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A M E R I C A N C O L L E G E O F



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## Pulmonary Rehabilitation\*

### Joint ACCP/AACVPR Evidence-Based Clinical Practice Guidelines

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**Background:** Pulmonary rehabilitation has become a standard of care for patients with chronic lung diseases. This document provides a systematic, evidence-based review of the pulmonary rehabilitation literature that updates the 1997 guidelines published by the American College of Chest Physicians (ACCP) and the American Association of Cardiovascular and Pulmonary Rehabilitation.

**Methods:** The guideline panel reviewed evidence tables, which were prepared by the ACCP Clinical Research Analyst, that were based on a systematic review of published literature from 1996 to 2004. This guideline updates the previous recommendations and also examines new areas of research relevant to pulmonary rehabilitation. Recommendations were developed by consensus and rated according to the ACCP guideline grading system.

**Results:** The new evidence strengthens the previous recommendations supporting the benefits of lower and upper extremity exercise training and improvements in dyspnea and health-related quality-of-life outcomes of pulmonary rehabilitation. Additional evidence supports improvements in health-care utilization and psychosocial outcomes. There are few additional data about survival. Some new evidence indicates that longer term rehabilitation, maintenance strategies following rehabilitation, and the incorporation of education and strength training in pulmonary rehabilitation are beneficial. Current evidence does not support the routine use of inspiratory muscle training, anabolic drugs, or nutritional supplementation in pulmonary rehabilitation. Evidence does support the use of supplemental oxygen therapy for patients with severe hypoxemia at rest or with exercise. Noninvasive ventilation may be helpful for selected patients with advanced COPD. Finally, pulmonary rehabilitation appears to benefit patients with chronic lung diseases other than COPD.

**Conclusions:** There is substantial new evidence that pulmonary rehabilitation is beneficial for patients with COPD and other chronic lung diseases. Several areas of research provide opportunities for future research that can advance the field and make rehabilitative treatment available to many more eligible patients in need.

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**Key words:** COPD; dyspnea; exercise training; guidelines; pulmonary rehabilitation; quality of life

**Abbreviations:** AACVPR = American Association of Cardiovascular and Pulmonary Rehabilitation; ACCP = American College of Chest Physicians; ADL = activity of daily living; CRDQ = Chronic Respiratory Disease Questionnaire; DAS = distractive auditory stimuli; DEXA = dual-energy x-ray absorptiometry; ESM = education and stress management; HR = heart rate; HRQOL = health-related quality of life; IMT = inspiratory muscle training; MRC = Medical Research Council; NETT = National Emphysema Treatment Trial; NPPV = noninvasive positive-pressure ventilation; PAV = proportional assist ventilation; P<sub>max</sub> = maximal inspiratory pressure; RCT = randomized controlled trial; SaO<sub>2</sub> = arterial oxygen saturation; TCEMS = transcutaneous electrical stimulation of the peripheral muscles;  $\dot{V}_E$  = minute ventilation;  $\dot{V}_{O_2}$  = oxygen uptake

**P**ulmonary diseases are increasingly important causes of morbidity and mortality in the modern world. The COPDs are the most common chronic lung diseases, and are a major cause of lung-related death and disability.<sup>1</sup> Pulmonary rehabilitation has emerged as a recommended standard of care for patients with chronic lung disease based on a growing body of scientific evidence. A previous set<sup>2,3</sup> of evidence-based guidelines was published in 1997 as a joint effort of the American College of Chest Physicians (ACCP) and the American Association of Cardiovascular and Pulmonary Rehabilitation

(AACVPR). Since then, the published literature in pulmonary rehabilitation has increased substantially, and other organizations have published important statements about pulmonary rehabilitation (*eg*, the American Thoracic Society and the European Respiratory Society<sup>4</sup>). The purpose of this document is to update the previous ACCP/AACVPR document with a systematic, evidence-based review of the literature published since then.

## EPIDEMIOLOGY OF COPD

In the United States, COPD accounted for 119,054 deaths in 2000, ranking as the fourth leading cause of death and the only major disease among the top 10 in which mortality continues to increase.<sup>5-8</sup> In persons 55 to 74 years of age, COPD ranks third in men and fourth in women as cause of death.<sup>9</sup> However, mortality data underestimate the impact of COPD because it is more likely to be listed as a contributory cause of death rather than the underlying cause of death, and it is often not listed at all.<sup>10,11</sup> Death rates from COPD have continued to increase more in women than in men.<sup>5</sup> Between 1980 and 2000, death rates for COPD increased 282% for women compared to only 13% for men. Also, in 2000, for the first time, the number of women dying from COPD exceeded the number of men.<sup>5</sup>

Morbidity from COPD is also substantial.<sup>5,12</sup> COPD develops insidiously over decades and because of the large reserve in lung function there is a long preclinical period. Affected individuals have few symptoms and are undiagnosed until a relatively advanced stage of disease. In a population survey in Tucson, AZ, Burrows<sup>13</sup> reported that only 34% of persons with COPD had ever consulted a physician, 36% denied having any respiratory symptoms, and 30% denied dyspnea on exertion, which is the primary symptom. National Health and Nutrition Examination Study III data estimate that 24 million US adults have impaired lung function, while only 10 million report a physician diagnosis of COPD.<sup>5</sup> There are approximately 14 million cases of chronic bronchitis reported each year, and 2 million cases of emphysema.<sup>14</sup> The National Center for Health Statistics for 1996 reported prevalence rates of chronic bronchitis and emphysema in older adults (*eg*, persons  $\geq$  65 years of age) of 82 per 1,000 men and 106 per 1,000 women.<sup>15</sup> In 2000, COPD was responsible for 8 million physician office visits, 1.5 million emergency department visits, and 726,000 hospitalizations.<sup>5</sup> COPD accounts for > 5% of physician office visits and 13% of hospitalizations.<sup>16</sup> National Health and Nutrition Examination Study III data from 1988 to 1994 indicated an overall prevalence of

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COPD of 8.6% among 12,436 adults (average age for entire cohort, 37.9 years).<sup>17</sup> In the United States, COPD is second only to coronary heart disease as a reason for Social Security disability payments.

Worldwide, the burden of COPD is projected to increase substantially, paralleling the rise in tobacco use, particularly in developing countries. An analysis by the World Bank and World Health Organization ranked COPD 12th in 1990 in disease burden, as reflected in disability-adjusted years of life lost.<sup>10</sup>

#### SEVERITY OF COPD

For consistency throughout the document, the panel used the description of severity of COPD as recommended by the Global Initiative for Chronic Obstructive Lung Disease<sup>18</sup> and the American Thoracic Society/European Respiratory Society Guidelines<sup>19</sup> based on FEV<sub>1</sub>, as follows: stage I (mild), FEV<sub>1</sub> ≥ 80% predicted; stage II (moderate), FEV<sub>1</sub> 50 to 80% predicted; stage III (severe), FEV<sub>1</sub> 30 to 50% predicted; and stage IV (very severe), FEV<sub>1</sub> < 30% predicted.

#### PULMONARY REHABILITATION

Rehabilitation programs for patients with chronic lung diseases are well-established as a means of enhancing standard therapy in order to control and alleviate symptoms and optimize functional capacity.<sup>2,4,14,20</sup> The primary goal is to restore the patient to the highest possible level of independent function. This goal is accomplished by helping patients become more physically active, and to learn more about their disease, treatment options, and how to cope. Patients are encouraged to become actively involved in providing their own health care, more independent in daily activities, and less dependent on health professionals and expensive medical resources. Rather than focusing solely on reversing the disease process, rehabilitation attempts to reduce symptoms and reduce disability from the disease.

Many rehabilitation strategies have been developed for patients with disabling COPD. Programs typically include components such as patient assessment, exercise training, education, nutritional intervention, and psychosocial support. Pulmonary rehabilitation has also been applied successfully to patients with other chronic lung conditions such as interstitial diseases, cystic fibrosis, bronchiectasis, and thoracic cage abnormalities.<sup>21</sup> In addition, it has been used successfully as part of the evaluation and preparation for surgical treatments such as lung transplantation and lung volume reduction sur-

gery.<sup>22–26</sup> Pulmonary rehabilitation is appropriate for any stable patient with a chronic lung disease who is disabled by respiratory symptoms. Patients with advanced disease can benefit if they are selected appropriately and if realistic goals are set. Although pulmonary rehabilitation programs have been developed in both outpatient and inpatient settings, most programs, and most of the studies reviewed in this document, pertain to outpatient programs for ambulatory patients.

#### DEFINITION

The American Thoracic Society and the European Respiratory Society have recently adopted the following definition of pulmonary rehabilitation: Pulmonary rehabilitation is 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 systemic manifestations of the disease. Comprehensive pulmonary rehabilitation programs include patient assessment, exercise training, education, and psychosocial support.<sup>4</sup>

This definition focuses on three important features of successful rehabilitation:

1. *Multidisciplinary*: Pulmonary rehabilitation programs utilize expertise from various health-care disciplines that is integrated into a comprehensive, cohesive program tailored to the needs of each patient.
2. *Individual*: Patients with disabling lung disease require individual assessment of needs, individual attention, and a program designed to meet realistic individual goals.
3. *Attention to physical and social function*: To be successful, pulmonary rehabilitation pays attention to psychological, emotional, and social problems as well as physical disability, and helps to optimize medical therapy to improve lung function and exercise tolerance.

The interdisciplinary team of health-care professionals in pulmonary rehabilitation may include physicians; nurses; respiratory, physical, and occupational therapists; psychologists; exercise specialists; and/or others with appropriate expertise. The specific team make-up depends on the resources and expertise available, but usually includes at least one full-time staff member.<sup>27</sup>

## METHODOLOGY AND GRADING OF THE EVIDENCE FOR PULMONARY REHABILITATION

In 1997, the ACCP and the AACVPR released an evidence-based clinical practice guideline entitled "Pulmonary Rehabilitation: Joint ACCP/AACVPR Evidence-Based Guidelines."<sup>2,3</sup> Following the approved process for the review and revision of clinical practice guidelines, in 2002 the ACCP Health and Science Committee determined that there was a need for reassessment of the current literature and an update of the original practice guideline. This new guideline is intended to update the recommendations from the 1997 document and to provide new recommendations based on a comprehensive literature review. The literature review and development of evidence tables were conducted by Carla Herreiras, MPH, the ACCP Clinical Research Analyst. The joint ACCP/AACVPR expert panel used the evidence to develop graded recommendations.

### *Expert Panel Composition*

The guideline panel was organized under the joint sponsorship of the ACCP and the AACVPR. Andrew Ries, MD, MPH, FCCP, Chair of the 1997 panel, served as Chair of the new panel. Panel members were evenly distributed between and selected by the two organizations with a goal of making the panel multidisciplinary and geographically diverse. Drs. Casaburi, Mahler, Make, and Rochester represented the ACCP, and Drs. Bauldoff, Carlin, Emery, and ZuWallack represented the AACVPR. Five panel members (Drs. Carlin, Casaburi, Emery, Mahler, and Make) had served on the previous guideline panel. In addition to several conference calls, the panel met for one 2-day meeting to review the evidence tables and become familiar with the process of grading recommendations. Writing assignments were determined by members' known expertise in specific areas of pulmonary rehabilitation. Each section of the guideline was assigned to one primary author and at least one secondary author. Sections were reviewed by relevant panel members when topics overlapped.

### *Conflict of Interest*

At several stages during the guideline development period, panel members were asked to disclose any conflict of interest. These occurred at the time the panel was nominated, at the first face-to-face meeting, the final conference call, and prior to publication. Written forms were completed and are on file at the ACCP.

### *Scope of Work*

The 1997 practice guideline on pulmonary rehabilitation focused on program component areas of

lower and upper extremity training, ventilatory muscle training, and various outcomes of comprehensive pulmonary rehabilitation programs, including dyspnea, quality of life, health-care utilization, and survival. Psychosocial and educational aspects of rehabilitation were examined both as program components and as outcomes.

For this review, the panel decided to focus on studies that had been published since the previous review, again concentrating on stable patients with COPD. Since there have been many advances and new areas of investigation since the previous document was written, the panel decided to expand the scope of this review rather than just update the previous one. Topics covered in this document include the following:

- Outcomes of comprehensive pulmonary rehabilitation programs: lower extremity exercise training; dyspnea; health-related quality of life (HRQOL); health-care utilization and economic analysis; survival; psychosocial outcomes; and long-term benefits from pulmonary rehabilitation;
- Duration of pulmonary rehabilitation;
- Postrehabilitation maintenance strategies;
- Intensity of aerobic exercise training;
- Strength training in pulmonary rehabilitation;
- Anabolic drugs;
- Upper extremity training;
- Inspiratory muscle training (IMT);
- Education;
- Psychosocial and behavioral components of pulmonary rehabilitation;
- Oxygen supplementation as an adjunct to pulmonary rehabilitation;
- Noninvasive ventilation;
- Nutritional supplementation in pulmonary rehabilitation;
- Pulmonary rehabilitation for patients with disorders other than COPD; and
- Summary and recommendations for future research.

### *Review of Evidence*

The literature review was based on the scope of the work as outlined in the previous section. The literature search was conducted through a comprehensive MEDLINE search from 1996 through 2004, and was supplemented by articles supplied by the guideline panel as well as by a review of bibliographies and reference lists from review articles and other existing systematic reviews. The literature search was limited to articles published in peer-reviewed journals only in the English language, and on human subjects. Inclusion criteria primarily included a population of persons with a diagnosis of COPD determined either by physical examination or by existing diagnostic criteria; however, those with other pulmonary conditions (*eg*, asthma or

interstitial lung disease) were also included. The search included randomized controlled trials (RCTs), meta-analyses, systematic reviews, and observational studies. The search strategy linked pulmonary rehabilitation or a pulmonary rehabilitation program with each key subcomponent, as listed in section on "Scope of Work." To locate studies other than RCTs, such as systematic reviews and metaanalyses, those key words were used in searching MEDLINE and the Cochrane databases. Informal review articles were included only for hand searching additional references. For the purpose of this review, *pulmonary rehabilitation* was defined operationally as studies involving exercise training plus at least one additional component. Associated outcomes across all components were dyspnea, exercise tolerance, quality of life and activities of daily life, and health-care utilization. An initial review of 928 abstracts was conducted by the ACCP Clinical Research Analyst and the Research Specialist. Full articles (a total of 202) were formally reviewed and abstracted by the Clinical Research Analyst, and a total of 81 clinical trials were included in all evidence tables. RCTs were scored using a simplified system that was based on methods of randomization, blinding, and documentation of withdrawals/loss to follow-up. This system follows a method that is based on a 3-point scale, which rates randomization (and appropriateness), blinding (and appropriateness), and tracking of withdrawals and loss to follow-up. Studies were graded on a scale of 0 to 5.<sup>28</sup> No formal quantitative analysis was performed due to the wide variation in methodologies reported in studies. Given the length of time required to prepare the final manuscript after the conclusion of the systematic literature review in December 2004, from which the tables were constructed, the committee was allowed to include reference to selected articles published in 2005 and 2006 in the text if the additional information provided by the newer publications was felt to be important.

#### *Strength of Evidence and Grading of Recommendations*

The ACCP system for grading guideline recommendations is based on the relationship between the strength of the evidence and the balance of benefits to risk and burden (Table 1).<sup>29</sup> Simply stated, recommendations can be grouped on the following two levels: strong (grade 1); and weak (grade 2). If there is certainty that the benefits do (or do not) outweigh risk, the recommendation is strong. If there is less certainty or the benefits and risks are more equally balanced, the recommendation is weaker. Several important issues must be considered when classifying recommendations. These include the quality of the evidence that supports estimates of benefit, risks,

**Table 1—Relationship of Strength of the Supporting Evidence to the Balance of Benefits to Risks and Burdens\***

Strength of Evidence	Balance of Benefits to Risks and Burdens			
	Benefits Outweigh Risks/Burdens	Risks/Burdens Outweigh Benefits	Evenly Balanced	Uncertain
	High	1A	1A	2A
Moderate	1B	1B	2B	
Low or very low	1C	1C	2C	2C

\*1A = strong recommendation; 1B = strong recommendation; 1C = strong recommendation; 2A = weak recommendation; 2B = weak recommendation; 2C = weak recommendation.

and costs; the importance of the outcomes of the intervention; the magnitude and the precision of estimate of the treatment effect; the risks and burdens of an intended therapy; the risk of the target event; and varying patient values.

