Medical Policy

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Title: Outpatient Pulmonary Rehabilitation

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Populations	Interventions	Comparators	Outcomes
Individuals: • With moderate-to-severe chronic obstructive pulmonary disease	Interventions of interest are: • Single course of outpatient pulmonary rehabilitation	Comparators of interest are: • Usual care without outpatient pulmonary rehabilitation	Relevant outcomes include: • Symptoms • Functional outcomes • Quality of life
Individuals: • With idiopathic pulmonary fibrosis	Interventions of interest are: • Single course of outpatient pulmonary rehabilitation	Comparators of interest are: • Usual care without outpatient pulmonary rehabilitation	Relevant outcomes include: • Symptoms • Functional outcomes • Quality of life
Individuals: • With bronchiectasis	Interventions of interest are:	Comparators of interest are:	Relevant outcomes include: • Symptoms

Populations	Interventions	Comparators	Outcomes
	• Single course of outpatient pulmonary rehabilitation	• Usual care without outpatient pulmonary rehabilitation	• Functional outcomes • Quality of life
Individuals: • With scheduled lung surgery for volume reduction, transplantation, or resection	Interventions of interest are: • Single course of preoperative outpatient pulmonary rehabilitation	Comparators of interest are: • Usual care without outpatient pulmonary rehabilitation	Relevant outcomes include: • Symptoms • Functional outcomes • Quality of life
Individuals: • Who have had lung volume reduction surgery	Interventions of interest are: • Single course of outpatient pulmonary rehabilitation	Comparators of interest are: • Usual care without outpatient pulmonary rehabilitation	Relevant outcomes include: • Symptoms • Functional outcomes • Quality of life
Individuals: • Who have had lung transplantation	Interventions of interest are: • Single course of outpatient pulmonary rehabilitation	Comparators of interest are: • Usual care without outpatient pulmonary rehabilitation	Relevant outcomes include: • Symptoms • Functional outcomes • Quality of life
Individuals: • Who have had lung cancer resection	Interventions of interest are: • Single course of outpatient pulmonary rehabilitation	Comparators of interest are: • Usual care without outpatient pulmonary rehabilitation	Relevant outcomes include: • Symptoms • Functional outcomes • Quality of life
Individuals: • Who have had an initial course of pulmonary rehabilitation	Interventions of interest are: • Repeat or maintenance outpatient pulmonary rehabilitation	Comparators of interest are: • Usual care without repeat or maintenance outpatient pulmonary rehabilitation	Relevant outcomes include: • Symptoms • Functional outcomes • Quality of life
Individuals: • With an indication for outpatient pulmonary rehabilitation	Interventions of interest are: • Single course of home-based pulmonary rehabilitation	Comparators of interest are: • Single course of ambulatory care–based pulmonary rehabilitation	Relevant outcomes include: • Symptoms • Functional outcomes • Quality of life

DESCRIPTION

Pulmonary rehabilitation (PR) is a multidisciplinary approach to reducing symptoms and improving quality of life in patients with compromised lung function. PR programs generally include a patient assessment followed by therapeutic interventions including exercise training, education, and behavior change.

Objective

The objective of this evidence review is to evaluate whether the use of pulmonary rehabilitation in patients with various lung conditions improves net health outcomes.

Background

In 2013, the American Thoracic Society (ATS) and the European Respiratory Society (ERS) defined pulmonary rehabilitation (PR) as a "comprehensive intervention based on a thorough patient assessment followed by patient-tailored therapies that include, but are not limited to exercise training, education, and behavior change."[1] PR programs are intended to improve patient functioning and quality of life. Most research has focused on patients with chronic obstructive pulmonary disease (COPD), although there has been some interest in patients with asthma, cystic fibrosis, or bronchiectasis.

Pulmonary Rehabilitation is also routinely offered to patients awaiting lung transplantation and lung volume reduction surgery. PR before lung surgery may stabilize or improve patients' exercise

tolerance, teach patients techniques that will help them recover after the procedure, and allow healthcare providers to identify individuals who might be suboptimal surgical candidates due to non-compliance, poor health, or other reasons.

POLICY

A. A single course of pulmonary rehabilitation in the outpatient ambulatory care setting may be considered **medically necessary** for treatment of chronic pulmonary disease for patients with moderate-to-severe disease who are experiencing disabling symptoms and significantly diminished quality of life despite optimal medical management.

B. A single course of pulmonary rehabilitation may be considered **medically necessary** in an outpatient ambulatory care setting as a preoperative conditioning component:
   1. for those considered appropriate candidates for lung volume reduction surgery; or
   2. for lung transplantation

C. Pulmonary rehabilitation programs are considered **medically necessary** following lung transplantation.

D. Pulmonary rehabilitation programs are considered **experimental / investigational** following other types of lung surgery, included but not limited to lung volume reduction surgery and surgical resection of lung cancer.

E. Multiple courses of pulmonary rehabilitation are considered **experimental / investigational**, either as maintenance therapy in patients:
   1. who initially respond; or
   2. who fail to respond; or
   3. whose response to an initial rehabilitation program has diminished over time

F. Home-based pulmonary rehabilitation programs are considered **experimental / investigational**.

G. Pulmonary rehabilitation programs are considered **experimental / investigational** in all other situations.

Policy Guidelines

1. A pulmonary rehabilitation outpatient program is a comprehensive program that generally includes team assessment, patient training, psychosocial intervention, exercise training, and follow-up.
2. Team assessment includes input from a physician, respiratory care practitioner, nurse, and psychologist, among others.
3. Patient training includes breathing retraining, bronchial hygiene, medications, and proper nutrition.
4. Psychosocial intervention addresses support system and dependency issues.
5. Exercise training includes strengthening and conditioning and may include stair climbing, inspiratory muscle training, treadmill walking, cycle training (with or without ergometer), and supported and unsupported arm exercise training. Exercise conditioning is an essential component of pulmonary rehabilitation. Education in disease management techniques

without exercise conditioning does not improve health outcomes of patients who have chronic obstructive pulmonary disease.
6. Follow-up to a comprehensive outpatient pulmonary rehabilitation program may include supervised home exercise conditioning.
7. Candidates for pulmonary rehabilitation should be medically stable and not limited by another serious or unstable medical condition. Contraindications to pulmonary rehabilitation include severe psychiatric disturbance (e.g., dementia, organic brain syndrome), and significant or unstable medical conditions (e.g., heart failure, acute cor pulmonale, substance abuse, significant liver dysfunction, metastatic cancer, disabling stroke).
8. Cessation of smoking for at least 3 months is required, immediately prior to the rehabilitation program.
9. For BCBSKS members, services provided in connection with an approved outpatient pulmonary rehabilitation program may be considered reasonable and necessary for up to 18 sessions in a single 6-week period, consideration may be made on a case-by-case basis for exceptions. Coverage for continued participation would be allowed only on a case-by-case basis with exit criteria taken into consideration.
10. Services must be furnished in a hospital outpatient setting. All settings must have a physician immediately available and accessible for medical consultations and emergencies at all times.

BENEFIT APPLICATION
Pulmonary rehabilitation must be performed in a facility approved by Blue Cross and Blue Shield of Kansas.

RATIONALE
The most recent literature update was performed through January 29, 2021.

Evidence reviews assess the clinical evidence to determine whether the use of a technology improves the net health outcome. Broadly defined, health outcomes are length of life, quality of life, and ability to function including benefits and harms. Every clinical condition has specific outcomes that are important to patients and to managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of a technology, 2 domains are examined: the relevance and the quality and credibility. To be relevant, studies must represent 1 or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. RCTs are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice. The following is a summary of the key literature to date.

This evidence review focuses on comprehensive, multidisciplinary programs that include an exercise component plus other modalities. Where there is a lack of evidence on multidisciplinary pulmonary rehabilitation programs, interventions that are strictly exercise will be considered. In this regard, exercise constitutes the primary intervention that improves outcomes and that, if exercise alone improves outcomes, then it would be expected that exercise plus other modalities would improve outcomes to the same degree or greater.

CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Clinical Context and Therapy Purpose

The purpose of a single course of outpatient pulmonary rehabilitation is to provide a treatment option that is an alternative to or an improvement on existing therapies, such as usual care without outpatient pulmonary rehabilitation, in patients with moderate-to-severe chronic obstructive pulmonary disease (COPD).

The question addressed in this evidence review is: Does the use of pulmonary rehabilitation in patients with moderate-to-severe COPD improve net health outcomes?

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest are individuals with moderate-to-severe COPD.

Interventions

The therapy being considered is a single course of outpatient pulmonary rehabilitation. Pulmonary rehabilitation programs include a patient assessment followed by therapeutic interventions including exercise training, education, and behavior change.

Patients with moderate-to-severe COPD are actively managed by pulmonologists and primary care providers in an outpatient clinical setting.

Comparators

Comparators of interest include usual care without outpatient pulmonary rehabilitation. Treatment includes physical exercise, diaphragmatic breathing, oxygen therapy, bronchodilators, and steroid regimens.

Patients with moderate-to-severe COPD are actively managed by pulmonologists and primary care providers in an outpatient clinical setting.

Outcomes

The general outcomes of interest are symptoms, functional outcomes, and quality of life.

The existing literature evaluating a single course of outpatient pulmonary rehabilitation as a treatment for moderate-to-severe COPD has varying lengths of follow up. While studies described below all reported at least 1 outcome of interest, at least 6 months duration of follow-up is desirable to fully assess outcomes.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

1. To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs.
2. In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
3. To assess longer term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
4. Studies with duplicative or overlapping populations were excluded.

