Title: Pulmonary Rehabilitation

Description/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 interest in patients with asthma, cystic fibrosis, or bronchiectasis.

PR 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.

Regulatory Status:

N/A

Medical Policy Statement

The safety and effectiveness of pulmonary rehabilitation have been established. It may be considered a useful therapeutic option when indicated.
Inclusionary and Exclusionary Guidelines (Clinically based guidelines that may support individual consideration and pre-authorization decisions)

The outpatient program generally includes team assessment, patient training, psychosocial intervention, supervised exercise and follow-up. Participation in pulmonary rehabilitation generally occurs for a period of 4-6 hours per week for 8-12 weeks. The program must have active medical supervision that includes, at a minimum, either a registered nurse, respiratory therapist or exercise physiologist providing direct supervision and a physician available on-site.

Inclusions:
Pulmonary rehabilitation is considered established for:
A. Preoperative conditioning prior to:
   • Lung volume reduction surgery, OR
   • Lung transplantation
B. Postoperative rehabilitation following lung transplantation
C. Individuals with chronic respiratory diseases, with medical documentation of the following:
   • A diagnosis of a chronic but stable respiratory system impairment that is under medical management; AND,
   • A pulmonary function test (PFT), within the past year, that shows forced vital capacity (FVC), forced expiratory volume in one second (FEV1) or diffusing capacity of the lungs for carbon monoxide (DLCO) (uncorrected for volume) less than 65% of predicted normal, AND,
   • Disabling symptoms that significantly impair the individual’s level of function
     NOTE: respiratory diseases may include: COPD (chronic bronchitis, emphysema), asthma, bronchiectasis, cystic fibrosis, interstitial lung disease, restrictive chest wall disease, pulmonary hypertension, lung cancer, respiratory impairment from neuromuscular disease, etc.

In addition to the above, there is medical documentation that the individual is:
   • Physically able, motivated and willing to participate in a pulmonary rehabilitation program; AND,
   • A nonsmoker, has quit smoking or is enrolled in a smoking cessation program; AND,
   • Expected to show measurable improvement in a reasonable and predictable time frame

Candidates for pulmonary rehabilitation should be medically stable and not limited by another serious or unstable medical condition. Contraindications to pulmonary rehabilitation may include:
   • Ischemic cardiac disease
   • Acute cor pulmonale
   • Severe pulmonary hypertension
   • Significant hepatic dysfunction
   • Metastatic cancer
   • Renal failure
   • Severe cognitive deficit
   • Psychiatric disease that interferes with memory and compliance
   • Substance abuse
- Disabling stroke

**Exclusions:**
- Multiple courses of pulmonary rehabilitation, either as maintenance therapy in patients who initially respond or in patients who fail to respond or whose response to an initial rehabilitation program has diminished over time
- Home-based pulmonary rehabilitation programs
- Pulmonary rehabilitation following lung surgeries other than lung transplant (e.g., lung volume reduction surgery and surgical resection of lung cancer)

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**CPT/HCPCS Level II Codes** *(Note: The inclusion of a code in this list is not a guarantee of coverage. Please refer to the medical policy statement to determine the status of a given procedure)*

**Established codes:**
- G0237
- G0238
- G0239
- G0302
- G0303
- G0304
- G0424
- S9473

**Other codes (investigational, not medically necessary, etc.):**
- G0305

**Note:** The above code(s) may not be covered by all contracts or certificates. Please consult customer or provider inquiry resources at BCBSM or BCN to verify coverage.

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**Rationale**

Evidence reviews assess the clinical evidence to determine whether the use of technology improves the net health outcome. Broadly defined, health outcomes are the 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 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 technology, two domains are examined: the relevance and the quality and credibility. To be relevant, studies must represent one 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 (PR) 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 will improve outcomes to the same degree or greater.

**CHRONIC OBSTRUCTIVE PULMONARY DISEASE**

**Clinical Context and Test 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.

The question addressed in this evidence review is: does the use of pulmonary rehabilitation in patients with various lung conditions improve net health outcomes.

The following PICOTS were used to select literature to inform this review.

**Patients**
The relevant population of interest are individuals with moderate-to-severe chronic obstructive pulmonary disease.

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

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

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

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

**Setting**
Patients with moderate-to-severe chronic obstructive pulmonary disease are actively managed by pulmonologists and primary care providers in an outpatient clinical setting.
Study Selection Criteria
Methodologically credible studies were selected using the following principles:

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

Systematic Reviews
Numerous randomized controlled trials (RCTs) and several systematic reviews of RCTs have been published. Most recently, Puhan et al (2016) published a Cochrane review that evaluated PR programs for patients who had an exacerbation of COPD. (3) To be included, the rehabilitation program needed 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 PR compared with usual care (odds ratio, 0.44; 95% confidence interval [CI], 0.21 to 0.91). Several secondary outcomes also favored the PR group. In a pooled analysis of 13 trials, there was a significantly greater improvement from baseline on the 6-minute walk distance (6MWD) in the PR 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 (HRQOL) found significantly greater improvement after PR 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 PR or were lost to follow-up; the study.

