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A Randomized Controlled Trial of Rollator-Style Walkers and Oxygen in Chronic Obstructive Pulmonary Disease

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ABSTRACT

Statement of Problem: The ability to walk, fundamental to a good quality of life, is affected by chronic obstructive pulmonary disease. Rollator-style walkers and oxygen are both used clinically to improve the ability to walk in people with mildly hypoxemia and exertional desaturation. However, there is little evidence on which is more efficacious and significant cost differences exist between the interventions. This trial directly compared rollator-style walkers to oxygen.

Methods: A single-blind randomized controlled crossover trial was used to assess the effect of rollator-style walkers compared to oxygen (4 liters per minute) on distance walked, oxygen saturation, perceived exertion, speed and number of rest breaks measured by the six-minute walk test. Open- and closed-ended questions were used to elicit the subject's values and feelings towards the interventions.

Results: Eleven participants were recruited (May 2001 to January 2002) from a tertiary rehabilitation centre. The patients mean age (± standard deviation) was 67.5 ± 16.6 years, mean percent predicted forced expiratory velocity in one second ($FEV_{1.0}$) was 26.1 ± 6.8 %, and mean PaO_2 was 61.2 ± 2.3 mmHg. There were no significant period by treatment interactions, or period effects on any outcome. Oxygen significantly outperformed the rollator-style walker on final oxygen saturation (7.8 percent (95% CI 5.0 to 10.6)) and perceived exertion (1.3 points (95% CI 0.1 to 2.4)) but there was no difference noted on distance walked (22.2 metres (95% CI: –76.7 to +32.4)) or speed (-0.02 metres/second (95% CI: -0.13 to 0.08)). Compared to unassisted walks, oxygen improved distanced walked (51.3 metres (95% CI 18.6 to 84.0)) but rollator-style walkers did not (31.4 metres (95% CI –3.4 to 66.2)). Participants indicated that both interventions improved their walking but more participants preferred the rollator-style walker.

Conclusions: In spite of oxygen reducing arterial desaturation, rollator-style walkers resulted in similar distance walked compared to oxygen. However, when compared to unassisted walks, oxygen appears to be more effective in increasing distance walked. Rollator-style walkers are a lower cost alternative to oxygen in individuals with COPD and exertional desaturation whose resting arterial oxygen is between 55 – 65 mmHg.

KEY WORDS: COPD, rollator-style walkers, oxygen, rehabilitation, six-minute walk

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This is dedicated to my patients, who gave me the motivation to start; to my parents, who taught me to believe in myself; and to Andy, whose love and support made this possible.

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CHAPTER ONE: INTRODUCTION

Chronic obstructive pulmonary disease (COPD), traditionally encompassing chronic bronchitis and emphysema, includes lung disease processes that result in reduced expiratory flow rates that are minimally reversible with bronchodilators. Individuals with moderate to severe COPD show reduced health related quality of life (HRQL), particularly on the dimensions related to physical function (1-4). The ability to walk is fundamental to independence and a good quality of life. Both rollator-style walkers and oxygen are routinely used to improve walking endurance, but it is unclear if rollator-style walkers (Appendix A) or oxygen are effective at improving the ability to walk in people with COPD, mild hypoxemia and exertional desaturation. Because COPD is highly prevalent, affecting an estimated half-million Canadians (5), and impacts on a patient's HRQL, and because the efficacy of the rollator-style walkers and oxygen is unclear, the improvement of a patient's ability to walk forms a clinically important issue.

PREVALENCE OF COPD

The National Population Health Survey (NPHS) surveyed over 17,000 Canadian adults and estimated COPD prevalence to range from 1.5 to 9.1% (6;7). Approximately half a million Canadians suffer from COPD (5). The prevalence varies by age and gender, likely as a result of historic variations in smoking patterns (5;6). The NPHS estimates COPD to occur in 5.7% (95% CI 4.9 – 6.6) of people aged $\geq$ 55 years (both genders) and as high as 7.8% (95% CI 5.2 - 10.5) and 9.1% (95% CI 5.4 – 12.9) in females and males over 75 years respectively

(Table 1). Based on the variation in prevalence by age, the largest number of Canadians with COPD falls into the 55 to 74 year-old age group; approximately 214,000 people (5).

The prevalence of the disease has been changing over time, likely based on changes in smoking patterns. The prevalence appears to be dropping for both men and women under 54 years and increasing for women between 55 and 74 years (5). These estimates, taken from the NPHS, relied on self-reports; the numbers are based on self-report of physician diagnosis. This may have led to under-reporting of COPD, because individuals are asymptomatic in the early stages of the disease. Mild COPD is often not clinically symptomatic, particularly in sedentary individuals, and includes people with lung function ($FEV_{1.0}$) as low as 60% of their predicted value. As a result, the true Canadian prevalence may be slightly higher than the estimate from the NPHS. Supporting this hypothesis was the finding, by the Third United States National Health and Nutrition Examination Survey, of low lung function in greater than 10% of the adult population over 45 years of age (8). The survey used laboratory assessment of pulmonary function from a random sample of 20,050 adults over the age of 17, which included people with asymptomatic disease. Low lung function was used as a proxy for the presence of COPD and was defined as forced expiratory volume in one second ($FEV_{1.0}$) less than 80% of the predicted value and the ratio of $FEV_{1.0}$ to forced vital capacity of less than 0.70 (8). This definition of low lung function is suggestive of COPD but is not sufficient for diagnosis and it may capture individuals with mild COPD who would not self-report a diagnosis of

COPD. Despite the bias introduced by self-reported disease, it is clear that COPD affects a large number of Canadian adults, and particularly aging adults.

Table 1. Prevalence of self-reported COPD by age and gender in Canada.

	Male			Female		
Age (years)	Percent	95% CI	Prevalence[3]	Percent	95% CI	Prevalence[3]
35 – 44[1]	1.8	1.0 – 2.5	75,700	3.5	2.4 – 4.6	106,200
45 – 54[1]	1.5	0.7 – 2.4		3.6	2.3 – 4.9	
55 – 64[1]	5.0	3.2 – 6.8	89,300	4.5	2.9 – 6.2	124,400
65 – 74[2]	6.6	4.5 – 8.8		4.5	3.0 – 6.0	
≥ 75[2]	9.1	5.4 – 12.9	46,800	7.8	5.2 – 10.5	56,000
≥ 55[2]	6.3	5.0 – 7.7		5.2	4.2 – 6.3	

[1] Chen et al. [reference (7)]
[2] Lacasse et al. [reference (6)]
[3] Prevalence is reported for 35 to 54 years, 55 to 74 years, and 75+ years [reference (5)]

MORBIDITY AND QUALITY OF LIFE RELATED TO COPD

COPD hospital morbidity, operationally defined as the number of hospital separations for COPD, has increased in the last twenty years in Canada. Age-standardized hospital separation rates for women increased by approximately 25% between 1980 and 1995, but the rate for men decreased slightly (6). In 1995, COPD was the primary diagnosis in 55,785 hospital separations (6). As with prevalence, there appears to be a gender effect, which may be related to variations in smoking patterns.

HRQL, measured by the Short-Form 36 (SF – 36) generic tool, is lower in individuals with COPD than in the general population (1-4). The SF – 36 reportes general HRQL through two subscales; physical component and mental component scores. There are eight further subscales that report of varying dimensions of HRQL including physical function, physical role, and general health. The SF – 36 scale ranges from zero to 100 where a higher score represents better HRQL. HRQL declines as COPD becomes more severe (1). Of particular relevance to the ability to walk are the scores seen on the physical function, physical role and general health scales (Table 2). Values for moderate and severe disease are presented along side values taken form the general population. People with mild COPD are not reported in the literature, likely because mild disease is often asymptomatic and undiagnosed. It is expected that this population would have values similar to their peers without COPD. Because physical ability is such an integral part of HRQL, it is hypothesized that any improvement in the ability to walk may improve HRQL scores.

Table 2. Health related quality of life changes in COPD by disease severity.

SF-36 Subscales	Canadian Norms[1] (25+ years) (n = 9395)[5]	(65–74 years) (n = 2921)[5]	COPD Severity Moderate[2] (n = 50)	Moderate[3] (n = 95)	Severe[4] (n = 19)
Physical Function	85.8 ± 20.0	75.7 ± 22.2	43.6 ± 28.5	46 ± 25	21.9 ± 21.8
Role: Physical	82.1 ± 33.2	76.2 ± 36.5	42.0 ± 40.5	44 ± 42	18.4 ± 34.2
General Health	77.0 ± 17.7	73.5 ± 18.4	43.5 ± 20.3	42 ± 22	32.6 ± 21.9

[1] Hopman et al. [reference (9)]
[2] Mahler et al. [reference (2)]
[3] Jones et al. [reference (3)]
[4] Moy et al. [reference (1)]
[5] Some categories included slightly more participants

ROLE OF INTERVENTIONS IN PULMONARY REHABILITATION

Pulmonary rehabilitation is defined as an interdisciplinary program of care for patients with chronic respiratory impairment that is individually tailored and designed to optimize physical and social performance and autonomy (10;11), which improves HRQL (12). This includes exercise training, education, and psychosocial and behavioural interventions (10;11). Current clinical practice often includes the prescription of rollator-style walkers, oxygen, or both in order to achieve these goals.

There is clear benefit from providing oxygen for people with COPD and resting PaO_2 of less than 55 mmHg. It increases exercise tolerance and life expectancy (13;14). There is moderate evidence of benefit for distance walked from the use of rollator-style walkers, by as much as 13%, for people with COPD who are severely impaired in their ability to walk (15-17). There is little evidence, however, for either intervention (rollator-style walkers or oxygen) in the small subgroup of individuals with mild hypoxemia (resting PaO_2 of 55 to 65 mmHg) and exertional desaturation ($\leq 88\%$) (18). Exertional desaturation refers to the decrease in PaO_2 during physical activity and can be measured indirectly through SaO_2. Lastly, there is no evidence to support the use of either intervention in the least impaired group ($PaO_2 > 65$mmHg) (17).

There are few risks from either intervention. The primary risk from oxygen, in this population, is the possibility $PaCO_2$ retention (19). $PaCO_2$ is the partial atmospheric pressure of carbon dioxide dissolved in the blood. The normal range is 35 – 45 mmHg. The amount of carbon dioxide in the blood is the primary indicator to the brain for initiation of respiration; therefore increased $PaCO_2$ levels reduce the drive to breathe. Secondary risks include the possibility of fire because oxygen supports combustion, risk of injury from the presence of oxygen canisters in the home, and irritation of the skin from the nasal cannula. There are no documented physical risks from the using the rollator-style walker in this population, however, it has been suggested that a rollator-style walker may increase mobility and independence thereby increasing their risk for falls and injury.

ECONOMIC BURDEN OF COPD

When considering the economic burden of disease there are three primary sources of direct costs; health care resources consumed, patient and family resources consumed and resources consumed from other sectors (20). In this situation, both rollator-style walkers and oxygen consume all three types due to the nature of their funding formulas, which are described below. The majority of the total cost of each intervention is publicly funded.

The total direct costs of rollator-style walkers and oxygen are substantially different from each other in Ontario. Oxygen is provided to eligible individuals with the province paying $400 per month or $24,000 over five years. In Ontario, approximately 63 million dollars were spent providing the home oxygen program in 1999 (21). Rollator-style walkers are provided to eligible individuals for approximately $500 with the province paying approximately $350 with expected use for five years.

The province of Ontario fully reimburses the cost of oxygen for residents over 65 years of age, for those who receive certain social benefits, and for those who reside in long term care facilities. The province reimburses all other residents for 75% of the $400 per month. For all residents, regardless of funding status, approval for use of oxygen is based on the criteria of resting PaO_2[a] of 55 mmHg or less, or SaO_2[b] of 88% or less in an individual whose condition and treatment regime has been stabilized. This decision has been based on randomized controlled trials that indicate oxygen supplementation under these conditions increases life expectancy (13;14). Individuals with a PaO_2 of 56 to 60

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[a] PaO_2 is defined as the partial atmospheric pressure of oxygen dissolved in the blood. The normal range is 90 – 106 mmHg.

[b] SaO_2 is defined as the percent saturation of oxygen in the haemoglobin. It is an indirect measure of PaO_2 and has a relationship with PaO_2 through the oxyhemoglobin dissociation curve. SaO_2 of 90% is approximately equal to a PaO_2 of 60 mmHg.

mmHg may be considered if they also demonstrate exercise-induced hypoxemia and documented improvement with oxygen. Lastly, individuals with PaO_2 of greater than 60 mmHg may be considered with additional clinical and laboratory finding through an appeals process but this is uncommon.

