Chapter 10
Field Exercise Testing: 6-Minute Walk and Shuttle Walk Tests

Annemarie L. Lee, Theresa Harvey-Dunstan, Sally Singh, and Anne E. Holland

10.1 Background to Field Exercise Testing

Assessment of exercise capacity is traditionally performed in a laboratory using cardiopulmonary exercise testing (CPET); however this method is time-consuming and requires expensive equipment and technical support, which may limit its application in some settings. As a result, the last three decades have seen the development of alternative approaches in the form of field-based walking tests. These are shown to be valid, reliable, and repeatable, are easy to perform for both the operator and the subject (although they do require initial training), and require little equipment. An added bonus of walking tests is that walking is a common and acceptable

A. L. Lee (✉)
Faculty of Medicine, Nursing and Health Sciences, Monash University, Frankston, VIC, Australia

Rehabilitation, Nutrition and Sport, La Trobe University, Bundoora, VIC, Australia

Institute for Breathing and Sleep, Austin Health, Heidelberg, VIC, Australia
e-mail: Annemarie.Lee@monash.edu

T. Harvey-Dunstan · S. Singh
Centre for Exercise and Rehabilitation Science, NIHR Leicester Biomedical Research Centre – Respiratory, Glenfield Hospital, Leicester, UK

Faculty of the College of Medicine, Biological Sciences and Psychology, University of Leicester, Leicester, UK
e-mail: sally.singh@uhl-tr.nhs.uk

A. E. Holland
Institute for Breathing and Sleep, Austin Health, Heidelberg, VIC, Australia

Alfred Health, Melbourne, VIC, Australia

Department of Rehabilitation, Nutrition and Sport, La Trobe University, Bundoora, VIC, Australia
e-mail: a.holland@alfred.org.au

D. A. Kaminsky, C. G. Irvin (eds.), *Pulmonary Function Testing*, Respiratory Medicine, https://doi.org/10.1007/978-3-319-94159-2_10

form of activity. This enables implementation across a variety of settings where people with chronic respiratory disease receive their care and is frequently used to guide exercise prescription for pulmonary rehabilitation programs.

The most commonly employed field walking tests are the 6-minute walk (6MWT) and the incremental shuttle walking tests (ISWT) and, its derivative, the endurance shuttle walking test (ESWT). The 6MWT is a self-paced test, while the ISWT is a maximal and incremental test that uses an audible prompt for progressive increases in walking speed. Within 3 min, the 6MWT achieves a plateau in VO_2 which is sustained for the remainder of the test. In contrast the ISWT demonstrates a gradual increase in VO_2 to the point of symptom limitation, matching closely the trajectory and peak values of the laboratory-based CPET.

The 6MWT and ISWT provide important information relevant to assessment of people with chronic respiratory disease, understanding treatment responses, and monitoring disease progress over time. In this chapter we will outline the rationale for each test, as well as their measurement properties, testing protocols, and interpretation. The testing procedures described in this chapter are consistent with those described in the European Respiratory Society/American Thoracic Society Technical Standard for field walking tests.

10.1.1 6-Minute Walk Test

10.1.1.1 Background

The 6MWT is a self-paced test of functional exercise capacity. The aim is to walk as far as possible in 6 min along a flat corridor. The main outcome is the 6-minute walk distance (6MWD), reported in meters or feet. Standardized instructions and encouragement are provided, to minimize variation in test performance. The 6MWT is widely used across many chronic respiratory diseases to assess functional capacity, estimate prognosis and disease progression, assess exertional desaturation, prescribe exercise for pulmonary rehabilitation, and assess response to treatments. It has been extensively studied, particularly in COPD, with good evidence for validity and reliability.

Validity

The validity of the 6MWT is well established in individuals with COPD, ILD, CF, and PAH and in individuals undergoing lung transplantation. There is a strong relationship between the 6MWD and other measures of exercise capacity, particularly peak oxygen uptake (VO_2 peak) from a CPET (correlation coefficients ranging from 0.40 to 0.80) and peak work (0.58–0.93). In patients with moderate to severe COPD, there is no difference in VO_2 peak between a CPET and a 6MWT, although the ventilatory requirements (peak carbon dioxide production, peak ventilation, and respiratory exchange ratio) during a 6MWT are lower. This may account for the excellent patient tolerance of the 6MWT across different chronic respiratory diseases. The

high physiological load imposed by the 6MWT suggests it is not truly a submaximal test, particularly in individuals with more severe disease. There is a moderate to strong relationship between the 6MWD and measures of physical activity during daily life (walking time, daily energy expenditure, time spent in vigorous physical activity, number of steps) in a range of patient populations (COPD, ILD, CF, PAH), which supports the notion that the 6MWT is best conceptualized as a test of functional exercise capacity.

The relationship of 6MWD to measures of respiratory function is weaker than the relationship to exercise capacity and physical function. In COPD, correlation coefficients for FEV_1 ranged from 0.31 to 0.70, although a stronger relationship has been reported in those with more severe disease. In ILD, the relationship between FVC or DLCO and 6MWD ranged from $r = 0.06$ to 0.61, while in PAH, mean PAP and 6MWD are weakly to moderately related ($r = -0.2$ to -0.62). In lung cancer, a moderate relationship was evident with FEV_1 $r = 0.53$. In bronchiectasis, 6MWD has a moderate relationship with FVC ($r = 0.52$). For patient-reported outcomes, the strength of the relationship is similar, with weak to moderate relationships between 6MWD and symptoms of dyspnea, fatigue, or health-related quality of life (HRQOL) reported in all disease groups. The 6MWD should be considered as a global measure of functional capacity which is influenced by many important body systems including respiratory, cardiovascular, musculoskeletal, neurological, and psychological function.

Reliability and Learning

The 6MWD is a highly reliable measure of functional exercise capacity, with excellent intraclass correlation coefficients (ICCs ranging from 0.72 to 0.99) across COPD, CF, ILD, and PAH. Despite its reliability, there is consistent evidence of a learning effect for the 6MWD, with most patients walking further on a second test. In 1514 people with COPD, the average learning effect was 27 m, with 82% of patients improving their 6MWD on the second test. The size of the learning effect is sufficiently large to be of clinical significance. For this reason, if the 6MWD is being used to evaluate the effect of an intervention (e.g., pulmonary rehabilitation or medication prescription), either as clinical practice or as part of research, at least two tests should be completed in order to obtain an accurate measurement of functional exercise capacity, with the longest distance recorded.