McCarthy et al (2015) published a Cochrane review that included RCTs assessing the effect of outpatient or inpatient PR on functional outcomes and/or disease-specific quality of life (QOL) outcomes in patients with COPD. (4) PR 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 the Cochrane reviewers, but article titles suggest a focus on patients with moderate-to-severe COPD. In the pooled analyses, there was statistically significantly greater improvement in all outcomes in the PR 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 (CRQ)—dyspnea, fatigue, emotional function, and mastery—the effect was larger than the accepted minimal clinically important difference (MCID) of 0.5 units. Also, the between-group difference in maximal exercise capacity exceeded the MCID of 4 watts and the between-group difference in 6MWD—an 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 four RCTs indicated that none evaluated a comprehensive PR program in patients who met criteria for mild COPD. Rather than being comprehensive PR programs, all interventions were exercise-based. One intervention included an educational component and another used a qigong intervention, which includes breathing and meditation in addition to exercise. Also, none of the RCTs enrolled a patient population only with 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 PR in patients with mild COPD from this systematic review.

Table 1. SR & MA Characteristics

<table>
<thead>
<tr>
<th>Study</th>
<th>Dates</th>
<th>Trials</th>
<th>Participants</th>
<th>Intervention</th>
<th>N, Range</th>
<th>Design</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Puhan (2016)</td>
<td>up to Mar 2010⁴ Mar 2010 to Oct 2015</td>
<td>20</td>
<td>PR patients (N=1477) that met inclusion criteria and had an exacerbation of COPD</td>
<td>Inpatient and outpatient PR</td>
<td>4866 (NR)</td>
<td>RCT</td>
<td>3-18mm</td>
</tr>
<tr>
<td>McCarthy (2015)⁵</td>
<td>up to Jul 2004, Jul 2004 to Mar 2014</td>
<td>65</td>
<td>Patients (n=3822) mean ages ranging from 31.3 to 74.1 years; residing in-patient, out-patient, community-based or home-based rehabilitation</td>
<td>Outpatient or inpatient PR greater than or equal to 4 wkst that includes exercise therapy +/- education and psychological support (range PR excer Prog. = 7wk to 6m)</td>
<td>3822 (694-1819)</td>
<td>RCT</td>
<td>greater than or equal to 24m</td>
</tr>
<tr>
<td>Rugbjerg (2015)⁵</td>
<td>2000-2015</td>
<td>4</td>
<td>patients with COPD and mild symptoms [mean ages 61.5 to 74.1 (n=489 total) according to dyspnea scores, mHRC greater than or equal to 1 when PR was compared to usual care]</td>
<td>patients with COPD and mild symptoms according to dyspnea scores, mHRC greater than or equal to 1 when PR was compared to usual care</td>
<td>489 (23-313)</td>
<td>RCT</td>
<td>greater than or equal to 24m</td>
</tr>
</tbody>
</table>

1 a previous review included information from studies up to this date

Table 2. SR & MA Results

<table>
<thead>
<tr>
<th>Study</th>
<th>Rate of hospital readmission</th>
<th>Baseline 6mo walk, distance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Puhan (2016)⁵</td>
<td>N=610</td>
<td>N=13</td>
</tr>
<tr>
<td>N=1477 PR compared with usual care</td>
<td>OR= (M-H, random, 95% CI 0.44 [0.28, 1.67])</td>
<td>MD=M-H, random, 95% CI 62.4m, 38.5 to 86.3 m</td>
</tr>
<tr>
<td>McCarthy (2015)⁵</td>
<td>N=313</td>
<td>4 studies</td>
</tr>
<tr>
<td>N=3822, 4 trials</td>
<td>OR= (M-H, random, 95% CI 0.44 [0.28, 1.67])</td>
<td>Pooled results, usual care=157 patients, PR=156 patients’ mean difference in walking distance (PR vs SC= PR greater than or equal to SC as PR (95% CI [15.76-35.65])</td>
</tr>
<tr>
<td>Health-related Quality of Life (SGRQ)</td>
<td>mean difference assessed at 18-24m, compared to baseline</td>
<td></td>
</tr>
<tr>
<td>Rugbjerg (2015)⁵</td>
<td>N=489 patients</td>
<td>Pooled results, mean difference in walking distance (n=157 in intervention group and 156 in control), MD=25.71m, favoring PR (95% CI [15.76-35.65]).</td>
</tr>
</tbody>
</table>

CT: confidence interval; PR=pulmonary rehabilitation

Section Summary: Chronic Obstructive Pulmonary Disease

Multiple RCTs and meta-analyses of RCTs have, for the most part, found improved outcomes (ie, functional ability, QOL) in patients with moderate-to-severe COPD who have a comprehensive PR program in the outpatient setting. There is limited evidence on the efficacy of repeated and/or prolonged PR programs, and the available evidence is mixed on whether these programs improve additional health outcome benefits.

IDIOPATHIC PULMONARY FIBROSIS
Clinical Context and Test 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 various lung conditions.

The following PICOTS were used to select literature to inform this review.

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

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

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

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

Timing
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 one 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.

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

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

a) To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;

b) In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.

c) To assess longer term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
d) Studies with duplicative or overlapping populations were excluded.

Jackson et al (2014) evaluated patients with idiopathic pulmonary fibrosis who were 40 to 80 years of age and had disease onset between 3 and 48 months before screening, abnormal pulmonary function, and a 6MWD between 150 and 500 meters. (10) In this pilot, patients were assigned to a PR program consisting of twice-weekly 2-hour rehabilitation sessions over 12 weeks (n=14) or usual care (n=11). Twenty-one of the 25 patients completed the 3-month intervention study. Reviewers did not report between-group statistics. Follow-up data at 3 months postintervention were reported by Gaunaurd et al (2014). (11) During the intervention, patients in the PR group had significantly greater self-reported physical activity, but, in the subsequent 3 months, activity levels in the 2 groups were similar. For example, at 6 months, pulmonary function measures (eg, total lung capacity, forced vital capacity [FVC], spirometry diffusion capacity) did not change significantly within either group. 6MWD was not reported.

