions in the previous 12 months	
Interventions	**PR components:** exercise + psychotherapy (motivational interviewing) + education/behaviour change **Exercise mode:** aerobic exercise and resistance training (strengthening) Timing: at hospital discharge Frequency: daily walking-based aerobic program and 3 times/week resistance training Intensity: NR Duration: 45 min Length: 10 weeks Supervision: No Adherence: NR Provider: physiotherapist Setting: home	
Control	**Usual care:** a follow-up appointment with the community COPD team or telephone follow-up after an inpatient review by a respiratory nurse specialist and an outpatient consultant review	
Outcomes	**Hospital readmissions:** 1 and 3 months **HRQoL:** Chronic Respiratory Questionnaire, dyspnoea, fatigue, emotion and mastery domains, 3 months **Cardiovascular submaximal capacity:** 1) incremental shuttle walk test (ISWT) mts, 2) endurance shuttle walking test (ESWT) seconds 3 months **Mortality:** CRQ, 3 months **Dyspnoea:** CRQ, 3 months	
Attrition	PR: preferred to do PR (n = 1), ankle fracture (n = 1), new dx terminal lung Ca (n = 1), not COPD (n = 1) Control: withdrawn died (n = 3)	
Notes	**Funding:** British lung foundation grant RB11-2 **Another identifier:** ISRCTN84599369	
Risk of bias		
Bias	**Author's judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low	Randomization was achieved using a computer-generated process
Allocation concealment (selection bias)	Low	Allocation was concealed through a computer-generated process
Blinding of participants (performance bias): Objective outcomes (i.e., FEV1)	Low	Participants were not blinded, but assumed that these outcomes cannot be influenced participants
Blinding of participants (performance bias): Subjective outcomes (i.e., HRQoL)	High	Participants were not blinded
Blinding of personnel (performance bias): Objective outcomes (i.e., FEV1)	Low	Personnel were not blinded, but assumed that these outcomes cannot be influenced by personnel
Blinding of personnel (performance bias): Subjective outcomes (i.e., HRQoL)	High	Personnel were not blinded
Blinding of outcome assessment (detection bias): Objective outcomes (i.e., FEV1)	Low	Outcome assessment performed by a blinded assessor
Blinding of outcome assessment (detection bias): Subjective outcomes (i.e., HRQoL)	Low	Outcome assessment performed by a blinded assessor
Incomplete outcome data (attrition bias)	Low	There was a similar rate of attrition in both treatment groups. Intention-to-treat analysis was performed and reported
Selective reporting (reporting bias)	High	Differences between the pre-specified outcomes in the registered protocol and the outcomes reported in the study
Khosravi 2020		
Study characteristics		

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Khosravi 2020	
Study characteristics	
Methods	**Study design:** RCT, parallel Country: Iran **Duration:** Not reported
Participants	60 participants PR n = 30, control n = 30 Female %: PR 21%, control 39% Age (mean, SD): PR 70.25 (7.5), control 71.79 (10.2) FEV% mean: NR **Other characteristics:** Education: reading and writing: PR 21 (75%), control 22 (78.6%) Primary of high school: PR 7 (25%), control 6 (21.4%) Job Farmer: PR 10 (35.7%), control8 (28.6%) Smoking (N, %): PR 18 (64.3%), control 13 (46.4%) **Inclusion criteria:** hospitalization with a definitive diagnosis of COPD exacerbation; consciousness; age above 60 years; speaking Farsi; lack of other debilitating physical or psychiatric diseases; and access of the patient or his/her companion to a phone **Exclusion criteria:** unwillingness to cooperate with the study and patient's death
Interventions	**PR components:** exercise (physical activities and training respiratory rehabilitation/breathing exercises) + psychotherapy + education/behaviour change **Exercise mode:** aerobic exercise and stretching Timing: during hospitalization Frequency: NR Intensity: NR Duration: 30 min Length: NR Supervision: yes Adherence: NR Provider: NR Setting**:** hospital and home
Control	**Usual care:** NR
Outcomes	**Hospital readmissions:** 1, 3, 6 months
Attrition	PR: failure to follow up: death (n = 1), complete de intervention (n = 1) control: failure to complete de intervention (n = 2)
Notes	**Funding:** research deputy of Rafsanjan University of Medical Sciences **Another identifier:** IRCT2017061822320N5

Risk of bias		
Bias	**Author's judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear	Insufficient information to allow a judgment
Allocation concealment (selection bias)	Unclear	No further information provided
Blinding of participants (performance bias): Objective outcomes (i.e., FEV1)	Low	No further information is provided, but assumed that these outcomes cannot be influenced by participants
Blinding of participants (performance bias): Subjective outcomes (i.e., HRQoL)	NA	NA
Blinding of personnel (performance bias): Objective outcomes (i.e., FEV1)	Low	No further her information is provided, but assumed that these outcomes cannot be influenced by personnel
Blinding of personnel (performance bias): Subjective outcomes (i.e., HRQoL)	NA	NA
Blinding of outcome assessment (detection bias): Objective outcomes (i.e., FEV1)	Low	No further information is provided, but assumed that these outcomes cannot be influenced by outcome assessor
Blinding of outcome assessment (detection bias): Subjective outcomes (i.e., HRQoL)	NA	NA
Incomplete outcome data (attrition bias)	Unclear	No further information is provided
Selective reporting (reporting bias)	Low	Outcomes were reported as planned

Kjaergaard 2020	
Study characteristics	
Methods	**Study design**: RCT, parallel Country: Denmark **Duration:** 7 weeks
Participants	150 participants (randomized) 131 participants assessed at 12 months PR n = 70, control n = 61 Female %: PR 59%, control 59% Age (mean, SD): PR 72.7 (9.4), control 74.4 (7.8) FEV% mean: PR 40.2, control 44.1 **Other characteristics:** Comorbidities: cancer, asthma, cardiac causes, urosepsis Smoking n (%): current: PR: 22 (31%), control: 15 (25%); former: PR 45 (64%), control 43 (70%); never: PR 3 (4%), control 3 (5%) Exposure pack-years: PR 40.6 (16.5%), control 43.5 (19.5%)

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Kjaergaard 2020	
Study characteristics	
	Inclusion criteria: hospitalization with an AECOPD, a diagnosis of COPD according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD), age >18 years, ability to walk 10 m independently (with or without a walking aid) **Exclusion criteria:** another disease (such as cancer or severe heart disease), difficulties in understanding and speaking Danish (e.g., due to dementia), residence outside Gentofte Hospital's recruitment area, discharge to a residence other than their own (e.g., nursing home), participation in another rehabilitation program or inability to provide informed consent
Interventions	**PR components:** exercise + education/behaviour change **Exercise mode:** resistance training (strengthening) Timing: within 2 weeks of hospital discharge Frequency: 2 sessions/week Intensity: submaximal exercise performance corresponding to 85% of VO2max calculated from the ISWT Duration: 90 min Length: 7 weeks Supervision: yes Adherence: early pulmonary rehabilitation group 58 (83%) Provider: physiotherapist Setting: hospital and home
Control	**Usual care:** PR initiated at 2-month follow-up
Outcomes	**Hospital readmissions:** 1, 3, 6 months **Cardiovascular submaximal capacity:** 1) endurance shuttle walking test (ESWT) seconds; 2) incremental shuttle walk test (ISWT) mts baseline, 2 and 6 months **Mortality:** 12 months **Impact of disease:** COPD assessment test (CAT) baseline, 2 and 6 months
Attrition	6 and 13 participants were excluded in the early and stable pulmonary rehabilitation groups respectively, mainly due to a diagnosis of asthma or start of another rehabilitation program
Notes	**Funding:** prevention fund of the capital region in Denmark **Another identifier:** NCT02987439

Risk of bias

Bias	Author's judgement	Support for judgement
Random sequence generation (selection bias)	Low	Randomization was achieved using a computer-generated process
Allocation concealment (selection bias)	Low	Allocation was concealed in sealed opaque envelopes
Blinding of participants (performance bias): Objective outcomes (i.e., FEV1)	Low	No further information is provided, but assumed that these outcomes cannot be influenced by participants
Blinding of participants (performance bias): Subjective outcomes (i.e., HRQoL)	High	No further information is provided, but the outcome is likely to be influenced by participants
Blinding of personnel (performance bias): Objective outcomes (i.e., FEV1)	Low	No further information is provided, but assumed that these outcomes cannot be influenced by personnel
Blinding of personnel (performance bias): Subjective outcomes (i.e., HRQoL)	High	No further information is provided, but the outcome is likely to be influenced by personnel
Blinding of outcome assessment (detection bias): Objective outcomes (i.e., FEV1)	Low	No further information is provided, but assumed that these outcomes cannot be influenced by outcome assessor
Blinding of outcome assessment (detection bias): Subjective outcomes (i.e., HRQoL)	High	No further information is provided, but the outcome is likely to be influenced by outcome assessor
Incomplete outcome data (attrition bias)	Low	There was a similar rate of attrition in both treatment groups
Selective reporting (reporting bias)	High	Differences between the pre-specified outcomes in the registered protocol and the outcomes reported in the study

