An Official American Thoracic Society/European Respiratory Society Statement: Key Concepts and Advances in Pulmonary Rehabilitation

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***Background*: Pulmonary rehabilitation is recognized as a core component of the management of individuals with chronic respiratory disease. Since the 2006 American Thoracic Society (ATS)/European Respiratory Society (ERS) Statement on Pulmonary Rehabilitation, there has been considerable growth in our knowledge of its efficacy and scope.**

***Purpose*: The purpose of this Statement is to update the 2006 document, including a new definition of pulmonary rehabilitation and highlighting key concepts and major advances in the field.**

***Methods*: A multidisciplinary committee of experts representing the ATS Pulmonary Rehabilitation Assembly and the ERS Scientific Group 01.02, "Rehabilitation and Chronic Care," determined the overall scope of this update through group consensus. Focused literature reviews in key topic areas were conducted by committee members with relevant clinical and scientific expertise. The final content of this Statement was agreed on by all members.**

***Results*: An updated definition of pulmonary rehabilitation is proposed. New data are presented on the science and application of pulmonary rehabilitation, including its effectiveness in acutely ill individuals with chronic obstructive pulmonary disease, and in individuals with other chronic respiratory diseases. The important role of pulmonary rehabilitation in chronic disease management is highlighted. In addition, the role of health behavior change in optimizing and maintaining benefits is discussed.**

***Conclusions*: The considerable growth in the science and application of pulmonary rehabilitation since 2006 adds further support for its efficacy in a wide range of individuals with chronic respiratory disease.**

Keywords: COPD; pulmonary rehabilitation; exacerbation; behavior; outcomes

OVERVIEW

Pulmonary rehabilitation has been clearly demonstrated to reduce dyspnea, increase exercise capacity, and improve quality of life in individuals with chronic obstructive pulmonary disease (COPD) (1). This Statement provides a detailed review of progress in the science and evolution of the concept of pulmonary rehabilitation since the 2006 Statement. It represents the consensus of 46 international experts in the field of pulmonary rehabilitation.

On the basis of current insights, the American Thoracic Society (ATS) and the European Respiratory Society (ERS) have adopted the following new definition of pulmonary rehabilitation: "*Pulmonary rehabilitation is a comprehensive intervention based on a thorough patient assessment followed by patient-tailored therapies that include, but are not limited to, exercise training, education, and behavior change, designed to improve the physical and psychological condition of people with chronic respiratory disease and to promote the long-term adherence to health-enhancing behaviors.*"

Since the previous Statement, we now more fully understand the complex nature of COPD, its multisystem manifestations, and frequent comorbidities. Therefore, integrated care principles are being adopted to optimize the management of these complex patients (2). Pulmonary rehabilitation is now recognized as a core component of this process (Figure 1) (3). Health behavior change is vital to optimization and maintenance of benefits from any intervention in chronic care, and pulmonary rehabilitation has taken a lead in implementing strategies to achieve this goal.

Noteworthy advances in pulmonary rehabilitation that are discussed in this Statement include the following:

- There is increased evidence for use and efficacy of a variety of forms of exercise training as part of pulmonary rehabilitation; these include interval training, strength training, upper limb training, and transcutaneous neuromuscular electrical stimulation.
- Pulmonary rehabilitation provided to individuals with chronic respiratory diseases other than COPD (i.e., interstitial lung disease, bronchiectasis, cystic fibrosis, asthma, pulmonary hypertension, lung cancer, lung volume reduction surgery, and lung transplantation) has demonstrated improvements in symptoms, exercise tolerance, and quality of life.
- Symptomatic individuals with COPD who have lesser degrees of airflow limitation who participate in pulmonary rehabilitation derive similar improvements in symptoms, exercise tolerance, and quality of life as do those with more severe disease.
- Pulmonary rehabilitation initiated shortly after a hospitalization for a COPD exacerbation is clinically effective, safe, and associated with a reduction in subsequent hospital admissions.
- Exercise rehabilitation commenced during acute or critical illness reduces the extent of functional decline and hastens recovery.
- Appropriately resourced home-based exercise training has proven effective in reducing dyspnea and increasing exercise performance in individuals with COPD.
- Technologies are currently being adapted and tested to support exercise training, education, exacerbation management, and physical activity in the context of pulmonary rehabilitation.
- The scope of outcomes assessment has broadened, allowing for the evaluation of COPD-related knowledge and self-efficacy, lower and upper limb muscle function, balance, and physical activity.
- Symptoms of anxiety and depression are prevalent in individuals referred to pulmonary rehabilitation, may affect outcomes, and can be ameliorated by this intervention.

In the future, we see the need to increase the applicability and accessibility of pulmonary rehabilitation; to effect behavior change to optimize and maintain outcomes; and to refine this intervention so that it targets the unique needs of the complex patient.

INTRODUCTION

Since the American Thoracic Society (ATS)/European Respiratory Society (ERS) Statement on Pulmonary Rehabilitation was published in 2006 (1), this intervention has advanced in several ways. First, our understanding of the pathophysiology underlying chronic respiratory disease such as chronic obstructive pulmonary disease (COPD) has grown. We now more fully appreciate the complex nature of COPD, its multisystem manifestations, and frequent comorbidities. Second, the science and

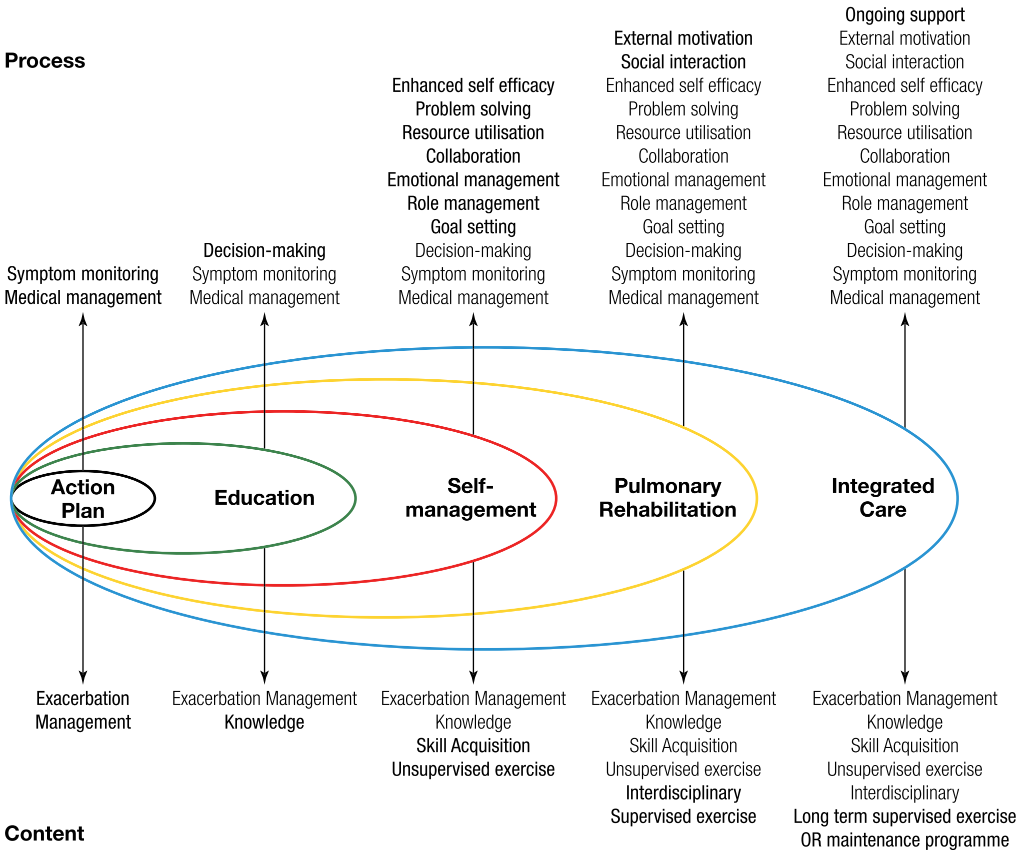

Figure 1. A spectrum of support for chronic obstructive pulmonary disease. Reprinted by permission from Reference 3.

application of pulmonary rehabilitation have evolved. For example, evidence now indicates that pulmonary rehabilitation is effective when started at the time or shortly after a hospitalization for COPD exacerbation. Third, as integrated care has risen to be regarded as the optimal approach toward managing chronic respiratory disease, pulmonary rehabilitation has established itself as an important component of this model. Finally, with the recognition that health behavior change is vital to optimization and maintenance of benefits from any intervention in chronic care, pulmonary rehabilitation has taken a lead in developing strategies to promote self-efficacy and thus the adoption of a healthy lifestyle to reduce the impact of the disease.

Our purpose in updating this ATS/ERS Statement on Pulmonary Rehabilitation is to present the latest developments and concepts in this field. By doing so, we hope to demonstrate its efficacy and applicability in individuals with chronic respiratory disease. By necessity, this Statement focuses primarily on COPD, because individuals with COPD represent the largest proportion of referrals to pulmonary rehabilitation (4), and much of the existing science is in this area. However, effects of exercise-based pulmonary rehabilitation in people with chronic respiratory disease other than COPD are discussed in detail. We hope to underscore the pivotal role of pulmonary rehabilitation in the integrated care of the patient with chronic respiratory disease.

METHODS

A multinational, multidisciplinary group of 46 clinical and research experts (Table 1) participated in an ATS/ERS Task Force with the charge to update the previous Statement (1). Task Force members were identified by the leadership of the ATS Pulmonary Rehabilitation Assembly and the ERS Scientific Group 01.02, "Rehabilitation and Chronic Care." Members were vetted for potential conflicts of interest according to the policies and procedures of ATS and ERS.

Task Force meetings were organized during the ATS International Congress 2011 (Denver, CO) and during the ERS Annual Congress 2011 (Amsterdam, The Netherlands) to present and discuss the latest scientific developments within pulmonary rehabilitation. In preparation, the Statement was split up into various sections and subsections. Task Force members were appointed to one or more sections, based on their clinical and scientific expertise. Task Force members reviewed new scientific advances to be added to the then-current knowledge base. This was done through identifying recently updated (published between 2006 and 2011) systematic reviews of randomized trials from Medline/PubMed, EMBASE, the Cochrane Central Register of Controlled Trials, CINAHL, the Physical Therapy Evidence Database (PEDro), and the Cochrane Collaboration, and supplementing this with recent studies that added to the evidence based on pulmonary rehabilitation (Table 2). The Task Force members selected the relevant papers themselves, irrespective of the study designs used. Finally, the Co-Chairs read all the sections, and together with an *ad hoc* writing committee (the four Co-Chairs, Linda Nici, Carolyn Rochester, and Jonathan Raskin) the final document was composed. Afterward, all Task Force members had the opportunity to give written feedback. In total, three drafts of the updated Statement were prepared by the four Co-Chairs; these were each reviewed and revised iteratively by the Task Force members. Redundancies within and across sections were minimized. This document represents the consensus of these Task Force members.

This document was created by combining a firm evidence-based approach and the clinical expertise of the Task Force members. This is a Statement, not a Clinical Practice Guideline. The latter makes specific recommendations and formally grades strength of the recommendation and the quality the scientific evidence. This Statement is complementary to two current documents on pulmonary rehabilitation: the American College of

TABLE 1. MULTIDISCIPLINARY COMPOSITION OF THE AMERICAN THORACIC SOCIETY/EUROPEAN RESPIRATORY SOCIETY TASK FORCE ON PULMONARY REHABILITATION

- Chest physicians/respirologists/pulmonologists
- Elderly care physician
- Physiotherapists
- Occupational therapist
- Nurses
- Nutritional scientist
- Exercise physiologists
- Methodologists
- Psychologists/behavioral experts
- Health economists

TABLE 2. METHODS CHECKLIST

	Yes	No
Panel assembly		
• Included experts from relevant clinical and nonclinical disciplines	X	
• Included individual who represents views of patients in society at large		X
• Included methodologist with documented expertise	X	
Literature review		
• Performed in collaboration with librarian		X
• Searched multiple electronic databases	X	
• Reviewed reference lists of retrieved articles	X	
Evidence synthesis		
• Applied prespecified inclusion and exclusion criteria		X
• Evaluated included studies for sources of bias	X	
• Explicitly summarized benefits and harms		X
• Used PRISMA to report systematic review		X
• Used GRADE to describe quality evidence		X
Generation of recommendations		
• Used GRADE to rate the strength of recommendations		X

Definition of abbreviations: GRADE = Grading of Recommendations Assessment, Development and Evaluation; PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

Chest Physicians and American Association of Cardiovascular and Pulmonary Rehabilitation (AACVPR) evidence-based guidelines (5), which formally grade the quality of scientific evidence, and the AACVPR Guidelines for Pulmonary Rehabilitation Programs, which give practical recommendations (6). This Statement has been endorsed by both the ATS Board of Directors (June 2013) and the ERS Executive Committee (February 2013).

DEFINITION AND CONCEPT

In 2006 (1), pulmonary rehabilitation was defined as "*an evidence-based, multidisciplinary, and comprehensive intervention for patients with chronic respiratory diseases who are symptomatic and often have decreased daily life activities. Integrated into the individualized treatment of the patient, pulmonary rehabilitation is designed to reduce symptoms, optimize functional status, increase participation, and reduce healthcare costs through stabilizing or reversing systemic manifestations of the disease.*"

Even though the 2006 definition of pulmonary rehabilitation is widely accepted and still relevant, there was consensus among the current Task Force members to make a new definition of pulmonary rehabilitation. This decision was made on the basis of recent advances in our understanding of the science and process of pulmonary rehabilitation. For example, some parts of a comprehensive pulmonary rehabilitation program are based on years of clinical experience and expert opinion, rather than evidence-based. Moreover, nowadays pulmonary rehabilitation is considered to be an interdisciplinary intervention rather than a multidisciplinary approach (7) to the patient with chronic respiratory disease. Finally, the 2006 definition emphasized the importance of stabilizing or reversing systemic manifestations of the disease, without specific attention to behavior change.

On the basis of our current insights, the ATS and the ERS have adopted the following new definition of pulmonary rehabilitation: "*Pulmonary rehabilitation is a comprehensive intervention based on a thorough patient assessment followed by patient-tailored therapies, which include, but are not limited to, exercise training, education, and behavior change, designed to improve the physical and psychological condition of people with chronic respiratory disease and to promote the long-term adherence of health-enhancing behaviors.*"

Pulmonary rehabilitation is implemented by a dedicated, interdisciplinary team, including physicians and other health care professionals; the latter may include physiotherapists, respiratory therapists, nurses, psychologists, behavioral specialist, exercise physiologists, nutritionists, occupational therapists, and social workers. The intervention should be individualized to the unique needs of the patient, based on initial and ongoing assessments, including disease severity, complexity, and comorbidities. Although pulmonary rehabilitation is a defined intervention, its components are integrated throughout the clinical course of a patient's disease. Pulmonary rehabilitation may be initiated at any stage of the disease, during periods of clinical stability or during or directly after an exacerbation. The goals of pulmonary rehabilitation include minimizing symptom burden, maximizing exercise performance, promoting autonomy, increasing participation in everyday activities, enhancing (health-related) quality of life, and effecting long-term health-enhancing behavior change.

This document places pulmonary rehabilitation within the concept of integrated care. The World Health Organization defines integrated care as "a concept bringing together inputs, delivery, management and organization of services related to diagnosis, treatment, care, rehabilitation and health promotion" (8). Integration of services improves access, quality, user satisfaction, and efficiency of medical care. As such, pulmonary rehabilitation provides an opportunity to coordinate care throughout the clinical course of an individual's disease.

EXERCISE TRAINING

Introduction

Exercise capacity in patients with chronic respiratory disease such as COPD is impaired, and is often limited by dyspnea. The limitation to exercise is complex and it would appear the limitation to exercise is dependent on the mode of testing (9). The exertional dyspnea in this setting is usually multifactorial in origin, partly reflecting peripheral muscle dysfunction, the consequences of dynamic hyperinflation, increased respiratory load, or defective gas exchange (10–12). These limitations are aggravated by the natural, age-related decline in function (13) and the effects of physical deconditioning (detraining). In addition, they are often compounded by the presence of comorbid conditions. Some of these factors will be partially amenable to physical exercise training as part of a comprehensive pulmonary rehabilitation program.

Considered to be the cornerstone of pulmonary rehabilitation (1), exercise training is the best available means of improving muscle function in COPD (14–18). Even those patients with severe chronic respiratory disease can often sustain the necessary training intensity and duration for skeletal muscle adaptation to occur (16, 19). Improvements in skeletal muscle function after exercise training lead to gains in exercise capacity despite the absence of changes in lung function (20, 21). Moreover, the improved oxidative capacity and efficiency of the skeletal muscles leads to a reduced ventilatory requirement for a given submaximal work rate (22); this may reduce dynamic hyperinflation, thereby adding to the reduction in exertional dyspnea (23). Exercise training may have positive effects in other areas, including increased motivation for exercise beyond the rehabilitation environment, reduced mood disturbance (24–26), less symptom burden (27), and improved cardiovascular function (28, 29). Optimizing medical treatment before exercise training with bronchodilator therapy, long-term oxygen therapy, and the treatment of comorbidities may maximize the effectiveness of the exercise training intervention.

Before starting an exercise training program, an exercise assessment is needed to individualize the exercise prescription, evaluate the potential need for supplemental oxygen, help rule out some cardiovascular comorbidities, and help ensure the safety of the intervention (30–35).

This patient assessment (35) may also include a maximal cardiopulmonary exercise test to assess the safety of exercise, to define the factors contributing to exercise limitation, and to identify a suitable exercise prescription (30).

Identifying a single variable limiting exercise in individuals with COPD is often difficult. Indeed, many factors may contribute directly or indirectly to exercise intolerance. Because of this, separating the various mechanisms contributing to exercise intolerance is often a largely academic exercise and is not always necessary or feasible. For example, deconditioning and hypoxia contribute to excess ventilation, resulting in an earlier ventilatory limitation. Consequently, exercise training and oxygen therapy could delay a ventilatory limit to exercise without altering lung function or the maximal ventilatory capacity. Analyzing the output from a cardiopulmonary exercise test may uncover otherwise hidden exercise-related issues, such as hypoxemia, dysrhythmias, musculoskeletal problems, or cardiac ischemia (30).

Physiology of Exercise Limitation

Exercise intolerance in individuals with chronic respiratory disease may result from ventilatory constraints, pulmonary gas exchange abnormalities, peripheral muscle dysfunction, cardiac dysfunction, or any combination of the above (10–12). Anxiety, depression, and poor motivation may also contribute to exercise intolerance (36); however, a direct association has not been established (37–39).

Ventilatory limitation. In COPD, ventilatory requirements during exercise are often higher than expected because of increased work of breathing, increased dead space ventilation, impaired gas exchange, and increased ventilatory demand as a consequence of deconditioning and peripheral muscle dysfunction. Adding to this increased demand is the limitation to maximal ventilation during exercise resulting from expiratory airflow obstruction and dynamic hyperinflation in individuals with COPD (40, 41). This leads to further increased work of breathing, increased load and mechanical constraints on the respiratory muscles (42, 43), with a resulting intensified sense of dyspnea.

Gas exchange limitation. Hypoxia directly increases pulmonary ventilation through augmenting peripheral chemoreceptor output and indirectly through stimulation of lactic acid production. Lactic acidemia resulting from anaerobic metabolism by the muscles during higher intensity exercise contributes to muscle task failure and increases pulmonary ventilation, as lactic acid buffering results in an increase in carbon dioxide production and acidosis stimulates the carotid bodies (44). Supplemental oxygen therapy during exercise, in hypoxemic and even in nonhypoxemic patients with COPD, allows for higher intensity training, probably through several mechanisms, including a decrease in pulmonary artery pressure, carotid body inhibition, and a decrease in lactic acid production, all resulting in a dose-dependent decrease in respiratory rate, and thereby a reduction in dynamic hyperinflation (41, 45–48).

Cardiac limitation. The cardiovascular system is affected by chronic respiratory disease in a number of ways, the most important being an increase in right ventricular afterload. Contributing factors include elevated pulmonary vascular resistance resulting from combinations of hypoxic vasoconstriction (49), vascular injury and/or remodeling (50, 51), and increased effective pulmonary vascular resistance due to erythrocytosis (52). An overloaded right ventricle may lead to right ventricular hypertrophy and failure (53). Right ventricular hypertrophy may also compromise left ventricular filling by producing septal shifts; these further reduce the ability of the heart to meet exercise demands (54). Other cardiac complications include tachyarrythmias and elevated right atrial pressure (due to air trapping). The latter may further compromise cardiac function during exercise (55, 56). Some of the substantial physiologic benefits from exercise training (57–60) may be due, in part, to an improvement in cardiovascular function (28, 29).

Limitation due to lower limb muscle dysfunction. Lower limb muscle dysfunction is frequent in individuals with chronic respiratory disease and is an important cause of their exercise limitation (61, 62). A summary of common skeletal muscle abnormalities in chronic respiratory disease is given in the ATS/ERS Statement on Skeletal Muscle Dysfunction in COPD (63). Peripheral muscle dysfunction in individuals with chronic respiratory disease may be attributable to single or combined effects of inactivity-induced deconditioning, systemic inflammation, oxidative stress, smoking, blood gas disturbances, nutritional impairment, low anabolic hormone levels, aging, and corticosteroid use (61, 63–70). Skeletal muscle dysfunction is frequently reported as fatigue; in many individuals this is the main limiting symptom, particularly during cycle-based exercise (71, 72). This could be related to the fact that the peripheral muscle alterations as described previously (63) render these muscles susceptible to contractile fatigue (73, 74).

The lactic acidosis resulting from exercising skeletal muscles at higher intensities is a contributory factor to exercise termination in healthy individuals, and may also contribute to exercise limitation in patient with COPD (75, 76). Patients with COPD often have increased lactic acid production for a given exercise work rate (57, 71), thereby increasing their ventilatory requirement (57). The increased ventilatory requirement imposes an additional burden on the respiratory muscles, which are already facing increased impedance to breathing. This rise in lactic acid is exacerbated by a tendency to retain carbon dioxide during exercise, further increasing acidosis and resultant ventilatory burden. Improving skeletal muscle function is therefore an important goal of exercise training programs.