Review of Evidence

Systematic Reviews

Numerous RCTs and several systematic reviews of RCTs have been published. Most recently, Puhan et al (2016) published a Cochrane review that evaluated pulmonary rehabilitation programs for patients who had an exacerbation of COPD.[2,] To be included, the rehabilitation program had to begin within 3 weeks of initiating exacerbation treatment and had to include physical exercise. Twenty trials (total N=1477 participants) met inclusion criteria. Rehabilitation was outpatient in 6 trials, inpatient in 12 trials, both inpatient and outpatient in 1 trial, and home-based in 1 trial. In a pooled analysis of 8 trials, there was a statistically significant reduction in the primary outcome (rate of hospital admissions) for pulmonary rehabilitation compared with usual care (odds ratio=0.44; 95% confidence interval [CI], 0.21 to 0.91). Several secondary outcomes also favored the pulmonary rehabilitation group. In a pooled analysis of 13 trials, there was a significantly greater improvement from baseline in the 6-minute walk distance in the pulmonary rehabilitation groups (mean difference [MD]=62.4 meters; 95% CI, 38.5 to 86.3 meters). Moreover, a pooled analysis of health-related quality of life found significantly greater improvement after pulmonary rehabilitation versus control (MD=-7.80; 95% CI, -12.1 to -3.5). However, in a pooled analysis of 6 trials, there was no statistically significant difference between groups in mortality rate (odds ratio=0.68; 95% CI, 0.28 to 1.67). Trials had a mean duration of only 12 months, which may not be long enough to ascertain a difference in mortality rates. Participants in all the studies included in this analysis could not be blinded and this may have introduced bias for outcomes to some degree. Also, some studies did not assess the outcomes of those participants who dropped out of the pulmonary rehabilitation or were lost to follow-up.

McCarthy et al (2015) published a Cochrane review that included RCTs assessing the effect of outpatient or inpatient pulmonary rehabilitation on functional outcomes and/or disease-specific quality of life in patients with COPD[3,]. Pulmonary rehabilitation programs had to be at least 4 weeks in duration and include exercise therapy with or without education and/or psychological support. Sixty-five RCTs (total N=3822 participants) met inclusion criteria. COPD severity was not specifically addressed by Cochrane reviewers, but article titles suggest a focus on patients with moderate-to-severe COPD. In pooled analyses, there was a statistically significantly greater improvement in all outcomes in pulmonary rehabilitation groups than in usual care groups. Also, between-group differences on key outcomes were clinically significant. For example, on all 4 important domains of the validated Chronic Respiratory Questionnaire (dyspnea, fatigue, emotional function, and mastery) the effect was larger than the accepted minimal clinically important difference of 0.5 units.

Also, the between-group difference in maximal exercise capacity exceeded the minimal clinically important difference of 4 watts and the between-group difference in 6 minute walk distance (a mean difference of 43.93 meters) was considered clinically significant.

Rugbjerg et al (2015) published a systematic review that identified 4 RCTs (total N=489 participants).[4,] Inspection of the trial designs for the 4 RCTs indicated that none evaluated a comprehensive pulmonary rehabilitation program in patients who met criteria for mild COPD. Rather than being comprehensive pulmonary rehabilitation programs, all interventions were exercise-based. One intervention included an educational component, and another used a qigong intervention, which included breathing and meditation in addition to exercise. Also, none of the RCTs enrolled a patient population with only mild COPD. Roman et al (2013)[5,] and Gottlieb et al (2011)[6,] included patients with moderate COPD, Liu et al (2012)[7,] included patients with mild-to-moderate COPD, and van Wetering et al (2010)[8,] included patients with moderate-to-severe COPD. Conclusions cannot be drawn about the efficacy of pulmonary rehabilitation in patients with mild COPD from this systematic review.

Tables 1 and 2 summarize the characteristics and results of Puhan et al (2016)[2,] and McCarthy et al (2015)[3,]. Rugbjerg et al (2015)[4,] is not included in the table because of study overlap.

Table 1. Systematic Review Characteristics

Study	Dates	Trials	Participants	Intervention	N (Range)	Design	Duration
Puhan (2016)[2,]	Up to Mar 2010*; Mar 2010 to Oct 2015	20	PR patients (N=1477) that met inclusion criteria and had an exacerbation of COPD	Inpatient and outpatient PR	1477 (26-389)	RCT	3-18 mo
McCarthy (2015) [3,]	Up to Jul 2004; Jul 2004 to Mar 2014	65	Patients (N=3822) mean ages ranging from 31.3 to 74.1 years; in-patient, out-patient, community-based or home-based rehabilitation program of ≥ 4 weeks on continuous oxygen; those with clinical diagnosis of moderate-to-severe COPD and best recorded FEV1 <0.7; exercise therapy/intervention (rehabilitation) vs. standard care (control)	Outpatient or inpatient PR ≥4 wk that includes exercise therapy +/- education and psychological support (range of PR exercise program = 7 wk to 6 mo)	3822 (12-350)	RCT	≥24 mo

COPD: chronic obstructive pulmonary disease; FEV1: forced expiratory volume in 1 second; mMRC: Modified Medical Research Council Dyspnea Scale; PR: pulmonary rehabilitation; RCT: randomized controlled trial.
* A previous review included information from studies up to this date.

Table 2. Systematic Review Results

Study	Rate of Hospital Readmission	6-minute Walk Distance
Puhan (2016)[2,]	n=810; 8 trials	n=819; 13 trials
N=1477		
PR compared with usual care	Relative effect (95% CI) OR=0.44 (0.21, 0.91)	Change from baseline, random effects (95% CI) MD= 62.38 m (38.45, 86.31 m)
McCarthy (2015)[3,]	NR	n=1879; 38 studies
N=3822		
PR compared with usual care	NR	Random, effect size (95% CI) MD=43.93 (32.64, 55.21)

CI: confidence interval; MD: mean difference; NR: not reported; OR: odds ratio; PR: pulmonary rehabilitation.

Section Summary: Chronic Obstructive Pulmonary Disease
Multiple meta-analyses of RCTs have, for the most part, found improved outcomes (i.e., functional ability, quality of life) in patients with moderate-to-severe COPD who have had a comprehensive pulmonary rehabilitation program in the outpatient setting. There is limited evidence on the efficacy of repeated and/or prolonged pulmonary rehabilitation programs, and that evidence is mixed on whether these programs impact additional health outcome benefits.

IDIOPATHIC PULMONARY FIBROSIS

Clinical Context and Therapy Purpose
The purpose of a single course of outpatient pulmonary rehabilitation is to provide a treatment option that is an alternative to or an improvement on existing therapies, such as usual care without outpatient pulmonary rehabilitation, in patients with idiopathic pulmonary fibrosis.

The question addressed in this evidence review is: Does outpatient pulmonary rehabilitation improve net health outcomes in patients with idiopathic pulmonary fibrosis?

The following PICO was used to select literature to inform this review.

Populations
The relevant population of interest are individuals with idiopathic pulmonary fibrosis.

Interventions
The therapy being considered is a single course of outpatient pulmonary rehabilitation. Pulmonary rehabilitation programs include a patient assessment followed by therapeutic interventions including exercise training, education, and behavior change.

Patients with idiopathic pulmonary fibrosis are actively managed by pulmonologists and primary care providers in an outpatient clinical setting.

Comparators
Comparators of interest include usual care without outpatient pulmonary rehabilitation. Treatment includes physical exercise, diaphragmatic breathing, oxygen therapy, and medication therapy.

Patients with idiopathic pulmonary fibrosis are actively managed by pulmonologists and primary care providers in an outpatient clinical setting.

Outcomes

The general outcomes of interest are symptoms, functional outcomes, and quality of life.

The existing literature evaluating a single course of outpatient pulmonary rehabilitation as a treatment for idiopathic pulmonary fibrosis has varying lengths of follow up. While studies described below all reported at least 1 outcome of interest, longer follow-up was necessary to fully observe outcomes. Therefore, at least 3 months of follow-up is considered necessary to demonstrate efficacy.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

1. To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs.
2. In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
3. To assess longer term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
4. Studies with duplicative or overlapping populations were excluded.

Review of Evidence

Systematic Reviews

The meta-analysis by Yu et al (2019) evaluated pulmonary rehabilitation for exercise tolerance and quality of life for patients with idiopathic pulmonary fibrosis.[9,] They analyzed results of 5 RCTs (N=190 participants). In addition to better 6 minute walk distance and Saint George's Respiratory Questionnaire results with pulmonary rehabilitation than with standard treatment (see Table 4), forced vital capacity was significantly higher for the pulmonary rehabilitation group (MD=3.69; 95% CI, 0.16 to 7.23; p=.04). However, pulmonary rehabilitation had no significant effect on lung diffusing capacity determined by the single-breath technique (MD=3.02; 95% CI, -0.38 to 6.42; p=.08). The results of this study suggest the benefits of pulmonary rehabilitation lie in its effect on quality of life, and it may slow the decline of lung function in patients with idiopathic pulmonary fibrosis. Cheng et al (2018) looked at 4 RCTs and evaluated results in terms of short-term (9-12 weeks) and long-term (6-12 months) outcomes.[10,] They found significant benefits in the short term as measured by 6 minute walk distance and Saint George's Respiratory Questionnaire, but the benefits did not last in the long term.

Table 3. Systematic Review Characteristics

Study	Dates	Trials	Participants	N (Range)	Design	Duration
Yu (2019)[9,]	2008-2016	5 (7 articles)	Patients with diagnosed IPF	190 (21-32)	RCTs	10 wk-11 mo

Cheng (2018)[10,]	2008-2017	4 (5 articles)	Patients with diagnosed IPF	142 (21-61)	RCTs	9 wk-11 mo

IPF: idiopathic pulmonary fibrosis; RCT: randomized controlled trial.

Table 4. Systematic Review Results

Study	**6-minute Walk Distance**		**SGRQ**	
Yu (2019)[9,]	5 trials;		3 trials;	
MD, fixed effects	48.60		-7.87	
95% CI	29.03 to 68.18		-11.44 to -4.30	
P value	<0.001		0.031	
Cheng (2018)[10,]	4 trials	2 trials	3 trials	2 trials
	Short-term (9-12 wk)	**Long-term (6-12 mo)**	**Short-term (9-12 wk)**	**Long-term (6-12 mo)**
WMD, random effects	38.38	17.02	-8.40	-3.45
95% CI	4.64 to 72.12	-26.87 to 60.81	-11.4 to -5.36	-8.55 to 1.64
P value	<0.05	0.43	<0.001	0.088

CI: confidence interval; MD: mean difference; SGRQ: Saint George's Respiratory Questionnaire (lower score is better); WMD: weighted mean difference.

Section Summary: Idiopathic Pulmonary Fibrosis
Two small systematic reviews of RCTs have evaluated pulmonary rehabilitation programs for patients with idiopathic pulmonary fibrosis. Significant differences favoring pulmonary rehabilitation over standard care were seen in 6 minute walk distance in the short term. At 3 months postintervention outcomes did not differ between groups.

BRONCHIECTASIS

Clinical Context and Therapy Purpose
The purpose of a single course of outpatient pulmonary rehabilitation is to provide a treatment option that is an alternative to or an improvement on existing therapies, such as usual care without outpatient pulmonary rehabilitation, in patients with bronchiectasis.

