

# **Exercise & Sports Science Australia (ESSA) position statement on exercise and chronic obstructive pulmonary disease.**

**Abbreviated Title.**      Exercise Guidelines for COPD

**Contact Information.**

## **ABSTRACT**

*OBJECTIVES:* Chronic obstructive pulmonary disease (COPD) results in airflow obstruction and a marked reduction in exercise capacity and health-related quality of life (HRQoL). Affecting over 1 in four Australians aged over 75 years, COPD remains one of the major causes of disability and death in the world. To date there have been over 80 randomised controlled trials examining the role of exercise training in a range of settings for individuals with COPD. This review will synthesise existing literature and provide health practitioners with broad evidence-based guidelines for exercise-training in this growing population.

*DESIGN:* Position stand.

*METHODS:* Synthesis of randomised controlled trials of exercise training and of existing guidelines for exercise in COPD. Systematic reviews of alternative modes of exercise training will also be reviewed.

*RESULTS:* There is convincing evidence that in adults with COPD, exercise-training improves exercise capacity, decreases symptoms such as dyspnoea and fatigue, and improves HRQoL. There is emerging evidence in this population that alternative modes of exercise training such as high intensity interval training (HIIT), aquatic based therapy, tai chi and neuromuscular electrical stimulation improve exercise outcomes when compared to no exercise.

*CONCLUSIONS:* For individuals with COPD, an exercise program of aerobic and strength exercises delivered over at least an 8-week period, that engages lower and upper body skeletal muscles, will deliver significant health improvements. Programs should be individualised, take into consideration relevant co-morbid conditions and be delivered appropriately qualified health practitioners experienced in clinical exercise prescription.

## 1. BACKGROUND

Chronic obstructive pulmonary disease (COPD) is characterised by airflow obstruction that is not fully reversible<sup>1</sup> and an abnormal inflammatory response of the lungs<sup>2,3</sup>. Airflow obstruction is the result of changes in the airways and parenchyma associated with emphysema and chronic bronchitis<sup>2,3</sup>. The emphysematous changes result in the destruction of alveolar walls and their attachments, compromising the patency of the airways and leading to airflow obstruction. The accompanying enlargement of the air spaces of the lung distal to the terminal bronchiole also reduce the area available for gas exchange. Chronic bronchitis is a hyper-secretory disorder characterised by excessive production and secretion of mucus within the bronchial tree. Additionally, chronic inflammation in the small airways leads to injury of the airway wall. The injury-repair cycle consequently results in structural remodelling of the airway walls and increased scar tissue and collagen formation, thus narrowing the airway lumen and causing “fixed” airway obstruction<sup>4</sup>.

In 2020, COPD is estimated to be the third-leading cause of death worldwide and is a major cause of lost disability adjusted life years<sup>5</sup>. In Australia, 7.5% of individuals aged over 40 years are affected by COPD that is at least of moderate severity, with the prevalence increasing with age (29% prevalence in adults aged  $\geq 75$  years)<sup>6</sup>. The risks for developing COPD encompass host factors and environmental exposures, and development of the disease is usually attributable to a combination of both. Host factors that exclusively contribute to COPD (e.g.  $\alpha 1$ -antitrypsin deficiency) are rare (less than 1%<sup>7</sup>). Thus, COPD is typically associated with environmental exposure to noxious particles and gases. Cigarette smoke is the primary risk factor, with 20-25% of smokers developing COPD<sup>8</sup>.

Cardinal symptoms of COPD include shortness of breath (dyspnoea), particularly on exertion, chronic cough and excess sputum production. Diagnosis is established through spirometry<sup>5</sup>, with a post-bronchodilator forced expired volume in one second (FEV<sub>1</sub>) and forced vital

capacity (FVC) ratio ( $FEV_1/FVC$ ) of less than 0.7 confirming the presence of persistent airflow obstruction<sup>5</sup>. Extrapulmonary symptoms such as cachexia (muscle wasting) and anaemia may occur, due at least in part to the systemic inflammatory response<sup>9</sup>. There is no cure for COPD; however, the recently updated COPD plan (COPD-X) provided by the Lung Foundation Australia provides an evidence-based stepwise plan for multidisciplinary management<sup>10</sup>. Management of COPD primarily entails smoking cessation and removal or modification of risk factors. Symptom reduction and exacerbation risk minimisation is also provided through short- and long-acting bronchodilator therapy (short and long acting beta agonists [SABA and LABA]; short and long acting antimuscarinics [SAMA and LAMA]) which, when combined with inhaled corticosteroids (ICS) are known as preventers. During an exacerbation, oral glucocorticosteroid may be prescribed. Referral for exercise training, typically to a pulmonary rehabilitation program, is also recommended for individuals with symptoms that limit participation in activities of daily living<sup>10,11</sup>.

## **2. EXERCISE INTOLERANCE AND DISABILITY IN COPD**

Individuals with COPD have reduced exercise capacity and poor health-rated quality of life (HRQoL)<sup>10</sup>. The progressive nature of the disease results in increased dyspnoea on exertion, leading to a vicious cycle of inactivity and deconditioning. Physical activity levels are markedly reduced<sup>12</sup>. The gradual deterioration in exercise capacity may be accompanied by psychosocial issues such as social isolation, depression, anxiety, and loss of independence, that exert an increasingly deleterious effect upon HRQoL<sup>5,13</sup>.

The systemic inflammation contributes to extrapulmonary manifestations and comorbid conditions such as cardiovascular disease, lung cancer and skeletal muscle dysfunction<sup>2,9,14,15</sup>. Both ventilatory limitation and skeletal muscle dysfunction contribute to the increased exertional dyspnoea and reduced exercise capacity<sup>15,16</sup>. Cardiovascular limitations,

nutritional deficiencies, and psychological factors may also play a role in the reduction in exercise capacity<sup>13,14</sup>.

### ***Ventilatory limitation***

Individuals with COPD are ventilatory limited, typically due to expiratory airflow limitation<sup>17,18</sup>. Gas trapping at rest and further gas trapping during exercise results in increased end-expiratory lung volumes on exertion (dynamic hyperinflation)<sup>17,18</sup>. As a result, many individuals with COPD breathe at higher operational lung volumes, placing elastic and threshold loads on the inspiratory muscles<sup>15,17,18</sup>. Tidal volume expansion is limited, meaning that ventilation is increased primarily through increased breathing frequency. Gas exchange abnormalities can also contribute to ventilatory limitation. Excess physiological dead space, intrapulmonary shunting, ventilation to perfusion mismatch and impaired lung diffusion capacity contribute to hypoxaemia, hypercapnia, and an increased ventilatory demand for a given level of physical activity<sup>4</sup>. Hypoxic vasoconstriction and structural remodelling of the pulmonary vasculature may also increase pulmonary vascular resistance and right ventricular afterload, while dynamic lung hyperinflation may impair right ventricular preload and limit cardiac output during exercise<sup>17</sup>.