Knaut 2020	
Study characteristics	
Methods	**Study design:** RCT, parallel Country: Brazil **Duration:** 4 weeks
Participants	26 participants PR n = 13, control n = 13 Female %: PR 61.5%, control 69.2% Age (mean, SD): PR 66.8 (9.49), control 69.3 (13.5) FEV% mean: PR (L) 0.75 ± 0.30, control 0.89 (0.32) **Other characteristics:** Smoking (pack-years) PR 46.0 (40.0–68.0), control 50.0 (31.8–92.0) BMI (kg/m2) PR 25.4 (5.29), control 23.3 (4.69) SGRQ: anxiety: PR 8.9 (6.9), control 7.4 (5.0); depression: PR 3.1 (3.1), control 5.3 (4.4) **Inclusion criteria:** patients diagnosed with AECOPD **Exclusion criteria:** lack of COPD diagnosis, patients who stayed less than 24 h in hospital, Glasgow score <15, Borg dyspnoea score >7, unstable heart disease, limited mobility, hemodynamic instability, and mechanical ventilation
Interventions	**PR components:** exercise only **Exercise mode:** aerobic exercise Timing: during hospitalization Frequency: NR Intensity: NR Duration: 15 min

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Knaut 2020	
Study characteristics	
	Length: 4 weeks Supervision: no Adherence: NR Provider: NR Setting: hospital
Control	**Usual care:** NR
Outcomes	**HRQoL:** St George's Respiratory Questionnaire, symptom, activity, impact and total domains 1 month **Cardiovascular submaximal capacity:** 6 MWD (m) baseline and 1 month **Dyspnoea:** mMRC baseline and 1 month
Attrition	NR
Notes	**Funding:** NR **Another identifier:** U1111-1166-7480

Risk of bias		
Bias	**Author's judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low	Randomization was achieved using sealed envelopes
Allocation concealment (selection bias)	Unclear	No further information is provided
Blinding of participants (performance bias): Objective outcomes (i.e., FEV1)	Low	No further information is provided, but assumed that these outcomes cannot be influenced by participants
Blinding of participants (performance bias): Subjective outcomes (i.e., HRQoL)	High	No further information is provided, but the outcome is likely to be influenced by participants
Blinding of personnel (performance bias): Objective outcomes (i.e., FEV1)	Low	No further information is provided, but assumed that these outcomes cannot be influenced by personnel
Blinding of personnel (performance bias): Subjective outcomes (i.e., HRQoL)	High	No further information is provided, but the outcome is likely to be influenced by personnel
Blinding of outcome assessment (detection bias): Objective outcomes (i.e., FEV1)	Low	No further information is provided, but assumed that these outcomes cannot be influenced by outcome assessor
Blinding of outcome assessment (detection bias): Subjective outcomes (i.e., HRQoL)	High	No further information is provided, but the outcome is likely to be influenced by outcome assessor
Incomplete outcome data (attrition bias)	Low	There was a similar rate of attrition in both treatment groups
Selective reporting (reporting bias)	High	Differences between the outcomes reported in the methods and in the results. Registered protocol not located

Liao 2015	
Study characteristics	
Methods	**Study design:** RCT, parallel Country: Taiwan **Duration:** 4 days
Participants	62 participants PR n = 31, control n = 31 Female %: PR 46.7%, control 32.3% Age median (range): PR 68.0 (44.0–89.0), control70.0 (52.0, 91.0) FEV% mean: NR **Other characteristics:** Comorbidities: PR 100%, control 90.3% **Inclusion criteria:** patients older than 65 years; in clear consciousness; diagnosed with shortness of breath or dyspnoea that was not caused by heart disease, pneumothorax, or pulmonary edema; had received bronchodilator aerosol therapy or antibiotic treatment, but had not been treated with an antitussive **Exclusion criteria:** patients with systolic blood pressure lower than 90 mmHg; blood oxygen concentration lower than SpO [2] = 90%; unstable psychological status, hemoptysis, pneumothorax, pulmonary edema, and the use of a respirator
Interventions	**PR components:** exercise + education/behaviour change + airway clearance **Exercise mode:** aerobic exercise and resistance training (strengthening) Timing: during hospitalization Frequency: 2 sessions/day Intensity: NR Duration: 70 min Length: 4 days Supervision: yes Adherence: NR Provider: physician, nurse Settings: hospital
Control	**Usual care:** usual care and health education, which included monitoring of the vital signs and the AECOPD symptoms, assessing the nutritional status, educating the smoking cessation, and providing the nasal O2 therapy
Outcomes	**Cardiovascular submaximal capacity:** 6 MWD (m), 3 months **Dyspnoea:** modified Borg scale, 3 months
Attrition	PR: discontinued intervention (n = 1) at discharge Control: no lost follow up
Notes	**Funding:** Chest hospital, Ministry of Health and Welfare, Taiwan (DOH100-HO-3053) **Another identifier:** NCT02329873

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Liao 2015

Study characteristics

Risk of bias

Bias	Author's judgement	Support for judgement
Random sequence generation (selection bias)	Low	Randomization was achieved through coin tossing
Allocation concealment (selection bias)	Unclear	No further information is provided
Blinding of participants (performance bias): Objective outcomes (i.e., FEV1)	Low	Participants were not blinded, but assumed that these outcomes cannot be influenced by participants
Blinding of participants (performance bias): Subjective outcomes (i.e., HRQoL)	High	Participants were not blinded
Blinding of personnel (performance bias): Objective outcomes (i.e., FEV1)	Low	Personnel were not blinded, but assumed that these outcomes cannot be influenced by personnel
Blinding of personnel (performance bias): Subjective outcomes (i.e., HRQoL)	High	Personnel were not blinded
Blinding of outcome assessment (detection bias): Objective outcomes (i.e., FEV1)	Low	Outcome assessment performed by a blinded assessor
Blinding of outcome assessment (detection bias): Subjective outcomes (i.e., HRQoL)	Low	Outcome assessment performed by a blinded assessor
Incomplete outcome data (attrition bias)	Low	There was a similar rate of attrition in both treatment groups
Selective reporting (reporting bias)	Low	Outcomes were reported as planned

Liao 2021

Study characteristics

Methods	**Study design:** RCT, parallel Country: China **Duration:** 12 weeks
Participants	80 participants PR n = 40, control n = 40 Female %: PR 18%, control 25% Age (mean, SD): PR 61.83 (6.63), control 61.21 (7.38) FEV% mean: PR 55.62, control 54.25 **Other characteristics:** Comorbidities: hypertension (PR 41%, control 47%); diabetes (PR 17%, control 18%); coronary heart disease (PR 19.4%, control 11.7%) **Inclusion criteria:** patients between 40 and 80 years; COPD was diagnosed according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines, and was diagnosed as AECOPD (have acute worsening respiratory symptoms, including worsening dyspnoea, worsening cough, increased sputum volume and/or purulent sputum); AECOPD patients treated with non-invasive ventilation; any regular exercise (at least 3 times a week) was not implemented within 6 months before this study; they could complete the sitting and lying Liuzijue exercise under guidance **Exclusion criteria:** severe cardiovascular, hepatorenal, and hematopoietic diseases, psychosis, or took part in other clinical studies
Interventions	**PR components:** exercise only **Exercise mode:** stretching Timing: during hospitalization Frequency: 2 sessions/day Intensity: 60–80% of the maximum heart rate Duration: 60 min Length: 12 weeks Supervision: yes Adherence: 70 (87.5%) after 9 months Provider: doctor, but no qualifications/expertise Setting: hospital and home
Control	**Usual care:** according to the GOLD guidelines, the control group received routine nursing, including medication, smoking cessation, and life instructions
Outcomes	**HRQoL:** Saint George's Respiratory Questionnaire, symptom, activity, impact and total domains, 3 months **Cardiovascular submaximal capacity:** 6 MWD (m), 3 months **Dyspnoea:** mMRC, 3 months **Re-exacerbations:** 6 months
Attrition	PR: lost follow up (n = 3), declined reassessment (n = 3) control: lost follow up (n = 4)
Notes	**Funding:** science and technology department of Sichuan province (2019YFS0391) **Another identifier:** ChiCTR2000034530

Risk of bias

Bias	Author's judgement	Support for judgement
Random sequence generation (selection bias)	Low	Randomization was achieved using a computer-generated process
Allocation concealment (selection bias)	Unclear	No further information is provided

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Liao 2021		
Study characteristics		
Blinding of participants (performance bias): Objective outcomes (i.e., FEV1)	Low	Participants were not blinded, but assumed that these outcomes cannot be influenced by participants
Blinding of participants (performance bias): Subjective outcomes (i.e., HRQoL)	High	Participants were not blinded
Blinding of personnel (performance bias): Objective outcomes (i.e., FEV1)	Low	Personnel were not blinded, but assumed that these outcomes cannot be influenced by personnel
Blinding of personnel (performance bias): Subjective outcomes (i.e., HRQoL)	High	Personnel were not blinded
Blinding of outcome assessment (detection bias): Objective outcomes (i.e., FEV1)	Low	Outcome assessment performed by a blinded assessor
Blinding of outcome assessment (detection bias): Subjective outcomes (i.e., HRQoL)	Low	Outcome assessment performed by a blinded assessor
Incomplete outcome data (attrition bias)	Low	There was a similar rate of attrition in both treatment groups
Selective reporting (reporting bias)	High	Differences between the pre-specified outcomes in the registered protocol and the outcomes reported in the study