The strength of evidence is classified, based on the quality of the data, into the following three categories: high (grade A); moderate (grade B); and low (grade C). The strongest evidence comes from well-designed RCTs yielding consistent and directly applicable results. In some circumstances, high-quality evidence can be the result of overwhelming evidence from observational studies. Moderate-quality evidence is based on RCTs with limitations that may include methodological flaws or inconsistent results. Studies other than RCTs that may yield strong results are also included in the moderate-quality category. The weakest type of evidence is that from other types of observational studies. It should be noted that the ACCP Health and Science Policy Committee has endorsed the principle that most relevant clinical studies provide evidence, even though the quality of that evidence is varied. Therefore, the reasons for excluding studies should be documented.

Table 2 describes the balance of benefits to risk and burden, and the level of certainty based on this balance. As stated above, the more certain the

**Table 2—Description of Balance of Benefits to Risks/Burdens Scale**

Benefits clearly outweigh the risks and burdens	Certainty of imbalance
Risks and burdens clearly outweigh the benefits	Certainty of imbalance
The risks/burdens and benefits are closely balanced	Less certainty
The balance of benefits to risks and burdens is uncertain	Uncertainty

balance, or lack thereof, the stronger the recommendation. Patient and community values are important considerations in clinical decision making and are factored into the grading process. In situations in which the benefits clearly do or do not outweigh the risks, it is assumed that nearly all patients would have the same preferences. For weaker recommendations, however, there may not be consistency in patient preferences.

In addition to recommendations, the committee included several statements when it thought that there was insufficient evidence to make a specific recommendation. These statements are included along with the recommendations but are not graded.

#### OUTCOMES OF COMPREHENSIVE PULMONARY REHABILITATION PROGRAMS

As currently practiced, pulmonary rehabilitation typically includes several different components, including exercise training, education, instruction in various respiratory and chest physiotherapy techniques, and psychosocial support. For this review, *comprehensive pulmonary rehabilitation* was defined as an intervention that includes one or more of these components beyond just exercise training, which is considered to be an essential, mandatory component.

In addition to the clinical trials reviewed in the evidence tables in this document, several systematic reviews and metaanalyses have been published within the past decade that support the beneficial effects from comprehensive pulmonary rehabilitation programs. In a Cochrane Review published in 2006, Lacasse<sup>30</sup> analyzed 31 RCTs in patients with COPD and concluded that rehabilitation forms an important component of the management of COPD. They reported statistically and clinically significant improvements in important domains of quality of life (i.e., dyspnea, fatigue, emotions, and patient control over disease). Improvement in measures of exercise capacity were slightly below the threshold for clinical significance. Similarly, after a systematic review, Cambach and colleagues<sup>31</sup> identified 18 articles for inclusion in a metaanalysis of outcome measures of exercise capacity and HRQOL in patients with COPD. They found significant improvements for exercise measures of maximal exercise capacity, endurance time, and walking distance, and for HRQOL measures in all dimensions of the Chronic Respiratory Disease Questionnaire (CRDQ) [*ie*, dyspnea, fatigue, emotion, and mastery]. Improvements in maximal exercise capacity and walking distance were sustained for up to 9 months after rehabilitation.

#### Lower Extremity Exercise Training

*Dyspnea*: In the previous evidence-based review document<sup>2,3</sup> the 1997 guidelines panel concluded that the highest strength of evidence (A) supported the recommendation for including lower extremity exercise training as a key component of pulmonary rehabilitation for patients with COPD. In addition, the panel concluded that there was high-grade evidence (A) that pulmonary rehabilitation improves the symptom of dyspnea in patients with COPD. This panel concluded that the evidence presented in Table 3 in this document further strengthens those conclusions and recommendations.

#### Recommendations

**1. A program of exercise training of the muscles of ambulation is recommended as a mandatory component of pulmonary rehabilitation for patients with COPD.** Grade of recommendation, 1A

**2. Pulmonary rehabilitation improves the symptom of dyspnea in patients with COPD.** Grade of recommendation, 1A

#### HRQOL

Regarding changes in HRQOL, the previous panel concluded that there was B level strength of evidence supporting the recommendation that “pulmonary rehabilitation improves health-related quality of life in patients with COPD.” Based on the current review, this panel believes that the additional published literature now available strengthens support for this conclusion and upgrades the evidence to grade A. In this document, the term *HRQOL* will be used interchangeably with the term *health status*.

In one of the larger RCTs reported (200 patients), Griffiths and colleagues<sup>32</sup> reported significant improvements in HRQOL 1 year after a 6-week pulmonary rehabilitation program. Troosters and colleagues<sup>33</sup> reported sustained improvement in HRQOL over 18 months after patients participated in a 6-month outpatient pulmonary rehabilitation program compared with the decline observed in the control group. The study reported by Green and colleagues<sup>34</sup> reported improvement in HRQOL after pulmonary rehabilitation and found that improvements after a 7-week intervention were greater than those after 4 weeks of pulmonary rehabilitation. Strijbos and colleagues<sup>35</sup> reported significant improvement in reported well-being after pulmonary rehabilitation that was maintained over 18 months in rehabilitation-treated subjects, while most patients in the control group felt unchanged or worse. Foglio and colleagues<sup>36</sup> reported sustained improvements

Table 3—Outcomes of Comprehensive Pulmonary Rehabilitation\*

Study/Year	Study Type	Country/Setting	Patients, Total		Outcomes	Results
			No.	No.		
Clark et al <sup>45</sup> /2000	RCT, comprehensive training vs control	Scotland/home	48		Peripheral muscle endurance and strength	Lower and upper body increase (p < 0.001 vs control group); endurance increase (p < 0.001 vs control group)
Wijlstra et al <sup>58</sup> /1996	RCT, home PRP vs control	Netherlands/home	45		Lung fx; endurance; strength	FEV <sub>1</sub> improved; IVC decreased; Wmax decreased
Strijbos et al <sup>35</sup> /1996	RCT: OP PRP vs home PRP vs control groups	Netherlands/OP	40		Exercise capacity; general QOL	Wmax and 4MWD (p = 0.001) all groups; at rest breath decrease (p < 0.001); QOL shows significant improvement at 12/18 mo
Bendstrup et al <sup>58</sup> /1997	Unblinded RCT: comprehensive PRP vs normal care group	Denmark/OP	47		ADL, QOL, exercise tolerance	ADL improvement at 12 wk (p = 0.004) and 24 wk (p = 0.007) post-PRP; HRQL improved post-PRP
Emery et al <sup>57</sup> /1998	Double-blind RCT: comprehensive PRP vs normal care vs control group	United States/OP	79		Physiologic assessment; HRQL; cognitive assessment	No significant change in physiological assessment; HRQL, NS for group, time, or interaction; no significant change in most cognitive parameters
Wedzicha et al <sup>39</sup> /1998	RCT: PRP with education vs education	United Kingdom/OP	126		Lung function, exercise tolerance/breathlessness, health status	Exercise performance increase (p < 0.0005 vs control group); exercise tolerance increase; significant change in QOL post-PRP
Engstrom et al <sup>59</sup> /1999	Blinded RCT: 12 mo PRP vs conventional care	Sweden/OP	50		Lung function and other physiologic factors; QOL	Walking distance/tolerance (13.5% and 12.1% increase, respectively; vs control group); QOL, no effect on SGRQ or Mood Adjective Check List
Troosters et al <sup>33</sup> /2000	RCT: 6 mo and 18 mo PRP vs usual care	Belgium/OP clinic	100		Pulmonary fx; exercise capacity; muscle strength and QOL	16 who died during trial had significantly lower FEV <sub>1</sub> (p < 0.001), DLCO (p < 0.001), walking distance (p < 0.05), and exercise capacity (p < 0.02); no significant effects of PRP on PF; QOL improved following PRP
Griffiths et al <sup>32</sup> /2000	Single blind RCT: comprehensive PRP vs standard care	United Kingdom/OP	200		Exercise capacity; HRQL	Health status measures including HRQL significantly improved
Green et al <sup>34</sup> /2001	Single blind RCT: short- vs long-term PRP	United Kingdom/OP	44		Endurance; HRQL	At 7 wk, patients had greater improvement in each outcome variable; total CRDQ score (p = 0.011) and domains of dyspnea (p = 0.021), emotion (p = 0.003), and mastery (p = 0.027)
Foglio et al <sup>36</sup> /2001	Single-blind RCT: repeat PRP vs no repeat	Italy/OP	61		Lung function; dyspnea; HRQL; HC utilization	No significant changes in lung function; exercise tolerance increased postrehabilitation, but not sustained; no significant changes in dyspnea/leg pain; hospitalization decreased
Finnerty et al <sup>37</sup> /2001	Double blind RCT: PRP vs routine care	United Kingdom/OP	100		HRQL; secondary outcomes walk distance	SGRQ decreased (p < 0.001); symptom score, ADL (p < 0.01 tx group); walk distance increased significantly
Berry et al <sup>63</sup> /2003	Single-blind RCT	United States/OP	140		Physical disability; V̇O <sub>2</sub> ; pulmonary function	Distance increase (p = 0.03); stair-climb increase (p = 0.05) at 18 mo; peak O <sub>2</sub> /PFT/physical activity scale (NS)
White et al <sup>42</sup> /2002	Not blinded RCT: upper and lower PRP vs brief advice	United Kingdom/OP	103		Pulmonary function; exercise capacity; HRQL	Walk distance (p < 0.001 tx group vs baseline) at 3 mo; HRQL, dyspnea (p < 0.001 vs tx group); fatigue and emotion (p < 0.01 vs tx group); mastery (p < 0.001 vs tx group); total CRDQ score (p < 0.05 tx group); all other parameters NS
Man et al <sup>45</sup> /2004	RCT: early PRP vs normal care	United Kingdom/OP	42		Exercise capacity; HRQL and general QOL	6MWD significant increased tx group (p = 0.0002); HRQL, significant improvement in all parameters measured; utilization, hospital admission, visits, days decreased in tx group vs control group

\*OP = outpatient; ADL = activities of daily living; QOL = quality of life; 4MWD = 4-min walk distance; 6MWD = 6-min walk distance; PRP = pulmonary rehabilitation program; PF = pulmonary function; SGRQ = St. George Respiratory Questionnaire; SF-36 = Medical Outcomes Study 36-item short form; DLCO = diffusing capacity of the lung for carbon monoxide; NS = not significant; IVC = inspiratory vital capacity; fx = function; tx = transplant; Wmax = maximum exercise work; HAD = hospital anxiety and depression scale.



in HRQOL up to 2 years after pulmonary rehabilitation. In a study of early pulmonary rehabilitation after hospital discharge for an exacerbation of COPD, Man and colleagues reported significant improvements in HRQOL measures. Finnerty and colleagues<sup>37</sup> reported marked improvements in HRQOL after pulmonary rehabilitation that persisted for 6 months. Similar findings were reported by Bendstrup and colleagues.<sup>38</sup> In the study reported by Wedzicha and colleagues,<sup>39</sup> which stratified patients according to baseline dyspnea, improvement in HRQOL after pulmonary rehabilitation was observed in patients with moderate dyspnea (Medical Research Council [MRC] score, 3 or 4) but not in control subjects or patients with severe baseline dyspnea (MRC score, 5). The study by Ries and colleagues<sup>40</sup> evaluated a maintenance program after pulmonary rehabilitation. However, observational results after pulmonary rehabilitation that had been administered to all patients before randomization demonstrated consistent improvements in several different measures of both general and disease-specific measures of HRQOL. Guell and colleagues<sup>41</sup> reported significant improvement in HRQOL that persisted, although diminished, for up to 2 years of follow-up after the pulmonary rehabilitation intervention.

Of the studies reported in Table 3, only one small study by White and colleagues<sup>42</sup> reported only modest improvements in measured HRQOL that did not consistently reach statistically or clinically significant levels. In addition to the studies reported in Table 3, which generally were performed in single specialized centers, two observational studies<sup>43,44</sup> provide strong evidence of the effectiveness of pulmonary rehabilitation as routinely practiced in clinical centers. Although neither of these studies<sup>43,44</sup> was an RCT, they provide important information regarding the generalizability of the practice of pulmonary rehabilitation beyond specialized centers and as currently practiced in the general medical community in the United States. A multicenter evaluation of pulmonary rehabilitation in 522 patients in nine centers throughout California<sup>43</sup> reported consistent improvements in symptoms of dyspnea and HRQOL after pulmonary rehabilitation. Similar findings were reported in a multicenter observational study in Connecticut.<sup>44</sup> In this study, significant improvement was reported in the pulmonary functional status scale in 164 patients in 10 centers and in the CRDQ in 60 patients in 3 centers. Also, in the National Emphysema Treatment Trial (NETT),<sup>26</sup> a randomized study that evaluated lung volume reduction surgery in 1,218 patients with severe emphysema, all subjects were required to complete a pulmonary rehabilitation program as part of the eligibility requirements before randomization. Pulmonary reha-

bilitation was conducted at the 17 NETT centers as well as at 539 satellite centers throughout the United States. Observational results demonstrated significant improvements in measures of exercise tolerance, dyspnea, and HRQOL after rehabilitation that were quite comparable among the specialized NETT centers and the largely community-based satellite centers.

#### *Recommendation*

**3. Pulmonary rehabilitation improves HRQOL in patients with COPD.** Grade of recommendation, 1A

#### *Health-Care Utilization and Economic Analysis*

Regarding changes in health-care utilization resulting from pulmonary rehabilitation, the previous panel concluded that there was B level strength of evidence supporting the recommendation that “pulmonary rehabilitation has reduced the number of hospitalizations and the number of days of hospitalization for patients with COPD.”

In the current review, some additional information is available about changes in health-care utilization after pulmonary rehabilitation. In the study by Griffiths and colleagues,<sup>32</sup> over 1 year of follow-up the number of patients admitted to the hospital was similar in both the pulmonary rehabilitation group and the control group (40 of 99 vs 41 of 101 patients); however, the number of days spent in the hospital was significantly lower in the rehabilitation patients (10.4 vs 21.0 days, respectively). In a subsequent cost-utility economic analysis of the results in this pulmonary rehabilitation trial, Griffiths and colleagues<sup>45</sup> found that the cost per quality-adjusted life-years indicated that pulmonary rehabilitation was, in fact, cost-effective and would likely result in financial benefits to the health-care system (quality-adjusted life-year is a measure of effectiveness that is commonly used in cost-effectiveness analyses, reflecting survival adjusted for quality of life, or the value that individuals place on expected years of life). In the trial reported by Foglio and colleagues,<sup>36</sup> results indicated a significant decrease in yearly hospitalizations and exacerbations > 2 years after pulmonary rehabilitation.

Goldstein and colleagues<sup>46</sup> conducted a cost analysis that was associated with an RCT of a 2-month inpatient pulmonary rehabilitation program (followed by 4 months of outpatient supervision) that produced statistically and clinically significant improvements in measures of HRQOL and exercise capacity. Although the cost analysis in this study was driven largely by the inpatient phase of the program and, as such, is not applicable to the large majority of outpatients programs, the authors found cost-effective-

ness ratios for the CRDQ component measures to range from \$19,011 to \$35,142 (in Canadian dollars) per unit difference. Even with the added costs associated with the inpatient program, these cost/benefit ratios are within a range that has been typically considered to represent reasonable cost-effectiveness for other widely advocated health-care programs.<sup>47</sup>

In a small randomized trial of early pulmonary rehabilitation after hospitalization for acute exacerbation, Man and colleagues<sup>48</sup> reported a significant reduction in emergency department visits and a trend toward reduced numbers of hospital admissions and days spent in the hospital over the 3 months after hospital discharge in the pulmonary rehabilitation group compared to the usual-care group. Also, in a multicenter randomized trial of a self-management program of patients with severe COPD, Bourbeau and colleagues<sup>49</sup> reported a significant reduction in the numbers of hospital admissions and days spent in the hospital in the year following the intervention compared to the usual-care control group.

In a multicenter, observational evaluation<sup>43</sup> of the effectiveness of pulmonary rehabilitation in centers throughout California (not included in Table 3), self-reported measures of health-care utilization were found to decrease substantially over 18 months of observation after the rehabilitation intervention. In the 3-month period prior to pulmonary rehabilitation, 522 patients reported 1,357 hospital days (2.4 per patient), 209 urgent care visits (0.4 per patient), 2,297 physician office visits (4.4 per patient), and 1,514 telephone calls to physicians (2.7 per patient). Over the 18 months after rehabilitation, the average per patient reported health-care utilization (in the past 3 months) was reduced approximately 60% for hospital days, 40% for urgent care visits, 25% for physician office visits, and 30% for telephone calls. It should be recognized that the results of an observational, noncontrolled study like this may be influenced by the selection of patients for pulmonary rehabilitation shortly after an exacerbation or episode of increased health-care utilization.