The question addressed in this evidence review is: Does the use of pulmonary rehabilitation in patients with bronchiectasis improve net health outcomes?

The following PICO was used to select literature to inform this review.

Populations
The relevant population of interest are individuals with bronchiectasis.

Interventions

The therapy being considered is a single course of outpatient pulmonary rehabilitation. Pulmonary rehabilitation programs include a patient assessment followed by therapeutic interventions including exercise training, education, and behavior change.

Patients with bronchiectasis are actively managed by pulmonologists and primary care providers in an outpatient clinical setting.

Comparators

Comparators of interest include usual care without outpatient pulmonary rehabilitation. Treatment includes physical exercise, diaphragmatic breathing, oxygen therapy, and medication therapy.

Patients with bronchiectasis are actively managed by pulmonologists and primary care providers in an outpatient clinical setting.

Outcomes

The general outcomes of interest are symptoms, functional outcomes, and quality of life.

The existing literature evaluating a single course of outpatient pulmonary rehabilitation as a treatment for bronchiectasis has varying lengths of follow up. While studies described below all reported at least 1 outcome of interest, 3-6 months duration of follow-up is desirable to fully assess outcomes.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

1. To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs.
2. In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
3. To assess longer term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
4. Studies with duplicative or overlapping populations were excluded.

Review of Evidence

Systematic Review

Lee et al (2017) published a systematic review of RCTs on pulmonary rehabilitation in patients with non-cystic fibrosis bronchiectasis.[11,] Reviewers identified 4 RCTs. They selected studies of exercise-only interventions as well as exercise combined with education and/or another intervention. The control intervention had to be something other than exercise-based. A pooled analysis of 3 RCTs immediately after an 8-week intervention found significantly greater incremental shuttle walk distance in the intervention compared with the control group (MD=66.6; 95% CI, 51.8 to 81.7). A pooled analysis of 2 trials found significantly greater improvement in the Saint George's Respiratory Questionnaire score postintervention (MD = -4.65; 95% CI, -6.70 to -2.60). There was no significant difference postintervention on the Leicester Cough Questionnaire (total) scores. Reviewers did not conduct meta-analyses beyond the immediate postintervention period.

Section Summary: Bronchiectasis
A systematic review of RCTs on pulmonary rehabilitation for patients with bronchiectasis found that some, but not all, outcomes improved more with pulmonary rehabilitation than with a non-exercise control condition immediately postintervention. Limited observational data would suggest that outcomes in patients with other respiratory conditions may benefit, but likely not as much as COPD patients.

PREOPERATIVE PULMONARY REHABILITATION PROGRAMS

Clinical Context and Therapy Purpose
The purpose of a single course of preoperative outpatient pulmonary rehabilitation is to provide a treatment option that is an alternative to or an improvement on existing therapies, such as usual care without outpatient pulmonary rehabilitation, in patients with scheduled lung surgery for volume reduction, transplantation, or resection.

The question addressed in this evidence review is: Does the use of pulmonary rehabilitation improve net health outcomes in patients undergoing lung surgery for volume reduction, transplantation, or resection?

The following PICO was used to select literature to inform this review.

Populations
The relevant population of interest are individuals with scheduled lung surgery for volume reduction, transplantation, or resection.

Interventions
The therapy being considered is a single course of preoperative outpatient pulmonary rehabilitation. Pulmonary rehabilitation programs include a patient assessment followed by therapeutic interventions including exercise training, education, and behavior change.

Patients with scheduled lung surgery for volume reduction, transplantation, or resection are actively managed by pulmonologists, general surgeons and thoracic surgeons.

Comparators
Comparators of interest include usual care without outpatient pulmonary rehabilitation. Treatment includes physical exercise, diaphragmatic breathing, oxygen therapy and medication therapy.

Patients with scheduled lung surgery for volume reduction, transplantation, or resection are actively managed by pulmonologists, general surgeons and thoracic surgeons.

Outcomes
The general outcomes of interest are symptoms, functional outcomes, and quality of life.

The existing literature evaluating a single course of preoperative outpatient pulmonary rehabilitation as a treatment for scheduled lung surgery for volume reduction, transplantation, or resection has varying lengths of follow up. While studies described below all reported at least 1 outcome of interest, 3- 6 months duration follow-up are desirable to assess outcomes.

Study Selection Criteria
Methodologically credible studies were selected using the following principles:

1. To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs.
2. In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
3. To assess longer term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
4. Studies with duplicative or overlapping populations were excluded.

Review of Evidence

Lung Volume Reduction Surgery
Pulmonary rehabilitation prior to lung volume reduction surgery represents a distinct subset of patients with COPD, and the National Emphysema Treatment Trial requires all candidates to undergo a vigorous course of pulmonary rehabilitation. The final National Emphysema Treatment Trial results supported the treatment effectiveness in a subset of patients with COPD.[12,]

Lung Transplantation
A systematic review of the literature on pulmonary rehabilitation for lung transplant candidates was published by Hoffman et al (2017). [13,] Interventions had to include exercise training but did not have to be part of a comprehensive pulmonary rehabilitation program and could have taken place in the inpatient or outpatient setting. Reviewers identified 6 studies (2 RCTs and 4 case series). Both RCTs evaluated the impact of exercise (not comprehensive pulmonary rehabilitation) on outcomes; additionally, 1 was conducted in the inpatient setting, and it included only 9 patients. Conclusions on the impact of a comprehensive pulmonary rehabilitation program before lung transplantation on health outcomes cannot be drawn from this systematic review.

LUNG CANCER RESECTION

Randomized Controlled Trials
Several small RCTs have evaluated preoperative pulmonary rehabilitation for patients undergoing lung cancer resection. Morano et al (2013) conducted a single-blind study in Brazil.[14,] Patients with non-small-cell lung cancer eligible for lung resection were randomized to 4 weeks of an exercise-only pulmonary rehabilitation program (5 sessions per week) or chest physical therapy; there were 12 patients in each group. All patients in the pulmonary rehabilitation group and 9 of 12 in the chest physical therapy group subsequently underwent surgery (the other 3 patients had inoperable disease). Several short-term postoperative outcomes were assessed. Patients in the pulmonary rehabilitation group spent significantly fewer days in the hospital (mean, 7.8 days) than patients in the chest physical therapy group (mean, 12.2 days; p=0.04). Also, patients in the pulmonary rehabilitation group spent fewer days with chest tubes (mean, 4.5 days) than the physical therapy group (mean, 7.4 days; p=0.03). The trial did not assess longer term functional outcomes after surgery.

Benzo et al (2011) conducted 2 small exploratory RCTs evaluating pulmonary rehabilitation before lung cancer resection.[15,] Eligibility criteria included having moderate-to-severe COPD and being scheduled for lung cancer resection either by open thoracotomy or by video-assisted

thoracoscopy. The first trial had poor recruitment, enrolling only 9 patients. The second study enrolled 19 patients into a 10-session, preoperative pulmonary rehabilitation program (n=10) or usual care (n=9). Mean number of days in the hospital was 6.3 in the pulmonary rehabilitation group and 11.0 in the control group (p=0.058). Three (33%) patients in the pulmonary rehabilitation group and 5 (63%) patients in the control group experienced postoperative pulmonary complications (p=0.23). The trial sample size was likely too small to detect statistically or clinically significant differences between groups. Trialists recommended conducting a larger multicenter randomized trial in this population.

Table 5. Summary of Key RCT Characteristics

Study	Countries	Sites	Dates	Participants	Interventions	
					Active	*Comparator*
Morano (2013)[14,]	Brazil	1	Mar 2008 to Mar 2011	Patients undergoing lung cancer resection and who have non-small cell lung cancer resection by open thoracotomy (or video-assisted); and previous pulmonary disease, interstitial lung disease, or obstructive airway disease, with impaired respiratory function by spirometry (N=24)	PR: Strength/endurance training + education; 5 sessions/wk for 4 wk (20 sessions) (n=12)	CPT breathing exercises + education; 5 sessions/wk for 4 wk (20 sessions) (n=12)
Benzo (2011)[15,]	US	2	NR	Patients who require lung cancer resection by open thoracotomy (or video-assisted); moderate-to-severe COPD (N=19)	PR: 10 preoperative PR sessions involving customized protocol with nonstandard components (exercise prescription based on self-efficacy, inspiratory muscle training; slow breathing) (n=10)	Usual care (n=9)

COPD: chronic obstructive pulmonary disease; CPT: chest physical therapy; NR: not reported; PR: pulmonary rehabilitation; RCT: randomized controlled trial;.

Table 6. Summary of Key RCT Results

Study	Hospital Stay at 4 Weeks, mean (SD)	ICU Stay (days) at 4 Weeks	Postoperative Hospitalizations
Morano (2013)[14,]	N=31 patients at t=0; 24 in analysis; 21 in final analysis	N=31 patients at t=0; 24 in analysis; 21 in final analysis	N
PR (exercise) n=12	7.8 (4.8)	2 (2-3)[a]	NR
CPT (control) n=9	12.2 (3.6)	2 (2-4.5)[a]	NR
P-value	0.04	0.20	NR

Study	Hospital Stay at 4 Weeks, mean (SD)	ICU Stay (days) at 4 Weeks	Postoperative Hospitalizations
Benzo (2011)[15,]	N=17	N=17	NR
PR arm	6.3 (3.0)	0.6 (1.9)[b]	NR
Usual care	11.0 (6.3)	1.7 (3.1)[b]	NR
P-value	0.06	0.39	NR

CI: confidence interval; CPT: chest physical therapy; ICU: intensive care unit; NR: not reported; PR: pulmonary rehabilitation; RCT: randomized controlled trial; SD: standard deviation.
[a] Median (25th-75th percentile).
[b] Mean (SD).

The purpose of the limitations tables (see Tables 7 and 8) is to display notable limitations identified in each study. This information is synthesized as a summary of the body of evidence following each table and provides the conclusions on the sufficiency of evidence supporting the position statement.

Table 7. Study Relevance Limitations

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Follow-Up[e]
Morano (2013)[14,]				3. No CONSORT reporting of harms was addressed	1. Short duration of follow-up (4-weeks)
Benzo (2011)[15,]	4. Recruitment not met.				