Partial funding of a rollator-style walker, up to 75% of the total cost, is provided to all qualifying adult residents of Ontario to a maximum of $350 (Information obtained from the Assistive Devices Program, Ontario Ministry of Health. 2002). Recipients of veterans and workplace injury pensions are fully funded through alternate sources. There are no restrictions on the provision of rollator-style walkers. Partial funding of rollator-style walkers is based on need, determined by an authorized occupational or physical therapist, for greater than six months.

SUMMARY

COPD is a moderately prevalent disease with an important contribution to morbidity in Canada. The lung impairment associated with COPD results in a reduced ability to walk and a lower HRQL. There is weak evidence to support the use of rollator-style walkers or oxygen in mildly hypoxic individuals with exertional desaturation and there is a substantial cost difference between the two interventions. Despite the state of the current evidence, the use of both interventions to improve the ability to walk is current practice. As a result, the efficacies of the two interventions need to be evaluated. The study, described here, made a direct comparison between rollator-style walkers and oxygen in COPD patients with mild hypoxia and exertional desaturation.

CHAPTER TWO: LITERATURE REVIEW

Rollator-style walkers and oxygen, separately or in combination, are used to improve the ability to walk in people with COPD. In fact, the suggestion that a rollator-style walker may be beneficial was noted in the literature as early as 1957 (22). The mechanism through which the improvement in walking ability occurs is different for both interventions. Supplemental oxygen may directly affect the amount of oxygen available to the body. Rollator-style walkers may work in a variety of ways including altering the physiology and mechanics of respiration, increasing confidence in the ability to walk, and altering the metabolic cost of walking. As a result, it is expected that each intervention will improve walking distance to different degrees.

No study has directly compared the two interventions for patients with COPD (PaO_2 55 to 65 mmHg) and exertional desaturation. There is some evidence comparing each intervention to unassisted walks, but these studies were completed on patients with a wide range of severity of COPD that does not reflect of the population with COPD who are mildly hypoxic and suffer from exertional desaturation.

THEORETICAL FRAMEWORK

Rollator-style walkers

Rollator-style walkers may improve the ability to walk in people with COPD through a variety of mechanisms that include altered physiology of respiration, altered metabolic cost of walking through slowed speed of gait, and increased confidence in the ability to walk.

Physiology of Respiration

Rollator-style walkers may increase distance walked by minimizing dynamic hyperinflation, which reduces the work of breathing. They may also further decrease the work of breathing by forward displacement of the abdominal organs.

Hyperinflation, a hallmark sign of COPD, refers to increased functional residual capacity and is caused by a restriction in the expiratory flow of air from the lungs. Increased functional residual capacity reduces the inspiratory capacity of the lungs. This is problematic for people with severe COPD because they require most of their available inspiratory capacity to perform activities of daily living. Dynamic hyperinflation refers to additional hyperinflation, which occurs during exertion or other periods of increased respiratory rate. Dynamic hyperinflation increases the work of breathing by further decreasing inspiratory capacity, increasing resistance of the lung tissue, and increasing the respiratory rate. Dynamic hyperinflation has been shown to reduce the inspiratory capacity in people with COPD over a period of exertion from 28.9 ± 6.7% to 24.1 ± 6.8% of the total lung volume during exertion (23). Dynamic hyperinflation also causes respiration to occur with higher alveolar resistance. This directly results in greater work of breathing because of the need to convert alveolar pressures from positive to negative at the end of expiration.

The role dynamic hyperinflation plays in restricting the distance people with COPD are able to walk has been evaluated indirectly. It has been shown that in people with COPD, dynamic hyperinflation, measured by inspiratory capacity at the start and end of exercise, occurs during treadmill walking (23). The ability to walk is also related to the perception of exertion. In addition, increased dynamic hyperinflation, measured by reduced in inspiratory capacity, is also highly correlated to higher perceived exertion during walking (r = -0.49) (23). Recent editorials have suggested that the focus of pulmonary function testing in COPD should routinely include the measurement of inspiratory capacity at rest and exertion for the purpose of estimating dynamic hyperinflation because of its link to exercise capacity (24).

Rollator-style walkers may reduce dynamic hyperinflation by altering the function of the shoulder muscles. Several muscles have dual roles as shoulder stabilizers / upper extremity movers and accessory muscles of inspiration; latissimus dorsi, pectoralis major and minor, and serratus anterior. When the scapula or humerus is stabilized they act as accessory inspiratory muscles of respiration (25). Importantly, regression analysis has suggested that inspiratory muscle strength is a strong predictor of exercise capacity (r = 0.50 to 0.58), measured on the 6MW or cycle ergometry (26). Supporting this hypothesis, it has been shown that body positions that involve bracing of arms allow higher levels of ventilation measured by ventilatory capacity (27). A similar relationship has been found by the introduction of handrail support during treadmill walking. Handrails significantly increase walking time and decrease oxygen consumption in normal individuals (28;29) and in those with peripheral vascular disease (30). Rollator-style walkers may provide the same effect as a handrail on a treadmill. Predictive equations for oxygen uptake (VO_2max), which is highly correlated with the 6MW, differentiate between walks with and without handrail support (31). Using the handrail reduces estimates of VO_2max (31). An increase in ventilatory requirements when the arms are elevated above the head has been shown to occur independently of ventilatory drive or metabolic demand further implicating these muscles in respiration (32). In contrast, a recent regression analysis of the impact of weight-bearing through the upper extremity as a predictor for distance walked on the 6MW showed no significant relationship (17).

Lastly, the work of breathing includes overcoming the resistance of the abdominal organ displacement; forward displacement of the abdominal contents may also allow the diaphragm to increase its participation in respiration (33). By altering posture, the use of a rollator-style walker encourages forward displacement of the abdominal contents, thereby reducing the amount of resistance generated by the abdominal organs and allowing more effective movement of the diaphragm.

Metabolic Cost of Walking

Rollator-style walkers may cause people with COPD to walk more slowly but enable them to walk for longer distances. Several studies have shown that rollator-style walkers slow the speed of walking in people with COPD (17;34). Slower speed of walking is consistent with the concept of pacing, which refers to regulating the intensity of activity. Pacing has been used in respiratory rehabilitation in order to allow people with COPD to perform activities of daily living while keeping the rate of ventilation below a level where dyspnea becomes symptomatic (10).

Research indicates that the metabolic demands increase when the speed of walking increases (35). This relationship has been shown to exist when the speed of walking is between 10 and 50 metres per minute in healthy individuals without rollator-style walkers (35). This is similar to the range of walking speeds often seen in people with COPD. It is not clear if slowing the natural speed, by the introducing a rollator-style walker, reduces metabolic demand. Studies in healthy elderly suggest they do not (36), however this is debatable because requiring healthy people to walk slowly may not be representative of a diseased population. Overall, individuals with COPD who walk more slowly appear to be able to walk longer distances (34).

Confidence

Dyspnea caused by walking may result in anxiety in people with COPD. Anxiety and panic associated with dyspnea may cause people with COPD to reduce their activity level (37) (Figure 1). The introduction of the rollator-style walker may increase confidence while walking by ensuring the individual has access to a place to rest and regain control over dyspnea at all times. As a result, people may be more likely to walk further distances. If this theorized relationship exists, then a break in the cycle of deconditioning and dyspnea proposed by Sassi-Dambron (37), may allow people with moderate and severe COPD to maintain their functional abilities for longer periods of time.

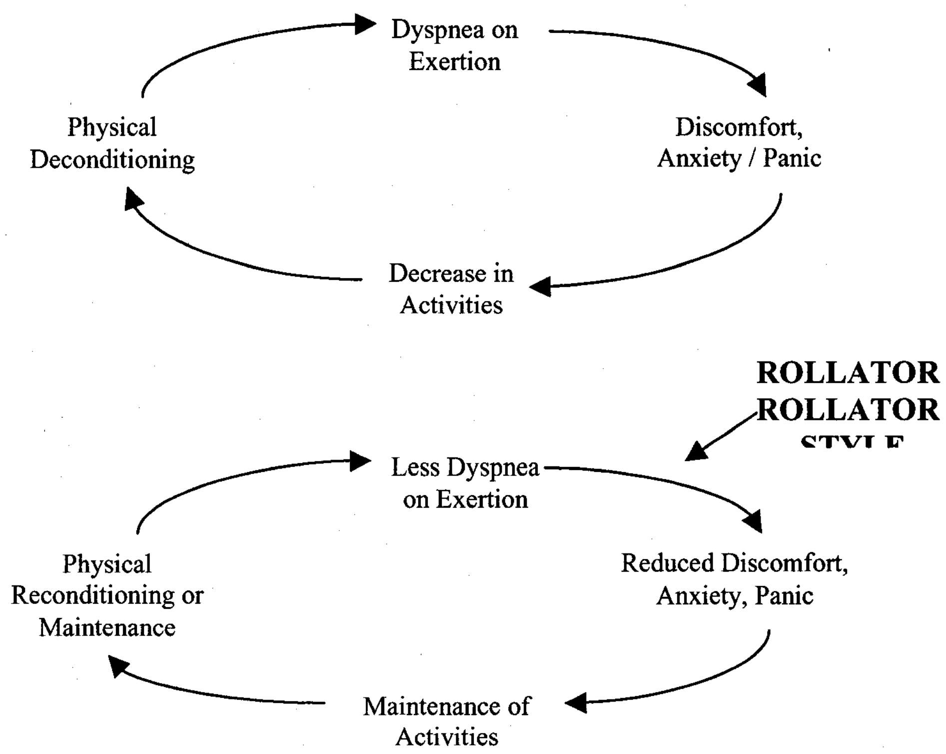

Figure 1. The hypothesized role of rollator-style walkers and impact of anxiety on walking ability in COPD (Adapted from Sassi-Dambron (37).

Summary

Rollator-style walkers may influence the distance walked by people with COPD through a variety of mechanisms including altering the physiology of respiration, reducing the metabolic demands of walking, and improving their confidence while walking.

Oxygen

Short-term supplemental oxygen improves exercise capacity in people with COPD and mild hypoxia (38-47). The means through which this improvement occurs is multi-factorial and not clearly understood (48). Specific mechanisms through which oxygen works includes the reduction in ventilatory requirement, altered perception of dyspnea, and improved tissue oxygenation in both respiratory and peripheral musculature (39;40;46-50). The longer term impact of supplemental oxygen has been poorly studied and the benefits are less clear (51). A recent meta-analysis of two publications showed improvement on resting PaO_2 but no significant change in distance walked on the 6MW, reduction in desaturation during exertion, and reduction in perceived exertion during exertion (51).

Reduced ventilatory requirements

Provision of supplemental oxygen has been shown to reduce ventilatory requirements for exertion, measured by lower levels of minute ventilation during exertion (39;46;49). This is postulated to delay the onset of maximum ventilatory capacity through the maintenance of available inspiratory capacity, and reduction of the effect of dynamic hyperinflation. This allows for longer periods of exertion and greater work to be completed (48;49).

Altered perception of dyspnea

The perception of dyspnea also limits exertion in people with COPD. Oxygen reduces this sensation, which in turn may allow for greater exercise capacity. The mechanisms through which this occurs are not clear but may include a reduction in chemoreceptor activity in the aortic and carotid bodies (39;40;48-50). Also, dynamic hyperinflation, described earlier, has been reported to explain 32% of the variability of exertional dyspnea (46).

Tissue oxygenation

It is known that supplemental oxygen during exertion can correct arterial desaturation by enriching the alveolar air (40;42;45;46;49;52). Systemic oxygen delivery may be estimated through arterial saturation. During exertion with supplemental oxygen the peripheral muscles have adequate oxygen supply reducing lactic acid production and extending the period of time they can exercise (46;49). This has been shown by correlating lactic acid level, oxygen levels and exercise capacity (46;49). In addition to improving the function of the peripheral musculature, it is hypothesized that inspiratory muscle fatigue may also be delayed by improved oxygenation of the respiratory muscular (50), and is corroborated by other research that indicates inspiratory strength may be a strong predictor of exercise capacity (26).

Summary

Oxygen may influence the distance walked by people with COPD through a variety of mechanisms including reduced ventilatory requirement, altered perception of dyspnea, and improved tissue oxygenation in both respiratory and peripheral musculature.

OUTCOME MEASURES: THE SIX-MINUTE WALK TEST

Among a wide selection of walking tests, the 6MW is a simple, inexpensive estimate of exercise capacity that is less invasive than treadmill or bicycle exercise testing. Within the 6MW, several subjective and objective indicators can be measured. These include distance walked, final oxygen saturation level, final level of perceived exertion, speed, and number of rest breaks required. The 6MW is a variation of an early walking test called the twelve-minute walk test (12MW). In people with moderate to severe COPD the 12MW shows excellent correlation with oxygen uptake, a measure of exercise capacity ($r = 0.72$) (53). The objective of the shorter two-minute and 6MW was to decrease patient burden while maintaining the relationship with exercise capacity. When the two-minute and the 6MW were compared, the 6MW discriminated better between individuals (54). Lastly, the 6MW also shows good correlation to maximum oxygen uptake ($r = 0.64$) (53). Based on this work, the 6MW is a good compromise because of its correlation with the exercise capacity and its lower burden on study participants.