Section Summary: Idiopathic Pulmonary Fibrosis
One small RCT has evaluated a comprehensive PR program in patients with idiopathic pulmonary fibrosis; at three months postintervention, outcomes did not differ between groups who did and did not receive PR.

BRONCHIECTASIS

Clinical Context and Test 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: what the safety and efficacy of pulmonary rehabilitation in patients with various lung conditions.

The following PICOTS were used to select literature to inform this review.

Patients
The relevant population of interest are individuals with bronchiectasis.

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

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

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

Timing
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 one outcome of interest, 3-6 months duration of follow-up is desirable to fully assess outcomes.

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

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

a) To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;

b) In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.

c) To assess longer term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.

d) Studies with duplicative or overlapping populations were excluded.

Lee et al (2017) published a systematic review of RCTs on PR in patients with non-cystic fibrosis bronchiectasis. (12) Reviewers identified four 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 St. George's Respiratory Questionnaire (SGRQ) 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 of data beyond the immediate postintervention period.

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

PR PROGRAMS BEFORE LUNG SURGERY

Clinical Context and Test 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 various conditions.

The following PICOTS were used to select literature to inform this review.

Patients
The relevant population of interest are individuals with scheduled lung surgery for volume
Interventions
The therapy being considered is a single course of preoperative outpatient pulmonary rehabilitation.

PR programs include a patient assessment followed by therapeutic interventions including exercise training, education, and behavior change.

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

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

Timing
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 one outcome of interest, 3-6 months duration follow-up are desirable to assess outcomes.

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

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

a) To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;

b) In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.

c) To assess longer term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.

d) Studies with duplicative or overlapping populations were excluded.

Lung Volume Reduction Surgery
PR prior to LVRS represents a distinct subset of patients with COPD, and the National Emphysema Treatment Trial requires all candidates to undergo a vigorous course of PR. The final National Emphysema Treatment Trial results supported the treatment effectiveness in a subset of patients with COPD. (13)

Lung Transplantation
A systematic review of the literature on PR for lung transplant candidates was published by Hoffman et al (2017). (14) Interventions had to include exercise training but did not have to be part of a comprehensive PR 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 PR) on outcomes; additionally, one was conducted in the inpatient setting, and the included only 9 patients. Conclusions on the impact of a
comprehensive PR program before lung transplantation on health outcomes cannot be drawn from this systematic review.

**Lung Cancer Resection**

Several small RCTs have evaluated preoperative PR for patients undergoing lung cancer resection. Morano et al (2013) published a single-blind study in Brazil. (15) Patients with non-small-cell lung cancer (NSCLC) eligible for lung resection were randomly assigned to 4 weeks of an exercise-only PR program (5 sessions per week) or chest physical therapy; there were 12 patients in each group. All patients in the PR 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 PR 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 PR group spent fewer days with chest tubes (mean, 4.5 days) than the physical therapy group (mean, 7.4 days; p=0.03). There was not a significant difference between groups in the length of hospital stay. The trial did not assess longer-term functional outcomes after surgery.

Benzo et al (2011) conducted 2 small exploratory RCTs evaluating PR before lung cancer resection. (16) Eligibility criteria included having moderate-to-severe COPD and being scheduled for lung cancer. The first trial had poor recruitment, enrolling only 9 patients. The second study enrolled 19 patients into a 10-session preoperative PR program (n=10) or usual care (n=9). Mean number of days in the hospital was 6.3 in the PR group and 11.0 in the control group (p=0.058). Three (33%) patients in the PR 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 and clinically significant differences between groups. Trialists recommended conducting a larger multicenter randomized trial in this population.

Bradley et al (2013), in a nonrandomized comparative study evaluated an outpatient-based PR intervention in 58 lung cancer patients who were candidates for surgery. (17) This U.K.-based study also evaluated a comparison group of 305 patients, also surgical candidates, who received usual care. Patients in the two 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 6MWD in the intervention group before and after participation in a 4-session presurgical PR program. In between-group analyses, there were not statistically significant differences between the intervention and comparisons groups in clinical outcomes such as postoperative pulmonary complications, readmissions, and mortality after surgery.
<table>
<thead>
<tr>
<th>Study</th>
<th>Countries</th>
<th>Sites</th>
<th>Dates</th>
<th>Participants</th>
<th>Interventions</th>
<th>Comparator</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marano (2013) [12]</td>
<td>Brazil</td>
<td>1</td>
<td>Mar 2008 to Mar 2011</td>
<td>Patients undergoing lung cancer resection (n=24) and who have non-small cell lung cancer resection by open thoracotomy (or video-assisted); and due to pulmonary disease, interstitial lung disease, or obstructive airway disease, with impaired respiratory function by spirometry.</td>
<td>PR: Strength/endurance training - education; 5 sessions/wk for 4 wks (20 sessions) (n=12)</td>
<td>CPT breathing exercises + education; 5 sessions/wk for 4 wks (10 sessions) (n=12)</td>
</tr>
<tr>
<td>Benzo (2011) [16]</td>
<td>US</td>
<td>2</td>
<td>NR</td>
<td>Patients who require lung cancer resection by open thoracotomy (or video-assisted); moderate-to-severe CCOPD (n=19 total patients)</td>
<td>PR: 10 preoperative PR sessions involving customized protocol with nonstandard components (exercise prescription based on self-efficacy, inspiratory muscle training; slow breathing) (n=10)</td>
<td>Usual care (n=9)</td>
</tr>
</tbody>
</table>

