

Pulmonary Rehabilitation for Mild COPD: A Systematic Review

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BACKGROUND: Pulmonary rehabilitation (PR) is effective in improving exercise capacity and health-related quality of life (HRQOL) in patients with moderate-to-very-severe COPD. Quadriiceps strength and HRQOL can be impaired in patients with mild COPD, therefore, patients at this grade may already benefit from PR. However, the impact of PR in patients with mild COPD remains unestablished. Thus, this systematic review assessed the impact of PR on exercise capacity, HRQOL, health-care resource use and lung function in patients with mild COPD. **METHODS:** The Web of Knowledge, EBSCO, MEDLINE, and SCOPUS databases were searched up to April 2013. Reviewers independently selected studies according to the eligibility criteria. **RESULTS:** Three studies with different designs (retrospective, one group pretest-posttest, and randomized controlled trial) were included. Out-patient PR programs were implemented in two studies, which included mainly aerobic, strength, and respiratory muscle training. The randomized controlled trial compared a PR home-based program, consisting of 6 months of walking and participating in ball games, with standard medical treatment. Significant improvements in exercise capacity (effect size [ES] 0.87–1.82) and HRQOL (ES 0.24–0.86) were found when comparing pretest-posttest data and when comparing PR with standard medical treatment. In one study, a significant decrease in hospitalization days was found (ES 0.38). No significant effects were observed on the number of emergency department visits (ES 0.32), number of hospitalizations (ES 0.219), or lung function (ES 0.198). **CONCLUSIONS:** Most of the PR programs had significant positive effects on exercise capacity and HRQOL in patients with mild COPD; however, their effects on health-care resource use and lung function were inconclusive. This systematic review suggests that patients with mild COPD may benefit from PR; however, insufficient evidence is still available. Studies with robust designs and with longer follow-up times should be conducted. *Key words:* pulmonary rehabilitation; mild chronic obstructive pulmonary disease; chronic obstructive pulmonary disease. [Respir Care 2014;59(4):588–594. © 2014 Daedalus Enterprises]

Introduction

COPD, independent of its severity, impacts the lives of patients and families as well as health-care systems.^{1,2}

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Therefore, it is imperative to plan health care for patients with COPD at all grades.

Pulmonary rehabilitation is defined as “an evidence-based, multidisciplinary, and comprehensive intervention for patients with chronic respiratory diseases who are symptomatic and often have decreased daily life activities”.³ This intervention is a recommended standard of care in the management of patients with COPD, and typically combines exercise training, education, and psychosocial sup-

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port.^{3,4} A meta-analysis conducted by Lacasse et al⁵ suggests that pulmonary rehabilitation is effective in relieving dyspnea and fatigue, and in improving patients' health-related quality of life (HRQOL). However, in this meta-analysis only studies including patients with moderate, severe, and very severe COPD were analyzed.

Recent evidence has shown that physical activity levels, quadriceps strength, and HRQOL can be already impaired in patients with mild COPD (best recorded FEV₁ ≥ 80% predicted),⁶⁻⁸ and these impairments worsen over time.⁸ Therefore, patients at this grade may also benefit from pulmonary rehabilitation programs. A systematic review⁹ about the influence of physical activity on mild-to-moderate COPD showed that physical activity significantly improved patients' physical fitness; however, no statistically significant beneficial effects were seen on HRQOL or dyspnea. Furthermore, the great proportion of patients analyzed in this review had moderate COPD. Therefore, the impact of pulmonary rehabilitation programs on patients with mild COPD remains unestablished.

Thus, this systematic review aimed to assess the impact of pulmonary rehabilitation on exercise capacity, HRQOL, health-care resource use, and lung function in patients with mild COPD.