#### *Recommendations*

**4. Pulmonary rehabilitation reduces the number of hospital days and other measures of health-care utilization in patients with COPD.** Grade of recommendation, 2B

**5. Pulmonary rehabilitation is cost-effective in patients with COPD.** Grade of recommendation, 2C

#### *Survival*

The previous panel concluded that there was little evidence (strength of evidence, C) regarding survival after pulmonary rehabilitation and made the recom-

mendation that “pulmonary rehabilitation may improve survival in patients with COPD.” Only one RCT<sup>50</sup> of pulmonary rehabilitation was included in the previous review. In that study of 119 patients, Ries and colleagues<sup>50</sup> reported 11% higher survival over 6 years after comprehensive pulmonary rehabilitation (67%) compared with an education control group (56%). This difference was not statistically significant. Other evidence for improved survival was derived from nonrandomized and observational studies. This lack of evidence does not necessarily indicate that pulmonary rehabilitation has no effect on survival, but in order to be reasonably powered to detect an effect of this magnitude the sample size would have to be a magnitude larger than those found in existing studies. The timed walk distance and MRC-rated dyspnea do improve with pulmonary rehabilitation, and these variables are correlated with survival in patients with COPD.

In the current review, few additional data were found regarding the effect of pulmonary rehabilitation on survival. Similar to previous published studies, the trial reported by Griffiths and colleagues<sup>32</sup> that followed 200 patients over 1 year found fewer deaths in the rehabilitation group (6 of 99 patients) compared with the control group (12 of 101 patients).

#### *Recommendation*

**6. There is insufficient evidence to determine whether pulmonary rehabilitation improves survival in patients with COPD. No recommendation is provided.**

#### *Psychosocial Outcomes*

Regarding psychosocial outcomes of pulmonary rehabilitation, the previous panel concluded that “scientific evidence was lacking” (strength of evidence, C). Reviews of the research literature pertaining to psychosocial outcomes of pulmonary rehabilitation programs indicate that comprehensive pulmonary rehabilitation is generally associated with enhanced psychological well-being (*ie*, reduced distress) and improved quality of life.<sup>51,52</sup> In addition, it has been found that increased self-efficacy associated with exercise may mediate the effect of exercise rehabilitation on quality of life.<sup>53</sup> Other positive psychosocial outcomes of exercise rehabilitation include improved cognitive function,<sup>54–56</sup> reduced symptoms of anxiety<sup>32,55</sup> and depression,<sup>32</sup> and improved patient perceptions of positive consequences of the illness.<sup>57</sup>

In the current review of randomized studies, Griffiths and colleagues<sup>32</sup> reported reduced symptoms of anxiety and depression following a 6-week

pulmonary rehabilitation program, with symptoms of depression remaining significantly reduced at the 12-month follow-up. Emery and colleagues<sup>55</sup> found reduced anxiety and improved cognitive function following a 10-week pulmonary rehabilitation intervention. In a study of 164 patients participating in pulmonary rehabilitation prior to being randomly assigned to a long-term follow-up intervention, Ries and colleagues<sup>40</sup> observed significant improvements in measures of depression and self-efficacy for walking immediately following the 8-week pulmonary rehabilitation program.

#### *Recommendation*

**7. There are psychosocial benefits from comprehensive pulmonary rehabilitation programs in patients with COPD.** Grade of recommendation, 2B

#### *Long-term Benefits From Pulmonary Rehabilitation*

The formal component of most pulmonary rehabilitation programs is of relatively short duration, usually ranging from 6 to 12 weeks. Regarding the issue of long-term benefits following the short-term intervention, the previous panel did not specifically address this topic but recommended it as an important area for future research. Since that time, additional important studies have addressed this topic. The next section discusses the issue of the duration of pulmonary rehabilitation treatment (*ie*, beyond 12 weeks).

Several clinical trials of 6 to 12 weeks of comprehensive pulmonary rehabilitation that have followed patients over a longer term have found that benefits typically persist for about 12 to 18 months after the intervention but gradually wane thereafter. In many ways, this is surprising given the severity of illness for many of these patients with chronic lung disease and the complex set of behaviors incorporated into pulmonary rehabilitation (*eg*, exercise training, breathing control techniques, complex treatment regimens with medications, use of supplemental oxygen, and relaxation or panic control techniques). More recent clinical trials substantiate these findings (Table 4).

Griffiths and colleagues<sup>32</sup> reported improvements in measures of exercise tolerance, HRQOL, anxiety, and depression after pulmonary rehabilitation that remained significant but declined gradually over 1 year of follow-up. The study reported by Wijkstra and colleagues<sup>58</sup> evaluated the effects of weekly vs monthly follow-up over the 18 months after pulmonary rehabilitation in a small sample of patients with COPD ( $n = 36$ ). They reported no long-term improvement in exercise tolerance in the two experimental groups, although this was better than the

decline observed in the control group. There were, however, more sustained improvements in dyspnea. Engstrom and colleagues<sup>59</sup> reported sustained improvement in exercise tolerance at 12 months after pulmonary rehabilitation with minimal improvements in either a general or disease-specific measure of HRQOL (although there was a trend for worsening HRQOL in the control group). Strijbos and colleagues<sup>35</sup> reported significant improvement in reported well-being after pulmonary rehabilitation that was maintained over 18 months (compared to most control subjects who reported being unchanged or worse). The study reported by Guell and colleagues<sup>41</sup> also found persistent, but diminished, benefits in measures of exercise tolerance, dyspnea, and HRQOL over the 2 years of follow-up after pulmonary rehabilitation.

The study reported by Ries and colleagues<sup>40</sup> examined the effects of a telephone-based maintenance program for 1 year after a short-term rehabilitation intervention. The experimental effects of the maintenance program are discussed in a subsequent section on postrehabilitation maintenance. However, as an observational study, it is notable that the control group (without postprogram maintenance) demonstrated a progressive decline in benefits over 2 years of follow-up. Another multicenter observational evaluation of the effectiveness of pulmonary rehabilitation in centers throughout California (not included in Table 3)<sup>43</sup> found that improvements in symptoms of dyspnea, HRQOL, and indexes of health-care utilization declined over 18 months but still remained above baseline levels.

#### *Recommendation*

**8. Six to twelve weeks of pulmonary rehabilitation produces benefits in several outcomes that decline gradually over 12 to 18 months.** Grade of recommendation, 1A. **Some benefits, such as HRQOL, remain above control levels at 12 to 18 months.** Grade of recommendation, 1C

#### DURATION OF PULMONARY REHABILITATION

There is no consensus of opinion regarding the optimal duration of the pulmonary rehabilitation intervention. From the patient's perspective, the optimal duration should be that which produces maximal effects in the individual without becoming burdensome. Significant gains in exercise tolerance, dyspnea, and HRQOL have been observed following inpatient pulmonary rehabilitation programs as short as 10 days<sup>60</sup> and after outpatient programs as long as 18 months.<sup>61</sup> Shorter program duration has the potential to reduce the cost per patient served and to

**Table 4—Long-term Effects of Pulmonary Rehabilitation\***

Study/Year	Study Type	Country/Setting	Patients, Total No.	Outcomes	Results
Wijkstra et al <sup>58</sup> / 1996	RCT: home PRP vs control group	Netherlands/ home	45	Lung fx; endurance; 6MWD; IM strength and endurance	FEV <sub>1</sub> improved in group B (p < 0.05 to baseline); Wmax decreased (p < 0.05 for control subjects); PIP/ endurance significant increase in group A only
Engstrom et al <sup>59</sup> /1999	RCT: single blind; long-term vs conventional care	Sweden/OP	50	Lung fx and other physiologic factors; QOL	Walk distance/tolerance significantly increased in tx group Sickness impact profile: decreased in control group
Griffiths et al <sup>32</sup> / 2000	RCT: single blind: 6-wk PRP vs conventional care	United Kingdom/OP	200	Exercise capacity; general health status; HRQL	Shuttle walk, SGRQ, SF-36, HAD statistically significant vs control group (6 wk) Shuttle walk, SGRQ, CRDQ, SF-36, and HAD statistically significant vs control group (12 wk)
Guell et al <sup>41</sup> / 2000	RCT: single-blind; long-term vs standard care	Spain/OP	60	Dyspnea, exercise, HRQL, hospital utilization	Treatment effects: FVC (p = 0.04); 10MWT (p = 0.0001); dyspnea (p = 0.0001); MRC scales (p = 0.0001); CRDQ score in all domains Exacerbations: control group, 207; tx group, 111 (p < 0.0001); hospitalization: control group, 39; tx group, 18
Foglio et al <sup>36</sup> / 2001	RCT: single-blind; repeat PRP vs no repeat	Italy/OP	61	Lung fx; symptoms; dyspnea; HRQL; health-care utilization	Lung fx/inspiratory muscle fx: NS; exercise tolerance: increased in tx group, not sustained; dyspnea/leg pain, NS; POD, short-term improvement (NS); utilization: hospitalization decreased
Brooks et al <sup>71</sup> / 2002	RCT: enhanced follow-up after PRP vs standard care	Canada/OP	109	Functional exercise capacity; HRQL	6MWD: distance, NS; time (p < 0.001); time × group interaction (p = 0.03); distance at 12 mo decreased (p < 0.001); HRQL: significant differences over time
Ries et al <sup>40</sup> / 2003	RCT: 12-mo maintenance vs standard care	United States/ OP	172	PFT, exercise tolerance, psychosocial measures, health-care utilization	At 12 mo, exercise tolerance/ health status significantly improved in tx vs control group; 6MWT decreased both groups At 24 mo, levels for all parameters were slightly higher than pre-PRP; utilization decreased in tx group

\*10MWT = 10-min walk test; MRC = Medical Research Council; PIP = peak inspiratory mouth pressure; 6 MWT = 6-min walk test; PFT = pulmonary function test; POD = perception of dyspnea. See Table 3 for abbreviations not used in the text.

spread limited resources.<sup>62</sup> On the other hand, longer program duration may produce greater gains and improved maintenance of benefits. This section will examine longer term pulmonary rehabilitation interventions (*ie*, beyond 12 weeks of treatment).

Successful pulmonary rehabilitation requires complex behavioral changes for which the patients' competence and adherence may be facilitated by longer exposure to treatment interventions and interactions with staff who provide reinforcement, encourage-

ment, and coaching. These changes include incorporating regular exercise into the patient's lifestyle; the use of breathing techniques, pacing and energy conservation strategies; and the use of medications and equipment, supplemental oxygen, and psychosocial adaptations. A number of external factors also influence program duration including health-care systems and reimbursement policies, access to programs, level of functional disability, health-care provider referral patterns, and the ability of individual patients to make progress toward treatment goals.

Few clinical trials have focused on the impact of program duration on rehabilitation outcomes, but existing data suggest that gains in exercise tolerance may be greater following longer programs (Table 5). For example, two other randomized trials compared 3 vs 18 months of low-intensity exercise training in pulmonary rehabilitation.<sup>63,64</sup> Berry and colleagues<sup>63</sup> demonstrated that the longer intervention led to a 6% increase in the 6-min walk distance, a 12% reduction in self-reported disability, and faster completion of stair climbing and overhead tasks. Foy and colleagues<sup>64</sup> showed that only male patients achieved greater gains in CRDQ scores following the 18-month program (compared to the 3-month program). In a 2005 published prospective trial involving seven outpatient programs (not in Table 5), Verrill and colleagues<sup>65</sup> demonstrated that patients achieved significant gains in exercise tolerance (6-min walk distance), dyspnea (University of California, San Diego Shortness of Breath Questionnaire), and health status (Medical Outcomes Study 36-item Short Form and the quality-of-life index) after 12 weeks of pulmonary rehabilitation. Following an additional 12 weeks of rehabilitation, exercise tolerance but not health status or dyspnea outcomes improved further, suggesting that program duration may not impact all outcomes equally.

Also in support of longer term exercise training, Troosters and colleagues<sup>33</sup> demonstrated that a 6-month outpatient pulmonary rehabilitation program composed of moderate-to-high-intensity aerobic and strength exercise training led to significant improvements in exercise performance and quality of life. Although this study did not compare the 6-month program with a shorter one, the benefits gained following the 6-month training program persisted 18 months after the completion of rehabilitation. This contrasts with the results of other studies<sup>35,50,66</sup> of pulmonary rehabilitation of shorter than 6 months duration in which benefits tended to decline progressively over the year following rehabilitation. Likewise, in the study by Guell and colleagues<sup>41</sup> (Table 4) a 12-month intervention (6 months of daily rehabilitation followed by 6 months of weekly supervision) led to gains in exercise toler-

**Table 5—Duration of Pulmonary Rehabilitation\***

Study/Year	Study Type	Country/Setting	Patients, Total No.	Outcomes	Results
Troosters et al <sup>33</sup> / 2000	RCT: 6 vs 18 mo vs usual care	Belgium/OP	100	Pulmonary fx; exercise capacity; muscle strength; QOL	Walking distance ( $p < 0.05$ ); exercise capacity ( $p < 0.02$ ); no significant effects of training program on PF measures vs usual care; improved quadriceps strength ( $p < 0.05$ ) and QOL ( $p < 0.001$ )
Foy et al <sup>64</sup> /2001	RCT: short- vs long-term PRP	United States/OP	140	Four domains of CRQ	Significant changes in short vs long term in all domains
Green et al <sup>34</sup> / 2001	RCT: single-blind; short- vs long-term PRP	United Kingdom/OP	44	Endurance; HRQL	CRDQ ( $p = 0.011$ ); dyspnea ( $p = 0.021$ ), emotion ( $p = 0.003$ ), mastery ( $p = 0.027$ )
Berry et al <sup>63</sup> / 2003	RCT: single-blind; short- vs long-term PRP	United States/OP	140	Physical function and disability; pulmonary function	Disability: $p = 0.016$ long- vs short-term Physical fx: increased walk distance ( $p = 0.03$ long-term); stair climb time ( $p = 0.05$ ) Pulmonary fx: NS

\*See Table 3 for abbreviations not used in the text.

ance, dyspnea, and health status that persisted over the 1 year after rehabilitation, although even these benefits tended to decline gradually over the second year of follow-up.

Green and colleagues<sup>34</sup> also demonstrated that patients with severe COPD achieved greater improvements in treadmill endurance, incremental shuttle walk distance, and quality of life following a 7-week outpatient pulmonary rehabilitation program compared with an identical program of only 4 weeks duration. However, patients who underwent the 4-week program were not reassessed at the 7-week time point to enable the direct comparison of outcomes.

A more recent trial (not in Table 5) readdressed this issue in a larger cohort of patients. Sewell and colleagues<sup>67</sup> randomized 100 patients with moderate-to-severe COPD (mean FEV<sub>1</sub>, 1.13 L) to receive 4 vs 7 weeks of outpatient rehabilitation. All patients were assessed at baseline, at the end of the rehabilitation intervention, and 6 months later. Patients in the 4-week training group were also evaluated at 7 weeks. Patients in both groups had significant improvements in exercise tolerance and health status. This study contrasts with the results of other published studies mentioned above in that it showed that the shorter 4-week intervention produced gains in exercise tolerance at both the 7-week and 6-month follow-up time periods that were comparable to those following the longer 7-week program. Finally, in an older trial Wijkstra and colleagues<sup>61</sup> showed that patients who underwent 18 months of home-based rehabilitation had greater sustained improvements in quality of life compared with patients who received twice-weekly rehabilitation over a 3-month period, but no difference was noted between groups in the magnitude of gains in the 6-min walk distance.

Overall, although some studies suggest that the duration of the pulmonary rehabilitation program impacts exercise tolerance improvement, it is less clear that other outcomes such as health status or dyspnea are similarly affected by program duration. Other studies<sup>60,67</sup> have demonstrated that even programs of short duration (*ie*, 10 days to 4 weeks) can produce significant benefits as well. Moreover, the effect of program duration on patient abilities to perform activities of daily living (ADLs) is uncertain. The clinical benefits of pulmonary rehabilitation may depend as much on program site and content as on duration.<sup>62</sup> Thus, given the variations in types of rehabilitation programs and differences in clinical study design, patient populations, health systems in different countries, program location, and program content, it is not possible at this time to draw firm conclusions regarding the optimal duration of pulmonary rehabilitation treatment.