Although it is strictly an estimate of maximum exercise capacity, the 6MW has further been noted by the American Thoracic Society as an appropriate assessment of activities of daily living specific to walking if administered with standardized encouragement and testing conditions (10). In addition, a survey of 99 pulmonary rehabilitation programs in North America indicated that 87% (62 / 71 responders) routinely use the 6MW for patient evaluation (55). An evaluation of patients with COPD ($n = 37$) showed that distance walked on the 6MW correlated with several subscales of the SF-36: physical function, bodily pain, and general health ($p < 0.05$) but not the other subscales (4). Lastly, test-retest reliability and construct validity have been documented to varying degrees for the three primary indicators of distance walked, perceived exertion, and oxygen saturation.

Distance Walked

Reliability has been well documented for the indicator of distance walked on the 6MW in populations with COPD. The 6MW has been shown to have a within-person standard deviation of less than six percent of their mean score (22.5 metres) after the first two test scores are excluded (56;57). The 6MW has been analyzed for its minimal clinically important difference in COPD by assessing change in distance walked to patients perceived change in function. The minimal clinically important difference has been estimated to fall between 30 and 54 metres (58;59). The estimate of fifty-four metres represents a verbally encouraged 6MW. More recently, however, the American Thoracic Society has stated that a change of 71 metres is required before a clinically important difference has occurred (60). Seventy-one metres represents the outer bound of the 95% confidence interval for the 54 metres estimate (60).

There is a well-documented learning curve for the distance ambulated on the 6MW (56;61-63) and this is also seen on the 12MW (64). The learning effect declines after the completion of two consecutive 6MW. The 6MW has been noted to have a steeper learning curve in young individuals (61). In addition, the administration of bronchodilators (inhaled salbutamol and oral theophylline) has been shown to alter the distance ambulated (58). In the COPD population, it has been shown that emotional status does not appear to affect performance on the 6MW (61;65;66).

Oxygen Saturation

Maintaining oxygen saturation levels during exertion may be a mechanism for improvement in distance walked. Pulse oximetry is used to estimate arterial oxygen saturation because it is less invasive than arterial blood gas testing. Pulse oximetry readings via ear oximetry correlate highly with arterial blood gas samples in a variety of monitors during exertion but not specifically will completing the 6MW ($r = 0.94$, $r = 0.88$) (67). Oximetry is more accurate at estimating change in saturation then measuring absolute value (68). A change of two to three percent in pulse oximetry is representative of a true directional change in saturation (67).

Perceived Exertion

The Borg scale of perceived exertion is a single question with a ten-point response scale that is numbered and worded (69). It is anchored at zero with "nothing at all" and at 10 with "maximal" (Appendix B). The modified Borg scale (English version) has been validated and analyzed for reliability. In study participants with COPD the modified Borg scale has been found to correlate with measures of minute ventilation ($r = 0.96 \pm 0.04$) and oxygen consumption ($r = 0.95 \pm 0.04$) (70). A strong relationship between modified Borg scores and minute ventilation ($r^2 = 0.75$) has also been shown to occur in healthy young subjects (71). There was no indication that the modified Borg rating varies over repeated short-term testing at the same level of exertion in individuals with COPD ($r = 0.993$) (70). Reproducibility has been shown to be fair on repeated testing over eight weeks ($r = 0.65$) (72). There is no available data on minimal clinically important change.

CRITIQUE OF CLINICAL TRIALS OF OXYGEN AND ROLLATOR-STYLE WALKERS

There is evidence that rollator-style walkers or oxygen improve walking distance when compared to unassisted walks, but there only one trial that directly compared rollator-style walkers to oxygen. Reduction in desaturation and perceived exertion are other outcomes that are infrequently evaluated in the literature. These secondary outcomes are important to evaluate because the results may assist us in understanding the mechanisms through which the interventions improve distance walked. A summary of the available literature follows, but no clear conclusions can be drawn on the comparisons between the two interventions.

Rollator-style walkers

Five studies, with a total sample size of only 90, evaluated the impact of rollator-style walkers compared to placebo. Four of the five studies used the 6MW, (15;17;73;74) and the fifth study used the 12MW (16). The study design and the populations evaluated were too diverse to support a meta-analysis; the participants studied in these five trials had a broad range of disease severity. People with moderate to severe COPD, defined as PaO_2 55 to 65 mmHg with exertional desaturation, were not adequately evaluated. The details of the populations and results can be found in Table 3 (page 37).

Distance Walked

The use of rollator-style walkers appeared to improve the distance walked by people with severe COPD but not with mild COPD. Three trials (n = 11, n =

12, $n = 19$) showed significant improvements ($p < 0.05$) on distance walked with a rollator-style walker on the 6MW and 12MW in a population of people with severe COPD ($FEV_{1.0}$ predicted = 29.6%, 33%, and 33.1%) (Table 3) (15-17). In the first trial, the mean distance improved from 225.8 (standard deviation (SD) 91.5) metres on the control walk to 259.4 (SD 94.2) metres resulting in a mean difference of 33.6 metres (15). This was a change considered important by some researchers (58;65). The second trial initially showed no difference between groups in a population of severe COPD ($PaO_2 < 55$mmHg) but post-hoc analysis of participants ($n = 6$) with the shortest distances walked showed a significant difference ($p < 0.05$) between groups (16). The mean distance improved from 388 (SD 258) metres to 435 (SD 232) metres and resulting in a mean difference of 69 metres over the 12MW. Eleven of twelve participants improved their distance walked but the large inter-subject variation may have caused the results to be non-significant. Unfortunately, the minimal clinically important difference for 12MW has not been established. Likewise, a third trial showed an improvement on distance walked in those who walked less than 300 metres at baseline, from 220.3 (SD 52.3) metres on an unassisted walk to 242.5 (SD 61.9) with a rollator-style walker ($p = 0.02$) (17).

Two trials did not show any difference between groups. The first publication ($n = 27$) studied people with moderate COPD (mean $FEV_{1.0}$ = 49% predicted) where an improvement may not have been expected (73). The second trial did not define the study population in terms of percent of predicted values, but likely had moderate COPD based on their absolute mean $FEV_{1.0}$ values (74). If this were true, we would not have expected to see an improvement.

Overall, the rollator-style walker contributed to improvement in distance walked by people with the most severe COPD. It appears that people with less severe COPD may not experience as great benefits. More research is required to define this relationship.

Oxygen Saturation

Rollator-style walkers appear to lessen exertional desaturation in COPD. Two trials, with a total sample of 38, evaluated the impact of rollator-style walkers on exertional desaturation (Table 3) (15;73). The results are summarized in Table 3. The first trial (n = 11) showed an absolute reduction of 2.2% ($p <$ 0.05) favouring the rollator-style walker group; saturation on the unaided walk dropped by 7.2% (SD 56) but only 5.0% (SD 4.0) with the rollator-style walker (15). Importantly, the reduction in exertional desaturation occurred despite the study participant in the rollator-style walker group walking further (mean difference = 33.6 metres). The population studied had severe COPD (mean $FEV_{1.0}$ predicted = 29.6%). A second trial (n = 27) showed a non-significant absolute difference of 0.6% favouring the rollator-style walker group (73). There was no significant difference between groups in distance walked. The study participants had moderate COPD (mean $FEV_{1.0}$ predicted = 49.5%) so we did not expect to see an improvement in this group. It has been suggested that two to three percent change is representative of a true directional change in saturation

(67), however the minimally clinical important difference has not been established.

There is a trend to suggest rollator-style walkers may reduce desaturation but overall there is weak evidence to support the effect of rollator-style walkers on exertional desaturation. Based on the theoretical model presented earlier, there is potential to improve exertional desaturation. More study is required to clarify this relationship.

Perceived Exertion

Three publications (total $n = 61$) evaluated the impact of rollator-style walkers on perceived exertion (Table 3) (15;17;74). The Borg Scale, described earlier, measured perceived exertion in these trials. One trial ($n = 11$) that studied participants with severe COPD (mean $FEV_{1.0}$ predicted = 29.6%) found a significant improvement of 1.3 / 10 ($p < 0.005$) when people used the rollator-style walker (15). The reduction in perceived exertion occurred despite the rollator-style walker group walking further (mean difference = 33.6 metres). The second study ($n = 10$) also found a significant difference of 1.6 / 10 ($p < 0.05$) favouring the rollator-style walker group (74). In this study, there was no significant difference in distance walked between the study groups. Likewise, a third study found a greater increase in perceived exertion, from the start to end of the walking test, with the rollator-style walker when compared to without the rollator-style walker (1.8 (SD 1.3) versus 2.7 (SD 1.9) / 10 points). The relationship with perceived exertion appeared more extreme when the more severely impaired participants (1.8 versus 3.2) were examined separately from the less severely impaired (1.7 versus 2.7) (17). Overall, there is evidence that using a rollator-style walker reduces perceived exertion. It is small, however, and it remains unclear how much change should be considered clinically important, even in the presence of statistical significance.

Summary

The literature only weakly supported the ability to walk further distances with a rollator-style walker compared to no intervention. In particular, the evidence suggested that people with the most severe COPD were primarily those showing improvements in distance walked. In addition, rollator-style walkers may lessen exertional desaturation and this improvement was seen even when the distance walked increased. Lastly, there was some evidence to suggest that perceived exertion was lower when using a rollator-style walker, but it was unclear if the improvement seen was clinically important.

Table 3. Publications evaluating rollator-style walker assisted versus unassisted walks on outcomes of distance, oxygen saturation and perceived exertion.

			Six-Minute Walk Test		
Study	Subjects	Compar-ison	Distance (metres) Mean (SD)	Oxygen Saturation Mean (SD)	Borg Scale Mean (SD)
Roomi et al.(73)	$n = 27$ Age: 75.1 yrs $FEV_{1.0}$: 49% ± 4.2	Unaided	210 (83)[3]	-6.0% (5.7)[3]	Not available
		RSW	212 (88)[3]	-5.4% (4.7)[3]	Not available
Dalton et al.(74)	$n = 10$ Age: 64.6 yrs $FEV_{1.0}$: 0.7 L	Unaided	222.6 (89)[3]	Not available	3.7 (1.9)[3]
		RSW	209.8 (94)[3]	Not available	2.1 (1.1)[1,3]
Honeyman et al. (15)	$n = 11$ Age: 71.3 ± 6.4 $FEV_{1.0}$: 29.6%±7.8	Unaided	225.8 (91.5)[3]	-7.2% (5.6)[3]	4.7 (2.0)[3]
		RSW	259.4 (94.2)[1,3]	-5.0% (4.0)[1,3]	3.4 (2.0)[1,3]
Solway et al. (17)	$n = 40$ Age: 67.7 ± 1.2 $FEV_{1.0}$: 36.1% ± 2.0 PaO_2: 65.2 ± 1.6 mmHg	Unaided	311.6 (105.0)[3]	No data available	Change: 2.7 (1.9)[3]
		RSW	317.0 (103.7)[3]	No data available	Change: 1.8 (1.3)[3]
			Twelve-Minute Walk Test		
Wesmiller et al. (16)	$n = 12$ Age: 62.8 $FEV_{1.0}$: 33% ± 12 $PaO_2 < 55$mmHg O_2 flow: 2.3 lpm	Unaided	388 (258)[2]	No data available	No data available
		RSW	435 (232)[2]	No data available	No data available

[1] Difference was significant to $p < 0.05$

[2] Values were converted from feet to metres; Difference was significant to $p < 0.05$ for subgroup who walked less than 305 metres on the unaided walk

lpm = litres per minute

[3] Converted from standard error or 95% confidence interval to standard deviation.

RSW = Rollator-style walker

Oxygen

The impact of supplemental oxygen on people with COPD has been studied more thoroughly than rollator-style walkers, but its effect on walking ability still remains unclear. A total of five clinical trials (total n = 80) have evaluated the impact of oxygen in mildly hypoxic people on self paced walking tests. The differences in methodology, outcomes, and populations prevented formal meta-analysis and the results of the studies are summarized in Table 4 (page 42). A recent systematic review on long-term ambulatory oxygen for the improvement of exercise tolerance in COPD only identified two studies and was also unable to complete meta-analysis (51). The authors concluded that there was inadequate evidence available to draw conclusions concerning the effectiveness of ambulatory oxygen therapy in people with COPD (51).

Distance

Four of the five publications assessed the impact of oxygen on distance walked measured by the 6MW (40;42;44;45) and the remaining study used an incremental shuttle walk test (52). All trials found that oxygen improved the distance walked when compared to either an unblinded baseline or blinded controlled walk. As the control condition, the studies blinded patients to oxygen by having them breathe compressed air.