Methods

Search Strategy

A systematic literature search was conducted between January and April 2013 on the following databases: Web of Knowledge (1970–2013), EBSCO (1974–2013), MEDLINE (1948–2013), and SCOPUS (1960–2013). The search terms used were organized using the PICO (Population, Intervention, Comparison, and Outcome) framework,¹⁰ the definition of Comparison (C) was omitted as it was aimed at finding a range of study designs, as follows: "COPD" OR "chronic obstructive pulmonary disease" OR "chronic bronchitis" OR "emphysema" OR "mild COPD" OR "early COPD" OR "GOLD 1" OR "GOLD I" AND "pulmonary rehabilitation" OR "respiratory rehabilitation" OR "exercise training" OR "physical activity" OR "exercise" AND "exercise capacity" OR "health-related quality of life" OR "health-care resource use" OR "lung function" OR "FEV₁". The reference lists of the included studies were hand searched for other potentially eligible studies. This systematic review was reported according to the PRISMA Group statement for preferred reporting items for systematic reviews and meta-analyses.¹¹

Selection Criteria

According to the PICO framework, studies were included if they met the following inclusion criteria.

1. Patients with mild COPD (FEV₁ ≥ 80% predicted⁶)
2. Pulmonary rehabilitation program (in-patient, out-patient, or home-based care) of at least 4 weeks^{4,5} that included exercise training with or without any form of education and/or psychological support
3. Comparison: Standard medical treatment or none
4. Outcomes: at least one of the following: exercise capacity, HRQOL, health-care resource use, and lung function

Studies were excluded if they did not include patients with mild COPD (studies with a subgroup of patients were retained in the analysis) and if they were review articles, abstracts of communications or meetings, conference proceedings papers, case reports, editorials, commentary to articles, study protocols, or unpublished papers. Papers without abstracts or written in languages other than English, Portuguese, and Spanish were also excluded.

Screening of Studies

The authors independently reviewed the titles, abstracts, and key words of every record. If the information given in the title, abstract, and/or key words suggested that the study might fit the inclusion criteria of the systematic review, the full article was retrieved for further assessment. From the full articles, the decision to exclude a study was based on the agreement of both authors. Disagreements were solved by reaching a consensus. Studies that did not fulfill the selection criteria of the systematic review were excluded. Once a study was excluded, a record of the article, including the reason for exclusion, was retained.

Quality Assessment

The methodological quality of each included study was independently assessed by the two authors, based on the checklist created by Downs and Black.¹² This checklist assesses the quality of both randomized and non-randomized studies of health-care interventions, and it is composed of 27 questions split into 5 sections: reporting, external validity, internal validity–bias, internal validity–confounding, and power.¹² According to previous systematic reviews,^{13,14} the scoring for question 27 dealing with statistical power was simplified to a choice of awarding either 1 point or 0 points, depending on whether there was sufficient power to detect a clinically important effect. The scores of the Downs and Black¹² checklist can be grouped into four quality levels: ≤ 14; poor; 15–19, fair; 20–25, good; and 26–28, excellent.^{13,14}

Data Extraction

The authors independently extracted data from the included studies. Disagreements were discussed until con-

sensus was reached. Data from the articles were extracted in a structured table format according to the following topics: first author's last name and year of publication, study design, participants' characteristics, type of intervention(s) or comparator(s) (if there were any), outcome measures used, and quantitative findings.

Data Analysis

To determine the consistency of the quality assessment performed by the 2 authors, an inter-observer agreement analysis using Cohen's kappa was performed. The value of Cohen's kappa ranges from 0 to 1, and can be categorized as slight (0.0–0.20), fair (0.21–0.40), moderate (0.41–0.60), substantial (0.61–0.80), or almost perfect (≥ 0.81) agreement.¹⁵ This statistical analysis was performed using PASW Statistics (version 18.0, SPSS, Chicago, Illinois).

Because of the different designs and outcome measures used in the selected studies a meta-analysis was not possible to conduct. To analyze the effects of pulmonary rehabilitation on mild COPD, the effect sizes were computed for the outcomes of interest. The effect sizes were interpreted as low (0.20), medium (0.50), and high (0.80) effect magnitudes.¹⁶ All quantitative data analyzes were performed using the software Comprehensive Meta-Analysis version 2 (Biostat, Englewood, New Jersey).¹⁷

Results

Study Selection

The databases search identified 5,728 records. After the removal of duplicate records, 4,766 records were screened for relevant content. During the title, abstract, and keyword screening, 4,745 articles were excluded. The full text of 21 potentially relevant articles was assessed, and 11 articles were excluded for the following reasons: (1) patients with mild COPD were not included ($n = 8$); (2) the effect of pulmonary rehabilitation programs was not assessed with the outcome measures of interest ($n = 1$); (3) quantitative data were not provided ($n = 1$); and (4) the study was not written in English, Portuguese, or Spanish ($n = 1$). Ten studies were retained. Eight of these studies included patients with mild COPD; however, results were not presented by COPD grade. The corresponding authors were contacted to provide data on patients with mild COPD. Only Liu et al¹⁸ made available the requested data, and therefore their study was included. The other 7 studies were excluded. Therefore, 3 original articles were included. The search for relevant articles within the reference list of the selected articles did not retrieve any further study (Fig. 1).