N=19

RCT: randomized controlled trial
PK= 1 Number randomized; Interactions; mode of delivery; dose (frequency/duration).
2 Key eligibility criteria

Table 4. Summary of Key RCT Results

<table>
<thead>
<tr>
<th>Study</th>
<th>ICU stay mean +/- SD at 4 weeks</th>
<th>Postoperative hospitalizations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marano (2013) [12]</td>
<td>N=31 patients at t=0; 24 in analysis; 21 in final analysis</td>
<td>N=31 patients at t=0; 24 in analysis; 21 in final analysis</td>
</tr>
<tr>
<td>PR (Exercise) n=12</td>
<td>6.8 +/- 4.8</td>
<td>2 (2-3) P = 0.04 (not significant)</td>
</tr>
<tr>
<td>CPT (control) n=9</td>
<td>12.2 +/- 3.6</td>
<td>2 (2-4.5) P = 0.04 (not significant)</td>
</tr>
<tr>
<td>Benzo (2011) [16]</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>PR arm compared to control average</td>
<td>mean days of 6.4 vs. 11.1, p=0.058</td>
<td>NR</td>
</tr>
</tbody>
</table>

CI: confidence interval; HR: hazard ratio; NNT: number needed to treat; OR: odds ratio; RCT: randomized controlled trial; RR: relative risk.

Table 5. Relevance Gaps

<table>
<thead>
<tr>
<th>Study</th>
<th>Population</th>
<th>Intervention</th>
<th>Comparator</th>
<th>Outcome</th>
<th>Follow Up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marano (2013) [15]</td>
<td>4. Recruitment not met.</td>
<td>3. No CONSORT reporting of harms was addressed</td>
<td>1. Short duration of follow-up (4-weeks)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benzo (2011) [16]</td>
<td>5. Clinical significant difference not supported.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The evidence gaps 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 Outcome 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 supported.
e Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.
Section Summary: Preoperative Pulmonary Rehabilitation Programs
The National Emphysema Treatment Trial has recommended administering PR before LVRS, which is considered the standard of care before LVRS and lung transplantation. However, there is a lack of large RCTs comparing PR with no PR for preoperative candidates undergoing LVRS, lung transplantation, or lung cancer resection. Moreover, the available studies evaluated exercise programs, but not necessarily comprehensive PR. Also, the few small RCTs and observational studies have reported short-term outcomes and have found inconsistent evidence of benefit even on these outcomes.

POSTOPERATIVE PULMONARY REHABILITATION PROGRAMS

Lung Volume Reduction Surgery

Clinical Context and Test 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 PICOTS were used to select literature to inform this review.

Patients
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. PR programs include a patient assessment followed by therapeutic interventions including exercise training, education, and behavior change.

Comparators
Comparators of interest include usual care without outpatient pulmonary rehabilitation.

Treatment includes physical exercise, diaphragmatic breathing, oxygen therapy and medication therapy.

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

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

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

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

a. To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;

b. In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.

c. To assess longer term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.

d. Studies with duplicative or overlapping populations were excluded.

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

**Section Summary: PR Programs After LVRS**
No comparative studies have evaluated PR programs after LVRS. One case series evaluated a comprehensive PR program after LVRS in 49 patients who had not received preoperative PR. HRQOL was higher at 3 to 6 months and 12 to 18 months postsurgery. The study did not provide data on patients who underwent LVRS and did not have postoperative PR, or on patients who had preoperative PR.
Lung transplantation

Clinical Context and Test 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 PICOTS were used to select literature to inform this review.

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

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

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

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

Timing
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 one outcome of interest, 3-6 months duration of follow-up is desirable to assess outcomes.

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

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

a. To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;

b. In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.

c. To assess longer term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.

d. Studies with duplicative or overlapping populations were excluded.

Exercise training after lung transplantation (not necessarily provided in comprehensive PR 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 two 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. (19)

**Randomized Controlled Trials**

Langer et al (2012) conducted an RCT in the U.K. that examined activity-related outcomes in lung transplant recipients after exercise training. (20) 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 usual care with instructions to exercise (n=19). Patients in both groups had 6 individual counseling sessions in the 6 months after 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 three-month intervention and one-year postdischarge, mean walking time was significantly longer in the intervention group. At 1 year, the exercise group walked a mean of 85 minutes per day and 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 6MWD 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) vs long (14-week) rehabilitation programs for patients who underwent lung transplantation. (21) The primary outcome was change in the 6-minute walking test (6MWT). Secondary outcomes included the strength of the quadriceps and hamstring muscles (as measured by an isokinetic dynamometer), and QOL (as measured by the 36-Item Short-Form Health Survey). In both the 7- and 14-week rehabilitation groups, participants increased their 6MWT (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>
<thead>
<tr>
<th>Study/Trial</th>
<th>Countries</th>
<th>Sites</th>
<th>Participants</th>
<th>Interventions</th>
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</tr>
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<tbody>
<tr>
<td>Langer (2012)</td>
<td>UK</td>
<td>1</td>
<td>Patients who received a single or double lung transplantation and had no nonoperative complications (N=40)</td>
<td>Exercise program (3x/wk for 3m) N=21</td>
<td>Usual Care with added “instruction to exercise” N=19</td>
</tr>
<tr>
<td>Fuller (2017)</td>
<td>US</td>
<td>1</td>
<td>Post-lung transplantation (LTX) patients aged greater than or equal to 18 years (N=66; 33 women; mean age, 51±13y) who had undergone either single LTX or bilateral LTX</td>
<td>Longer-duration (14wk) rehabilitation program after LTX</td>
<td>Shorter (7wk) rehabilitation program after LTX</td>
</tr>
</tbody>
</table>