### Recommendation

**9. Longer pulmonary rehabilitation programs (beyond 12 weeks) produce greater sustained benefits than shorter programs.** Grade of recommendation, 2C

### POSTREHABILITATION MAINTENANCE STRATEGIES

Although the benefits of pulmonary rehabilitation have been demonstrated up to 2 years following a short-term intervention,<sup>41</sup> most studies suggest that the clinical benefits of pulmonary rehabilitation tend to wane gradually over time. This is underscored in 12-month follow-up data from a cohort of patients with COPD who had completed a 10-week comprehensive pulmonary rehabilitation program.<sup>68</sup> At the end of the 10-week program, participants were given a structured home exercise program to follow. At the follow-up evaluation 1 year later, participants who had continued with the “prescribed” exercise routine maintained the gains that had been achieved in physical endurance, psychological functioning, and cognitive functioning during the initial intervention. However, participants who did not maintain the exercise routine exhibited significant declines in all areas of functioning, including exercise endurance, psychological functioning, and cognitive functioning.

Interest has thus arisen in strategies to maintain the benefits of pulmonary rehabilitation over time, such as repeated courses of rehabilitation treatment or maintenance interventions. In the study by Foglio and colleagues,<sup>36</sup> although repeated pulmonary rehabilitation interventions spaced 1 year apart led to significant short-term gains similar to those seen following an initial 8-week outpatient program, no additive, long-term physiologic benefits were noted. A study by Ries and colleagues<sup>40</sup> demonstrated that a 12-month maintenance intervention (consisting of monthly supervised exercise and educational reinforcement sessions and weekly telephone contacts) following an initial 8-week outpatient pulmonary rehabilitation program led to modest improvements in the maintenance of walking endurance, health status, and health-care utilization compared with usual care following pulmonary rehabilitation over a 1-year follow-up period. However, a gradual decline in these outcomes was noted over time in both patient groups, and the initial benefits of the maintenance intervention were no longer evident at 24 months of follow-up. In a separate study by Puente-Maestu and colleagues,<sup>69</sup> a 13-month maintenance program (consisting of patient self-governed walking 4 km per day at least 4 days per week with supervised sessions every 3 months) led to small gains in

tolerance of high-intensity constant-work-rate exercise and quality of life after an initial 8 weeks of lower extremity training (two different regimens), but the effects of the maintenance program on the ability to perform lower intensity exercise or ADLs were not tested. Grosbois and colleagues<sup>70</sup> showed that 18 months of both self-managed, home-based, and center-based supervised exercise maintenance were beneficial in maintaining the benefits in maximal exercise tolerance following a 7-week outpatient pulmonary rehabilitation program. In this study, center-based exercise maintenance afforded no benefits over the patient self-managed, home-based approach. Other studies<sup>71</sup> have failed to demonstrate any benefit of maintenance programs following the short-term rehabilitation intervention. Although most studies have not yet assessed how maintenance programs truly impact patients' ability to perform daily activities outside of the program setting, participation after pulmonary rehabilitation in regular exercise such as walking has been associated with a slower decline in HRQOL and dyspnea during ADLs.<sup>72</sup>

Thus, the role of maintenance pulmonary rehabilitation interventions following initial structured programs remains uncertain at this time, and the benefits of such interventions studied to date are modest, at best. Additional research is needed to clarify the relative impact of the many factors that can impact duration benefits from short-term pulmonary rehabilitation, such as the maintenance program structure, content, and location; exacerbations of respiratory disease; complications of other medical comorbidities; and the absence of reimbursement for continued patient participation. An additional important topic that must be addressed in the future is that of long-term patient participation. A relatively small number of patients who are offered a community-based exercise maintenance program will accept it and adhere to it.<sup>73</sup> Moreover, among those persons who do enroll in maintenance programs, attrition is problematic, resulting from factors such as disease exacerbations, loss of interest and/or motivation, transportation barriers, depression, program costs, and other personal issues affecting patients' lives. Additional work is needed to evaluate the optimal methods to incorporate short-term rehabilitation strategies into long-term disease management programs for patients with chronic lung disease.

### Recommendation

**10. Maintenance strategies following pulmonary rehabilitation have a modest effect on long-term outcomes.** Grade of recommendation, 2C

## INTENSITY OF AEROBIC EXERCISE TRAINING

Exercise training is one of the key components of pulmonary rehabilitation. The exercise prescription for the training program is guided by the following three parameters: intensity; frequency; and duration. The characteristics of exercise programs in pulmonary rehabilitation for patients with COPD have not been extensively investigated.

As noted by the previous panel and a 2005 review,<sup>74</sup> for most patients with COPD with limited maximum exercise tolerance, training intensities at higher percentages of maximum (*ie*, peak exercise) are well-tolerated, and physiologic training effects (*eg*, increase in aerobic capacity and anaerobic threshold with reduced ventilatory demand) have been documented as a result of (relatively) high-intensity aerobic training. Although it has not been conclusively demonstrated in patients with COPD, higher intensity training may result in better physiologic training effects, including reduced minute ventilation ( $\dot{V}E$ ) and heart rate (HR), and, thus, less dyspnea at submaximal exercise. In this context, the term *high-intensity training* for patients with COPD refers to patients exercising close to individual peak levels and is relative to the markedly reduced peak exercise levels in these patients. In previous studies, *high-intensity training targets* have been operationally defined to be at least 60 to 80% of the peak work rate achieved in an incremental maximum exercise test.<sup>75,76</sup> This should not be interpreted to represent training at high absolute work levels.

There have only been two randomized studies<sup>77,78</sup> published since the previous panel report that have evaluated the intensity of exercise during pulmonary rehabilitation in patients with COPD. Gimenez and colleagues<sup>77</sup> randomized 13 patients to high-intensity or moderate-intensity lower extremity exercise training daily for a period of 6 weeks. High-intensity exercise was performed on a cycle ergometer using a protocol of 1-min periods at peak oxygen uptake ( $\dot{V}O_2$ ) followed by 4-min periods at 40 to 45% of peak  $\dot{V}O_2$ . The moderate-intensity exercise group pushed an oxygen cart for a similar duration of 45 min per session. High-intensity training resulted in greater physiologic improvements (*eg*, improvement in maximum  $\dot{V}O_2$ ). High-intensity exercise, but not low-intensity exercise, also resulted in decreased dyspnea at rest and during submaximal exercise, and increased the 12-min walk distance. Vallet and colleagues<sup>78</sup> randomized 24 subjects to exercise at an HR achieved at the anaerobic or gas exchange threshold (high intensity) or at an HR of 50% of maximal cardiac frequency reserve (low intensity). Stationary cycle ergometry was performed for 45 min 5 days per week for 4 weeks. Subjects who

trained at the higher gas exchange threshold intensity exhibited improvement in maximum exercise  $\dot{V}O_2$  and a greater decrease in  $\dot{V}E$  compared to those who trained with low-intensity exercise.

The physiologic benefits of higher intensity exercise training with the associated reduction in  $\dot{V}E$  at similar workloads may be expected to result in better outcomes from pulmonary rehabilitation. The few small controlled randomized studies<sup>77,78</sup> available confirm these expectations. However, the effects of high-intensity training on other key patient-centered outcomes such as quality of life, shortness of breath, and ability to perform ADLs have not been investigated rigorously.

Moreover, the impact of exercise intensity on the important outcome of maintenance of exercise training has not been evaluated. As in other populations, it is possible that lower intensity exercise training may be associated with better long-term adherence than higher intensity training.

### Recommendations

**11. Lower extremity exercise training at higher exercise intensity produces greater physiologic benefits than lower intensity training in patients with COPD.** Grade of recommendation, 1B

**12. Both low-intensity and high-intensity exercise training produce clinical benefits for patients with COPD.** Grade of recommendation, 1A

## STRENGTH TRAINING IN PULMONARY REHABILITATION

Although always recognized as important, improving the function of the muscles of the arms and legs has recently become a central focus of pulmonary rehabilitation. In the course of everyday activities, these muscles are asked to perform two categories of tasks. Endurance tasks require repetitive actions over an extended period of time; walking, cycling, and swimming are examples. Strength tasks require explosive performance over short time periods; sprinting, jumping, and lifting weights are examples. For individuals whose muscles are weak, another category of strength-related tasks may become relevant, such as maintaining balance while standing, rising from a chair, or hoisting objects above head level.

Different characteristics of skeletal muscle enable the performance of endurance and strength tasks. Endurance is facilitated by having machinery capable of the aerobic metabolism of nutrients. Predominance of type I fibers, dense capillarity, high concentrations of enzymes subserving oxidative metabolism, and high mitochondrial density all pro-

mote muscle endurance. In contrast, strength is facilitated in muscles, the fibers of which are high in number and large in cross-section, with high fractions of type II fibers.

Some work<sup>79–81</sup> has shown that the skeletal muscles of patients with COPD are, in general, dysfunctional. Some structural and biochemical abnormalities would predict poor aerobic function (*eg*, poor capillarization and type II fiber predominance). However, compared to age-matched healthy subjects, patients with COPD also have low muscle mass,<sup>82,83</sup> especially in the muscles of ambulation; this predicts poor muscle strength.<sup>83–85</sup>

In healthy subjects, strength-training programs, in which progressive resistance methods are used to increase the ability to exert or resist force,<sup>86</sup> are capable of profoundly altering muscle structure and biochemistry, even in older subjects.<sup>87–90</sup> An important principle of training specificity dictates that training programs featuring endurance activities (*eg*, treadmill walking and bicycle riding) yield muscle changes that improve endurance, while training programs that feature tasks requiring strength (*eg*, machine weights, free weights, elastic resistance, and lifting the body against gravity) yield muscle changes improving strength. However, more recent work<sup>91,92</sup> has shown that the muscles of elderly subjects may also show improvements in aerobic characteristics after a program of strength training.

In patients with COPD, there is a strong scientific basis for implementing endurance-training programs in regard to both design and benefits. In comparison, programs of strength training have been explored in clinical trials only in more recent years. Since the last review, eight randomized clinical trials relevant to strength training have been published (Table 6), which is a considerable advance on the one study published prior to 1997. This older study (Simpson and colleagues<sup>93</sup>) was not included in the previous review and so has been included in the current analysis. These nine studies<sup>93–101</sup> can be separated into those that allow comparison between a control group (*ie*, either no exercise or endurance exercise)<sup>93–98</sup> and a strength-trained group, and those that allow comparison between an endurance-trained group and a group receiving a combined endurance-training and strength-training intervention.<sup>97,99–101</sup> The latter comparison is especially relevant to rehabilitative practice in which the question is whether the addition of strength training to an endurance-training program produces additional benefits.

The six randomized clinical trials<sup>93–98</sup> examining the responses of patients with COPD to a program of strength training have sufficient commonality to be examined as a group. With one exception,<sup>95</sup> the



**Table 6—Strength Training\***

Study/Year	Study Type	Country/Setting	Patients, Total No.	Outcomes	Results
Bernard et al <sup>99/</sup> 1999	RCT: not blinded; aerobic training vs aerobic/strength	Canada/OP	45	Muscle function, PF, exercise capacity, QOL	Muscle function: significant increases in strength group Work rate: increase in strength group 6MWD: improved ( $p < 0.0005$ both groups) HRQL: improved ( $p < 0.05$ both groups) Maximum weight lifted ( $p < 0.001$ vs control; four of five exercises) Endurance: increased ( $p < 0.001$ vs control subjects)
Clark et al <sup>95/</sup> 2000	RCT: training vs control	United Kingdom/OP	43	Muscle strength; endurance	Significant improvement in all outcomes in exercise training group PF: changes NS
Spruit et al <sup>96/</sup> 2002	RCT: resistance vs endurance	Belgium/OP	48	PF; exercise capacity; endurance; HRQL	Endurance: significant increase in all groups Strength: significant increase in all groups; HRQL: improved fatigue and emotion
Ortega et al <sup>97/</sup> 2002	RCT: endurance vs strength vs combined vs control	Spain/OP	72	PF; peak exercise parameters; capacity; muscle strength; HRQL	Upper and lower body strength increased in tx group
Panton et al <sup>101/</sup> 2004	RCT: resistance vs aerobic	United States/OP	18	PF; blood measures; strength; 12MWT; ADL	HR, SaO <sub>2</sub> , RPE, RPD: no change 12MWT: increase in tx group ADL: improvements in tx group
Kongsgaard et al <sup>96/</sup> 2004	RCT: resistance vs control	Denmark/OP	18	Body measurements; dynamic strength; maximum leg extension power; normal/maximum gait speed; stair climb; ADL	Anthropometric parameters: no change; decrease in FEV <sub>1</sub> , NS in control group Significant relationships among changes in strength, physical function, power; CSA, MVC, knee extension trunk flex, power ( $p < 0.05$ resistance); 5 RM (kg), N-gait ( $p < 0.001$ resistance)
Mador et al <sup>100/</sup> 2004	RCT: endurance vs combined training	United States/OP	32	PF, exercise testing, QOL, muscle measurements	ADL: improvement ( $p < 0.05$ ) in tx group Muscle strength: increases in combined vs endurance only QOL: improvements in both groups Exercise performance: NS in both groups Exercise endurance: significant increase in both groups
Casaburi et al <sup>94/</sup> 2004	RCT: blinded; placebo vs resistance	United States/OP	47	Body composition; muscle strength, endurance, PF, blood measures, safety measures	Body composition: weight gain: NS in placebo groups; increase in tx groups; lean mass increase significant in tx groups Endurance: significant increase in tx groups Peak O <sub>2</sub> update, peak work rate, lactic acid: significant changes in tx group

\*12MWT = 12-min walk time; CSA = cross-sectional area; MVC = maximum isometric extension; RPE = rate of perceived exertion; RPD = rate of perceived dyspnea; RM = range of movement; N-gait = normal gait. See Table 3 for abbreviations not used in the text.

average disease severity was moderately severe (FEV<sub>1</sub> range, 38 to 48% predicted). The exception is the study of Clark and colleagues<sup>95</sup> in which patients with very mild COPD were studied (average FEV<sub>1</sub>, 77% predicted). Collectively, the total number of patients studied was moderate, with the strength-trained group in the various studies comprising 6 to 26 subjects (total, 99 subjects). The training apparatus, exercise repetition, and intensity progression varied among studies (see Storer<sup>102</sup> for a review of suitable strength-training strategies). Program length ranged from 8 to 12 weeks; sessions were held two or three times per week, and session length (when stated) ranged from 40 to 90 min. These program characteristics are similar to those known to be effective in healthy subjects.<sup>103</sup>

The recorded outcomes of these studies include changes in strength, endurance, muscle mass, and disease-specific HRQOL. All six studies<sup>93–98</sup> reported improvements in strength. A variety of testing apparatuses were used, and it should be stressed that the measures of strength used in these studies were effort, motivation, and practice dependent. In all studies but one,<sup>96</sup> the change in exercise endurance was also assessed. Results were mixed. The peak exercise level in an incremental cycle ergometer test showed a statistically significant increase in only one of five studies<sup>98</sup>; the duration of a constant-work-rate task increased in three of five studies<sup>93,95,97</sup>; and the 6-min walk distance increased in one of the two studies in which it was assessed.<sup>98</sup> In two studies in which it was measured, muscle mass (assessed by MRI of a quadriceps cross-section<sup>96</sup> or dual-energy x-ray absorptiometry [DEXA] scan of lean leg mass<sup>94</sup>) increased significantly (by 4% and 3%, respectively).

Four studies<sup>97,99–101</sup> allowed a comparison of benefits to COPD patients between a combined strength-training and endurance-training program and an endurance-training program alone. These studies examined patients with, on average, moderately severe to severe disease (mean FEV<sub>1</sub> range, 33 to 45% predicted). The number of patients included in the strength-training-plus-endurance-training group ranged from 9 to 21 (total, 55 patients). Training programs were 8 to 12 weeks in duration; sessions were held two or three times per week; the duration of strength training per session was generally not stated (it was 45 min in the study by Bernard and colleagues<sup>99</sup>). Strength-training exercises were included for both the arms and the legs.