### ***Skeletal muscle dysfunction***

It is now well-recognised that changes in peripheral skeletal muscle function contribute to the disability associated with the COPD<sup>15</sup>. Lower limb fatigue and discomfort are important contributing factors to exercise intolerance in people with COPD<sup>19</sup>. Studies have shown muscle fibre atrophy, changes in fibre composition with a selective loss of type I fibres<sup>20,21</sup>, reduced capillary to fibre ratio<sup>21</sup>, and a reduction in oxidative enzyme activity<sup>22</sup> of skeletal muscle in people with COPD. These changes contribute to an early reliance on anaerobic metabolism during exercise resulting in an early onset of lactic acidosis, a greater non-

metabolic carbon dioxide production and excessive ventilatory response<sup>15</sup>, which further contributes to the ventilatory limitation in COPD.

### **3. THE ROLE OF EXERCISE TRAINING IN THE MANAGEMENT OF COPD**

Therapeutic exercise, delivered through an exercise-based rehabilitation program such as pulmonary rehabilitation, is recognised as an essential component of the management of people with COPD with convincing evidence that it improves exercise capacity, decreases symptoms such as dyspnoea and fatigue, and improves HRQoL<sup>23,24</sup>. The average magnitude of change in these outcomes exceeds the threshold for the minimal clinical important difference. Moreover, there is evidence that well implemented exercise-based rehabilitation programs, embedded into comprehensive pulmonary rehabilitation, result in reduced hospitalisations and long-term health economic benefits<sup>25,26</sup>.

A summary of the RCTs examining exercise-based rehabilitation is shown in Table 1. A more detailed summary of these RCTs is included in Supplementary Table. The primary source for this Table are the 65 RCTs from the recent Cochrane review by McCarthy et al<sup>23</sup> (which has now closed) and an additional search using the same search terms and inclusion criteria as the Cochrane review date (26<sup>th</sup> March, 2014) up until March, 2019. This search yielded an additional 1364 articles which, following a title, abstract and article review, resulted in a further 20 studies (see Supplementary Table).

#### ***Alternative and adjuncts to ‘traditional’ exercise training programs***

##### ***High intensity interval training***

There has been a reasonably large body of work examining the role of high intensity interval exercise (HIIT) training in COPD<sup>27,28</sup>. This type of training is predominantly undertaken on a cycle ergometer whereby repeat short bouts of exercise, prescribed at intensities at or near  $W_{peak}$ , are separated by periods of rest or lower intensity exercise<sup>27</sup>. Studies in people with

COPD compared short duration (exercise period < 180s), high intensity (80-150%  $W_{peak}$ ) interval exercise with traditional continuous exercise training<sup>27,28</sup>. However, despite training at higher intensities, when interval and continuous exercise were matched for total amount of work completed, there were no greater improvements in exercise capacity, HRQoL or any greater physiological adaptations with HIIT in COPD<sup>27,28</sup>. It should be noted however, that when interval exercise is prescribed at the same absolute intensity as continuous exercise (i.e. not HIIT) then individuals with COPD are able to achieve greater amounts of work, demonstrate less dynamic hyperinflation, desaturate less and are less breathless<sup>29</sup>. Interval exercise, prescribed at the same intensity as continuous exercise, has been used for individuals unable to tolerate continuous bouts of exercise training<sup>11,23,26</sup>.

#### *Inspiratory muscle training*

Several of the studies used inspiratory muscle training (IMT) as an adjunct to whole-body therapeutic exercise programs. In people with COPD, IMT applied at loads that exceed 30% of the maximum inspiratory pressure (MIP) improved the pressure-generating capacity of the inspiratory muscles<sup>30</sup>. However, the clinical efficacy of IMT in terms of exercise capacity, dyspnoea and HRQoL, over and above the benefits achieved with therapeutic exercise alone, remains contradictory<sup>31,32</sup>. Whilst an earlier meta-analysis suggested that IMT may convey some clinical benefit<sup>33</sup>, two large RCTs published in 2018 reported negligible benefit of adding IMT to a program of therapeutic exercise in terms of improvements in exercise capacity and HRQoL, even in those with more severe disease<sup>31,32</sup>.

#### *Exercise in water, active mind-body movement therapies and neuromuscular electrical stimulation*

Several systematic reviews have been published examining alternative approaches or adjuncts to therapeutic exercise in this population. Cochrane reviews have examined the role

of water-based exercise<sup>34</sup>, active mind-body movement therapies (e.g. yoga, tai chi)<sup>35,36</sup> and neuromuscular electrical stimulation (NMES)<sup>37</sup> in COPD.

Exercising in water has been proposed as an alternative to land-based exercise and provides buoyancy to support body weight, resistance to movement and a warm environment<sup>34</sup>. Water-based exercise is likely to be especially relevant for those who experience discomfort with walking and/or cycling due to comorbid conditions (e.g. osteoarthritis)<sup>34</sup>. In people with COPD, when compared to no exercise, water-based exercise programs have been shown to improve both exercise capacity and HRQoL<sup>34</sup>. The magnitude of this change is similar to that seen with land-based exercise training.

Studies using active mind-body movement therapies such as Tai Chi have shown improvements in HRQoL when compared to an unsupervised exercise program<sup>36</sup>. One study in people with COPD reported that, compared to no exercise, a 12-week program of Tai Chi conducted twice weekly, increased both HRQoL and endurance shuttle walk distance<sup>38</sup>. The exercise intensity of Tai Chi corresponded to approximately 50% of  $VO_{2\text{reserve}}$  ( $VO_{2\text{peak}} - VO_{2\text{rest}}$ )<sup>38</sup>. However, adding Tai Chi to a traditional exercise program does not appear to provide any additional benefit<sup>35</sup>.

Adding NMES of the peripheral muscles has also been trialled as a strategy to improve exercise capacity. This intervention involves placing conductive pads over the muscle (usually the quadriceps) that are then attached to a stimulation unit. Increasing the stimulation activates the intramuscular nerve branches and muscle fibres resulting in muscle contraction. In COPD, when compared to no exercise, the application of NMES to the quadriceps muscle improves peripheral muscle strength and endurance, as well as exercise capacity<sup>37</sup>. Nevertheless, there is little evidence to suggest that combining NMES with a traditional exercise program provides additional benefit over and above what is achieved with traditional

exercise alone<sup>37</sup>. The primary benefit for NMES would appear to be for severely debilitated individuals, unable to participate in more-traditional whole-body exercise programs<sup>37</sup>.