Limitations due to respiratory muscle dysfunction. The diaphragm of individuals with COPD adapts to chronic overload and has greater resistance to fatigue (77, 78). As a result, at identical absolute lung volumes, the inspiratory muscles are capable of generating more pressure than those of healthy control subjects (79–81). However, patients with COPD often have static and dynamic hyperinflation, which places their respiratory muscles at a mechanical disadvantage. Thus, despite adaptations in the diaphragm, both functional inspiratory muscle strength (82) and inspiratory muscle endurance (83) are compromised in COPD. As a consequence, respiratory muscle weakness, as assessed by measuring maximal respiratory pressures, is often present (82–86). This contributes to hypercapnia

(87), dyspnea (88, 89), nocturnal oxygen desaturation, and reduced exercise performance (71, 90).

Exercise Training Principles

The general principles of exercise training in individuals with chronic respiratory disease are no different from those for healthy individuals or even athletes. For physical training to be effective the total training load must reflect the individual's specific requirements, it must exceed loads encountered during daily life to improve aerobic capacity and muscle strength (i.e., the training threshold), and must progress as improvement occurs. Various modes of training will be required for improvements in cardiorespiratory endurance, strength, and/or flexibility. The text below provides details on endurance training, interval training, resistance training, neuromuscular electrical stimulation, and respiratory muscle training.

Endurance Training

Since the previous Statement new science has been reported on the endurance training component of pulmonary rehabilitation, especially in the area of its widened scope. However, the aims of the intervention and the principles of the exercise prescription have not changed substantially. The aims are to condition the muscles of ambulation and improve cardiorespiratory fitness to allow an increase in physical activity that is associated with a reduction in breathlessness and fatigue. Higher intensity endurance exercise training is commonly used by pulmonary rehabilitation programs (91). However, for some individuals, it may be difficult to achieve the target intensity or training time, even with close supervision (60). In this situation, low-intensity endurance training or interval training are alternatives (92, 93). Recently, the number of steps per day has been suggested as an alternative yet tangible target of exercise training (94); this may emerge as an important concept in pulmonary rehabilitation (95).

Endurance exercise training in the form of cycling or walking exercise is the most commonly applied exercise modality in pulmonary rehabilitation (23, 59, 60). The framework recommended by the American College of Sports Medicine (*ACSM's Guidelines for Exercise Testing and Prescription* on Frequency, Intensity, Time, and Type [FITT]) can be applied in pulmonary rehabilitation (96). Endurance exercise training in individuals with chronic respiratory disease is prescribed at the same frequency: three to five times per week. A high level of intensity of continuous exercise (>60% maximal work rate) for 20 to 60 minutes per session maximizes physiologic benefits (i.e., exercise tolerance, muscle function, and bioenergetics) (96). A Borg dyspnea or fatigue score of 4 to 6 (moderate to [very] severe) or Rating of Perceived Exertion of 12 to 14 (somewhat hard) is often considered a target training intensity (97).

Walking (either ground-based or on a treadmill) and biking (using a stationary cycle ergometer) are optimal exercise modalities if tolerated by the individual. Walking training has the advantage of being a functional exercise that can readily translate to improvement in walking capacity. If the primary goal is to increase walking endurance, then walking is the training modality of choice (98) in this situation. Biking exercise places a greater specific load on the quadriceps muscles than walking (9) and results in less exercise-induced oxygen desaturation (99).

Since the previous Statement, there has been an increased awareness of the efficacy of leisure walking as a mode of exercise training in COPD. This is highlighted by a randomized controlled trial of a 3-month outdoor Nordic walking exercise program (1 h of walking at 75% of initial maximal heart rate three times per week) versus control (no exercise) in 60 elderly individuals with moderate to severe COPD (100). After 3 months of training, those in the Nordic walking group spent more time walking and standing, had an increased intensity of walking, and increased their 6-minute walk distance compared with the control group. These improvements were sustained at 6 and 9 months after the initial 3-month intervention. This result was reinforced by a randomized study of 36 individuals with COPD that compared walking with outdoor cycle training on walking outcome, the endurance shuttle walk time (98). Both groups trained indoors for 30 to 45 minutes per session, three times weekly over 8 weeks. The walk training group increased their endurance shuttle walk time significantly more than did the cycle training group, providing evidence for ground walking as a preferred mode of exercise training to improve walking endurance.

Interval Training

Interval training may be an alternative to standard endurance training for individuals with chronic respiratory disease who have difficulty in achieving their target intensity or duration of continuous exercise because of dyspnea, fatigue, or other symptoms (60, 101). Interval training is a modification of endurance training in which high-intensity exercise is regularly interspersed with periods of rest or lower intensity exercise. This may result in significantly lower symptom scores (93) despite high absolute training loads, thus maintaining the training effects of endurance training (93, 102, 103), even in cachectic individuals with severe COPD (104). The practical difficulty of interval training is its mode of delivery, which typically requires a cycle-based program and continuing the regimen in unsupervised settings.

Since the previous Statement there has been considerable research interest in interval training in COPD, with the publication of several randomized, controlled trials (102, 105–110) and systematic reviews (111, 112). Overall, these studies have found no clinically important differences between interval and continuous training modes in outcomes including exercise capacity, health-related quality of life, and skeletal muscle adaptation immediately after training. Longer term effects of or adherence to interval training have not been investigated.

To date, most studies in COPD have matched the total work performed by continuous training and interval training groups, and found similar training adaptations (93, 109, 113). Whether it might be possible to achieve greater total work using interval training, and therefore achieve even larger training adaptations, remains currently unknown. In contrast, for individuals with chronic heart failure a high-intensity interval training program was superior to moderate-intensity continuous training at matched work for both exercise capacity and quality of life (114). The reason for this difference in outcomes between patient populations is unclear. However, the high prevalence of chronic heart failure in individuals undergoing pulmonary rehabilitation suggests that high-intensity interval training may have a useful role for individuals with comorbid disease.

The efficacy of interval training versus endurance training in decreasing dyspnea during the exercise training is unclear. Evidence available at the time of the previous Statement suggested that in COPD, interval training resulted in lower symptom scores while allowing for higher training intensities (93, 109). Subsequent studies have found no difference in symptoms between continuous and interval training (105, 106); however, these studies have used slightly longer training intervals (1 min or more, compared with 30 s in previous studies). It is possible that during high-intensity interval training, shorter intervals (<1 min) are required to achieve lower symptom scores (111). Indeed, the metabolic response during interval training seems comparable to the metabolic load during simple, self-paced domestic activities of daily life (115).

There is no evidence regarding the role of interval training for individuals with respiratory conditions other than COPD. Extrapolating from COPD studies, when continuous training is curtailed by severe dyspnea or oxyhemoglobin desaturation (as in interstitial lung disease), interval training may be a reasonable strategy to increase exercise intensity and training adaptations.

In summary, interval training and continuous training appear to be equally effective in COPD. Interval training may be a useful alternative to continuous training, especially in symptom-limited individuals who are unable to tolerate high-intensity continuous training. Further research is necessary regarding its applications in chronic respiratory diseases other than COPD.

Resistance/Strength Training

Resistance (or strength) training is an exercise modality in which local muscle groups are trained by repetitive lifting of relatively heavy loads (116–118). Resistance training is considered important for adults to promote healthy aging (119) and also appears to be indicated in individuals with chronic respiratory disease (21, 120), such as those with COPD, who have reduced muscle mass and strength of their peripheral muscles, relative to healthy control subjects (65, 121). These systemic manifestations of COPD are related to survival, health care use, and exercise capacity (61, 122–125). Further, as falling appears to be common among people with COPD (126, 127), and muscle weakness is an important risk factor for falls in the older population (128), optimizing muscle strength is likely to be an important goal of rehabilitation in this population. In addition to the expected effects on muscle strength, it is possible that resistance training may also assist with maintaining or improving bone mineral density (129), which has been shown to be abnormal low (e.g., osteoporosis or osteopenia) in about 50% of individuals with COPD (130, 131).

Of note, endurance training, which is the mainstay of exercise training in pulmonary rehabilitation programs, confers suboptimal increases in muscle mass or strength compared with programs that include specific resistance exercise (15, 132, 133). Resistance training has greater potential to improve muscle mass and strength than endurance training (21, 120, 132, 134–136), two aspects of muscle function that are only modestly improved by endurance exercises (23). Moreover, strength training results in less dyspnea during the exercise period, thereby making this strategy easier to tolerate than endurance constant-load training (101).

The optimal resistance training prescription for patients with chronic respiratory disease is not determined, as evidenced by the wide variation in its application among clinical trials (117). The American College of Sports Medicine recommends that, to enhance muscle strength in adults, 1 to 3 sets of 8 to 12 repetitions should be undertaken on 2 to 3 days each week (116). Initial loads equivalent to either 60 to 70% of the one repetition maximum (i.e., the maximal load that can be moved only once over the full range of motion without compensatory movements [137]) or one that evokes fatigue after 8 to 12 repetitions are appropriate. The exercise dosage must increase over time (the so-called *overload*) to facilitate improvements in muscular strength and endurance. This increase occurs when an individual can perform the current workload for 1 or 2 repetitions over the desired number of 6 to 12, on 2 consecutive training sessions (116). Overload can be achieved by modulating several prescriptive variables: increasing the resistance or weight, increasing the repetitions per set, increasing the number of sets per exercise, and/or decreasing the rest period between sets or exercises (116, 118). Because the optimal resistance training approach for patients with chronic respiratory disease is not known, clinicians often follow these recommendations. Alternative models for progression in training intensity, such as daily undulating periodized resistance training (e.g., making alterations in training volume and intensity on a daily basis [138]) may be advantageous (139), but data are lacking.

Clinical trials in COPD have compared resistance training with no training and with endurance training. Lower limb resistance training consistently confers gains in muscle force and mass compared with no exercise training (136, 140–143). The effects on other outcomes are less consistent. It appears that the capacity for increased lower limb muscle force to translate into increased maximal or submaximal exercise capacity is dependent, at least in part, on the magnitude of the training load. Studies that have used loads equal to or exceeding 80% of one repetition maximum throughout the training program have reported improvements in submaximal exercise capacity (21, 120) and peak power measured via cycle ergometry (142) as well as peak walk speed measured over a 30-m track (140). Similar findings have been reported in individuals with chronic heart failure (144). In some (120, 136), but not all studies (141), training loads between 50 and 80% of one repetition maximum were sufficient to improve endurance exercise capacity. Training programs that appear to have used more modest loads are ineffective at conferring gains in exercise capacity (143).

When added to a program of endurance constant-load exercise, resistance training confers additional benefits in muscle force, but not in overall exercise capacity or health status (15, 117, 132, 133). However, gains in quadriceps muscle strength may optimize performance of tasks that specifically load these muscles, such as stair-climbing and sit-to-stand (145). Resistance training for the muscles of the upper limbs has been demonstrated to increase the strength of the upper limb muscles and translate this into improvements in related tasks, such as the 6-minute peg board and ring test (146, 147).

Resistance exercise elicits a reduced cardiorespiratory response compared with endurance exercise (101). That is, resistance exercise demands a lower level of oxygen consumption and minute ventilation, and evokes less dyspnea (101). In the clinical setting, this makes resistance exercise an attractive and feasible option for individuals with advanced lung disease or comorbidities who may be unable to complete high-intensity endurance or interval training because of intolerable dyspnea (60, 101). It may also be an option for training during disease exacerbations (148).

In summary, the combination of constant-load/interval and strength training improves outcome (i.e., exercise capacity and muscle strength [15]) to a greater degree than either strategy alone in individuals with chronic respiratory disease, without unduly increasing training time (132).

Upper Limb Training

Many problematic activities of daily living in individuals with chronic respiratory disease involve the upper extremities, including dressing, bathing, shopping, and many household tasks (149). Because of this, upper limb training is typically integrated into an exercise regimen. Examples of upper extremity exercises include aerobic regimens (e.g., arm cycle ergometer training) and resistance training (e.g., training with free weights and elastic bands, which provide resistance). Typical muscles targeted are the biceps, triceps, deltoids, latissimus dorsi, and the pectorals.

Complementing a previous review (134), a systematic review of upper limb training in COPD published since the previous Statement demonstrates that upper limb resistance training improves upper limb strength (150). This review included all forms of upper limb training, categorizing the trials as offering supported (cycle ergometry) and unsupported (including free weights/lifting a dowel/throwing a ball) exercise programs. The outcome measures across the trials were diverse, making firm conclusions challenging. However, the analysis indicated that improvements in upper limb performance were equivocal. Furthermore, it was difficult to determine whether upper limb training led to additional benefit in health-related quality of life or dyspnea associated with activities of daily living.

Since the above review two trials of unsupported resistance training (146, 147) have been published. The first was (146) a 3-week inpatient trial that compared unsupported upper extremity training plus pulmonary rehabilitation with pulmonary rehabilitation alone. The between-group comparison identified significant gains in the upper limb training group in the 6-minute ring test, an upper limb activities test. Perhaps unsurprisingly, there was no additional benefit detected in the 6-minute walk test (6MWT). The second trial (147) compared upper extremity resistance training with a sham intervention; both groups participated in an endurance and strength-based lower limb exercise training regimen. Compared with the control group, the intervention group had improvements in upper limb performance but there was no change in health-related quality of life or dyspnea during activities of daily living. Taken together, the evidence suggests that upper extremity training increases upper limb function in patients with COPD. However, the optimal approach to training remains to be determined. Furthermore, it is not clear whether and to what extent specific gains in upper limb function translate into improvements in broader outcomes such as health-related quality of life.

Flexibility Training

Although flexibility training is a component of many exercise regimens and is commonly provided in pulmonary rehabilitation, there are, to date, no clinical trials demonstrating its effectiveness in this particular setting. Improved thoracic mobility and posture may increase the vital capacity in patients with chronic respiratory disease (151). Because respiration and posture have a coupled relationship, a thorough evaluation includes both the assessment and treatment of patients with chronic respiratory disease (152). Common postural impairments include thoracic kyphosis, increased chest anterior–posterior diameter, shoulder elevation and protraction, and trunk flexion (152–154). Postural abnormalities are associated with a decline in pulmonary function, decreased quality of life, poor bone mineral density, and increased work of breathing (155, 156). Postural deviations are known to alter body mechanics, resulting in back pain, which in turn alters breathing mechanics (155). One approach in pulmonary rehabilitation is to have patients perform both upper and lower body flexibility exercises (including stretching of major muscle groups such as the calves, hamstrings, quadriceps, and biceps, as well as range of motion exercises for the neck, shoulders, and trunk) at least 2–3 days/week (153).

Neuromuscular Electrical Stimulation

Transcutaneous neuromuscular electrical stimulation (NMES) of skeletal muscle is an alternative rehabilitation technique wherein muscle contraction is elicited, and selected muscles can thereby be trained, without the requirement for conventional exercise. Electrical stimulation of the muscle is delivered according to a specific protocol in which the intensity (amplitude), frequency, duration, and wave form of the stimulus are chosen to achieve the desired muscle response (157–159). The electrical stimulus amplitude (intensity) determines the strength of muscle contraction.

Muscle contraction induced by electrical stimulation does not lead to dyspnea, poses minimal cardiocirculatory demand (158, 160–165), and bypasses the cognitive, motivational, and psychological aspects involved in conventional exercise that may hinder or prevent effective exercise training (166). As such, it is suited for deconditioned individuals with severe ventilatory and/or cardiac limitation, including those hospitalized with acute disease exacerbations or respiratory failure. Small, relatively inexpensive, portable electrical stimulators are also suitable for home use, and therefore may benefit persons who are too disabled to leave their homes, require home mechanical ventilation, or who lack access to traditional pulmonary rehabilitation programs (167).

NMES improves limb muscle strength, exercise capacity, and reduces dyspnea of stable outpatients with severe COPD and poor baseline exercise tolerance (159, 162, 167), and NMES can be continued during acute COPD exacerbations (167, 168). In a randomized, sham-controlled trial, transcutaneous nerve stimulation applied over traditional acupuncture points led to within- and between-group increases in multiple outcome variables, including FEV_1; 6-minute walk distance; quality of life, as measured by the St. George's Respiratory Questionnaire (SGRQ); and β-endorphin levels (169). In another study, individuals with COPD with low body mass index, severe airflow limitation, and severe deconditioning who had been released from hospitalization for exacerbations achieved greater improvements in leg muscle strength and dyspnea during activities of daily life after a 4-week treatment with NMES plus active limb mobilization and slow walking as compared with the same mobilization regimen without NMES (170). NMES added to active limb mobilization also augments gains in mobility among bed-bound individuals with chronic hypercapnic respiratory failure due to COPD who are receiving mechanical ventilation (171). It also preserves muscle mass (172) and helps prevent critical illness neuromyopathy among critically ill individuals in the intensive care unit (173). The mechanisms by which NMES improves muscle function and exercise capacity or performance are incompletely understood. The pattern of muscle fiber activation during NMES may differ from that which occurs during conventional exercise (174–176). The precise electrical stimulation protocol chosen may also impact the rehabilitation outcomes of NMES. Specifically, the frequency of stimulus delivered likely determines the types of muscle fibers activated (177). A NMES stimulus frequency up to 10 Hz likely preferentially activates slow-twitch fibers and may selectively improve resistance to fatigue (178), whereas a frequency greater than 30 Hz may activate both types of fibers, or may selectively recruit fast-twitch fibers and enhance power (179). Studies conducted to date in individuals with COPD who have demonstrated gains in both muscle strength and endurance have used stimulus frequencies ranging from 35 to 50 Hz (158, 162, 167, 171). Effects of low-frequency NMES have not been studied in individuals with COPD (159). Some investigators advocate delivery of a combination of stimulus frequencies during NMES training to most closely mimic normal motor neuron firing patterns and have maximal impact on muscle function (180, 181). The duration of benefits in muscle function after a limited period (e.g., several weeks) of NMES muscle training has not, to date, been studied in individuals with chronic respiratory disease. There are no formal patient candidacy guidelines for NMES.

Contraindications to NMES are primarily based on expert opinion. Most care providers do not perform NMES on individuals with implanted electrical devices such as pacemakers or implanted defibrillators; or persons with seizure disorder, uncontrolled cardiac arrhythmias (particularly ventricular), unstable angina, recent myocardial infarction, intracranial clips, and/or total knee or hip replacement (160, 161, 163). Individuals with severe osteoarthritis of the joints to be mobilized by the muscles to be stimulated, or persons with severe peripheral edema or other skin problems wherein desired placement of electrodes would be limited, may also be poor candidates for NMES.

NMES is safe and generally well tolerated. The adverse effect reported most commonly is mild muscle soreness that usually resolves after the first few NMES sessions (177), and that in part relates to the stimulus amplitude and frequency chosen. Pulse amplitudes greater than 100 mA may lead to intolerable muscle discomfort. Some individuals are unable to tolerate NMES even at lower stimulus amplitudes and gains in exercise tolerance may depend on the patient's ability to tolerate incremental training stimulus intensities (182). At the start of NMES training, stimulus amplitudes that lead to nonpainful muscle contraction are applied, and incremental gains in the stimulus amplitude are made over the course of the training program, according to patient tolerance.

Taken together, evidence suggests that is a promising training modality within pulmonary rehabilitation, particularly for severely disabled patients with COPD. It remains unclear whether NMES is effective for individuals with COPD with a higher degree of baseline exercise tolerance (183). Moreover, the impact of NMES in clinically stable individuals with chronic respiratory conditions other than COPD has not been evaluated.

Inspiratory Muscle Training

The pressure-generating capacity of the inspiratory pump muscles is reduced in individuals with COPD (121). This is primarily due to the deleterious effects of pulmonary hyperinflation, which serves to shorten and flatten the diaphragm, placing it at a mechanical disadvantage (79). The reduced pressure-generating capacity of the inspiratory muscles contributes to both exercise intolerance and the perception of dyspnea in individuals with COPD (61, 89). Endurance exercise training, despite conferring large gains in exercise capacity and reducing dyspnea, does not appear to improve the pressure-generating capacity of the inspiratory muscles (21, 184, 185), likely because the ventilatory load during whole-body exercise is of insufficient magnitude to confer a training adaptation. For this reason, there has been interest in applying a specific training load to the inspiratory muscles in individuals with weakened inspiratory muscles, in an effort to increase exercise capacity and reduce dyspnea.

The most common approach to inspiratory muscle training (IMT) uses devices that impose a resistive or a threshold load. The properties of these devices have been described elsewhere (186, 187). In individuals with COPD, IMT performed with loads equal to or exceeding 30% of an individual's maximal inspiratory pressure [PI_{max}]) confers gains in inspiratory muscle strength and endurance (188, 189). Studies of IMT in individuals with COPD have investigated the effects of IMT in isolation and of IMT added to whole-body exercise training.

Meta-analyses of IMT, compared with sham IMT or no intervention, in individuals with COPD demonstrate significant improvements in inspiratory muscle strength and inspiratory muscle endurance (188, 189). In addition, significant and clinically meaningful reductions in dyspnea during activities of daily living and increases in peak inspiratory flow were observed (188). Improvements have been demonstrated in walk distance, but not peak power achieved during cycle ergometry testing (188). Small gains, which may not be clinically important, have been shown in health-related quality of life (188, 189).

IMT given as an adjunct to whole-body exercise training has an additional benefit on inspiratory muscle strength and endurance, but not on dyspnea or maximal exercise capacity (188–190). Because whole-body exercise training confers substantial improvements in exercise capacity, dyspnea, and health-related quality of life (91) it seems that detecting further improvement using IMT is difficult.

It is possible that IMT as an adjunct to whole-body exercise training may benefit those individuals with COPD with marked inspiratory muscle weakness. Indeed, the added effect of IMT on functional exercise capacity just failed to reach statistical significance in those individuals with COPD and inspiratory muscle weakness (189, 191). This finding, however, needs to be confirmed prospectively.

Although the nature of IMT programs differs considerably among studies, the use of an interval-based program with loaded breathing, interspersed with periods of rest, has been shown to optimize the training loads that can be tolerated as well as the rate of change in PI_{max} (192). Gains in inspiratory muscle function are lost 12 months after cessation of the IMT program (193).

In summary, current evidence indicates that IMT used in isolation does confer benefits across several outcome areas. However, its added benefit as an adjunct to exercise training in COPD is questionable. It is conceivable that IMT might be useful when added to whole-body exercise training in individuals with marked inspiratory muscle weakness or those unable to participate in cycling or walking because of comorbid conditions, but this idea needs to be evaluated prospectively.

Maximizing the Effects of Exercise Training

Relatively few clinical trials have evaluated the potential role of adjuncts designed to enhance the positive effects of exercise training in patients with chronic respiratory disease. The following outlines some of the research in this area.