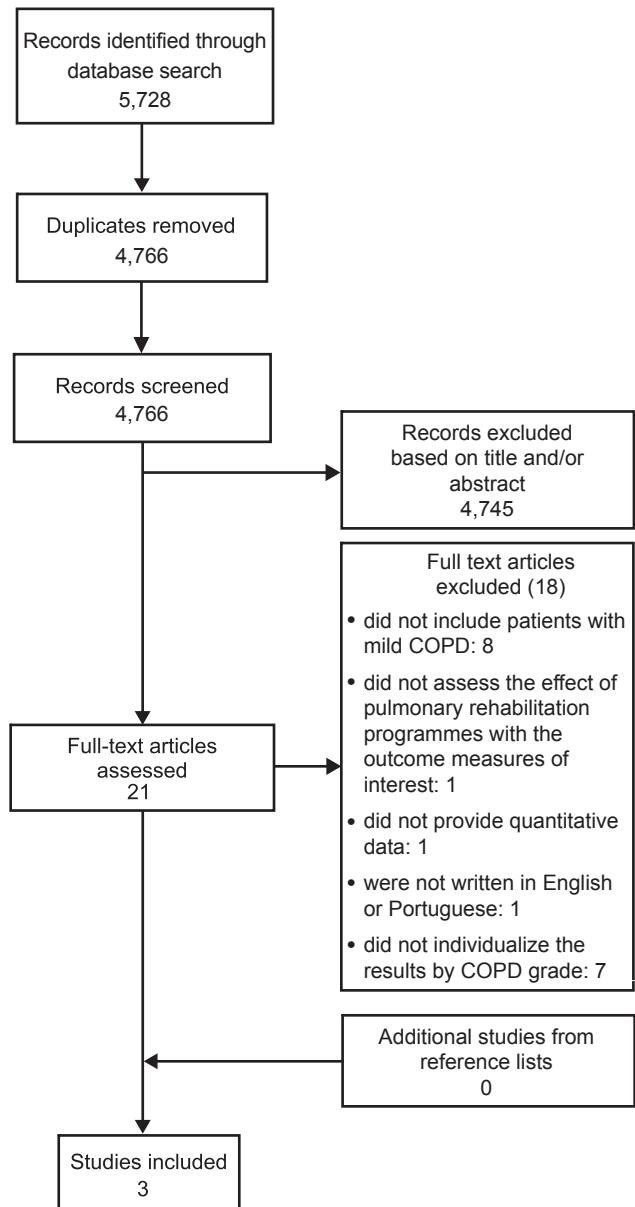


Fig. 1. Flowchart of included studies.

Quality Assessment

The articles included in this review scored 14–20 on the Downs and Black¹² scale with a mean of 16.7 ± 3.1 (Table 1). The agreement between the 2 authors was substantial (kappa = 0.686, 95% CI 0.507–0.842, $P = .001$). Results indicate that the quality of the studies varied among poor,¹⁹ fair,²⁰ and good.¹⁸ The 3 studies scored particularly poorly in the following items: description of adverse events, sample representativeness, patient and assessor blinding, adjustment for confounding factors in the analysis, and power.

Table 1. Quality Assessment Using the Downs and Black¹² Scale

Studies	Reporting										External Validity			Internal Validity										Power	Total		
														Bias					Confounding								
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23			24	25
Golmohammadi et al ¹⁹	1	1	1	1	0	1	1	0	1	1	0	0	1	0	0	1	0	1	1	1	0	0	0	0	1	0	14
Riario-Sforza et al ²⁰	1	1	1	1	1	1	1	0	0	1	0	0	1	0	0	1	1	1	1	1	1	1	0	0	0	0	16
Liu et al ¹⁸	1	1	1	1	1	1	1	0	1	1	0	0	0	0	1	1	1	1	1	1	1	1	1	1	0	1	20

Study Characteristics

Study characteristics are presented in Table 2. The included studies had different designs that included retrospective,¹⁹ one-group pretest-posttest,²⁰ and randomized controlled.¹⁸ The 3 studies recruited a total of 100 patients receiving specialized care. Golmohammadi et al¹⁹ did not provide data on age and gender ratio of the 31 patients with mild COPD. In the other 2 studies, age ranged from 41 to 83 y, and the number of male patients included were approximately double the number of female patients (47:22).