LTX: lung transplantation; RCT: randomized controlled trial.
1 Number randomized, intervention, mode of delivery, dose (frequency/duration).
2 Key eligibility criteria
Munro et al (2009) published a case series that evaluated a comprehensive PR program after lung surgery. The seven-week program, which started one month postsurgery, consisted of one hour of supervised exercise three times a week and a weekly group education session facilitated by a multidisciplinary team (eg, 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% 1 month, postsurgery and 81% at 3 months. Similarly, 6MWD 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 PR program is unknown.

**Section Summary: PR Programs After Lung Transplantation**
A systematic review of exercise training after lung transplantation (not necessarily provided in a comprehensive PR program) identified seven controlled and uncontrolled studies and 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 postsurgical exercise intervention walked more 1-year postdischarge and had a significantly greater 6MWD. The most recent RCT (2017) did not identify a difference in outcomes with longer duration of PR. Findings on other outcomes were mixed. Case series data also support improvement in the 6MWD after postoperative PR.

**Lung Cancer Resection**

**Clinical Context and Test 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 PICOTS were used to select literature to inform this review.

**Patients**
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. PR programs include a patient assessment followed by therapeutic interventions including exercise training, education, and behavior change.

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

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

**Timing**
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 one outcome of interest, 3-6 months duration of follow-up is desirable to assess outcomes.

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

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

a. To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;

b. In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.

c. To assess longer term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.

d. Studies with duplicative or overlapping populations were excluded.

Stigt et al (2013) published an RCT evaluating a multicomponent postsurgery PR program in patients with resectable lung cancer. (23) The trial was conducted in the Netherlands. Before thoracotomy, 57 patients were randomized to PR or usual care. The 12-week PR 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 (PR=23, usual care=26) were analyzed. The primary end point was QOL, 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, 6MWD (a secondary outcome) improved significantly more in the PR group than in the usual care group at three months. The between-group difference in 6MWD was 94 meters (p=0.024). A limitation of this analysis is that only 8 of 23 patients in the PR performed a 6MWT 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 6MWT.

An exercise-only intervention after lung cancer surgery (not comprehensive PR) was evaluated in an RCT published by Edvardsen et al (2015). (24) This single-blind study was conducted in Norway and included lung cancer patients at four to six weeks postsurgery. Sixty-one patients were randomized to an exercise program 3 times a week for 20 weeks or 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% 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; p=0.002). This trial did not report other functional outcomes (eg, 6MWD).

**Subsection Summary: Lung Cancer Resection**
A single RCT has evaluated a comprehensive PR 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 PR programs to those who have had lung resection.

**REPEAT AND MAINTENANCE PULMONARY REHABILITATION PROGRAMS**
Clinical Context and Test Purpose
The purpose of repeat or 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 repeat or 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 repeat or maintenance pulmonary rehabilitation improve net health outcomes in patients who have various lung conditions.

The following PICOTS were used to select literature to inform this review.

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

Interventions
The therapy being considered is repeat or maintenance outpatient pulmonary rehabilitation. PR programs include a patient assessment followed by therapeutic interventions including exercise training, education, and behavior change.

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

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

Timing
The existing literature evaluating repeat or 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 one outcome of interest, l3-6 months duration follow-up is desirable to assess outcomes.

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

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

a. To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;

b. In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.

c. To assess longer term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.

d. Studies with duplicative or overlapping populations were excluded.
Both repeat and maintenance PR programs provide additional rehabilitation services after initial participation in a PR program. Program categories are not strictly defined but repeat programs are generally considered to be those that include patients who failed to respond to an initial program or whose response to an initial rehabilitation program diminished over time. In contrast, maintenance programs tend to be those designed to extend the effects of the initial PR program, and they are open to all patients who successfully completed an initial program.

**Repeat Pulmonary Rehabilitation Program**

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 PR program. (25) Initially, patients completed a 6-week inpatient program or a 12-week outpatient program. The repeat PR program lasted 3 weeks and consisted of exercise and education; patients could choose inpatient or outpatient versions. Over 6 months, 41 patients developed an exacerbation and 12 did not. Seven patients withdrew from the study, and the remaining 34 were randomized to a repeat PR program within 1 month of the exacerbation (n=17) or to no repeat PR 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 PR 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 HRQOL, as measured on the 4 domains of the CRQ score. There was no statistically significant difference between groups in mean change in CRQ 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 MCID. In the control group, the magnitude of change in all domains did not meet the MCID. Change in the 6MWD (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 PR 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 PR programs cannot be drawn from 1 study with 33 subjects.