López-López 2019	
Study characteristics	
Methods	**Study design:** RCT, parallel Country: Spain **Duration:** 1 week
Participants	66 participants PR: self-management (SM) n = 22; physical activity (PT) n = 22; control n = 22 Female (%): NR Age (mean, SD): PR (SM) 72.63 (7.37), PT 71.20 (11.53), control 71.35 (9.88) FEV% mean: PR (SM) 38.77, PT 36.58, control 34.50 **Inclusion criteria:** older than 40 years; diagnosed with severe COPD according to the criteria of the Global initiative for chronic Obstructive Lung Disease (GOLD 3 or 4); hospitalized due to acute exacerbation of COPD and agreed to participate **Exclusion criteria:** severe comorbidities, such as unstable cardiovascular disease, orthopaedic diseases in the upper and lower limbs, motor sequelae from neurological or visual disorders that interfere with the ability to perform physical exercise; cognitive impairment that could interfere with the evaluation and the treatment; and those who did not agree to participate in the study
Interventions	**PR components:** exercise + education/behaviour change **Exercise mode:** resistance training (strengthening) Timing: during hospitalization Frequency: 1 session/day Intensity: NR Duration: NR Length: 1 week Supervision: yes Adherence: NR Provider: physiotherapist Settings: hospital
Control	**Usual care:** control: standard medical treatment prescribed by the doctor (consisting of bronchodilators, inhaled corticosteroids, and antibiotics). Exercise control (PT): control group treatment plus neuromuscular stimulation therapy on quadriceps accompanied by lower limbs exercises
Outcomes	**HRQoL:** EQ-5D, mobility, personal, daily activities, pain, anxiety/depression and VAS domains at discharge and 3 months **Dyspnoea:** Modified scale Borg at discharge and 3 months
Attrition	At 3 months SM n = 0, control n = 3, PT n = 1
Notes	**Funding:** Fundacion Progreso y Salud (FPS) and Boehringer Ingelheim Spain, SA. Project code: PI-0370–2014 **Another identifier:** NCT02515318

Risk of bias		
Bias	**Author's judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low	Randomization was achieved using a computer-generated process
Allocation concealment (selection bias)	Low	Allocation was concealed by an individual unaware of study aims
Blinding of participants (performance bias): Objective outcomes (i.e., FEV1)	NA	NA
Blinding of participants (performance bias): Subjective outcomes (i.e., HRQoL)	High	No further information is provided, but the outcome is likely to be influenced by participants
Blinding of personnel (performance bias): Objective outcomes (i.e., FEV1)	NA	NA
Blinding of personnel(performance bias): Subjective outcomes (i.e., HRQoL)	High	No further information is provided, but the outcome is likely to be influenced by personnel
Blinding of outcome assessment (detection bias): Objective outcomes (i.e., FEV1)	NA	NA
Blinding of outcome assessment (detection bias): Subjective outcomes (i.e., HRQoL)	Low	Outcome assessment performed by a blinded assessor
Incomplete outcome data (attrition bias)	Low	There was a similar rate of attrition in both treatment groups

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López-López 2019		
Study characteristics		
Selective reporting (reporting bias)	High	Differences between the pre-specified outcomes in the registered protocol and the outcomes reported in the study
López- López 2021		
Study characteristics		
Methods	**Study design:** RCT, parallel Country: Spain **Duration:** 9 days	
Participants	43 participants PR global exercise group (GEG) n = 13, control n = 16, functional electrostimulation group (FEG) n = 14 Female (%): NR Age (mean, SD): PR GEG 74.92 (7.07), control 70.98 (9.22), FEG 75.80 (8.61) FEV% mean: PR GEG 32.46, control 33.41, FEG 37.12 **Other characteristics:** Comorbidities: Charles Comorbidity Index (mean, SD): PR GEG 5.69 (1.65), control 4.77 (1.40), FEG 2.80 (1.47); hospital stay (days): PR GEG 10.33 (3.05), control 11.00 (5.29), FEG: 7.47 (3.50) **Inclusion criteria:** 1) patients with a diagnosis of COPD made according to the criteria of the American Thoracic Society (ATS), 2) with a moderate to severe COPD (GOLD III-IV (FEV1% < 50), 3) hospitalized AECOPD patients, 4) with hypoxemia at rest defined as resting SpO2 between 89 and 93%, 5) who agreed to participate **Exclusion criteria:** severe comorbidities that could interfere with the evaluation or with the treatment, as well as contraindications of electrotherapy	
Interventions	**PR components:** exercise only **Exercise mode:** aerobic exercise, resistance training (strengthening), stretching Timing: during hospitalization Frequency: 1 session/day Intensity: GEG: the intensity of the treatment was adapted taking into account the subject's response (the perceived dyspnoea and fatigue during the exercise). FEG and control NR. Duration: 60 min Length: 9 days Supervision: yes Adherence: all of the patients carried out the program every day during the hospital stay Provider: physiotherapist Setting: hospital	
Control	**Usual care:** standard medical treatment prescribed by the doctor (consisting of bronchodilators, inhaled corticosteroids, and antibiotics)	
Outcomes	**HRQoL:** EQ-5D, mobility, personal care, daily activities, pain, anxiety/depression, and VAS domains at discharge	
Attrition	There have been no dropouts in any of the three included groups during the study	
Notes	**Funding:** FPU grant of the Spanish ministry of education **Another identifier:** NCT04295655	
Risk of bias		
Bias	**Author's judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low	Randomization was achieved using a computer-generated process
Allocation concealment (selection bias)	Low	Allocation was concealed in sealed opaque envelopes
Blinding of participants (performance bias): Objective outcomes (i.e., FEV1)	NA	NA
Blinding of participants (performance bias): Subjective outcomes (i.e., HRQoL)	High	Participants were not blinded
Blinding of personnel (performance bias): Objective outcomes (i.e., FEV1)	NA	NA
Blinding of personnel (performance bias): Subjective outcomes (i.e., HRQoL)	High	Personnel were not blinded
Blinding of outcome assessment (detection bias): Objective outcomes (i.e., FEV1)	NA	NA
Blinding of outcome assessment (detection bias): Subjective outcomes (i.e., HRQoL)	Low	Outcome assessment performed by a blinded assessor
Incomplete outcome data (attrition bias)	Low	There was a similar rate of attrition in both treatment groups
Selective reporting (reporting bias)	High	Differences between the pre-specified outcomes in the registered protocol and the outcomes reported in the study
Lu 2020		
Study characteristics		
Methods	**Study design:** RCT, parallel Country: China **Duration:** 8 weeks	
Participants	82 participants PR n = 41, Control n = 41 Female %: none Age (mean, SD): PR 67.4 (7.1), control 68.3 (6.8) FEV% mean (admission-not evaluated, at discharge in both groups): PR 30.5, control 31.4	

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Lu 2020	
Study characteristics	
	Inclusion criteria: men or women aged 60 to 80 lung function in the previously year must satisfy: FEV1/FVC<70% after using bronchodilator and FEV1%pre <50%, ability to perform ZSRE under instruction **Exclusion criteria:** history of previous pulmonary rehabilitation exercise, presence of accompanying pneumonia, pneumothorax, pleural effusion, pulmonary embolism, bronchial asthma, tumour, fever of unknown origin, vasculitis, and/or connective tissue disease, presence of serious primary diseases in major organs/systems including heart, liver, kidneys, or hematopoietic system, presence of waist, back, and/or limb dysfunction or postoperative status, presence of mental disorders or cognitive impairment, poor compliance or refusal to perform rehabilitation exercises
Interventions	**PR components:** exercise only **Exercise mode:** resistance training (strengthening) Timing: during hospitalization Frequency: hospitalization (three times daily), home rehabilitation two video calls per week Intensity: NR Duration: NR Length: 8 weeks Supervision: yes Adherence: NR Provider: rehabilitation group started ZSRE under the instruction of the researchers (1 doctor or nurse who was familiar with ZSRE) Setting: hospital and home
Control	**Usual care:** patients in the control group did not perform any rehabilitation exercise but routine drug therapy
Outcomes	**Cardiovascular submaximal capacity:** 6 MWD (m) at discharge and 9 weeks **Dyspnoea:** mMRC baseline and 9 weeks **Impact of disease:** COPD assessment test (CAT) at discharge and 9 weeks
Attrition	Five patients in the PR and four patients in the control lost to follow-up. One patient in control died. Among all the patients lost to follow-up, two patients in the IG and two in the control stopped because they moved too far away. One in the PR and two in the control changing the contact information without informing; one patient in the PR was reluctant to continue ZSRE preferred outdoor activities; one patient in the PR was excluded from analysis because his family could not upload rehabilitation exercises video
Notes	**Funding:** National natural science foundation of China (Grant number 30971317) (NNSFC, China) and the 13th five-year research and development project of China (Grant number 2016YFC1304600) **Another identifier:** ChiCTR–ION–16008854

Risk of bias

Bias	Author's judgement	Support for judgement
Random sequence generation (selection bias)	Low	Randomization was achieved using a random digits table
Allocation concealment (selection bias)	Unclear	No further information is provided
Blinding of participants (performance bias): Objective outcomes (i.e., FEV1)	Low	No further information is provided, but assumed that these outcomes cannot be influenced by participants
Blinding of participants (performance bias): Subjective outcomes (i.e., HRQoL)	High	Participants were not blinded
Blinding of personnel (performance bias): Objective outcomes (i.e., FEV1)	Low	No further information is provided, but assumed that these outcomes cannot be influenced by personnel
Blinding of personnel (performance bias): Subjective outcomes (i.e., HRQoL)	High	Personnel were not blinded
Blinding of outcome assessment (detection bias): Objective outcomes (i.e., FEV1)	Low	Outcome assessment performed by a blinded assessor
Blinding of outcome assessment (detection bias): Subjective outcomes (i.e., HRQoL)	Low	Outcome assessment performed by a blinded assessor
Incomplete outcome data (attrition bias)	Low	There was a similar rate of attrition in both treatment groups. Data from participants lost during the study is reported
Selective reporting (reporting bias)	Low	Outcomes were reported as planned