When the 6MWD is applied to stage disease or assess morbidity, the presence and magnitude of the learning effect may be of lesser relevance, and one test may be sufficient. However, if the information obtained influences treatment decisions (e.g., decisions regarding transplantation or other surgical management), repeat testing should be considered. The learning effect may be moderated by test repetition and the duration between tests. For example, for people with COPD undertaking pulmonary rehabilitation, the learning effect is less if the test is repeated within a short period of time, such as the end of rehabilitation, but may reemerge by 3 months following rehabilitation. Clinicians should be mindful that learning effect may return after a longer duration of time between tests, and in these circumstances, two tests should be completed.

The reliability of other outcomes obtained during a 6MWT, including nadir oxyhemoglobin saturation and heart rate response, is more variable and may be influenced by the type of respiratory disease. For oxyhemoglobin saturation, excellent reliability is evident in COPD and CF, but in individuals with ILD, this measure may be influenced by the presence of underlying vascular disease, which can reduce oximetry signal quality and reduce reliability. For individual patients in whom detecting desaturation is the key indication for the 6MWT, this may influence further clinical decision-making. In COPD and CF, heart rate (HR) measures are more variable compared to oxyhemoglobin saturation, with differences between tests being from −4 bpm to +8 bpm. While this may be of little significance for some individual patients, those suspected of concurrent heart disease or a history of abnormal heart rate or rhythms, the degree of variability in this measure during the 6MWT may warrant additional measures to clarify HR response.

10.2 Relationship of 6MWT to Clinical Outcomes

The 6MWD has a strong relationship to important clinical outcomes in individuals with chronic respiratory disease, with a lower 6MWD consistently associated with increased mortality and morbidity. In COPD, the 6MWD threshold below which mortality is increased has varied across studies from 200 to 350 m, with similar values reported in IPF and PAH. The 6MWD is a component of the BODE index, a multidimensional disease rating for COPD which includes body mass index (BMI), degree of obstruction (FEV_1), functional exercise capacity (6MWT), and degree of dyspnea; in the BODE index, a 6MWD of less than 350 m predicts increased mortality. For individuals with COPD undergoing bilateral lung volume reduction survey, a reduced 6MWT distance (200 m or less) has been associated with a longer length of hospital stay (greater than 3 weeks) and increased likelihood of mortality within 6 months of surgery. Lower distances (<357 m) are also associated with an increased risk of exacerbation-related hospitalization. This metric is also associated with lung transplant waitlist mortality. For this reason, 6MWD is part of the lung allocation score and included as a standard component of pretransplant evaluation. In non-small cell lung carcinoma, the 6MWD offers a moderate prediction of postoperative outcomes and survival in those with advanced disease.

Monitoring of oxygen saturation during the 6MWT provides the opportunity to detect exercise-induced desaturation. The 6MWT is more sensitive for detecting exercise-induced desaturation compared to cardiopulmonary exercise testing, probably because it involves walking rather than cycling. Desaturation during a 6MWT is associated with greater disease severity and progression, more rapid decline in FEV_1, and worse prognosis. In addition, evidence of desaturation during a 6MWT can be used to establish the need for supplemental oxygen therapy, either during daily life or during pulmonary rehabilitation. The distance-saturation product (DSP) is defined as the product of the 6MWD and the nadir SpO_2 when the test is conducted on room air. A DSP ≤200 m% predicts mortality in individuals with IPF; the DSP is also an independent predictor of health-related quality of life (HRQOL) in people with sarcoidosis.

Although less commonly applied in clinical practice, HR monitoring during a 6MWT may provide additional information related to morbidity and mortality. The heart rate response (HRR) is the reduction in HR with rest following the exercise period. An abnormal HRR at 1 min (prolonged recovery, usually defined as ≤13–18 beats per min) is a predictor of clinical deterioration in people with idiopathic PAH and of mortality in people with IPF and is a significant predictor of an acute exacerbation of COPD.

10.3 Reference Equations for 6MWD

Reference equations describe the 6MWD for healthy individuals and allow results to be presented as a percentage of the predicted value. A large number of published reference equations are available for both children and adults. Factors influencing the 6MWD in healthy adults include age, height, weight, sex, grip strength, and percentage of maximum heart rate attained during walking. However the reference equations were generated using a wide range of different methods and in different populations. For instance, the walking tracks ranged from 20 to 50 m, and test repetition ranged from one to four 6MWTs. As a result, there is marked variability in the predicted 6MWD generated by different equations.

The impact of this variation in predicted 6MWD across reference equations is demonstrated in Fig. 10.1. A 74-year-old lady with COPD has FEV_1 48%, height

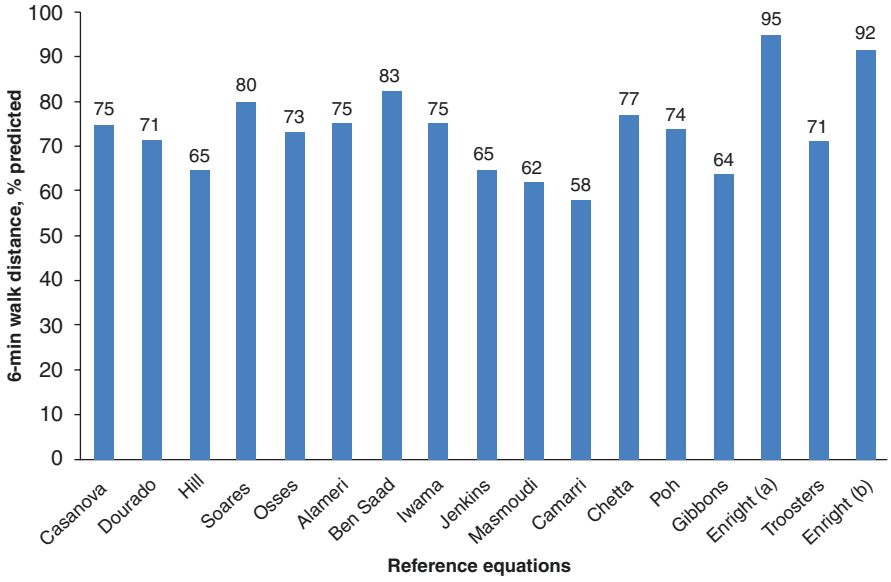

Fig. 10.1 Impact of different reference equations on the 6-minute walk percent predicted for a 74-year-old lady with COPD, FEV_1 48%, height 162 cm, weight 80 kg, 6MWD 365 m, 83% of predicted maximum HR

162 cm, and weight 80 kg. Her 6MWD is 365 m, and she reaches 83% of her predicted maximum HR. Her 6MWD ranges from 58% to 95% of the predicted maximum value, depending on the reference equation used. This could substantially affect interpretation. For this reason, it is recommended that if a reference equation is used, it should be one that was developed in a similar population that in whom it is being applied, using a similar 6MWT protocol. The name of the reference equation should also be provided.