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use.
[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4. Not the intervention of interest.
[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.
[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical significant difference not supported.
[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

Table 8. Study Design and Conduct Limitations

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Follow-Up[d]	Power[e]	Statistical[f]
Morano (2013)[14,]	4.Inadequate control for selection bias: the			1. High loss to follow-	1. Power is	

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Follow-Up[d]	Power[e]	Statistical[f]
	participants were not evenly randomized			up or missing data	not reported	
Benzo (2011)[15,]						

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
a Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.
b Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.
c Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.
d Follow-Up key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).
e Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.
f Statistical key: 1. Intervention is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Intervention is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated.

Observational Study

Bradley et al (2013), in a nonrandomized comparative study, evaluated an outpatient-based pulmonary rehabilitation intervention in 58 lung cancer patients who were candidates for surgery.[16,] This United Kingdom based study also evaluated a comparison group of 305 patients, also surgical candidates, who received usual care. Patients in the 2 groups were matched by age, lung function, comorbidities, and type of surgery. In a within-group analysis, there was a statistically significant 20-meter improvement in 6 minute walk distance in the intervention group before and after participation in a 4-session presurgical pulmonary rehabilitation program. In between-group analyses, there were no statistically significant differences between the intervention and comparisons groups in clinical outcomes such as postoperative pulmonary complications, readmissions, and mortality after surgery.

Section Summary: Preoperative Pulmonary Rehabilitation Programs

The National Emphysema Treatment Trial has recommended administering pulmonary rehabilitation before lung volume reduction surgery, which is considered the standard of care before lung volume reduction surgery and lung transplantation. However, there is a lack of large RCTs comparing pulmonary rehabilitation with no pulmonary rehabilitation for preoperative candidates undergoing lung volume reduction surgery, lung transplantation, or lung cancer resection. The available studies evaluated exercise programs and comprehensive pulmonary rehabilitation. Also, the few small RCTs and observational studies have reported on short-term outcomes and have found inconsistent evidence of benefit even on these outcomes.

LUNG VOLUME REDUCTION SURGERY POSTOPERATIVE PULMONARY REHABILITATION PROGRAMS

Clinical Context and Therapy Purpose

The purpose of a single course of outpatient pulmonary rehabilitation is to provide a treatment option that is an alternative to or an improvement on existing therapies, such as usual care

without outpatient pulmonary rehabilitation, in patients who have had lung volume reduction surgery.

The question addressed in this evidence review is: Does the use of postoperative pulmonary rehabilitation improve net health outcomes in patients who have undergone lung volume reduction surgery?

The following PICO was used to select literature to inform this review.

Populations
The relevant population of interest are individuals who have had lung volume reduction surgery.

Interventions
The therapy being considered is a single course of outpatient pulmonary rehabilitation. Pulmonary rehabilitation programs include a patient assessment followed by therapeutic interventions including exercise training, education, and behavior change.

Patients who have had lung volume reduction surgery are actively managed by pulmonologists, general surgeons and thoracic surgeons in an outpatient clinical setting.

Comparators
Comparators of interest include usual care without outpatient pulmonary rehabilitation. Treatment includes physical exercise, diaphragmatic breathing, oxygen therapy and medication therapy.

Patients who have had lung volume rehabilitation surgery are actively managed by pulmonologists, general surgeons and thoracic surgeons in an outpatient clinical setting.

Outcomes
The general outcomes of interest are symptoms, functional outcomes, and quality of life.

The existing literature evaluating a single course of outpatient pulmonary rehabilitation as a treatment for individuals who have had lung volume rehabilitation surgery has varying lengths of follow up. While studies described below all reported at least 1 outcome of interest, 3-6 months duration of follow-up is desirable to assess outcomes.

Study Selection Criteria
Methodologically credible studies were selected using the following principles:

1. To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs.
2. In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
3. To assess longer term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
4. Studies with duplicative or overlapping populations were excluded.

Review of Evidence

No RCTs evaluating comprehensive pulmonary rehabilitation programs after lung volume reduction surgery were identified. Bering et al (2009) reported on a case series involving 49 patients with severe emphysema who participated in a pulmonary rehabilitation program after lung volume reduction surgery.[17,] Patients underwent lung volume reduction surgery at a single center and had not received pulmonary rehabilitation at that institution pre-surgery. After hospital discharge, patients underwent an outpatient comprehensive pulmonary rehabilitation program for 4 hours a day, 5 days a week for 2 weeks. The program included a multidisciplinary team with a variety of components, including dietary, physical therapy, physical exercise, psychosocial, occupational therapy, and respiratory therapy. The primary outcome was health-related quality of life measured by the 36-Item Short-Form Health Survey. Compared with pre-lung volume reduction surgery scores, significantly better scores were achieved on the Physical Component Summary and Mental Component Summary at both time 2 (3-6 months post-lung volume reduction surgery) and time 3 (12-18 months post-lung volume reduction surgery). Study limitations included no comparison with patients who had lung volume reduction surgery and no pulmonary reduction, and the difficulty disentangling the impact of lung volume reduction surgery from that of pulmonary rehabilitation on outcomes. Moreover, patients had not received pulmonary rehabilitation before lung volume reduction surgery, so the treatment effects of presurgery versus post surgery lung volume reduction surgery could not be determined.

Section Summary: Lung Volume Reduction Surgery Postoperative Pulmonary Rehabilitation Programs

No comparative studies have evaluated pulmonary rehabilitation programs after lung volume reduction surgery. One case series evaluated a comprehensive pulmonary rehabilitation program after lung volume reduction surgery in 49 patients who had not received preoperative pulmonary rehabilitation. Health-related quality of life was higher at 3 to 6 months and 12 to 18 months post-surgery. The study did not provide data on patients who underwent lung volume reduction surgery and who did not have postoperative pulmonary rehabilitation or on patients who had preoperative pulmonary rehabilitation.

LUNG TRANSPLANTATION POSTOPERATIVE PULMONARY REHABILITATION PROGRAMS

Clinical Context and Therapy Purpose

The purpose of a single course of outpatient pulmonary rehabilitation is to provide a treatment option that is an alternative to or an improvement on existing therapies, such as usual care without outpatient pulmonary rehabilitation, in patients who have had lung transplantation.

The question addressed in this evidence review is: Does the use of pulmonary rehabilitation improve net health outcomes in patients who have undergone lung transplantation?

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest are individuals who have had lung transplantation.

Interventions

The therapy being considered is a single course of outpatient pulmonary rehabilitation. Pulmonary rehabilitation programs include a patient assessment followed by therapeutic interventions including exercise training, education, and behavior change.

Patients who have had lung transplantation are actively managed by pulmonologists and primary care providers in an outpatient clinical setting.

Comparators

Comparators of interest include usual care without outpatient pulmonary rehabilitation. Treatment includes physical exercise, diaphragmatic breathing, oxygen therapy, and medical therapy.

Patients who have had lung transplantation are actively managed by pulmonologists and primary care providers in an outpatient clinical setting.

Outcomes

The general outcomes of interest are symptoms, functional outcomes, and quality of life.

The existing literature evaluating a single course of outpatient pulmonary rehabilitation as a treatment for individuals who have had lung transplantation has varying lengths of follow up. While studies described below all reported at least 1 outcome of interest, 3-6 months duration of follow-up is desirable to assess outcomes.

Methodologically credible studies were selected using the following principles:

1. To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs.
2. In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
3. To assess longer term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
4. Studies with duplicative or overlapping populations were excluded.

Review of Evidence

Exercise training after lung transplantation is reported in the literature but not necessarily provided in comprehensive pulmonary rehabilitation programs. Wickerson et al (2010) published a systematic review of the available literature in which the researcher had evaluated any exercise intervention in conjunction with lung transplantation. Seven studies (a cohort made of RCTs, controlled trials, and prospective cohorts) met the inclusion criteria, including 2 randomized controlled trials targeting lumbar bone mineral density. Also included in the review were uncontrolled studies that reported improvement in functional status as a byproduct of an exercise-program intervention.[18,]

Randomized Controlled Trials

Langer et al (2012) conducted an RCT in the United Kingdom that examined activity-related outcomes in lung transplant recipients after exercise training.[19,] The trial included 40 patients

who underwent single- or double-lung transplantation and had an uncomplicated postoperative period. Following hospital discharge, patients were randomized to a supervised exercise program 3 times a week for 3 months (n=21) or to usual care with instructions to exercise (n=19). Patients in both groups had 6 individual counseling sessions in the 6 months post discharge. Six patients dropped out of the trial, 3 in each group. The primary outcome was daily walking time, assessed by activity monitors. At the end of the 3-month intervention and 1-year post discharge, mean walking times were significantly longer in the intervention group. At 1 year, the exercise group walked a mean of 85 minutes per day while the control group walked a mean of 54 minutes per day (p=0.006). Other outcomes related to daily physical activity were reported as secondary outcomes and some, but not all, significantly favored the intervention group. Mean 6 minute walk distance at 1 year was 86% of predicted in the exercise group and 74% of predicted in the control group (p=0.002). The trial had a relatively small sample size and may have been underpowered to detect clinically meaningful differences between groups on secondary outcomes.

Fuller et al (2017) published an RCT reporting on the impact of short (7-week) versus long (14-week) rehabilitation programs for patients who underwent lung transplantation.[20,] The primary outcome was change in the 6-minute walk test. Secondary outcomes included the strength of the quadriceps and hamstring muscles (as measured by an isokinetic dynamometer), and quality of life (as measured by the 36-Item Short-Form Health Survey). In both the 7- and 14-week rehabilitation groups, participants increased their 6-minute walk test (mean improvement in 7-week group, 202 meters vs. 14-week group, 149 meters). At 6 months after transplantation, the mean difference between groups was 59.3 meters, favoring the 7-week group (95% CI, 12.9 to 131.6 meters). The increases in strength in quadriceps and hamstring muscles in both groups did not differ statistically. The 36-Item Short-Form Health Survey summary scores of the domains of physical health and mental health both increased over time with no significant difference between groups at any time point.

Table 9. Summary of Key RCT Characteristics

Trial	Countries	Sites	Participants	Interventions	
				Active	*Comparator*
Langer (2012)[19,]	UK	1	Patients aged 40-65 y who had undergone a single or bilateral LTX with no postoperative complications (N=40)	Exercise program (3 x/wk for 3 mo) (n=21)	Usual care with added instruction to exercise (n=19)
Fuller (2017)[20,]	US	1	Post-LTX patients aged ≥18 years (N=66; 33 women; mean age=51+/-13 y) who had undergone either single LTX or bilateral LTX (N=66)	Longer-duration (14-wk) rehabilitation program after LTX	Shorter (7-wk) rehabilitation program after LTX

LTX: lung transplantation; RCT: randomized controlled trial; U.K. United Kingdom.