The two trials with the least biased methods suggest that oxygen, flowing at two litres per minute, improves the distance walked on the 6MW between 12.1% and 19.2% (40;42;44). When the amount of oxygen provided was increased to four litres per minute the improvement increased to 34.5% (SD 17.8) with no further improvement seen at higher oxygen concentrations (40). More biased studies, in which the controlled or compressed air walk was always performed first, suggested an improvement with oxygen (2 litres per minute) between 8.9% and 15.1% (42;45). A large retrospective study (*n* = 50) showed an improvement of 9.7% with oxygen at two litres per minute (41).

Of importance, only one sample included study participants within our population of interest, those with exertional desaturation (45). The amount of oxygen provided varied between participants, but was always kept high enough to prevent desaturation, and resulted in a mean improvement of 15.1% (45).

The trend of improved exercise capacity is also seen in cycle ergometry, but the increases are not directly applicable to walking because need to bear weight on the extremities is eliminated, altering the metabolic demands. Two studies (*n* = 24) show improvement in symptom-limited incremental cycle time of 15% to 38% with supplemental oxygen of approximately five litres per minute (39;43). This supports the wide range of improvements seen on the 6MW.

Overall, there is consistent evidence to indicate that supplemental oxygen improves the distance walked by people with COPD and mild hypoxia. The magnitude of improvement is unclear because of biased design and inclusion of non-desaturating populations. However, oxygen is likely to improve performance by more than 10%.

Oxygen Saturation

Provision of oxygen during exertion reduces oxygen desaturation (40;42;45). Three trials, with a total sample of 56, observed the effect of oxygen on desaturation on the 6MW (40;42;45). Two studied the impact on the percentage desaturation (40;45) while the third study documented the lowest oxygen saturation (42). Oxygen (2 litres per minute) improved the minimum saturation from 75% to 81% (42). The mean improvement in percent desaturation was 4.8% and 7.8% at two and four litres per minute respectively, based on an initial mean desaturation of 15% (40). No further improvement was seen at higher flow rates (40). A third study measured desaturation but provided oxygen at a flow rate to correct desaturation so the results do not clarify the role of oxygen (45).

Perceived Exertion

Four studies, with a total sample of 66, evaluated the impact of oxygen on perceived exertion over the 6MW (40;42;44;45). All studies showed an improvement on their chosen outcome, 100 millimetre visual analogue scale or the Borg scale of perceived exertion. The magnitude was not clearly interpretable because each study recorded the outcome differently and clinical significance has not been established.

The trend of improved dyspnea is not clearly seen in exercise testing stationary bicycles (cycle ergometry). One study (n = 12) showed no change in dyspnea with supplemental oxygen of approximately five litres per minute when measured at the end of the exercise test (39). However, the total time cycled was longer with oxygen than with compressed air. When dyspnea was measured at the isotime it showed a reduction from 8.5 to 6.5 on a ten-point scale ($p = 0.01$). Isotime was defined as the time at which the exercise test ended with compressed air. It is important to note that cycle ergometry does not require the person to bear weight through their legs and so may not be applicable to the ability to walk. Overall, it appears that the use of oxygen may reduce perceived exertion but these results are based on small studies and require more substantiation.

Summary

The use of supplemental oxygen has a positive impact on distance walked, improvement in saturation, and perceived exertion on the 6MW in people with COPD and mild hypoxia. It is not clear how large these changes are, and whether the subgroup of those who desaturate with exertion are different than those who do not desaturate.

Table 4. Publications evaluating oxygen assisted versus unassisted walks on outcomes of distance, oxygen saturation and perceived exertion.

Author	Participants	Comparison	Results (6MW) Distance: Metres Mean (SD)	Oxygen Saturation Mean (SD)	Perceived Exertion Mean (SD)
				Total Desaturation	Final: Borg
Jolly et al. (45)	$n = 11$ Age = 67 (SE 2) FEV_1= 36 (SE 4) % PaO_2 = 74 (SE 2) mmHg	Control[2]	391 (119) [5]	9.9 (3.1) [5]	5.82 (1.5) [5]
		Oxygen (O_2) (3-12 lpm)	450 (96) [5]	3.45 (3.0) [5]	3.73 (2.0) [5]
				Change from Desaturation	Final: 10 cm VAS
Leach et al. (40)	$n = 20$ Age = 63.4 (SD 7.2) FEV_1= 0.74(SD 0.25) L PaO_2= 65.7 (SD17.9) mmHg[1]	Air[3]	228 (95% range: 64 to 811)	15% (95% range: 1 to 34)	9 (range 4 – 10)
		O_2 (2 lpm)	+19.2% (15.5) [5]	-4.8% (4.8) [5]	7 (range 3 – 9)
		O_2 (4 lpm)	+34.5% (17.8)[5]	-7.8% (4.6) [5]	5 (range 2 – 9)
		O_2 (6 lpm)	+36.3% (17.8) [5]	-7.9% (4.6) [5]	5 (range 1 – 8)
				Lowest saturation	Change: 10 cm VAS
Roberts et al. (42)	n =15 Age = 67.5 (SD 6.2) FEV_1= 31 (SD 8.1) % PaO_2= 52.5 (SD 7.2) mmHg[1]	Air[4]	271 (92)	75% (11)	44.7mm (23.8)
		O_2 (2 lpm)	295 (89)	81% (7)	35.3mm (34.5)
Woodcock et al. (44)	$n = 10$ Age = 62 (range 43–70) FEV_1=0.71 (SD 0.29) L PaO_2= 72.6 (SD 11.4) mmHg[1]	Air	289 (332) [5]	Not available	7.93 (4.8) [5]
		O_2 (4 lpm)	324 (275) [5]		6.64 (6.7)
			Shuttle Walk Test		
				Lowest median saturation	
Garrod et al (52)	n =14 FEV_1= 32 (SD 9.4) PaO_2= 63.0 (SD 9.3) mmHg[1]	Air	189 (110)	78.0%	Not available
		O_2 (2 lpm)	204 (106)	88.5%	

[1] Values were converted from kPa to mmHg (1 mmHg = 0.133 kPa).
[2] Walk was with room air (unblinded) and always first.
[3] Air refers to compressed air provided through mask or nasal prongs.
[4] Walk with compressed air was always first.
[5] Standard error and 95% confidence intervals converted to standard deviation.

Rollator-style walkers versus Oxygen

The relative efficacy of rollator-style walkers and supplemental oxygen in people with moderate COPD and exertional desaturation has not been well studied. Grant (1972) studied the effect of oxygen or a rollator-style walker in five participants with COPD (34). The rollator-style walker used in this study was a tripod-style rollator-style walker (three wheels) whereas we used a four-wheeled rollator rollator-style walker in our study. The tripod rollator-style walker likely has similar effects as the four wheeled rollator-style walker. As shown in Table 5, the results indicated that the use of oxygen out-performed the rollator-style walker for distance walked. However, the results are questionable because the authors did not use a standardized outcome measure, did not randomize the order of interventions (oxygen always after rollator-style walker), and used a flow of oxygen (100%) inappropriate for long-term use. The subjects studied would now be considered too healthy for oxygen therapy. The documented learning curve of standardized walking tests suggests that one could expect the second test (oxygen) to always outperform the first (rollator-style walker) (61;62). The trial did not evaluate perceived exertion or desaturation as outcomes. In summary, there is no appropriate evidence comparing the two interventions.

Table 5. Publication evaluating rollator-style walker assisted versus oxygen assisted walks on outcomes of distance, oxygen saturation and perceived exertion.

			"Walk as far as possible."		
Author	Participants	Comparison	Distance Mean (SE)	Saturation	Perceived Exertion
Grant et al. (12)	*n* = 5 Age: 55 - 65 yrs $FEV_{1.0}$ < 0.6L PaO_2: 62 - 78 mmHg	Oxygen (100%)	316 (75)	Not available	
		Rollator-style walker	198 (22)		

CHAPTER THREE: OBJECTIVES

The primary purpose of this study was to evaluate whether a rollator-style walker was more efficacious at increasing distance walked when compared to supplemental oxygen (4 litres per minute) in people with mildly hypoxic COPD and exertional desaturation. Quantitative research has suggested that both interventions improve the ability to walk but study populations and methodologies are inconsistent. Oxygen reduces or corrects exertional desaturation, whereas rollator-style walkers effect additional body systems including balance, walking speed, confidence and the physiology of respiration without likely effect saturation. However, based on a review of the literature, it is debatable which intervention is superior, therefore two-tailed testing was planned for all outcomes.

The second purpose of the study was to contribute to the understanding of mechanisms that may allow rollator-style walkers to increase the ability to walk. In order to complete this, oxygen saturation and perceived exertion were evaluated at the end of each walking test. It is hypothesized that oxygen would improve oxygen saturation at the end of each walk more than the rollator-style walker because supplemental oxygen increases uptake of oxygen from the lungs to the blood stream. It is hypothesized that the rollator-style walker would reduce perceived exertion more than oxygen by reducing the metabolic demands of walking and by improving the efficiency of respiration. This may be through a combination of slowed speed of gait and increased confidence with the rollator-style walker. In addition, there is a poor relationship between oxygen saturation, which oxygen corrects but rollator-style walkers do not, and the sensation of dyspnea. Lastly, we also measured speed of walking and number of rest breaks to identify changes in the style or quality of gait. This will also contribute to the understanding of the mechanisms through which the interventions alter walking.

The final purpose of this study was to examine the participant's feelings and relationship to the rollator-style walker when compared to oxygen. Clinical experience has suggested that some patients may prefer to use rollator-style walkers because the rollator-style walker has a less medical appearance, however other patients may prefer not to use a rollator-style walker because it may be associated with aging. Often, patients may perceive the introduction of long-term supplemental oxygen as entering the end-stage of their disease. As a result, these values may influence clinical decision making to a greater extent than the difference in distance walked.

The three objectives allow qualitative and quantitative analyses to be used. By using several outcome measures within the study, a broader understanding of the research question can be achieved. This is important for clinicians and patients, who consider not only the efficacy of an intervention, but also its costs and acceptability to patients.

CHAPTER FOUR: METHODS

A single-blind randomized controlled crossover trial was used to assess the effect of rollator-style walkers and compressed air, compared to oxygen, on distance walked, final oxygen saturation, perceived exertion, speed and number of rest breaks as measured by the 6MW (Figure 2). Compressed air contained the same percentage of oxygen as ambient air.

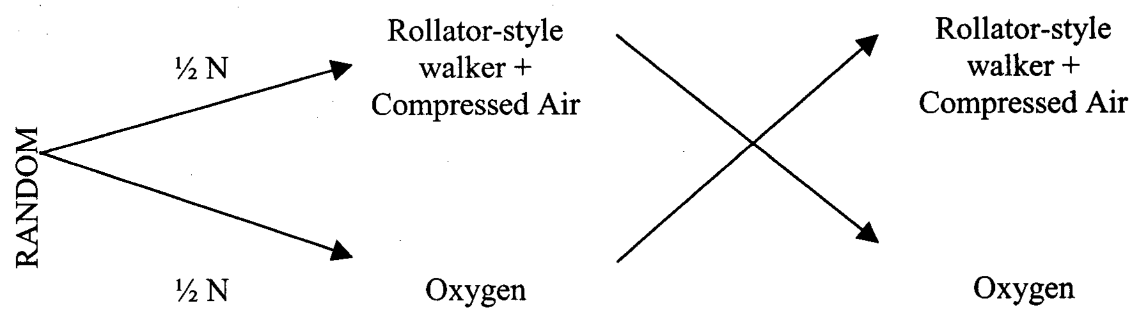

Figure 2. Illustration of study design.

PARTICIPANTS

Participants were recruited from a tertiary pulmonary rehabilitation clinic. Ambulatory adults, from The Ottawa Hospital – The Rehabilitation Centre (Pulmonary Rehabilitation Program), with moderate to severe COPD were included if they met the following criteria: $FEV_{1.0} < 40\%$ of their predicted value, exertional desaturation < 89% for less than or equal to two minutes on the 6MW, and resting PaO_2 55 to 65 mmHg on room air. Participants were excluded if they had had an acute exacerbation of their COPD in the past four weeks, if they were unable to walk independently, if their walking was limited by factors other than COPD, or if they were unable to understand and use the Borg Scale of Perceived Exertion. All participants gave written informed consent prior to participating in the study. The study was given approval by the Rehabilitation Centre Research Ethics Board.