Whilst there is a growing body of evidence for alternative approaches to exercise training in COPD, it is also worth noting that: (i) reviews of alternative approaches to therapeutic exercise only include between 5 and 12 studies<sup>34,37</sup> (i.e. much less than the 65 included in the review of more traditional exercise training<sup>23</sup>), (ii) many of the conclusions are based on low-quality evidence, and (iii) the estimate of the effects were accompanied by wide 95% confidence intervals, which offer little precision for the prescribing therapist.

### ***Outcome measures***

Common assessments used to evaluate the effect of exercise training on exercise capacity include the 6MWT, incremental shuttle walk test (ISWT) and the cardiopulmonary exercise test (CPET)<sup>39</sup>. Regarding the assessment of other constructs, such as HRQoL, the St George's Respiratory Questionnaire (SGRQ) and the Chronic Respiratory Disease Questionnaire (CRDQ) are the most commonly used disease-specific measure (Supplementary Table). Further, the COPD Assessment Test (CAT) is also a popular tool to assess health status in this population. The assessment of peripheral muscle strength, though likely to be important, is less commonly measured. In clinical practice, hand-held dynamometry is often used to quantify upper limb muscle strength, including grip strength. However, the distribution of muscle weakness in people with COPD is not uniform, and the strength of upper limb musculature, may not accurately reflect lower limb muscle strength<sup>15</sup>. Assessment of lower limb muscle strength, such as the quadriceps, can be challenging. Hand-held dynamometry has been used in non-laboratory-based settings however the technique requires some assessment skill. Accurate assessment of quadriceps often requires more sophisticated equipment such as a commercial dynamometer (eg Biodex®).

#### 4. LIMITATIONS OF EVIDENCE

Whilst the reviews examining the role of traditional and alternative/adjunct approaches to therapeutic exercise training in people with COPD<sup>23,34-36,40</sup> suggest a benefit for exercise capacity and HRQoL, the quality of evidence included in these reviews was typically downgraded. This was due, at least in part, to the high risk of performance bias and inconsistency in results (i.e. statistical heterogeneity)<sup>41</sup>. Further trials of therapeutic exercise versus usual care cannot change these limitations and the most recent Cochrane review of therapeutic exercise is now closed<sup>41</sup>. Rather than examining the effect of exercise training (compared with no exercise training) on outcomes such as exercise capacity, HRQoL and symptoms, future work should focus on addressing issues such as; (i) the effect of therapeutic exercise on survival, (ii) strategies to maintain the benefits achieved following an exercise program and, (iii) optimising the translation of benefits achieved following an exercise program into increased participation in physical activity during daily life<sup>41</sup>.

A further possible limitation to the evidence is that many of the RCTs of therapeutic exercise in COPD exclude people with co-morbid conditions likely to limit exercise capacity, such as severe osteoarthritis, cardiac disease and peripheral vascular disease<sup>23</sup>. However, it is well recognised that people with COPD present with multiple co-morbid conditions with previous studies suggesting that 29% of people with COPD referred to a rehabilitation program had five or more co-morbid conditions<sup>42</sup>. Therefore, the estimate of the effect of therapeutic exercise provided to date, may be overly ambitious for the people who are typically referred to a clinical therapeutic exercise program.

Another consideration when examining the evidence for therapeutic exercise is that the estimate of the effect relates to between-group differences. Even though, in a group of people with COPD, an exercise intervention is likely to produce large, clinically meaningful improvements in exercise capacity, HRQoL, dyspnoea and fatigue there is clear evidence that

the response varies considerably between individuals<sup>43</sup>. In fact, nearly half of all people with COPD who complete an exercise-based rehabilitation program have a moderate or minimal response<sup>43</sup>. Further work is needed to identify strategies and approaches that allow non-responders to become responders to exercise training.

## **5. SPECIAL CONSIDERATIONS**

One of the more contentious issues for clinicians involved in the delivery of an exercise-based rehabilitation program for COPD is how to manage transient exertional desaturation. It is generally accepted that those who have met the criteria for long-term oxygen therapy (LTOT) should use supplemental oxygen when exercising<sup>11</sup>. However, the challenge is managing those who have acceptable arterial oxygen saturation at rest and do not meet the requirements to be prescribed LTOT, but demonstrate severe transient exertional desaturation. Whilst most would argue that severe transient exertional desaturation is something to be avoided, there is no clear evidence that severe transient exertional desaturation is dangerous<sup>44</sup> or that using supplemental oxygen during exercise training to minimise this desaturation is beneficial<sup>45-47</sup>. Indeed, a recently completed study, the largest RCT to date, examined exercise training combined with either oxygen supplementation or sham (air) in individuals with COPD who desaturated below 90% during a 6MWT, found no benefit in training on oxygen in terms of changes in exercise capacity or HRQoL<sup>48</sup>. There is wide disparity in the management of this issue and the level of desaturation tolerated by clinicians delivering a pulmonary rehabilitation program appears arbitrary<sup>49</sup>.

### ***Uptake, adherence and completion***

Despite the strong evidence for the benefits of exercise training offered as part of a pulmonary rehabilitation program, accessing these programs is a major challenge.

Astonishingly, studies conducted in seven countries over 18 years (1995–2013) show the proportion of people living with COPD who access these programs is <2%<sup>50</sup>. Of those

referred, one third did not attend their initial assessment and just less than half of those who commenced completed the program<sup>50</sup>. A recent review extracted data from 48 studies to provide an overview of factors which influenced referral, uptake, attendance and/or completion of pulmonary rehabilitation programs<sup>51</sup>. Based on the results of this study, some strategies that may optimise participation in pulmonary rehabilitation are; (i) improved knowledge of referral processes, (ii) positive influence of referring doctor, (iii) improved understanding of perceived benefits and safety of exercise for this population and (iv) overcoming issues related to transport and parking costs associated with attending hospital-based programs.

## **6. RECOMMENDATIONS**

Most therapeutic exercise programs for COPD are based on recommendations developed by the American College of Sports Medicine (ACSM)<sup>52</sup>, The American Thoracic Society(ATS)/European Respiratory Society (ERS)<sup>11</sup> and/or the American Association of Cardiovascular and Pulmonary Rehabilitation (AACVPR)<sup>53</sup>. Evidence based guidelines have also been published by the Lung Foundation/Thoracic Society of Australia and New Zealand (TSANZ)<sup>25</sup>, the British Thoracic Society (BTS)<sup>54</sup> and the Canadian Thoracic Society (CTS)<sup>55</sup>. For a comparison of these guidelines readers are directed toward a recently published, comparative review of major guidelines by the AACVPR<sup>56</sup>. From the practical perspective of establishing and delivering a therapeutic exercise program, readers are directed to the Lung Foundation of Australia and the Pulmonary Rehabilitation Toolkit<sup>57</sup>. This peer-reviewed, updated site provides an evidence-based approach for the management of COPD, including the prescription of therapeutic exercise.