Osadnik 2014	
Study characteristics	
Methods	**Study design:** RCT, parallel Country: Australia **Duration:** until discharge or 24 h without sputum
Participants	92 participants PR n = 46, control n = 46 Female %: PR 38%, control 33% Age (mean, SD): PR 69.5 (9.8), control 67.8 (11.6) FEV% mean: PR 37.3, control 44.4 **Other characteristics:** Comorbidities (%): respiratory comorbidity: PR 40%, control 40%, cardiac comorbidity: PR 51%, control 44%. Pack-years (mean, SD): PR 72.3 (45.9), control 56.0 (41.3) **Inclusion criteria:** patients hospitalized due to an AECOPD, with evidence of sputum expectoration or a history of chronic sputum production ('regularly expectorated sputum on most days'), who provided informed consent **Exclusion criteria:** respiratory condition deemed more significant than COPD (e.g., clinical history of primary bronchiectasis, asthma or lung cancer requiring active therapy) even if coexistent with COPD; established airway clearance routines; breathing via an artificial airway; PEP therapy was contraindicated (undrained pneumothorax; significant haemoptysis; recent facial, oral, oesophageal or skull surgery/

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Osadnik 2014	
Study characteristics	
	trauma; surgical or non-surgical lung volume reduction procedures, lung transplantation or pneumonectomy within the last 6 months)
Interventions	**PR components:** exercise + education/behaviour change **Exercise mode:** aerobic exercise Timing: during hospitalization Frequency: exercise 1 session/day, PEP 1 supervised/day plus 2 unsupervised/day Intensity: NR Duration: 50 min Length: until discharge or 24 h without sputum Supervision: mixed/partially Adherence: NR Provider: physiotherapists Setting: hospital
Control	**Usual care:** medical therapy including bronchodilators, corticosteroids, antibiotics, supplemental oxygen, prescribed in accordance with COPDX guidelines; non-invasive ventilation (NIV) if indicated, prescribed according to hospital protocols; and allied health assessment and intervention, as required. Physiotherapists delivered a standardized physical exercise training regime that commenced as early as possible with the aim of achieving 30 min/day of walking or equivalent lower limb exercise
Outcomes	**Hospital Readmission:** 6 months **HRQoL:** St George's Respiratory Questionnaire, symptom, activity impact and total domains 2 and 6 moths **Cardiovascular submaximal capacity:** 6 MWD (m) at discharge, 2 and 6 months **Mortality:** 6 months **Dyspnoea:** mMRC at discharge, 2 months, and 6 months **Re-exacerbations:** 6 months
Attrition	PG at discharge n = 1 (death), 8 weeks n = 1 (death), 6-month n = 3 (death 2, lung transplant 1); control at discharge n = 1 (death), 8 weeks n = 2 (death and lung transplant), 6-month n = 4 (death)
Notes	**Funding:** Australian physiotherapy association, Physiotherapy research foundation (S10-010), the institute for breathing and sleep, and La Trobe University **Another identifier:** NCT01101282

Risk of bias		
Bias	**Author's judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low	Randomization was achieved using a computer-generated process
Allocation concealment (selection bias)	Low	Allocation was concealed in sealed opaque envelopes
Blinding of participants (performance bias): Objective outcomes (i.e., FEV1)	Low	Participants were not blinded, but assumed that these outcomes cannot be influenced by participants
Blinding of participants (performance bias): Subjective outcomes (i.e., HRQoL)	High	Participants were not blinded
Blinding of personnel (performance bias): Objective outcomes (i.e., FEV1)	Low	Personnel were not blinded, but assumed that these outcomes cannot be influenced personnel
Blinding of personnel (performance bias): Subjective outcomes (i.e., HRQoL)	High	Personnel were not blinded
Blinding of outcome assessment (detection bias): Objective outcomes (i.e., FEV1)	Low	Outcome assessment performed by a blind assessor
Blinding of outcome assessment (detection bias): Subjective outcomes (i.e., HRQoL)	Low	Outcome assessment performed by a blind assessor
Incomplete outcome data (attrition bias)	High	More than 20% missing data for some timepoints
Selective reporting (reporting bias)	Low	Outcomes were reported as planned

Puhan 2012	
Study characteristics	
Methods	**Study design:** RCT, parallel Country: Switzerland **Duration:** 12 weeks
Participants	36 participants (randomized) 28 participants assessed at end PR n = 15, control n = 13 Female %: PR 37%, control 47% Age (mean, SD): PR 67.5 (9.8), control 66.5 (6.2) FEV% mean: PR 42.7, control 46.3 **Other characteristics:** Comorbidities %: at least 1 comorbidity PR 74%, control 82%; pack-years (mean, SD): PR 58.6 (34.8), control 57.6 (21.9) **Inclusion criteria:** patients with COPD, Global Initiative for Chronic Obstructive Lung Disease stages II–IV; 40 years or older; had just undergone treatment of an acute exacerbation in private pulmonary practices and acute care clinics in Switzerland. Patients had to have suffered from at least 2 exacerbations in the previous 2 years requiring in- or outpatient care and needed to have been diagnosed with COPD during a stable phase within 3 years before enrolment. They needed to be in a medical condition that allowed immediate pulmonary rehabilitation or recovery at home **Exclusion criteria:** hospitalization for other reasons than a COPD exacerbation; long-term non-invasive ventilation (except for continuous pressure ventilation for obstructive sleep apnoea, which was allowed); other lung diseases such as doctor-diagnosed asthma. Who were not eligible for either treatment arm because

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Puhan 2012	
Study characteristics	
	of an impaired level of consciousness, acute confusion, acute changes on the radiograph or electrocardiogram or arterial pH < 7.35, orthopaedic, rheumatologic, cardiovascular, or neurological disorders that inhibit exercise training, gymnastics or guided walking tours, inability to follow patient education in German, French or Italian or mental disorders (e.g., substance abuse, psychosis, dementia)
Interventions	**PR components:** exercise + education/behaviour change **Exercise mode:** aerobic exercise, resistance training (strengthening) Timing: within 2 weeks exacerbation Frequency: NR Intensity: NR Duration: NR Length: 12 weeks Supervision: yes Adherence: NR Provider: NR Setting: hospital and home
Control	**Usual care:** PR starting 6 months after randomization and in a stable state
Outcomes	**Mortality:** 18 months **Re-exacerbations:** 18 months **HRQoL:** Chronic Respiratory Questionnaire, dyspnoea, fatigue, emotion, and mastery domains, 6, 12, 18 months **Dyspnoea:** mMRC, 6, 12, 18 months
Attrition	Did not start rehabilitation early PR n = 4, late PR n = 4
Notes	**Funding:** Swiss Lung League (SLL), SLL of the cantons of Aargau, Grisons, Lucerne, Nidwalden, Solothurn, Thurgau, Valais, Vaud, and Zurich, the Klinik Barmelweid, the 4 clinics of Crans-Montana (Quadrimed), the Höhenkliniken of Zurich as well as Astra Zeneca Switzerland **Another identifier:** Protocol not reported

Risk of bias

Bias	Author's judgement	Support for judgement
Random sequence generation (selection bias)	Low	Randomization was achieved using a computer-generated process
Allocation concealment (selection bias)	Low	Allocation was concealed through central randomization and minimization
Blinding of participants (performance bias): Objective outcomes (i.e., FEV1)	Low	No further information is provided, but assumed that these outcomes cannot be influenced by participants
Blinding of participants (performance bias): Subjective outcomes (i.e., HRQoL)	High	No further information is provided, but the outcome is likely to be influenced by participants
Blinding of personnel (performance bias): Objective outcomes (i.e., FEV1)	Low	No further information is provided, but assumed that these outcomes cannot be influenced by personnel
Blinding of personnel (performance bias): Subjective outcomes (i.e., HRQoL)	High	No further information is provided, but the outcome is likely to be influenced by personnel
Blinding of outcome assessment (detection bias): Objective outcomes (i.e., FEV1)	Low	No further information is provided, but assumed that these outcomes cannot be influenced by outcome assessor
Blinding of outcome assessment (detection bias): Subjective outcomes (i.e., HRQoL)	High	No further information is provided, but the outcome is likely to be influenced by outcome assessor
Incomplete outcome data (attrition bias)	Low	Less than 5% missing data. Intention-to-treat analysis was performed and reported
Selective reporting (reporting bias)	High	Differences between the pre-specified outcomes in the registered protocol and the outcomes reported in the study

Seymour 2010	
Study characteristics	
Methods	**Study design:** RCT, parallel Country: United Kingdom **Duration:** 8 weeks
Participants	60 participants PR n = 30, control n = 30 Female %: PR 57%, control 53% Age (mean, SD): PR 67 (10), control 65 (10) FEV% mean: PR 52, control 52 **Other characteristics:** Comorbidities: hypertension n = 22, stable treated ischemic heart disease n = 13, type 2 diabetes mellitus n = 10 Pack-years, median (IQR): PG 44 (30–61), control 40 (23–57) **Inclusion criteria:** patients with a diagnosis of COPD prior to admission, admitted to hospital for a period in excess of 24 h and commenced on oral corticosteroid therapy (30–40 mg prednisolone) and/or antibiotic therapy, willing to enrol on to a pulmonary rehabilitation program within a week of discharge **Exclusion criteria:** comorbidities precluding exercise testing or training, attendance at a pulmonary rehabilitation class in the preceding year
Interventions	**PR components:** exercise + education/behaviour change **Exercise mode:** aerobic exercise, resistance training (strengthening) Timing: within 1 week of hospital discharge Frequency: 2 sessions/week Intensity: NR Duration: 120 min Length: 8 weeks