INTERVENTIONS

The study participants participated in the study by attending two study days separated by two to five days. On both study days the participants completed three practice 6MW without intervention to minimize the well-documented learning effect. The practice 6MW were followed by one 6MW with the intervention set-up (rollator-style walker with compressed air or oxygen). The participants rested between each walking test for a minimum of fifteen minutes or until heart rate, oxygen saturation, and perceived exertion returned to baseline values. Pulse oximetry was used to measure oxygen saturation and the Borg Scale of Perceived Exertion was used to measure perceived exertion. The study protocol is shown in Appendix C.

If the participant had a current prescription for bronchodilator inhalers, the medication was given 30 minutes prior to the first 6MW. We standardized encouragement at two-minute intervals because it has been shown to affecct performance positively during the 6MW (Appendix D) (57;61). Time of day is thought to affect the ability of individuals with COPD to walk therefore the time of day over the two study visits was kept consistent for each participant.

Oxygen or compressed air were delivered at four litres per minute via nasal cannula. The participants used a rollator-style walker with the handle height adjusted to the level of the subject's wrist crease for the rollator-style walker intervention. The assessor walked slightly behind the participant with soft-soled shoes to avoid altering the subject's speed. It has been suggested that the clicking of the assessor's shoes may alter the pace at which the participant chooses to walk. The walk took place in a 30-meter straight corridor and was measured to the nearest meter. Four sets of chairs were available for rest breaks whose locations were standardized. Distances were chosen in order to minimize interference with the walking route.

The assessor carried the oxygen / air canister so that the intervention was not contaminated by the need to carry additional weight (40). Although this is strictly not a reflection of the work of managing oxygen in the community, it was necessary in order to isolate the effect of oxygen alone. There were several other reasons that the assessor carried the canisters. The weight of the air canister is not equal to the oxygen canister; air canisters are made of steel and oxygen canisters are made of aluminium. Most individuals use small lightweight canisters of oxygen for use in the community, however these were not available for air and using them for the oxygen only would not have allowed for blinding to the interventions. Lastly, by having the assessor carry the canister, we felt that the community situation was somewhat replicated because most patients do not carry their oxygen canisters but pull or push the canister on a cart. Oxygen and air dosing was standardized at four litres per minute because this flow rate should be adequate to correct exertional desaturation (40;75).

This was a single blind study, where only the study subject was blinded to one of the interventions. The participants were provided with air at the same flow rate during the rollator-style walker intervention as the flow of oxygen during the oxygen intervention. The canister was shrouded in order to obscure any identifying marks. Oxygen and air have the same odour and sensation and should be indistinguishable. The assessor was not blinded for practical reasons and neither the assessor nor the participant could be blinded to the rollator-style walker. In order to assess the validity of the blind, the participants were asked what gas (oxygen or air) they thought they were breathing prior to each intervention (fourth) walk. Lastly, prior to the first walk on the second study date the following question "Has anything happened since your last visit to change your ability to walk?" to assess the stability of the disease and the associated disability.

RANDOMIZATION

The crossover design is a variation of a traditional randomized controlled trial where each participant receives each intervention sequentially, and thereby acts as his / her own control. The participants are randomized in terms of the order in which they receive the interventions. Participants were randomized into receiving the rollator-style walker first, or the oxygen first. A blocked randomized design was used to ensure equal groupings. Blocking was done by groups of four.

Allocation concealment was maintained through numbered opaque envelopes and the sequence was concealed until the participant was enrolled in the study. Allocation concealment reduces bias by preventing the researcher from influencing into which study arm that the participant is randomized (76).

A third party generated the allocation sequence. Participants were screened by the respirologist associated with the pulmonary rehabilitation program and the program secretary distributed the randomization envelopes to the researcher once the participant had been enrolled into the study.

SAMPLE SIZE

Sample size calculations, based on distance walked on the 6MW in previous studies, indicated that evaluation of 18 participants would be required to ensure this study had adequate power (77). Both 54m and 30m have been used by researchers to estimate the minimal clinically important difference (MCID) for the 6MW in people with moderate and severe COPD (56;58). In order to ensure adequate power 30 m was chosen. A two-tailed alpha of 0.05 and power of 0.8 were chosen. These are standard choices for detecting difference between interventions.

Standard deviation of the 6MW when applied to a population with moderate to severe COPD has been estimated to be 99 metres (78). This agrees with the standard deviation used by researchers at the University of Toronto currently using the six minute walk test as an outcome measure for similar research (17). Their estimate was based on an analysis of clients in a Toronto pulmonary rehabilitation program.

The correlation coefficient between repeated 6MW was estimated to be 0.9. The two-, six- and 12-minute walk tests were evaluated for their repeatability and the correlation was between 0.864 and 0.955 (54). This high level of correlation between tests may reflect the learned skill this population has in judging their tolerance to activity.

Therefore, the sample size calculation was as follows:

Effect Size: *MCID / SD of outcome measure*
= 30 m / 99 m = 0.3030

Modifier: $= 1/\sqrt{(1-r)}$; *where* $r = 0.9$;
$= 1/\sqrt{(1-0.9)}$
$= 1/\sqrt{(0.1)}$
$= 1/0.316$

Effect Size * Modifier $= 0.3030 * (1/0.316)$
$= 0.3030/0.316$
$= 0.958$

Interpolation from tables estimated the sample size to be 18 (77).

STATISTICAL METHODS

Crossover trials are used when studying stable chronic diseases and short-term interventions that do not permanently alter the disease process (79;80). Crossover designs result in smaller sample size requirements, caused by reduced variation because the participants act as their own controls (81). The disadvantage of using a crossover design is that if violation of several key assumptions occurs only the first period data can be used for analysis. This causes the study to become underpowered to detect a difference between interventions. The key assumptions include the absence of period by treatment interaction and period effect (79;81). Period by treatment interaction occurs when the efficacy of the intervention varies across periods (79). Period effects are systematic changes in the outcome by period, potentially related to temporal changes in the disease (79). They may also be related to systematically occurring external forces such as seasonal changes resulting in different performance during one period. An example of this would occur in a clinical trial evaluating a outcomes important to COPD. If the first period was always in the winter and the second period always occurred during the summer when humidity and pollution levels are higher one would expect performance on any outcome to be systematically worse during the second period.

A general understanding of the components of a two-period crossover design can be understood through the "mean cell model", shown in Table 6 (82). Treatment sequence refers to the order in which the interventions were received; treatment period refers to the study day on which the interventions were received.

The effect of an arbitrarily selected reference treatment A is represented by β_0 and the effect of the other treatment, is represented by $\beta_0 + \beta_1$. Hence, β_1 represents the mean difference between treatments. Period effects are represented by β_2. β_2 is found in both cells of the second period because period effects represent differences in treatment effect that effect both interventions. Lastly, β_3 represents period by treatment interaction and is found in one treatment cell because is represents an interaction between a period and one treatment. Importantly, when β_3 or β_2 are shown to be significantly different from zero, analysis is completed on period one data only. When β_3 and β_2 are shown not to be significantly different from zero analyses include data from both periods.

Table 6. Illustration of the components of the two-period crossover design.

	Treatment Period	
Treatment Sequence	1	2
(A) → (B)	Mean $_{A1} = \beta_0$	Mean $_{B2} = \beta_0 + \beta_1 + \beta_2$
(B) → (A)	Mean $_{B1} = \beta_0 + \beta_1$	Mean $_{A2} = \beta_0 + \beta_2 + \beta_3$

Data analysis was completed using SAS 8.0 (SAS Institute Inc., Cary, N.C.) software. Analysis was based on a model of mean within-person sums and differences, pooled by period, shown in Table 7. The test estimates and variances derived from this model are more precisely estimated than the "mean cell model" because the individual treatment differences (and sums) are utilized instead of the mean cell values. Using the mean of individual treatment differences to estimate the incremental treatment effect results in values that have statistical independence from each other. This is done by creating a unique sum (t) and difference (d) for each study subject followed by a mean sum and difference for each treatment sequence. This differs from the "mean cell model" approach where both the within-subject and between-subject variance needs to be recognized.

This approach was used for the continuous outcomes of distance walked, final oxygen saturation, final perceived exertion, and speed. Median values were compared for the number of rest breaks taken over the walking test.

Table 7. Individual and mean sums and differences model for analysis of two period crossover clinical trials.

		Treatment Periods			
Treatment Sequences (i)	Subject *k*	1 Y_{i1k}	2 Y_{i2k}	Sum $Y_{i1k}+Y_{i2k} = a_{ik}$	Difference $Y_{i1k}-Y_{i2k} = D_{ik}$
1	$n = 5$	$Y_{i1.}$	$Y_{i2.}$	$\bar{a}_{i.}$	$\bar{d}_{i.}$
2	$n = 6$	$Y_{i1.}$	$Y_{i2.}$	$\bar{a}_{i.}$	$\bar{d}_{i.}$

Parameters were estimated by equations one through three for period by treatment interaction (β_3), period effect (β_2), and treatment effect (β_1) respectively.

Equation 1. $\beta_3 = \bar{a}_{1.} - \bar{a}_{2.}$

Equation 2. $\beta_2 = \frac{1}{2}(\bar{d}_{1.} + \bar{d}_{2.})$

Equation 3 $\beta_1 = \frac{1}{2}(\bar{d}_{1.} - \bar{d}_{2.})$

The estimate of treatment effect (β_1), is a pooled estimate of the mean difference of the two sequences ($\frac{1}{2}(\bar{d}_{1.} - \bar{d}_{2.})$). When unequal samples are used in each sequence an effect occurs in which the smaller sequence contributes more weight to the pooled mean difference. This *sequence* effect is minimized with increased sample size. Importantly, one needs to assess the impact of the sequence effect on the outcome by comparing the pooled mean difference, the mean difference without considering study design, and the minimal clinically important difference that the study is attempting to detect.

Variance estimates for period by treatment interaction are shown in Equation 4 and for period and direct treatment effects in Equation 5. These equations represent the sums of squares to create an estimate of pooled between subject variance.

Equation 4 $\sigma^2_t = [\sum(a_{1k} - \bar{a}_{1.})^2 + \sum(a_{2k} - \bar{a}_{2.})^2]/((n_1+n_2)-2)$

Equation 5 $\sigma^2_d = [\sum(D_{1k} + \bar{d}_{1.})^2 + \sum(D_{2k} + \bar{d}_{2.})^2]/ ((n_1+n_2)-2)$

All estimates were tested using the t-statistic. Equations 6 through 8 show the equations for period by treatment interaction, period effect, and direct treatment effects respectively.

Equation 6 $T_{\beta 3} = (\bar{a}_{1.} - \bar{a}_{2.}) / [\sqrt{(1/n_1 + 1/n_2)}\ \sigma^2_a]$

Equation 7 $T_{\beta 2} = [\frac{1}{2}(\bar{d}_{1.} + \bar{d}_{2.})] / [\sqrt{(1/n_1 + 1/n_2)(\sigma^2_D/4)}]$

Equation 8 $T_{\beta 1} = [\frac{1}{2}(\bar{d}_{1.} - \bar{d}_{2.})] / [\sqrt{(1/n_1 + 1/n_2)(\sigma^2_D/4)}]$

Final analysis was based on 11 participants who completed the study protocol. The outcomes of distance walked, final saturation, final perceived exertion score and speed on the 6MW were analyzed. The assumptions for analysis of a crossover design were tested; normal distribution of the outcomes, period by treatment interaction and period effect were evaluated. A post-hoc power analysis was completed, the validity of the blind was tested, and stabilization of the learning effect on the 6MW was evaluated. Once we were satisfied that the assumptions had been met, a t-test was used to test overall within-patient differences for distance walked, final oxygen saturation, final perceived exertion, and speed on the 6MW. In order to account for the possibility that either intervention may outperform the other, two-tailed tests for significance were always used. In addition, the Students t-test was used to assess the mean difference in distance walked between rollator-style walkers and baseline as well as oxygen and baseline. This was completed after establishing that there were no period effects present in the baseline data (practice walking test three). The median values for number of rest-breaks were compared. Lastly, we completed qualitative analysis by categorizing the responses to the open-ended questions and generating themes.

CHAPTER FIVE: RESULTS

STUDY FLOW

New and returning clients of the Pulmonary Rehabilitation Program at the Ottawa Hospital – Rehabilitation Centre were screened for inclusion in the study between May 2001 and January 2002. Ninety-eight new and seventy-five[c] returning clients with lung disease were screened for potential eligibility. Nineteen met the initial eligibility criteria of diagnosis of COPD (excluding asthma and restrictive lung disease), presence of exertional desaturation for at least two minutes on the 6MW, and $FEV_{1.0} \leq 40\%$ of predicted value. One was referred for medical care and became unavailable. Two declined to participate because they felt they were too well to be involved in a study using oxygen. Further screening for eligibility detected that three had arterial oxygen levels out of inclusion range (PaO_2 of 55 to 65 mmHg). One participant had a very poor memory and after initial screening it become evident that he / she would be unable to reliably use the Borg Scale of perceived exertion as well as potentially unable to give informed consent. Lastly, one participant was excluded from the analysis because, although the participant showed exertional desaturation during the screening 6MW, there was no evidence of it during the study; the lowest recorded oxygen saturation was 93%.