The recommendations (below) developed for Exercise and Sports Science Australia have been based primarily from the information obtained from the summary of RCTs (Supplementary

Table). In developing these recommendations, the authors have also consulted guidelines from the ACSM, ATS, ERS AACVPR, TSANZ, BTS and CTS<sup>11,52,53,56,25,54,55</sup>, as well as the Pulmonary Rehabilitation Toolkit<sup>57</sup>. A summary of exercise recommendations is included in Table 2.

Given the likelihood of co-morbid conditions such as cardiovascular disease and the older age of the participants, it is recommended each participant undergoes a medical review prior to commencing an exercise program. Medical therapy should be optimised and participants should have received advice or commenced on appropriate risk management programs such as smoking cessation or removal from exposure to other environmental hazards contributing to COPD<sup>10</sup>.

Aerobic exercise should be prescribed for upper and lower limbs. Lower limb exercise, such as walking or cycling, is recommended. Walking exercise can be undertaken as free (ground-based) walking or on a treadmill if attending a gym or using at home. Walking speeds can be calculated using the average speed achieved during the 6MWT. A walking speed equivalent to 80% of the average 6MWT speed is recommended at the start of an exercise program<sup>57</sup>. Training work rate on a cycle ergometer can be set at either a percentage of the  $W_{peak}$  measured during a CPET or estimated from equations derived from the 6MWD<sup>58</sup>. Intensity of exercise can also be set based on the severity of dyspnoea or rating of perceived exertion (RPE) using either the modified Borg scale (3-4) or the original Borg scale (12-14), respectively. After the initial prescription, intensity is usually titrated according to symptoms by increasing walking speed and grade (if using a treadmill) and/or the power on the cycle ergometer. Heart rate appears to be rarely used guide exercise intensity in people with moderate to severe lung disease<sup>23,57</sup>. High intensity interval training can be also be prescribed provided the participant is able to sustain short duration exercise at or near a peak power. We would recommend that

the duration of exercise is kept short, one minute or less, to minimise an excessive ventilatory response which may limit further exercise.

The inclusion of stretching and flexibility exercises in a rehabilitation program for COPD has been recommended by the ACSM, ATS and the AACVPR<sup>11,52,53</sup>, despite there being no clinical trials in this area. Slow movements that involve sustained stretch for up to 60s for the major muscle groups of the upper and lower limb that can be conducted either at the beginning and/or the end of the rehabilitation program. Given that individuals with COPD are older, balance exercises could also be included with the flexibility program<sup>59</sup>.

Water-based exercise may also be prescribed, particularly for those with underlying musculoskeletal conditions which may limit exercise activity due to pain. For individuals with severe disease and more debilitated NMES may be useful. Where possible, these modalities should be considered as a 'bridge' to allow the person to participate in whole-body exercise training.

With regards to monitoring, it is recommended that both symptoms (i.e. dyspnoea) and oxygen saturation are monitored during exercise training. Dyspnoea can be monitored using the modified Borg scale adapted for breathlessness<sup>60</sup>. Based on current evidence, the absolute level of desaturation at which an individual should stop exercising remains arbitrary. The Australian Lung Foundation notes that individuals who desaturate below 88% even when participating in interval training should be assessed to determine the benefit of supplemental oxygen<sup>57</sup>. On the other hand, the technical standard for field walking tests in chronic respiratory disease endorsed by the ATS/ERS suggest ceasing an exercise test when SpO<sub>2</sub> is ≤ 80%<sup>39</sup>. Yet, a recent review of 549 individuals with chronic lung disease found that oxygen desaturation below 80% during the 6MWT was not associated with an increased risk of adverse event<sup>44</sup>. We would recommend that both symptoms and SpO<sub>2</sub> are constantly

monitored throughout testing and training. We recommend different criteria for the cessation of exercise, for exercise **testing** vs exercise **training**. Ceasing exercise **testing** when  $SpO_2$  is  $\leq 80\%$  would be safe and conservative approach<sup>39</sup>. Exercise testing may be recommenced when  $SpO_2$  is  $>85\%$ <sup>39</sup>. However, during aerobic **training**, we would recommend that clinicians apply higher thresholds for the minimal acceptable level of  $SpO_2$ , such as  $<85\%$  or  $<88\%$  and recommence exercise when  $SpO_2$  is  $>90\%$ . During both testing and training, in addition to monitoring  $SpO_2$ , clinicians also need to closely monitor symptoms which may be associated with a cardiac limitation, such as excessive shortness of breath, dizziness and chest tightness or pain, and be guided by these when deciding to impose a rest and/or cease exercise. The decision to halt exercise testing or training should be made based on the evaluation of all signs and symptoms, not just the degree of desaturation<sup>39</sup>.

The optimal exercise training frequency and duration is three to five times per week (often achieved as a combination of supervised and unsupervised sessions) ideally for 40 to 60 min per session. Shorter duration (20-40 min) programs could be used at commencement. Individuals with COPD initially unable to complete a continuous exercise bout due to the onset of intolerable symptoms should complete shorter bouts of interval exercise as tolerated to achieve a total exercise time of 20 to 40 min per session. As exercise tolerance increases, interval exercise can be progressed, by increasing the exercise period duration and decreasing the duration and/or frequency of the rest periods. Total exercise time can also be extended to 40-60 minutes as tolerance increases. Upper limb exercise can be prescribed using arm ergometry or undertaking 'shelving' (i.e. lifting small weights from waist to over the shoulder height) tasks. The special considerations are outlined in Table 2.

Respiratory medications should be optimised prior to commencing an exercise program<sup>10</sup>. Regular bronchodilator therapy should be continued when undertaking exercise program; most participants do not require additional short-acting bronchodilators prior to exercise.

Table 3 outlines the common COPD medications and the potential side effects which may affect exercise performance.

Resistance exercise is also recommended to improve peripheral muscle strength and endurance for upper and lower limbs. Where available, weight machines and free weights should be employed to ensure an accurate prescription. The intensity can be fixed as a percentage of a repetition maximum (RM); however, the RPE could also be used to set the training intensity. More 'functional' exercise such as step-ups and sit to stands can also be prescribed to improve strength, these being particularly useful for home-based exercise programs. Duration and frequency details are outlined in Table 2.

We would endorse the inclusion of home-based program consisting of both aerobic and resistance exercises for the upper and lower limbs. Depending on the frequency of the supervised exercise program, the home-based program could be undertaken at least two to three days per week and consist of at least 30 minutes of walking exercise and functional strengthening exercises for the upper and lower limb. On completion of a supervised program, participants should be encouraged to continue with a maintenance exercise program for three to five days per week. Walking at least 30 minutes in duration is recommended, at a similar intensity prescribed during the supervised exercise program. It is also recommended that participants continue with a once weekly supervised exercise class or have their unsupervised maintenance program reviewed every three to six months<sup>57</sup>.