10.4 Meaningful Change in 6MWD

Minimal Important Difference

The minimal important difference (MID) is the smallest difference in score in the outcome of interest that informed patients or informed proxies perceive as important and which would lead the patient or health professional to consider a change in the management. There have been a number of studies investigating the MID for 6MWD in adults with chronic lung disease, including over 5600 patients. Most are in COPD, with smaller numbers of trials in ILD and PAH, and most studies have been conducted in the context of a rehabilitation program. Recent studies report consistent estimates for the MID in the range 25–33 m, with a median value of 30 m. The MID estimates are consistent across patient groups and across study methods. At present there is no evidence that the MID varies according to disease severity or baseline 6MWD, although there are few studies examining these questions.

Current standards for the conduct and interpretation of the 6MWT suggest an MID of 30 m should be used in adult patients with chronic respiratory disease. As a result, a change in 6MWD of at least 30 m would need to occur in order to be confident that true clinical change had occurred between testing occasions.

Impact of Interventions on 6MWD

The 6MWD is responsive to common interventions in people with chronic respiratory disease, particularly for those involving exercise training and surgery. Following outpatient pulmonary rehabilitation in COPD, the mean improvement in 6MWD was 44 m (95% 33–55 m), from 38 studies of 1879 participants. Following hospitalization for an acute exacerbation, the mean improvement in 6MWD was 62 m (95% CI 38–86 m). In ILD, the improvement in 6MWD following rehabilitation is reported as 44 m (95% CI 26–63 m). In bronchiectasis, the degree of change was 41 m (95% CI 19–63 m). The 6MWD may be less responsive to pharmacological interventions. In trials of bronchodilator therapy for COPD or selective and nonselective endothelin receptor antagonists in people with PAH, the degree of change in 6MWD has varied between 6 m and 54 m. Following lung volume reduction surgery in people with COPD, the degree of improvement in 6MWD has been reported as high as 98 m.

10.5 Factors Affecting the 6-Minute Walk Distance

The 6MWD is highly sensitive to small changes in test methodology. The factors shown to influence 6MWD, and the magnitude of their effect on the measured distance, are presented in Table 10.1. Many of these effects exceed the MID. As a result of the substantial impact of variations in methodology, standardization of the testing procedure is very important.

Methodological factors requiring particular attention include:

- Use of standardized encouragement. Recommended phrases are provided below.
- Consistency in provision of supplemental oxygen within an individual, where 6MWD will be compared over time. This includes the method of transporting the supplemental oxygen, which can have a significant impact on 6MWD due to the added weight.
- Clear documentation regarding method for transporting supplemental oxygen (by patient or by tester) and use of gait aids.
- Treadmill testing is not recommended as 6MWD is substantially reduced.
- Track length and layout should be consistent between tests. To facilitate comparison across centers, a straight track, 30 m in length, has been recommended.

10.5.1 Performing the 6MWT

A 6MWT should be performed in a flat, straight corridor that is relatively free of pedestrian traffic. A course of 30 m is recommended, to be consistent with the courses on which most reference equations have been generated. The ends of the course should be marked such that they are clearly visible to the patient. Prior to the test, patients should take their usual medications at the usual times. Strenuous

Table 10.1 Factors affecting the 6-minute walk distance

Change to methodology	Average effect on 6-minute walk distance
Instructions (far vs fast)	↑ 53 m
Supplemental oxygen	↑ 35 m
Continuous track	↑ 34 m
Encouragement	↑ 30 m
Repeat testing	↑ 27 m
Rollator	↑ 14 m
Outdoors	No difference
Home (vs hospital)	↓ 27 m
Shorter track (10 m vs 30 m)	↓ 50 m
Treadmill	↓ 102 m

Data are from Holland et al. 2014

exercise should be discouraged on the day of the test. If respiratory function tests are to be performed on the same day, then these should be performed prior to the 6MWT due to the potential impact of exercise on respiratory function measures. Subsequent 6MWTs should ideally be performed at a similar time of day to the first test.

Contraindications and Precautions to the 6MWT

Because the 6MWT is a strenuous test which frequently elicits a VO_2 similar to CPET, it is recommended that the same contraindications and precautions are used. An extensive list has been published. Comorbidities and medication use should be recorded prior to the test.

Baseline Measurements

Patients should be seated in a chair close to the starting line. Measures to be taken at baseline, prior to test performance, are resting SpO_2 and HR from pulse oximetry; dyspnea and fatigue using a validated scale; and blood pressure, if this has not recently been documented.

Patient Instructions

Standardized instructions should be given before the test begins. These should be given every time the test is performed, regardless of whether the patient has previously performed the test. The ERS/ATS Technical Standard recommends specific, standardize wording be used.

Measurements Taken During the 6MWT

Continuous pulse oximetry should be performed during the 6MWT, in order to accurately determine the lowest SpO_2. This measure has important clinical implications for assessment of disease progression and need for oxygen therapy. The assessor should ensure that a quality signal is obtained. The assessor should not "pace" the patient during the test but should walk sufficiently behind the patient such that the pulse oximeter readings can be observed without influencing the patient's walking speed. This is usually achieved by placing the pulse oximeter in a pouch which is hung over the patient's torso.

Rests

The patient can rest at any time during the test, either in sitting or standing. However, the timer keeps going up until 6 min, to give the patient opportunity to resume walking when able, if SpO_2 is $\geq$85%. Record the start and end time of each stop.

Stopping the 6MWT

The Technical Standard suggests that the 6MWT is ceased if the SpO_2 falls to 80%, as this is associated with a very low rate of adverse events. The rate of adverse events if the SpO_2 is allowed to fall below 80% is not known. If the SpO_2 recovers to 85%, then the patient is asked to recommence walking. Other reasons the assessor may cease a test include chest pain, intolerable dyspnea, leg cramps, staggering or loss of balance, diaphoresis, or pale appearance. Emergency procedures should be instituted according to local protocols, including administration of oxygen as required.

Test Repetition
Due to the learning effect, two 6MWT are required in order to obtain a baseline value against which subsequent 6MWDs can be compared. The Technical Standard suggests an interval of 30 min between 6MWTs to allow physiological measures and symptoms (SpO_2, HR, blood pressure, dyspnea, and fatigue) to return to baseline.

Use of Oxygen During the 6MWT
If the patient has been prescribed oxygen therapy, then this should be used during the 6MWT. Ideally the flow rate should be kept constant for subsequent tests; if this is not possible due to a change in the patient's oxygen prescription, then this should be clearly documented, as direct comparison of 6MWD will not be possible. Oxygen should not be titrated during any 6MWT where 6MWD will be reported, as this is not reproducible and likely to have a highly significant effect on distance walked. For any test where oxygen is used, ensure that the flow rate, oxygen delivery device, and method by which it is transported (by patient or assessor, backpack or trolley, etc.) are recorded.