Pharmacotherapy. BRONCHODILATORS. In individuals with chronic airflow limitation, pharmacologic therapy is one of the key components of disease management, used to prevent and control symptoms, reduce exacerbations, and improve exercise tolerance and health status (194). Inhaled bronchodilators primarily act on airway smooth muscle, and not only improve expiratory flow in individuals with airflow limitation but also reduce resting (195) and dynamic hyperinflation (196). Both short-acting (197) as well as long-acting bronchodilators (196) increase exercise capacity in COPD. Bronchodilator therapy may be especially effective in enhancing exercise performance in individuals with a ventilatory exercise limitation (74). With optimal bronchodilation, the primary locus of exercise limitation may change from dyspnea to leg fatigue, thereby allowing individuals to exercise their peripheral muscles to a greater degree. This illustrates the potential synergy between pharmacologic and nonpharmacologic treatments.

Optimizing the use of maintenance bronchodilator therapy within the context of a pulmonary rehabilitation program for COPD results in augmentation of exercise tolerance benefits (198, 199), possibly by allowing individuals to exercise at higher intensities. Therefore, optimization of bronchodilator therapy before exercise training in patients with airflow limitation is generally routine in pulmonary rehabilitation. Although inhaled corticosteroids are indicated for individuals with severe COPD and recurrent exacerbations (200), no effects on exercise capacity have been shown (201).

ANABOLIC HORMONAL SUPPLEMENTATION. Exercise training programs that are part of pulmonary rehabilitation have been shown to induce morphologic and biochemical changes in the exercising muscles that enhance exercise tolerance (202). In recent years, research interest has been given to pharmacologic supplements that enhance these effects. In concept, agents can been targeted either at enhancing muscle strength (inducing muscle fiber hypertrophy) or endurance (increasing capillary density, mitochondrial number, aerobic enzyme concentration), thereby enhancing the effects of, respectively, strength training or endurance training. To date, no anabolic supplement has received sufficient study to be considered for routine inclusion in pulmonary rehabilitation programs.

Anabolic steroids (testosterone and its analogs) increase muscle mass and decrease fat mass. In healthy younger and older men, testosterone increases muscle mass and strength in a dose-dependent fashion (203). In men, side effects also increase in a dose-dependent fashion; these include an increase in hemoglobin, a decrease in high-density cholesterol, and (most worrisome) the potential for increasing the growth rate of prostate cancer foci (204). Therefore, raising the circulating testosterone level much above the levels seen in healthy young men seems unwise. Anabolic steroids have been administered to women (205), but identifying an anabolic steroid dose that yields muscle hypertrophy without yielding virilization has proven difficult (206). Selective androgen receptor modulators have the potential to yield anabolic effects similar to testosterone and its analogs without prostate stimulation (in men) or virilization (in women) (207); large-scale trials have yet to be reported.

Low testosterone levels are common in men with COPD (67). Studies in which testosterone analogs have been administered have generally demonstrated increases in muscle mass, but have failed to yield consistent evidence of muscle strength improvement (208–210). In a 10-week study involving 47 men with COPD and low circulating testosterone levels, the effects of intramuscular injections of testosterone enanthate (100 mg weekly) were compared with a three-times-weekly strength training program (141). Subjects were divided into four groups: (*1*) neither intervention; (*2*) testosterone alone; (*3*) strength training alone; or (*4*) both testosterone and strength training. In the two groups receiving single interventions, both lean body mass (measured by dual-energy X-ray absorptiometry scan) and leg muscle strength (measured by one-repetition maximum of leg press) increased. Improvements in the group receiving the combined intervention were approximately additive. No adverse effects were detected in this short-term study. Quadriceps muscle biopsy analysis showed that both interventions had significant anabolic effects (211).

Growth hormone is a peptide hormone secreted by the pituitary; it exerts an anabolic effect on skeletal muscle principally through stimulation of hepatic production of insulin-like growth factor-1 (212). Studies in healthy subjects have often demonstrated increases in muscle mass, but seldom have yielded strength increases. Two small studies in individuals with COPD have similarly shown lean mass increases without evidence of peripheral muscle endurance or strength improvement (213, 214). Ghrelin is a peptide secreted by the stomach that stimulates growth hormone secretion and may have other effects, including appetite stimulation. Only one study has been reported investigating the impact of ghrelin on cachexia in individuals with COPD (215).

Other anabolic drugs have had limited investigation. Megestrol acetate has been shown to increase appetite and body weight in underweight individuals with COPD (216). However, the drug is anabolic to fat but not muscle, likely because circulating testosterone levels are suppressed.

Oxygen and helium–hyperoxic gas mixtures. For safety reasons, individuals who are receiving long-term oxygen therapy have this continued during exercise training, but flow rates may need to be increased to maintain adequate oxygenation. Oxygen supplementation increases exercise tolerance and reduces breathlessness in individuals with COPD in the laboratory setting (46), even in those with mild hypoxemia or exercise oxygen desaturation (47).

Studies testing the efficacy of oxygen supplementation as an adjunct to exercise training have had inconsistent results. In nonhypoxemic individuals with moderate to severe COPD without exercise-induced oxygen desaturation, oxygen supplementation (compared with compressed air) allowed for higher training intensities and resulted in enhanced cycle-based endurance capacity (46). In contrast, in individuals with severe COPD and exercise-induced oxygen desaturation, training with supplemental oxygen did not influence exercise tolerance or health status when compared with training on room air, although there was a small difference in dyspnea (217). Although methodological differences may help explain these differences in results (37), the evidence to date does not appear to provide unequivocal support for the widespread use of oxygen supplementation during exercise training for all individuals with COPD (205), apart from those already receiving long-term oxygen therapy. Individualized oxygen titration trials may identify individuals with COPD who respond to oxygen supplementation during exercise testing (218).

Since the previous Statement, a single-blind, randomized controlled trial compared ambulatory oxygen (vs. supplemental air) as an adjunct to pulmonary rehabilitation in patients with COPD who were nonhypoxemic at rest but who had exercise-induced oxygen desaturation. Only those individuals who at baseline assessment improved exercise endurance with supplemental oxygen were included in the study. The use of ambulatory oxygen in this select group greatly improved endurance walking distance (219). Unfortunately, the outcome assessment was done on the gas to which they were randomized, whereas baseline assessment was on room air, which means it is impossible to tell whether this is an acute gas effect or a training effect.

Studies testing the potential benefits of helium–hyperoxic gas (HH) mixtures as adjuncts to exercise training in COPD have also had varied results. In a crossover study, individuals with COPD inhaling the less dense, 70 to 30% helium–oxygen mixture had greater functional exercise capacity compared with when they breathed room air or supplemental oxygen alone (220). However, in normoxemic individuals with moderate to severe COPD, 2 months of pulmonary rehabilitation with HH did not improve exercise capacity when compared with training breathing oxygen alone or breathing room air (221). In another study HH during pulmonary rehabilitation allowed for increased intensity and duration of exercise performed by nonhypoxemic individuals with COPD. Indeed, HH resulted in greater improvements in constant-load exercise time and health status than those observed with air (222). The practical application of HH as an adjunct in pulmonary rehabilitation exercise training, in particular the potential benefits versus costs, remains to be established.

Noninvasive ventilation. During exercise in people with COPD, expiratory flow limitation and increased respiratory frequency may provide insufficient time for lung emptying during expiration. This results in an increase in end-expiratory lung volume, known as dynamic hyperinflation, where breathing takes place at lung volumes closer to total lung capacity (41). Dynamic hyperinflation increases the intrinsic positive end-expiratory pressure and increases the elastic work of breathing. This is associated with high levels of dyspnea and termination of exercise at low workloads (41, 223, 224). Noninvasive positive pressure ventilation (NPPV) unloads the respiratory muscles and reduces work of breathing during exercise in COPD (225, 226). NPPV is associated with acute reductions in dyspnea (227), improved gas exchange (228), increased minute ventilation (226), and longer exercise duration (227). As a result, NPPV may be useful as an adjunctive therapy to pulmonary rehabilitation.

NPPV has been tested as an adjunct to exercise training. Since the previous Statement, a systematic review evaluating the effects of noninvasive positive pressure ventilation (NPPV) in individuals with COPD, provided as an adjunct to pulmonary rehabilitation, has been published (229). This concluded that NPPV used as an adjunct to exercise-based pulmonary rehabilitation (either nocturnally or during a rehabilitation program) appears to augment the effects of an exercise program, probably by allowing increased work load to be performed by resting or unloading the respiratory muscles. The benefit appears to be most marked in individuals with severe COPD, and higher positive pressures (as tolerated) may lead to greater improvements. Moreover, the addition of NPPV during sleep in combination with pulmonary rehabilitation in severe COPD results in improved exercise tolerance and quality of life, presumably due to resting the respiratory muscles at night (230–232).

Because NPPV is a difficult and labor-intensive intervention, it may be practically feasible only in hospitals or other therapy units that have significant experience in its use, and only in those individuals who have demonstrated benefit from this therapy. The latter are more likely those with severely impaired lung function (229). It may also be possible to use NPPV in hospitalized individuals to improve tolerance of exercise early during recovery from an acute exacerbation (233), with a goal of providing inspiratory pressures of greater than 10 cm H_2O, subject to the tolerance of the patient. Further research is required evaluating the cost-effectiveness and patient perception of NPPV as an adjunctive rehabilitation technique.

Breathing strategies. As stated earlier, individuals with COPD may have dynamic hyperinflation (234, 235), which limits their exercise capacity. Because breathing retraining focuses on slowing the respiratory rate, primarily through prolonged expiration, it may be beneficial in reducing dyspnea via reducing exercise-induced dynamic hyperinflation (234). Adaptive breathing strategies have been employed using yoga breathing (236), pursed-lips breathing (235), and computer-aided breathing feedback (236). Studies have shown that individuals who undergo breathing training are able to adopt a slower, deeper pattern of breathing (234–236). Pursed-lips breathing was successful in reducing dyspnea after a 6-minute walk (235), and computer-aided breathing feedback was successful in reducing dynamic hyperinflation (234). Studies employing these adaptive breathing strategies are small (n = 64 [234], 40 [235], and 11 [236]) and although expert opinion strongly supports their use, more evidence is needed to make definitive recommendations on their use in pulmonary rehabilitation (237).

Walking aids. The use of a rollator to assist with ambulation has been demonstrated to increase functional exercise capacity and reduce dyspnea on exertion in some individuals with COPD (238–240). Those most likely to benefit appear to be characterized by marked impairments in functional exercise capacity (i.e., a 6-min walk distance less than 300 or 400 m) (239, 240) and/or the need to rest during a 6-minute walk test due to intolerable dyspnea (239). The mechanism underlying the improvement appears to relate to fixation of the arms on the rollator, coupled with the forward lean position serving to increase the maximal voluntary ventilation and pressure-generating capacity of the respiratory muscles (240–242). Individuals who are deemed suitable for these devices by pulmonary rehabilitation staff report high levels of satisfaction with their use in a domiciliary environment (243). Moreover, a rollator is useful for carrying an oxygen cylinder by individuals who are receiving long-term oxygen therapy, it is easily transportable (e.g., folding, lightweight), and provides a readily available place to sit.

In addition to the rollator, other walking aids such as a modern draisine (a bicycle without pedals) may increase outdoor exercise performance (244). Moreover, during an acute exacerbation of COPD more supportive gait aids, such as gutter frames, may facilitate greater independence with activities of daily living (245). To date, it is unknown whether and to what extent using a rollator or other similar devices optimizes the response to exercise training or increases physical activity in daily life.

PULMONARY REHABILITATION IN CONDITIONS OTHER THAN COPD

Most individuals enrolled in pulmonary rehabilitation have COPD (4). However, individuals with chronic respiratory disorders other than COPD experience similar symptom burden and activity limitation, and some stand to benefit from the pulmonary rehabilitation intervention. Since the previous Statement there have been a number of randomized controlled trials and uncontrolled trials investigating the effects of pulmonary rehabilitation in people with chronic respiratory disorders other than COPD (Table 3). Whereas the previous Statement indicated that recommendations for individuals without COPD were based on pathophysiology and clinical judgment, there is now more robust evidence to support inclusion of some of these patient groups in pulmonary rehabilitation programs.

Interstitial Lung Disease

Exercise intolerance is a key feature of the interstitial lung diseases (ILDs), and is often associated with marked dyspnea on exertion. Poor exercise tolerance is associated with reduced quality of life (246) and poor survival (247). Exercise limitation in ILD is related to altered respiratory mechanics, impaired gas exchange, and circulatory limitation (248). Peripheral muscle dysfunction is also emerging as an important contributor to exercise limitation (249, 250). Exercised-induced hypoxia and pulmonary hypertension are common in the ILDs. It is likely that physical deconditioning plays a similar role in ILD as it does in other chronic respiratory diseases, with avoidance of activities that provoke dyspnea and fatigue and reduction in physical activity (251). Treatment with corticosteroids and immunosuppressants, as well as systemic inflammation, oxidative stress, nutritional impairments, physical inactivity, and aging, may also impact on peripheral muscle function in some individuals with ILD (250).

Emerging evidence suggests that pulmonary rehabilitation may result in meaningful short-term benefits in patients with ILD. Although the mechanisms of respiratory limitation in COPD and ILD differ, the similarities in clinical problems (exercise intolerance, muscle dysfunction, dyspnea, impaired quality of life) suggest that pulmonary rehabilitation may also benefit these patients. Two randomized, controlled trials have demonstrated short-term improvements in functional exercise tolerance, dyspnea, and quality of life after pulmonary rehabilitation in the ILDs (252, 253). However, the magnitude of these benefits was smaller than that generally seen in COPD (254, 255), and no ongoing effects were evident 6 months after training (252). This may reflect the challenges in providing pulmonary rehabilitation for conditions such as idiopathic pulmonary fibrosis (IPF) that can be rapidly progressive (256). Huppmann and colleagues included 402 individuals with ILD during an 11-year period and showed that pulmonary rehabilitation has a positive impact on functional status and quality of life (257).

TABLE 3. EXERCISE-BASED REHABILITATION IN PATIENTS WITH CHRONIC RESPIRATORY DISEASE OTHER THAN CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Population	Evidence for PR	Outcomes of PR	Special Considerations	Specific Assessment Tools
Interstitial lung disease	Two RCTs of exercise training (252, 253); one observational pulmonary rehabilitation study (257); one systematic review (255)	Improved 6-min walk distance, dyspnea, and quality of life. Magnitude of benefits smaller than that seen in COPD (254, 255). Benefits not maintained at 6 mo (254, 255).	Exercise-induced desaturation and pulmonary hypertension are common. Supplemental oxygen should be available and appropriate monitoring of oxyhemoglobin saturation during exercise is indicated.	An IPF-specific version of the St. George's Respiratory Questionnaire is available, with fewer items than the standard version (732)
Bronchiectasis	One RCT of exercise ± inspiratory muscle training (269); one large retrospective study of standard PR (270)	Improvement in incremental shuttle walk test distance and endurance exercise time. Benefits maintained after 3 mo only in group that did inspiratory muscle training in addition to whole-body exercise training (269). Benefits of equivalent magnitude to those seen in COPD (270).	Role of airway clearance techniques not yet established. Importance of inspiratory muscle training muscle training unclear—associated with better maintenance of benefit in RCT (269).	Consider measuring impact of cough, e.g., Leicester Cough Questionnaire (733)
Cystic fibrosis	Six RCTs of aerobic training (734–736), anaerobic training (736, 737), combined training (738), and partially supervised sports (739); one systematic review (261)	Improvements in exercise capacity, strength, and quality of life; slower rate of decline in lung function; effects not consistent across trials	Walking exercise decreases sputum mechanical impedance (263), indicating a potential role for exercise in maintaining bronchial hygiene. No specific recommendations regarding pulmonary rehabilitation are included in CF infection control guidelines (264); however, it is noted that people with CF should maintain a distance of at least 3 ft from all others with CF when in the outpatient clinic setting. Local infection control policies may preclude participation in group exercise programs.	CF-specific quality of life questionnaires are available—Cystic Fibrosis Quality of Life Questionnaire (740) and the Cystic Fibrosis Questionnaire (741)
Asthma	One systematic review (742); two RCTs of exercise training (280, 281)	Improved physical fitness, asthma symptoms, anxiety, depression, and quality of life (280, 281, 742)	Preexercise use of bronchodilators and gradual warm-up are indicated to minimize exercise-induced bronchospasm. Cardiopulmonary exercise testing may be used to evaluate for exercise-induced bronchospasm (282).	Consider measures of asthma symptoms and asthma-specific quality of life measures, e.g., Asthma Quality of Life Questionnaire (743)
Pulmonary hypertension	One RCT (296); two prospective case series (288, 295)	Improved exercise endurance, WHO functional class, quality of life, peak $\dot{V}O_2$ (288, 295, 296), increased peak workload (295), and increased peripheral muscle function (288)	Care must be taken to maintain $Sa_{O_2} > 88\%$ during exercise and supplemental O_2 should be available. BP and pulse should be monitored closely. Telemetry may be needed for patients with known arrhythmias. Avoid falls for patients receiving anticoagulant medication. Light or moderate aerobic, and light resistive training are recommended forms of exercise (5). High-intensity exercise, activities that involve Valsalva-like maneuvers or concurrent arm/leg exercises are generally not recommended. Close collaboration between PR providers and pulmonary hypertension specialists is needed to ensure safe exercise training. Exercise should be discontinued if the patient develops lightheadedness, chest pain, palpitations, or syncope.	Cambridge Pulmonary Hypertension Outcome Review (CAMPHOR) (744) WHO Functional Class (745) SF-36 (571) Assessment of Quality of Life instrument (AQoL) (746)

(Continued)

TABLE 3. (CONTINUED)

Population	Evidence for PR	Outcomes of PR	Special Considerations	Specific Assessment Tools
Lung cancer	Preoperative PR: Small, uncontrolled observational studies (311, 312)	Improved exercise tolerance (311, 312), possible change in status from noncandidate for surgical resection to operative candidate	Short duration e.g. 2-4 wk), up to 5 times per week, needed to avoid delay in potential curative surgery	Functional Assessment of Cancer Therapy-Lung Cancer (FACT-L) (747, 748)
	Postoperative PR: Small uncontrolled trials (308, 315, 316); two RCTs comparing aerobic training, resistive training or both in postsurgical lung cancer patients is ongoing (317, 318); one systematic review (307)	Increased walking endurance, increased peak exercise capacity, reduced dyspnea and fatigue (308, 315, 316). Variable impact on quality of life (307)		Trial Outcome Index (748, 749) Functional Assessment of Cancer Therapy Fatigue Scale (750, 751)
	Medical treatment: Case series of patients with nonresectable stage III or IV cancer (309)	Improved symptoms and maintenance of muscle strength (309)		
Lung volume reduction surgery	Prospective observational study (321); analysis of data from the National Emphysema Treatment Trial; a small case series (efficacy of home-based PR before LVRS) (320)	Pre-LVRS PR and exercise training: Improved exercise capacity (peak workload, peak $\dot{V}O_2$, walking endurance), muscle strength, dyspnea, and quality of life (320, 321)	Oxygen saturation should be monitored. Explanations of the surgical procedure, postoperative care including chest tubes, lung expansion, secretion clearance techniques and importance of early postoperative mobilization should be included in the educational component of PR.	Quality of Well Being Score (319, 752) Usual outcome assessments for COPD, such as CRQ (516) and SGRQ (515), are appropriate. Consider generic tools such as SF-36 (571) to allow comparison with population normative values postoperatively.
Lung transplantation	Pretransplant PR: One RCT comparing interval versus continuous training (323); small uncontrolled trials evaluate benefits of pretransplant PR, including Nordic walking (324, 753–755)	Pretransplant PR: Improved exercise tolerance and well-being (753–755)	Exercise prescription must be tailored to patients with severe end-stage lung disease and to specific considerations pertaining to the disease for which the transplant is being considered. Patients may require lower intensity or interval training. Hemodynamic parameters and oxygenation should be monitored closely; O_2 should be available. Educational component should cover surgical techniques, risks, benefits of the surgery, postoperative care (controlled cough, incentive spirometry, chest tubes, wound care, secretion clearance techniques, importance of early mobilization), risk and benefits of immunosuppressive agents.	SF-36 and other assessment tools appropriate for the individual disease state
	Post-transplant PR: Two RCTs; a few cohort studies; one systematic review assessed PR after lung transplantation (153, 327, 334, 756)	Post-transplant PR: Increased muscle strength, walking endurance, maximal exercise capacity, and quality of life (153, 327, 334, 756)		

Definition of abbreviations: BP = blood pressure; CF = cystic fibrosis; COPD = chronic obstructive pulmonary disease; CRQ = Chronic Respiratory Questionnaire; IPF = interstitial pulmonary fibrosis; LVRS = lung volume reduction surgery; PR = pulmonary rehabilitation; RCT = randomized controlled trial; Sa_{O_2} = oxygen saturation; SF-36 = Short Form-36; SGRQ = St. George's Respiratory Questionnaire; $\dot{V}O_2$ = aerobic capacity; WHO = World Health Organization.

The published international Statement on the management of IPF (258) makes a weak positive recommendation for pulmonary rehabilitation, stating that although the majority of individuals with IPF should be treated with pulmonary rehabilitation, it may not be reasonable in a minority.

Cystic Fibrosis

There have been no high-quality randomized controlled trials of pulmonary rehabilitation in cystic fibrosis (CF) since the previous Statement, possibly reflecting the established role of exercise training in general CF management. Participation in regular exercise across their life span is a critical part of the treatment regimen for people with CF (259). Higher levels of physical fitness have been associated with better survival in CF (260). A Cochrane review shows improvements in exercise capacity, strength, and quality of life after exercise training, with some evidence of a slower decline in lung function (261); however, these effects are not consistent across trials. Higher levels of exercise capacity and physical activity are associated with higher bone mineral density in people with CF (262), suggesting that exercise may have an important role in maintenance of bone health. Walking exercise decreases sputum mechanical impedance (263), indicating a potential role for exercise in maintaining bronchial hygiene, a crucial aspect of CF care.

No specific recommendations regarding pulmonary rehabilitation are included in CF infection control guidelines (264); however, people with CF are advised to maintain a distance of at least 3 feet from all others with CF when in the outpatient clinic setting, given the potential risk of cross-infection with antibiotic-resistant bacteria. Local infection control policies may preclude participation of people with CF in standard group-based pulmonary rehabilitation programs.

Bronchiectasis

Bronchiectasis, unrelated to cystic fibrosis, is also characterized by cough with purulent sputum, recurrent pulmonary infections, and dyspnea (265). People with bronchiectasis experience reduction in both exercise capacity and health-related quality of life (266). Reduction in exercise capacity has been associated with structural alterations to lung tissue, progressive airflow obstruction, dyspnea secondary to dynamic hyperinflation, and psychological morbidity (266–268). Pulmonary rehabilitation for people with bronchiectasis aims to improve exercise capacity, through effects on aerobic capacity and peripheral muscle, as well as to enhance disease management and improve quality of life.