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Seymour 2010	
Study characteristics	
	Supervision: yes Adherence: NR Provider: physiotherapists Setting: hospital
Control	**Usual care:** patients were provided with general information about COPD and offered outpatient appointments with their general practitioner or respiratory team
Outcomes	**Hospital readmission:** 3 months **HRQoL:** 1) Saint George's Respiratory Questionnaire (Symptom, activity, impact and total), 2) Chronic Respiratory Questionnaire (dyspnoea, fatigue, emotion, and mastery), 3) EQ-5D (VAS domains), 3 months each one **Cardiovascular submaximal capacity:** 1) incremental shuttle walk test (ISWT), mts, 2) endurance shuttle walking test (ESWT), seconds, 3 months each one **Re-exacerbations:** 3 months
Attrition	PR death (n = 1), failed to attend reassessment at 3 month (n = 3), control reassessment at 3 months (n = 4)
Notes	**Funding:** British lung foundation - project Grant (P04/8), medical research council UK, European respiratory society, and national institute for health **Another identifier:** NCT00557115

Risk of bias		
Bias	**Author's judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear	No further information is provided
Allocation concealment (selection bias)	Unclear	No further information is provided
Blinding of participants (performance bias): Objective outcomes (i.e., FEV1)	Low	Participants were not blinded, but assumed that these outcomes cannot be influenced participants
Blinding of participants (performance bias): Subjective outcomes (i.e., HRQoL)	High	Participants were not blinded
Blinding of personnel (performance bias): Objective outcomes (i.e., FEV1)	Low	No further information is provided, but assumed that these outcomes cannot be influenced by personnel
Blinding of personnel (performance bias): Subjective outcomes (i.e., HRQoL)	High	No further information is provided, but the outcome is likely to be influenced by personnel
Blinding of outcome assessment (detection bias): Objective outcomes (i.e., FEV1)	Low	Assessors were not blinded, but assumed that these outcomes cannot be influenced by outcome assessors
Blinding of outcome assessment (detection bias): Subjective outcomes (i.e., HRQoL)	High	Assessors were not blinded
Incomplete outcome data (attrition bias)	Low	There was a similar rate of attrition in both treatment groups. Intention-to-treat analysis was performed and reported
Selective reporting (reporting bias)	Low	Outcomes were reported as planned

Song 2014	
Study characteristics	
Methods	**Study design:** RCT, parallel Country: South Korea **Duration:** 8 weeks
Participants	40 participants PR n = 20, control n = 20 Female %: PR 44%, control 27% Age (mean, SD): PR 66.6 (11.1), control 68.1 (6.5) FEV% mean: PR 57, control 60 **Inclusion criteria:** a diagnosis of moderate COPD, based on the Global Initiative for Chronic Obstructive Lung Diseases (GOLD) staging system, confirmed discharge date at the discretion of the responsible medical doctors, age between 65 and 75 years; capable of independent mobility **Exclusion criteria:** history of other lung diseases, including pneumoconiosis, bronchiectasis, pulmonary tuberculosis, primary pulmonary hypertension, pulmonary embolism, and interstitial lung disease; any concomitant diseases that could interfere with the general condition such as diabetes, cardiovascular disease, renal failure, cancer, mental disease; neuromuscular impairment that would interfere with the patient's mobility
Interventions	**PR components:** exercise + psychotherapy (motivational interviewing) + education/behaviour change **Exercise mode:** aerobic exercise and stretching Timing: day before discharge Frequency: NR Intensity: NR Duration: 120 min Length: 8 weeks Supervision: mixed/partially Adherence: NR Provider: nurses Setting: hospital and home
Control	**Usual care:** education on COPD management, proven benefits of exercise, and maintaining daily activities. After the completion of the data collection procedure, participants in the control group were provided with the materials used for experimental groups and invited to receive an SCSI

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Song 2014		
Study characteristics		
Outcomes	**HRQoL:** Saint George's Respiratory Questionnaire, symptom, activity, impact and total domains, 2 months **Cardiovascular submaximal capacity:** 6 MWD (m), 2 months	
Attrition	6 patients dropped out: 2 patients in the control did not complete the second month measurement, PR 2 patients failed to complete the intervention and 1 patient the second month measurement	
Notes	**Funding:** Yonsei University research fund of 2009 **Another identifier:** protocol not reported	
Risk of bias		
Bias	**Author's judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear	No further information is provided
Allocation concealment (selection bias)	Unclear	No further information is provided
Blinding of participants (performance bias): Objective outcomes (i.e., FEV1)	Low	Participants were not blinded, but assumed that these outcomes cannot be influenced by participants
Blinding of participants (performance bias): Subjective outcomes (i.e., HRQoL)	High	Participants were not blinded
Blinding of personnel (performance bias): Objective outcomes (i.e., FEV1)	Low	Personnel were not blinded, but assumed that these outcomes cannot be influenced by personnel
Blinding of personnel (performance bias): Subjective outcomes (i.e., HRQoL)	High	Personnel were not blinded
Blinding of outcome assessment (detection bias): Objective outcomes (i.e., FEV1)	Low	Assessor were not blinded, but assumed that these outcomes cannot be influenced by outcome assessors
Blinding of outcome assessment (detection bias): Subjective outcomes (i.e., HRQoL)	High	Assessors were not blinded
Incomplete outcome data (attrition bias)	Low	There was a similar rate of attrition in both treatment groups
Selective reporting (reporting bias)	Low	Outcomes were reported as planned

Zhang 2020	
Study characteristics	
Methods	**Study design:** RCT, parallel Country: China **Duration**: 12 weeks
Participants	208 participants PR n = 92, control n = 97 Female %: PR 23.5%, control 24.7% Age (mean, SD): PR 65.53 (6.64), control 66.31 (7.91) FEV% mean: PR 46.37, control 44.05 **Other characteristics:** Comorbidities (n): none PR 15, control 16; 1–2 comorbidities PR 48, control 48; 3 above comorbidities PR 22, control 25 Education n (%): primary or lower PR 29 (34.1), control 33 (37.1); middle school PR: 34 (40.0), control 36 (40.4); high school or higher PR: 20 (22.5), control 22 (25.9) Smoking Status n (%): current smoker PR 20 (23.5), control 20 (22.5); ex-smoker PR 39 (45.9), control 35 (39.3); non-smoker PR 26 (30.6), control 34 (38.2) Stage of COPD (n): 2) PR 33, control 30; 3) PR 36, control 36; 4) PR: 19, control 20 **Inclusion criteria:** age ≥40 years old, diagnosis of COPD according to GOLD guideline (FEV1/FVC <70% after use of bronchodilator), including COPD stage 2 (moderate, FEV1 ≤50%–80% predicted), 3 (severe, FEV1 ≤30%–<50% predicted), or 4 (very severe, FEV1 <30% predicted), hospitalized at least once due to COPD exacerbation during the last 12 months, and not intending to move to another city within the next 2 years **Exclusion criteria:** unable to provide accurate information or follow instructions, unable to walk even during periods of COPD, and currently involved in another program
Interventions	**PR components:** exercise + psychotherapy + education/behaviour change **Exercise mode:** aerobic exercise, stretching, and Tai-chi Timing: during hospitalization Frequency: 2 sessions/week Intensity: NR Duration: 55 min Length: 12 weeks Supervision: yes Adherence: NR Provider: physiotherapist, Tai-chi mentor, and respiratory nurse Setting: hospital and home
Control	**Usual care:** education about self-management, exercise training, medication, and seeking health care when necessary. Each patient in this group got a pamphlet addressing self-management of COPD, including symptom recognition, smoking cessation, physical exercise, medication use, oxygen therapy, and nutrition. Contact information was printed in the pamphlet for a health-counselling service. Besides the intervention and usual care, both groups received prescriptions from physicians according to individual disease status
Outcomes	**Readmission (times):** baseline, 3, 6, 12 months and 12–24 months **Readmission (days):** baseline, 3, 6, 12 months and 12–24 months **Cardiovascular submaximal capacity:** 6 MWD (m) baseline, 3, 6, 12 months and 12–24 months **Dyspnoea:** mMRC baseline, 3, 6, 12 months and 12–24 months **Impact of disease:** COPD assessment test (CAT) baseline, 3, 6, 12 months and 12–24 months

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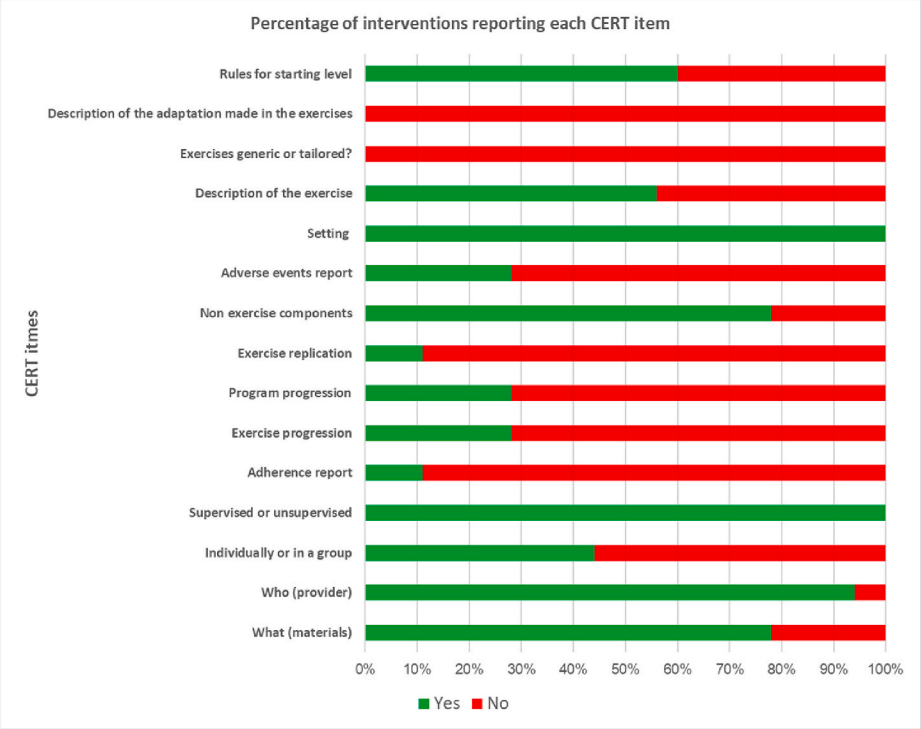
Zhang 2020	
Study characteristics	
Attrition	PR: at 3 months: lack of ability to do physical exercise: (n = 7), lack of interest to participate: (n = 5). At 6 months: died (n = 1), move to another city (n = 1). At 12 months: move to another city (n = 1). At 24 months: Lost follow up (n = 2), lack of interest to participate (n = 2) Control at 3 months: died (n = 1), lack of ability to do physical exercise: (n = 2), lack of interest to participate: (n = 4). At 6 months: died (n = 1), lack of interest to participate (n = 1). At 12 months: died (n = 1), lack of interest to participate (n = 1), lost follow up (n = 1). At 24 months: Lost follow up (n = 1), move another city (n = 1), lack of interest to participate (n = 1)
Notes	**Funding:** China medical board and national key research and development program of China (2018YFC1313600) **Another identifier:** ChiCTR-TRC-14005108