The pulmonary rehabilitation programs implemented by Golmohammadi et al¹⁹ and by Riario-Sforza et al²⁰ were both out-patient programs, with duration between 6 and 8 weeks and frequency between 2 and 3 sessions a week. The exercise training sessions lasted between 60 and 90 min, and included mainly aerobic training, strength training, and respiratory muscle training. Both programs included an educational component. Liu et al¹⁸ implemented a home-based pulmonary rehabilitation program, consisting of 1 week of pursed-lip breathing and aerobic training under the supervision of health professionals followed by 6 months of peer-led walking and participation in ball games for 60 min twice a week. This study also had a control group that received standard medical treatment, consisting of health education and recommendations to exercise by themselves.

Synthesis of the Results

Exercise Capacity

Exercise capacity was assessed in 2 studies by the 6-min walk distance.^{18,20} Significant improvements in exercise capacity were found when comparing pretest-posttest data (effect size (ES) 0.87)²⁰ and when comparing pulmonary rehabilitation with standard medical treatment (ES 1.82).¹⁸

HRQOL

HRQOL was measured in 2 studies using distinct instruments, that is, the St George Respiratory Questionnaire (SGRQ)¹⁹ and the Zhongshan COPD questionnaire.¹⁸ A small improvement in SGRQ symptoms (ES 0.34) and

activity (ES 0.49) scores, and a medium improvement in SGRQ impact score (ES 0.66) were found after pulmonary rehabilitation.¹⁹ A significant improvement in HRQOL (Zhongshan COPD questionnaire total score) favored the pulmonary rehabilitation group (ES 0.86).¹⁸ The Zhongshan COPD questionnaire also provided information on 4 subscales of HRQOL: activity of daily living, social participation, depression, and anxiety. Improvements in anxiety (ES 0.85), activity of daily living (ES 0.47), and depression (ES 0.46) favored the pulmonary rehabilitation group. Social participation did not change significantly in any of the groups (ES 0.24).

Health Care Resource Use

The number of hospitalization days were decreased after pulmonary rehabilitation (ES 0.38).¹⁹ The number of emergency department visits also decreased (ES 0.32).¹⁹ The number of hospitalizations in the pulmonary rehabilitation group after 6 months was not significantly different from that of the control group (ES 0.22).¹⁸

Lung Function

Pulmonary rehabilitation had no significant effect on lung function (ES 0.2).¹⁸

Discussion

Most of the pulmonary rehabilitation programs implemented in the 3 studies analyzed had significant positive effects on the exercise capacity and HRQOL of patients with mild COPD. However, the effects of these programs on health-care resource use and lung function were inconclusive.

Two studies^{18,20} analyzed the impact of pulmonary rehabilitation on exercise capacity with the 6-min walk test, and a statistically significant improvement was found. The improvement in the distance walked after pulmonary rehabilitation was ~37 m in one study¹⁸ and 63 m in the other.²⁰ Since the minimally important difference for the 6-min walk test is expected to be between 25 and 35 m in patients with moderate and severe COPD,^{21,22} we can hypothesize that in both studies the clinically important effect was achieved. Nevertheless, this has to be interpreted

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Table 2. Impact of Pulmonary Rehabilitation Programs in Patients With Mild COPD