One randomized controlled trial has shown improvements in exercise tolerance after pulmonary rehabilitation compared with a control group (269). A large retrospective study suggests that the magnitude and duration of benefit for exercise capacity and quality of life were similar to those observed in COPD (270). Interestingly, the benefits of pulmonary rehabilitation were better maintained at 3 months in a group that undertook inspiratory muscle training (IMT) in addition to whole-body exercise training (269); however, other data suggest that benefits may be well maintained in the absence of IMT (270). Further data regarding the role of IMT in bronchiectasis are required. Likewise, the role of airway clearance techniques as part of pulmonary rehabilitation for bronchiectasis requires further study. There may be an opportunity for individuals with bronchiectasis to learn airway clearance techniques during a pulmonary rehabilitation program.

Neuromuscular Disease

There are no clinical trials specifically evaluating the effectiveness of pulmonary rehabilitation in patients with neuromuscular disease. Indeed, because the neuromuscular diseases are such a heterogeneous group of conditions with varied symptoms and functional limitations, and often markedly differing prognoses (271, 272), evidence-based studies would be difficult to do. The current Task Force recognizes that individuals with neuromuscular disease are often referred to pulmonary rehabilitation for training with and adaptation to NIPPV equipment such as biphasic positive airway pressure, as well as assessment of the need for adaptive assistive equipment. Nevertheless, for detailed information on general rehabilitation in individuals with neuromuscular disease the Task Force refers to existing systematic reviews (271, 273) and a detailed narrative review (274) regarding the efficacy of exercise training across this diverse group of individuals.

Asthma

Asthma causes recurrent episodes of wheezing, dyspnea, chest tightness, and coughing (275). Some individuals with asthma may avoid physical activity because of dyspnea on exertion, or the fear of triggering symptoms. Adults with asthma have been reported to have lower levels of physical fitness than their peers; as well, their reduced capacity to undertake daily activities increased levels of psychological distress and reduced health-related quality of life (276–278). Importantly, regular physical activity has been shown to reduce the risk of asthma exacerbations in individuals with asthma (279).

Although it has long been the assumption that exercise training improves physical fitness in asthma, new data suggest that exercise training also has important effects on psychosocial outcomes and symptoms. Two randomized controlled trials have shown that exercise training improves asthma symptoms, anxiety, depression, and quality of life in people with moderate to severe, persistent asthma (280, 281). These data strengthen the rationale for inclusion of adults with persistent asthma in pulmonary rehabilitation programs. Preexercise use of bronchodilators and gradual warm-up are indicated to minimize exercise-induced bronchospasm. Cardiopulmonary exercise testing may be used to evaluate for exercise-induced bronchospasm (282).

Pulmonary Arterial Hypertension

Pulmonary arterial hypertension (PAH) is a group of severe disorders defined by progressive elevation of pulmonary vascular resistance in the small pulmonary arteries and arterioles that causes progressive dyspnea, severe activity limitation, and eventually death due to right heart failure (283). Previously, because of the absence of effective PAH treatment strategies, short life expectancy, and risk of sudden cardiac death with exercise, experts used to recommend significant limitations in physical activities, avoiding exercise including pulmonary rehabilitation (PR) programs (283). However, the advent of multiple-targeted medical therapies has significantly altered the prognosis of this disorder, allowing individuals to live longer with increased functional ability. Given the trend of improved prognosis and function, the role for exercise training in individuals with PAH has been revisited (284).

Individuals with PAH have an abnormal pulmonary vascular response to exercise, and severe muscle deconditioning is commonly present (285). Exercise capacity is also limited, in part, by impaired cardiac response to peripheral muscle demand, similar to that seen in individuals with COPD and chronic heart failure. The risks of cardiovascular complications during exercise are diminished with the current use of standard therapies because of the improvements in hemodynamics and exercise capacity. Concurrent morbidities, such as depression, anxiety, social isolation, and osteoporosis, are common in individuals with PAH (286, 287). Physical inactivity and skeletal muscle dysfunction have also been observed, with a higher degree of dysfunction if more severe PAH is present (285, 288–294).

The rationale for pulmonary rehabilitation, including exercise endurance training, would be to improve mobility, social interaction, exercise tolerance, and quality of life, as is demonstrated in other pulmonary diseases (5). The risk of sudden death with moderate exercise has been largely hypothetical. Multiple observations indicate that a regular, low-level exercise regimen may be both safe and beneficial for individuals with PAH. In addition, pulmonary rehabilitation programs can benefit individuals with PAH through multiple educational and comprehensive management strategies.

In individuals with optimized disease-targeted medical therapy, pulmonary rehabilitation may be of benefit (295). Limited published data in three recent studies suggest that pulmonary rehabilitation can improve exercise capacity and quality of life in individuals with severe PAH (288, 295, 296). The initial prescription is generally formulated on the basis of an exercise test such as cardiopulmonary exercise testing or 6-minute walk test along with evaluation of exertional symptoms. The optimal exercise training program remains currently unknown. Slow, incremental exercise protocols at low intensity and short duration are often used initially. On the basis of observed hemodynamic responses to exercise in this patient population, it would be prudent to avoid interval training because of the associated rapid changes in pulmonary hemodynamics and risk of syncope. On the basis of symptoms and heart rate/oxygenation response, the intensity and duration of exercise may be advanced as tolerated (284). However, the target level for exercise training is generally kept at a submaximal level. Although light-intensity resistance exercise may be included, this is generally performed only when the patient can comply with appropriate breathing patterns to avoid the Valsalva-type maneuver (118). Historically, clinicians may have advocated a practice of avoiding strengthening exercises performed with arms raised above the head or shoulders. There is no evidence base to support this practice and currently no restrictions for upper or lower extremity strengthening exercises in pulmonary rehabilitation in the framework of monitoring and managing clinical status. Range of motion exercises and flexibility training can also be performed safely by these individuals. Blood pressure, pulse rate, and oxygen saturation are monitored during exercise (284). Standards of care and suspension of exercise are implemented if the patient develops chest pain, lightheadedness, palpitations, hypotension, or syncope. One must also be cautious to avoid interruption of intravenous vasodilator therapy and to prevent falls for individuals taking anticoagulants.

Lung Cancer

Deconditioning, muscle weakness, fatigue, cachexia, and anxiety and concurrent COPD (297) frequently result in disability among individuals with lung cancer. Dyspnea and depressed mood also contribute to impaired quality of life (298). Physical inactivity may be an underlying cause (299, 300). Therefore, these processes can be improved after pulmonary rehabilitation (301, 302).

Exercise training improves strength, well-being, and health status among individuals with lung cancer who are undergoing chemotherapy (303–305) as well as exercise endurance, cycling work performance, fatigue, and quality of life of individuals with lung cancer who have undergone treatment (306–308). Individuals with stage IIIb and stage IV non–small cell lung cancer undergoing medical therapy and who are able to complete 8 weeks of rehabilitation achieve reduction in symptoms with maintenance of walking endurance and muscle strength (309); however, many are unable to complete the program. Multimodality chest physiotherapy with breathing exercises may also help to control symptoms (310).

Low exercise tolerance is associated with poor thoracic surgical outcomes and reduced survival among individuals with lung disease. Preoperative pulmonary rehabilitation can optimize individuals' exercise tolerance and overall medical stability before lung cancer resection surgery (311–314). Improvement in exercise performance may also render a patient initially considered inoperable to become a candidate for potentially curative surgery. The duration of preoperative rehabilitation for individuals with lung cancer must be dictated by medical necessity. A short duration (2–4 wk) of preoperative pulmonary rehabilitation is feasible, but its safety and benefits, especially *vis à vis* postoperative outcomes need confirmation in larger randomized controlled trials. Case series data suggest that it improves exercise capacity, but no changes in quality of life have been seen (307). Participation in exercise training sessions up to five times per week may be helpful to optimize gains in exercise capacity for individuals undergoing a short-duration preoperative exercise-based pulmonary rehabilitation program.

Uncontrolled trials have shown that pulmonary rehabilitation after lung cancer resection surgery improves walking endurance, increases peak exercise capacity, and reduces dyspnea and fatigue (308, 315, 316). Variable effects on quality of life have been reported (307). A randomized controlled trial has shown that an aerobic and strength training program commenced in the immediate postoperative period improves strength compared with a control group; however, there was no effect on 6-minute walk distance (6MWD) or quality of life (317). A randomized trial comparing the effect of aerobic training, resistive training, or a combination of the two on exercise capacity, symptoms, pulmonary function, and cardiac and muscle function in postsurgical lung cancer individuals is currently ongoing (318). Further work is needed to assess the impact of pre- and postoperative pulmonary rehabilitation on perioperative complications and survival.

Lung Volume Reduction Surgery

The National Emphysema Treatment Trial (NETT) (319), wherein 1,218 individuals underwent outpatient pulmonary rehabilitation before and after randomization to lung volume reduction surgery (LVRS) versus medical care, demonstrated that individuals with upper lobe–predominant emphysema and baseline low exercise capacity after preoperative pulmonary rehabilitation had gained a survival benefit at 24 months after LVRS. Individuals in the surgery group also had greater gains in exercise capacity, timed walking distance, quality of life, pulmonary function, and dyspnea.

Pulmonary rehabilitation administered before LVRS is safe and effective (320, 321). In the NETT study, pulmonary rehabilitation led to significant improvements in peak exercise workload (cycle ergometry), walking endurance (6-min walk test), dyspnea, and quality of life (321). Improvements in peak aerobic capacity and muscle strength can also result from pulmonary rehabilitation before LVRS (320). No increased incidence of adverse events has been reported in pulmonary rehabilitation for individuals with severe COPD preparing for LVRS as compared with persons with more moderate severity of disease. Pulmonary rehabilitation program content for individuals preparing for LVRS generally follows existing pulmonary rehabilitation guidelines for individuals with COPD. The educational component includes detailed explanations of the surgical procedure, chest tubes, lung expansion and secretion clearance techniques, and postoperative mobilization processes. After LVRS, pulmonary rehabilitation is helpful in reversing deconditioning, improving mobility and monitoring oxygenation and the need for medications, and may potentially reduce some of the postoperative complications. It is unclear whether preoperative improvement in exercise tolerance in pulmonary rehabilitation leads to greater benefits from LVRS, lower postoperative complication rate, or postoperative mortality benefit.

Lung Transplantation

Pulmonary rehabilitation plays an essential role in the management of individuals both before and after lung transplantation (322). Pretransplant pulmonary rehabilitation can help individuals to optimize and maintain their functional status before surgery and can provide the patient with a comprehensive knowledge base regarding the upcoming surgery and the postoperative medications, monitoring requirements, and potential complications. As impaired exercise capacity is an important predictor of thoracic surgery outcomes and survival (322), increased exercise tolerance achieved in pulmonary rehabilitation has the potential to improve surgical outcomes. The exercise training regimen used depends in part on the underlying disease for which the patient is undergoing transplantation. In general, individuals have severe exercise limitation and gas exchange disturbances, and may require low-intensity exercise or interval training. Hemodynamic parameters and oxygenation are monitored closely. Individuals continue the exercise achieved in pulmonary rehabilitation up to the time of surgery. Close partnering and communication between the patient, referring care provider, and pulmonary rehabilitation staff is crucial, to identify potential problems and to enable adaptation of the individual's medical therapy and/or exercise prescription if the patient's condition changes. The education component covers the risks and benefits of surgery, topics related to care in the postoperative period (controlled coughing, chest tubes, wound care, secretion clearance techniques, etc.), risks and benefits of immunosuppressive agents, and planning for the required follow-up visits and testing.

Gloeckl and colleagues studied the effect of interval training versus continuous training in lung transplant candidates with COPD (323). Interval training was associated with a lower dyspnea sensation during exercise and fewer unintended breaks, but achieved similar improvements in exercise capacity compared with continuous training. Preliminary results from Jastrzebski and colleagues suggest that Nordic walking is also safe, feasible, and effective in patients with end-stage lung disease referred for lung transplantation (324).

Exercise intolerance and functional disability often persist after lung transplantation despite restoration of normal (or near normal) lung function and gas exchange. Skeletal muscle dysfunction plays an important role in this exercise impairment (325–327). Indeed, muscle weakness present preoperatively can worsen in the early weeks after transplantation (327). Muscle weakness may be present up to 3 years after transplantation (328–331) and peak exercise capacity may be decreased to 40–60% of predicted up to 2 years after transplantation (332, 333). Immunosuppressive medications can worsen muscle function (333). It is possible that some elements of this muscle dysfunction may be amenable to exercise training in pulmonary rehabilitation.

Rehabilitation begun in the first 24–48 hours after surgery is focused on optimizing lung expansion and secretion clearance, as well as on breathing pattern efficiency, upper and lower extremity range of motion, strength, and basic transfer and gait stabilization activities. Precautions with intensive aerobic or strength training, particularly that involving the upper extremities, are required for 4–6 weeks to allow incisional healing. As skeletal muscle strength and endurance gradually improve, individuals may ultimately be able to undertake higher intensity exercise training than they were able to achieve preoperatively, because they are less ventilatory-limited after transplantation.

A recent systematic review identified seven studies (randomized controlled trials, controlled trials, and prospective cohorts) of exercise training on functional outcomes of exercise training on lung transplantation recipients (334). Although the overall quality of the studies was deemed fair to moderate, positive outcomes of pulmonary rehabilitation were observed in areas of maximal and functional exercise capacity, skeletal muscle function, and lumbar bone mineral density. Further work is needed to understand the degree to which these benefits derive from structured rehabilitation versus the natural healing process. Also, not all transplant recipients achieve expected gains in muscle strength or exercise capacity after rehabilitation. The reason for this is unclear and requires further investigation.

BEHAVIOR CHANGE AND COLLABORATIVE SELF-MANAGEMENT

Introduction

The symptom burden, functional impairment, and impaired quality of life in patients with chronic respiratory disease are not simply consequences of the underlying physiological disorder (335) but also depend on the patient's adaptation to the illness, its comorbidities, and its treatments (336). Reflecting this fact, the educational component of pulmonary rehabilitation has gradually evolved from a traditional, didactic approach to the promotion of adaptive behavior change, especially collaborative self-management (337).

Collaborative self-management strategies promote self-efficacy (i.e., the confidence in successfully managing one's health) through increasing the patients' knowledge and skills required to participate with health care professionals in optimally managing their illness (338). This multifaceted approach can be implemented through pulmonary rehabilitation (91, 339).

Self-management includes core generic strategies, such as goal setting, problem solving, decision-making, and taking action based on a predefined action plan. These strategies should apply to any individual with any chronic respiratory disease. Action plans for the early recognition and treatment of COPD exacerbations have been shown to reduce health care use, improve time to recovery, and reduce costs (340–344). Action plans are integral to pulmonary rehabilitation, but can also be used independently using a case manager.

Examples of positive adaptive behaviors include adherence to medication, maintaining regular exercise and increased physical activities, changing nutritional habits, breathing regulation techniques, and applying energy-saving strategies during activities of daily living (339). The multifaceted approach to achieve collaborative self-management skills and behaviors can be facilitated through pulmonary rehabilitation in a group or on an individual therapy basis (91). Self-management training involves collaboratively helping individuals acquire and practice these skills to optimize and maintain benefits (Table 4) (338). Collaborative self-management strategies aimed at the prevention, early recognition, and treatment of COPD exacerbations are especially beneficial (5, 341).

This section briefly outlines the theory of behavior change as the foundation of self-management and provides examples of behavior change interventions and self-management skills. Although these strategies pertain to most chronic respiratory diseases, most of the evidence has been published regarding individuals with COPD.

Behavior Change

Cognitive behavior therapy (CBT) is effective in inducing behavior change in individuals with chronic respiratory disease, such as COPD (345), with a positive effect achieved after only a limited number of sessions. CBT offers relatively simple and structured techniques that can be incorporated by the members of the multidisciplinary team.

Operant conditioning. Operant conditioning refers to the principle that the reoccurrence of behavior is dependent on its consequences (346). Positive consequences (rewards) elicit stronger effects than negative consequences (punishments), and short-term consequences elicit stronger effects than long-term consequences. An example would be that the patient experiences increased exercise tolerance after the use of a breathing technique;

TABLE 4. EDUCATIONAL TOPICS CONCERNING SELF-MANAGEMENT

- Normal pulmonary anatomy and physiology
- Pathophysiology of chronic respiratory disease
- Communicating with the health care provider
- Interpretation of medical testing
- Breathing strategies
- Secretion clearance techniques
- Role and rationale for medications, including oxygen therapy
- Effective use of respiratory devices
- Benefits of exercise and physical activities
- Energy conservation during activities of daily living
- Healthy food intake
- Irritant avoidance
- Early recognition and treatment of exacerbations
- Leisure activities
- Coping with chronic lung disease

this experience then acts as a reinforcer, increasing the likelihood of continued use of breathing techniques in the future. The sometimes greater compliance with fast-acting versus maintenance bronchodilation may be due to operant conditioning. In practice, health care professionals may be more effective if they provide less advice (education) on "how to do it," but rather encourage individuals to experiment with new adaptive behaviors to experience the benefits of this new behavior.

Changing cognitions. Social cognitive theory proposes that response to consequences mediates behavior, and that behavior and emotions are largely regulated in an antecedent fashion through cognitive processes (347). The consequences of a behavior lead to expectations of behavioral outcomes. The ability to form these expectations (beliefs) provides the ability to predict the outcomes of actions before they are performed. In chronic illness, cognitions are ideas or beliefs the patient has concerning their illness; these beliefs are strong determinants of emotions and behavior. Cognition, memory, and reasoning skills change over time as a function of experience. Cognitions affect behavior and emotions. For example, a patient who has the cognition, "this medication is not effective," will likely stop using it. Cognitions can also influence behavior indirectly. A patient with dyspnea may believe, "I am suffocating." This in turn induces anxiety or panic, which induces avoidance of activities associated with this unpleasant symptom.

Enhancement of self-efficacy. It is important to emphasize the patient's paramount role in optimizing and maintaining his/her health. This perception of self-efficacy—confidence in successfully managing one's health—plays a major role in acquiring new adaptive behaviors (348). Several strategies can be used by the health professional to enhance a patient's self-efficacy (338), including (*1*) mastery experiences, (*2*) explicit experiences provided by peer models, (*3*) social persuasion, and (*4*) positive mood. Prior experience of individuals in carrying out the behaviors is the most effective. Individuals who have experienced failures in the past may need to reattribute the perceived causes of this failure ("I was not adequately prepared then, but now I know exactly how to . . ."). Individuals who have (successfully) completed pulmonary rehabilitation in the past and are willing to share their positive experiences with new individuals (349) can provide a strong modeling effect. Groups can be useful in helping individuals to learn explicitly through a sharing of experiences, reinforce learning, change self-image, and discourage passivity.

Addressing motivational issues. Importantly, motivation is not a prerequisite to enrolling in pulmonary rehabilitation; rather it is one of its major goals. Increasing motivation and changing cognitions occur simultaneously when individuals experience positive benefits from new adaptive behaviors in an interactive manner (348). Self-efficacy beliefs play an important role in the self-regulation of motivation. However, to date there is no measure of motivation applied successfully in pulmonary rehabilitation.

Collaborative Self-Management

Self-management training for COPD, as part of a multiple-component disease management intervention, has demonstrated positive outcomes (350). In pulmonary rehabilitation, self-management trains individuals in gaining personal care and health behaviors skills, and fosters confidence (self-efficacy) in applying these skills on an everyday basis. Core generic skills of self-management include goal setting, problem solving, decision-making, and taking action based on a predefined action plan. Collaborative self-management interventions, tailored to the individual patient, place individuals and health care professionals in partnerships: health professionals help individuals make informed decisions enabling achievement of treatment goals. Individuals and health professionals mutually agree on patient goals; these goals can be outlined in a written summary or action plan. Individuals are primarily responsible for day-to-day management of the illness, in collaboration with the health care professional. Involving individuals in goal setting increases knowledge (351), enhances self-efficacy and self-management abilities, and improves outcomes (352).

A systematic review (350) of disease management trials in COPD demonstrated that self-management training, as part of a multiple-component disease management intervention that includes delivery system, decision support, and clinical information systems, can reduce health care use. However, this review concluded that interventions that apply self-management alone are unlikely to show this benefit.

A Cochrane review of COPD self-management education evaluated their effect on health care use (342). The conclusion from this review of 14 randomized trials was that self-management training reduced the probability of at least one hospital admission compared with usual care: odds ratio (OR), 0.64; 95% confidence interval (CI), 0.47 to 0.89 with a 1-year number needed to treat (NNT) of 10 for individuals with a 51% risk of exacerbation and an NNT of 24 for those with a 13% risk. However, data were insufficient to formulate clear recommendations regarding the form and contents of self-management programs in COPD. Virtually all the studies showing benefits from self-management education in COPD (342) have in common an action plan for exacerbations and case management.

Advance Care Planning

Advance care planning is often inadequate in chronic respiratory diseases (256, 353). Advance care planning is the process of communication between individuals and professional caregivers that includes, but is not limited to, options for end-of-life care and the completion of advance directives (354, 355). This reflects the notoriously inaccurate prognosis of the individual patient (356), the fact that death may occur at any time because of intercurrent illness (357), and the unfortunate situation when decisions on end-of-life care often occur at a time when the patient's decision-making ability is compromised (358, 359). For example, when questioned in the month before they died, only 31% of the individuals with advanced COPD estimated their life expectancy to be less than 1 year (360). Multiple studies have shown that individuals with advanced COPD had concerns about dying, but did not discuss this with their clinician (353, 361).

The failure to understand the likelihood of death from COPD is another important barrier to initiating discussions about end-of-life care (362, 363). Only 25% of individuals entering pulmonary rehabilitation reported having an advance directive (364), 19% report discussing advance directives with their clinician, and 14% thought that their clinician understood their wishes

TABLE 5. EDUCATIONAL TOPICS CONCERNING ADVANCE CARE PLANNING

- Diagnosis and disease process
- Prognosis
- Patient autonomy in medical decision-making
- Life-sustaining treatments
- Advance directives documents
- Surrogate decision-making
- Durable powers of attorney for health care
- Discussing advance care planning with health care professionals and family caregivers
- Process of dying
- Prevention of suffering

Taken from References 365, 370, 757, and 758.

for end-of-life care (365). Nevertheless, 94% had opinions about intubation and 99% wanted to discuss advance directives with their clinician (365). Despite the need for advance directive education, only about one-third of U.S. pulmonary rehabilitation programs provide some form of advance directives education (366); data from Europe are not available.