In all four studies, improvement in measures of muscle strength was superior in the group receiving a strength-training component to that seen among those receiving endurance training alone. In one study,<sup>101</sup> measures of ADLs improved more

in the combined-training group. However, measures of the increase in exercise endurance were comparable in the two groups (with the exception of the study by Panton and colleagues,<sup>101</sup> who found a superior increase in the 12-min walk distance in the combined-training group). Two studies<sup>99,101</sup> assessed muscle mass changes; neither detected significant changes in subjects performing endurance training alone, while both showed increases in the groups in whom a strength-training program was added (8% increase in thigh cross-section by CT scan<sup>99</sup> and 5% increase in whole-body lean mass by DEXA scan<sup>101</sup>).

These data can be interpreted to indicate that well-designed strength-training programs increase muscle strength and mass in patients with moderate-to-severe COPD. Strength training, when delivered as an isolated intervention may improve disease-specific quality of life but does not seem to produce additional gains when added to a program of endurance training. Strength training does not produce endurance benefits as consistently as does specific endurance training.

It should be emphasized that, to date, all cited trials featuring combined programs have added a strength-training component to an endurance-training program (*ie*, essentially doubling the time spent training) rather than substituting part of the endurance-training program with an endurance component. Therefore, whether it is wise for rehabilitation practitioners to include a strength-training component in a session of fixed duration by reducing the time spent in endurance activities cannot be assessed at this time. Importantly, no serious adverse effects of strength training have been reported; these preliminary data suggest that strength training is safe in patients without obvious contraindications (*eg*, severe osteoporosis). Little information is available on the long-term benefits of strength training in the pulmonary rehabilitation patient. Whether strength gains persist and whether adverse consequences of weakness occur (*eg*, decreased mobility or injuries due to falls) cannot be determined. Larger, longer term trials are required to resolve these issues. Finally, muscle biopsy studies of the cellular and biochemical adjustments following strength training have yet to be reported; such studies should help to determine the extent to which strength training ameliorates the muscle dysfunction seen in COPD patients.

#### *Recommendation*

**13. The addition of a strength-training component to a program of pulmonary rehabilitation increases muscle strength and muscle mass.** Strength of evidence, 1A

## ANABOLIC DRUGS

Since exercise-training interventions are a cornerstone in pulmonary rehabilitation and yield benefits, at least in part, by improving the function of the exercising muscles, it seems reasonable to hypothesize that pharmaceutical agents that improve muscle function in similar ways might be useful adjuncts to rehabilitative therapy. However, the list of drugs that might be suitable for clinical trials is quite limited. In particular, no agent that is capable of directly improving the aerobic characteristics of muscle has been studied in a clinical trial. It is plausible that erythropoietin might be of use in anemic patients with COPD; increasing muscle oxygen delivery might increase exercise endurance as it has in other patient groups,<sup>104,105</sup> but this has not been tested in a clinical trial.

Drugs that produce muscle hypertrophy have been identified and studied to determine whether they elicit improvements in muscle strength. Growth hormone, generally administered by daily injection, has been shown to induce modest increases in muscle mass. However, improved functionality has been difficult to demonstrate.<sup>106,107</sup> In the only study in COPD, Burdet and colleagues<sup>108</sup> studied 16 underweight patients with COPD who received daily growth hormone injections for 3 weeks. Lean body mass (assessed by DEXA scan) increased 2.3 kg in the growth-hormone group compared with 1.1 kg in the placebo group. No differences in maximum inspiratory pressure, handgrip strength, or incremental cycle ergometer exercise capacity were detected between groups. The 6-min walk distance decreased significantly in the growth-hormone group. Clearly, growth hormone cannot be recommended as an adjunct therapy for pulmonary rehabilitation at this time.

In men, therapy with testosterone and its analogs has been shown to increase muscle mass, decrease fat mass, and improve muscle strength. Well-controlled trials of testosterone supplementation in healthy young men<sup>109,110</sup> and older men<sup>111</sup> have demonstrated that muscle mass and strength increase with a linear dose-response relationship; an appreciable hypertrophic response is seen within the physiologic range of circulating testosterone levels. Further, hypogonadal men show increases in muscle mass and strength in response to physiologic doses of testosterone.<sup>112</sup> The side effects of testosterone administration are of concern; lipid abnormalities, polycythemia, and liver function abnormalities have been reported.<sup>113</sup> In older men who may harbor subclinical foci of prostate cancer, testosterone administration may enhance the growth of these foci.<sup>114</sup> More recent experience suggests that substan-

tially supraphysiologic doses of testosterone should be avoided in older men.<sup>111</sup> A number of formulations of testosterone are available; it can be administered by injection, transdermal patch, transdermal gel, and orally.<sup>115</sup> Oral administration, however, has often been associated with elevations in liver function test results. There have also been some preliminary studies<sup>116</sup> of testosterone administration in women. Circulating levels of testosterone in women are roughly 10-fold lower than those in men, and high testosterone doses are inevitably associated with virilization.<sup>117</sup> Whether lower doses that are not associated with virilization will have substantial anabolic effects on muscle remains to be seen.

A rationale for testosterone supplementation in men with COPD is that circulating levels have been shown to be lower than those seen in healthy young men and are often lower than those in age-matched control subjects.<sup>94,118,119</sup> Since the publication of the previous rehabilitation guidelines, five RCTs<sup>94,120-123</sup> have appeared in which testosterone or its analogs (collectively known as *anabolic steroids*) have been administered to patients with COPD. These trials are similar, in that patients with moderately severe COPD were studied (mean FEV<sub>1</sub> range, 34 to 49% predicted). All studies were limited to men, except for the study of Schols and colleagues,<sup>122</sup> in which women received half the drug dose that men received. In three of the studies,<sup>120-122</sup> all participants received a rehabilitation-type program. All studies used relatively low doses, and no clear drug-related adverse reactions (with the exception of a modest increase in hematocrit<sup>94</sup>) have been reported.

Schols and colleagues<sup>122</sup> administered nandrolone decanoate or placebo by injection every 2 weeks for 8 weeks to approximately 130 patients who also received nutritional supplementation. Although no differences in body weight change were observed between these groups, in the nandrolone group weight gain was predominantly in lean mass, whereas in the placebo group weight gain was predominantly fat. No difference in changes in the 6-min walk distance or peak inspiratory pressure was detected.

Ferreira and colleagues<sup>121</sup> administered oral stanozolol or placebo daily for 27 weeks to 23 underweight patients with COPD. DEXA scanning revealed an increase in lean mass of approximately 2 kg and a 5% increase in thigh circumference, which are changes that were not seen in the control group. No differences were detected in 6-min walk distance or incremental cycle ergometer testing results.

Creutzberg and colleagues<sup>120</sup> administered nandrolone decanoate or placebo by IM injection every 2 weeks for 8 weeks to 63 men with COPD. Fat-free mass increased by 1.7 kg in the nandrolone group compared to 0.3 kg in the placebo group. No signif-

icant differences were seen between groups in incremental cycle ergometer exercise capacity or HRQOL. Muscle strength was assessed, but no differences were detected in handgrip strength or isokinetic leg strength testing results.

Svartberg and colleagues<sup>123</sup> administered testosterone enanthate or placebo by injection every 4 weeks for 26 weeks to 29 men with COPD. DEXA scanning revealed a 1.1-kg increase in lean mass and a 1.5-kg decrease in fat mass in the testosterone group. No exercise outcomes were assessed. No difference in quality of life, as assessed by the St. George respiratory questionnaire was detected, but better sexual quality of life and erectile function was noted.

Casaburi and colleagues<sup>94</sup> studied 47 men with COPD and low testosterone levels (mean total testosterone level, 320 ng/dL). Subjects received 100 mg of testosterone enanthate or placebo by IM injection for 10 weeks. Half of the group receiving testosterone also underwent a strength-training program. Testosterone therapy yielded a 2.2-kg increase in lean body mass; the group receiving both testosterone and strength training experienced a 3.3-kg increase in lean mass. Average leg press strength increased by 12% in the testosterone group and by 22% in the group receiving testosterone therapy plus strength training. No improvements in incremental or constant-work-rate cycle ergometer exercise tolerance were demonstrated.

In summary, anabolic steroid administration has consistently been shown to increase lean (presumably muscle) body mass in men with moderate-to-severe COPD. As expected on theoretical grounds, no improvement in endurance exercise capacity was detected. In one study,<sup>94</sup> but not in another,<sup>120</sup> an increase in the strength of the muscles of ambulation was detected. No evidence for improvements in quality of life has been obtained. It is premature to suggest that the administration of anabolic steroids be incorporated into rehabilitative programs for patients with COPD. Only roughly 150 patients have received this intervention and only with relatively short-term exposures; whether the benefits outweigh the risks in the long term cannot be determined at this time.

### Recommendation

**14. Current scientific evidence does not support the routine use of anabolic agents in pulmonary rehabilitation for patients with COPD.** Grade of recommendation, 2C

### UPPER EXTREMITY TRAINING

Upper extremity exercise training specifically impacts the arms and has been shown to increase arm

work capacity while decreasing  $\dot{V}O_2$  for a comparable work level. Postulated mechanisms for improvement in upper extremity function from such training in patients with chronic lung diseases include desensitization to dyspnea, better muscular coordination, and metabolic adaptations to exercise.

The previous 1997 guidelines panel recommended that “strength and endurance training of the upper extremities improves arm function in patients with COPD” and that “arm exercises are safe, and should be included in rehabilitation programs for patients with COPD” (strength of evidence, B). This was based on five randomized trials and one observational study.

The methodology of the earlier studies varied considerably. Arm training alone appeared to be less effective than leg training<sup>124</sup>; however, when combined with leg training, a significant improvement in functional status was noted compared to either modality alone.<sup>124,125</sup> Arm training by weight lifting significantly improved work capacity, reduced ventilatory requirements,<sup>126</sup> and reduced both metabolic and ventilatory requirements (*ie*,  $O_2$  uptake,  $CO_2$  production, and  $\dot{V}E$ ) following training.<sup>127</sup> Greater benefit in unsupported arm work (with reduced metabolic cost) was seen with unsupported arm exercise when compared to supported arm exercise via ergometry.<sup>211</sup>

Since the previous guideline, one observational study<sup>128</sup> and three RCTs<sup>129–131</sup> were identified that address upper extremity training (Table 7). They further support the conclusion that arm training positively impacts arm activity tolerance and that arm exercise improves ventilatory requirements by reducing ventilation and the associated  $\dot{V}O_2$ .

The study by Holland and colleagues<sup>129</sup> compared arm training combined with lower limb training vs lower limb training alone. The combined-training group reported a significant improvement in arm endurance ( $p = 0.02$ ) compared to the group undergoing lower limb training alone. In addition, the combined-training group demonstrated a trend toward reduced Borg score for perceived dyspnea ( $p = 0.07$ ). No difference in perceived fatigue ratings was noted.

Unsupported arm exercise has been shown to increase upper extremity activity tolerance and endurance when compared to control subjects.<sup>130,131</sup> Epstein and colleagues<sup>131</sup> evaluated respiratory muscle strength, endurance, and exercise capacity in 26 persons with severe COPD. The arm-exercise group demonstrated increased muscle recruitment from the diaphragm, reduced oxygen cost during arm elevation, increased endurance time ( $p < 0.05$ ), and reduced ventilation. No differences were seen between groups for  $\dot{V}E$  and mean inspiratory flow. Bauldoff and colleagues<sup>130</sup> studied unsupported arm

**Table 7—Upper Extremity Training\***

Study/Year	Study Type	Country/Setting	Patients, Total No.	Outcomes	Results
Bauldoff et al <sup>130/</sup> 1996	RCT; upper arm vs control	United States/home	20	Exercise ability; disability; fatigue and ADL	Time effect; NS for treatment, time × treatment Fatigue score: time × treatment (p = 0.0012); NS for time or treatment alone
Epstein et al <sup>131/</sup> 1997	RCT; not blinded; upper arm vs respiratory muscle training	United States/OP (IP for those who could not commute)	26	Respiratory muscle strength, endurance, exercise capacity	Breathlessness: NS Muscle recruitment: increase significant after arm elevation Muscle strength: NS Unsupported arm exercise: response similar in both groups Endurance time: increased (p < 0.05 vs tx group)
Franssen et al <sup>128/</sup> 2002	Prospective case-control	Netherlands/IP	33	Energy efficiency and exercise performance; pulmonary fx	Resting energy expenditure: significantly increased COPD Upper/lower extremity testing: significant difference in COPD vs control groups Pulmonary function: significant improvement in COPD posttraining Mechanical efficiency: NS
Holland et al <sup>129/</sup> 2004	RCT; single-blind; upper limb vs control	Australia/OP or home	38	Exercise capacity, symptoms, QOL	Endurance: significant improvement in tx group Borg score: decrease in tx group (p = 0.06) Arm fatigue: NS QOL; significant increase in all CRDQ domains

\*IP = inpatient. See Table 3 for abbreviations not used in the text.

training in 20 patients with moderate-to-severe COPD over an 8-week period. They noted significant improvement over time in ratings of perceived fatigue ( $p = 0.03$ ) and a trend toward improvement in arm endurance ( $p = 0.07$ ) in the arm-training group compared with control subjects. No difference was seen for ratings of perceived dyspnea.

In a prospective, case-control observational study, Franssen and colleagues<sup>128</sup> compared 33 stable patients with COPD to 20 healthy age-matched and gender-matched control subjects. Resting energy expenditure was significantly increased in the COPD group, and both lower and upper extremity tests demonstrated significantly lower peak workload, peak  $\dot{V}O_2$  and carbon dioxide output, respiratory exchange ratio, and end-exercise ventilation in the COPD patients. There were no significant differences in mechanical efficiency between the groups. As the mechanical efficiency and exercise capacity did not appear to be affected uniformly in patients with COPD, the relative preservation of upper limb activities may influence exercise-training prescriptions in the pulmonary rehabilitation of patients with COPD.

In summary, the new evidence provides additional support for the use of upper extremity exercise training in pulmonary rehabilitation for patients with COPD by demonstrating improvement in upper limb exercise capacity and reduced ventilation and  $\dot{V}O_2$  cost during arm activity following unsupported arm training. Given the lack of randomized studies comparing unsupported vs supported arm exercise, the best type of arm training is unknown.

### Recommendation

**15. Unsupported endurance training of the upper extremities is beneficial in patients with COPD and should be included in pulmonary rehabilitation programs.** Grade of recommendation, 1A

### IMT

In general, patients with COPD have weak inspiratory muscles.<sup>132,133</sup> In fact, biopsy specimens from patients with mild-to-moderate COPD show reduced force generation per cross-sectional area.<sup>134</sup> The major clinical consequences of inspiratory muscle weakness for patients are breathlessness and exercise impairment. The rationale for IMT is that increasing the strength and/or endurance of the respiratory muscles has the potential to improve these clinical outcomes. To date, clinical trials of IMT have been performed in endurance athletes, in patients with chronic respiratory diseases (*ie*, asthma, cystic fibrosis, and COPD), chronic heart failure,

chronic cervical spinal cord injury, and muscular dystrophy, before cardiothoracic surgery, and to assist weaning from mechanical ventilatory support.

The 1997 guidelines panel concluded that “the scientific evidence at the present time does not support the routine use of ventilatory muscle training as an essential component of pulmonary rehabilitation” and that “ventilatory muscle training may be considered in selected patients with COPD who have decreased respiratory muscle strength and breathlessness” (strength of evidence, B).

In the current review, six investigations of IMT were identified (Table 8)<sup>137,206–210</sup> that met the following criteria: randomized trial involving patients with COPD and a treatment and a control group; use of a resistance, threshold, or flow device for IMT; and inclusion of appropriate physiologic (*ie*, inspiratory muscle strength [maximal inspiratory pressure (P<sub>imax</sub>)] and/or endurance and exercise performance) and clinical (*ie*, dyspnea ratings and/or health status) outcome measures. These six studies included a total of 169 patients with COPD (range, 17 to 32 subjects per study) who completed the trials, which lasted from 2 months to 1 year in duration. In addition, a metaanalysis by Lotters and colleagues<sup>135</sup> and a review article by Lisboa and Borzone<sup>136</sup> were also considered.

The 1997 guidelines panel raised various concerns about the methodology of studies evaluating IMT. For example, one question regarding the previous studies was: “Is the training stimulus adequate to induce an expected physiologic response?” All of the six new studies that were reviewed (Table 8) provided subjects with an appropriate training stimulus such that the respective IMT group achieved improvement in respiratory muscle function compared with the control group.