Risk of bias		
Bias	**Author's judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low	Randomization was achieved using block randomization
Allocation concealment (selection bias)	Low	Allocation was concealed through the statistical staff; recruitment staff had no access
Blinding of participants (performance bias): Objective outcomes (i.e., FEV1)	Low	Participants were not blinded, but assumed that these outcomes cannot be influenced participants
Blinding of participants (performance bias): Subjective outcomes (i.e., HRQoL)	High	Participants were not blinded
Blinding of personnel (performance bias): Objective outcomes (i.e., FEV1)	low	Personnel were not blinded, but assumed that these outcomes cannot be influenced by personnel
Blinding of personnel (performance bias): Subjective outcomes (i.e., HRQoL)	High	Personnel were not blinded
Blinding of outcome assessment (detection bias): Objective outcomes (i.e., FEV1)	Low	Outcome assessment performed by a blinded assessor
Blinding of outcome assessment (detection bias): Subjective outcomes (i.e., HRQoL)	Low	Outcome assessment performed by a blinded assessor
Incomplete outcome data (attrition bias)	Low	There was a similar rate of attrition in both treatment groups
Selective reporting (reporting bias)	High	Differences between the pre-specified outcomes in the registered protocol and the outcomes reported in the study

Appendix 6. Completeness reporting of exercise interventions in the pulmonary rehabilitation: total sample and type of pulmonary rehabilitation subgroup

Completeness of exercise interventions reporting in the pulmonary rehabilitation programs (n = 18).



Exercise + education/behavioural change (Exe + E/BC) (n = 9): This subgroup reported levels similar to those of the total sample (main text).

The reporting of supervision and non-exercise components was 100%, and description of the exercises (67%) was the highest across subgroups. None of the studies in this subgroup reported on adherence or exercise replication.

Exercise + education/behavioural change + psychological support (Exe + E/BC + Psycho) (n = 5): Overall, this subgroup had the lowest levels of reporting across subgroups, with four items with null reporting. Of note, provider, supervision, non-exercise components, and setting reached full reporting (100%).

Exercise only (Exe) (n = 4): The most reported items in this subgroup were what? supervision, and setting (full reporting), whereas non-exercise components, adaptations, and rules for starting levels had no reporting.

CERT item	Total sample (n = 18)	Exercise plus Education/behavioural change (n = 9)	Exercise plus Education/behavioural change plus psychological support (n = 5)	Exercise only (n = 4)
	n (%)	n (%)	n (%)	n (%)
What (materials)	14 (78%)	7 (78%)	3 (60%)	4 (100%)
Who (provider)	17 (94%)	9 (100%)	5 (100%)	3 (75%)
Individually or in a group	8 (44%)	4 (44%)	2 (40%)	2 (50%)
Supervised or unsupervised	18 (100%)	9 (100%)	5 (100%)	4 (100%)
Adherence report	2 (11%)	0 (0%)	1 (20%)	1 (25%)
Exercise progression	5 (28%)	2 (22%)	1 (20%)	2 (50%)
Program progression	5 (28%)	2 (22%)	0 (0%)	3 (75%)
Exercise replication	2 (11%)	0 (0%)	0 (0%)	2 (50%)
Non exercise components	14 (78%)	9 (100%)	5 (100%)	0 (0%)
Adverse events report	5 (28%)	2 (22%)	1 (20%)	2 (50%)
Setting	18 (100%)	9 (100%)	5 (100%)	4 (100%)
Description of the exercise	10 (56%)	6 (67%)	2 (40%)	2 (50%)
Exercises generic or tailored?	6 (33%)	1 (11%)	2 (40%)	3 (75%)
Description of the adaptation made in the exercises	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Rules for starting level	1 (6%)	1 (11%)	0 (0%)	0 (0%)

Appendix 7. Outcome measures, timepoints, and comparisons across included studies

Outcome and studies	PR mode	Time points (Weeks: wks)	Tool
Hospital readmissions			
Benzo, 2016 (n = 215)	PR (Exe + E/BC)	End: 4 wks Long-term: 12, 24, 36, 48 wks	Administrative data (e.g., clinical records)
Seymour, 2010 (n = 60)	PR (Exe + E/BC)	End: 12 wks	
Osadnik, 2014 (n = 92)	PR (Exe + E/BC)	Long-term: 24 wks	
Johnson-Warrington, 2016 (n = 78)	PR (Exe + E/BC + Psycho)	End: 12 wks	
Khosravi, 2020 (n = 60)	PR (Exe + E/BC + Psycho)	End: 4 wks Long-term: 12, 24 wks	
Zhang, 2020 (n = 208)	PR (Exe + E/BC + Psycho)	End: 12 wks Long-term: 24, 48, 96 wks	
Kjaergaard 2020 (n = 150)	Early PR vs late PR PR (Exe + E/BC)	Long-term: 48 wks	
HQRoL			
Benzo, 2016 (n = 215)	PR (Exe + E/BC)	Long-term: 24, 48 wks	CRQ
Borges, 2014 (n = 46)	PR (Exe + E/BC)	End: 1 wk Long-term: 4 wks	SGRQ
He, 2015 (n = 101)	PR (Exe + E/BC)	End: 2 wks	CRQ
López- López 2019 (n = 66)	PR (Exe + E/BC)	End: 1 wks Long-term: 12 wks	EQ-5D
Osadnik, 2014 (n = 92)	PR (Exe + E/BC)	End: 8 wks Long-term: 24 wks	SGRQ
Seymour, 2010 (n = 60)	PR (Exe + E/BC)	End: 12 wks	SGRQ/CRQ/EQ-5D
Deepak, 2014 (n = 60)	PR (Exe + E/BC + Psycho)	End: 12 wks	SGRQ
Johnson-Warrington, 2016 (n = 78)	PR (Exe + E/BC + Psycho)	End: 12 wks	CRQ
Song, 2014 (n = 20)	PR (Exe + E/BC + Psycho)	End: 8 wks	SGRQ
Knaut, 2014 (n = 26)	PR (Exe)	End: 4 wks	SGRQ
Liao, 2021 (n = 80)	PR (Exe)	End: 12 wks	SGRQ
López- López 2021 (n = 43)	PR (Exe)	End: 2 wks	EQ-5D
Puhan 2012 (n = 36)	**Early PR vs late** PR PR (Exe + E/BC)	Long-term: 24, 48, 72 wks	CRQ
Cardiovascular submaximal capacity			
Borges, 2014 (n = 46)	PR (Exe + E/BC)	End: 1 wk	6 MWD (m)
He, 2015 (n = 101)	PR (Exe + E/BC)	End: 2 wks	6 MWD (m)
Liao, 2015 (n = 62)	PR (Exe + E/BC)	End: 12 wks	6 MWD (m)
Osadnik, 2014 (n = 92)	PR (Exe + E/BC)	End: 8 wks Long-term: 24 wks	6 MWD (m)
Seymour, 2010 (n = 60)	PR (Exe + E/BC)	End: 12 wks	ISWT (mts) ESWT (sec)
Deepak, 2014 (n = 60)	PR (Exe + E/BC + Psycho)	End: 12 wks	6 MWD (m)