Advance care planning can be effective in changing outcomes for individuals and their loved ones and provide support for use of advance directives (358, 367–369). Pulmonary rehabilitation provides the opportunity to facilitate advance care and directive education (Table 5) to encourage completion of living wills and durable powers of attorney for health care, patient–physician discussions about advance directives, and discussions about options for life support (370, 371).

BODY COMPOSITION ABNORMALITIES AND INTERVENTIONS

Introduction

Body composition abnormalities are prevalent in COPD and affect prognosis. Although body composition abnormalities are probably common to all advanced respiratory diseases, most of the medical literature, to date, has focused on individuals with COPD. Therefore, the information given below relates predominantly to this disease.

Abnormalities in weight are traditionally classified on the basis of body mass index (BMI, body weight in kilograms divided by height in meters squared) as underweight (<21 kg/m^2), normal weight (21–25 kg/m^2), overweight ($>$25–30 kg/m^2), and obese ($>$30 kg/m^2). The BMI, however, does not reflect changes in body composition that may occur with aging or with acute or chronic disease. These changes may include (*1*) a shift from fat-free mass (FFM) toward fat mass, (*2*) an accelerated loss of the FFM during periods of weight loss, (*3*) a redistribution between the intracellular and extracellular water compartment of the FFM during acute (disease-induced) metabolic stress, and (*4*) a redistribution of the fat mass compartment from peripheral (subcutaneous) fat to ectopic fat (372).

Independent of COPD spirometric severity staging, 20–30% of normal weight individuals with COPD are characterized by a shift in body composition toward muscle wasting and relative abundance of fat mass (373). Furthermore, there appears to be a disproportionate increase in visceral fat mass in individuals with COPD that is not limited to obese patients (372, 374). Whereas weight loss and underweight status are most prevalent in advanced disease and in the emphysematous phenotype (375), obesity and fat abundance are more prevalent in mild COPD (376).

Weight loss and an underweight status are associated with increased mortality, independent of the degree of airflow obstruction, whereas weight gain in those with a BMI below 25 kg/m^2 appears to be associated with decreased mortality (377, 378). In advanced COPD, low FFM and mid–thigh muscle cross-sectional area are associated with increased mortality independent of BMI, whereas obesity is associated with decreased mortality (the obesity paradox) (122, 124, 125). The abundance of fat mass and increased visceral fat mass is related to enhanced systemic inflammation and decreased insulin sensitivity (379). This potentially contributes to increased cardiovascular (mortality) risk in COPD, and could be an important novel target for pulmonary rehabilitation, in particular in early disease stages.

Muscle mass constitutes the major part of fat-free mass. A simple field test to estimate FFM in clinically stable individuals is bioimpedance analysis (BIA) using a validated prediction equation that is appropriate regarding age, sex, and race (380). BIA underestimates FFM in extremely wasted individuals (due to shrinkage of intracellular mass) (381) and overestimates FFM in unstable individuals with extracellular water expansion. A clear age dependency of body composition calls for application of age-adjusted percentiles to define normal values for FFM. An FFM index less than the 10th percentile clearly reflects severe disability (124, 125).

Interventions to Treat Body Composition Abnormalities

Since the previous Statement several studies aimed at improving body composition abnormalities in COPD have had positive outcomes; these include a 6-month intervention of dietary counseling and food fortification (382); a multimodal intervention of nutrition and anabolic steroids integrated into pulmonary rehabilitation for advanced COPD (377, 383, 384); and an intervention including nutritional therapy and counseling plus exercise training in patients with COPD with less severe airway obstruction (385).

Weight loss and fat wasting may be caused by a negative energy balance due to either elevated energy requirements, reduced dietary intake, or both; muscle wasting is the consequence of an imbalance between muscle protein synthesis and breakdown (386). Impairment in energy balance and protein balance may occur simultaneously, but these processes can be dissociated. Depending on the body composition abnormality, intervention strategies will be oriented toward restoring energy and protein balance (weight loss), restoring protein balance (hidden muscle wasting), or decreasing energy balance while maintaining protein balance (obesity and visceral fat expansion).

Since the publication of the previous Statement, it has been demonstrated that a 6-month intervention consisting of dietary counseling and food fortification resulted in significant body weight gain and fat mass with maintenance of fat-free mass compared with a control group (382). In addition, three randomized controlled trials have investigated the efficacy of multimodal intervention, including nutrition and anabolic steroids, integrated into pulmonary rehabilitation for advanced COPD or chronic respiratory failure (377, 383, 384). This combined approach was indeed successful in improving body weight, fat-free mass, exercise tolerance, and even survival in compliant individuals. However, the relative influence of the various components could not be determined.

n-3 polyunsaturated fatty acids (PUFAs) improve muscle maintenance, probably through modulating systemic inflammation. Although an earlier trial had negative results (387), 3 months of nutritional supplementation enriched with PUFAs used as an adjunct to exercise training did indeed result in decreased systemic inflammatory markers including C-reactive protein, tumor necrosis factor-α, and IL-8 (388). On the basis of a systematic literature review, creatine supplementation does not improve exercise capacity, muscle strength, or health-related quality of life in individuals with COPD receiving pulmonary rehabilitation (389).

Because muscle wasting is not limited to advanced disease, early intervention may be indicated to improve or maintain physical functioning. Accordingly, a 4-month intervention consisting of exercise and standardized nutritional supplements followed by a 20-month maintenance program (including counseling and supplements on indication) in patients with COPD with less severe airway obstruction resulted in significant long-term beneficial effects on fat-free mass, skeletal muscle function and 6-minute walking distance in muscle-wasted individuals with COPD compared with usual care (385). Cost analysis furthermore revealed significantly lower hospital admission costs in the intervention group (385).

Special Considerations in Obese Subjects

Reflecting the dramatic increase in the global prevalence of obesity, an increasing number of individuals with chronic respiratory diseases and coexisting obesity will be referred for pulmonary rehabilitation (390). In addition, a growing number of persons with obesity-related respiratory disorders such as "obesity hypoventilation syndrome" and "obstructive sleep apnea" may be referred for pulmonary rehabilitation if functional limitations are present. Pulmonary rehabilitation is an ideal setting in which to address the needs of these people. Specific interventions may include exercise training, nutritional education, restricted calorie meal planning, encouragement for weight loss, psychological support, and training with and acclimatization to noninvasive positive pressure ventilation.

The respiratory consequences of obesity alone are well described (391, 392). A reduction in functional residual capacity resulting from reduced respiratory system compliance is the hallmark of isolated obesity, while airway function and diffusion capacity are preserved (391). In COPD, obesity reduces resting lung hyperinflation (393), possibly explaining the finding that obese individuals with this disease may not have as severe dyspnea or exercise impairment as nonobese individuals with similar degrees of airflow obstruction (393). In another study, peak oxygen uptake was also greater during constant work rate cycling exercise among overweight and obese individuals with COPD with hyperinflation, although exercise endurance time, dyspnea ratings, and lung volumes were not different as compared with the normal weight group (394). However, in contrast to weight-supported exercise, obesity may have a negative impact on weight-bearing exercise tolerance: despite less severe airflow obstruction and comparable constant work rate cycling endurance time, individuals with COPD with obesity had lower 6MWT distances compared with overweight and normal weight individuals (395).

Two studies indicated that obesity did not adversely affect the magnitude of gains made in pulmonary rehabilitation (395, 396). At present, the optimal exercise training strategy and target BMI for obese individuals with COPD remain unknown. Also, the effects of weight loss on symptoms, lung function, and exercise tolerance in obese individuals with COPD are currently unclear.

Because obese persons often have systemic hypertension, cardiovascular disease, diabetes mellitus, osteoarthritis, and other morbidities (397, 398), and those with obesity hypoventilation syndrome and/or obstructive sleep apnea may have pulmonary hypertension, pulmonary function testing, assessment of gas exchange, echocardiography, and/or cardiopulmonary exercise testing or pharmacologic stress testing can be considered before initiation of pulmonary rehabilitation, to identify factors contributing to the patient's functional limitation. Specialized equipment such as wheelchairs, walkers, recumbent bicycles, or chairs may be needed to accommodate persons of extreme weight (244, 399), and the weight limits of available exercise equipment must be considered. Walking, low-impact aerobics, and water-based exercise are suitable for persons too heavy to use a treadmill or cycle ergometer (400). Extra staff may be needed to assist in mobility training of the morbidly obese patient.

PHYSICAL ACTIVITY

Physical inactivity is common in COPD and is associated with poor outcomes, independent of lung function abnormality. Because of this and the fact that new technologies have been developed to directly measure activity, pulmonary rehabilitation is beginning to focus on this outcome area. Studies to date of pulmonary rehabilitation translating gains in exercise capacity into increased physical activity have had mixed results.

Although it had been assumed that individuals with COPD are physically inactive resulting from their adoption of a sedentary lifestyle, this clinical impression has been substantiated in several studies (401, 402). In one study of directly measured physical activity in 50 individuals with COPD compared with 25 healthy elderly individuals (403), patients with COPD spent significantly less time walking and standing and more time sitting and lying than their control subjects. Of note, walking time correlated poorly with the degree of airflow limitation.

Another study of 163 individuals with COPD and 29 with chronic bronchitis but no airflow limitation (404) demonstrated that directly measured physical activity decreases as disease severity increases. In subsequent studies (402, 405), physical activity in COPD was found to be associated with multiple factors, including FEV_1; diffusing capacity; the 6-minute walk distance; peak aerobic capacity; quadriceps and expiratory muscle strength; fibrinogen, C-reactive protein, and tumor necrosis factor-α levels; health status; and dyspnea, fatigue, degree of emphysema, and frequency of exacerbations.

Physical inactivity in COPD is associated with poor outcome, including increased mortality risk. In one study (406), those individuals with COPD receiving long-term oxygen therapy who reported regular outdoor activity had a 4-year survival of 35% versus 18% if they reported no regular outdoor activity. In analyses of two Danish cohorts (407), questionnaire-assessed activity predicted 10-year survival in individuals with COPD: survival was approximately 75% among those who rated their activity level as high versus 45% among those who rated their activity level as low.

More recently, two longitudinal studies of physical activity directly measured by motion detectors worn on the body demonstrated a relationship between physical inactivity and increased mortality risk. In one, a study of 170 clinically stable patients with COPD (408), directly measured physical activity using an activity monitor was the strongest predictor of 4-year survival: physical activity was a stronger predictor of survival than lung function, the 6-minute walk distance, echocardiographic assessment of cardiovascular status, Doppler-assessed peripheral vascular disease, body mass index and fat-free mass index, dyspnea, health status, depression symptoms, and multiple systemic biomarkers (408). Showing similar results, in another study of 173 patients with moderate to severe COPD (409) physical activity measured from a triaxial accelerometer predicted survival over 5–8 years. This association was present in univariate and multivariate models. For the latter, comorbidity, endurance time, and activity counts (vector magnitude units) were retained as independent predictors of mortality.

Lower levels of physical activity also predict hospitalization (409) or rehospitalization in individuals with COPD hospitalized for an exacerbation (410, 411), and may indeed be associated with a faster decline in lung function (412).

Those individuals with COPD with higher levels of exercise tolerance do tend to have higher levels of directly measured everyday activity (403). However, although acceptable levels of exercise capacity/tolerance can be considered permissive of physical activity, it does not mandate higher levels of physical activity. Physical activity as a behavior is probably determined by a complex set of factors including health beliefs, personality characteristics, exercise-associated symptoms, mood, past behaviors, social and cultural factors and external factors, such as climate (413, 414). Thus, activity level has a strong behavioral component as well as a physical component.

Because physical activity in individuals with chronic respiratory disease such as COPD is low and this inactivity is associated with poor prognosis, increasing activity is a desirable outcome.

However, two interventions that are recognized to improve exercise tolerance, bronchodilator administration and ambulatory oxygen therapy, have failed to demonstrate significant increases in physical activity levels (415, 416).

The pulmonary rehabilitation intervention, with components aimed at increasing exercise tolerance and improving self-efficacy, could be considered as a potentially good candidate to promote physical activity. Indeed, at least 10 trials have been published in the past decade investigating whether pulmonary rehabilitation increases activity level. Most of these studies have been summarized recently (417–419). Some of these studies have features that might be considered suboptimal: several had small sample sizes and several had periods of activity monitoring that were less than the 7 days hypothesized to be necessary for accurate assessment (420). The results of these studies are inconsistent: four have demonstrated statistically significant increases in activity level after pulmonary rehabilitation (421–424), whereas six have not (425–430). No study characteristics seem to consistently explain these differences. However, a sustained increase in physical activity requires structural behavior change by the patient.

The above disparity in physical activity outcome among the nine clinical trials highlights the fact that there is, to date, little knowledge of how to transfer the gains in exercise capacity that pulmonary rehabilitation yields into enhanced participation in daily life activities. In addition, it is not known how much improvement in physical activity is clinically relevant or meaningful. This is compounded by the fact that a multitude of different activity monitors have been used in testing, and the optimal mode of reporting (movements, estimated steps, energy expenditure, etc.) is not known (431). However, any increase in the proportion of individuals meeting the required amount of physical activity for healthy aging would be a significant benefit for both individuals and society. Future research could focus on whether pulmonary rehabilitation enhances the proportion of individuals meeting these goals (30 min of physical activity in addition to normal daily activities at moderate intensity on at least 5 d/wk) (119). Modifications to pulmonary rehabilitation might be considered to help achieve this goal.

One small study suggested that the use of simple pedometer devices may provide individuals with real-time feedback on their physical activity levels (95) and thereby increase activity. When appropriate guidance could be given, this may enhance physical activity levels, much like in healthy subjects (432). Further research is necessary to determine the effectiveness of a feedback approach like this. Another study showed that individuals walked more after Nordic walking training was given; this appealed to individuals and could be done in groups (100). Whether other behavioral interventions may help to achieve a long-term change toward a more physically active lifestyle remains to be investigated. A future challenge will be to merge exercise training requirements (i.e., prescribed high-intensity exercise tailored to improve exercise tolerance) with behavioral modification promoting healthy physical activity levels (i.e., moderate intense exercise on 5 of 7 d/wk) (419).

TIMING OF PULMONARY REHABILITATION

Pulmonary Rehabilitation in Early Disease

Traditionally, most pulmonary rehabilitation programs enroll individuals with severe to severe COPD (91). However, newer data suggest that patients with less severe disease also improve significantly across several outcome areas (110, 433). The rationale for including patients in pulmonary rehabilitation with lesser degrees of airflow limitation stems from the fact that the correlation between the degree of airflow limitation, dyspnea, health status, and exercise performance is weak (335, 434, 435). Moreover, low physical activity, problematic activities of daily living, dynamic hyperinflation with exercise, lower limb weakness, osteoporosis, anxiety, and depression may also occur in mild to moderate airflow limitation (62, 115, 131, 149, 402, 436–438).

Vogiatzis and colleagues showed that functional capacity and morphologic and typologic adaptations to a 10-week pulmonary rehabilitation program in lower limb muscle fibers were similar across Global Initiative for Chronic Obstructive Lung Disease (GOLD) stages II to IV (110). Moreover, a community-based pulmonary rehabilitation program was effective in individuals with mild or moderate COPD who had impaired exercise performance at baseline (433). In a 2-year randomized controlled trial, 199 individuals with COPD were randomized to either an INTERdisciplinary COMmunity-based COPD management program (INTERCOM) or usual care. The program included 4 months of formal training and 20 months of maintenance supervised cycle-based exercise training, education, nutritional therapy, and smoking cessation counseling. At 2 years, between-group differences in favor of the treatment group were maintained in components of health status, dyspnea, cycle endurance time, and walk distance. These results suggest that pulmonary rehabilitation can lead to positive outcomes irrespective of the degree of lung function impairment, with the timing of pulmonary rehabilitation rather depending on the individual's clinical status. By improving exercise tolerance and physical activity, promoting self-efficacy and behavior change, and reducing exacerbations, pulmonary rehabilitation at an earlier stage of disease has the potential to markedly alter the course of the disease.

Pulmonary Rehabilitation and Exacerbations of COPD

There is now evidence of the role of pulmonary rehabilitation in acute disease, specifically during and after hospitalization for acute exacerbations of chronic obstructive pulmonary disease (AECOPD). This evidence includes several randomized controlled trials, and an updated Cochrane review (439).

AECOPD is associated with worsening lung function, symptoms, and activity (440–444), a substantial decline in functional status and health-related quality of life, psychological distress (444–447), and increased morbidity and mortality (443). Furthermore, it represents one of the most common reasons for hospital admission, and results in a substantial proportion of COPD-related health care costs (448). Impairments in lung function may persist for several months (440, 449). Exercise capacity and activity levels are markedly reduced during and after an exacerbation and may persist for weeks, months, or years after hospital discharge (444, 450). Those immobilized during respiratory failure requiring mechanical ventilatory support are particularly at risk. Reduced physical activity associated with AECOPD is likely a major contributor to skeletal muscle dysfunction, particularly of the lower limbs (444). Recent data suggest that significant physical inactivity is an independent risk factor for mortality (408) and is associated with a faster rate of decline in lung function (412). Physical inactivity after AECOPD is associated with readmission with subsequent exacerbation (407, 410).

Given the role of pulmonary rehabilitation in improving exercise capacity, activity level, skeletal muscle function, and health-related quality of life in stable patients, it appears logical to consider pulmonary rehabilitation in the acute setting. Pulmonary rehabilitation can be initiated during hospitalization for AECOPD. Although ventilatory limitation may preclude aerobic exercise training during AECOPD, resistance training of the lower extremity muscles during hospitalization for AECOPD is well tolerated, safe, and improves muscle strength and 6-minute walk distance (148, 451). Neuromuscular electrical stimulation (NMES) is an alternative safe and effective training method that can prevent muscle function decline and hastens recovery of mobility for hospitalized individuals, particularly in critical care (159, 171, 172).

Pulmonary rehabilitation initiated early (e.g., within 3 wk) after AECOPD hospitalization is feasible, safe, and effective, and leads to gains in exercise tolerance, symptoms, and quality of life (439, 452–460). Pulmonary rehabilitation in the posthospitalization period also reduces health care use, readmissions, and mortality (439, 456, 459, 460).

The Cochrane review of randomized trials comparing outcomes of pulmonary rehabilitation versus usual care after an AECOPD, updated in 2011 (439), included nine trials that enrolled 432 individuals. In four trials, inpatient pulmonary rehabilitation was initiated within 3–8 days of AECOPD hospital admission; in three trials, outpatient rehabilitation was initiated after the inpatient exacerbation; in one study individuals started either in- or outpatient rehabilitation; and in one trial outpatient rehabilitation was started after the hospital-at-home treatment of an exacerbation. Pulmonary rehabilitation significantly improved exercise capacity and health-related quality of life. No adverse events were reported in three studies providing this information. Pulmonary rehabilitation reduced the chance of a hospital admission significantly, by at least 42% (pooled OR, 0.22; 95% CI, 0.08 to 0.58) over a median follow-up of 25 weeks, although other trials have shown less reduction in health care use (461, 462). The chance of mortality was also reduced significantly by at least 16% (OR, 0.28; 95% CI, 0.10 to 0.84). This evidence suggests that pulmonary rehabilitation is an effective and safe intervention after AECOPD.

Further work is required to determine the minimal duration of pulmonary rehabilitation required to achieve beneficial outcomes after AECOPD, the duration of benefits, and whether individuals with exacerbations of other chronic respiratory diseases (e.g., bronchiectasis, asthma, pneumonia, acute respiratory distress syndrome [ARDS] survivors) may also benefit from pulmonary rehabilitation. It is also not known whether there are subgroups for which pulmonary rehabilitation provided during or early after AECOPD is beneficial, for example, after a prolonged ICU stay. In addition, the optimal time relative to AECOPD to initiate pulmonary rehabilitation is unknown. A small trial evaluated pulmonary rehabilitation efficacy initiated immediately after an exacerbation versus after returning to a stable pulmonary state (463). This head-to-head comparison did not show any difference in AECOPD over 18 months of follow-up. Chronic Respiratory Questionnaire domain scores were higher for individuals with early rehabilitation, but not statistically significant. Studies involving posthospitalization outpatient pulmonary rehabilitation have shown low uptake and adherence rates (460–462). Transportation, psychological morbidity associated with AECOPD, and general frailty are frequent and important barriers to posthospitalization pulmonary rehabilitation (464). Inpatient rehabilitation is a successful intervention for persons with severe functional limitation and/or ongoing needs for daily medical and/or nursing care (465). Alternative approaches may include home-based pulmonary rehabilitation (457, 466) and self-management programs (342, 467), although these have not been tested rigorously in the immediate post–acute phase setting. The multidisciplinary nature of pulmonary rehabilitation, whether in the hospital or after hospital discharge, provides a unique opportunity to assess and engage the patient, to refer for smoking cessation in active smokers, promote physical activity and self-management skills to induce long-term behavioral changes, to identify and treat nutritional insufficiency and psychological morbidity, and to introduce palliative care to selected individuals. A substantial percentage of individuals hospitalized with AECOPD lack a prior diagnosis of COPD (468, 469), and as such comprise a patient group that has yet to be offered care for or education about their disease.

Early Rehabilitation in Acute Respiratory Failure

The progress of intensive care medicine has dramatically improved survival of critically ill individuals, especially in individuals with ARDS (470). However, improved survival is often associated with general deconditioning, functional impairment, and reduced health-related quality of life after intensive care unit (ICU) discharge (447, 471, 472). This indicates the need for rehabilitation after ICU and hospital discharge (471), and underscores the need for assessment and measures to prevent or attenuate deconditioning and loss of physical function during ICU stay. Clinical interest and scientific evidence have given support to safe and early physical activity and mobilization in critically ill patient with respiratory failure by an interdisciplinary ICU team (473–477). Assessment of cooperation, cardiorespiratory reserve, muscle strength, joint mobility, functional status, and quality of life is involved in planning early mobilization and physical activity. Assessment of muscle strength is particularly important in guiding progressive ambulation (474) and predicting outcomes (478). Muscle strength in ICU patients can be measured in alert patients with the Medical Research Council (MRC) dyspnea grade, handgrip dynamometer, and handheld dynamometer. In unconscious individuals, measurement of muscle thickness by ultrasound is available as a nonvalidated test (479). Several protocols have been developed to enhance early mobilization and physical activity. All address safety, clinical assessment including cardiorespiratory and neurological status, level of cooperation, and functional status (muscle strength, mobility), and provide steps to gradually increase physical activity and mobilization in the critically ill (474, 480).