Another key concern is the type of IMT. The major training methods are threshold loading, resistive breathing, and targeted flow. Five of the six new studies<sup>206–210</sup> used threshold loading, which has the advantage of being independent of inspiratory flow rate but requires a build up of negative pressure before flow begins. In addition, threshold loading enhances the velocity of inspiratory muscle contraction, which appears favorable by shortening inspiratory time, thus allowing more time for exhalation and lung emptying. The sixth study<sup>137</sup> trained subjects with an incentive flowmeter that provided visual feedback.

One of the most important questions relates to the types of patients with COPD (*ie*, phenotypes) concerns who should be considered for IMT. In the six new trials (Table 8),<sup>137,206–210</sup> patients were recruited based on a diagnosis of COPD and a willingness to participate in the study. No specific patient

**Table 8—Inspiratory Muscle Training\***

Study/Year	Study Type	Country/Setting	Patients, Total No.	Outcomes	Results
Lisboa et al <sup>206</sup> /1997	RCT; double-blind; 30% vs 10% inspiratory pressure training	Chili/home	20 with chronic airflow limitation/none noted	Max respiratory pressure, changes in dyspnea, exercise tolerance	<p>P<sub>max</sub>: Group 1: significant increase at 2 wk Group 2: significant increase at 5 wk Between groups: NS at 10 wk Dyspnea at 10 wk: significant decrease (p = 0.036 group 1 vs group 2) Walk distance: group 1: significant increase (p &lt; 0.01) with decrease in dyspnea (p &lt; 0.05) Borg score: significant difference between groups (p &lt; 0.05) W<sub>max</sub>: NS Pulmonary function: group 1: significant increase (p &lt; 0.001) Intensity: equal both IMT groups Muscle Strength/Endurance: increase both IMT groups Exercise Performance: Peak work rate: IMT/Cycling increase (p &lt; 0.01); O<sub>2</sub> uptake (p &lt; 0.01); Heart rate, Tidal Volume, breathlessness, leg fatigue: NS Dyspnea/Fatigue: improved in cycling group Spirometry: NS P<sub>max</sub>: increased IMT (p &lt; 0.003) V<sub>O<sub>2</sub></sub>max: W<sub>max</sub>: NS Walk distance: increased IMT (p &lt; 0.05 vs control) Borg Score: no change Dyspnea: change IMT (p &lt; 0.003) QOL: treatment effect greater all domains P<sub>max</sub>: increase in IMT group P<sub>emax</sub>: NS (p &gt; 0.05) Endurance: increase IMT (p &lt; 0.05) Dyspnea: decrease IMT (p &lt; 0.05) HRQL: improved IMT (p &lt; 0.05) TI; T<sub>rot</sub>; V<sub>t</sub>: NS Breathing patterns: change (p &lt; 0.05) both groups PF: NS posttraining all groups; P<sub>max</sub>: increase in IMT and combined groups (p &lt; 0.005 both groups) Endurance: inspiratory muscle: increase (p &lt; 0.001 IMT and combined groups) Walk distance: increase (p &lt; 0.05) in all three training groups Borg score: dyspnea × IMT (p &lt; 0.05) Spirometry: NS either group (IMT and control) Inspiratory muscle strength/endurance: P<sub>max</sub>, increase (p &lt; 0.005 both groups); endurance, same pattern 6MWT: significant improvement in both groups Dyspnea: NS between groups Borg score: decrease in both groups</p>
Larson et al <sup>207</sup> /1999	RCT; single-blind; IMT vs cycle training vs IMT/cycle vs control group	United States/home	130	Respiratory muscle strength and endurance, performance, dyspnea, fatigue	
Sanchez Riera et al <sup>137</sup> /2001	RCT; double-blind; IMT vs control group	Spain/home	20	PF; inspiratory muscle endurance, exercise capacity and performance, dyspnea, QOL	
Covey et al 2001 <sup>208</sup>	RCT; single-blind; IMT vs control group	United States/OP	27	Respiratory muscle performance and endurance; dyspnea; HRQL	
Weiner et al <sup>209</sup> /2003	RCT; double-blind; IMT vs expiratory training vs both vs control group	Israel/OP	32	Lung function; walk distance; respiratory muscle strength and endurance; dyspnea	
Weiner et al <sup>210</sup> /2004	RCT; double-blind; IMT vs low-load training group	Israel/OP	38	Lung fx, endurance, inspiratory muscle strength and endurance, dyspnea	

\*IMT = inspiratory muscle training; TI = inspiratory time; T<sub>rot</sub> = total breathing cycle time; P<sub>emax</sub> = maximal expiratory pressure; V<sub>O<sub>2</sub></sub>max = maximum V<sub>O<sub>2</sub></sub>; V<sub>t</sub> = tidal volume. See Tables 3 and 4 for abbreviations not used in the text.

phenotypes, such as stage of COPD, evidence of inspiratory muscle weakness, degree of hyperinflation, severity of breathlessness, level of exercise impairment, and/or reduced health status, were considered for inclusion or exclusion criteria in these studies. In a metaanalysis, Lotters and colleagues<sup>135</sup> found that neither the degree of severity of COPD nor hyperinflation had any effect on the efficacy of IMT. However, subgroup analysis revealed that those patients with inspiratory muscle weakness (*ie*, P<sub>Imax</sub> ≤ 60 cm H<sub>2</sub>O) improved P<sub>Imax</sub> significantly more with IMT combined with exercise training compared to patients without inspiratory muscle weakness.

The consideration of outcome measures is also important to assess the benefits of IMT. Overall, the six investigations summarized in Table 8<sup>137,206–210</sup> show consistent improvements in inspiratory muscle function, increases in exercise performance, and reductions in dyspnea. These data generally support the findings of the metaanalysis by Lotters and colleagues<sup>135</sup> that IMT by itself significantly increased inspiratory muscle strength and endurance, significantly improved dyspnea related to ADLs and during exercise, and showed a nonsignificant trend for an increase in exercise capacity.

Collectively, the positive results of the six new studies<sup>137,206–210</sup> (Table 8) provide further support for the efficacy (both physiologic and patient-centered outcomes) of IMT. However, each study was performed at a single institution and included relatively small numbers of patients with COPD. Based on this information, the panel continues to recommend that IMT be considered in selected patients with COPD who have decreased inspiratory muscle strength and breathlessness despite receiving optimal medical therapy. The panel believes that a large-scale, multicenter RCT should be performed with appropriate statistical power to more completely examine the role of IMT in treating patients with COPD. Appropriate patient characteristics, training methodologies, and outcome measures are important considerations.

### *Recommendation*

**16. The scientific evidence does not support the routine use of IMT as an essential component of pulmonary rehabilitation.** Grade of recommendation, 1B

### *Education*

The 1997 guidelines panel agreed that “education is generally considered to be a necessary, but not sufficient, part of pulmonary rehabilitation” but did not review the topic independent of the other com-

ponents because it could not identify a sufficient number of studies that were focused solely on education. The panel reviewed education along with the psychosocial and behavioral components and recommended that “although scientific evidence is lacking, expert opinion supports the inclusion of educational and psychosocial interventions as components of comprehensive pulmonary rehabilitation programs for patients with COPD” (strength of evidence, C).

Patient education is a central component of most pulmonary rehabilitation programs. Education classes are generally conducted in a lecture/discussion format and may cover a wide variety of topics regarding the management of chronic lung disease. The scientific evidence for education in the 1997 guidelines was based on four randomized studies and one observational study.<sup>138–142</sup> Three of these studies<sup>138–140</sup> demonstrated mild improvement in dyspnea. One of these studies<sup>140</sup> compared dyspnea self-management to health education as the control, finding that the self-management group reported decreased dyspnea on baseline dyspnea index/transitional dyspnea index. In addition, both forms of education resulted in significant improvement in dyspnea. Conflicting results were reported in the two additional studies reviewed.<sup>141,142</sup> One study<sup>141</sup> found that education imparted no benefit on coping skills, while the second study<sup>142</sup> reported increased psychological distress following an education intervention.

In the current review, four new RCTs were identified.<sup>49,55,143,144</sup> The results of all of these studies demonstrate that education alone has no independent benefit (Table 9).

In the study by Emery and colleagues,<sup>55</sup> a three-group design tested comprehensive pulmonary rehabilitation vs education and stress management (ESM) vs a waiting-list group in 79 stable patients with COPD using blinded data collectors. The findings were that the pulmonary rehabilitation group demonstrated significant improvements in endurance exercise, maximum  $\dot{V}O_2$ , psychological well-being, and illness-related impairment when compared to the education group ( $p < 0.05$ ). Significant improvement was seen over time for anxiety as well as cognitive function in the pulmonary rehabilitation group vs the education group ( $p < 0.05$ ). However, all groups achieved significant improvement in mental efficiency over time. The authors concluded that comprehensive pulmonary rehabilitation produced significant improvements in endurance exercise, anxiety, and cognitive performance when compared to either the education-alone group or to the waiting-list group.

The study by Stulbarg and colleagues<sup>144</sup> also used



**Table 9—Education in Pulmonary Rehabilitation\***

Study/Year	Study Type	Country/Setting	Total N	Outcomes	Results
Wedzicha et al <sup>39/</sup> 1998	RCT: PRP with education vs education	United Kingdom/ OP	126	Lung fx, exercise tolerance/ breathlessness, health status assessment	Exercise performance increase ( $p < 0.0005$ vs control); exercise tolerance increase ( $p < 0.001$ in moderate dyspneic group) QOL: CRDQ difference postrehabilitation ( $p = 0.051$ vs control group); interaction between exercise and severity ( $p = 0.043$ ); CRDQ total score ( $p < 0.0001$ in moderate dyspnea exercise group) EADL scores: no change any group Physiologic: NS; pulmonary function: unchanged all groups
Emery et al <sup>55/</sup> 1998	RCT: blinded; comprehensive PRP vs education vs control	United States/OP	79	Pulmonary fx; HRQL; psychological well-being	Psychological: depression (time $\times$ group interaction $p < 0.05$ ); anxiety ( $p < 0.05$ time $\times$ group interaction). HRQL: NS Cognitive: mental efficiency ( $p < 0.001$ time main effect); verbal processing ( $p < 0.01$ time effect; $p < 0.001$ time $\times$ group interaction) Health knowledge: time main effect ( $p < 0.001$ ); test scores increase ( $p < 0.001$ education and exercise groups)
Ringbaek et al <sup>143/</sup> 2000	RCT: PRP with education vs control	Denmark/OP	45	6MWT; dyspnea; QOL	No significant effects of PRP on physical performance or well-being found 6MWT: improved ( $p < 0.001$ ) Breathlessness: decrease ( $p < 0.04$ exposure and training group vs DM group)
Stulbarg et al <sup>144/</sup> 2002	RCT; single-blind	United States/OP	115	Pulmonary fx; exercise performance; POD; HRQL	HRQL: CRDQ dyspnea, decrease ( $p < 0.001$ ); CRDQ fatigue, emotional fx, mastery ( $p < 0.001$ vs training group); SF-36, all subscales improved

\*DM = daily movement; EADL = extended activities of daily living scale. See Tables 3 and 4 for abbreviations not used in the text.

a three-group design evaluating education in the form of (1) dyspnea self-management alone vs (2) dyspnea self-management with minimal exercise training (4 sessions) vs (3) dyspnea self-management with extensive exercise training (24 sessions) in 115 patients with moderate-to-severe COPD with single blinding. Significant improvement was seen in the training group for 6-min walk distance ( $p < 0.001$ ). Both the program-exposure group and the exercise-training group reported significant improvement in shortness of breath that was not seen in the self-management group ( $p < 0.04$ ). Improvements in CRDQ subscales were seen primarily in the exercise-training group ( $p < 0.003$ ), supporting the hypothesis that improvement in dyspnea was related to the number of exercise sessions undertaken. No improvements in dyspnea or function were seen in the self-management group.

In the third study by Ringbaek and colleagues,<sup>143</sup> an 8-week pulmonary rehabilitation program plus education was compared to conventional care in 45 stable patients with moderate COPD without the blinding of either the participants or the research staff. No significant differences were seen between the group receiving pulmonary rehabilitation plus education compared to the control group. Of note, the authors concluded that the absence of significant differences might be due to the brevity of the program (8 weeks), the selection of patients with moderate COPD, or type II error.

In the final study by Bourbeau and colleagues,<sup>49</sup> a self-management program was compared to usual care in 191 patients with COPD. The 2-month program was composed of weekly visits by nurses or allied health professionals including exercise evaluation and home-based instruction in an exercise-training program. Monthly telephone calls were conducted in months 3 to 12. The number of hospital admissions related to COPD exacerbations was reduced significantly in the intervention group vs the usual-care group (40%), as well as the number of hospital admissions related to other problems (57%). In addition, significant reductions in the numbers of emergency department visits (41%) and unscheduled physician visits (59%) were seen. These results suggest that a self-management program provided by health professionals reduced health-care service utilization.

In summary, there continues to be limited research that is specific to the impact of education on the key outcomes of pulmonary rehabilitation in patients with COPD. Nevertheless, current practice and expert opinion suggest that there are important benefits of patient education, independent of pulmonary rehabilitation, including active patient participation in a partnership with health-care providers to

achieve collaborative self-management and patient adherence to health-enhancing behaviors. Patient education is included as an important recommendation in current clinical practice guidelines for COPD.<sup>18,145</sup>

Patient education remains an integral component of comprehensive pulmonary rehabilitation, possibly limiting the ability to differentiate the benefits of education alone. Discriminating the effect of educational topics vs exercise is difficult as they are generally administered together and appear to be highly related. The previous 1997 guidelines panel thought that education outside of a comprehensive pulmonary rehabilitation program was not sufficient to improve the well-being of patients with COPD. The new evidence on using education and self-management education supports this conclusion, since none of the studies found a benefit for education alone in the absence of exercise training.

#### *Recommendation*

**17. Education should be an integral component of pulmonary rehabilitation. Education should include information on collaborative self-management, and the prevention and treatment of exacerbations.** Grade of recommendation, 1B

#### PSYCHOLOGICAL AND BEHAVIORAL COMPONENTS OF PULMONARY REHABILITATION

Based on little published evidence, the 1997 guidelines panel concluded that “Evidence to date does not support the benefits of short-term psychosocial interventions as single therapeutic modalities, but longer term interventions may be beneficial” and that “expert opinion supports the inclusion of education and psychosocial interventions as components of comprehensive pulmonary rehabilitation programs for patients with COPD.”

#### *Psychological Distress in COPD*

Some studies<sup>146,147</sup> have confirmed that there is a relatively high prevalence of psychological distress among patients with COPD. Depression and anxiety are the most commonly reported psychological concerns. However, due to the variety of methods utilized in measuring depression and anxiety, prevalence estimates for clinically significant depression vary from 7 to 57%,<sup>148</sup> and estimates for clinically significant anxiety vary from 10 to 96%.<sup>149,150</sup> Data indicate that clinical depression may not be associated with mortality among patients with COPD.<sup>151</sup> However, no studies have evaluated the influence of

depressive symptoms on survival among patients with COPD, despite evidence among patients with cardiac disease that mortality is associated with depressive symptoms. Studies<sup>54,152,153</sup> also have documented changes in cognitive functioning among patients with COPD, including impairments in memory performance and higher cognitive skills (eg, attention and complex visual-motor processes, abstraction ability, and verbal tasks).

Overall, psychological distress is an important clinical feature of COPD because patients with COPD are more likely than age-matched peers to report symptoms of distress, especially depression and anxiety. In addition, psychological distress among patients with COPD predicts impaired quality of life and restricted ADLs.<sup>154</sup> Functional capacity is more strongly associated with emotional/psychosocial factors (eg, depression, anxiety, somatization, low self-esteem, attitudes toward treatment, and social support) than with traditional physiologic indicators.<sup>155</sup> Although psychological factors are associated with functional performance, the influence of psychological factors on disease progression and mortality is unknown.