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Outcome and studies	PR mode	Time points (Weeks: wks)	Tool
Johnson-Warrington, 2016 (n = 78)	PR (Exe + E/BC + Psycho)	End: 12 wks	ISWT (mts) ESWT (sec)
Song, 2014 (n = 20)	PR (Exe + E/BC + Psycho)	End: 8 wks	6 MWD (m)
Zhang, 2020 (n = 208)	PR (Exe + E/BC + Psycho)	End: 12wks Long-term: 24, 48, 96 wks	6 MWD (m)
Knaut, 2014 (n = 26)	PR (Exe)	End: 4 wks	6 MWD (m)
Liao, 2021 (n = 80)	PR (Exe)	End: 12 wks	6 MWD (m)
Lu, 2020 (n = 82)	PR (Exe)	End: 8 wks	6 MWD (m)
Kjaergaard 2020 (n = 150)	**Early PR vs late PR** PR (Exe + E/BC)	End: 8 wks Long-term: 24 wks	ISWT (mts) ESWT (sec)
Physical activity levels			
Benzo, 2016 (n = 215)	PR (Exe + E/BC)	Long-term: 24 and 48 wks	Physical activity monitor
Mortality			
Benzo, 2016 (n = 215)	PR (Exe + E/BC)	Long-term: 48 wks	Administrative data
Osadnik, 2014 (n = 92)	PR (Exe + E/BC)	Long-term: up: 24 wks	Administrative data
Johnson-Warrington, 2016 (n = 78)	PR (Exe + E/BC + Psycho	Long-term: 12 wks	Administrative data
Kjaergaard 2020 (n = 150)	**Early PR vs late PR** PR (Exe + E/BC)	Long-term: 48 wks	Administrative data
Puhan 2012 (n = 36)	**Early PR vs late PR** PR (Exe + E/BC)	Long-term: 72 wks	Administrative data
Dyspnoea			
He, 2015 (n = 101)	PR (Exe + E/BC)	End: 2 wks	mMRC
Johnson-Warrington, 2016 (n = 78)	PR (Exe + E/BC)	End: 12 wks	CRQ
Liao, 2015 (n = 62)	PR (Exe + E/BC)	End: 12 wks	Modified Borg scale
Lopez, 2019 (n = 66)	PR (Exe + E/BC)	End: 1 wk Long-term: 12 wks	Modified Borg scale
Osadnik, 2014 (n = 92)	PR (Exe + E/BC)	End: 8 Long-term: 24 wks	mMRC
Deepak, 2014 (n = 60)	PR (Exe + E/BC + Psycho	End: 12 wks	mMRC
Zhang, 2020 (n = 208)	PR (Exe + E/BC + Psycho	End: 12 wks Long-term: 24, 48, 96 wks	mMRC
Knaut, 2014 (n = 26)	PR (Exe)	End: 4 wks	mMRC
Liao, 2021 (n = 80)	PR (Exe)	End: 12 wks	mMRC
Lu, 2020 (n = 82)	PR (Exe)	End: 8 wks	mMRC
Puhan 2012 (n = 36)	**Early PR vs late PR** PR (Exe + E/BC)	Long-term: 24, 48, 56 wks	mMRC
Re-exacerbation			
Seymour, 2010 (n = 60)	PR (Exe + E/BC)	Long-term: 12 wks	Administrative data
Osadnik, 2014 (n = 92)	PR (Exe + E/BC)	Long-term: 24 wks	Administrative data
Benzo, 2016 (n = 215)	PR (Exe + E/BC)	Long-term: 48 wks	Administrative data
Liao, 2021 (n = 80)	PR (Exe)	Long-term: 24 wks	Administrative data
Puhan 2012 (n = 36)	**Early PR vs late PR** PR (Exe + E/BC)	Long-term: 56 wks	Administrative data
Impact of disease			
He, 2015 (n = 101)	PR (Exe + E/BC)	End: 2 wks	COPD (CAT test)
Lu, 2020 (n = 82)	PR (Exe + E/BC)	End: 8 wks Long-term: 12 wks	COPD (CAT test)
Zhang, 2020 (n = 208)	PR (Exe + E/BC + Psycho	End: 8 wks Long-term: 24, 48, 96 wks	COPD (CAT test)
Kjaergaard 2020 (n = 150)	**Early PR vs late PR** PR (Exe + E/BC)	Long-term: 8, 24 wks	COPD (CAT test)

A: aerobic. BC: behaviour change. CAT: The COPD Assessment Test. Con: control. COPD: Chronic obstructive pulmonary disease. CRQ: Chronic Respiratory Disease Questionnaire. E: education. EQ-5D: EuroQoL-5D. ESWT: Endurance Shuttle Walk Test. Exe: exercise. Exp: experimental or intervention group. ISWT: Incremental Shuttle Walk Test. mMRC: Modified Medical Research Council. Psycho: psychotherapy. R: resistance. S: Stretching. SGRQ: St. George's Respiratory Questionnaire. wk (s): week(s). 6 MWD: Six-minute walk test.

Appendix 8. Risk of bias assessment

Selection bias (random sequence generation and allocation sequence concealment)

Fifteen (83%) studies described adequate methods of random sequence generation [33–35,37–43,46,47,49–51] while the remaining three (17%) studies were rated as unclear risk of selection bias as there was no further information [36,44,45]. Ten studies lacked information about allocation concealment and were assessed as being at unclear risk of bias for this domain [33,35,36,39,43–47,49]. In eight (44%) studies allocation concealment was clearly described and therefore these studies were judged at low risk of bias for this domain [34,37,38,40–42,50,51].

Performance bias (blinding of participants and personnel) and detection bias (blinding of outcome assessment)

Objective outcomes: We rated blinding of participants and personnel as low risk in fourteen (78%) studies [33–35,37–39,41–47,50] and as high risk in two (11%) studies [36,49]. Two studies (11%) did not report objective outcomes [40,51]. Blind assessment of objectives outcomes was reported in fifteen (83%) studies, and these were assessed as at low risk of bias [33–35,37–39,41–47,50]. He 2015 [36] did not blind outcome assessment (high risk of bias).

Subjective outcomes: All the studies reported subjective outcomes except for Khosravi 2020 [45]. Blinding of participants and personnel was not possible due to the nature of PR itself, so that the studies were judged to be at high risk of bias. Eight (44%) studies were at high risk of detection bias, as these included self-reported outcomes [33,35,36,38,42–44,46], while the remaining nine (50%) studies described adequate blinding of outcome assessment [34,37,39–41,47,49–51].

Attrition bias (incomplete outcome data)

We judged fifteen (83%) studies to be at low risk of attrition bias (low overall attrition) [33,34,36–40,42–44,46,47,49–51]. Two (11%) studies had high risk of bias (uneven attrition across groups) [35,41], whereas Khosravi 2020 [45] was rated as unclear risk due to incomplete information on the rates and reasons for participants being excluded from the analysis in each group.

Reporting bias (selective outcome reporting)

Eleven (44%) studies [33,34,36–38,40,42,46,47,50,51] had high risk of bias due to either not reporting all the outcomes as stated in their protocol, or missing data. Seven (39%) studies reported all the outcomes specified in the methodology and were judged at low risk of reporting bias [35,39,41,43–45,49].

Appendix 9. Summary of Findings table for all timepoints

Outcomes	Anticipated absolute effects*(95% CI)		Relative effect (95% CI)	N° of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with usual care	Risk with pulmonary rehabilitation				
Hospital readmissions (COPD-related): end of intervention (4–12 weeks), assessed with administrative data	239 per 1000	**134 per 1000** (86–206)	**RR 0.56** (0.36–0.86)	590 (5 RCTs)	⨁⨁⨁◯ Moderate[a]	Pulmonary rehabilitation probably reduces COPD-related hospital readmissions compared to usual care. One study (Kjærgaard 2020, n = 131) found evidence of no difference between early and late PR in readmissions throughout the 12month follow-up period (HR 0.79, 95% CI 0.47 to 1.23)
Hospital readmissions (COPD-related): long-term (12 weeks follow-up), assessed with administrative data	194 per 1000	**87 per 1000** (47–167)	**RR 0.45** (0.24–0.86)	270 (2 RCTs)	⨁⨁◯◯ Low[a,b]	Pulmonary rehabilitation may reduce COPD-related hospital readmissions compared to usual care at 12 weeks follow-up.
Hospital readmissions (COPD-related): long-term (24 weeks follow-up), assessed with administrative data	362 per 1000	**228 per 1000** (170–304)	**RR 0.63** (0.47–0.84)	455 (3 RCTs)	⨁⨁⨁◯ Moderate[a]	Pulmonary rehabilitation probably reduces COPD-related hospital readmissions compared to usual care at 24 weeks follow-up.
Hospital readmissions (COPD-related): long-term (36 weeks follow-up), assessed with administrative data	330 per 1000	**205 per 1000** (129–324)	**RR 0.62** (0.39–0.98)	214 (1 RCT)	⨁⨁◯◯ Low[a,b]	Pulmonary rehabilitation may reduce COPD-related hospital readmissions compared to usual care at 36 weeks follow-up.
Hospital readmissions (COPD-related): long-term (48 weeks follow-up), assessed with administrative data	556 per 1000	**389 per 1000** (322–472)	**RR 0.70** (0.58–0.85)	395 (2 RCTs)	⨁⨁◯◯ Low[a,b]	Pulmonary rehabilitation may reduce COPD-related hospital readmissions compared to usual care at 48 weeks follow-up.
Hospital readmissions (COPD-related): long-term (49–96 weeks follow-up), assessed with administrative data	775 per 1000	**519 per 1000** (411–651)	**RR 0.67** (0.53–0.84)	174 (1 RCT)	⨁⨁◯◯ Low[a,b]	Pulmonary rehabilitation may reduce COPD-related hospital readmissions compared to usual care at 48–96 weeks follow-up.
Health-related quality of life, HRQoL: end of intervention (median 3 weeks), assessed with: CRQ, SGRQ, and EQ-5D: higher scores mean improvement	SMD **0.78 SD higher** (0.35 higher to 1.22 higher)		–	416 (8 RCTs)	⨁◯◯◯ Very low[c,d]	The evidence is very uncertain about the effect of pulmonary rehabilitation on HRQoL compared to usual care. One study (Puhan 2012, n = 28) found evidence of no difference between early and late PR in any of the CRQ domains (dyspnea, fatigue, emotional function, and mastery) at 6-, 12-, or 18- months follow-up. All analyses were adjusted for baseline values of the outcome, age and FEV1.
HRQoL: long-term (4–12 weeks follow-up), assessed with SGRQ and EQ-5D: higher scores mean improvement	SMD **0.16 higher** (0.31 lower to 0.63 higher)		–	70 (2 RCTs)	⨁◯◯◯ Very low[a,e]	The evidence is very uncertain about the effect of pulmonary rehabilitation on HRQoL compared to usual care at 4–12 weeks follow-up.
HRQoL: long-term (24 weeks follow-up), assessed with CRQ and SGRQ: higher scores mean improvement	SMD **0.06 higher** (1.11 lower to 1.22 higher)		–	302 (2 RCTs)	⨁◯◯◯ Very low[a,d,e]	The evidence is very uncertain about the effect of pulmonary rehabilitation on HRQoL compared to usual care at 24 weeks follow-up.
HRQoL: long-term (48 weeks follow-up), assessed with CRQ: higher scores mean improvement	SMD **0.79 higher** (0.51 higher to 1.07 higher)		–	214 (1 RCT)	⨁◯◯◯ Very low[a,e]	The evidence is very uncertain about the effect of pulmonary rehabilitation on HRQoL compared to usual care at 48 weeks follow-up.
Cardiovascular submaximal capacity: end of intervention (median 8 weeks), assessed	SMD 0.73 higher (0.48 higher to 0.99 higher)		–	495 (8 RCTs)	⨁⨁⨁◯ Moderate[c]	Pulmonary rehabilitation probably results in a large increase in cardiovascular submaximal