Recording Performance on the 6MWT
The primary outcome is the 6MWD, in meters or feet. During the tests the assessor should record the number of laps and the number of meters/feet walked in the final part-lap, so that a total distance walked can be reported. If the test is performed twice, then the best 6MWD should be reported, along with other variables recorded on the same test. The SpO_2 and HR at baseline and end test, the lowest SpO_2 recorded during the test, and the symptom scores obtained before and after the test should also be reported. It is also informative to ask the patient about what prevented them from walking further/faster during the test (dyspnea, leg fatigue, or others). If the patient stopped during the test, then the number of stops and the total time stopped are reported. This provides alternative metrics to describe disease progression and may assist with exercise prescription in pulmonary rehabilitation. An example of a recording form is available with the Technical Standard.

10.5.2 Safety Considerations for the 6MWT

The rate of adverse events during the 6MWT in people with chronic respiratory diseases is very low, particularly when the test has been conducted to an established protocol, which incorporates cessation of the test with oxygen desaturation less than 80%. With this protocol applied, one study documented complications on 6% of tests, with the most common complication being oxygen desaturation. Intolerable symptoms, including dyspnea, severe wheeze, lightheadedness, low back pain, chest pain, and tachycardia, were also noted. Predictors of desaturation during a 6MWT were a lower FEV_1 and lower pre-6MWT oxygen saturation.

The absence of documented long-term adverse sequelae related to oxygen desaturation may influence the differing approaches between clinical practices regarding

permissible oxygen desaturation during a 6MWT. Some centers advocate for test termination before significant desaturation has the opportunity to occur, while others lend support an individual clinicians' judgment and experience regarding the safety level for cessation of a 6MWT for this metric. The safety of the 6MWT if severe desaturation (<80%) is permitted has not been documented.

10.6 Clinical Example Using the 6MWD

The following example illustrates the use of the 6MWT in clinical practice.

Mr. C is a 66-year-old gentleman who presents to a respiratory clinic with dyspnea and cough of 6-month duration. His respiratory function tests show a mild restrictive pattern with FVC 67% predicted and TLCO 60% predicted. Mr. C has no history of relevant exposures. High-resolution computed tomography shows a honeycombing pattern consistent with idiopathic pulmonary fibrosis (IPF).

The best of two 6MWDs at initial clinic visit is relatively well preserved at 520 m or 77% predicted using reference equations from Jenkins et al. The lowest SpO_2 during 6MWT is 92%, decreased from resting SpO_2 of 96%.

A diagnosis of IPF is confirmed after review by a multidisciplinary meeting. Mr. C is prescribed with pirfenidone, which he tolerates well. At repeat clinic visit 6 months later, his respiratory function tests are stable. His 6MWD shows a small increase (+22 m) which is not clinically significant, and his nadir oxygen saturation is unchanged at 91%.

Twelve months later Mr. C returns to clinic, reporting an increase in his dyspnea. There has been a small reduction in respiratory function (5% in FVC and TLCO). However, there has been a highly significant reduction in 6MWD, falling from 540 m to 480 m, with lowest SpO_2 of 86%. Mr. C's physician recommends that he remains on pirfenidone. He also refers Mr. C to pulmonary rehabilitation and to the oxygen clinical for consideration of ambulatory oxygen.

Key Points

- The 6MWT at baseline allows both assessment of Mr. C's functional capacity and exertional oxygen saturation.
- Regular monitoring of the 6MWD can alert clinicians to any significant changes, either improvement or decline. In this case the first follow-up 6MWD provided assurance that Mr. C's functional capacity remained stable. The second follow-up 6MWD showed a highly significant decline, indicating that more intensive treatment and monitoring may be required.
- The 6MWT provides sensitive information about exertional desaturation that can alert clinicians to change over time and suggests when initiation of oxygen therapy could be considered. It will also assist pulmonary rehabilitation practitioners to design a safe and effective training strategy for Mr. C.

10.6.1 Incremental Shuttle Walk Test (ISWT)

10.6.1.1 Background

The ISWT was developed as a way of performing an objective and standardized measure of functional capacity in patients with COPD. This test is performed around a 10-meter course, at speeds dictated by an external auditory cue. The speed of walking increases every minute and provokes a symptom-limited maximal performance. The primary outcome of the ISWT is distance which is recorded in meters to the last completed shuttle. Since initial development, it has been adopted for use in other respiratory and chronic conditions. The ISWT was developed and modified from earlier work where a test using a 20-m running track was used to measure the peak oxygen uptake ($\dot{V}O_2$Peak) in a sporting population. By adapting the incremental levels reported by Léger and Lambert, the ISWT was developed to include similar multistage speeds.

Validity
The ISWT distance related well to $\dot{V}O_2$Peak, the gold standard measure of cardiorespiratory fitness, during a CPET ($r = 0.88$). When comparing the distances walked between the ISWT to the previously established 6MWD, there was a good correlation ($r = 0.68$). From the initial validation data, Singh et al. established the following regression equation:

Estimated $\dot{V}O_2$Peak ($ml.min^{-1}.kg^{-1}$) = 4.19 (95% CI 1.12 to 7.17) + 0.025 (0.018 to 0.031) distance (m).

For patients with COPD, a moderate correlation has been observed between the ISWT and quadriceps strength ($r = 0.47$), symptom burden using the COPD assessment tool (CAT; $r = 0.50$), and physical activity ($r = 0.54$). Only weak correlations have been reported in COPD between ISWT distance and age or lung function, as might be expected. For patients with lung cancer, the ISWT correlates moderately to quadriceps and inspiratory muscle strength but only weakly to lung function. There is evidence that the ISWT is also a valid tool for use in bronchiectasis with moderate correlations observed for $\dot{V}O_2$Peak, steps per day, MRC, and peak workload.

For patients with asthma, the ISWT has been validated in those who do not demonstrate exercise-induced bronchodilation. When comparing the response between the ISWT and a constant work rate (CWR) treadmill-based CPET test, there were similar responses in ventilatory efficiency ($\dot{V}E/\dot{V}CO_2$ 32 ± 8 vs 19.7); however, the ISWT elicited a greater ventilatory demand than the CWR treadmill test (VE/MVV 0.5 ± 0.2 vs 0.4 ± 0.2). This may have been a relative effect of comparing an incremental test to a CWR test which was performed at 40% of an incremental alternative. The development of a modified ISWT (MST) has demonstrated a strong relationship in $\dot{V}O_2$Peak ($r = 0.95$, $p < 0.01$) for adult patients with cystic fibrosis. This relationship was expressed as $\dot{V}O_2$Peak = 6.83 [95% CI, 2.85–10.80] + 0.028 [0.019–0.024] × MST distance.