### *Psychosocial Interventions*

During the past decade, there have been very few studies evaluating nonexercise psychosocial interventions among patients with COPD. Rose and colleagues<sup>156</sup> reviewed studies evaluating psychosocial interventions to treat anxiety and panic. They described only one study<sup>55</sup> published since 1995 with a randomized control group. Participants in this study were randomly assigned to one of the following three groups: exercise with ESM (designed to provide the standard of care in pulmonary rehabilitation); ESM (designed to provide participants with the psychosocial components of rehabilitation minus any exercise training); and a nonintervention waiting list. Outcomes from participants in the ESM group reflected the effects of a psychosocial intervention. The results indicated that ESM participants achieved significant increases in their knowledge about and treatment of COPD, but there were no effects of ESM on indicators of anxiety, depression, or quality of life. In addition, ESM participants did not exhibit changes in cognitive function. Thus, the data indicate that ESM alone in the absence of exercise had a minimal impact on psychosocial functioning. These data are consistent with the results of a 2005 study<sup>157</sup> indicating that patients with COPD who attended an educational lecture series in addition to undergoing exercise training did not experience any benefits beyond those experienced by participants in exercise training without education or those who underwent

exercise training with activity training. Despite the absence of any apparent benefit from educational training in the latter study, it is noteworthy that the retention of participants assigned to the educational group was 100% at 12 weeks compared to 64% and 84%, respectively, in the other two groups. Thus, the educational intervention may have facilitated aspects of program adherence that the other regimens did not.

### *Health Behavior Interventions*

Behavioral factors are important in the preventive care and rehabilitation of patients with COPD. Specifically, smoking is well known to be the primary risk factor for the onset of COPD. Diagnosis with COPD is not always a sufficient health threat to motivate smokers to quit. Data regarding smoking cessation interventions among pulmonary rehabilitation patients are sparse. In a 2005 study<sup>158</sup> of patients with COPD who were smoking, participants were randomly assigned to either a smoking cessation educational intervention or to usual care. Participants were recruited at various primary care sites throughout the Netherlands. The results indicated that quit rates in the intervention group were approximately double those in the usual-care group (16% vs 9%, respectively). These data confirm that a diagnosis of COPD is not a sufficient stimulus to initiate the process of smoking cessation, but educational information may facilitate quitting in some patients.

### *Conclusions*

The data suggest that depression and anxiety are more common among patients with COPD than in the public at large. Data indicate that psychosocial intervention may facilitate behavioral changes, such as smoking cessation, as well as the management of symptoms, including dyspnea. However, psychosocial interventions alone may not lead to reduced psychological distress.

### *Recommendations*

**18. There is minimal evidence to support the benefits of psychosocial interventions as a single therapeutic modality.** Grade of recommendation, 2C

**19. Although no recommendation is provided, since scientific evidence is lacking, current practice and expert opinion support the inclusion of psychosocial interventions as a component of comprehensive pulmonary rehabilitation programs for patients with COPD.**

## OXYGEN SUPPLEMENTATION AS AN ADJUNCT TO PULMONARY REHABILITATION

It was demonstrated > 25 years ago that long-term oxygen supplementation prolongs survival in patients with COPD and severe resting hypoxemia.<sup>159,160</sup> More recently, the usefulness of oxygen therapy in improving outcomes from pulmonary rehabilitation in patients with COPD has been evaluated in several RCTs. A distinction must be made between the immediate effect of oxygen on exercise performance and its usefulness in the exercise-training component of pulmonary rehabilitation.<sup>161</sup> This section will review the latter.

As an adjunct to exercise training, supplemental oxygen therapy has been studied in the following two situations: (1) patients who are severely hypoxemic at rest or with exercise; and (2) patients who do not have severe hypoxemia. The rationale for these studies is that supplemental oxygen therapy improves dyspnea and exercise capacity in patients with COPD and hypoxemia,<sup>162,163</sup> and even in those without exercise-induced hypoxemia,<sup>164</sup> possibly allowing them to train at higher intensities. These studies, which evaluated exercise performance and, in some instances, HRQOL, are summarized in Table 10.

Rooyackers and colleagues<sup>165</sup> randomized 24 patients with severe COPD who were referred to pulmonary rehabilitation and who experienced hypoxemia during exercise testing (arterial oxygen saturation [SaO<sub>2</sub>] at maximum exercise, < 90%) into the following two groups: (1) exercise training with room air; and (2) exercise training with supplemental oxygen administered at a rate of 4 L/min. The exercise-training intensity was increased as tolerated, but the work rate was adjusted to keep SaO<sub>2</sub> at

> 90% in all patients. Health status was measured using the CRDQ. In prerehabilitation testing, compared with breathing room air, the use of supplemental oxygen was associated with greater maximal cycle exercise performance and 6-min walk distances. However, exercise training with supplemental oxygen did not enhance the benefits of exercise training with respect to exercise performance measured while breathing room air or on health status measurements. These negative results might be explained by the fact that the mean work rate during interval cycle exercise training during the last 6 weeks was not significantly different between the two groups ( $p = 0.12$ ).

Garrod and Wedzicha<sup>166</sup> randomized 25 patients with severe COPD and exercise-hypoxemia into 18 sessions of exercise training breathing room air or supplemental oxygen (4 L/min) over 6 weeks. Patients were instructed to exercise as long as possible at a high intensity. In the short term, supplemental oxygen therapy improved the shuttle walk distance and symptoms of dyspnea in test results before rehabilitation. However, supplemental oxygen therapy with exercise training did not enhance the postrehabilitation gains in exercise performance, health status, or questionnaire-measured functional status. These results might be explained by the fact that the group receiving oxygen supplementation did not have significantly higher oxygen saturation levels than the nonsupplemented group. There was a small improvement in exertional dyspnea following rehabilitation with oxygen therapy.

Wadell and colleagues<sup>167</sup> randomized 20 patients with COPD and exercise-induced hypoxemia into training with or without supplemental oxygen (at a rate of 5 L/min). Training involved 30-min sessions

**Table 10—Oxygen Supplementation as an Adjunct to Exercise Training\***

Study/Year	Design	Hypoxia	Patients, No.	Duration	Between-Group Differences After Exercise Training†
Rooyackers et al <sup>165</sup> / 1997	RCT; O <sub>2</sub> vs RA; SaO <sub>2</sub> kept at > 90%; blinding not stated	Yes	24	50 sessions over 10 wk	No differences in peak work rate, peak $\dot{V}O_2$ , 6MWT, or health status
Garrod et al <sup>166</sup> / 2000	RCT; double blind; O <sub>2</sub> vs RA	Yes	25	18 sessions over 6 wk	No difference in shuttle walk test, health status, ADL scale; less postrehabilitation dyspnea with O <sub>2</sub> treatment
Wadell et al <sup>167</sup> / 2001	RCT; O <sub>2</sub> vs RA; SaO <sub>2</sub> kept at > 90%, patient blinded to tx group	Yes	20	24 sessions over 8 wk	No difference in exercise performance or health status
Emtner et al <sup>168</sup> / 2003	RCT; double-blind; O <sub>2</sub> vs RA group	No	29	21 sessions over 7 wk	O <sub>2</sub> group achieved higher levels of exercise training and greater increases in constant work rate testing

\*RA = room air. See Tables 3 and 4 for abbreviations not used in the text.

†Testing conducted with patients breathing room air.

on a treadmill three times weekly for 8 weeks. Training intensity was individualized to target dyspnea and perceived exertion ratings and to maintain  $\text{SaO}_2$  at  $> 90\%$ . Oxygen supplementation led to longer walk test distances before and after rehabilitation. However, there were no significant between-group differences in exercise-training effects at the end of the rehabilitation period, when patients were tested either while breathing room air or supplemental oxygen. In fact, there was a trend for greater improvement in those patients who trained while breathing room air.

The studies described above evaluated the effect of oxygen in patients who experienced hypoxemia during exercise. More recently, Emtner and colleagues<sup>168</sup> evaluated the use of supplemental oxygen as an adjunct to exercise training in patients with COPD who did not meet the standard criteria for oxygen supplementation. Unlike previous studies, this randomized trial was double-blinded. Twenty-nine patients without significant exercise-induced oxygen desaturation were randomized to receive compressed air or oxygen (at a rate of 3 L/min) during high-intensity exercise training. Patients were trained in 21 sessions over a 7-week period with a target intensity of 75% of the baseline peak work rate on a cycle ergometer, which was progressively adjusted according to the patient's perceived level of dyspnea and fatigue. The results indicated that patients receiving oxygen were able to train at higher intensities. After exercise training, endurance time at a constant work rate improved more in the group receiving supplemental oxygen therapy (14.5 min) compared with the group breathing room air (10.5 min;  $p < 0.05$ ). This improvement in exercise performance was accompanied by a reduction in respiratory rate at isotime during the tests. A recent metaanalysis<sup>169</sup> of these trials concluded that there was a trend toward greater improvement in constant-work-rate test results and health status with oxygen supplementation, but the opposite effect was present with the 6-min walk test distance.

In summary, the use of continuous supplemental oxygen for patients with COPD and severe resting hypoxemia is clearly indicated and recommended as a part of routine clinical practice. From a safety perspective, there is a strong rationale to administer supplemental oxygen during exercise training for patients with severe resting or exercise hypoxemia. However, while oxygen use improves maximal exercise performance acutely in the laboratory, studies testing its effect in enhancing the exercise-training effect have produced inconsistent results. This may reflect differences in methodology among the studies, especially with respect to intensity targets for training. Of note, most of the studies reviewed

evaluated supplemental oxygen administered at a rate of 3 to 5 L/min, which is higher than that used in the typical clinical setting. As described above, one well-designed study<sup>168</sup> of supplemental oxygen therapy for nonhypoxemic patients with COPD who trained at high intensity showed greater improvement in exercise capacity with oxygen therapy. The long-term benefit when supplemental oxygen is discontinued and the effect on other outcomes such as HRQOL remain to be determined.

#### *Recommendations*

**20. Supplemental oxygen should be used during rehabilitative exercise training in patients with severe exercise-induced hypoxemia.**

Grade of recommendation, 1C

**21. Administering supplemental oxygen during high-intensity exercise programs in patients without exercise-induced hypoxemia may improve gains in exercise endurance.**

Grade of recommendation, 2C

#### NONINVASIVE VENTILATION

Noninvasive positive-pressure ventilation (NPPV) includes the techniques of continuous positive airway pressure, pressure support, and proportional assist ventilation (PAV). A metaanalysis<sup>170</sup> of nocturnal NPPV in stable hypercapnic patients with COPD, which included four eligible trials, showed that this therapy did not improve lung function, gas exchange, or sleep efficiency, but may have led to an increased walk distance. The rationale for NPPV as an adjunct to exercise training is that through unloading the respiratory muscles, the decreased work of breathing might allow for improved tolerance of exercise training and the ability to achieve higher levels of exercise intensity.<sup>171</sup> In a systematic review of NPPV in seven trials that met specified inclusion criteria (describing a total of 65 patients with COPD), van't Hul and colleagues<sup>172</sup> concluded that dyspnea and exercise endurance were significantly improved in the short term with the application of this therapy. However, these short-term effects on dyspnea and exercise performance must be differentiated from the ability of repeated NPPV use to enhance outcomes from pulmonary rehabilitation.

In this evidence-based review, we were able to identify several trials that evaluated NPPV as an adjunct to an exercise training or pulmonary rehabilitation program (Table 11). Garrod and colleagues<sup>173</sup> randomized 45 patients with severe COPD to 12 weeks of exercise training with or without nocturnal NPPV via nasal mask. The median settings for NPPV were 16 cm  $\text{H}_2\text{O}$  inspiratory and 4 cm  $\text{H}_2\text{O}$  expira-

**Table 11—Noninvasive Ventilation as an Adjunct to Exercise Training\***

Study/Year	Design	Patients, No.	Duration	Between-Group Differences After Exercise Training
Garrod et al <sup>173/</sup> 2000	Nocturnal NPPV vs SB	45	16 sessions over 8 wk	The nocturnal NPPV group had increased shuttle walk distance and health status compared to the control group
Bianchi et al <sup>174/</sup> 2002	PAV vs SB	33	18 sessions over 6 wk	No significant differences in exercise tolerance, dyspnea, leg fatigue, or health status
Hawkins et al <sup>175/</sup> 2002	PAV vs SB	19	18 sessions over 6 wk	Higher training intensity with PAV, higher peak work rate, trend for lower lactate at iso-work rate
Johnson et al <sup>176/</sup> 2002	NPPV vs heliox vs SB	39	12 sessions over 6 wk	NPPV allowed for longer exercise training duration; no difference in peak workload
Costes et al <sup>177/</sup> 2003	NPPV vs SB	14	24 sessions over 8 wk	The NPPV group had a greater increase in peak $\dot{V}O_2$ ; no differences in exercise endurance or lactate measured at isotime
van't Hul et al <sup>178/</sup> 2006	Inspiratory pressure support vs SB	29	24 sessions over 8 wk	Inspiratory pressure support group had greater improvement in shuttle walk distance and cycle endurance time

\*SB = spontaneous breathing.

tory bilevel pressure ventilation. Compared with the exercise-training-only group, those patients using nocturnal NPPV as an adjunct to exercise training had a significantly increased shuttle walk distance (72 m) and greater improvement in health status.

Two trials<sup>174,175</sup> evaluated the adjunctive effect of NPPV during supervised exercise training. Bianchi and colleagues<sup>174</sup> randomized 33 men with moderate-to-severe COPD (mean FEV<sub>1</sub>, 44% predicted) beginning a 6-week pulmonary rehabilitation program into receiving mask PAV or spontaneous breathing during exercise training. Five of the 18 patients in the PAV group dropped out because of lack of compliance with the equipment. There were no between-group differences in dyspnea, leg fatigue, exercise performance, or health status. In a similar trial, but including patients with more severe disease (mean FEV<sub>1</sub>, 27% predicted), Hawkins and colleagues<sup>175</sup> found that PAV during 6 weeks of high-intensity cycle exercise training led to better outcomes. Compared to those patients breathing without assistance during exercise training, the PAV group had a 15.2% higher training intensity, higher peak work rate, and a trend ( $p = 0.09$ ) of lower lactate levels at the isowork rate. There was no significant between-group difference in exercise endurance.

Johnson and colleagues<sup>176</sup> randomized 39 patients with severe COPD (mean FEV<sub>1</sub>, 34% predicted) who were undergoing 6 weeks of pulmonary rehabilitation into the following three groups: (1) heliox breathing; (2) nasal NPPV therapy; and (3) spontaneous breathing during exercise training. Bilevel pressure ventilation was administered via nasal mask, with inspiratory positive airway pressure at 8 to 12 cm H<sub>2</sub>O (as tolerated) and expiratory positive airway pressure at 2 cm H<sub>2</sub>O. NPPV allowed for a longer exercise time during training, but there were no between-group differences in the percentage change in peak workload.

Costes and colleagues<sup>177</sup> randomized 14 patients with severe COPD into NPPV or spontaneous-breathing groups. Bilevel pressure ventilation settings were adjusted to tolerance. All were given 24 sessions of exercise training over 8 weeks. The NPPV group demonstrated greater improvement in peak  $\dot{V}O_2$  following exercise training compared to the group trained conventionally.

More recently, van't Hul and colleagues<sup>178</sup> randomized 29 patients with COPD into the following two groups: (1) inspiratory pressure support (10 cm H<sub>2</sub>O) as an adjunct to an 8-week high-intensity cycle exercise-training program; and (2) sham therapy (inspiratory support at 5 cm H<sub>2</sub>O) with exercise training. Although both the patients and the investigator assessing the outcomes were blinded to the treatment group, the physiotherapists supervising exercise training were not. Significant between-group improvements in favor of the treatment group were seen in shuttle walk distance and cycle endurance time.

In summary, several randomized trials have compared spontaneous breathing with NPPV as an adjunct to exercise in patients with COPD. Obvious methodological issues exist with respect to blinding patients and investigators, differences in exercise training and outcome assessments, and the small numbers of subjects. However, it appears that this therapy does confer an immediate postrehabilitation benefit in improving exercise tolerance in selected patients with more advanced disease.

### Recommendation

**22. As an adjunct to exercise training in selected patients with severe COPD, noninvasive ventilation produces modest additional improvements in exercise performance.** Grade of recommendation, 2B

## NUTRITIONAL SUPPLEMENTATION IN PULMONARY REHABILITATION

Poor nutritional status is associated with increased morbidity and mortality in patients with moderate-to-severe COPD.<sup>179</sup> Prior studies have investigated the effects of dietary supplementation on patients with COPD, as summarized in a relatively recent metaanalysis.<sup>180</sup> Summary data indicate that nutritional support/supplementation does not have a clinically significant effect on lung function or functional abilities. No studies have evaluated the effects of behavioral weight management (gain or loss) among patients with COPD.