**Maintenance Pulmonary Rehabilitation Program**

In 2012, an Ontario Health Technology Assessment evaluated PR for patients with COPD. (26) Reviewers identified 3 RCTs (total N=284 participants) assessing maintenance PR programs for individuals with COPD who successfully completed an initial PR 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 programs. One program also included an unsupervised exercise component, and 1 included educational sessions. Reviewers judged study quality as generally poor due to methodologic limitations (eg, inadequate information on randomization, allocation concealment, and 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 6MWD 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 MCID to be 25 to 35 meters walked, and meta-analysis of study 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. A total of 143 patients attended an initial 8-week outpatient PR 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 two weeks and supervised training sessions every two weeks. The control group was advised to exercise at home without supervision. Some outcomes but not others favored the intervention group at two years but outcomes did not differ significantly between groups at three years. For example, compared with baseline, at 2 years the 6MWD 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 6MWD decreased by 4 meters in the intervention group and decreased by 33 meters in the control group (p=0.119). The CRQ dyspnea score, at 2 years compared with baseline, decreased 0.4 points in the intervention group and 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 PR to standard care without maintenance PR in patients with COPD who had completed at least 60% of an initial PR program. One hundred forty-eight patients were randomized, 110 (74%) completed the trial and were included in the analysis. The maintenance program consisted of a two-hour every three months for one 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-PR) in the CRQ dyspnea domain. Among trial completers, mean CRQ dyspnea score changed from 2.6 to 3.2 among patients receiving maintenance PR and from 2.5 to 3.3 among controls. The difference between groups was not statistically significant. Secondary outcomes, including other CRQ domains, scores on the endurance shuttle walk test, and number of exacerbations or hospitalizations, also did not differ significantly between groups.

**Section Summary: Repeat and Maintenance PR Programs**
A limited number of RCTs are available to evaluate repeat or 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 repeat and maintenance PR programs on health outcomes in patients with COPD is insufficient.

**HOME-BASED PULMONARY REHABILITATION PROGRAMS**

**Clinical Context and Test 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 PICOTS were used to select literature to inform this review.

**Patients**
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. PR programs include a patient assessment followed by therapeutic interventions including exercise training, education, and behavior change.

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.

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

Timing
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.

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

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

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

Evaluation of home-based PR 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 U.S. health care system.

Systematic Reviews
Several RCTs and systematic reviews of RCTs have assessed home-based PR programs. Among the systematic reviews, Liu et al (2014) identified 18 RCTs evaluating home-based PR programs. (29) Most trials compared PR with usual care, and none of the selected trials compared home-based and clinic-based programs. Only 2 studies 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 two to four studies. For example, a pooled analysis of 3 studies (n=112 patients) reporting the St. George’s Respiratory Questionnaire total score found statistically significant improvement in symptoms with home-based PR 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 6MWD after 12 weeks in the PR 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) identified 12 RCTs comparing home-based PR with PR in another setting or to standard care in patients with COPD. (30) The comparison intervention in three studies was a hospital-based program; in eight trials, it was standard care; and in one trial, both comparisons were made. The methodologic quality of the studies 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 PR with standard care reported on between-group differences in QOL; in all three studies, differences were reported as statistically significant. The two trials that reported differences in exercise capacity found home-based PR to result in significantly greater improvement in the 6MWD or constant work rate test than standard care. On the other hand, in the three trials comparing home-based PR and hospital-based programs, there were no statistically significant differences between groups in QOL changes. Moreover, in the two trials that assessed maximal work level and the two trials that assessed the 6MWD, outcomes did not differ significantly from home-based or hospital-based PR 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). (31) However, this review combined home and community-based PR programs in analyses so no conclusions can be drawn on the impacts of home-based programs compared with programs based in the ambulatory care setting.

**Randomized Controlled Trials**

A study with a relatively large sample size, and that compared home-based PR with outpatient clinic-based PR was published by Maltais et al (2008). (32) 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 PR programs; 252 patients were included. All patients initially completed a four-week self-management educational program. They were then randomized to receive eight 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 CRQ 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 one year was considered clinically unimportant. The trial did not evaluate a comprehensive PR program.

**Section Summary: Home-Based PR Programs**

Most studies of home-based PR have compared it with standard care. Very few studies have compared home-based PR with hospital or clinic-based PR and those available are mostly of low quality. Therefore, there is insufficient evidence to determine comprehensive PR programs conducted in the home setting are at least as effective as comprehensive PR 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 PR, the evidence includes numerous randomized
controlled trials (RCTs) and systematic reviews. Relevant outcomes are symptoms, functional outcomes, and quality of life. The published studies found improved outcomes (ie, functional ability, quality of life) in patients with moderate-to-severe COPD who underwent a comprehensive PR program in the outpatient setting. Among the many randomized trials, the structure of the PR programs varied, so it is not possible to provide guidance on the optimal components or duration of a PR program. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals with idiopathic pulmonary fibrosis who receive a single course of outpatient PR, the evidence includes an RCT. The relevant outcomes are symptoms, functional outcomes, and quality of life. The number of controlled studies is limited. One small RCT evaluated a comprehensive PR program in patients with idiopathic pulmonary fibrosis; at three months postintervention, outcomes did not differ in groups that did and did not receive PR. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals with bronchiectasis who receive a single course of outpatient PR, the evidence includes RCTs, systematic reviews, and observational data. Relevant outcomes are symptoms, functional outcomes, and quality of life. A systematic review of four RCTs on PR for patients with bronchiectasis found that some, but not all outcomes, improved more with PR than with nonexercise control conditions immediately after the intervention. The evidence is insufficient to determine the effects of the technology on health outcomes.