Reliability and Learning

The reliability of the ISWT for patients with COPD is strong when measured by intraclass correlation coefficients (ICC 0.88–0.93). While not measured with ICCs, initial data by Singh et al. reported an excellent correction between tests one and two ($r = 0.98$). This is also the case for patients with bronchiectasis and CF. The reliability of the ISWT has not been reported in either ILD or asthma.

Initial testing of the ISWT suggested a significant learning effect of 31 m between tests one and two, but this reduced to 2 m between tests two and three. A similar learning effect was also reported in a recent systematic review where a pooled mean difference of 20 m was reported in over 600 patients. For same-day repeatability, a learning effect of 20–40 m has been reported. For physiological variables, same-day repeatability of the ISWT has been described as −56 L/min for $\dot{V}O_2$Peak (coefficient of repeatability (CR) of 414 L/min), 56 L/min for $\dot{V}CO_2$Peak (CR of 329 L/min), 0.09 for RER (CR of 0.24), 4 bpm for end test HR (CR 13 bpm), and 0 for end test SpO_2 (CR of 4%). Expert opinion would suggest that two tests should be performed when establishing a baseline ISWT, with the best distance recorded. Recent audit data in the United Kingdom highlights that this is not routine practice for many clinical services. Many services may struggle with this repetition in terms of time and provision; however, its completion allows for accurate assessment of exercise performance and prescription required for optimal exercise training as recommended internationally.

Repeatability of the ISWT within other respiratory populations is unclear. In ILD the learning effect is suggested to be 29 m, while for bronchiectasis, this effect was absent between tests with only a 4-meter difference. In a population of adult patients with CF, there was no difference between the distance walked on two tests (mean 0, 95% CI −1–1). Repeatability of the ISWT has not been confirmed in adult patients with asthma.

10.7 ISWT as a Clinical Indicator

Performance of the ISWT has proven useful for predicting mortality in patients with COPD with a suggested distance threshold of <170 m indicating greater mortality and in predicting hospital readmission following an acute exacerbation of COPD. The test has also been incorporated into the multidimensional tool, the iBODE (body mass index, degree of airflow obstruction, dyspnea, and exercise capacity (by ISWT)), which has proven valuable as a composite measure for the categorization and prediction of outcome in patients with COPD. This has not been duplicated in other respiratory conditions.

10.8 Reference Equations

Numerous reference equations have been published for predicting $\dot{V}O_2$Peak from the ISWT. One of these studies was conducted in a South American population and was not age matched to a COPD population; however, another based in India grouped patients by three age ranges. A European-based study observed that age, body mass index (BMI), FEV_1, quadriceps strength, and physical activity explained 50% of the variation in the ISWT distance. No predictive equations have been reported within other respiratory populations.

10.9 Meaningful Change in the ISWT

Minimal Important Difference
The minimal important difference (MID) for the ISWT for patients with COPD and following pulmonary rehabilitation has been estimated at 48 m. This measure was calculated using a patient preference approach, rather than a statistical model. For patients with non-CF bronchiectasis, an MCID of 35 m has been identified.

Impact of Interventions on ISWT
The ISWT is sensitive in identifying exercise-induced desaturation in patients with COPD, and distance walked is sensitive for identifying improvements in oxygenation when ambulatory oxygen was administered. This study identified a significant increase of 33 m in ISW distance when patients received supplemental ambulatory oxygen when compared to air. Interestingly these authors also identified a significant reduction of 29 m in ISW distance in persons carrying an air cylinder when compared to an unencumbered control walk. This highlights the benefits of supplemental oxygen but also that the method of ambulation (i.e., carrying with a backpack or on a walker) should be documented, enabling standardization of the test on subsequent visits. The use of a walking aid has also demonstrated a useful tool worthy of prescription for increasing walking distance for patients with COPD.

The ISWT is sensitive to exercise-based interventions such as pulmonary rehabilitation for patients with COPD and a variety of respiratory and long-term chronic diseases (such as heart failure). Studies report a range of ISWT responses to pulmonary rehabilitation from 36 to 61 m. A pooled mean improvement of 40 m has been suggested in the latest Cochrane Review; however, only half of the studies achieved the suggested MID. An effect size of 0.65 has also been reported for the ISWT following pulmonary rehabilitation. For patients with ILD, significant improvements in ISWT distance have been reported following pulmonary rehabilitation; however, these gains were not observed for those patients prescribed with oxygen therapy. A recent systematic review in patients with non-CF bronchiectasis has suggested improvement of the ISWT following pulmonary rehabilitation with weighted mean difference of 67 m, coinciding with improvements in health status.

With relation to the sensitivity of the ISWT to detect changes following bronchodilation, significant improvements of 30 m have been reported following the administration of nebulized salbutamol and ipratropium. This was not however translated into any significant improvements in breathlessness scores. For patients with chronic asthma, the response of the ISWT has not been reported following either bronchodilation or exercise-based interventions.

10.9.1 Endurance Shuttle Walk Test (ESWT)

10.9.1.1 Background

The ESWT is an endurance or constant work rate derivative of the ISWT, using the same walking track and setup but with a different protocol. The primary outcome of the ESWT is time and should be reported in seconds or percent change following an intervention. For this test, after an initial warm-up period of 2 min, the speed of walking is kept constant. The speed of walking is derived from the results of the ISWT, and therefore the ESWT cannot be completed as a stand-alone test. The test was developed as a submaximal measure of function for the assessment of disability in patients with COPD as a companion to the ISWT. As such, an accurate prediction of 85% peak performance is dependent upon the patient completing an adequate ISWT prior to calculating the appropriate speed of the ESWT. An added benefit of performing an ESWT is that it allows a health-care provider to prescribe a level of exercise at a given threshold value, enabling accurate and optimal aerobic training. It also serves as a responsive outcome measure. At the present time, the majority of ESWT data has been reported within the COPD population; however there is growing use of this test within other respiratory populations.

Validity
There is limited evidence regarding the validity of the ESWT. However, during the developmental stages of the ESWT, the test was validated against a laboratory-based constant work rate treadmill test in patients with COPD. The ESWT and treadmill constant work rate test elicited similar physiological and metabolic responses for $\dot{V}O_2$Peak, $\dot{V}_E$Peak, breaths per minute, tidal volume, and heart rate per minute, when tests were performed at both 75 and 85% predicted $\dot{V}O_2$Peak (using the ISWT equation). This was not the case when patients performed near maximal testing (95% $\dot{V}O_2$Peak).