Physical activity and exercise in the unconscious patient. Individuals who are critically ill need to be positioned upright (well supported), and rotated when recumbent to avoid adverse effects on cardiorespiratory function, soft tissue, joints, nerve impingement, and skin breakdown. Rehabilitation in ICU patients with respiratory failure was considered contraindicated in more than 40% of ICU bed days, mainly due to sedation and renal replacement issues (481). However, treatment modalities, such as passive cycling, joint mobilization, muscle stretching, and neuromuscular electrical stimulation, do not interfere with renal replacement or sedation. Passive stretching or range of motion exercises are particularly important in the management of immobile individuals. Continuous passive motion (CPM) prevents contractures in individuals with critical illness and respiratory failure with prolonged inactivity (482). In critically ill individuals, 3 hours of CPM three times per day reduced fiber atrophy and protein loss, compared with passive stretching for 5 minutes, twice daily (482). Exercise training early during ICU stay is often more challenging. Technological development includes the bedside cycle ergometer for active or passive leg cycling during bed rest, permitting prolonged continuous mobilization and rigorous control of exercise intensity and duration. Training intensity can be continuously adjusted to the patient's health status and physiological responses to exercise. A randomized controlled trial of early application of daily bedside (initially passive) leg cycling in critically ill individuals showed improved functional status, muscle function, and exercise performance at hospital discharge compared with standard physiotherapy (477). In immobile individuals, NMES has been used to prevent disuse muscle atrophy. In acute critically ill individuals with respiratory failure, unable to move actively, reductions in muscle atrophy (172) and critical illness neuropathy (173) were observed when using NMES. NMES of the quadriceps in individuals with protracted critical illness, in addition to active limb mobilization, enhanced muscle strength and hastened independent transfer from bed to chair (171).

Physical activity and exercise in the alert patient. Mobilization refers to physical activity sufficient to elicit acute physiological effects that enhance ventilation, central and peripheral perfusion, circulation, muscle metabolism, and alertness. Strategies—in order of intensity—include transferring in bed, sitting over the edge of the bed, moving from bed to chair, standing, stepping in place, and walking with or without support. Standing and walking frames enable early mobilization of critically ill individuals. Transfer belts facilitate heavy lifts and protect both the patient and clinicians. Early mobilization was studied in two trials (474, 476). Morris and colleagues (474) demonstrated in a prospective cohort study that individuals with respiratory failure receiving early mobility therapy had reduced ICU and hospital stay with no differences in weaning time or hospital costs versus usual care. In a randomized controlled trial, Schweickert and colleagues observed that early physical and occupational therapy improved functional status at discharge, shortened duration of delirium, and increased ventilator-free days. These findings did not result in reduced length of ICU or hospital stay (476). Aerobic training and muscle strengthening, in addition to routine mobilization, improve walking distance more than mobilization alone in ventilated individuals with chronic respiratory failure (458). A randomized controlled trial showed that a 6-week upper and lower limb training program improved limb muscle strength, ventilator-free time, and functional outcomes in individuals requiring long-term mechanical ventilation compared with usual care (483). These results are in line with a retrospective analysis of individuals on long-term mechanical ventilation who participated in whole-body training and respiratory muscle training (484). In individuals recently weaned from mechanical ventilation (485), upper limb exercise enhanced effects of general mobilization on exercise endurance and dyspnea. Low-resistance multiple repetitions of resistive muscle training can augment muscle mass, force generation, and oxidative enzymes. Daily sets of repetitions within the patient's tolerance should be commensurate with their goals. Resistive muscle training can include use of pulleys, elastic bands, and weight belts. The chair cycle and bed cycle allow performance of an individualized exercise training program. The intensity of cycling can be adjusted to the individual's capacity, ranging from passive cycling via assisted cycling to cycling against increasing resistance.

The amount of rehabilitation performed in ICUs is often inadequate and often better organized in weaning centers or respiratory ICUs (458, 486). The rehabilitation team in the ICU (e.g., physicians, physiotherapists, nurses, and occupational therapists) prioritizes and identifies aims and parameters of treatment modalities of early mobilization and physical activity, ensuring these modalities are therapeutic and safe by appropriate monitoring of vital functions. Transfer of patients with acute respiratory failure to the respiratory ICU substantially improved ambulation, independent of the underlying pathophysiology. These data suggest that the ICU environment may contribute to unnecessary immobilization (486). Garzon-Serrano and colleagues observed that physical therapists mobilize critically ill individuals to higher levels of mobilization than nursing staff (487). Transferring a patient from the ICU to the respiratory ICU increased the number of individuals ambulating threefold versus pretransfer rates (486). Ideally, physiotherapists will be heavily involved in implementing mobilization plans, exercise prescription, and making recommendations for progression of the rehabilitation strategy, jointly with medical and nursing staff (488).

Role for rehabilitation in weaning failure. A small proportion of individuals with respiratory insufficiency fail to wean from mechanical ventilation, and require a disproportionate amount of resources. There is accumulating evidence that weaning problems are associated with failure of the respiratory muscles to resume ventilation (489). Inspiratory muscle training (IMT) may be beneficial in individuals with weaning failure. Uncontrolled trials of IMT have shown an improvement in inspiratory muscle function and reduction in duration of mechanical ventilation and weaning time (490). A randomized controlled trial comparing IMT at moderate intensity (about 50% of maximal inspiratory pressure [$P_{I_{max}}$]) versus sham training in individuals with weaning failure showed that a statistically significant, larger proportion of the training group (76%) could be weaned compared with the sham group (35%) (491). Addition of IMT in critically ill individuals initiating mechanical ventilation has shown contrasting findings. Caruso and colleagues submitted individuals to IMT for 30 minutes/day. IMT failed to improve $P_{I_{max}}$, reduce weaning duration, or decrease reintubation rate (492). However, Cader and colleagues observed that twice-daily IMT sessions at 30% of $P_{I_{max}}$ for 5 minutes improved $P_{I_{max}}$, and reduced the weaning period (3.6 vs. 5.3 d in the control group) (493).

Assessment and treatment of these individuals focus on deconditioning (muscle weakness, joint stiffness, impaired functional exercise capacity, and physical inactivity) and respiratory issues (retained airway secretions, atelectasis, and respiratory muscle weakness). Evidence-based targets are deconditioning and weaning failure; a variety of modalities for exercise training and early mobility are evidence based and must be implemented depending on the stage of the patient's acute respiratory failure, comorbidities, and level of consciousness and cooperation. Patient mobilization plans and exercise prescription are a multidisciplinary team responsibility, involving physical therapist, occupational therapist, medical doctor, and nursing staff.

Long-Term Maintenance of Benefits from Pulmonary Rehabilitation

In the absence of any maintenance strategy, benefits of pulmonary rehabilitation appear to diminish over 6–12 months, with quality of life better maintained than exercise capacity (17, 494, 495). The reasons for this decline are multifactorial, including decrease in adherence to therapy, especially long-term regular exercise, progression of underlying disease and comorbidities, and exacerbations (496). Regardless of the causes, developing ways to extend the effects of pulmonary rehabilitation is an important goal.

Maintenance exercise training programs. Several new randomized controlled trials have examined the effects of maintenance strategies after pulmonary rehabilitation (428, 497, 498). Evidence for supervised exercise training maintenance therapy remains equivocal, with one study finding no additional benefits of weekly sessions over routine follow-up (497) and another reporting that weekly sessions resulted in improved exercise capacity but not health-related quality of life (499). Reducing the frequency of supervision to once per month demonstrated no significant benefits for either outcome measure (499).

Ongoing communication to improve adherence. In one study, weekly phone calls improved 6-minute walk distance but not health-related quality of life (428). Another study showed no benefits from monthly telephone follow-up (497). In contrast, a home exercise program accompanied by monthly phone calls improved 6-minute walk distance and health-related quality of life after 3 weeks of inpatient pulmonary rehabilitation (500), although ongoing participation in exercise was not encouraged for the control subjects, which may not reflect usual care.

Repeating pulmonary rehabilitation. Repeating pulmonary rehabilitation to maintain outcomes includes repeat sessions to (*1*) prevent decline in pulmonary rehabilitation outcomes, and (*2*) after decline of function, for example, with AECOPD. Repeating pulmonary rehabilitation in the first format has equivalent effects of the initial program (501, 502) although optimal timing remains unclear. In the second format, a pilot randomized controlled trial of abbreviated pulmonary rehabilitation after AECOPD did not improve exercise or quality of life compared with completing rehabilitation within 12 months of AECOPD (453). Nevertheless, excluding individuals who experienced a second AECOPD during follow-up, repeat pulmonary rehabilitation yielded benefits in the dyspnea domain of the Chronic Respiratory Questionnaire (453).

Other methods of support. No studies have evaluated the clinical impact of consumer-led support groups after pulmonary rehabilitation. However, qualitative data indicate that individuals who have completed pulmonary rehabilitation value opportunities for ongoing peer support, through group activities with others who have similar needs and experiences (503).

PATIENT-CENTERED OUTCOMES

Patient-centered outcomes have historically been used for patient assessment and measurement of change or impact of pulmonary rehabilitation in chronic respiratory disease. The strongest evidence of impact from pulmonary rehabilitation has been for improvement in symptoms, exercise performance, and quality of life in individuals with COPD (18). Outcomes described in this section outline key measures used in pulmonary rehabilitation.

Studies have focused on accurately defining and describing relevant outcomes and their measurement and interpretation. Analyses of outcomes have included descriptions of relevant change, such as the minimal (clinically) important difference (MID). The MID has been defined as the smallest difference in a measurable clinical parameter that indicates a meaningful change in the condition for better or for worse, as perceived by the patient, clinician, or investigator (504). MIDs derived from group means reflect a group response (505, 506), and cannot be used to interpret changes in individuals. There may additionally be a discrepancy between the MID and statistical significance in reported change. Challenges to consider when interpreting results include the time frame within which to demonstrate change in behavior, which may be particularly important for direct measures of behaviors, for example, physical activity. Determination of the impact of a pulmonary rehabilitation program requires, at minimum, that measurements be taken before the program begins and after the program is finished. Moreover, long-term outcome measurement can offer important understanding of the impact of pulmonary rehabilitation (17, 451). The methods to measure outcomes of pulmonary rehabilitation discussed below pertain largely to individuals with COPD. The optimal methods for measuring these outcomes among participants with chronic respiratory disorders other than COPD are as yet uncertain; in some cases the outcome measures overlap. However, this is an emerging area of study, and some additional tools used in studies of pulmonary rehabilitation for disorders other than COPD that may be better suited to some outcomes measurement in individual non-COPD disorders are listed in Table 3. Questionnaires fall broadly into two categories: generic (e.g., the 36-item Short-Form Health Survey [SF-36], EuroQol-5 dimension questionnaire [EQ-5D], and Hospital Anxiety and Depression Scale [HADS]), allowing a legitimate comparison between different diseases; and disease specific. In general, disease-specific questionnaires are favored as outcome measures for pulmonary rehabilitation.

For the purposes of this section, we will limit our review to those symptom measures that have been used in pulmonary rehabilitation to evaluate symptoms as an outcome with clear documentation of traditional psychometric properties of reliability, validity, and responsiveness (507, 508). Other considerations in selecting instruments for symptom assessment in pulmonary rehabilitation include the following: clinical usefulness, length of time needed to complete the measurement, administration requirements (e.g., the ease of scoring and whether the test needs to be delivered with a member of the rehabilitation team), and time frame over which the symptoms are measured (509).

Quality-of-Life Measurements

The concepts of quality of life, health-related quality of life, functional impairment, and symptoms often are used interchangeably and many definitions of these concepts exist (510). General theories define health status as an overall concept, covering domains of physiological functioning, symptoms, functional impairment, and quality of life (511, 512). Health-related quality is a component of the broader concept of quality of life and is defined as satisfaction with health. These domains of health status have been shown to be divided into many more concrete subdomains (513). Ideally, health status assessment to evaluate effects of treatment is tailored to the treatment needs of the individual patient.

Several generic and disease-specific instruments are available that measure health status and its domains. Although generic instruments are considered to be less discriminative and less sensitive to change, the SF-36 has been shown to detect improvement after pulmonary rehabilitation (514). The St. George's Respiratory Questionnaire (SGRQ) (515) and Chronic Respiratory Disease Questionnaire (CRQ; and its self-reported version [516, 517]) are the most widely used disease-specific questionnaires. They have been shown to be sensitive to change (91, 518, 519) and have defined thresholds indicating the MID (520–522).

All instruments have important limitations (523). First, disease-specific questionnaires typically measure subjective accounts of pulmonary symptoms and functional impairment (524). Although these represent important aspects of health status, other aspects of health status are important as well. In addition, instruments that show subjective change may not directly indicate actual behavior change. As discussed previously, discrepancies are reported between what the patient is able to do, what the patient really does, and what the patient subjectively believes he or she can do (525). Second, most instruments contain only a few subscales. The recently developed COPD Assessment Test (CAT) contains only a single score (526). This indicates that these instruments measure at best only a few aspects of health status. This is potentially a drawback in research and in clinical practice because patient-tailored treatment requires a detailed picture of the many subdomains of a patient's health status. Then again, the CAT is short and easily understood by individuals and clinicians and also improves after pulmonary rehabilitation (527, 528). To obtain a detailed picture of a patient, instruments may be used in combined fashion (529). Third, most instruments require complex scoring procedures. Fourth, instruments lack normative data indicating whether a certain score indicates normal functioning or abnormal functioning. The Nijmegen Clinical Screening Instrument (NCSI) was developed as a health status questionnaire to circumvent these

TABLE 6. DYSPNEA, FATIGUE, AND MULTIPLE SYMPTOM MEASURES USED IN PULMONARY REHABILITATION

			Psychometric Properties				
Symptom	Type and Name of Measure	References	Reliable	Valid	Responsive	Purpose	Time Frame
Dyspnea	Short-term						
	Borg	17, 534, 535, 759	✓	✓	✓	Discriminative and evaluative	Current
	VAS	536–540	✓	✓	✓	Discriminative and evaluative	Current
	Situational						
	MRC	541–543	✓	✓	✓	Discriminative	Are you ever
	BDI	540, 544–546	✓	✓	✓	Discriminative	Current
	SOBQ	18, 547	✓	✓	✓	Discriminative and evaluative	Last few weeks
	Impact						
	CRQ (dyspnea subscale)	17, 538, 548	✓	✓	✓	Discriminative and evaluative	Last 2 wk
	PFSDQ	549	✓	✓	✓	Discriminative and evaluative	Today, most days, current
	PFSDQ-M (dyspnea subscale)	550	✓	✓	✓	Discriminative and evaluative	Today, most days, current
Fatigue	Short-term						
	Borg	534, 551	✓	✓	✓	Discriminative and evaluative	Current
	VAS	539	✓	✓	✓	Discriminative and evaluative	Current
	Impact						
	CRQ (fatigue subscale)	17, 538, 548	✓	✓	✓	Discriminative and evaluative	Last 2 wk
	PFSDQ-M (fatigue subscale)	550	✓	✓	✓	Discriminative and evaluative	Today, most days, current
	FACIT-fatigue	552, 553	✓	✓	✓	Discriminative and evaluative	Previous 7 d
	MFI	554, 555	✓	✓	NR	Discriminative	Previous few days
	CIS	760	✓	✓	✓	Discriminative and evaluative	Last 2 wk
Multiple symptoms	CAT	526, 527	✓	✓	✓	Discriminative and evaluative	Current
	SGRQ symptoms domain	17, 515	✓	✓	✓	Discriminative and evaluative	Previous 3 or 12 mo

Definition of abbreviations: BDI = Baseline Dyspnea Index; Borg = Borg Scale; CAT = COPD Assessment Test; CIS = checklist individual strength; CRQ = Chronic Respiratory Questionnaire; FACIT = Functional Assessment of Chronic Illness Therapy; MFI = Multidimensional Fatigue Inventory; MRC = Medical Research Council; NR = not reported; PFSDQ = Pulmonary Functional Status and Dyspnea Questionnaire; PFSDQ-M = Pulmonary Functional Status and Dyspnea Questionnaire, modified version; PFSS = Pulmonary Functional Status Scale; SGRQ = St. George's Respiratory Questionnaire; SOBQ = Shortness of Breath Questionnaire; VAS = Visual Analog Scale.

limitations (523). Nevertheless, the NCSI needs further exploration before it can be generally recommended. Finally, in participants with disorders other than COPD, other tools to assess quality of life may be needed to understand the impact of the disease and to measure the impact of pulmonary rehabilitation.

Symptom Evaluation

Individuals with chronic respiratory disease often have symptoms such as dyspnea, fatigue, cough, weakness, sleeplessness, and psychological distress (256, 436, 530–532). Breathlessness is the most commonly reported symptom for individuals with COPD, and may be present at rest and on exertion (533). Reducing dyspnea is an important aim of pulmonary rehabilitation. Dyspnea assessment instruments can be divided into the following: short-term intensity tools (17, 534–540), situational measures (18, 541–547), and impact measures (17, 538, 548–550). Fatigue assessment instruments are divided into short-term intensity tools (534, 539, 551) and impact measures (17, 538, 548, 550, 552–555). Instruments for assessment of multiple symptoms include the SGRQ (17, 515), CRQ (556), and CAT (526, 527). Table 6 shows the psychometric properties, usefulness, time frame, and administration properties of instruments to assess dyspnea, fatigue, and other symptoms.

The presence of symptoms, their severity and impact, are the individual's perception of the sensations, are difficult to measure, and in the context of pulmonary rehabilitation are largely assessed with questionnaires. Questionnaires have typically been developed to discriminate between groups of individuals or to evaluate change in a patient given a specific treatment, such as pulmonary rehabilitation (557, 558).

Depression and Anxiety

Up to 40% of persons with COPD have symptoms of depression or anxiety (559). The prevalence can be higher if disease is advanced and among those using supplemental oxygen (560). An investigation of the prevalence of anxiety and depression in 701 individuals with COPD entering pulmonary rehabilitation found rates of 32% with anxiety and 27% with depression (436). The presence of depressive or anxious symptoms does not necessarily indicate the presence of a depressive or anxiety disorder (according to the *Diagnostic and Statistical Manual of Mental Disorders*, 4th edition [DSM-IV]). Therefore, programs often screen individuals to rule out untreated major depression or anxiety disorders, which may impact participation in, and reduce the benefit from, pulmonary rehabilitation (561).

In a systematic review and meta-analysis, three randomized control trials (n = 269) of comprehensive pulmonary rehabilitation demonstrated a reduction in short-term anxiety and depression (559). Gains in anxiety and depression postrehabilitation are most likely to be observed in those presenting with significant baseline anxiety and depression (26, 202). The National Emphysema Treatment Trial found that anxiety and depression were associated with significantly worse functional capacity as measured by the 6-minute walk distance and maximal exercise capacity (watts), measured on a cycle ergometer (562). In the ECLIPSE (Evaluation of COPD Longitudinally to Identify Predictive Surrogate Endpoints) study, patients with COPD with poor 6MWD had a worse mean SGRQ-C (SGRQ for COPD) activity score; a higher percentage of patients had symptoms of dyspnea (modified MRC [mMRC] $\geqslant$ 2) and depressive symptoms (Center for Epidemiological Studies Depression [CES-D] $\geqslant$ 16), which remained after stratification for GOLD stages and after correction for sex, age, body weight, and country (563).

Some reports incorporating psychotherapy into pulmonary rehabilitation have demonstrated improvement in psychological symptoms (564, 565); however, this area is relatively underexplored. Supervised exercise combined with stress management education in pulmonary rehabilitation may offer management strategies for persons with anxiety and depression (26). Further research is needed to explore how to maintain the impact of pulmonary rehabilitation on anxiety and depression.

Importantly, anxiety and panic can lead to alterations in breathing pattern that often result in severe progressive dynamic hyperinflation that can in turn precipitate frequent emergency department visits and/or outright respiratory failure. Incorporation of breathing training and coping strategies for recognition and management of anxiety/panic in pulmonary rehabilitation has potential to reduce such events and improve patient outcomes.

Functional Status

Functional status refers to the way an individual is able to complete activities that are necessary so that basic physical, psychological, and social needs are met. Measurement of functional status can be multidimensional, with functional capacity referring to the individual's maximal potential to perform and activity. Functional performance is a measure of what an individual actually does in daily life. It is frequently the inability to perform daily activities such as walking, stair climbing, bathing, and so on (149), that drives individuals with chronic respiratory diseases to seek health care advice, and not surprisingly a common goal of individuals attending pulmonary rehabilitation is to improve their ability to successfully complete domestic tasks (including energy conservation techniques) as well as generally to be more physically active (339, 422, 423).

Because a large variability in individual goals and physical limitations is present, walking may not be an important goal for the individual patient; indeed, a large study suggested that up to one-third of individuals do not describe walking as an important goal (149). There are several dimensions to individuals' daily activities, including frequency, duration, degree of difficulty of the activity, and performance satisfaction, which currently are not reflected in any one instrument. Questionnaires can be considered to provide a "snapshot" of activities individuals believe they perform in their daily life and, most importantly, activities they potentially resume as a result of pulmonary rehabilitation. Functional status scales normally consist of a predefined list of activities that have been found to be problematic for individuals with COPD. Individuals then rate their ability to complete these tasks against a defined response scale. Scales commonly employed include the Manchester Respiratory Activities of Daily Living Scale (566), Pulmonary Functional Status and Dyspnea Questionnaire (549) and its shorter version (550), the Pulmonary Functional Status Scale (short form) (567), and the London Chest Activity of Daily Living (LCADL) (568–570).

An alternative approach to assess functional performance is an individualized scale, such as the Canadian Occupational Performance Measure (COPM) (537). The COPM is an individualized measure of functional performance that has been shown to be reliable and sensitive to change after pulmonary rehabilitation (423).

Domains from health status measures also evaluate various aspects of activity such as impact on daily life. Measures with a physical domain include the Medical Outcomes Study (MOS/SF-36) (571), SGRQ (572), Chronic Respiratory Questionnaire (516) and Seattle Obstructive Lung Questionnaire (SOLQ) (573).

Direct observations of problematic activities of daily life are time-consuming, but will provide detailed insight into the performance of problematic activities of daily life by individuals with chronic respiratory disease. Indeed, such observations may even provide insight into the task-related oxygen uptake, ventilation, and symptoms (115). A standardized activity of daily life test has been developed as an outcome measure for pulmonary rehabilitation, requiring the patient to perform a set routine of tasks (574). Exercise capacity measured by field tests is sometimes used as a surrogate measure for functional evaluation. However, activity performance and exercise capacity are distinct domains. For example, field tests such as the 6-minute walk test do not correlate strongly with (self-reported or accelerometer-objectified) physical activity levels (403, 575) or problematic activities of daily life (149).