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Outcomes	Anticipated absolute effects*(95% CI)		Relative effect (95% CI)	Nº of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with usual care	Risk with pulmonary rehabilitation				
with 6 MWT and ISWT: higher scores are better						capacity compared to usual care. One study (Kjærgaard 2020, n = 131), reported that participants in early PR gained 33.9 m more than those in the late PR group at 2 months, measured by ISWT (MD 33.9 m, 95% CI 4.2 to 63.7). This effect did not reach the MID of 47.5 m (68). No between-group differences were observed at 6 months (MD 17.7, 95% CI −13.3 to 48.7).
Cardiovascular submaximal capacity: long-term (24 weeks follow-up), assessed with 6 MWT: higher scores are better	The mean MD **45.7** cardiovascular **higher** submaximal (52.11 lower to capacity was **0**143.5 higher)		–	273 (2 RCTs)	⨁◯◯◯ Very low[a,d,e]	The evidence is very uncertain about the effect of pulmonary rehabilitation on cardiovascular submaximal capacity compared to usual care at 24 weeks follow-up.
Cardiovascular submaximal capacity: long-term (48 weeks follow-up), assessed with 6 MWT: higher scores are better	The mean MD **85.7** cardiovascular **higher** submaximal (69.13 higher to capacity was **0**102.27 higher)		–	181 (1 RCT)	⨁◯◯◯ Very low[b,f]	The evidence is very uncertain about the effect of pulmonary rehabilitation on cardiovascular submaximal capacity compared to usual care at 48 weeks follow-up.
Cardiovascular submaximal capacity: long-term (48–96 weeks follow-up), assessed with 6 MWT: higher scores are better	The mean MD **68.4** cardiovascular **higher** submaximal (52.11 higher to capacity was **0** 84.69 higher)		–	174 (1 RCT)	⨁◯◯◯ Very low[b,f]	The evidence is very uncertain about the effect of pulmonary rehabilitation on cardiovascular submaximal capacity compared to usual care at 48–96 weeks follow-up.
Physical activity levels: end of intervention (4 weeks), assessed with physical activity monitors	One study (Benzo 2016, n = 92) found evidence of no difference in any physical activity between the pulmonary rehabilitation and control arms at any time point (effect estimates were not reported).			(1 RCT)	⨁◯◯◯ Very low[a,b]	The evidence is uncertain about the effect of pulmonary rehabilitation on physical activity levels compared to usual care.
Mortality: end of intervention (12 weeks), assessed with administrative data	83 per 1000	**12 per 1000** (1–228)	**RR 0.15** (0.01–2.74)	71 (1 RCT)	⨁◯◯◯ Very low[e,f]	The evidence is uncertain about the effect of pulmonary rehabilitation on mortality compared to usual care. Two studies found evidence of no difference between early and late PR on mortality. In Kjærgaard 2020 (n = 131), one-year cumulative mortality rate in the early PR group (13%) did not differ from that in the late PR group (10%) (adjusted HR from the Cox proportional hazard model 1.04, 95% CI 0.36 to 3.01). Similarly, Puhan 2012 (n = 28) reported that 2 patients died in each group.
Mortality: long-term (24 weeks follow-up), assessed with administrative data	136 per 1000	**91 per 1000** (27–300)	**RR 0.67** (0.20–2.20)	88 (1 RCT)	⨁◯◯◯ Very low[e,f]	The evidence is uncertain about the effect of pulmonary rehabilitation on mortality compared to usual care at 24 weeks follow-up.
Mortality: long-term (48 weeks follow-up), assessed with administrative data	113 per 1000	**93 per 1000** (42–205)	**RR 0.82** (0.37–1.81)	214 (1 RCT)	⨁◯◯◯ Very low[a,e]	The evidence is uncertain about the effect of pulmonary rehabilitation on mortality compared to usual care at 48 weeks follow-up.
Dyspnea: end of intervention (median 8 weeks), assessed with mMRC (0–4, MCID 0.5): lower is better	MD **0.42 points lower** (0.57 lower to 0.27 lower) The mean dyspnea: end of intervention was **2.4** points		–	586 (7 RCTs)	⨁⨁◯◯ Low[c]	Pulmonary rehabilitation may reduce dyspnea slightly compared to usual care. One study (Puhan 2012, n = 28) assessed self-reported dyspnea with mMRC. Participants in the early PR group reported less dyspnea than those in late PR at 6-months (MD 0.83, 95% CI 0.10 to 1.57). These gains disappeared at 12- and 18-month follow-up (MD at 18 months 0.27, 95% CI –0.45 to 1.00).
Dyspnea: long-term (12–96 weeks), assessed with mMRC: lower is better	Not pooled		–	628 (2 RCTs)	⨁◯◯◯ Very low[b,c]	The evidence is uncertain about the effect of pulmonary rehabilitation on dyspnea compared to usual care at long-term follow up.

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Outcomes	Anticipated absolute effects*(95% CI)		Relative effect (95% CI)	Nº of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with usual care	Risk with pulmonary rehabilitation				
Re-exacerbations: 12–48 weeks follow-up, assessed with administrative data	The median re-exacerbations: 12–48 weeks follow-up was **0.9** number of re-exacerbations	MD **0.18 number of re-exacerbations lower** (0.22 lower to 0.14 lower)	–	372 (3 RCTs)	⨁⨁◯◯ Low[b,f]	Pulmonary rehabilitation may reduce the number of re-exacerbations slightly compared to usual care at 12–48 weeks follow-up. One study (Puhan 2012, n = 28) reported evidence of no difference between early and late PR in re-exacerbations over the 18-month follow-up (RR 0.96, 95% CI 0.84 to 1.94).
Impact of disease: end of intervention assessed with CAT (8 items, scale 0 to 40): lower is better	The mean impact of disease: end of intervention was **18** points	MD **3.94 points lower** (5.04 lower to 2.83 lower)	–	355 (3 RCTs)	⨁◯◯◯ Very low[a,b,g]	The evidence is uncertain about the effect of pulmonary rehabilitation on impact of disease compared to usual care. One study (Kjærgaard 2020, n = 131) found evidence of no difference between early and late PR in the CAT scores at either 2 month (MD −1.4, 95% CI −3.4 to 0.6) or 6 months (MD −1.4, 95% CI −3.5 to 0.6).
Impact of disease: long-term (12–24 weeks follow-up), assessed with CAT: lower is better	The mean impact of disease: long-term, 12–24 weeks follow-up was **18** points	MD **5.05 points lower** (6.95 lower to 3.15 lower)	–	257 (2 RCTs)	⨁⨁◯◯ Low[a,b]	Pulmonary rehabilitation may result in a large reduction in impact of disease at 12–24 weeks follow-up.
Impact of disease: long-term (48 weeks follow-up), assessed with CAT: lower is better	The mean impact of disease: long-term, 48 weeks follow-up was **22** points	MD **4.5 points lower** (5.62 lower to 3.38 lower)	–	181 (1 RCT)	⨁⨁◯◯ Low[a,b]	Pulmonary rehabilitation may result in a large reduction in impact of disease at 48 weeks follow-up
Impact of disease: long-term (49–96 weeks follow-up), assessed with CAT: lower is better	The mean impact of disease: long-term, 48–96 weeks follow-up was **22** points	MD **4.2 points lower** (5.5 lower to 2.9 lower)	–	174 (1 RCT)	⨁⨁◯◯ Low[a,b]	Pulmonary rehabilitation may result in a large reduction in impact of disease at 48–96 weeks follow-up

Population: individuals with acute exacerbation of chronic pulmonary disease (AECOPD).
Setting: clinic/hospital (44%) and mixed (clinic/hospital and home, 44%).
Intervention: pulmonary rehabilitation (PR).
Comparison: usual care.
*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CAT: COPD assessment test; **CI:** confidence interval; **COPD:** chronic obstructive pulmonary disease; **CRQ:** Chronic Respiratory Questionnaire; **HR:** hazard ratio; **HRQoL:** Health-related quality of life; **ISWT:** Incremental Shuttle Walk Test; **MCID:** Minimal clinically important difference; **MD:** mean difference; **mMRC:** Modified Medical Research Council Dyspnea Scale; **RR:** risk ratio; **SGRQ:** St George's Respiratory Questionnaire; **SMD:** standardized mean difference; **6MWT:** Six Minute Walk Test.
GRADE Working Group grades of evidence.
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect. **Very low certainty:** we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.
Explanations.
a. Issues of selection and reporting biases.
b. Small sample size.
c. Issues of selection, detection, attrition, and selective reporting biases.
d. High statistical heterogeneity (I^2=>80%).
e. Wide confidence intervals and small sample size.
f. Issues of blinding and selective reporting biases.
g. High statistical heterogeneity (I^2>60%).

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Further reading

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