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[c] The number of new clients was accurate. The number of returning clients was estimated based on the ratio of new to returning clients from September to November 2002 due to a bookkeeping error for May to December 2001.

DEMOGRAPHICS

The eleven study participants were recruited over an eight-month period. Despite the care taken to estimate how many patients may be available to participate in the study, the familiar study participant attrition occurred whereby patient numbers declined as the study began. The participants represented a population of mildly hypoxic people with COPD and exertional desaturation and their characteristics are shown in Table 8. The participants were severely impaired in respiratory function measured by $FEV_{1.0}$ and desaturated for a minimum of two minutes on the 6MW.

Table 8. Demographic characteristics of study participants (n = 11).

Characteristic	Mean (SD)	Range
Age (years)	67.5 (16.6)	39.1 – 91.7
Height (cm)	167.7 (11.9)	155.0 – 190.0
Weight (kg)	73.2 (12.2)	54.0 – 92.0
FVC (litres)	1.76 (0.57)	1.03 – 2.98
FVC (% predicted)	48.8 (12.7)	32.0 – 69.0
$FEV_{1.0}$ (litres)	0.72 (0.18)	0.45 – 1.14
$FEV_{1.0}$ (% predicted)	26.1 (6.8)	18.0 – 40.0
PaO_2 (mmHg)	61.2 (2.3)	57.4 – 64.4
	n (%)	
Sex (female)	5 (45.5)	
Oxygen (users)	3 (27.3)	

Eleven study participants completed 64 unassisted 6MW, 11 6MW with oxygen, and 11 6MW with a rollator-style walker over two study periods. One participant was only able to complete two unassisted 6MW prior to the intervention tests.

ASSUMPTIONS FOR USE OF THE SIX-MINUTE WALK TEST

Learning Effect of the Six-Minute Walk Test

There was evidence that the learning effect, documented in previous studies, stabilized by the third unassisted walk in our study sample (61;62). Study participants improved from 218 ± 77 metres to 232 ± 86 metres between walk one and two and changed minimally between walk two and three (235 ± 89 metres). The results are summarized in Figure 3. The results of one participant were not included in the estimate of learning effect because he was only able to complete two unassisted walking tests. Because there was no mean difference between the distances walked on test two and three, we treated this one subject's second walk as his baseline walk for the remaining analysis. We used the third unassisted walk for the baseline value of all other participants.

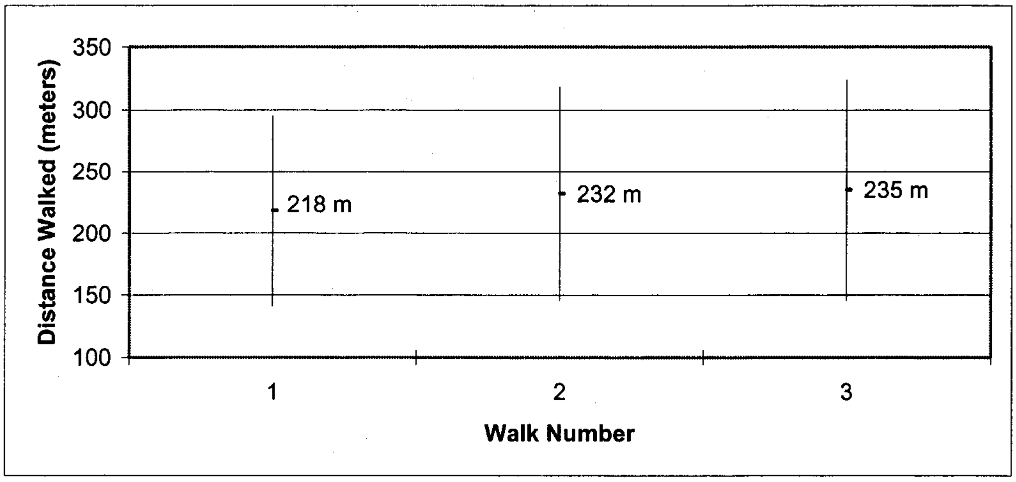

Figure 3. Mean (SD) distance walked on each practice walking test by ten participants over two study days (20 practice walks at each walk number).

The standard deviation increased over progressive tests with the greatest variation seen on walk number three. This suggests that the change in distance walked was not uniform over the entire sample; some decreased between walk two and three and others continued to increase their distance walked. The percent predicted of $FEV_{1.0}$, age, body mass index (weight in kilograms / height^2 in metres) of participants who deteriorated or maintained their distance walked between walk two and three were compared to those who continued to improve. There were no differences noted on percent-predicted $FEV_{1.0}$, forced vital capacity. The participants who continued to improve after walk two were younger (59.5 ± 13.1 versus 74.9 ± 13.1 years) and lighter, measured by body mass index (22.8 versus 27.7) than those who did not.

ASSUMPTIONS FOR ANALYSIS OF STUDY DESIGN

Blinding to Oxygen

We tested the validity of oxygen blind by asking the participant to guess what they were breathing during administration of the gas, which occurred just prior to starting each intervention walking test. A total of 22 guesses were made; 11 guesses on each of two study days. Ten guesses were 'unsure' what they were breathing; five while breathing oxygen and five while breathing air. The remaining participants did not identify what they were breathing with more accuracy than might have occurred by chance. The Fisher's Exact chi-square test of association was not significant (p = 0.54). Under each condition 83% guessed they were breathing oxygen. See Table 9.

Table 9. Validity of oxygen blind when participants were asked what they believed they were breathing prior to intervention walking test.

Intervention	Guess			
	Air	Oxygen	Unsure	Total
Air	1	5	5	11
Oxygen	1	5	5	11
Total	2	10	10	22

Disease Stability

The underlying assumption in a crossover design is that the condition under investigation is stable. In order to confirm the stability of the walking impairment measured by the 6MW, the participants were asked at the start of the second study visit "*Has anything had happened between the first and second study date that might change your ability to walk*". All eleven participants indicated that nothing had happened that might affect his or her ability. We felt confident that there was no change in the subject's ability to walk between the two study days, which ranged from two to seven days apart.

Normal Distribution of Data

It was required that the data would have a normal distribution in order to complete a statistical test for difference between interventions. This requirement was met by the outcome measures of distance, oxygen saturation, perceived exertion and speed. See Table 10. Minor differences were noted between the mean and median values for distance walked under both intervention conditions, but not for final saturation or exertion. The Shapiro-Wilk test of normality did not show a significant deviation from the normal distribution, with the exception of final saturation under the oxygen condition. For this exception, the mean and median were nearly identical and the deviation was caused by one observation. Lastly, there were no significant deviations noted in the baseline data, defined as the third practice test on the first study day.

Table 10. Univariate measures for the validation of the normal distribution assumption on the outcomes of distance, final oxygen saturation, final perceived exertion and speed

	Baseline ($n = 11$)	Rollator-style walker ($n = 11$)	Oxygen ($n = 11$)
Distance (metres)			
Mean	244.4	275.7	295.6
Median	248.0	240.0	312.0
Standard Deviation	85.0	108.2	82.4
Kurtosis	-1.08	0.03	-0.32
Skew	-0.30	0.83	-0.69
Shapiro-Wilk	0.93, $p = 0.45$	0.94, $p = 0.52$	0.94, $p = 0.55$
Final saturation (%)			
Mean	85.3	86.1	93.9
Median	85.0	86.5	94.0
Standard Deviation	2.0	2.7	2.8
Kurtosis	-0.26	-1.41	3.57
Skew	0.71	-0.13	-1.54
Shapiro-Wilk	0.91, $p = 0.25$	0.94, $p = 0.61$	0.85, $p = 0.04$
Final exertion (points)			
Mean	4.9	4.6	3.4
Median	5.0	4.0	3.0
Standard Deviation	2.7	2.2	2.1
Kurtosis	0.10	-0.86	0.85
Skew	0.82	0.05	0.40
Shapiro-Wilk	0.88, $p = 0.12$	0.96, $p = 0.81$	0.92, $p = 0.38$
Speed (metres / second)			
Mean	0.80	0.83	0.85
Median	0.79	0.78	0.87
Standard Deviation	0.22	0.27	0.24
Kurtosis	-0.08	0.01	-0.64
Skew	0.34	0.76	0.05
Shapiro-Wilk	0.97, $p = 0.93$	0.95, $p = 0.60$	0.97, $p = 0.87$

Power To Detect Difference Between Interventions for Distance

The results of the unassisted six-minute walk test supported the estimates used for the sample size calculation. The standard deviation of our sample was 92.5 metres and the Pearson correlation coefficient (r) between repeated unassisted (2nd and 3rd) 6MW varied from 0.94 to 0.99 depending on the study day. Based on interpolation from tables, the sample size required for the chosen power ($\beta = 0.80$, $\alpha = 0.05$) ranged from less than nine to 17. The details are shown in Table 11. The most likely estimate of sample size requirement was less than nine based on an estimated of MCID (30 metres), the mean estimate of correlation from our study sample (0.97), and the SD of the unassisted walking tests (92.5 metres) from our study sample.

Table 11. Sample size calculation and post-hoc power analysis for distance walked on the six minute walk test.

	Sample Size Calculation		Post-hoc Sample Size Calculation	
Alpha	0.05		0.05	
Beta	0.80		0.80	
Between Participant SD (metres)	99.0		92.5	
Pearson Correlation Coefficient (r)	0.90		0.97	
MCID (metres)	30	52	30	52
Effect Size	1.0	1.7	1.9	3.2
Sample Size	17	< 9	< 9	< 9

MCID: Minimal clinically important difference.

To verify the power calculation, a second evaluation was completed using the true sample standard deviation of the difference (28.1 metres) between practice walk two and three suggested by Cohen (77) and the range of MCID reported in the literature. The power was interpolated from tables (77) and resulted in a power of 0.75 for MCID = 30 metres, 0.85 for MCID = 54 metres, and > 0.85 for MCID = 71 metres.

1. Effect Size A: $= MCID / SD_z$; where $z_i = (x_i - y_i)$
$= 30 / 28.1$
$= 1.1$
2. Effect Size B: $= MCID / SD_z$; where $z_i = (x_i - y_i)$
$= 54 / 28.1$
$= 1.9$
3. Effect Size C: $= MCID / SD_z$; where $z_i = (x_i - y_i)$
$= 71 / 28.1$
$= 2.5$

Treatment by Period Interaction and Period Effects

The assumptions of absence of period by treatment interaction and period effect were met; there was no statistically significant period by treatment interaction or period effect for distance walked, final saturation, final perceived exertion or speed. The results of assumption testing are reported in Table 12.

Table 12. Test estimates for period by treatment interaction and period effect for the outcomes of distance, final oxygen saturation, final perceived exertion and speed.

Outcome		Effect Estimate	95% CI	Variance	*p*-value
Distance	Interaction[1]	-96.4	-217.3 – 24.6	31186.2	0.10
	Period Effect	-24.7	-79.3 – 29.9	6355.4	0.08
Saturation	Interaction	-2.4	-5.6 – 0.8	19.2	0.10
	Period Effect	0.2	-2.6 – 3.0	14.9	0.22
Exertion	Interaction	-2.6	-5.3 – 0.1	15.3	0.08
	Period Effect	-0.3	-1.4 – 0.9	2.8	0.16
Speed	Interaction	0.25	-0.59 – 0.09	0.25	0.11
	Period Effect	-0.05	-0.15 – 0.06	0.17	0.08

[1] Interaction refers to period by treatment interaction.

TREATMENT EFFECT

At baseline, defined as practice walk test three on study day one, the mean distance walked (± standard deviation) was 244.4 ± 85.0 metres. The mean oxygen saturation was 85.3 ± 2.0 percent. The mean perceived exertion was 4.9 ± 2.7 points out of a possible ten where a lower score is more desirable. The mean speed was 0.80 ± 0.22 metres per second. Lastly, the median (25% – 75%) number of rest breaks at baseline was 1 (0 – 2).

Under the oxygen condition, the mean distance walked was 295.6 ± 82.4 metres, with a mean final saturation of 93.9 ± 2.8 percent, and perceived exertion of 3.4 / 10 ± 2.1 points. The mean speed of walking was 0.85 ± 0.2 metres per second. Under the rollator-style walker condition the mean distance walked was 275.7 ± 108.2 metres, perceived exertion was 4.6 ± 2.2 points, and final oxygen saturation was 86.1 ± 2.7 percent. The mean walking speed was 0.83 ± 0.2 metres per second.