## **7. CONTRAINDICATIONS**

Both the ATS/ERS note that there are a few contraindications to therapeutic exercise in COPD<sup>11</sup>. As with any exercise program, however, absolute and relative contraindications for exercise, as outlined by the ACSM, should be observed<sup>52</sup>. These include neurological,

orthopaedic and cardiac disorders which may put the patient at unacceptable risk with performing exercise.

## **8. SUMMARY**

For individuals with COPD, exercise-based rehabilitation is a highly effective, safe, non-invasive therapeutic treatment option for improving exercise capacity and HRQoL. Exercise has been prescribed for individuals with severe disease in both an outpatient and inpatient setting. Challenges for this intervention remain; limited availability of supervised rehabilitation programs, poor referral and uptake patterns constrain the potential positive effects. Improved access and greater uptake of supervised exercise programs will improve outcomes and make a profound difference to the HRQoL for individuals with COPD.

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**Table 1. Summary of exercise training doses reported in randomised controlled trials of exercise training in people with chronic obstructive pulmonary disease**

Number of Studies	N	Mean Age (yr)	Mean FEV <sub>1</sub> (%)	Setting	Mode	Measures used to prescribe exercise intensity	Frequency (days/wk)	Duration (min)	Length (wk)	Measures used to evaluate program
83	4,502	65±4 (52 to 77)	46±13 (27 to 90)	IP/OP/ Comm/ Home	ULT; LLT; IMT; STR	W <sub>peak</sub> ; %VO <sub>2peak</sub> ; RPE; modified BORG; 6MWT speed; ISWT speed; RM	3.2 ± 1.6 (1 to 7)	55 ± 24 (30 to 120)	14 (4 to 52)	6MWT; HRQoL; W <sub>peak</sub> , VO <sub>2peak</sub>

Data for age, FEV<sub>1</sub>(%), frequency, duration and length are presented as mean ± standard deviation of the mean. Data in brackets represent the range (minimum to maximum).

**N:** Number.

**Age:** mean age in years (yr), combined control and exercise groups.

**FEV<sub>1</sub> (%):** mean forced expiratory volume in one second percentage predicted combined control and exercise groups.

**Setting:** site at which exercise program conducted. IP: inpatient; OP: outpatient; Comm: community; Home: home based.

**Mode:** mode of exercise training. ULT: upper limb training; LLT: lower limb training; IMT: inspiratory muscle training; STR: strength training.

**Measures used to prescribe exercise intensity:** W<sub>peak</sub>: peak power on cycle ergometer; VO<sub>2peak</sub>: peak rate of oxygen consumption; RPE: rating of perceived exertion; modified BORG: 0-10 breathlessness scale; 6MWT: six minute walk test; CPET: cardiopulmonary exercise test; ISWT: incremental shuttle walk test; RM repetition maximum.

**Frequency:** number of days per week of exercise training.

**Duration:** duration of each session in minutes.

**Length:** length of program in weeks.

**Measures used to evaluate program:** 6MWT: six minute walk test; HRQoL: health-related quality of life; W<sub>peak</sub>: peak power on cycle ergometer; VO<sub>2peak</sub>: peak rate of oxygen consumption.

**Table 2. Exercise prescription recommendations for chronic obstructive pulmonary disease**

Type of exercise	Intensity	Frequency	Time	Special considerations
<p>Aerobic</p> <ul style="list-style-type: none"> <li>• Lower limb: Walking (treadmill), cycling (ergometry or OG)</li> <li>• Upper Body: ergometry, shelving tasks</li> </ul>	<ul style="list-style-type: none"> <li>• RPE: 3-4 (modified BORG) or 12-14, BORG</li> <li>• Dyspnoea: 3-4 (modified BORG)</li> <li>• 40-60% <math>W_{peak}</math> cycle ergometer</li> <li>• 80% of 6MWT speed on treadmill</li> </ul>	<ul style="list-style-type: none"> <li>• 3-5 days per week</li> <li>• 1-2 bouts per day</li> </ul>	<ul style="list-style-type: none"> <li>• 30-60 min per session</li> <li>• Shorter sessions if &gt; 1 bout per day</li> <li>• Shorter interval exercise if unable to complete continuous exercise. Circuit training approach using 4-6 minute circuits for different upper and body exercise.</li> </ul>	<ul style="list-style-type: none"> <li>• Monitor status, consider modifying exercise if exacerbation</li> <li>• Adjust intensity for angina/ischaemia, hemodynamic instability</li> <li>• Monitor dyspnoea and <math>S_pO_2</math> regularly. Note upper limb may elicit greater dyspnoea</li> <li>• Depending on symptoms, during exercise testing cease exercise for <math>S_pO_2 \leq 80\%</math> and recommence exercise <math>S_pO_2 &gt; 85\%</math></li> <li>• During exercise training, cease exercise for <math>S_pO_2 \leq 85\%</math> and recommence exercise <math>S_pO_2 &gt; 90\%</math></li> <li>• Consider medication interactions (<math>\beta</math>-blockers) associated with co-morbid conditions</li> </ul>
<p>Resistance</p> <ul style="list-style-type: none"> <li>• Machine/free weights</li> <li>• Body weight</li> </ul>	<ul style="list-style-type: none"> <li>• 30-40% of 1 RM (upper body); 50-60% 1RM (lower body)</li> <li>• or 8-15 comfortable reps</li> </ul>	<ul style="list-style-type: none"> <li>• 2-3 days per week</li> </ul>	<ul style="list-style-type: none"> <li>• 10-20 min/d</li> <li>• 8-10 exercises (major muscle groups), 10-15 reps</li> </ul>	<ul style="list-style-type: none"> <li>• Goals to <math>\uparrow</math> SkM strength &amp; endurance</li> <li>• Avoid valsalva manoeuvre</li> <li>• Circuit training if safe</li> <li>• Changes in upper and lower body strength can be measured using hand-held dynamometer. Handgrip strength also be measured</li> </ul>
Flexibility exercises		<ul style="list-style-type: none"> <li>• 3-5 days per week</li> </ul>	30-60 s each muscle	<ul style="list-style-type: none"> <li>• Completed at the beginning/end of the session</li> </ul>
Aqua Therapy	<ul style="list-style-type: none"> <li>• RPE: 3-4 (modified</li> </ul>	<ul style="list-style-type: none"> <li>• 1-2 per week</li> </ul>	<ul style="list-style-type: none"> <li>• 30-60 min per session</li> </ul>	<ul style="list-style-type: none"> <li>• Head up activity and ensure no CI for undertaking exercise in the water</li> </ul>

	BORG) or 12-14, BORG •Dyspnoea: 3-4 (modified BORG)			
NMES	•Maximum tolerable	•4 to 7 days per week •1-2 sessions per day	•30 to 60 min per session	•Only prescribed for individuals with severe disease and unable to undertake weight-bearing exercise due to severe breathlessness. Most commonly applied to quadriceps. Stimulation frequency commonly set at between 35 and 50 Hz. Protocols that target improvements in endurance may be characterised by low-frequency, high duty-cycle. Protocol that target improvements in strength may be characterised by e. high-frequency, low duty-cycle.