Studies	Design	Participants	Intervention	Outcome Measures	Findings
Golmohammadi et al ¹⁹ (2004)	Retrospective	31 patients with mild COPD	Setting: out-patient Duration: 6 or 8 wk Frequency: 2 or 3 times/wk Exercise training Duration: 90 min Components: breathing exercises, endurance training, upper extremity strength training, inspiratory muscle training Education: adaptations in activities of daily living, relaxation techniques, nutritional counseling, psychosocial support.	SGRQ symptoms SGRQ activity SGRQ impact Emergency department visits Hospitalization days	SGRQ symptoms: Pre 48.3; Post 42.3; <i>P</i> = .07 SGRQ activity: Pre 55.3; Post 48.7; <i>P</i> = .01 SGRQ impact: Pre 30.8; Post 23; <i>P</i> = .01 Emergency department visits: Pre 41.2 ± 13; Post 13.6 ± 7.9; <i>P</i> = .085 Hospitalization days: Pre 123.9 ± 75; Post 12.9 ± 12.9; <i>P</i> = .043
Riario-Sforza et al ²⁰ (2009)	One group Pretest-posttest	37 patients with mild COPD 24 M, 13 F 64.6 ± 9.8 (41–83) y	Setting: out-patient Duration: 6 wk Frequency: 2 times/wk Exercise training Duration: 90 min Components: warm-up, endurance training, strength training of the arm, shoulder and trunk muscle groups; respiratory muscle training. Education	6MWD	6MWD: Pre 355 ± 63m; Post 418 ± 78m
Liu et al ¹⁸ (2012)	RCT	Experimental group 15 patients with mild COPD 10 M, 5 F 56.4 ± 8.2 (46–72) y Control group 17 patients with mild COPD 13 M, 4 F 58.9 ± 6 (46–67) y	Experimental group Setting: Home-based Duration: 6 mo Frequency: 2 times/wk Exercise training Duration: 60 min Components: walking and participation in ball games Education: pursed-lip breathing, aerobic exercises. Control group Standard medical treatment: health education, advised to continue exercising.	6MWD Zhongshan COPD questionnaire: ADL Anxiety Depression Social participation Total score Hospitalizations due to AECOPD FEV ₁	Experimental group 6MWD: Pre 407.4 ± 16.9; Post 444.6 ± 22.5; <i>P</i> = .001 Zhongshan COPD questionnaire ADLs: Pre 22 ± 3.1; Post 19.5 ± 2.7; <i>P</i> = .001 Anxiety: Pre 13.9 ± 2.4; Post 12.3 ± 1.7; <i>P</i> = .002 Depression: Pre 12.3 ± 1.7; Post 11.1 ± 1.4; <i>P</i> = .011 Social participation: Pre 12.7 ± 2.5; Post 12.7 ± 1.9; <i>P</i> = .892 Total Score: Pre 60.8 ± 5.4; Post 55.7 ± 4.8; <i>P</i> = .001 Hospitalizations: Pre 1.2 ± 0.4; Post 1 ± 0.4; <i>P</i> = .082 FEV ₁ : Pre 87.2 ± 4.1% predicted; Post 87.5 ± 3.7% predicted; <i>P</i> = .442 Control group 6MWD: Pre 403.1 ± 21; Post 401.6 ± 26.7; <i>P</i> = .756 Zhongshan COPD questionnaire ADL: Pre 21.3 ± 3.2; Post 20.8 ± 2.8; <i>P</i> = .324 Anxiety: Pre 14 ± 2.9; Post 14.35 ± 2.9; <i>P</i> = .496 Depression: Pre 12.1 ± 2.0; Post 11.9 ± 2; <i>P</i> = .699 Social participation: Pre 12.7 ± 2.5; Post 12.2 ± 2.3; <i>P</i> = .245 Total score: Pre 60.1 ± 4; Post 59.2 ± 3.3; <i>P</i> = .440 Hospitalizations: Pre 1.3 ± 0.6; Post 1.1 ± 0.5; <i>P</i> = .083 FEV ₁ : Pre 87.7 ± 5% predicted; Post 86.7 ± 4.3% predicted; <i>P</i> = .221

Data are presented as mean ± SD.
SGRQ= St George Respiratory Questionnaire
M= male
F= female
RCT= randomized controlled trial
6MWD= 6-min walk distance
ADLs= activities of daily living
AECOPD= acute exacerbation of COPD
Pre= pretest
Post= post-test

with caution, as the minimally important difference for the 6-min walk distance in patients with mild COPD has not been established.