Table 10. Summary of Key RCT Results

Study	Daily Walking Time	Mean Improvement in 6MWD From Baseline (SD)	6MWD Difference Between Groups
Langer (2012) [19,]			
N=40	N=34 (final)	NR	NR
3-mo exercise program (baseline/final)=21/18	Mean=85 min/day at 1 y (SD=27 min)	NR	NR
Usual care (baseline/final)=19/16	Mean=54 min/day at 1 y (SD=30 min)	NR	NR
Mean difference	26 min (adjusted)	NR	NR
95% CI	8 to 45 min	NR	NR
P-value	0.0006	NR	NR
Fuller (2017) [20,]			
N=66	NR	N=64 at 6 mo	N=64 at 6 mo
Longer-duration (14 wk) PR program	NR	+149 m (169 m)	NA
Shorter-duration (7 wk) PRprogram	NR	+202 m (72 m)	NA
P-value	NR	0.5	NR
Mean difference	NR	NA	59.3 m favoring 7-wk group
95% CI	NR	NR	12.9 to 131.6 m

6MWD: 6-minute walk distance; CI: confidence interval; NR: not reported; OR: odds ratio; RCT: randomized controlled trial; SD: standard deviation.

The purpose of the limitations tables (see Tables 11 and 12) is to display notable limitations identified in each study. This information is synthesized as a summary of the body of evidence following each table and provides the conclusions on the sufficiency of evidence supporting the position statement.

Table 11. Study Relevance Limitations

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Follow-Up[e]
Langer (2012)[19,]					
Fuller (2017)[20,]	1. Selection criteria not clear		2. Fitness activity monitor not validated as comparator for this clinical scenario.		

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.

[a] Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use.
[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4. Not the intervention of interest.
[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.
[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical significant difference not supported.
[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

Table 12. Study Design and Conduct Limitations

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Follow-Up[d]	Power[e]	Statistical[f]
Langer (2012)[19,]		1. Patients not blinded. Blinding not feasible. Outcome assessment not blinded.				
Fuller (2017)[20,]		1. Patients not blinded. Blinding not feasible. Outcome assessment not blinded.			1,2. Power is affected by small sample size, underpowered to detect meaningful differences	

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.
[b] Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.
[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.
[d] Follow-Up key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).
[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.
[f] Statistical key: 1. Intervention is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Intervention is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated.

Case Series

Munro et al (2009) published a case series that evaluated a comprehensive pulmonary rehabilitation program after lung surgery.[21,] The 7-week program, which started 1 month post surgery, consisted of 1 hour of supervised exercise 3 times a week and a weekly group education session facilitated by a multidisciplinary team (e.g., nurse, dietician, occupational therapist, social worker). Compared with baseline, on program completion, both forced expiratory volume in 1 second and forced vital capacity had improved significantly ($p<0.001$). For example, mean forced expiratory volume in 1 second was 71% at 1 month, post-surgery and 81% at 3 months. Similarly, 6 minute walk distance improved significantly: mean distance was 451 meters at 1

month and 543 meters at 3 months posttransplant. The study lacked a control group. Hence, the degree of improvement that would have occurred without participation in a pulmonary rehabilitation program is unknown.

Section Summary: Lung Transplantation Postoperative Pulmonary Rehabilitation Programs
A systematic review of exercise training after lung transplantation (not necessarily provided in a comprehensive pulmonary rehabilitation program) identified 7 controlled and uncontrolled studies but did not pool study findings. Neither RCT identified reported functional outcomes, but the uncontrolled studies did report improvements in functional outcomes. An RCT, published after the systematic review, found that patients who had a post-surgical exercise intervention walked more 1-year post-discharge and had a significantly greater 6 minute walk distance. The most recent RCT (2017) did not identify a difference in outcomes with longer duration of pulmonary rehabilitation. Findings on other outcomes were mixed. Case series data also support improvement in the 6-minute walk distance after postoperative pulmonary rehabilitation.

LUNG CANCER RESECTION POSTOPERATIVE PULMONARY REHABILITATION PROGRAMS

Clinical Context and Therapy Purpose
The purpose of a single course of outpatient pulmonary rehabilitation is to provide a treatment option that is an alternative to or an improvement on existing therapies, such as usual care without outpatient pulmonary rehabilitation, in patients who have had lung cancer resection.

The question addressed in this evidence review is: Does the use of outpatient pulmonary rehabilitation improve net health outcomes in patients who have had lung cancer resection surgery?

The following PICO was used to select literature to inform this review.

Populations
The relevant population of interest are individuals who have had lung cancer resection.

Interventions
The therapy being considered is a single course of outpatient pulmonary rehabilitation. Pulmonary rehabilitation programs include a patient assessment followed by therapeutic interventions including exercise training, education, and behavior change.

Patients who have had lung cancer resection are actively managed by pulmonologists, oncologists, and primary care providers in an outpatient clinical setting.

Comparators
Comparators of interest include usual care without outpatient pulmonary rehabilitation. Treatment includes physical exercise, diaphragmatic breathing, oxygen therapy and medical therapy.

Patients who have had lung cancer resection are actively managed by pulmonologists, oncologists, and primary care providers in an outpatient clinical setting.

Outcomes

The general outcomes of interest are symptoms, functional outcomes, and quality of life.

The existing literature evaluating a single course of outpatient pulmonary rehabilitation as a treatment for individuals who have had lung cancer resection has varying lengths of follow up. While studies described below all reported at least 1 outcome of interest, 3-6 months duration of follow-up is desirable to assess outcomes.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

1. To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs.
2. In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
3. To assess longer term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
4. Studies with duplicative or overlapping populations were excluded.

Review of Evidence

Randomized Controlled Trials

Stigt et al (2013) published an RCT evaluating a multicomponent post surgery pulmonary rehabilitation program in patients with resectable lung cancer.[22,] The trial was conducted in the Netherlands. Before thoracotomy, 57 patients were randomized to pulmonary rehabilitation or usual care. The 12-week pulmonary rehabilitation program started 4 weeks after surgery and consisted of exercise training, pain management, and visits with a medical social worker. The trial was terminated early because the institution started offering video-assisted thoracoscopic surgery, at which point few patients chose thoracotomy. Data on 49 patients (pulmonary rehabilitation=23, usual care=26) were analyzed. The primary endpoint was quality of life, as measured by the difference between groups in change in the total St. George's Respiratory Questionnaire score from baseline to 12 months. This difference was 2.71 points, which was not statistically significant (p=0.69). However, 6 minute walk distance (a secondary outcome) improved significantly in the pulmonary rehabilitation group versus the usual care group at 3 months. The between-group difference in 6 minute walk distance was 94 meters (p=0.024). A limitation of this analysis is that only 8 of 23 patients in the pulmonary rehabilitation performed a 6 minute walk distance at 3 months; the other 15 patients had dropped out or did not take the test. Eleven of 25 patients in the usual care group performed the 6 minute walk distance.

An exercise-only intervention after lung cancer surgery (not comprehensive pulmonary rehabilitation) was evaluated in an RCT published by Edvardsen et al (2015).[23,] This single-blind trial was conducted in Norway and included lung cancer patients at 4 to 6 weeks post surgery. Sixty-one patients were randomized to an exercise program 3 times a week for 20 weeks or to usual care. The exercise intervention took place at local fitness centers and was supervised by trained personal trainers and physical therapists. The significantly greater improvement was reported for the primary outcome (change in peak oxygen uptake from baseline to the end of the intervention) in the intervention group than in the control group (between-group difference, 0.26 L/min; p=0.005.) Findings on secondary outcomes were mixed. For example, the between-group difference in forced expiratory volume in 1 second was 0.6% of predicted (95% CI, -4.2% to

5.4%; p=0.738) and the difference in stair run was 4.3 steps (95% CI, 1.6 to 7.1 steps; p=0.002). This trial did not report other functional outcomes (e.g., 6 minute walk distance).

Section Summary: Lung Cancer Resection Postoperative Pulmonary Rehabilitation Programs
A single RCT has evaluated a comprehensive pulmonary rehabilitation program in patients who underwent thoracotomy for lung cancer. The trial was terminated early, had a high dropout rate, and reported mixed findings. An exercise-only intervention in patients who had lung cancer surgery had mixed findings and did not evaluate functional outcomes. Current evidence is not sufficiently robust to draw conclusions on the utility of pulmonary rehabilitation programs to those who have had lung resection.

REPEAT OUTPATIENT PULMONARY REHABILITATION PROGRAMS

Clinical Context and Therapy Purpose
The purpose of repeat outpatient pulmonary rehabilitation is to provide a treatment option that is an alternative to or an improvement on existing therapies, such as usual care without repeat outpatient pulmonary rehabilitation, in patients who have had an initial course of pulmonary rehabilitation.

The question addressed in this evidence review is: Does the use of repeat pulmonary rehabilitation improve net health outcomes in patients who have various lung conditions?

The following PICO was used to select literature to inform this review.

Populations
The relevant population of interest are individuals with lung conditions who have had an initial course of pulmonary rehabilitation.

Interventions
The therapy being considered is repeat outpatient pulmonary rehabilitation. Pulmonary rehabilitation programs include a patient assessment followed by therapeutic interventions including exercise training, education, and behavior change. Repeat pulmonary rehabilitation programs provide additional rehabilitation services after initial participation in a pulmonary rehabilitation program.

Patients who have had an initial course of pulmonary rehabilitation are actively managed by pulmonologists and primary care providers in an outpatient clinical setting.

Comparators
Comparators of interest include usual care without repeat outpatient pulmonary rehabilitation. Treatment includes physical exercise, diaphragmatic breathing, oxygen therapy, and medical therapy.

Patients who have had an initial course of pulmonary rehabilitation are actively managed by pulmonologists and primary care providers in an outpatient clinical setting.

Outcomes

The general outcomes of interest are symptoms, functional outcomes, and quality of life.

The existing literature evaluating repeat outpatient pulmonary rehabilitation as a treatment for individuals who have had an initial course of pulmonary rehabilitation has varying lengths of follow up. While studies described below all reported at least 1 outcome of interest, 3-6 months duration follow-up is desirable to assess outcomes.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

1. To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs.
2. In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
3. To assess longer term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
4. Studies with duplicative or overlapping populations were excluded.