**Preparation for Lung Surgery**

For individuals with scheduled lung surgery for volume reduction, transplantation, or resection who receive a single course of outpatient PR, 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 PR with no PR for preoperative candidates undergoing lung volume reduction surgery (LVRS), lung transplantation, or lung cancer resection. Moreover, the available studies have evaluated exercise programs, but not necessarily comprehensive PR programs. Also, the few small RCTs and observational studies have reported short-term outcomes and inconsistent evidence of benefit even on these outcomes. The evidence is insufficient to determine the effects of the technology on health outcomes.

**PR After Lung Surgery**

For individuals who have had LVRS who receive a single course of outpatient PR, 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 PR program after LVRS in 49 patients who had not received preoperative PR. Health-related quality of life was higher at 3 to 6 months and at 12 to 18 months postsurgery. The series did not provide data on patients who underwent LVRS and did not have postoperative PR, or patients who had preoperative PR. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have had lung transplantation who receive a single course of outpatient PR, the evidence includes RCTs, systematic reviews, and observational studies. Relevant outcomes are symptoms, functional outcomes, and quality of life. Neither of the 2 RCTs identified in a 2010 systematic review reported 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 one year postdischarge 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 PR. Case series data also support improvements in 6MWD after postoperative PR. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have had lung cancer resection who receive a single course of outpatient PR, the evidence includes an RCT. Relevant outcomes are symptoms, functional outcomes, and quality of life. One small RCT have evaluated a comprehensive PR 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 the effects of the technology on health outcome.

**Repeat or Maintenance Rehabilitation**
For individuals who have had an initial course of PR who receive repeat or maintenance outpatient PR, the evidence includes RCTs. Relevant outcomes are symptoms, functional outcomes, and quality of life. There are only a few RCTs and many of them have methodologic limitations and/or did not report clinically significant outcomes. The evidence is insufficient to determine the effects of the technology on health outcome.

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

**SUPPLEMENTAL INFORMATION**

**Practice Guidelines and Position Statements**

**American Thoracic Society and European Respiratory Society**
A2015 joint statement on pulmonary rehabilitation (PR) was issued by the American Thoracic Society and the European Respiratory Society. (1), The statement included the following relevant conclusions:

- “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 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.”

**American College of Physicians et al**
Joint guidelines on the management of COPD were issued by the American College of Physicians, the American College of Chest Physicians, American Thoracic Society, and European Respiratory Society (33): 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).”

American College of Chest Physicians et al
In 2007, joint guidelines on PR for COPD and other chronic respiratory diseases were issued by American College of Chest Physicians and the American Association of Cardiovascular and Pulmonary Rehabilitation. (see Table 1) (34)

Table 9. Pulmonary Rehabilitation Guidelines for Chronic Respiratory Diseases

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>GOR</th>
</tr>
</thead>
<tbody>
<tr>
<td>A program of exercise training of the muscles of ambulation is recommended as a mandatory component of pulmonary rehabilitation for patients with COPD</td>
<td>1A</td>
</tr>
<tr>
<td>Pulmonary rehabilitation improves the symptoms of dyspnea and improves health-related quality of life in patients with COPD</td>
<td>1A</td>
</tr>
<tr>
<td>Six to 12 weeks of pulmonary rehabilitation produces benefits in several outcomes that decline gradually over 12 to 18 months</td>
<td>1A</td>
</tr>
<tr>
<td>Both low- and high-intensity exercise training produce clinical benefits for patients with COPD</td>
<td>1A</td>
</tr>
<tr>
<td>Unsupported endurance training of the upper extremities is beneficial in patients with COPD and should be included in pulmonary rehabilitation programs</td>
<td>1A</td>
</tr>
<tr>
<td>Higher-intensity exercise training of the lower extremities produces greater physiologic benefits than lower-intensity training in patients with COPD</td>
<td>1B</td>
</tr>
<tr>
<td>Evidence does not support the routine use of inspiratory muscle training as an essential component of pulmonary rehabilitation</td>
<td>1B</td>
</tr>
<tr>
<td>Education should be an integral component of pulmonary rehabilitation; it should include information on collaborative self-management and prevention and treatment of exacerbations</td>
<td>1B</td>
</tr>
<tr>
<td>Pulmonary rehabilitation is beneficial for some patients with chronic respiratory diseases other than COPD</td>
<td>1B</td>
</tr>
</tbody>
</table>

COPD: chronic obstructive pulmonary disease; GOR: grade of recommendation.

U.S. 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 2.
**Government Regulations**

**National:**

National Coverage Determination (NCD) for Pulmonary Rehabilitation Services (240.8)

Effective date 9/25/2007, Implementation date 1/7/2008

**Item/Service Description**

**A. General**

PULMONARY REHABILITATION was defined in a 1999 joint statement of the American Thoracic Society and the European Respiratory Society as a multi-disciplinary program of care for patients with chronic respiratory impairment that is individually tailored and designed to optimize physical and social performance and autonomy and an evidence-based, multidisciplinary, and comprehensive intervention for patients with chronic respiratory diseases who are symptomatic and often have decreased daily life activities. Integrated into the individualized treatment of the patient, PULMONARY REHABILITATION is designed to reduce symptoms, optimize functional status, increase participation, and reduce health care costs through stabilizing or reversing systematic manifestations of the disease. Although services that make up PULMONARY REHABILITATION individually may be covered under Medicare and fall into various applicable benefit categories, the Centers for Medicare & Medicaid Services (CMS) has determined that the Social Security Act (the Act) does not expressly define a comprehensive PULMONARY REHABILITATION Program as a Part B
benefit. In addition, respiratory therapy services are identified as covered services under the Comprehensive Outpatient Rehabilitation Facility benefit and defined in 42 CFR 410.100(e)(1) to (2)(vi).