CI: contraindications; OG: Overground; RM: repetition maximum; 6MWT: six minute walk test; SkM: skeletal muscle; SpO<sub>2</sub>: oxygen saturation; W<sub>peak</sub>: peak work rate

**Table 3. Summary of medications (and exercise-specific side-effects) commonly prescribed for people of chronic obstructive pulmonary disease**

Medication	Action	Groups	Generic examples	Exercise-specific side effects <sup>61</sup>
$\beta_2$ -agonists	<ul style="list-style-type: none"> <li>stimulate <math>\beta_2</math>-receptors on airway smooth muscle and mast cells resulting in bronchodilatation and inhibition of mast cell mediator release</li> </ul>	<ul style="list-style-type: none"> <li>Short acting <math>\beta_2</math> agonists (SABA –“Relievers”)</li> </ul>	<ul style="list-style-type: none"> <li>Salbutamol</li> <li>Terbutaline</li> </ul>	<ul style="list-style-type: none"> <li>Increased heart rate/palpitations</li> <li>Tremor</li> <li>Cardiac arrhythmias (rare)</li> <li>metabolic acidosis (rare, respiratory compensation due to increased lactate levels)</li> <li>Peripheral vasodilation (rare)</li> </ul>
		<ul style="list-style-type: none"> <li>Long acting <math>\beta_2</math> agonists (LABA)</li> </ul>	<ul style="list-style-type: none"> <li>Formoterol</li> <li>Salmeterol</li> <li>Indacaterol</li> </ul>	
Anti-muscarinic Drugs	<ul style="list-style-type: none"> <li>Block the muscarinic effects of acetylcholine on nicotinic receptors resulting in airway . smooth muscle relaxation</li> </ul>	<ul style="list-style-type: none"> <li>Short-acting muscarinic antagonists – (SAMA)</li> </ul>	<ul style="list-style-type: none"> <li>Ipratropium</li> </ul>	<ul style="list-style-type: none"> <li>Cardiac arrhythmias (rare)</li> <li>Dry mouth, throat irritation, cough</li> <li>Headache (common&gt;1%)</li> <li>ECG changes (rare)</li> <li>Dizziness</li> </ul>
		<ul style="list-style-type: none"> <li>Long-Acting muscarinic antagonists – (LAMA)</li> </ul>	<ul style="list-style-type: none"> <li>Tiotropium</li> <li>Aclidinium</li> <li>Glycopyrronium</li> <li>Umeclidinium</li> </ul>	
Corticosteroids	<ul style="list-style-type: none"> <li>Suppress airway inflammation through genomic and non-genomic pathways</li> </ul>	<ul style="list-style-type: none"> <li>Inhaled corticosteroids (ICS, “Preventers”)</li> </ul>	<ul style="list-style-type: none"> <li>Fluticasone (as furoate or propionate)</li> <li>Budesonide</li> <li>Beclometasone</li> <li>Ciclesonide</li> </ul>	<ul style="list-style-type: none"> <li>Osteoporosis screening recommended for adults on long term high dose ICS</li> </ul>
Combination	<ul style="list-style-type: none"> <li>Corticosteroids/<math>\beta_2</math> agonist</li> </ul>	<ul style="list-style-type: none"> <li>ICS/LABA combinations</li> </ul>	<ul style="list-style-type: none"> <li>Budesonide/formoterol</li> <li>Fluticasone furoate /Vilanterol</li> <li>Fluticasone Propionate /Salmeterol</li> <li>Futicasone Propionate /Formoterol (*PBS asthma only)</li> </ul>	<ul style="list-style-type: none"> <li>See individual agent side effect profile</li> </ul>

	• Muscarinic/ $\beta_2$ agonist	• LAMA/LABA combinations	• Tiotropium/Olodaterol • Aclidinium/Formoterol • Glycopyrronium/Indacaterol • Umeclidinium/Vilanterol	• See individual agent side effect profile
	• Corticosteroids/Muscarinic/ $\beta_2$ agonist	• ICS/LAMA/LABA	• Fluticasone Furoate/Umeclidinium/Vilanterol	• See individual agent side effect profile

**Note: All side effects described are dose-dependent**

**Supplementary Table. Exercise Training Dose from Randomised Controlled Trials examining exercise training in patients with chronic obstructive pulmonary disease**

Author year	N(EX)	Age (yr)	FEV <sub>1</sub> (%)	Setting	Mode	Intensity	Frequency (days/wk)	Duration (mins)	Length (wk)	Outcomes
Barakat 2008	71 (35)	65	43	OP	ULT; LLT	40% VO <sub>2max</sub>	3	30	14	6MWD:↑; QoL:↑
Baumann 2012	81 (37)	64	46	Comm	ULT; LLT; INT; STR	4-6 RPE (modified BORG)	1	30-60	26	6MWD:↑; Wmax:↑; QoL:↑
Behnke 2000	30 (15)	66	36	IP/Home	LLT	75% 6MWT	7	45	10d(IP)/28(home)	6MWD:↑; QoL:↑
Bendstrup 1997	32(16)	65	-	OP	ULT; LLT; STR	maximum tolerable walk speed	3	60	12	6MWD:↑; QoL:↑
Booker 1984	69(32)	65	-	Home	LLT	-	-	-	9	6MWD:↔
Borghi-Silva 2009	34(20)	67	34	OP	LLT	70% CPET walk speed	3	40	6	6MWD:↑
Boxall 2005	46 (23)	77	39	Home	ULT; LLT	low intensity, symptom limited	7	6-30min	12	6MWD:↑; QoL: ↑
Busch 1988	14(7)	66	27	Home	LLT; STR	symptom limited, 20RM strength	5	individualised	18	-
Cambach 1997	23(15)	62	59	Comm	ULT; LLT	60-75% W <sub>max</sub> , row/cycle ≥60% HR <sub>max</sub>	2	90	12	6MWD:↑; QoL:↑
Casaburi 2004	24(12)	69	38	OP	STR	Strength, 60-80% 1RM	3	strength only	10	Wmax:↑; VO <sub>2peak</sub> :↑
Casey 2013	350(178)	69	59	Comm	-	-	-	-	8	ISWT ↔, QoL:↑
Cebollero 2012	36(28)	68	46	OP	-	-	2	-	12	6MWD:↑; QoL:↑
Chan 2011	136(69)	74	90	Comm	LLT	-	7	60	12	6MWD:↔; QoL:↔
Chlumsky 2001	19(13)	64	46	OP	LLT	-	2	30	8	6MWD:↔; QoL:↔
Clark 1996	48(32)	57	-	OP/home	ULT; LLT	-	7	na	12	-
Cochrane 2006	124(74)	-	-	OP	ULT; LLT	-	2	120	6	-
Cockcroft 1981	34(18)	61	-	IP/Home	ULT; LLT	-	7	na	6d(IP)/28(home)	-