The choice between standardized functional status scales and individualized measures carries a tradeoff between time involved in completion, and scoring and sensitivity to change in individual individuals. Functional status scales offer ease of completion as these are self-completed, but the activities are predetermined. Individualized measures offer greater insight into individual patient occupational and daily activity limitations, but are more time intensive to complete. Whichever measurement is chosen, reappraisal of functional performance is central to understanding whether changes in exercise capacity after rehabilitation translate into meaningful improvements in the patient's daily life. This is an important area for further study.

Exercise Performance

Exercise training is a major component of pulmonary rehabilitation and therefore exercise performance-related outcomes are consistently used to objectively assess the individual patient's response to pulmonary rehabilitation and to evaluate the efficacy of the intervention. Exercise performance captures the integrated and multisystemic effects of disease severity, including skeletal muscle dysfunction, aging, comorbidity, motivation, and cognition. Exercise performance tests include field walking tests and laboratory treadmill or cycle ergometer tests.

Field walking tests are low-cost, require little equipment, are suitable for evaluation in the community setting, and are considered to be more reflective of daily living than laboratory-based treadmill or cycle ergometer tests. The most established is the self-paced 6-minute walk test (6MWT) (563, 576, 577), which has been used in many pulmonary rehabilitation clinical trials in COPD (91). The 6MWT is also a well-recognized outcome measure in other chronic conditions such as pulmonary hypertension and chronic heart failure (578).

The MID for COPD was previously considered to be 54 m (95% CI, 37–71 m) (506), although other studies support lower values in the range of 25 to 35 m (505, 579, 580). Average improvements after pulmonary rehabilitation are approximately 50 m (91). The test requires a 30-m or greater walking course. There are several sources of variability and a learning effect associated with the measurement (581–584). Using the established, recommended protocol is critical to obtaining reliable, valid, and reproducible test results.

Externally paced field walking tests include the incremental shuttle walk test (ISWT) (585) and the endurance shuttle walk test (ESWT), which are performed over a 10-m course (586). Paced tests are considered more standardized than the 6MWT as the walking speed is set and less influenced by motivation or self-selected pacing. Practice walks are required (585, 586). The ISWT is a true symptom-limited maximal exercise capacity test, and distance walked relates strongly to peak aerobic capacity (587). Improvements in ISWT after pulmonary rehabilitation are consistently reported between 50 and 75 m (17, 456, 460), exceeding the ISWT MID of 47.5 m (588). The ESWT is a constant walking speed test performed at a set speed based on performance during the ISWT, and therefore cannot be conducted independent of the ISWT. There is some evidence to suggest that the ESWT may be more responsive to intervention than the 6MWT or constant-load cycling, at least regarding bronchodilator therapy (589–592). With pulmonary rehabilitation, ESWT increases by at least 180 seconds (or 80–90% of baseline) (460, 497, 586, 592). The MID for the ESWT has been suggested to be between 60 and 115 seconds with bronchodilation (593), although the same investigators were unable to secure an equally precise value of MID using a similar anchor-based approach after pulmonary rehabilitation (593).

Treadmill tests have the advantages of requiring less space than field walk tests and routinely allowing measurement of more complex physiological and metabolic data. Furthermore, speed (and incline) can be adjusted and set, allowing standardization of progressive and constant workload protocols. Existing cardiopulmonary treadmill exercise protocols (e.g., the Bruce protocol [594, 595]) are often too taxing for individuals with chronic respiratory disease or designed for other purposes (e.g., the Balke protocol [596]), although more specific protocols for individuals with COPD have been described (597). The treadmill may provide a less stable platform than the cycle ergometer, and caution is required in older individuals, particularly those with severe arthritis and/or poor balance. The cost and complexity of equipment also limit widespread use, and the MID has not been well established for incremental or endurance treadmill tests. Nevertheless, treadmill-based exercise tests are responsive to pulmonary rehabilitation. Previous studies have shown an improvement in peak aerobic capacity of 0.1 to 0.2 L/min (approximately 10–20% of baseline) (18, 598, 599) with incremental treadmill protocols, and a greater than 80% increase from baseline endurance time with constant speed (high workload) treadmill walking (18, 598).

Like the treadmill, the cycle ergometer requires less space than field walking tests, allows more complex physiological data to be routinely recorded, and is amenable to both incremental and endurance protocols. It provides a more stable platform than the treadmill, and cycling performance may be less affected by obesity than walking (395). However, some argue that cycling may not be familiar to many individuals with chronic respiratory disease, and consequently not as relevant to daily activities. The incremental cycle test permits measurement of peak work rate as well as peak aerobic capacity, and has high reproducibility (600). Estimating peak work load based on sex, age, height, weight, degree of airflow limitation, and 6MWT is inaccurate in individuals with COPD (34), reinforcing the need for an exercise test to assess exercise capacity and prescribe a training regimen.

There is variability in the response to change in peak work rate or peak aerobic capacity with pulmonary rehabilitation (18, 91, 451), averaging at an 8- to 12-W increase in peak work load and a 10–20% improvement in peak aerobic capacity from baseline (18, 598, 599). The MID for incremental cycle ergometer tests has been suggested as a 4-W increase in peak work load (505).

The endurance, constant-load cycle test (usually at 70–85% of baseline peak work load or peak aerobic capacity) is reliable and reproducible in individuals with COPD (601, 602). Endurance time consistently improves with pulmonary rehabilitation by more than 80% from baseline (18, 120, 198, 598, 603). The proposed MID for this test is in the range of 100–105 seconds (604, 605). Other variables during endurance cycling that may provide some indication of exercise performance include isotime dyspnea and minute ventilation, as well as inspiratory capacity, a reflection of dynamic hyperinflation, which have also been shown to be reliable and reproducible in COPD (601).

Most measures of exercise performance are responsive to pulmonary rehabilitation. The choice of test is usually determined by time considerations, cost constraints, availability, and familiarity with the measures, and the objectives of measuring exercise performance. The most commonly reported tests, however, are field-based walking tests. For example, if the objective is to assess the effects on lower limb function, a cycling test may be preferable to a walking test. If the aim is to assess the effects on pulmonary mechanics or breathlessness, a cycling test may not be ideal as leg symptoms or lower limb muscle fatigue may limit exercise performance in individuals with chronic respiratory disease (9). Exercise-induced oxygen desaturation is commonly assessed using a walking protocol (99). When assessing the efficacy of the pulmonary rehabilitation intervention, endurance tests are more responsive, although the incremental test is an essential and necessary prelude to setting constant loads. The MID can be helpful to the clinician; however, caution must be exercised in the interpretation as this may vary according to the severity of the patient's respiratory disease and medical comorbidities, and the nature of the intervention. The change from baseline performance is also important (580, 593). Consideration is also given to the composition and nature of the particular pulmonary rehabilitation program; for example, a cycling performance measure is likely to be more sensitive to change with a predominantly cycle-training intervention (466).

Physical Activity

Physical activity is increasingly considered important in chronic respiratory disease given the benefits of regular physical activity in the prognosis of chronic respiratory diseases (289, 290, 401, 407, 408). Physical activity has been traditionally defined as "any bodily movement produced by skeletal muscles that results in energy expenditure" (94), and this definition has been adapted to physical activity in daily life as "the totality of voluntary movement produced by skeletal muscles during everyday functioning" (94). Thus, physical activity refers to the quantification of physical activity, and differs from closely related concepts such as the adaptations individuals make to carry out activities, or symptoms associated with physical activity (431). This section aims to describe and discuss the use of instruments commonly used to quantify physical activity in daily life before and after pulmonary rehabilitation.

Three types of instruments are commonly used to quantify the changes in physical activity in daily life after pulmonary rehabilitation: subjective methods, measures of energy expenditure, and motion sensors, as described in detail previously (431). In brief, subjective methods (questionnaires, diaries) have been used to quantify duration, frequency, and intensity of physical activity (606, 607). Although results of the physical activity questionnaires may be useful as a group estimate, some degree of misclassification is likely to occur (608, 609). Energy expenditure methods yield estimates of metabolic costs of activity. The doubly labeled water technique yields an estimate of carbon dioxide output over a period of 1–2 weeks, but the methodology is rather expensive, and temporal resolution is limited (610). Portable metabolic measurement systems are capable of accurate assessment of metabolic rate (611), but the requirement that the subject breathe through a mouthpiece or facemask makes long-term monitoring impractical. Motion sensor technology has advanced significantly over the last few years, with a wide variety of equipment available (431). These devices range in complexity from mechanical step counters to monitors capable of long-term electronic data storage. Current-day activity monitors generally rely on accelerometry to record movement and its intensity (420, 612). Multisensor monitors record additional variables relevant to activity (e.g., body temperature, heat flux, heart rate). Some monitors claim to provide an estimate of energy expenditure (613). Accuracy of measurement for all types of activity is likely an unrealistic expectation. The choice among devices requires careful consideration of convenience, patient acceptability, validity, reliability, responsiveness, cost, and purpose of use. In general, measurement periods of 3 days or more have been found useful to appropriately characterize activity patterns and methods of analysis of the resulting data (404). These monitors have proven to be useful in both cross-sectional and interventional studies of activity level and may be seen as reference standards to capture the amount and intensity of physical activity (431). However, they are not able to capture patient perceptions of physical activity. Physical activity instruments generally have been shown to be responsive to pulmonary rehabilitation in individuals with COPD (418).

Finally, the choice between the various types of instruments to measure physical activity as an outcome of pulmonary rehabilitation requires that the users (clinicians, researchers, individuals, and health care providers) clearly define *a priori* which specific domain(s) of physical activity is (are) pursued (614).

Knowledge and Self-Efficacy

Improving individuals' knowledge of how to manage their disease is a foundation of pulmonary rehabilitation, and several new instruments have been developed in this area. Individuals with COPD have information needs that are poorly met (615, 616). For example, a large Canadian survey described by Hernandez and colleagues (615) reported that respondents' knowledge was poor in several domains including the causes of COPD, the consequences of inadequate therapy, and the management of exacerbations. Wilson and colleagues reported similar findings (616). Notable progress has been made in the attempt to evaluate both the information needs of individuals and the efficacy of education programs in pulmonary rehabilitation. The Lung Information Needs Questionnaire (LINQ [617]) was developed to identify the information needs from a patient's perspective. It is a self-administered, 16-item, tick-box questionnaire. The reliability and validity of the LINQ have been established. It has been shown to be effective at detecting the information needs of individuals before pulmonary rehabilitation and is also sensitive to changes after pulmonary rehabilitation (618).

The Bristol COPD Knowledge Questionnaire (BCKQ [619]) is a 65-item self-completed questionnaire that covers 13 topics. The tool was developed to test individuals' knowledge of COPD. This questionnaire has been shown to be reliable, valid, and sensitive to change in both conventional pulmonary rehabilitation programs and education-only interventions (620).

As stated previously, self-efficacy has been described as the belief that one can successfully execute particular behaviors to produce certain outcomes (348). Self-efficacy is rapidly being recognized as an important concept that is likely to be crucial in helping us to understand how improvements in exercise capacity can be translated into greater functional performance and also to increase self-management skills (338, 621). Self-efficacy has also been associated with long-term adherence in pulmonary rehabilitation (622). A number of tools have been developed to measure improvements in self-efficacy after pulmonary rehabilitation (623). Although not routinely reported, the COPD Self-Efficacy Scale (CSES) has been used in a number of studies (624, 625). The PRAISE (Pulmonary Rehabilitation Adapted Index of Self-Efficacy) tool has been shown to be a reliable and sensitive measure of self-efficacy in individuals attending pulmonary rehabilitation (623).

Outcomes in Severe Disease

Clinically significant improvements in exercise capacity and dyspnea after pulmonary rehabilitation are seen in individuals with severe disability (626) and those with chronic respiratory failure (627). In individuals with severe disease, improvements in exercise tolerance and dyspnea after pulmonary rehabilitation have been documented using standard pulmonary rehabilitation outcome measures (458, 626). However, it is possible that not all the domains of quality of life relevant to this group are captured with standard tools. Since the previous Statement there have been new data published regarding the assessment of quality of life in people with chronic respiratory failure.

The Maugeri Respiratory Failure Questionnaire (MRF-28 [627]) was developed to assess quality of life in people with chronic respiratory failure. The MRF-28 has good test–retest reliability in individuals with COPD and chronic respiratory failure, with better construct validity than the CRQ in this patient group (628). The MRF-28 correlates with measures of activities of daily living (628) and is sensitive to changes after pulmonary rehabilitation in people with COPD and chronic respiratory failure. A large prospective study found significant improvements in all domains of the MRF-28 (e.g., daily activity, cognitive function, and invalidity) and the total score after an inpatient pulmonary rehabilitation program (629).

The outcomes described in this section outline key measures used to evaluate the effectiveness of pulmonary rehabilitation. A stronger evidence base and improved tools for outcome measurement have further enhanced the science and quality of pulmonary rehabilitation. Controversies remain regarding evaluation of group versus individual response, the number of characteristics to evaluate, and the timing of outcome evaluation. Further work is needed to determine optimal methods of outcomes measurement for individuals with disorders other than COPD.

Composite Outcomes

In patients with COPD there is increasing interest in the use of multidimensional indices to characterize the severity of the disease and better predict outcomes. Such indices are popular as they combine measures that reflect the pulmonary and systemic manifestations of the disease and have been associated with important clinical outcomes such as hospitalization and mortality (630–633). Arguably the most well-known of these indices is the BODE Index (630), which combines measures of body mass index, airflow obstruction, functional limitation resulting from dyspnea, and functional exercise capacity. As pulmonary rehabilitation reduces dyspnea and increases exercise capacity, the BODE Index is responsive to change after this intervention (634). The I-BODE, in which the incremental shuttle walking test has been used as an alternative measure of exercise for the 6-minute walk test, may also be responsive to pulmonary rehabilitation (635), but this still has to be shown. Other indices (631–633) do not include a measure of exercise capacity; they may be less responsive to change on completion of pulmonary rehabilitation.

PROGRAM ORGANIZATION

Although all pulmonary rehabilitation programs share essential features, the available resources, program setting, structure, personnel, and duration vary considerably among different health care systems (636, 637). Therefore, by necessity, this review of program organization must be general in nature.

Patient Selection

Pulmonary rehabilitation can be adapted for any individual with chronic respiratory disease. There is good evidence that this intervention is beneficial, irrespective of baseline age and levels of disease severity (638–640), although many individuals are not referred until they have advanced disease. Although individuals with severe disease certainly stand to benefit, referral at a milder disease stage would allow for more emphasis on preventive strategies and maintenance of physical activity. Conversely,

TABLE 7. CONDITIONS APPROPRIATE FOR REFERRAL TO PULMONARY REHABILITATION

Obstructive diseases
- COPD (including α_1-antitrypsin deficiency)
- Persistent asthma
- Diffuse bronchiectasis
- Cystic fibrosis
- Bronchiolitis obliterans

Restrictive diseases
- Interstitial lung diseases
- Interstitial fibrosis
- Occupational or environmental lung disease
- Sarcoidosis
- Connective tissue diseases
- Hypersensitivity pneumonitis
- Lymphangiomyomatosis
- ARDS survivors
- Chest wall diseases
- Kyphoscoliosis
- Ankylosing spondylitis
- Posttuberculosis syndrome

Other conditions
- Lung cancer
- Pulmonary hypertension
- Before and after thoracic and abdominal surgery
- Before and after lung transplantation
- Before and after lung volume reduction surgery
- Ventilator dependency
- Obesity-related respiratory disease

Definition of abbreviations: ARDS = acute respiratory distress syndrome; COPD = chronic obstructive pulmonary disease.

individuals with chronic respiratory failure can also benefit from the integrated approach to care found in pulmonary rehabilitation, especially given the fact that these individuals are medically complex and have highly variable individual needs and goals (641).

Frequent reasons for referral to pulmonary rehabilitation include persistent respiratory symptoms (dyspnea, fatigue) and/or functional status limitations despite otherwise optimal therapy. A list of conditions considered appropriate for this intervention is shown in Table 7.

A Clinical Practice Guideline Update for COPD endorsed by the American College of Physicians (ACP), American College of Chest Physicians (ACCP), ATS, and ERS (642) recommended that clinicians should prescribe pulmonary rehabilitation for symptomatic individuals with an FEV_1 less than 50% predicted, and may consider pulmonary rehabilitation for symptomatic or exercise-limited individuals with an FEV_1 greater than 50% predicted. Although abnormalities noted on standard pulmonary function testing are helpful to confirm diagnosis and to characterize the patient's physiologic abnormalities, pulmonary function variables (such as FEV_1) are not the sole criteria for selection for pulmonary rehabilitation. As the severity of chronic respiratory disease, such as COPD, is often influenced by much more than the physiologic derangements alone (335, 435, 541), the current Task Force believes that better indications for pulmonary rehabilitation may exist but need to be studied and confirmed. Indeed, response to pulmonary rehabilitation cannot be predicted by the degree of airflow limitation (110, 639).

Reductions in health status, exercise tolerance, physical activity, muscle force, occupational performance, and activities of daily living, and increases in medical resource consumption, are evaluated in individuals with chronic respiratory disease and used in the selection process. Indications that commonly lead to referrals to pulmonary rehabilitation are listed in Table 8.

Contraindications to pulmonary rehabilitation are few, but include any condition that would place the patient at substantially increased risk during pulmonary rehabilitation, or any condition that would substantially interfere with the rehabilitative process. The majority of individuals are likely to benefit from the educational component, but for some the exercise program may present insurmountable difficulties (e.g., severe arthritis, neurological disorders) or may even put patients at risk (e.g., uncontrolled cardiac disease). In reality, many seemingly contraindicating problems can be addressed or the pulmonary rehabilitation process can be adapted to allow the patient to participate.

TABLE 8. INDICATIONS FOR INDIVIDUALS WITH CHRONIC RESPIRATORY DISEASE THAT COMMONLY LEAD TO REFERRAL TO PULMONARY REHABILITATION

- Dyspnea/fatigue and chronic respiratory symptoms
- Impaired health-related quality of life
- Decreased functional status
- Decreased occupational performance
- Difficulty performing activities of daily living
- Difficulty with the medical regimen
- Psychosocial problems attendant on the underlying respiratory illness
- Nutritional depletion
- Increased use of medical resources (e.g., frequent exacerbations, hospitalizations, emergency room visits, MD visits)
- Gas exchange abnormalities including hypoxemia

Comorbidities

COPD is commonly associated with one or more medical comorbidities. These comorbidities, in part, reflect several of the systemic manifestations of the disease (643, 644), and have significant impact on individuals' symptoms and medical outcomes. Indeed, the importance of comorbidities and systemic manifestations of COPD is reflected in the Global Initiative for Chronic Obstructive Disease definition of COPD, which states that "COPD, a common preventable and treatable disease, is characterized by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and the lung to noxious particles or gases. Exacerbations and comorbidities contribute to the overall severity in individual individuals" (22). It is now clear that COPD is a heterogeneous disease with many manifestations reaching far beyond the lungs. These systemic manifestations are likely to be, at least in part, the result of shared mechanisms that also contribute to the structural and functional changes within the lungs, including systemic inflammation, altered apoptosis, and oxidative stress (643). Inflammation and tissue injury–induced mediator release in the lungs caused by cigarette smoking may spill over into the systemic circulation and lead to tissue injury in other organs. Also, some of the comorbidities seen in individuals with COPD may result from common risk factors such as smoking, rather than resulting from COPD per se. Irrespective of the pathogenesis, it is important to recognize and consider comorbidities and systemic manifestations of COPD, as each has an important impact on patient assessment and management.

Medical comorbidities commonly associated with COPD include cardiovascular disease (hypertension, coronary artery disease, systolic and/or diastolic congestive heart failure, arrhythmias), metabolic disturbances (hyperlipidemia, diabetes mellitus, osteoporosis, and osteoarthritis), skeletal muscle dysfunction, anemia, infections, obstructive sleep apnea, renal insufficiency, swallowing dysfunction, gastroesophageal reflux, lung cancer, anxiety, depression, and cognitive dysfunction (130, 436, 645–655). Although not all individuals manifest all the comorbidities, most individuals have at least one, especially as the disease progresses to a more advanced stages of airflow obstruction. In one analysis of the prevalence of comorbidities associated with COPD, 32% had one other condition, and 39% had two or more concurrent medical conditions (656). Another analysis reported that the median number of comorbidities among individuals with COPD was nine (657).

Medical comorbidities of COPD impact individuals and the health care system in several important ways. First, they increase health care use (658) and health care costs (656). They also lead to increases in symptoms and morbidity, as well as worsen disability and patient-reported quality of life (131, 436, 643, 646, 647, 653, 654, 659). Moreover, they generally increase the complexity of individual individuals' medication regimen, which in turn has the potential to reduce adherence to medications, reduce symptom control, and increase risk of adverse medication effects (660). Importantly, the presence of comorbidities is associated with increased hospitalizations and mortality (661–665). Notably, and particularly important *vis à vis* consideration of individuals for inclusion in pulmonary rehabilitation programs, atherosclerosis begins early in the course of COPD, and tends to worsen with increasing severity of airflow obstruction (666). Cardiovascular disease is the leading cause of mortality for individuals with mild to moderate COPD (667, 668), and individuals are at increased risk of death from myocardial infarction independent of age, sex, and smoking status (669). The presence of COPD also increases the mortality associated with ischemic heart disease (670).

The frequency of multiple comorbidities raises several important practical considerations for the assessment and management of individuals with COPD. To date, no formal guidelines exist to direct a standard approach to diagnosis and assessment of comorbidities in individuals with COPD. Nevertheless, recognition of comorbidities is essential because treating the comorbidities can have a beneficial effect on COPD and vice versa, and early intervention may actually influence the course and prognosis of the disease. For example, statin therapy improves cardiovascular outcomes, and can also reduce COPD exacerbations, improve exercise capacity, and reduce COPD-related and all-cause mortality (671). Inhibitors of angiotensin-converting enzyme may also improve both cardiovascular and COPD outcomes (672).

Physical activity and regular exercise are both recommended and beneficial not only for individuals with COPD, but also for individuals with cardiovascular disease, musculoskeletal disease, obesity, diabetes, peripheral vascular disease, and most other chronic medical conditions (144, 673–676). The benefits of cardiac rehabilitation are well recognized (676, 677), and indeed the profile of skeletal muscle dysfunction is similar between individuals with COPD and those with congestive heart failure (678, 679). Thus, exercise training in the context of pulmonary rehabilitation is extremely important for individuals with COPD and comorbidities.