Review of Evidence

Repeat pulmonary rehabilitation programs provide additional rehabilitation services after initial participation in a pulmonary rehabilitation program. Repeat programs are generally those that include patients who failed to respond to an initial program or whose response to an initial rehabilitation program diminished over time.

Carr et al (2009) prospectively identified Canadian patients with moderate-to-severe COPD who experienced an acute exacerbation within 12 months of participating in a pulmonary rehabilitation program.[24,] All patients had initially completed a 6-week inpatient program or a 12-week outpatient program. Patients were then randomized to receive 3 weeks of pulmonary rehabilitation therapy or usual care. The repeat pulmonary rehabilitation program consisted of exercise and education; patients could choose inpatient or outpatient versions. Over a mean of 14 ± 11 weeks, 41 patients developed an exacerbation. Seven patients withdrew from the trial, and the remaining 34 were randomized to a repeat pulmonary rehabilitation program within 1 month of the exacerbation (n=17) or to no repeat pulmonary rehabilitation program (n=17). One patient in the intervention group dropped out; of the remaining 33 patients, 25 (76%) experienced an exacerbation of moderate severity; the remaining 8 had severe exacerbations. Nine (56%) of 16 patients in the intervention group chose an inpatient program, and 7 chose an outpatient program. Patients were assessed before the repeat pulmonary rehabilitation program, immediately after (3 weeks later), and again 12 weeks after the beginning of the exacerbation 5 weeks after completing the repeat rehabilitation program). The primary outcome was change in health-related quality of life, as measured on the 4 domains of the chronic respiratory questionnaire score. There was no statistically significant difference between groups in mean change in chronic respiratory questionnaire scores. Among patients in the intervention group, the magnitude of improvement in the domains of dyspnea (0.7 points) and fatigue (0.5 points) met or exceeded the minimal clinically important difference. In the control group, the magnitude of change in all domains did not meet the minimal clinically important difference. Change in the 6 minute walk distance (a secondary outcome) did not differ significantly between groups at either follow-up. Outcomes were not reported separately for the inpatient or outpatient programs (this evidence review addresses outpatient programs). Trialists recommended that future evaluations

of repeat pulmonary rehabilitation programs include patients with more serious exacerbations, last longer than 3 weeks, and start as close in time as possible to the exacerbation. Conclusions about repeat pulmonary rehabilitation programs cannot be drawn from 1 study with 33 subjects.

Section Summary: Repeat Outpatient Pulmonary Rehabilitation Programs
Evidence for repeat pulmonary rehabilitation program includes 1 small randomized study. Additional larger RCTs are needed before conclusions can be made about the effectiveness of repeat pulmonary rehabilitation.

MAINTENANCE OUTPATIENT PULMONARY REHABILITATION PROGRAMS

Clinical Context and Therapy Purpose
The purpose of maintenance outpatient pulmonary rehabilitation is to provide a treatment option that is an alternative to or an improvement on existing therapies, such as usual care without maintenance outpatient pulmonary rehabilitation, in patients who have had an initial course of pulmonary rehabilitation.

The question addressed in this evidence review is: Does the use of maintenance pulmonary rehabilitation improve net health outcomes in patients who have various lung conditions?

The following PICO was used to select literature to inform this review.

Populations
The relevant population of interest are individuals with lung conditions who have had an initial course of pulmonary rehabilitation.

Interventions
The therapy being considered is maintenance outpatient pulmonary rehabilitation. Pulmonary rehabilitation programs include a patient assessment followed by therapeutic interventions including exercise training, education, and behavior change. Maintenance pulmonary rehabilitation programs provide additional rehabilitation services after initial participation in a pulmonary rehabilitation program. Maintenance programs tend to be designed to extend the effects of the initial pulmonary rehabilitation program, and they are open to all patients who successfully completed an initial program.

Patients who have had an initial course of pulmonary rehabilitation are actively managed by pulmonologists and primary care providers in an outpatient clinical setting.

Comparators
Comparators of interest include usual care without maintenance outpatient pulmonary rehabilitation. Treatment includes physical exercise, diaphragmatic breathing, oxygen therapy and medical therapy.

Patients who have had an initial course of pulmonary rehabilitation are actively managed by pulmonologists and primary care providers in an outpatient clinical setting.

Outcomes
The general outcomes of interest are symptoms, functional outcomes, and quality of life.

The existing literature evaluating maintenance outpatient pulmonary rehabilitation as a treatment for individuals who have had an initial course of pulmonary rehabilitation has varying lengths of follow up. While studies described below all reported at least 1 outcome of interest, 3-6 months duration follow-up is desirable to assess outcomes.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

1. To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs.
2. In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
3. To assess longer term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
4. Studies with duplicative or overlapping populations were excluded.

Review of Evidence

In 2012, an Ontario Health Technology Assessment evaluated pulmonary rehabilitation for patients with COPD.[25,] Reviewers identified 3 RCTs (total N=284 participants) assessing maintenance pulmonary rehabilitation programs for individuals with COPD who had successfully completed an initial pulmonary rehabilitation program. The trials excluded patients who had experienced a recent acute exacerbation of COPD. All maintenance programs consisted of supervised exercise sessions; program duration was 3 months in 1 program and 12 months in the other 2. One program also included an unsupervised exercise component and another included educational sessions. Reviewers judged study quality as generally poor due to methodologic limitations (e.g., inadequate information on randomization, allocation concealment, blinding, and lack of clarity around the use of an intention-to-treat analysis). In a pooled analysis of data from 2 trials (n=168 patients), there was a significantly greater improvement in 6 minute walk distance in patients who participated in the maintenance program than in those in a control group (MD=22.9 meters; 95% CI, 5.2 to 40.7 meters). The confidence interval was wide, indicating lack of precision in the pooled estimate. Also, reviewers considered the minimal clinically important difference to be 25 to 35 meters walked, and meta-analysis of trial findings did not meet this threshold of difference between groups.

Several RCTs were published after the Ontario assessment. Guell et al (2017) published findings of a 3-year trial of patients with severe COPD.[26,] A total of 143 patients attended an initial 8-week outpatient pulmonary rehabilitation program, and 138 were then randomized to a 3-year maintenance program (n=68) or a control group (n=70). The maintenance intervention consisted of home-based exercises, calls from a physical therapist every 2 weeks, and supervised training sessions every 2 weeks. The control group was advised to exercise at home without supervision. Some outcomes but not others favored the intervention group at 2 years, but outcomes did not differ significantly between groups at 3 years. For example, compared with baseline, at 2 years the 6 minute walk difference increased by 2 meters in the intervention group and decreased by 32 meters in the control group (p=0.046). At 3 years, compared with baseline, the 6 minute walk distance decreased by 4 meters in the intervention group and decreased by 33 meters in the control group (p=0.119). The chronic respiratory questionnaire dyspnea score, at 2 years compared with baseline, decreased by 0.4 points in the intervention group and by 0.3 points in the control group (p=0.617); findings were similar at 3 years. The trial also had a high dropout rate.

Wilson et al (2015) published a single-blind RCT comparing maintenance pulmonary rehabilitation to standard care without maintenance pulmonary rehabilitation in patients who had COPD and had completed at least 60% of an initial pulmonary rehabilitation program.[27,] One hundred forty-eight patients were randomized; 110 (74%) completed the trial and were included in the analysis. The maintenance program consisted of a 2-hour session every 3 months for 1 year. The session included an hour of education and an hour of supervised individualized exercise training. The primary efficacy outcome was change from baseline (post-pulmonary rehabilitation) in the chronic respiratory questionnaire dyspnea domain. Among trial completers, mean chronic respiratory questionnaire dyspnea score changed from 2.6 to 3.2 among patients receiving maintenance pulmonary rehabilitation and from 2.5 to 3.3 among controls. The difference between groups was not statistically significant. Secondary outcomes, including other chronic respiratory questionnaire domains, scores on the endurance shuttle walk test, and a number of exacerbations or hospitalizations, also did not differ significantly between groups.

Section Summary: Maintenance Outpatient Pulmonary Rehabilitation Program
A limited number of RCTs are available to evaluate maintenance rehabilitation programs. Due to the paucity of RCTs, methodologic limitations of available trials, and lack of clinically significant findings, the evidence to determine the effect of maintenance pulmonary rehabilitation programs on health outcomes in patients with COPD is insufficient.

HOME-BASED PULMONARY REHABILITATION PROGRAMS

Clinical Context and Therapy Purpose
The purpose of a single course of home-based pulmonary rehabilitation is to provide a treatment option that is an alternative to or an improvement on existing therapies, such as a single course of ambulatory care–based pulmonary rehabilitation, in patients with an indication for outpatient pulmonary rehabilitation.

The question addressed in this evidence review is: Does the use of home-based pulmonary rehabilitation programs improve net health outcomes in patients with various lung conditions?

The following PICO was used to select literature to inform this review.

Populations
The relevant population of interest are individuals with an indication for outpatient pulmonary rehabilitation.

Interventions
The therapy being considered is a single course of home-based pulmonary rehabilitation. Pulmonary rehabilitation programs include a patient assessment followed by therapeutic interventions including exercise training, education, and behavior change.

Patients with an indication for home-based pulmonary rehabilitation are managed by pulmonologists, primary care providers, and ancillary clinical personnel.

Comparators

Comparators of interest include a single course of ambulatory care–based pulmonary rehabilitation. Treatment includes physical exercise, diaphragmatic breathing, oxygen therapy, and medical therapy.

Patients with an indication for home-based pulmonary rehabilitation are managed by pulmonologists, primary care providers and ancillary clinical personnel.

Outcomes

The general outcomes of interest are symptoms, functional outcomes, and quality of life.

The existing literature evaluating a single course of home-based pulmonary rehabilitation indicates that 3-6 months duration of follow-up is desirable to assess outcomes.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

1. To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs.
2. In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
3. To assess longer term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
4. Studies with duplicative or overlapping populations were excluded.

Review of Evidence

Systematic Reviews

Evaluation of home-based pulmonary rehabilitation programs requires evidence that these programs are at least as effective as programs conducted in the ambulatory care setting. The programs also need to be comprehensive and be feasible in the United States health care system.