Author year	N(EX)	Age (yr)	FEV <sub>1</sub> (%)	Setting	Mode	Intensity	Frequency (days/wk)	Duration (mins)	Length (wk)	Outcomes
De Souto Araujo 2012	32(21)	63	45	Comm	ULT; LLT; STR	Cycle 5 RPE, UL: 50% 1 RM	3	90	8	6MWD:↔; QoL:↑
Deering 2011	44(25)	68	64	OP	ULT; LLT; IMT	-	OP (1), home (3)	30-60	7	6MWD:↔; ISWT↑; QoL:↔
Elci 2008	78(39)	59	47	Comm/home	ULT; LLT; STR	75% of 6MWT; Resistance: 0.3-2 kg	OP(2), home(5)	10-30min	12	6MWD:↑; QoL:↔
Emery 1998	50(25)	66	-	OP	ULT; LLT; STR	-	7 (first 5 wk) then 3 (next 5wk)	45-90	10	Wmax:↑
Engström 1999	50(26)	66	32	OP/home	ULT; LLT; INT	Interval, 42:85% Wmax	2	45	52	6MWD:↑; Wmax:↑; QoL:↔
Faager 2004	20(10)	71	27	IP/Home	ULT; LLT	-	1	90	8	6MWD: ↑
Faulkner 2010	20(10)	-	-	Comm	ULT; LLT; STR	-	1	90	8	ISWT ↔; QoL:↔
Fernandez 2009	41(27)	67	35	Home	ULT; LLT; IMT; STR	-	5	>60	52	6MWD:↑; QoL: ↑
Finnerty 2001	65(36)	69	41	OP	ULT; LLT; STR	-	2	60	6	6MWD: ↑; QoL: ↑
Gohl 2006	10(9)	58	58	Comm	ULT; LLT	-	-	-	52	6MWD:↑; QoL:↔
Goldstein 1994	78(38)	65	35	IP/OP/Home	ULT; LLT; INT	-	3	>30	8(IP), 24(OP)	6MWD: ↑; Wmax:↔; QoL:↑
Gomez 2006	97(64)	65	69	Comm	ULT; LLT	-	-	-	12	6MWD:↔; QoL:↔
Gosselink 2000	70(37)	61	42	OP	ULT; LLT; STR	Cycle, 60-80%Wmax; Walk, 60-80% 6MWT; Strength:60% 1RM	3 then 2	90	24	6MWD: ↑; Wmax: ↑; QoL:↑
Gottlieb 2011	61(35)	74	65	Comm	ULT; LLT; STR	16-17 RPW (Borg, 6-20)	2	90	7	6MWD: ↑; QoL: ↑
Griffiths 2000	184(93)	68	40	OP/home	ULT; LLT	80% of max ISWT speed	3	40	6	ISWT↑; QoL:↑
Güell 1995	60(30)	65	35	OP/home	LLT	-	2 (first 12wk), 5 (next 12 wk)	30	12	6MWD:↑; Wmax:↔; QoL:↑
Güell 1998	35(18)	67	35	OP	LLT	50% of Wmax	5	30	8	6MWD:↑; QoL:↑

Author year	N(EX)	Age (yr)	FEV <sub>1</sub> (%)	Setting	Mode	Intensity	Frequency (days/wk)	Duration (mins)	Length (wk)	Outcomes
Gurgun 2013	46(30)	65	41	OP	ULT; ULT; STR	50% ISWT; Cycle 50-80% VO <sub>2peak</sub>	2	60-80	8	6MWD:↑; ISWT↑; QoL:↑
Hernandez 2000	37(20)	64	73	Home	LLT	70% ISWT	6	60	12	Wmax:↔; ISWT ↔ QoL:↑
Hoff 2007	12(6)	62	48	OP	STR	85-90% 1RM	3	strength only	8	Wmax ↔
Jones 1985	14(8)	64	-	Home	-	-	-	-	10	Wmax:↔
Karapolat 2007	45(26)	66	57	OP	-	RPE 3 (modified Borg)	3	>30	8	6MWD:↑; QoL: ↑
Lake 1990	14(7)	66	-	OP	ULT; LLT; INT	-	3	60	8	6MWD:↑; Wmax:↑
Lindsay 2005	50(25)	70	-	Comm	ULT; LLT	-	1	-	6	6MWD: ↔; QoL:↔
Liu 2012	67 (32)	62	61	IP/home	ULT; LLT	-	3	60	24	6MWD:↑
McGavin 1977	24(12)	59	-	Home	LLT	-	5	2-10min	?12	Wmax: ↑
McNamara 2013	53(38)	71	59	OP	ULT; LLT	3-5 RPE, 80% 6MWT	3	60	8	6MWD:↑; ISWT↑ QoL:↑
Mehri 2007	38(20)	52	-	OP	LLT	Dependent on the patients' ability and tolerance	2	-	8	-
Mendes De Oliveira 2010	85(56)	66-71	41-52	OP/home	ULT; LLT; STR	50% 1RM; 60-80% of max HR achieved on 6MWT	3	>30	12	6MWD:↑
Nalbant 2011	29(14)	71	58	Nursing home	ULT; LLT	-	3	90	24	-
O'Shea 2007	54(27)	68	51	OP/home	ULT; STR	8-12 reps, 3 sets	3	strength only	12	6MWD:↔; QoL:↔
Ozdemir 2010	50(25)	63	54	OP	ULT; LLT	-	3	35	4	6MWD:↔; QoL:↑
Paz-Diaz 2007	24(10)	64	32	OP	ULT; LLT	80% VO <sub>2max</sub> (treadmill and cycle ergometer)	3	60	8	QoL: ↑
Petty 2006	222(149)	68	-	Home	ULT; LLT	-	-	-	8	-
Reardon 1994	20(10)	66	34	OP	ULT; LLT; IMT; STR	70-85% of HRmax, RPE 3 (modified Borg)	2	90	6	-