Reliability and Learning
For patients with COPD, the learning effect for the ESWT has been reported as 60 s between tests one and two, when the test is performed at 85% predicted $\dot{V}O_2$Peak obtained from the ISWT. While this was not statistically significant, there was a significant increase in distance between tests one and three by 74 s. The same authors who developed the ESWT also suggested a nonsignificant mean increase in ESWT duration of 12 s between tests one and two when measuring on the same day

in 68 patients with COPD. This small difference in duration was confirmed by Bland and Altman (BA) plots where the coefficient of repeatability was ±100 s. Further studies have reported test-retest differences of −7 to −2 s. These data also identified some variability in ESWT performance associated with longer endurance time. This variation may be evident in patients who walk for longer as they are more sensitive to external influences such as motivation, mood, or boredom.

10.9.1.2 Meaningful Change in ESWT

Minimum Important Difference

Different values have been proposed for the MID of the ESWT, depending on the nature of the intervention. While Pepin et al. reported an MID of 45–85 s (or 60–115 m) following bronchodilation, the authors were unable to determine an MID for pulmonary rehabilitation using a preference-based approach. These authors did however report that a distribution-based analysis suggested an MID of 186–203 s. This was equivalent to 136% change in performance. Borel et al. (2014) more recently reported a similar MID range following a bronchodilation intervention of tiotropium plus additional fluticasone/salmeterol (fixed-dose combination), proposing that an improvement of 56–61 s, or distance of 70–82 m, was meaningful to patients. For patients with a diagnosis of respiratory failure, an MID in the range of 186–199 s or 154–164 m has been reported when anchored to health-related quality of life and exercise capacity.

Impact of Interventions

It is generally accepted that a constant work rate test is likely to be more sensitive to an intervention than a maximal exercise test, and this is observed when comparing the ISWT and ESWT. Given the increasing awareness of the responsive properties of the ESWT, there is a growing use of the test in clinical trials.

There is growing literature on ESWT response to bronchodilation. Pepin et al. have reported the response of the ESWT on two separate occasions found similar significant improvements (164 and 144 s, respectively) along with strong effect sizes (ES) of 0.93 and 0.66. Brouillard and colleagues reported similar responses with a significant improvement of 117 s and a moderate ES (0.56) following bronchodilation with salmeterol. A more recent study of tiotropium reported a difference of 117 s following 3 weeks of therapy. These improvements in exercise function were also translated into significant improvements in breathlessness at end test.

Response of ESWT to pulmonary rehabilitation has been reported as significant with improvement of 160 s from baseline and a strong ES of 2.90. Other trials have also reported significantly high responses with improvements ranging from 293 to 408 s. Unfortunately, the ESWT has not been included in any large Cochrane Reviews to date, and this may be a consequence of the small volume of literature available at the time of the review. However, a recent systematic review by Singh et al. reported the test responsiveness with standardized response means ranging from 0.52 to 1.27, with two of the six studies reported evaluating pulmonary rehabilitation.

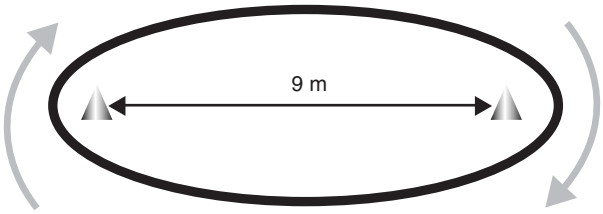

Fig. 10.2 Layout and conduct of the Shuttle Walk Test

10.10 Performing the ISWT and ESWT

Both incremental and endurance SWT utilize a 10-meter track marked with cones at either end Fig. 10.2. The remaining 1 m is accounted for in the turn required at either end of the track. The ISWT is a maximal and progressive symptom-limited test that is externally paced using an incremental speed which is indicated using an audio signal. The ESWT is a constant work rate test, which requires that an ISWT is performed first to establish the workload. The test should be conducted in a quiet corridor or dedicated exercise testing room. Standardized encouragement is required for both tests.

Contraindications and Precautions
As the ISWT is designed to elicit maximal exercise performance, the same contraindications and precautions as a CPET should be applied (TS).

Baseline Measurements
Before the test, physiological parameters should be collected including blood pressure, pulse rate, and oxygen saturation along with scales of perceived exertion and breathlessness.

Patient Instructions
Initial test instructions are given by the audio recording and are reproduced in the Technical Standard. An operator should pace the patient for the first minute/level of the test before stepping away, unless closer supervision is required for patient safety. Patients should not run during the ISWT. When running, $\dot{V}O_2$Peak increases in direct proportion to velocity and therefore is more efficient than walking. This change in metabolic demand would therefore render the predictive equation of the ISWT invalid.

Setting the Speed for the ESWT
The ESWT is calculated as a percentage of peak performance of the ISWT (e.g., 70–85% estimated $\dot{V}O_2$Peak) or a percentage of the peak speed achieved. The ESWT includes a warm-up period of 1.5 min, after which the patient should be paced for the first two shuttles. When choosing an appropriate speed, an operator should calculate the predicted $\dot{V}O_2$Peak (4.19 + (0.025 * ISWT distance)) followed by the percentage work the patient needs to work at (i.e., 70–85%). This percent-predicted $\dot{V}O_2$Peak can then be used to identify the appropriate walking speed for the ESWT.

Encouragement
For the ISWT, as the speed of walking increases every minute, indicated by a triple bleep, the patient should be advised:

"You now need to increase your speed of walking."

During both ISWT and ESWT, only one verbal cue can be used to encourage the patient to pick up their speed; if they are more than 0.5 m from the marker when the bleep sounds:

"You need to increase your speed to keep up with the test."

No other verbal cues should be given.

Measures Taken during the SWTs
The assessor counts the number of shuttles completed during the test. It is advisable to time the performance as an additional measure, to confirm manual recording of the number of shuttles completed.

Stopping the SWTs
The test is ceased if the patient is more than 0.5 of a meter from the marker when the auditory cue sounds for a second successive shuttle. The test is also ceased if the patent indicates symptom limitation (e.g., too breathless or tired to continue). It may also be terminated at the assessor's discretion should there be a drop of SpO_2 below 80%, an increase in cardiac frequency above 85% predicated heart rate maximum, or the patient feeling generally unwell. For an ESWT, the test should last between 180 and 480 s in duration, allowing for an optimal physiological response to the point of symptom limitation. If a patient exceeds this time, the test should be stopped and the patient allowed to rest. Once the patient has rested, a further test should be completed at one or two levels above the first. The operator's decision on prescribed speed should be guided by the patient's physiological and self-reported response to the first test.

Test Repetition
Due to the learning effect on the ISWT, two tests are recommended to obtain an accurate baseline. Repeat testing should occur following a 30-min rest or sufficient time to allow recovery of all physiological and symptom measures to baseline. Two tests do not appear to be required for an accurate baseline ESWT measurement. After an intervention the ESWT should be repeated at the same speed as at baseline, in order to accurately identify any treatment effects.