Several RCTs and systematic reviews of RCTs have assessed home-based pulmonary rehabilitation programs. Among the systematic reviews, Liu et al (2014) identified 18 RCTs evaluating home-based pulmonary rehabilitation programs.[28,] Most trials compared pulmonary rehabilitation with usual care, and none of the selected trials compared home-based with clinic-based programs. Only 2 trials were conducted in the United States, and both were published in the 1990s. All trials reported different outcomes over different timeframes, and pooled analyses only included data from 2 to 4 studies. For example, a pooled analysis of 3 studies (n=112 patients) reporting the Saint George's Respiratory Questionnaire total score found statistically significant improvements in symptoms with home-based pulmonary rehabilitation compared with control (effect size, -11.33; 95% CI, -16.37 to -6.29). A pooled analysis of data from 4 studies (n=167 patients) found a significantly increased 6 minute walk distance after 12 weeks in the pulmonary rehabilitation group compared with control (effect size, 35.9; 95% CI, 9.4 to 62.4). The latter analysis had a wide confidence interval, indicating an imprecise estimate of effect.

Vieira et al (2010), in a systematic review, identified 12 RCTs comparing home-based pulmonary rehabilitation with pulmonary rehabilitation in another setting or with standard care in patients

who had COPD.[29,] The comparison intervention in 3 trials was a hospital-based program; in 8 trials, it was standard care; and in 1 trial, both comparisons were made. The methodologic quality of the trials was considered average to poor, and most had small sample sizes and relatively short follow-up durations. Reviewers did not pool trial findings, and findings of individual studies were mixed. Three trials that compared home-based pulmonary rehabilitation with standard care reported on between-group differences in quality of life; in all 3 studies, differences were reported as statistically significant. The 2 trials that reported differences in exercise capacity found home-based pulmonary rehabilitation to result in significantly greater improvements in the 6 minute walk distance or constant work rate test than standard care. On the other hand, in the 3 trials comparing home-based pulmonary rehabilitation and hospital-based programs, there were no statistically significant differences between groups in quality of life changes. Moreover, in the 2 trials that assessed maximal work level and the 2 trials that assessed the 6 minute walk distance, outcomes did not differ significantly from home-based or hospital-based pulmonary rehabilitation programs. Reviewers commented that their analysis was limited by the generally low quality of the randomized trials and short-term length of follow-up.

Another systematic review was published by Neves et al (2016).[30,] However, this review combined home- and community-based pulmonary rehabilitation programs in analyses so no conclusions can be drawn on the impact of home-based programs compared with programs based in the ambulatory care setting.

Randomized Controlled Trial

A study with relatively large sample size and that compared home-based pulmonary rehabilitation with outpatient clinic-based pulmonary rehabilitation was published by Maltais et al (2008).[31,] This noninferiority trial was conducted in Canada. Eligibility criteria included stable COPD for at least 4 weeks before study participation and no previous participation in pulmonary rehabilitation programs; 252 patients were included. All patients initially completed a 4-week self-management educational program. They were then randomized to 8 weeks of self-monitored home-based exercise training or outpatient hospital-based exercise training. The exercise program included aerobic and strength exercises conducted 3 times a week. Patients were followed for 40 weeks after completion of the exercise program. Both interventions produced similar improvements in the chronic respiratory questionnaire dyspnea domain scores at 1 year: improvement in dyspnea of 0.62 (95% CI, 0.43 to 0.80) units in the home intervention (n=107) and 0.46 (95% CI, 0.28 to 0.64) units in the outpatient intervention (n=109). The difference between treatments at 1 year was considered clinically unimportant. The trial did not evaluate a comprehensive pulmonary rehabilitation program.

Section Summary: Home-Based Pulmonary Rehabilitation Programs

Most studies of home-based pulmonary rehabilitation have compared it with standard care. Very few studies have compared home-based pulmonary rehabilitation with a hospital or clinic-based pulmonary rehabilitation, and those available are mostly of low quality. Therefore, there is insufficient evidence to determine whether comprehensive pulmonary rehabilitation programs conducted in the home setting are at least as effective as comprehensive pulmonary rehabilitation programs in the ambulatory care setting.

Summary of Evidence

Chronic Pulmonary Disease Rehabilitation

For individuals with moderate-to-severe chronic obstructive pulmonary disease (COPD) who receive a single course of outpatient pulmonary rehabilitation, the evidence includes numerous systematic reviews of randomized controlled trials (RCTs). Relevant outcomes are symptoms, functional outcomes, and quality of life. The published studies found improved outcomes (i.e., functional ability, quality of life) in patients with moderate-to-severe COPD who underwent a comprehensive pulmonary rehabilitation program in the outpatient setting. Among the many randomized trials, the structure of the pulmonary rehabilitation programs varied, so it is not possible to provide guidance on the optimal components or duration of a pulmonary rehabilitation program. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with idiopathic pulmonary fibrosis who receive a single course of outpatient pulmonary rehabilitation, the evidence includes 2 systematic reviews of RCTs. Relevant outcomes are symptoms, functional outcomes, and quality of life. The number of controlled studies is limited. One small RCT evaluated a comprehensive pulmonary rehabilitation program in patients with idiopathic pulmonary fibrosis; at 3 months postintervention, outcomes did not differ between groups that did and did not receive pulmonary rehabilitation. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with bronchiectasis who receive a single course of outpatient pulmonary rehabilitation, the evidence includes a systematic review of RCTs. Relevant outcomes are symptoms, functional outcomes, and quality of life. The systematic review of 4 RCTs on pulmonary rehabilitation for patients with bronchiectasis found that some, but not all, outcomes, improved more with pulmonary rehabilitation than with nonexercised control conditions immediately after the intervention. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Although most published evidence on outpatient pulmonary rehabilitation for chronic pulmonary diseases assesses COPD, observational studies have reported on outcomes from pulmonary rehabilitation for other chronic pulmonary diseases. Clinical guidelines from pulmonary organizations have supported the use of outpatient pulmonary rehabilitation for individuals who are experiencing disabling symptoms and have significantly diminished quality of life despite optimal medical management. Therefore, outpatient pulmonary rehabilitation may be considered medically necessary for this population.

Preparation for Lung Surgery

For individuals with scheduled lung surgery for volume reduction, transplantation, or resection who receive a single course of outpatient pulmonary rehabilitation, the evidence includes RCTs and observational studies. Relevant outcomes are symptoms, functional outcomes, and quality of life. There is a lack of large RCTs comparing pulmonary rehabilitation with no pulmonary rehabilitation for preoperative candidates undergoing lung volume reduction surgery, lung transplantation, or lung cancer resection. Moreover, the available studies have evaluated exercise programs, but not necessarily comprehensive pulmonary rehabilitation programs. Also, the few small RCTs, and observational studies have only reported short-term outcomes and inconsistent evidence of benefit even on these outcomes. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Findings from the National Emphysema Treatment Trial have suggested that pulmonary rehabilitation is an appropriate component of care for patients with COPD before undergoing lung volume reduction surgery. Also, pulmonary rehabilitation is considered standard of care in patients undergoing lung transplantation to maximize preoperative pulmonary status. Thus, pulmonary rehabilitation may be considered medically necessary for patients considered appropriate candidates for lung volume reduction surgery or lung transplantation.

Pulmonary Rehabilitation After Lung Surgery

For individuals who have had lung volume reduction surgery who receive a single course of outpatient pulmonary rehabilitation, the evidence includes a case series. Relevant outcomes are symptoms, functional outcomes, and quality of life. No published RCTs were identified. The case series evaluated a comprehensive pulmonary rehabilitation program after lung volume reduction surgery in 49 patients who had not received preoperative pulmonary rehabilitation. Health-related quality of life was higher at 3 to 6 months and 12 to 18 months post surgery. The series did not provide data on patients who underwent lung volume reduction surgery and did not have postoperative pulmonary rehabilitation, or patients who had preoperative pulmonary rehabilitation. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have had lung transplantation who receive a single course of outpatient pulmonary rehabilitation, the evidence includes RCTs, a systematic review, and a case series. Relevant outcomes are symptoms, functional outcomes, and quality of life. Neither of the 2 RCTs identified in a 2010 systematic review reported on functional outcomes, but uncontrolled studies have reported improvements in functional outcomes. An RCT, published after the systematic review, found that patients who had a postsurgical exercise intervention walked more 1 year post discharge than before and had a significantly greater 6-minute walk distance. Findings on other outcomes were mixed. The most recent RCT (2017) did not identify a difference in outcomes with longer duration of pulmonary rehabilitation. Case series data also support improvements in 6-minute walk distance after postoperative pulmonary rehabilitation. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have had lung cancer resection who receive a single course of outpatient pulmonary rehabilitation, the evidence includes 2 RCTs. Relevant outcomes are symptoms, functional outcomes, and quality of life. One small RCT evaluated a comprehensive pulmonary rehabilitation program in patients who underwent thoracotomy for lung cancer. The trial was terminated early, had a high dropout rate, and reported mixed findings. An exercise-only intervention in patients who had lung cancer surgery had mixed findings and did not evaluate functional outcomes. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Repeat or Maintenance Pulmonary Rehabilitation

For individuals who have had an initial course of pulmonary rehabilitation who receive repeat or maintenance outpatient pulmonary rehabilitation, the evidence includes an RCT. Relevant outcomes are symptoms, functional outcomes, and quality of life. This small RCT had methodologic limitations and did not report inpatient and outpatient outcomes separately; it also

lasted only 3 weeks. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Home-Based Pulmonary Rehabilitation
For individuals who have an indication for outpatient pulmonary rehabilitation who receive a single course of home-based pulmonary rehabilitation, the evidence includes RCTs and systematic reviews. Relevant outcomes are symptoms, functional outcomes, and quality of life. Most studies of home-based pulmonary rehabilitation have compared outcomes with standard care. Very few have compared home-based pulmonary rehabilitation with the hospital- or clinic-based pulmonary rehabilitation, and the available studies are mostly of low quality. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

SUPPLEMENTAL INFORMATION
The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the evidence review conclusions.