<u>Rollator-style walker versus Oxygen</u>

Data from both periods were combined for analysis. There was no clinically or statistically significant difference between the rollator-style walker and oxygen on the primary outcome of distance walked. The pooled mean difference between oxygen and rollator-style walkers was -22.2[d] metres (95%

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[d] This represents a pooled mean difference were sequence A, (n = 5), was weighted more than sequence B, (n = 6), by $\beta_1 = ½ (\bar{y}_{1.} - \bar{y}_{2.})$ (Equation 3 - page 57). The mean difference, calculated by directly comparing the two interventions, and ignoring the study design is $mean_{rollator\text{-}style\ walker} - mean_{oxgyen}$ = 275.7 – 295.6 = -19.9.

Confidence Interval (CI) –76.7 to +32.4) favouring oxygen. Not surprisingly, a significant difference was found for final oxygen saturation. On average, the final saturation was 7.8 (95% CI 5.0 to 10.6) percentage points higher with oxygen compared with the rollator-style walker. This represents a true directional change in saturation, although the clinical relevance of correcting exertional desaturation is not clear in this population. A statistically significant difference was found on final perceived exertion. When participants walked with oxygen they experienced a level of perceived exertion that was 1.3 (95% CI 0.1 to 2.4) points lower than with the rollator-style walker. Higher scores represent greater exertion. The clinical significance of this difference for this population is not clear because the minimal clinically important difference has not been reported in the literature. Lastly, there were no significant differences noted on speed walked; the mean difference was 0.02 metres per second (95% CI -0.13 to 0.08) metres per second. The results are reported in Table 13. There was a small difference on the number of rest breaks taken on the 6MW. The median values for both interventions were zero, but participants in the top quartile took one or more rest breaks while using the rollator-style walker compared to no rest breaks taken when they used the oxygen accounting for the greater distance walked with oxygen in spite of similar walking speeds.

Table 13. Treatment effect for outcomes of distance (metres), final oxygen saturation (percentage points), final perceived exertion (points), speed (metres / second) and number of rest breaks.

	Mean Difference	95% CI	p-value
Distance (metres)	-22.2	-76.7 – 32.4	0.29
Saturation (%)	-7.8	-10.6 – -5.0	0.0001
Exertion (points / 10)	1.3	0.1 – 2.4	0.02
Speed (metres / second)	-0.02	-0.13 – 0.08	0.30
	Median (25% - 75%)		
	Rollator-style walker	Oxygen	
Rest Breaks	0 (0 – 1)	0 (0 – 0)	

<u>Oxygen and Rollator-style walkers versus Baseline</u>

Prior to comparing rollator-style walkers to baseline (unassisted walking test three) and oxygen to baseline, the absence of systematic differences between study days in the unassisted walks was completed using the same method to assess for period effects in the intervention data ($\beta_2 = \frac{1}{2}(\bar{d}_{1.} + \bar{d}_{2.})$). The results indicated that there was no evidence of systematic changes in distance walked (-16.3 (95% CI –48.7 to 16.1)), final saturation (-1.3 (95% CI –4.0 to 1.4)), or perceived exertion (0.5 (95% CI –0.5 to 1.4)) at the end of the baseline walk, by study day. There were significant period effects noted for speed (-0.05 (95% CI –0.11 to –0.01) and therefore no further testing was done for this outcome.

There were no significant differences between baseline values and outcomes using the rollator-style walker on distance walked (mean difference 31.4 metres, 95% CI -3.4 to 66.2), saturation (mean difference 0.7 percentage points, 95% CI -1.4 to 2.8), or perceived exertion (mean difference 0.3 points, 95% CI -0.8 to 1.3). However, there were significant differences on all outcomes for oxygen compared to the baseline values, including distance walked (mean difference 51.3 metres, 95% CI 18.6 to 84.0), saturation (mean difference 8.6 percentage points, 95% CI 5.9 to 11.4), and perceived exertion (mean difference 1.5 points, 95% CI 0.4 to 2.7). Testing was not completed for walking speed due the presence of period effect. By excluding period two data there would be insufficient data available.

QUALITATIVE ANALYSIS

Participants were asked both closed and open-ended questions about their experience with the rollator-style walker. The responses to the open-ended question are summarized in Table 14. Responses to open-ended question, "Do you have anything that you would like to say about your experience with, or your thoughts about, using the rollator-style walker?", suggested that some individuals found the rollator-style walkers helpful and would purchase them. The responses also showed that there were significant barriers to the use of the rollator-style walker in homes and in the community. The variety of responses highlights the variation in individual response to the interventions. Answers to closed-ended questions suggested that oxygen improved the ability to walk more than the rollator-style walker, however rollator-style walkers were the preferred intervention.

Table 14. Responses to open-ended question "Do you have anything else you would like to say about the walker" grouped by response type.

Positive Responses	
Physical	I can see myself going further because I don't have to carry the tank (oxygen).
	Without the walker I don't have the stability I should.
	Steadies me.
	My back was not as bad with the walker.
	I can walk further with the walker.
	I can get fitter with the walker.
	Doesn't make you 100% but much better, helps my breathing so I can walk better.
Psychological	It's security, something to hold onto.
	More confidence because I can sit down anytime I want to.
	I am only 44. I was a little apprehensive but after the 1st time it was a blessing in disguise.
	Walker is a big help, it gives me confidence.
	I can rest outside. I can sit on it.
	I don't mind the way the walker looks.
	Feelings don't matter – I will use whatever I have to (to walk)
Other	...difficult without it.
	...do shopping with the walker (e.g. milk).
	...use it to walk (with) the dog.
Negative Responses	
Physical	My house is not equipped for it
	It limits where I can go
	Too awkward around the house
	Areas where you can use the walker are limited
Psychological	I would use it but I would feel embarrassed because of my age (39)
	...not use it at the mall because people would stare
	As you get older these things (visual look of walker) are less important but you also get more stubborn
	Makes you feel like you are getting old
Other	I could use the (grocery) cart at (specific grocery store)
	Can borrow a walker from the Legion
	Would not use it for everyday stuff
	It (walker) is about the same as the stick but I am used to the stick
	Only use it (walker) for preplanned walks

Negative responses to the open-ended question included physical, psychological and other barriers to the use of the rollator-style walker. Physical barriers within the home and community, which would restrict mobility, were identified. This also included issues of awkwardness of the rollator-style walker. Psychological barriers were also noted; issues of embarrassment, reaction of other people, and negative feelings related to aging. Lastly, the responses indicated that there were other viable options other than purchase of a rollator-style walker available to the participants that may achieve the same results. This included using alternates to rollator-style walkers such as canes or grocery carts, and borrowing from community organizations.

The positive responses were also grouped as physical, psychological and other reasons for the use of the rollator-style walker. Physical reasons mentioned by the participants included impact on other body systems other than improving respiratory limitations in the ability to walk, including improved balance and fitness. One respondent noted that a concurrent medical problem might be assisted with the rollator-style walker. It was also noted that the rollator-style walker might provide assistance in managing concurrent oxygen therapy. Psychological reasons were related primarily to confidence or overcoming feelings about how the rollator-style walker looked. Lastly, other positive responses were related to specific tasks that may be easier with the rollator-style walker.

Closed-ended questions were asked following the end of each intervention walk. The participants were asked to rate the last (intervention) walk they completed. After walking with either oxygen or the rollator-style walker, over 90% of the participants stated it made their ability to walk 'a lot better' or 'a little better'. None of the participants rated the rollator-style walker or oxygen as making their walking 'a little worse' or 'a lot worse'. Slightly more participants rated the oxygen as 'a lot better' and the rollator-style walker 'as a little better'. See Figure 4.

After the completion of both study days the participants were asked if they preferred walking with or without the rollator-style walker. The question was structured to maintain the oxygen blind. Seven participants (64%) indicated they preferred the rollator-style walker intervention and four (36%) preferred the oxygen intervention.

Lastly, participants were asked if they would consider purchasing a rollator-style walker and / or oxygen based on their experience. The participants were informed of the cost to themselves prior to answering the question. Six (55%) of the participants indicated they would, and five indicated they would not purchase a rollator-style walker. Six (67%) participants indicated they would purchase oxygen, but there were two missing responses from this question.

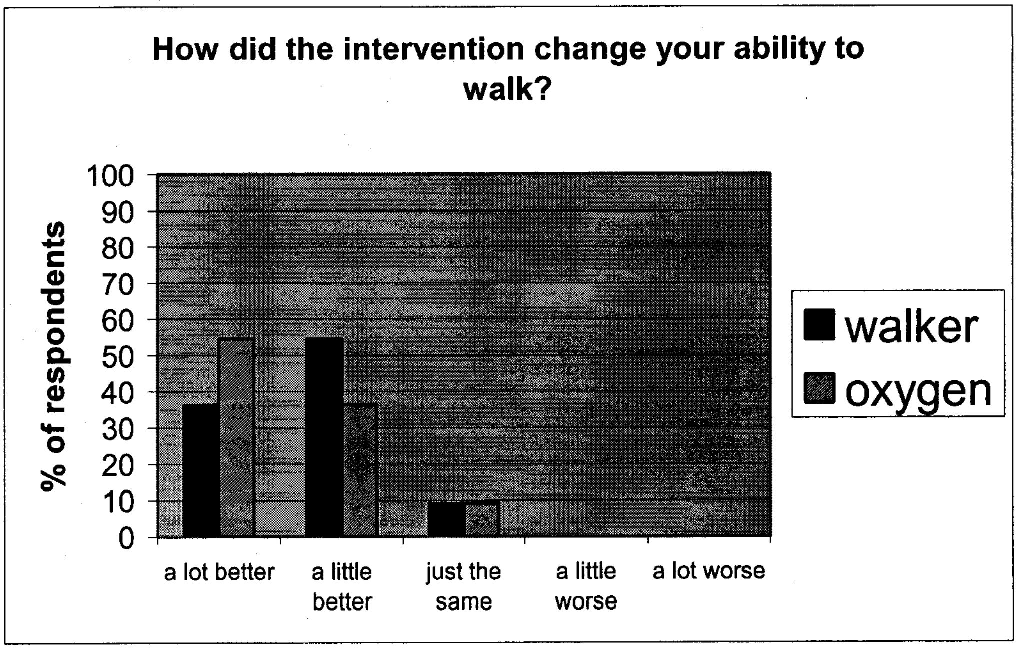


Figure 4. Results of closed-ended questions on improvement in ability to walk.

CHAPTER SIX: DISCUSSION

Understanding the difference in treatment effect between rollator-style walkers and oxygen is important for the management of people with mildly hypoxic COPD. Oxygen supplementation in patients with PaO_2 below 55 mmHg has been shown to prolong life (13;14), however, there is controversy over the use of oxygen in mildly hypoxic individuals. Its use does not appear to extend life, and although exercise capacity is clearly improved with oxygen, there is no conclusive evidence to support its longer-term impact on exercise capacity or walking ability. In addition, clinically, there may be resistance to the use of oxygen by people with severe COPD, perhaps because its medical appearance is associated with declining health status. Lastly, oxygen is expensive to provide on a long-term basis. Rollator-style walkers, unlike oxygen, are essentially risk-free, much less costly, and there may be greater acceptance among patients; however, the evidence to support the ability of the rollator-style walker to increase exercise capacity is less well understood. Therefore we compared the two interventions to each other and to the baseline unassisted walking ability.

TREATMENT EFFECT

Being able to walk is a fundamental component of the physical dimension of quality of life. Our study showed no statistical or clinically important differences in distance walked on the 6MW between rollator-style walkers or oxygen. Importantly, the inability to show difference occurred despite adequate power to detect a difference of 34 metres if one truly existed. In addition, the lack of significant difference occurred even though oxygen allowed for both signifcantly higher levels of oxygen saturation and lower levels of perceived exertion when compared to the rollator-style walker. There were no significant differences in the speed at which the participants walked. It was unclear whether there were differences in rest breaks due to the low number of rests that were taken by participants under any walking condition. Overall it appears that oxygen may outperform rollator-style walkers on distance walked on the 6MW in people with mildly hypoxic COPD by approximately 22 metres, a value that is both statistically and clinically unimportant.

Post-hoc testing was completed to compare oxygen to baseline and rollator-style walkers to baseline separately. Estimates of treatment effect suggested that while oxygen produced significantly improvements to distance walked on the 6MW, the difference was not large and the distance was not clinically important. Rollator-style walkers did not show either clinical or statistical differences from unassisted baseline scores. The results were also consistent with oxygen, but not rollator-style walkers, correcting exertional desaturation. Overall, it is not clear if it was the interventions that did not produce expected changes in the ability to walk, or if the outcome measure chosen did not offer adequate time for these improvements to make themselves known. This issue of clinical relevance of the 6MW choice is discussed in more detail in following sections.