Use of Oxygen
In order to interpret change over time, the SWTs should be performed with oxygen delivered at the same flow rate and by the same method, where possible. The delivery system, flow rate, and method of carrying the oxygen (patient or assessor, backpack or trolley, etc.) should be documented on the testing form.

Recording Performance
The primary outcome of the ISWT is distance, reported as an accumulation of 10-m lengths. The minimum distance is 0 m if patients fail to complete the first shuttle, and the maximum is 1020 m. It can also be reported as percent predicted, noting the reference equation used. The ESWT is reported as time (minutes and seconds), although it can also be expressed as distance. The recording form should include

SpO_2, heart rate, dyspnea, and fatigue scores at the beginning and end of the test, as well as the lowest SpO_2 recorded during the test. The reason for test termination should be recorded. Examples of recording forms are available with the Technical Standard.

10.11 Safety of the Shuttle Walk Tests

Subjects with angina or a recent myocardial infarction (1 month) should be discussed with the referring physician and testing under physician supervision when clinically safe. Stable exertional angina is not an absolute contraindication for a field walking test, but subjects with these symptoms should perform the test after using their anti-angina medication, and rescue nitrate medication should be readily available. Indeed, the ISWT has been used as an outcome for cardiac rehabilitation and is therefore a safe test to perform on patients with cardiac disease.

10.12 Clinical Examples Using the ISWT and ESWT

The following examples illustrate the use of the ISWT and ESWT in clinical practice:

ISWT example: Patient with COPD referred for pulmonary rehabilitation. Mr. A, a 69-year-old gentleman, attended a pulmonary rehabilitation assessment clinic during the winter. He had a confirmed diagnosis of COPD with post-bronchodilator spirometry of FEV_1 54% predicted and FEV_1/FVC 52%. He had an MRC breathlessness score of four, regular sputum production, and cough. No cardiovascular symptoms on questioning. He had a symptom burden score (CAT score) of 30 and CRQ-dyspnea score of 2.2 indicating he was disabled with breathlessness. Comorbidities consisted of hypertension (managed with an ACE inhibitor and a diuretic) and previous DVT and PE for which he was on warfarin. Mr. A also had a BMI of 38.3 $kg.m^{-2}$. He was treated with a combination inhaler (steroid/long-acting β_2-agonist), along with long-acting muscarinic receptor antagonist (LAMA) and a short-acting $Beta_2$-agonist (SAMA) for acute relief. This gentleman's 85% heart rate maximum (HRmax) was estimated at 128.

At rest he had finger oximetry (SpO_2) of 93% on room air and a pulse rate (regular) of 92 with a blood pressure of 120/65. His Borg breathlessness score was one. No ankle swelling and JVP were unremarkable.

Mr. A performed 120 m in his first ISWT, and test termination was due to breathlessness and leg fatigue. At end test, his SpO_2 was 90% (nadir SpO_2 was 90%) on room air and a pulse rate (regular) at 133 with a blood pressure of 136/72. His perceived breathlessness score was five and rate of perceived exertion was 17. These values returned to baseline within minutes after a short period of rest. A second test

was performed after 30 min. This second test measured 20 m less than the first (100 m) but with the same test termination (breathlessness and leg fatigue). At end test his SpO_2 was 92% on room air and a pulse rate (regular) at 103 with a blood pressure of 120/65. His perceived breathlessness score was five and rate of perceived exertion was 17.

Mr. A expressed that he was really happy with the distance that he had covered at the speed he had performed.

Key Notes

- Mr. A presents as a very symptomatic patient with moderate COPD (GOLD 2) with a very high CAT (30), an MRC of four, and an extreme breathlessness when measured using the CRQ dyspnea.
- The best test performed by Mr. A was test one despite both tests eliciting levels of severe breathlessness and leg fatigue. This is indicted by the first test provoking a good cardiovascular response to just above his predicted 85%HRmax. There was adequate rise in blood pressure within acceptable level for an exercise test.
- Mr. A displayed a decrease in his SpO_2 to 90%. While this would not constitute an additional prescription of oxygen, it would be clinically wise to monitor this during exercise training for any additional desaturation that may warrant further assessment.
- Given that Mr. A has a history of hypertension, the ISWT may identify excessive rises or even decompensation at end test if there was a drop in blood pressure below 10% of resting BP. It is therefore suggested that blood pressure is measured in all patients presenting in clinic for an ISWT. This allows a thorough interrogation of the systemic responses to exercise and hence optimizes the safety of patients entering pulmonary rehabilitation.
- ESWT example: calculation and performance of the ESWT.
- Using the example above, we can assume that Mr. A performed an accurate test (we know he performed a good maximal test due to his responses) and that his predicted $\dot{V}O_2$Peak, using the following predictive equation ($\dot{V}O_2$Peak (ml/min/kg) = 4.19 + (0.025 * ISWT distance)) was 7.19 (ml/min/kg).
- When choosing the speed for the ESWT, we calculate 85% of his predicated $\dot{V}O_2$Peak (7.19 * 0.85 = 6.11 (ml/min/kg). If we use the published equations, we find that in order for Mr. A to perform an endurance test at 60.11 (ml/min/kg) $\dot{V}O_2$Peak, the speed of choice was approximately 2.72 km/h (the closest level to the prediction).
- Using this calculation, Mr. A completed an ESWT at level four. The duration of his test was 240 s, exceeding the lower threshold of 3 min for conducting a good test. His end test responses were SpO_2 was 94% on room

air and a pulse rate (regular) at 118 with a blood pressure of 133/72. His perceived breathlessness score was five and rate of perceived exertion was 15. Reason for termination was breathlessness and leg fatigue.

- This endurance test elicited the suggested duration of a CWR test (180 s) and elicited a submaximal response at 85% of his predicted $\dot{V}O_2$Peak. When compared to his maximal test, these physiological responses are noted with less desaturation and less increase in cardiovascular outputs. While Mr. A reported severe breathlessness, his perceived leg fatigue was less than the ISWT.
- In terms of exercise prescription, level four would be an optimal training prescription for Mr. A with the aim to increase the duration of his walks over time. Clinically, and if Mr. A was finding training at level four too hard, the health-care professional could decrease to level three and be guided by the Borg breathlessness scale to gauge training efficiency.
- On completing pulmonary rehabilitation, the test should be repeated at the same level (level four in Mr. A's case). This enables the greatest changes to be assessed. If a new ESWT was calculated from a new ISWT, any treatment effect may be lost.

Selected References

American Thoracic S, American College of Chest P. ATS/ACCP statement on cardiopulmonary exercise testing. Am J Respir Crit Care Med. 2003;167(2):211–77.