Indications and Limitations of Coverage
B. Nationally Covered Indications
N/A
C. Nationally Non-Covered Indications
N/A
D. Other
The CMS has determined that a national coverage determination (NCD) for pulmonary rehabilitation is not appropriate at this time. Local contractors should continue to make decisions under §1862(a) (1) (A) of the Act through their local coverage determination (LCD) process or by case-by-case adjudication.

Local:
There is no local coverage determination.

(The above Medicare information is current as of the review date for this policy. However, the coverage issues and policies maintained by the Centers for Medicare & Medicare Services [CMS, formerly HCFA] are updated and/or revised periodically. Therefore, the most current CMS information may not be contained in this document. For the most current information, the reader should contact an official Medicare source.)

Related Policies

- Cardiac Rehabilitation
- Lung and Lobar Lung Transplant
- Lung Volume Reduction Surgery (Retired)

References


The articles reviewed in this research include those obtained in an Internet based literature search for relevant medical references through 4/8/19, the date the research was completed.
<table>
<thead>
<tr>
<th>Policy Effective Date</th>
<th>BCBSM Signature Date</th>
<th>BCN Signature Date</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>7/12/02</td>
<td>7/12/02</td>
<td>7/12/02</td>
<td>Joint policy established</td>
</tr>
<tr>
<td>9/10/03</td>
<td>9/10/03</td>
<td>10/3/03</td>
<td>Joint policy established</td>
</tr>
<tr>
<td>2/25/05</td>
<td>2/25/05</td>
<td>2/25/05</td>
<td>Routine maintenance</td>
</tr>
<tr>
<td>5/1/07</td>
<td>3/1/07</td>
<td>3/30/07</td>
<td>Routine maintenance</td>
</tr>
<tr>
<td>9/1/07</td>
<td>7/2/07</td>
<td>7/2/07</td>
<td>Routine maintenance</td>
</tr>
<tr>
<td>11/1/08</td>
<td>8/19/08</td>
<td>10/28/08</td>
<td>Code update only</td>
</tr>
<tr>
<td>11/1/09</td>
<td>8/18/09</td>
<td>8/18/09</td>
<td>Routine maintenance</td>
</tr>
</tbody>
</table>
| 7/1/10               | 4/20/10              | 4/20/10            | Routine maintenance  
Code update – G0424 added to policy. |
| 7/1/11               | 4/19/11              | 5/3/11             | Routine maintenance |
| 9/1/13               | 6/19/13              | 6/26/13            | Routine maintenance; reformatted description and rationale to mirror BCBSA; updated policy criteria. |
| 7/1/15               | 4/21/15              | 5/8/15             | Routine maintenance  
Inclusions updated to include pulmonary rehabilitation prior to lung volume reduction surgery and lung transplant.  
Statement added to exclusions for pulmonary rehabilitation following lung surgeries other than lung transplant (e.g., lung volume reduction surgery and surgical resection of lung cancer.)  
Added procedure codes G0302-G0305 |
<p>| 7/1/16               | 4/19/16              | 4/19/16            | Routine maintenance |
| 7/1/17               | 4/18/17              | 4/18/17            | Routine maintenance |
| 7/1/18               | 4/17/18              | 4/17/18            | Routine maintenance |</p>
<table>
<thead>
<tr>
<th>Date</th>
<th>Date</th>
<th>Date</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>9/1/18</td>
<td>6/19/18</td>
<td>6/19/18</td>
<td>Request to add respiratory therapist and exercise physiologist for supervision. CMS section updated. Inclusions re-formatted, examples of respiratory disease provided.</td>
</tr>
<tr>
<td>9/1/19</td>
<td>6/18/19</td>
<td></td>
<td>Routine maintenance</td>
</tr>
</tbody>
</table>

Next Review Date: 2nd Qtr, 2020
BLUE CARE NETWORK BENEFIT COVERAGE
POLICY: PULMONARY REHABILITATION

I. Coverage Determination:

<table>
<thead>
<tr>
<th>Commercial HMO (includes Self-Funded groups unless otherwise specified)</th>
<th>Covered, policy criteria apply</th>
</tr>
</thead>
<tbody>
<tr>
<td>BCNA (Medicare Advantage)</td>
<td>See Government Regulations section. If there is no NCD or LCD, medical policy criteria apply.</td>
</tr>
<tr>
<td>BCN65 (Medicare Complementary)</td>
<td>Coinsurance covered if primary Medicare covers the service.</td>
</tr>
</tbody>
</table>

II. Administrative Guidelines:

- The member's contract must be active at the time the service is rendered.
- Coverage is based on each member's certificate and is not guaranteed. Please consult the individual member's certificate for details. Additional information regarding coverage or benefits may also be obtained through customer or provider inquiry services at BCN.
- The service must be authorized by the member's PCP except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Services must be performed by a BCN-contracted provider, if available, except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Payment is based on BCN payment rules, individual certificate and certificate riders.
- Appropriate copayments will apply. Refer to certificate and applicable riders for detailed information.
- CPT - HCPCS codes are used for descriptive purposes only and are not a guarantee of coverage.