Practice Guidelines and Position Statements
Guidelines or position statements will be considered for inclusion in 'Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

American Thoracic Society and European Respiratory Society
A 2015 joint statement on pulmonary rehabilitation was issued by the American Thoracic Society and the European Respiratory Society.[32,] The statement included the following relevant conclusions:

- "Pulmonary rehabilitation (PR) has demonstrated physiological, symptom-reducing, psychosocial, and health economic benefits in multiple outcome areas for patients with chronic respiratory diseases."
- "The evidence indicates that patients who benefit from PR include not only persons with moderate to severe airflow limitation but also those with mild to moderate airflow limitation with symptom-limited exercise tolerance, those after hospitalization for COPD [chronic obstructive pulmonary disease] exacerbation, and those with symptomatic non-COPD respiratory conditions."
- "Patients graduating from a PR program stand to benefit from a home, community-based, or program-based maintenance exercise program to support the continuation of positive exercise behavior."

In 2017, the Society issued a joint statement on the management of COPD exacerbation.[33,] For patients hospitalized with a COPD exacerbation, they suggest "the initiation of pulmonary rehabilitation within 3 weeks after hospital discharge" (strength: conditional; quality of evidence: very low). In addition, "[they] suggest not initiating pulmonary rehabilitation during hospitalization" (strength: conditional; quality of evidence: very low).

American College of Physicians

In 2011, Joint guidelines on the management of stable COPD were issued by the American College of Physicians, the American College of Chest Physicians, American Thoracic Society, and European Respiratory Society.[34,] The guidelines recommended that "clinicians should prescribe pulmonary rehabilitation for symptomatic patients with an FEV [forced expiratory volume] <50% predicted (Grade: strong recommendation, moderate-quality evidence). Clinicians may consider pulmonary rehabilitation for symptomatic or exercise-limited patients with an FEV >50% predicted (Grade: weak recommendation, moderate-quality evidence)."

United States Preventive Services Task Force Recommendations
Not applicable

Ongoing and Unpublished Clinical Trials
Some currently unpublished trials that might influence this review are listed in Table 13.

Table 13. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
NCT03326089	Short and Long-term Effects of Oxygen Supplemented Pulmonary Rehabilitation in Idiopathic Pulmonary Fibrosis	20	Sep 2022
Unpublished			
NCT03299504	Factors Predicting Success in Lung Transplant Recipients Who Have Participated in the COLTT Program (Daily Intensive Post-hospitalization Rehabilitation): A Retrospective Review	105	Apr 2018 (last updated 08/24/18)
NCT03244137	Effects of Pulmonary Rehabilitation on Cognitive Function in Patients With Severe to Very Severe Chronic Obstructive Pulmonary Disease	100	Dec 2019 (last updated 01/07/20)
NCT02426437	Examining Pulmonary Rehabilitation on Discharged COPD Patients	150	Dec 2020
NCT02842463	Use of the 6-minute Stepper Test to Individualize Pulmonary Rehabilitation in Patients With Mild to Moderate Chronic Obstructive Pulmonary Disease	80	June 2020
NCT03244137	Effects of Pulmonary Rehabilitation on Cognitive Function in Patients With Severe to Very Severe Chronic Obstructive Pulmonary Disease	100	Dec 2019 (completed)
NCT02887521	Pulmonary Rehabilitation Before Lung Cancer Resection	194	Oct 2019 (completed)

NCT: national clinical trial.

CODING

The following codes for treatment and procedures applicable to this policy are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

CPT/HCPCS

S9473	Pulmonary rehabilitation program, nonphysician provider, per diem

ICD-10 Diagnoses (Effective October 1, 2015)

D38.1	Neoplasm of uncertain behavior of trachea, bronchus and lung
D81.810	Biotinidase deficiency
D84.1	Defects in the complement system
E84.11	Meconium ileus in cystic fibrosis
E84.9	Cystic fibrosis, unspecified
E88.89	Other specified metabolic disorders
I26.01	Septic pulmonary embolism with acute cor pulmonale
I26.02	Saddle embolus of pulmonary artery with acute cor pulmonale
I26.09	Other pulmonary embolism with acute cor pulmonale
I26.90	Septic pulmonary embolism without acute cor pulmonale
I26.92	Saddle embolus of pulmonary artery without acute cor pulmonale
I26.93	Single subsegmental pulmonary embolism without acute cor pulmonale
I26.94	Multiple subsegmental pulmonary emboli without acute cor pulmonale
I26.99	Other pulmonary embolism without acute cor pulmonale
I27.0	Primary pulmonary hypertension
J41.8	Mixed simple and mucopurulent chronic bronchitis
J43.0	Unilateral pulmonary emphysema [MacLeod's syndrome]
J43.1	Panlobular emphysema
J43.2	Centrilobular emphysema
J43.8	Other emphysema
J43.9	Emphysema, unspecified
J44.9	Chronic obstructive pulmonary disease, unspecified
J47.0	Bronchiectasis with acute lower respiratory infection
J47.1	Bronchiectasis with (acute) exacerbation
J47.9	Bronchiectasis, uncomplicated
J84.10	Pulmonary fibrosis, unspecified
J84.17	Other interstitial pulmonary diseases with fibrosis in diseases classified elsewhere
J84.89	Other specified interstitial pulmonary diseases
J99	Respiratory disorders in diseases classified elsewhere
M32.13	Lung involvement in systemic lupus erythematosus
M33.01	Juvenile dermatomyositis with respiratory involvement
M33.11	Other dermatomyositis with respiratory involvement
M33.21	Polymyositis with respiratory involvement
M34.0	Progressive systemic sclerosis
M34.1	CR(E)ST syndrome
M34.2	Systemic sclerosis induced by drug and chemical
M34.81	Systemic sclerosis with lung involvement

M34.82	Systemic sclerosis with myopathy
M34.83	Systemic sclerosis with polyneuropathy
M34.89	Other systemic sclerosis
M35.02	Sjogren syndrome with lung involvement
P27.0	Wilson-Mikity syndrome
P27.1	Bronchopulmonary dysplasia originating in the perinatal period
P27.8	Other chronic respiratory diseases originating in the perinatal period
P27.9	Unspecified chronic respiratory disease originating in the perinatal period
Q21.0	Ventricular septal defect
Q33.4	Congenital bronchiectasis
T80.0xxA	Air embolism following infusion, transfusion and therapeutic injection, initial encounter
T81.718A	Complication of other artery following a procedure, not elsewhere classified, initial encounter
T81.72xA	Complication of vein following a procedure, not elsewhere classified, initial encounter
T82.817A	Embolism of cardiac prosthetic devices, implants and grafts, initial encounter
T82.818A	Embolism of vascular prosthetic devices, implants and grafts, initial encounter

REVISIONS	
08-17-2010	Policy added to the bcbsks.com web site.
06-07-2012	Description section updated
	In Policy section: ▪ Revised wording on A from: "A single course of pulmonary rehabilitation in the outpatient care setting may be considered medically necessary for outpatient treatment of chronic pulmonary disease for patients with moderate-to severe disease who are experiencing disabling symptoms and significantly diminished quality of life in spite of optimal medical management." to: "A single course of pulmonary rehabilitation in the outpatient care setting may be considered medically necessary for outpatient treatment of moderate to severe chronic pulmonary impairment for patients who are experiencing disabling symptoms and significantly diminished quality of life in spite of optimal medical management." ▪ Added the following criteria: "D. Home-based pulmonary rehabilitation programs are considered experimental / investigational."
	Policy Guidelines updated ▪ Revised 8 from: "Cessation of smoking for at least 3 months is required." to: "Cessation of smoking for at least 3 months is required, immediately prior to the rehabilitation program." ▪ Revised 9 from: "Coverage is allowed for up to 18 sessions or 6 weeks. Additional services will be reviewed on a case-by-case basis." to: "For BCBSKS members, services provided in connection with an approved outpatient pulmonary rehabilitation program may be considered reasonable and necessary for up to 18 sessions, usually 3 sessions a week in a single 6-week period. Coverage for continued participation would be allowed only on a case-by-case basis with exit criteria taken into consideration." ▪ Removed "physician's office" from 10 to read, "Services must be furnished in a hospital outpatient setting. All settings must have a physician immediately available and accessible for medical consultations and emergencies at all times."
	Rationale section updated
	In Coding section: ▪ Updated CPT and Diagnosis nomenclature
	References updated
07-12-2013	Description section reviewed
	Rationale section updated
	In Coding section: ▪ ICD-10 codes added

REVISIONS	
	References updated
06-23-2015	Description section updated
	In Policy section: ▪ In Item A removed "chronic pulmonary impairment for patients" and added "of chronic pulmonary disease for patients with" and "disease" to read, "A single course of pulmonary rehabilitation in the outpatient care setting may be considered medically necessary for outpatient treatment of chronic pulmonary disease for patients with moderate-to-severe disease who are experiencing disabling symptoms and significantly diminished quality of life in spite of optimal medical management." ▪ In Item B added "ambulatory care" to read, "…medically necessary in an outpatient ambulatory care setting…" ▪ Added the new medically necessary indication of "Pulmonary rehabilitation programs are considered medically necessary following lung transplantation." ▪ Added the new experimental / investigational indications of "Pulmonary rehabilitation programs are considered experimental / investigational following other types of lung surgery, included but not limited to lung volume reduction surgery and surgical resection of lung cancer." And "Pulmonary rehabilitation programs are considered experimental / investigational in all other situations."
	Rationale section updated
	References updated
07-20-2016	In the Title removed "Programs" to read "Outpatient Pulmonary Rehabilitation"
	Description section updated
	In Policy section: ▪ In Item A added "ambulatory" and "despite"; removed "outpatient" and "in spite" to read "A single course of pulmonary rehabilitation in the outpatient ambulatory care setting may be considered medically necessary for treatment of chronic pulmonary disease for patients with moderate-to-severe disease who are experiencing disabling symptoms and significantly diminished quality of life despite optimal medical management." ▪ In Item B revised "and" to "or" between indications
	Rationale section updated
	In Coding section: ▪ Removed coding notation
	References updated
04-28-2017	Description section updated
	Rationale section updated
	References updated
10-01-2017	In Coding section: ▪ Revised ICD-10 Code Nomenclature: M33.01, M33.11
05-09-2018	Description section updated
	Rationale section updated
	References updated
07-01-2019	Description section updated
	Rationale section updated
	References updated
10-01-2019	In Coding section: ▪ Added ICD-10 codes: I26.93, I26.94
05-05-2021	Description section updated
	Rationale section updated
	References updated
10-01-2021	In Coding Section (Effective 10-01-2021) Revised nomenclature for ICD-10 code M35.02 to read:

REVISIONS	
	Sjogren syndrome with lung involvement
01-03-2022	In Coding section Removed HCPCS code G0424 terminated (effective 01-01-2022)

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