Bolton CE, Bevan-Smith EF, Blakey JD, Crowe P, Elkin SL, Garrod R, Greening NJ, Heslop K, Hull JH, Man WD, Morgan MD, Proud D, Roberts CM, Sewell L, Singh SJ, Walker PP, Walmsley S. British Thoracic Society pulmonary rehabilitation guideline development G, British Thoracic Society standards of care C. British Thoracic Society guideline on pulmonary rehabilitation in adults. Thorax. 2013;68(Suppl 2):ii1–30.

Borel B, Pepin V, Mahler DA, Nadreau E, Maltais F. Prospective validation of the endurance shuttle walking test in the context of bronchodilation in COPD. Eur Respir J. 2014;44(5):1166–76. https://doi.org/10.1183/09031936.00024314.

Celli B, Cote C, Lareau S, Meek P. Predictors of survival in COPD: more than just the FEV1. Respir Med. 2008;102(Suppl 1):S27–35.

Chandra D, Wise R, Hrishikesh S, et al. Optimising the 6-min walk test as a measure of exercise capacity in COPD. Chest. 2012;142:1545–52.

Dyer CA, Singh SJ, Stockley RA, Sinclair AJ, Hill SL. The incremental shuttle walking test in elderly people with chronic airflow limitation. Thorax. 2002;57(1):34–8.

Eaton T, Young P, Milne D. Six-minute walk, maximal exercise tests: reproducibility in fibrotic interstitial pneumonia. Am J Respir Crit Care Med. 2005;171:1150–7.

Granger C, denehy L, Parry S, Martin J, Dimitriadis T, Sorohan M, Irving L. Which field walking test should be used to assess functional exercise capacity in lung cancer? An observational study. BMC Pulm Med. 2015;15:89.

Harrison SL, Greening NJ, Houchen-Wolloff L, Bankart J, Morgan MD, Steiner MC, Singh SJ. Age-specific normal values for the incremental shuttle walk test in a healthy British population. J Cardiopulm Rehabil Prev. 2013;33(5):309–13.

Hernandes N, Wouters E, Meijer K, et al. Reproducibility of 6-minute walking test in patients with COPD. Eur Respir J. 2011;38:261–7.

Hill K, Dolmage TE, Woon L, Coutts D, Goldstein R, Brooks D. Comparing peak and submaximal cardiorespiratory responses during field walking tests with incremental cycle ergometry in COPD. Respirology (Carlton, Vic). 2012;17(2):278–84.

Holland A, Spruit M, Singh S. How to carry out a field walking test in chronic respiratory disease. Breathe. 2015;11(2):129–39.

Holland A, Spruit M, Troosters T, Puhan M, Pepin V, Saey D, MCCormack M, Carlin B, Sciurba F, pitta F, Wanger J, MacIntyre N, Kaminsky D, Culver B, Revill S, Hernandres N, Andrianopoulos V, Camillo C, Mitchell K, Lee A, Hill C, Singh S. An official European Respiratory Society / American Thoracic Society technical standard: field walking tests in chronic respiratory disease. Eur Respir J. 2014;44(6):1428–46.

Leger LA, Lambert J. A maximal multistage 20-m shuttle run test to predict VO2 max. Eur J Appl Physiol Occup Physiol. 1982;49(1):1–12.

Mador MJ, Modi K. Comparing various exercise tests for assessing the response to pulmonary rehabilitation in patients with COPD. J Cardiopulm Rehabil Prev. 2016;36(2):132–9.

McKeough ZJ, Leung RW, Alison JA. Shuttle walk tests as outcome measures: are two incremental shuttle walk tests and two endurance shuttle walk tests necessary? Am J Phys Med Rehabil. 2011;90(1):35–9.

Pepin V, Laviolette L, Brouillard C, Sewell L, Singh SJ, Revill SM, Lacasse Y, Maltais F. Significance of changes in endurance shuttle walking performance. Thorax. 2011;66(2):115–20.

Probst VS, Hernandes NA, Teixeira DC, Felcar JM, Mesquita RB, Goncalves CG, Hayashi D, Singh S, Pitta F. Reference values for the incremental shuttle walking test. Respir Med. 2012;106(2):243–8.

Puente-Maestu L, Palange P, Casaburi R, Laveneziana P, Maltais F, Neder JA, O'Donnell DE, Onorati P, Porszasz J, Rabinovich R, Rossiter HB, Singh S, Troosters T, Ward S. Use of exercise testing in the evaluation of interventional efficacy: an official ERS statement. Eur Respir J. 2016. doi: ERJ-00745-2015 [pii];47:429.

Revill SM, Noor MZ, Butcher G, Ward MJ. The endurance shuttle walk test: an alternative to the six-minute walk test for the assessment of ambulatory oxygen. Chron Respir Dis. 2010;7(4):239–45.

Sandland CJ, Morgan MD, Singh SJ. Detecting oxygen desaturation in patients with COPD: incremental versus endurance shuttle walking. Respir Med. 2008;102(8):1148–52.

Singh S, Puhan M, Andrianopoulos V, Hernandes N, Mitchell K, Hill C, Lee A, Camillo C, Troosters T, Spruit M, Carlin B, Wanger J, Pepin V, Saey D, Pitta F, Kaminsky D, MCCormack M, MacIntyre N, Culver B, Sciurba F, REvill S, Delafosse V, Holland A. An official systematic review of the European Respiratory Society / American Thoracic Society: measurement properties of field walking tests in chronic respiratory disease. Eur Respir J. 2014;44(6):1447–78.

Singh SJ, Jones PW, Evans R, Morgan MD. Minimum clinically important improvement for the incremental shuttle walking test. Thorax. 2008;63(9):775–7.

Singh SJ, Morgan MD, Hardman AE, Rowe C, Bardsley PA. Comparison of oxygen uptake during a conventional treadmill test and the shuttle walking test in chronic airflow limitation. Eur Respir J. 1994;7(11):2016–20.

Singh SJ, Morgan MD, Scott S, Walters D, Hardman AE. Development of a shuttle walking test of disability in patients with chronic airways obstruction. Thorax. 1992;47(12):1019–24.

Spruit M, Polkey M, Celli B, Edwards L, Watkins M, Pinto-Plata V, Vestbo J, Calverley P, Tal-Singer R, Agusti A, Coxson H, Lomas D, MacNee W, Rennard S, Silverman E, Crim C, Yates J, Wouters E, investigators EoCltipseEs. Predicting outcomes from 6-minute walk distance in chronic obstructive pulmonary disease. J Am Med Dir Assoc. 2012;13(3):291–7.

Van Gestel A, Clarenbach C, Stowhas A, et al. Prevalence and prediction of exercise-induced oxygen desaturation in patients with chronic obstructive pulmonary disease. Respiration. 2012;84:353–9.