The HRQOL was assessed using 2 instruments: the SGRQ¹⁹ and the Zhongshan COPD questionnaire.²³ In the study of Golmohammadi et al,¹⁹ the improvements were all statistically significant, with the exception of the SGRQ symptoms domain. Lacasse et al⁵ and Puhan et al,²⁴ reviewing the benefits of pulmonary rehabilitation in patients with COPD, also verified that the results of the SGRQ symptoms domain were not statistically significant. These findings suggest that this SGRQ domain may be the less responsive to pulmonary rehabilitation programs. In the study of Liu et al¹⁸ statistically significant improvements in HRQOL favored pulmonary rehabilitation in comparison with the standard medical treatment. The pulmonary rehabilitation programs implemented in the studies by Liu et al¹⁸ and Golmohammadi et al¹⁹ improved the HRQOL of patients with mild COPD. Because physical activity levels and HRQOL can be impaired in patients with mild COPD,^{7,8} and the limited evidence available shows that these health domains can be improved with pulmonary rehabilitation programs, more studies with robust study designs are needed to establish these benefits at an early stage of the disease.

Prevention of respiratory exacerbations is one of the major goals of COPD management.²⁴ The effects of pulmonary rehabilitation on the number of exacerbations was not directly assessed in any of the included studies, instead health-care resource use was examined. Pulmonary rehabilitation did not have a statistically significant effect on the number of hospitalizations when compared with standard medical treatment.¹⁸ A statistically significant decrease in the number of emergency department visits after pulmonary rehabilitation was also not found; however, a significant decrease in the number of hospitalization days was observed.¹⁹ In patients with mild COPD, the role of pulmonary rehabilitation in preventing exacerbations and its severity remains unclear. This is mainly due to the lack of studies, but probably is also due to the implementation of pulmonary rehabilitation programs with distinct training regimens and therefore different effects of dosage.²⁵

Pulmonary rehabilitation had no effect on lung function.¹⁸ This was expected because previous studies^{26,27} have shown that no changes in lung function were observed in patients with moderate-to-very-severe COPD after conventional pulmonary rehabilitation programs. However, a matched controlled trial performed in patients with moderate and severe COPD shows that after 3 y of out-patient pulmonary rehabilitation the decline in FEV₁ was significantly lower in the pulmonary rehabilitation group compared with the control group (standard treatment).²⁸ In patients with mild COPD, it is still unknown whether in the long run pulmonary rehabilitation can delay the de-

cline of lung function and therefore disease progression. This needs to be investigated in well-designed longitudinal studies.

This review has important limitations that need to be considered. First, only 3 studies with small sample sizes were included, and the oldest study was published in 2004. This may be because of the difficulty in recruiting patients with mild COPD, because most of them are asymptomatic and do not look for medical assistance. Additionally, this may be a result of the relatively new interest in pulmonary rehabilitation research in mild COPD and of publication bias (studies with statistically significant results are more likely to be published than those with nonsignificant results). Second, a number of well-designed studies including patients with mild COPD were excluded as results were not individualized by COPD grade. The inclusion of these studies would probably consolidate the findings of this review. Third, all studies had different methodological designs and implemented different pulmonary rehabilitation programs regarding the setting, duration, and components. This might be due to the absence of specific guidelines for pulmonary rehabilitation programs for patients with mild COPD. Further research from randomized controlled trials is therefore needed to define the most appropriate specificities of pulmonary rehabilitation for this population. Fourth, mainly the short-term effects of pulmonary rehabilitation were assessed. Only Golmohammadi et al¹⁹ analyzed the benefits of pulmonary rehabilitation in terms of emergency department visits and hospitalization days 1 y after pulmonary rehabilitation. However, the long-term benefits of pulmonary rehabilitation in terms of exercise capacity and HRQOL for patients with mild COPD remains uncertain. Therefore, long-term studies are also required.

Conclusions

Most of the pulmonary rehabilitation programs implemented in the included studies had significant positive effects on the exercise capacity and HRQOL of patients with mild COPD. Nevertheless, the effects of these programs on health-care resource use and lung function were inconclusive. This systematic review suggests that patients with mild COPD may benefit from pulmonary rehabilitation as part of the management of their disease; however, insufficient evidence is still available. Further research with robust study designs and longer follow-up times is urgently needed to inform guidelines for pulmonary rehabilitation in patients with mild COPD.

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