There remains very little information regarding the effects of nutritional supplementation used in conjunction with a comprehensive pulmonary rehabilitation program. Only one study<sup>181</sup> has investigated the effects of nutritional supplementation administered during a comprehensive pulmonary rehabilitation program. In this double blind, randomized trial, 85 patients with chronic lung disease were randomized to receive either (1) carbohydrate supplementation or (2) a nonnutritive placebo during a 7-week pulmonary rehabilitation program. The aim was to augment exercise performance with the use of carbohydrate supplementation. Outcomes measured included physical performance, health status, and body weight and composition. Twenty-five patients were unable to complete the study and were not included in the final analysis. Significant increases in shuttle walk distance and HRQOL (as measured by the CRDQ) were noted in both groups. In well-nourished patients (*ie*, body mass index > 19 kg/m<sup>2</sup>), improvement in shuttle walk performance was significantly greater in the nutritionally supplemented group (mean difference between groups, 27 m; 95% confidence interval, 1 to 53 m;  $p < 0.05$ ). The increase in shuttle walk performance correlated with increases in total carbohydrate intake.

The overall effects of nutritional supplementation in this single study are difficult to determine given the significant number of patients who did not complete the study and the fact that improvement was noted in both experimental groups. This study suggests that exercise-training results in a negative energy balance that can be overcome by supplementation, and in selected patients, may improve the outcome of training.

### *Recommendation*

**23. There is insufficient evidence to support the routine use of nutritional supplementation in the pulmonary rehabilitation of patients with COPD. No recommendation is provided.**

## PULMONARY REHABILITATION FOR PATIENTS WITH DISORDERS OTHER THAN COPD

Although they have not been studied as well to date, patients with respiratory disorders other than COPD can also benefit substantially from pulmonary rehabilitation. Indeed, the scientific rationale for providing pulmonary rehabilitation to patients with non-COPD diagnoses is the same as that for patients with COPD. General principles of rehabilitation treatment emphasize the adaptation of multidisciplinary treatment strategies to the needs of individual patients. Pulmonary rehabilitation programs provide an ideal setting to address both common and individual concerns for patients with a variety of different chronic lung diseases.

As in COPD, persons with other forms of chronic respiratory disease commonly experience deconditioning and exercise intolerance, disabling symptoms of dyspnea and fatigue, impaired health status and quality of life, systemic inflammation, nutritional impairments, and/or muscle dysfunction (related to deconditioning, loss of fat-free mass, and/or corticosteroid use) that collectively impair functional status along with abnormalities of pulmonary function. These comorbidities that are associated with chronic respiratory disease can potentially be addressed and corrected with rehabilitation strategies including exercise training and other interventions such as nutritional support, despite the presence of irreversible abnormalities of lung function. Moreover, pulmonary rehabilitation programs provide the opportunity to educate and train patients in adapting to complex treatment interventions such as immunosuppressive medications, oxygen therapy, noninvasive ventilation, tracheostomy, lung volume reduction surgery, or lung transplantation. Optimal outcomes from these depend on patient understanding and compliance with therapeutic recommendations, but there is minimal time typically available in the routine clinical care setting for patient education, training, and coaching for the complex behavioral changes included in treatment recommendations. Pulmonary rehabilitation can assist patients in adjusting complex interventions such as the technical requirements for oxygen supplementation or noninvasive ventilation. Patients undergoing lung transplantation or lung volume reduction surgery are frequently required to participate in preoperative and postoperative pulmonary rehabilitation, in part, to provide needed education and support.

Modification of the relative emphasis on the core program components and overall program content of pulmonary rehabilitation may be required to maintain patient safety and to meet individual patient needs and goals.<sup>182</sup> The goals of pulmonary rehabil-

itation for patients with chronic lung diseases other than COPD may differ from the standard goals for patients with COPD. Education of the rehabilitation program staff regarding the pathophysiology, symptoms, mechanisms of exercise limitation, natural course, and signs of disease destabilization as well as the therapeutic interventions specific for each of the various respiratory disorders is essential, as is close communication with referring physicians and the program medical director. Pulmonary rehabilitation staff must be familiar with the recommended methods of assessing patient exercise capacity, must be able to develop and safely implement the exercise program, and to identify situations in which specialized equipment or room setup may be required. Additional specific expertise may be needed in developing appropriate rehabilitation programs for non-COPD patients with disease-specific input from physical, occupational, and respiratory therapists, nurses, health psychologists, dieticians, respiratory physicians, and, when necessary, physiatrists or neurologists. Disease-appropriate and age-appropriate tools for the assessment of exercise capacity, health status, and quality of life should be utilized, and efforts must be made to integrate topics relating to non-COPD diagnoses in situations in which the patient group is composed predominantly of COPD patients. Individual patient education sessions and additional written and/or video materials may be needed.

Although most of the studies conducted and published to date investigating the outcomes of pulmonary rehabilitation for disorders other than COPD are uncontrolled trials or case series, RCTs are beginning to emerge.<sup>183,184</sup> The strength of existing evidence supporting the use of pulmonary rehabilitation varies across the different diseases. Thus far, existing data suggest that, as in COPD, exercise training and rehabilitation improve exercise tolerance and/or health status/quality of life for persons with asthma,<sup>183,185,186</sup> bronchiectasis,<sup>187</sup> cystic fibrosis,<sup>184,188,189</sup> interstitial lung disease and restrictive chest wall disease,<sup>21,190,191</sup> pulmonary hypertension,<sup>192</sup> obesity-related respiratory disease,<sup>193,194</sup> and lung cancer,<sup>195,196</sup> and selected patients with respiratory impairment from neuromuscular diseases.<sup>197–200</sup> For some patients with neuromuscular disease, pulmonary rehabilitation may not include traditional exercise training, but may instead focus on acclimatization to NPPV, optimization of functional status, and maintenance of the ability to live independently through the use of adaptive/assistive equipment (*eg*, walkers or sock reachers). Caution must be taken to avoid excess muscle fatigue, especially among persons with degenerative neuromuscular disorders. Further research is needed to identify optimal train-

ing regimens, program structures, and outcome measurement tools that are useful in pulmonary rehabilitation for patients with respiratory disorders other than COPD.

#### *Recommendations*

**24. Pulmonary rehabilitation is beneficial for patients with some chronic respiratory diseases other than COPD.** Grade of recommendation, 1B

**25. Although no recommendation is provided since scientific evidence is lacking, the current practice and expert opinion suggest that pulmonary rehabilitation for patients with chronic respiratory diseases other than COPD should be modified to include treatment strategies specific to individual diseases and patients, in addition to treatment strategies common to both COPD and non-COPD patients.**

#### SUMMARY AND RECOMMENDATIONS FOR FUTURE RESEARCH

The field of pulmonary rehabilitation has continued to develop and mature substantially since the publication of the previous evidence-based guidelines in 1997. Additional published literature has added substantially to the scientific basis of pulmonary rehabilitation interventions as well as outcomes. The new data that have been examined further strengthen the evidence that supports the benefits of lower extremity exercise training in pulmonary rehabilitation and the improvement expected in symptoms of dyspnea from comprehensive pulmonary rehabilitation programs. The evidence supporting important changes in HRQOL has also been strengthened in new studies. Although there is some additional evidence, there is still a need for more systematic studies of the effect of pulmonary rehabilitation on health-care costs and utilization. The question is still open about whether pulmonary rehabilitation improves survival in patients with COPD. Trends observed in existing studies suggest that pulmonary rehabilitation may have a modest effect on survival, but a larger study powered to address survival would add important new information to the field and would have a significant impact on future health policy decisions. There is also a need for more studies about psychosocial outcomes and interventions. New evidence adds support for the inclusion of psychosocial components in comprehensive pulmonary rehabilitation programs and the important beneficial effects of such programs on psychosocial health, but more is clearly needed. Several promising studies lend continued support for upper extremity training as a means of achieving



important benefits in ADLs for many patients with disabling chronic lung diseases. There remains little evidence to support the routine inclusion of specific ventilatory muscle training in pulmonary rehabilitation. There is little evidence that education alone, outside the context of comprehensive pulmonary rehabilitation treatment, is beneficial. However, there have been no systematic studies evaluating educational delivery, topic selection, and reinforcement of information. Investigation may be warranted regarding patient-specific learning styles, the duration of educational sessions, topic selection, and the use of educational reinforcement. Finally, emerging data have demonstrated that exercise training and pulmonary rehabilitation are beneficial for patients with respiratory disorders other than COPD.

An important area for future research relates to the duration of pulmonary rehabilitation treatment and strategies to help patients sustain benefits over a longer period of time. The existing literature strongly indicates that the typical 6-week to 12-week comprehensive pulmonary rehabilitation program produces benefits that are sustained for approximately 12 to 18 months. This, in itself, is remarkable in the face of progressive chronic lung diseases. However, it is likely that new treatment strategies could be developed to help patients maintain the benefits from pulmonary rehabilitation over longer periods of time. Changes in the typical program structure, the period of intervention, the more efficient use of limited resources, as well as the tailoring of the rehabilitation intervention to different clinical phenotypes of COPD (eg, with or without peripheral or respiratory muscle weakness, and depleted or nondepleted fat-free mass) may allow principles of pulmonary rehabilitation to be adapted to longer term chronic disease management, improve postprogram maintenance of benefits, and allow many more patients who are in need to benefit from pulmonary rehabilitation. The development of better postprogram strategies to help patients adhere to rehabilitative treatments and to better maintain the complex behavior changes acquired in pulmonary rehabilitation might extend the duration of benefits.

Interesting new evidence in the literature highlights several areas for fruitful future research in relation to pulmonary rehabilitation, and the treatment of patients with chronic lung diseases. Possible topics include strength training in addition to endurance exercise training (and optimal methods for such strength-training protocols), better definition of optimal exercise-training regimens, supplemental oxygen therapy for patients with less severe resting hypoxemia or hypoxemia specific to exercise or sleep, use of noninvasive ventilatory assistance as an adjunct to exercise training, nutritional supplementa-

tion, and use of rehabilitation strategies for patients with chronic lung diseases other than COPD.

One interesting new area for future research is to further define the role for the transcutaneous electrical stimulation of the peripheral muscles (TCEMS) as a rehabilitative strategy for patients with COPD and other forms of chronic respiratory disease. Studies published thus far have demonstrated that TCEMS in the muscles of ambulation can lead to significant improvements in muscle strength, exercise endurance, dyspnea,<sup>201,202</sup> and  $\dot{V}O_2$  max<sup>201</sup> among stable patients with moderate-to-severe COPD, as well as in severely deconditioned patients with severe airflow obstruction and low body mass index who are recovering from acute COPD exacerbations.<sup>203</sup> TCEMS also may facilitate improvement in mobility among bed-bound patients with COPD and respiratory failure requiring mechanical ventilation.<sup>204</sup> This safe, well-tolerated technique can even be performed during COPD exacerbations and may help to prevent functional decline during COPD exacerbations.<sup>201</sup> Further work is needed to clarify which subpopulations of patients benefit most from this technique, to define the role of TCEMS as a routine component of pulmonary rehabilitation, and to understand the mechanisms by which TCEMS confers its benefits among patients with chronic lung disease.

One novel approach to encouraging adherence is through the use of distractive auditory stimuli (DAS). A 2002 RCT<sup>205</sup> of the effects of DAS (*ie*, listening to music while exercising) on exercise adherence and exercise outcomes among patients with COPD who had completed a pulmonary rehabilitation program found no differences in amount of exercise, velocity of exercise, or physical symptoms during the study period between DAS participants and control subjects receiving standard care. However, participants in the DAS group experienced reductions in dyspnea during ADLs and a significant increase in exercise endurance (as determined by the 6-min walk distance). Thus, DAS may help to distract participants from exercise-related dyspnea and may help patients to increase exercise duration during individual bouts.

Finally, an important area of research in COPD relates to the importance of exacerbations in influencing the natural history of the disease, and in accelerating the subsequent morbidity and mortality. Preliminary evidence<sup>48</sup> suggests that pulmonary rehabilitation after an exacerbation could improve mortality in these high-risk patients. Additional work in this area would be very important.

In summary, this is an exciting time that is full of opportunities in the field of pulmonary rehabilitation. Pulmonary rehabilitation has now become well

established as a recommended treatment that can provide important benefits to substantial numbers of disabled patients with chronic lung diseases. A review of the various components of pulmonary rehabilitation also highlights opportunities, and challenges, for future research that have the potential to improve and broaden the scope of pulmonary rehabilitation practice for the large population of patients with chronic lung diseases, most of whom do not currently have access to such programs.

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#### SUMMARY OF RECOMMENDATIONS

**1. A program of exercise training of the muscles of ambulation is recommended as a mandatory component of pulmonary rehabilitation for patients with COPD.**

*Grade of Recommendation: 1A*

**2. Pulmonary rehabilitation improves the symptom of dyspnea in patients with COPD.**

*Grade of Recommendation: 1A*

**3. Pulmonary rehabilitation improves health-related quality of life in patients with COPD.**

*Grade of Recommendation: 1A*

**4. Pulmonary rehabilitation reduces the number of hospital days and other measures of health-care utilization in patients with COPD.**

*Grade of Recommendation: 2B*

**5. Pulmonary rehabilitation is cost-effective in patients with COPD.**

*Grade of Recommendation: 2C*

**6. There is insufficient evidence to determine if pulmonary rehabilitation improves survival in patients with COPD. No recommendation is provided.**

**7. There are psychosocial benefits from comprehensive pulmonary rehabilitation programs in patients with COPD.**

*Grade of Recommendation: 2B*

**8. Six to 12 weeks of pulmonary rehabilitation produces benefits in several outcomes that decline gradually over 12 to 18 months.**

*(Grade of Recommendation: 1A)*

**Some benefits, such as health-related quality of life, remain above control at 12 to 18 months.**

*(Grade of Recommendation: 1C)*

**9. Longer pulmonary rehabilitation programs (12 weeks) produce greater sustained benefits than shorter programs.**

*Grade of Recommendation: 2C*

**10. Maintenance strategies following pulmonary rehabilitation have a modest effect on long-term outcomes.**

*Grade of Recommendation: 2C*

**11. Lower-extremity exercise training at higher exercise intensity produces greater-physiologic benefits than lower-intensity training in patients with COPD.**

*Grade of Recommendation: 1B*

**12. Both low- and high-intensity exercise training produce clinical benefits for patients with COPD.**

*Grade of Recommendation: 1A*

**13. Addition of a strength training component to a program of pulmonary rehabilitation increases muscle strength and muscle mass.**

*Strength of evidence: 1A*

**14. Current scientific evidence does not support the routine use of anabolic agents in pulmonary rehabilitation for patients with COPD.**

*Grade of Recommendation: 2C*

**15. Unsupported endurance training of the upper extremities is beneficial in patients with COPD and should be included in pulmonary rehabilitation programs.**

*Grade of Recommendation: 1A*

**16. The scientific evidence does not support the routine use of inspiratory muscle training as an essential component of pulmonary rehabilitation.**

*Grade of Recommendation: 1B*

**17. Education should be an integral component of pulmonary rehabilitation. Education should include information on collaborative self-management and prevention and treatment of exacerbations.**

*Grade of Recommendation: 1B*

**18. There is minimal evidence to support the benefits of psychosocial interventions as a single therapeutic modality.**

*Grade of Recommendation: 2C*

**19. Although no recommendation is provided since scientific evidence is lacking, current practice and expert opinion support the inclusion of psychosocial interventions as a component of comprehensive pulmonary rehabilitation programs for patients with COPD.**

**20. Supplemental oxygen should be used during rehabilitative exercise training in patients with severe exercise-induced hypoxemia.**

*Grade of Recommendation: 1C*

**21. Administering supplemental oxygen during high-intensity exercise programs in patients without exercise-induced hypoxemia may improve gains in exercise endurance.**

*Grade of Recommendation: 2C*

**22. As an adjunct to exercise training in selected patients with severe COPD, noninvasive ventilation produces modest additional improvements in exercise performance.**

*Grade of Recommendation: 2B*

**23. There is insufficient evidence to support the routine use of nutritional supplementation in pulmonary rehabilitation of patients with COPD. No recommendation is provided.**

**24. Pulmonary rehabilitation is beneficial for some patients with chronic respiratory diseases other than COPD.**

*Grade of Recommendation: 1B*

**25. Although no recommendation is provided since scientific evidence is lacking, current practice and expert opinion suggest that pulmonary rehabilitation for patients with chronic respiratory diseases other than COPD should be modified to include treatment strategies specific to individual diseases and patients in addition to treatment strategies common to both COPD and non-COPD patients.**

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## **Pulmonary Rehabilitation\***

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