The presence of comorbidities does need to be considered in the context of choosing individuals for and monitoring individuals within pulmonary rehabilitation programs, to ensure individuals' safety. The prerehabilitation medical history and physical examination evaluate for common comorbidities associated with COPD, because other health care providers may not have considered these issues before referral. Echocardiography is recommended in the GOLD guidelines for individuals with COPD who have signs of congestive heart failure and/or concerning symptoms, such as exertion-related dizziness or chest pain, with or without a history of respiratory failure (22). A baseline resting ECG can be considered, as 20% of the individuals with COPD entering a pulmonary rehabilitation program have ischemic ECG changes (655). Whether a patient requires further cardiac investigations, such as echocardiography or cardiac stress testing (including pharmacologic or exercise-based stress testing), before program enrollment can be decided in consultation with other specialists, including cardiologists, who may be needed to determine safe exercise parameters. A cardiopulmonary exercise test may be considered in individuals who have multiple potential factors contributing to their activity intolerance, to characterize the mechanisms of exercise impairment and guide a safe exercise training prescription. Cardiovascular, orthopedic, and neurologic issues and anemia require particular consideration regarding safe formulation of the exercise plan. Special equipment needs must be considered. Realistic training goals are formulated that meet the individual's daily life needs. Where available, attention is paid to results of recent complete blood counts and chemistries, bone density testing, as well as to any available assessments of cognitive function, psychological well-being, or sleep disturbances. The medical director and/or pulmonary rehabilitation program coordinator interfaces with the primary care provider and/or other specialty care providers to suggest additional diagnostic testing before pulmonary rehabilitation where needed. Screening questionnaires for anxiety, depression, and/or cognitive impairment may be undertaken in the pulmonary rehabilitation baseline patient assessment (436). In some cases, pulmonary rehabilitation care providers may also suggest further interventions (e.g., nutritional counseling, mental health care, cognitive testing, etc.) based on their observations of the patient during pulmonary rehabilitation.

In addition to the issues regarding baseline patient assessment and ensuring patient safety, the presence of comorbidities poses the challenge of fitting individuals with varying and complex needs into a group rehabilitation setting. It also leads to the need for broadened pulmonary rehabilitation staff training to enable and ensure recognition of symptoms of comorbidities such as angina, changes in vital signs, dizziness, near-syncope, unsteadiness, claudication, bone/joint pain, anxiety, poor recall of items taught or difficulty completing questionnaires, poor attentiveness or somnolence during education sessions, or difficulty using selected exercise equipment.

To date, little is known about the impact of medical comorbidities on attendance, completion, and outcomes of pulmonary rehabilitation. One study found that the presence of major medical comorbidities did not adversely impact patient attendance of pulmonary rehabilitation (680). Two retrospective studies suggested that the presence of cardiovascular comorbidity might adversely affect the magnitude of gains made in pulmonary rehabilitation outcomes such as the 6-minute walk test or SGRQ (681, 682). In one of these, a higher Charlson Comorbidity Index (a composite index of multiple comorbidities [683]) was also negatively correlated with 6-minute walk test and SGRQ outcomes (682). However, a subsequent prospective study of 316 individuals monitored over 1 year did not convincingly demonstrate adverse effects of comorbidities on pulmonary rehabilitation outcomes (684). In this study, 62% of the individuals reported comorbidities (hypertension, hyperlipidemia, coronary artery disease, and diabetes were most frequent), and more than 45% of these individuals had significant gains in all pulmonary rehabilitation outcomes tested. However, individuals with two or more comorbidities had lesser gains in SGRQ scores, and persons with osteoporosis had lower gains in the 6-minute walk test. Further research is needed to better understand the relationship between the presence of comorbidities and outcomes of pulmonary rehabilitation.

Rehabilitation Setting

Pulmonary rehabilitation can be provided in inpatient and outpatient settings, and exercise training can also be provided in the individual's home. Outpatient settings include hospital outpatient departments, community facilities, and physiotherapy clinics. Inpatient rehabilitation is offered in hospitals with specialized rehabilitation care for individuals in a stable pulmonary state or after an exacerbation, or it can be initiated during inpatient acute care including intensive care units.

Home-based and community-based exercise training. Although exercise training in pulmonary rehabilitation is traditionally given under direct supervision at the pulmonary rehabilitation center, newer evidence suggests that exercise training in the home environment can be as effective (466, 685). Transferring the site of exercise training into the home setting would be more convenient and broaden the scope of pulmonary rehabilitation. Diversity of service delivery is an emerging area for rehabilitation providers. A number of studies comparing home- and hospital-based programs have been published since the previous Statement (466, 685, 686). The largest study (466) was designed as an equivalence study of (appropriately resourced) home versus outpatient exercise training after a 4-week educational program (e.g., Living Well with COPD). Important outcomes were equivalent for both groups. Interestingly, the groups had a lower than anticipated response in the 6MWT, but both demonstrated equivalent and meaningful improvements in cycle endurance time; the exercise training program was largely cycle based for both groups and this partly explains the results. The efficacy and safety of a home-based exercise training program was also confirmed in a randomized prospective study of 50 individuals with severe COPD who used long-term supplemental oxygen (687), although there were some home visits incorporated into the study. Albores and colleagues tested the effectiveness of a 12-week home exercise program based on a user-friendly computer system (five or more days per week) in 25 clinically stable patients with COPD (688). Significant improvements in exercise performance, arm-lift and sit-to-stand repetitions, and health status scores were noted.

Regarding outpatient programs, there is no strong evidence to suggest any difference in outcome between hospital-based and non–hospital-based programs for individuals with moderate to severe COPD.

A number of factors need to be considered when choosing the rehabilitation setting. These include characteristics of a particular health care setting or system, such as availability of inpatient or outpatient programs, transportation to and from the pulmonary rehabilitation program, availability of long-term programs, and payment considerations including coverage by health care insurance or other payers. If both inpatient and outpatient settings are an option, patient-specific factors need to be considered that include disease severity, stable or unstable (after exacerbation) pulmonary state, the degree of disability, and the extent of comorbidities. These factors determine the extent of supervision needed during physical exercise, the need for different modalities of physical exercise, or the need for more individualized patient education, occupational, psychosocial, and/or nutritional interventions.

As popularity and lack of capacity increase demand, other venues for effective rehabilitation will need to be found. Ideally these will have convenient access yet maintain the quality and effectiveness of conventional programs. New technology also has a part to play in improving services by telemonitoring or provision of remote rehabilitation to inaccessible regions.

Technology-assisted exercise training. Telehealth (telemonitoring and telephone support) is a promising way of delivering health services to individuals, particularly for those living in isolated areas or without access to transportation; however, to date, there is limited evidence of the use of technology for pulmonary rehabilitation. The technology employed ranges from simple pedometers through to mobile phone technology to support the exercise training component of pulmonary rehabilitation. Liu and colleagues (689) reported the application of a remotely monitored endurance exercise training program completed at home. Using a cell phone–based system, music of an appropriate tempo (matching prescribed speed from the ISWT) was loaded to facilitate the correct intensity of training; adherence was also monitored using the global positioning system on the phone. This intervention demonstrated good compliance and significant improvement, compared with the control group, in terms of clinical outcomes for individuals with moderate to severe COPD, with improvements in walking distance (ISWT), inspiratory capacity, and Short Form-12 (SF-12) quality-of-life questionnaire scoring at 12 weeks and persisting until the end of the study period of 1 year. In addition, the intervention was associated with fewer acute exacerbations and hospitalizations, although the study was not powered to detect changes in admission rates. A large controlled trial (n = 409) has shown that a pulmonary rehabilitation program delivered from a large, expert rehabilitation center to smaller, regional centers via videoconferencing resulted in equivalent outcomes for exercise capacity and quality of life (690). One other small trial in individuals with moderate to severe COPD who had completed at least 12 sessions of outpatient pulmonary rehabilitation found that telemonitoring by health care professionals reduced primary care contacts for respiratory issues compared with usual care (691). However, there were no differences between the groups in emergency room visits, hospital admissions, hospital days or contacts with the specialist COPD community nurse team (690, 691).

A systematic review of pedometer feedback in promoting activity in a variety of adult outpatient populations suggests that pedometers are effective in this regard, but only if they employ a physical activity target, such as 10,000 steps (432). A small randomized controlled trial looked at the value of a pedometer (no targets set) with daily phone calls to individuals with COPD; after 2 weeks there was a small increase in 6MWT distance in the intervention group, and an increase in physical activity measured on a activity monitor, but little increase in pedometer activity (692). A much longer activity counseling and pedometer-based intervention was offered to another small group of individuals with COPD; over a 12-week period important changes in activity were observed in the group that initially achieved fewer than 10,000 steps, but not in those individuals who were already fairly active (693). The aspects of counseling and behavior change are critical to the success of the pulmonary rehabilitation program. Indeed, de Blok and colleagues showed that the use of the pedometer, in combination with exercise counseling and the stimulation of lifestyle physical activity, is a feasible addition to pulmonary rehabilitation that may improve outcome and maintenance of rehabilitation results (95).

There is more evidence on the effects of telemedicine for COPD disease management, which may pave the way to "tele-rehabilitation." A systematic review found four randomized trials comparing home telemonitoring with usual care, and six trials comparing telephone support with usual care (694). There is a great deal of variability between studies in terms of interventions and approach. Results showed that home telehealth (home telemonitoring and telephone support) decreased rates of hospitalization and emergency department visits, whereas findings for hospital days varied between studies. The mortality rate tended to be greater in the telephone-support group compared with usual care, but the difference was not statistically significant (risk ratio, 1.21; 95% CI, 0.84 to 1.75) (694).

Program Duration, Structure, and Staffing

There remains no consensus on the optimal duration of pulmonary rehabilitation. Duration of rehabilitation for the individual patient is ideally set by continued progress toward goals and optimization of benefit; in reality it is also influenced by the resources of the program and reimbursement issues. Since the previous Statement, there has been a systematic review of the optimal duration of pulmonary rehabilitation (695). This review, which included five randomized controlled trials (all had been published before the previous Statement), was inconclusive. A meta-analysis was not possible because of the heterogeneity of the program delivery and outcomes. The authors concluded that it is not clear at this stage what the optimal duration of a rehabilitation program might be. However, longer programs are thought to produce greater gains and maintenance of benefits, with a minimum of 8 weeks recommended to achieve a substantial effect (695–697). Optimal duration for the individual can be considered the longest duration that is possible and practical, because programs longer than 12 weeks have been shown to produce greater sustainable benefits than shorter programs (5, 422, 697). Improvement in functional exercise capacity seems to plateau within 12 weeks of the start of the pulmonary rehabilitation program, despite continued training (422, 426, 698, 699). Then again, changes in daily physical activity levels were seen only after 6 months of pulmonary rehabilitation in individuals with moderate to severe COPD (419, 422). These changes had not occurred after 3 months despite marked improvements in exercise capacity and quality of life at that time (422), suggesting that longer program duration is required to achieve change in health-enhancing behavior. To date, pulmonary rehabilitation programs differ in duration among countries, and, in turn, may currently not have the desired duration to achieve change in health-enhancing behavior (4, 419, 636).

The number of sessions per week offered by pulmonary rehabilitation programs also varies; whereas outpatient programs commonly meet 2 or 3 days/week, inpatient programs are usually planned for 5 days/week. The session length per day is generally 1–4 hours, which is usually within the attention span and physical capability of a patient with chronic respiratory disease (4, 636). The impact of once versus twice weekly supervised pulmonary rehabilitation has been reported in a small randomized controlled trial; although the data suggested the interventions were equivalent, both groups failed to make significant improvements in exercise tolerance (700).

There remains no evidence-based guidance for optimal staff-to-patient ratios in pulmonary rehabilitation. In general, staffing for pulmonary rehabilitation is as variable as the structural design. The predominant clinical discipline of the program coordinator and supporting professional staff varies globally, with physical therapists in the majority in Australia, South America, and Europe, whereas respiratory therapists most commonly direct programs in the United States. Despite this variability, there is no one best staffing structure (701). The multidisciplinary nature of pulmonary rehabilitation allows collaboration between enthusiastic and motivated professionals from all areas who have expertise in caring for individuals with chronic respiratory disease. Program staff can vary from a rural hospital with a medical director and a program coordinator as the sole staff to a large academic medical center with an extensive team of rehabilitation professionals. Team size may be less relevant so long as the team members are clinically competent (702) in delivering the essential components of pulmonary rehabilitation and patient safety is maintained. The optimal staff-to-patient ratios in pulmonary rehabilitation are unknown because they have not been studied. The AACVPR uses ratios of 1:4 for exercise training, 1:8 for educational sessions, and 1:1 for complex patients (703); the British Thoracic Society uses ratios of 1:8 for exercise training (with a minimum of 2) and 1:16 for educational sessions (704). These ratios are based on experience and opinion.

Program Enrollment

Up to half (8–50%) (464) of individuals who are offered pulmonary rehabilitation will not enroll in this intervention. A systematic review of 15 articles evaluating adherence in pulmonary rehabilitation (464) determined the following major barriers to enrollment: (*1*) disruption to the patient's established routine; (*2*) travel, transportation, and location of the program; (*3*) influence of the patient's health care provider; (*4*) lack of perceived benefit from the program; and (*5*) inconvenient timing of the program. In addition, social support appears to be an important factor negatively influencing enrollment (705), with those who were divorced, widowed, or living alone less likely to attend. Some factors could be altered to improve uptake, such as greater recognition of the value of rehabilitation by the providers of health care (706), whereas other factors could not be changed (i.e., programs that are geographically not available to individuals or affordable). This is an area that merits further study.

Program Adherence

The definition of noncompletion (i.e., dropout) of a program varies in the literature. Usually attending at least one session is required; however, noncompletion has been defined in one study as declining to participate in the program (705). Noncompletion of a pulmonary rehabilitation program varies considerably from study to study, ranging from 10 to 32% (464). The major issues for noncompletion include illness and comorbidities, travel, transportation, lack of perceived benefits, smoking, depressive symptoms, lack of support, deprivation, and perceived impairment (561, 707, 708). However, it should be noted that the aforementioned factors do not necessarily restrict a patient's entry into a program. For example, programs enrolling current smokers find that many are motivated to stop smoking in the rehabilitation environment and many programs offer strategies for smoking cessation. Likewise, symptoms of depression have been shown to improve after rehabilitation. It is possible, however, that those with the most severe symptoms may benefit from treatment for their depression before or during the program. Although the lack of social support is related to noncompletion of programs, a study (623) found that those living alone had the highest scores of self-efficacy. These findings suggest that those living alone have the internal drive to reach their goals. Of concern is data showing that health care providers are not fully supportive of pulmonary rehabilitation for their patients (706, 709, 710). This provides additional support for the need for greater education of health care providers regarding the comprehensive treatment of individuals with COPD, a group whose members are the major users of rehabilitation.

Graves and colleagues (711) evaluated the effectiveness of a group "opt-in" session before individualized assessment and entry into pulmonary rehabilitation in an observational study using historical controls. The intention was to improve intake and retention rates. Those attending the opt-in session heard directly from the rehabilitation staff a description of both the enrollment process and the general concepts of pulmonary rehabilitation. Intake and retention rates were compared with those from before this session was offered. Because individuals could opt out after the initial session, the percentage attending the individualized assessment (the first official pulmonary rehabilitation session) was actually smaller than before this was offered: 59 versus 75%. However, a significantly higher proportion of individuals who participated in the group opt-in session and began rehabilitation graduated: 88 versus 76%. Dropout rates due to illness were similar in both groups, but dropout rates not due to illness were significantly lower in the group that participated in the opt-in session: 5 versus 15%. Therefore, an opt-in session may need to be considered.

Program Audit and Quality Control

Although the evidence for pulmonary rehabilitation in a research setting is strong, the translation to widespread clinical practice must be supported by a high standard of quality to ensure that individuals are receiving the same effective therapy. This is achieved when individual programs use strict measurement of appropriate outcome measures, transparent audit of progress, and adherence to safety standards. Unless these principles are upheld, rehabilitation will cease to be as effective when demand and capacity increase. Indeed, program-centered outcomes can identify areas that are successful and those that are in need of reorganization or modification to maintain or improve quality. Program metrics worthy of evaluation include program attendance, adherence to home exercise prescription, patient satisfaction, and translation of program components into a self-management program. The need for pulmonary rehabilitation program audits has been recognized internationally and can be program specific or regionally oriented. Please see References 712–716 for region-specific examples.

HEALTH CARE USE

Pulmonary rehabilitation programs have important economic consequences. These might include a decrease in the demand for primary and secondary health care services and medication use, although an increase is also possible because of earlier and more likely problem identification and referral. These potential cost savings are balanced against the program costs, which include staff time, equipment costs, capital costs, and overhead costs. The resulting total cost impact needs to be related to the gain in health outcomes to calculate the incremental cost-effectiveness, which is the additional cost per unit of additional effect, in comparison with an alternative treatment. The most frequently reported cost–effectiveness ratio is the cost per quality-adjusted life-year (QALY) ratio.

Program Costs

The costs of pulmonary rehabilitation programs strongly depend on the duration, frequency, and setting of the program (inpatient, outpatient, community-based, or home-based). At least 11 studies reported the costs of pulmonary rehabilitation programs, which vary considerably (451, 497, 717–725). This is, at least in part, due to the differences in content and duration of the pulmonary rehabilitation programs.

A study that directly compared the costs per session found higher costs per session of a community-based pulmonary rehabilitation program compared with a sessions of a hospital-based pulmonary rehabilitation (497). No studies reported the costs of programs delivered at a patient's home (466).

Impact on Health Care Use

Several studies investigated whether pulmonary rehabilitation leads to a decrease in the number of physician or other caregiver visits, hospital days, and medication use. In general, these studies tend to show some benefit in these important outcome areas. The effect of pulmonary rehabilitation in the perihospitalization period may be more pronounced; these results are discussed earlier in this document. Studies comparing health care use before and after pulmonary rehabilitation found significant reductions in the number of hospital admissions and hospital days (634, 717, 726–729). Pulmonary rehabilitation was also found to significantly reduce emergency room visits (728, 729) and physician visits (728). Results based on randomized trials were less conclusive. Although several studies comparing pulmonary rehabilitation with usual care found a trend toward reduced hospitalizations in the pulmonary rehabilitation group (456, 462, 730), this effect was significant only in two of five trials (17, 460). The largest randomized controlled trial, by Griffiths and colleagues, found a reduction in number of hospital admissions, hospital days, and primary care home visits during the year after a 6-week outpatient rehabilitation program compared with usual care (17). Only one study reported the impact of pulmonary rehabilitation on absence from paid work. No significant difference was found in the number of days of sick leave in individuals with asthma randomized to a 4-week inpatient pulmonary rehabilitation program or usual care (731). However, subgroup analyses of this study found significant reductions in the number of days of sick leave in individuals with a previous physician diagnosis of asthma and in individuals who were non- or ex-smokers at the time of randomization (731).

Impact on Medical Costs

Several studies comparing medical costs before and after pulmonary rehabilitation found a reduction in these costs (717, 721, 728, 729). Reductions in costs for hospitalizations and emergency room visits were found to range between 30 and 90% (717, 721, 729). The estimated costs per patient for acute care, physician, and other health care provider visits and physiotherapy sessions were reported to decrease by more than 50% (728).

Cost-Effectiveness

To the best of our knowledge, only four studies have presented a full economic evaluation of a pulmonary rehabilitation program (497, 720, 722, 723). Goldstein and colleagues reported the cost-effectiveness of an 8-week inpatient rehabilitation program followed by 16 weeks of outpatient training in individuals with severe stable COPD. The costs required for a single patient to achieve the minimal clinically important improvement in various components of the Chronic Respiratory Questionnaire were Can $28,993 for mastery, Can $38,270 for emotional function, Can $47,548 for dyspnea, and Can $51,027 for fatigue (720). A 1-year study by Griffiths and colleagues presented the cost-effectiveness of a 6-week outpatient rehabilitation program and found this program to be more effective (+0.03 QALY per patient [95% CI, 0.002 to 0.058]) and potentially cost saving compared with standard care (–£152 [95% CI, –881 to 577]) (722). In contrast to the dominance of pulmonary rehabilitation in the study by Griffiths and colleagues, the 2-year incremental cost–effectiveness ratio of an interdisciplinary community-based program for individuals with COPD (INTERCOM program) compared with usual care was found to be €32,400 per QALY gained (723). This cost–effectiveness ratio decreased to €8,400 per QALY gained if five individuals referred to inpatient rehabilitation during the study were excluded from the analyses. Waterhouse and colleagues reported an economic evaluation performed alongside a randomized trial with a 2 × 2 factorial design, investigating the effect of 6 weeks of community-based pulmonary rehabilitation versus outpatient hospital-based rehabilitation and telephone follow-up versus standard follow-up to maintain effects (497). Although both programs resulted in significant improvements in exercise capacity and generic and disease-specific health-related quality of life, no significant differences were found between the hospital and community-based groups and the two different types of follow-up in the short term or after 18 months. The gain in QALYs was 0.03 (95% CI, –0.13 to 0.07) per patient and costs were £867 (95% CI, –631 to 2,366) lower in the community-based group compared with the hospital-based group. Attrition was high in this study, with outcomes analyzed only for about 50% of randomized individuals.

Comparison of the various estimates of cost-effectiveness is complicated by differences in the content and intensity of pulmonary rehabilitation, outcome measures, target population, and comparator. More studies thoroughly investigating the cost-effectiveness of pulmonary rehabilitation programs in terms of costs per QALY gained are needed to reach definite conclusions.

MOVING FORWARD

This Task Force identifies the following major areas that need to be addressed further in the coming years:

1. Increasing the scope of pulmonary rehabilitation: This includes further defining its efficacy in patients with diseases other than COPD, in those hospitalized for exacerbations, and in those with critical illness. Furthermore, it is important to explore the disease-modifying potential of pulmonary rehabilitation in those with milder chronic respiratory disease.
2. Increasing the accessibility to pulmonary rehabilitation: This includes developing robust models for alternative forms of delivery, defining the role of telehealth and other new technologies, advocating for funding to ensure viability of existing pulmonary rehabilitation programs, fostering the creation of new programs, increasing clinician and patient awareness of the benefits of pulmonary rehabilitation, and identifying and overcoming barriers to participation.
3. Optimizing pulmonary rehabilitation components to influence meaningful and sustainable behavior change: This includes further developing collaborative self-management strategies and ways to translate gains in exercise capacity into increased physical activity.
4. Further understanding and addressing the heterogeneity and multisystem complexity of COPD and other forms of chronic respiratory disease: This includes defining phenotypes and using this information in optimizing the impact of the pulmonary rehabilitation.

This official statement was prepared by an *ad hoc* subcommittee of the ATS Assembly on Pulmonary Rehabilitation and the ERS Scientific Group 01.02 "Rehabilitation and Chronic Care."

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