Author year	N(EX)	Age (yr)	FEV <sub>1</sub> (%)	Setting	Mode	Intensity	Frequency (days/wk)	Duration (mins)	Length (wk)	Outcomes
Ringbaek 2000	45(24)	63	47	OP	ULT; LLT; STR	RPE 4-5 (modified BORG)	2	60	8	6MWD:↔; QoL:↔
Simpson 1992	28(14)	72	40	OP	ULT; STR	Initially 50% -85% 1RM	3	strength only	8	6MWD:↔; QoL:↑
Singh 2003	40(20)	na	27	Home	LLT	-	7	60	4	6MWD:↑; QoL:↑
Sridhar 2008	122(61)	70	46	OP/home	-	-	2	60	4	QoL:↑
Strijbos 1996	30(15)	62	42	OP	LLT	70% Wmax	2	60	12	Wmax:↑
Theander 2009	26(12)	65	34	OP/home	ULT, LLT, STR	-	2	60	12	6MWD:↔; QoL:↔
Vallet 1994	20(10)	59	56	IP	LLT	-	-	-	8	6MWD:↑
Van Wetering 2010	199(102)	67	59	Comm	ULT; LLT; STR	-	2 then 7(home)	30-60	16	6MWD:↑; Wmax:↑; QoL:↑
Vijayan 2010	31(16)	na	-	-	ULT; LLT	-	5	90	8	6MWD:↑
Weiner 1992	24(12)	64	36	OP	ULT; LLT; IMT; STR	50% Wmax; IMT 15% -80% of P <sub>lmax</sub>	3	60	24	-
Wen 2008	41(32)	68	-	OP	LLT	Highest tolerated/Anaerobic threshold level	2	-	12	-
Wijkstra 1994	43(28)	63	44	OP/home	ULT; LLT; IMT	60-75% Wmax	2	60	12	6MWD:↔; Wmax: ↑; QoL:↑
Xie 2003	50(25)	54	41	Home	LLT	-	6	60	12	Wmax: ↑; ISWT ↔
						Additional RCT's from March 2016-2018				
Arslan 2016	65(32)	-	-	Home	LLT	Low to moderate intensity walking program	3	33-41	8	-
Borghi-Silva 2014	20(10)	66.5	33.5	OP	LLT	75% peak CPET speed & modified Borg <4	3	30	12	6MWD:↑; VO <sub>2peak</sub> :↑
Chen 2017	49(25)	-	-	OP	LLT	-	-	-	8	6MWD:↑; QoL:↑
Chen 2015	36(?)	-	-	OP	-	-	OP (2), home (1)	-	4	6MWD:↑; QoL:↑

Author year	N(EX)	Age (yr)	FEV <sub>1</sub> (%)	Setting	Mode	Intensity	Frequency (days/wk)	Duration (mins)	Length (wk)	Outcomes
Cheriamane 2014	89(45)	59.63	50.63	OP	-	-	OP (2), home (2)	-	-	6MWD:↑; QoL:↑
de Roos 2018	52(26)	70	67	OP/home	LLT; STR	-	OP (2), home (1)	OP (60), home (30)	10	6MWD:↑; QoL:↑
Duruturk 2016	28(15)	62.41	60.81	OP	LLT	50-70% of the VO <sub>2max</sub> , modified Borg score 4-7	3	20-30	6	6MWD:↑; VO <sub>2peak</sub> :↑; QoL:↑
Farias 2014	34(18)	67.38	53.6	OP	LLT	Modified Borg score <5	OP (2), home (3)	40-60	8	6MWD:↑; Wmax:↑; QoL:↑
Jayasheela 2017	30(15)	-	-	OP	-	-	-	<120	12	6MWD:↑; QoL:↑
Kortianou 2014	30(20)	-	53	-	-	100% WRpeak (30 secs ex/30 secs rest)	3	40	12	Daily PAL
Leite 2015	16(10)	62.19	51.25	OP	LLT	60-100% of peak velocity reached in incremental test (vVO <sub>2peak</sub> ). Adjusted every 4/52	3	30-50 continuous (wk 1-8); 5×3-min interval (wk 9-12)	12	VO <sub>2peak</sub> :↑
Majewska-Pulsakowska 2016	22 (9)	64.19	60.46	OP	LLT	Individualised, ased on treadmill exercise test results	3	23-45	8	MET:↔; FEV1:↔; QoL:↔
Min 2017	-	-	-	-	ULT; LLT	-	3	30	8	QoL:↑
Pradella 2015	44(29)	63.39	47.34	Home	ULT; LLT	60-70% HRmax	3	15-40	8	6MWD:↑; QoL:↑
Roos 2017	45(21)	70.2	66.5	Comm/Home	LLT; STR	-	Comm (2), home (1)	60	10	6MWD:↑; QoL:↑
Tsai 2017	36(19)	73.94	63.78	Home	LLT; STR	Cycle: 60-80% of Wpeak; walking training: 80% 6MWT speed	3	~60	8	6MWD:↑; QoL:↑
Varas 2018	40(21)	67	48	Comm	LLT	Walking speeds based on last level completed during ISWT	5	30-60	8	ESWT:↑; QoL:↑
Wootton 2014	143(95)	68.66	43	OP	LLT	80% 6MWT speed, 3-4 on modified dyspnea Borg scale	3	30-45	8	6MWD:↔; QoL:↑
Wu 2015	30(15)	-	-	OP	LLT	80% W <sub>peak</sub>	3	30	12	VO <sub>2peak</sub> :↑
Zambom-Ferraresi 2015	36(28)	68.77	44.72	OP	LLT; STR	Strength: 50-70% 1RM, 6-12 reps, 3-4 sets; LLT: 40-85% Wmax (65-90% HRpeak)	2	LLT 20-35; STR 90	12	6MWD:↑; Wmax:↑; QoL:↑

#### Legend:

N: Number; EX (number in exercise group)

Age: age in years (yr), combined control and exercise groups

FEV<sub>1</sub>(%): Forced expiratory volume in one second percentage predicted;

Setting: Site at which exercise program conducted. OP: outpatient; IP: inpatient; home: home based; Comm: Community

Mode: Mode of exercise training. ULT: upper limb training; LLT: lower limb training; IMT: Inspiratory muscle training; STR: strength

Intensity: Intensity of exercise training. Wmax: maximal power on cycle ergometer; VO<sub>2</sub>max: maximal oxygen consumption; RPE: rating of perceived breathlessness;

modified BORG: 0-10 breathlessness scale; 6MWT: six minute walk test; CPET: cardiopulmonary exercise test; Interval: interval training; ISWT: intermittent shuttle walk test; RM Repetition maximum;

Frequency: Number of days per week of exercise training

Duration: Duration of each session in minutes

Length: Length of program in weeks

Outcomes: Reported outcomes from the study. 6MWD: six minute walk distance; VO<sub>2</sub>peak: peak oxygen consumption; QoL: quality of life.

Note where we could not determine data from the study we have used a “-”

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