POTENTIAL MECHANISM OF ACTION

Reduction in maximum ventilatory capacity (V_E) restricts the exercise capacity in people with COPD. This occurs because V_E is reached quickly during exertion. The reduction in maximum ventilatory capacity occurs for a variety of reasons that include the presence of hyperinflation and airway obstruction at rest, and increased minute ventilation, less efficient use of the diaphragm, respiratory muscle fatigue and increased sensation of dyspnea during exertion (46;72). It may be possible to increase distance walked through two mechanisms: altering the relationship between ventilation and work performed or altering the relationship between distance walked and work performed. Because distance walked is directly related to the amount of work performed, approaching maximum ventilation restricts the ability to walk further distances. Oxygen has been shown to affect the relationship between ventilation and work (46;72), whereas rollator-style walkers may affect both relationships. Figure 5 illustrates the hypothesized relationship between work and ventilation under room air condition.

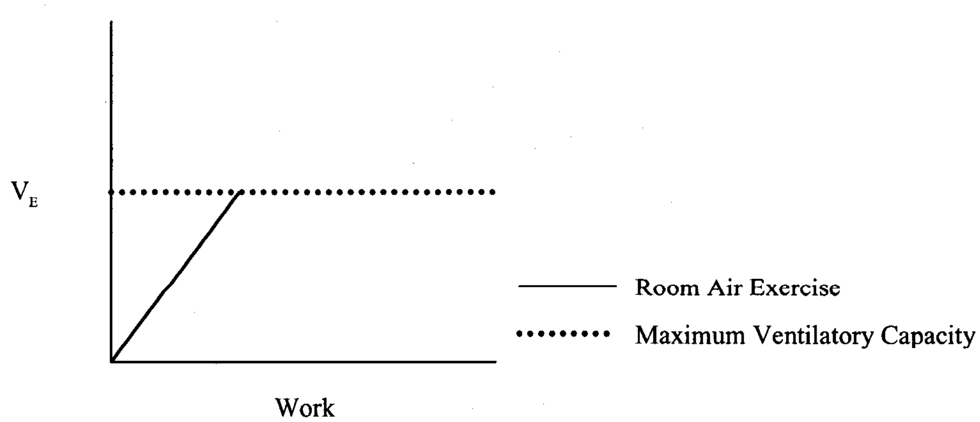


Figure 5. Relationship between ventilation, maximum ventilatory capacity and work in COPD.

Oxygen

It has been shown that oxygen is able to increase the amount of work performed in people with COPD by delaying the onset of maximum ventilatory capacity through reducing the slope of the relationship between work and ventilation (46;72). Figure 6 illustrates this relationship.

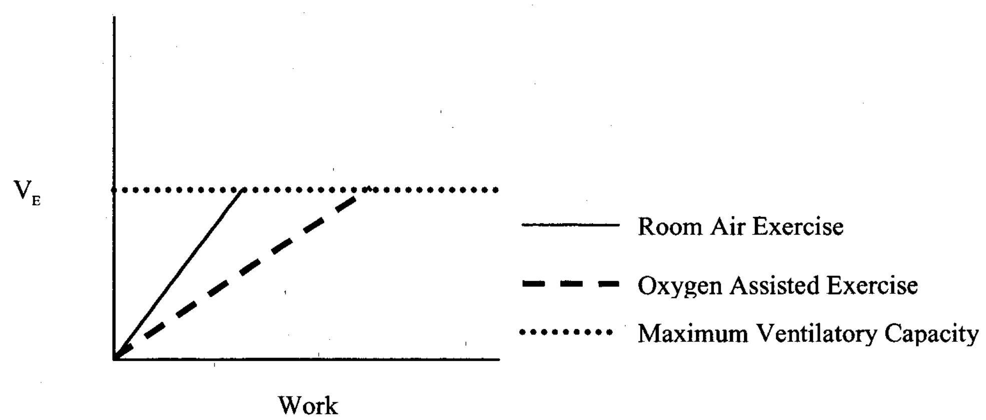


Figure 6. The hypothesized impact of oxygen on the relationship between ventilation and work.

This is supported by research that has shown that total ventilation during oxygen-supplemented exercise is lower than ventilation during room air exercise for the same amount of work completed in people with COPD (46;72). In addition, a greater amount of total work can be completed with oxygen supplementation compared to breathing room air (46;72). Our study data showed that oxygen increased the distance walked compared to room air walking tests.

Although we did not measure ventilation, we did note a small decrease in perceived exertion, which is highly correlated with measures of ventilation.

Rollator-style walker

The mechanism through which rollator-style walkers may increase work performed is not well understood. We hypothesized several mechanisms, which included altering the relationship between ventilation and work and the relationship between work and distance walked. Altering the relationship between work and ventilation, illustrated in Figure 7, was hypothesized to occur because stabilization of the accessory muscles of respiration may delay the onset of dynamic hyperinflation possibly through reduction of respiratory rate. A reduction in anxiety, as noted by the qualitative measures, may also reduce respiratory rate. In addition, the rollator-style walker may allow more effective use of the diaphragm through forward displacement of the abdominal contents. Lastly, we also suggest that the maximum ventilatory capacity may be less fixed than previously believed, and by increasing confidence the individual may be less limited by the frightening sensation of dyspnea. This was supported by a reduction in perceived exertion in spite of a longer distance walked and no improvement in oxygen saturation.

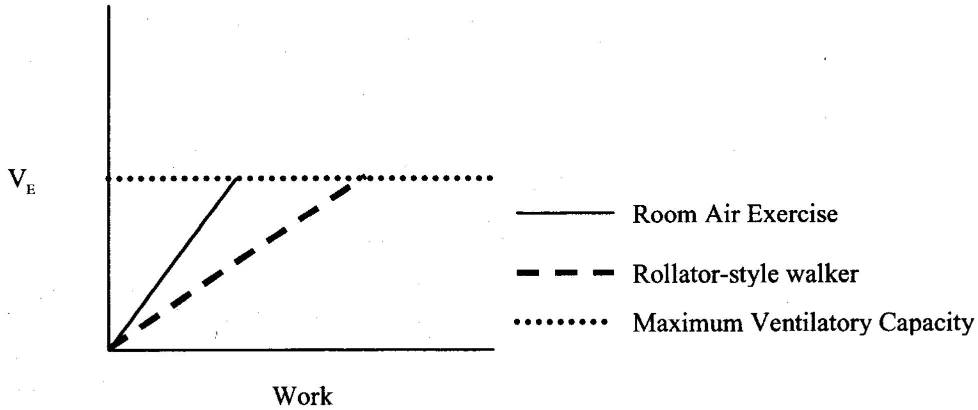


Figure 7. The hypothesized impact of rollator-style walkers on the relationship between ventilation and work.

The rollator-style walker may also alter the relationship between work and distance (Figure 8). It is known that more efficient gait patterns are metabolically less costly to the body therefore allowing further distance to be generated with the same amount of work performed.

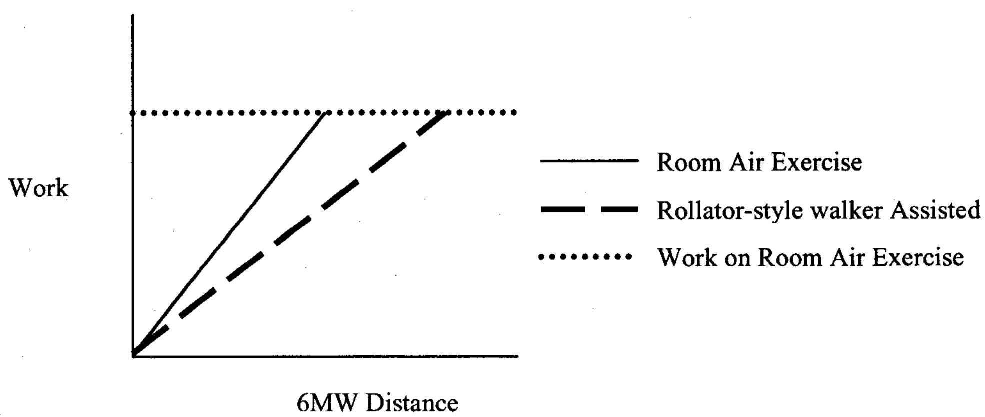


Figure 8. The hypothesized impact of rollator-style walkers on the relationship between work and six minute walk distance.

Statements made in the open ended component of the study about increased balance and confidence with the rollator-style walker support this hypothesis. It is unclear how the speed of gait may have affected this relationship. In our study, the speed increased, whereas we had hypothesized that is would decrease. However our subjects walked so slowly that slowing them down more may actually increase the metabolic costs for walking. There is a U-shaped relationship between work and speed where increased speed to a more normal range actually reduces the metabolic cost but increases in speed beyond this level increases the cost. Therefore the results of our study, which suggested increased speed, do not clarify the hypothesis that rollator-style walkers reduce the metabolic demands of walking.

In conclusion, it has been previously documented that oxygen changes the relationship between work and ventilation in people with COPD. By changing this relationship the distance walked is inherently increased. The rollator-style walker is less well studied. We hypothesized that it may increase distance walked by altering the relationship between work and ventilation and it may further act by altering the relationship between work and distance. Because both mechanisms may be at work assessing the combined effect of rollator-style walkers and oxygen is important, however we were unable to do that in this study due to demand on the study participants. In addition, work that has been completed assessing the relationship between work, ventilation and oxygen needs to be completed on rollator-style walker-assisted exercise.

QUALITATIVE ANALYSIS

Both the open and closed-ended questions showed that there were psychological and physical issues that would influence a person's decision to use a rollator-style walker. It was the first time these issues have been addressed in a systematic fashion.

Embarrassment was seen within the comments. Some participants felt they were too young or stated they would not be willing to tolerate the age-related association to the rollator-style walker. Our two youngest participants (39 and 44 years) both commented that their age was a factor contributing towards not wanting to use the rollator-style walker. Despite their similarity in age and illness, one participant considered using it while the other participant refused despite the fact that (s)he indicated it improved the ability to walk.

The use of wheelchairs is widely understood to be dependent on environmental accessibility but this has not been documented with rollator-style walkers. Clinically, however, it is common practice to ask about house layout during an assessment for rollator-style walker prescription. As a result the identification of physical barriers was not unexpected. Many homes are not large enough to accommodate a rollator-style walker, particularly those homes with stairs, and it is difficult to move a rollator-style walker in and out of a car. Community barriers continue to be perceived as a problem; despite the gradual shift in our communities to ensure buildings and sidewalks are accessible.

As expected, there were some comments suggesting the rollator-style walker assisted with other health problems such as balance and back pain. This may be a factor in why some individuals appeared to improve much more than others, even with the same lung impairment. Confounding health problems were not assessed in this study so we were unable to perform any subgroup analysis. Confounding health problems would be an important variable to include for future research.

Lastly, one participant identified the potential benefit of placing the oxygen tank in the rollator-style walker instead of carrying it. Requiring a person to carry an oxygen tank has been noted in the literature to reduce the distance walked by as much as 14% (40). This would be a benefit for patients who used both therapies concurrently.

The comments highlight a trend often seen clinically. Patients will refuse to use an intervention that is clinically beneficial. They often become labelled as unwilling to help themselves or non-compliant. Pharmaceutical, surgical or other medical interventions often have a clearer risk profile and as a result it may be easier for practitioners to understand why a patient would refuse an intervention. Non-invasive interventions, such as a rollator-style walker, do not have this clear risk profile. The barriers that were identified are real and need to be considered by the practitioners just as they would the potential risks of other interventions.

IMPACT ON CLINICAL DECISION MAKING

Decision-making requires the results of studies that use mean differences in groups of people, to be applied to an individual. When there are few differences between two interventions on clinically relevant outcomes, issues other than efficacy become more important. The differences between using oxygen and rollator-style walkers are few. The difference in distance walked is not clinically or statistically important; the difference in perceived exertion statistically favours oxygen but the clinical importance of such a small difference is not clear; and although oxygen corrects exertional desaturation, the relevance of doing so is not clear. As a result, the issues that may influence clinical decision-making include cost, risk, personal values, and environmental accessibility.

Oxygen is more costly than a rollator-style walker. Over five years the difference amounts to nearly 24,000 Canadian dollars. The risk profile, although not extreme for either intervention still needs to be considered. The primary risk with oxygen is CO_2 retention. Patients who decide to use long-term supplemental oxygen must understand the consequences of increasing their flow of oxygen beyond the prescribed level, and be willing to attend regular check-ups to ensure their arterial blood gas evaluations fall within acceptable ranges. The qualitative component of this study indicated that some people, in spite of showing an improvement on objective measures, place value on the negative consequences of using a rollator-style walker such as embarrassment. Lastly, environmental accessibility for the rollator-style walker needs to be considered. An individual who improves their walking ability with a rollator-style walker and desires to use a rollator-style walker may live in a house with stairs or a community that is not barrier free.

STRENGTHS AND LIMITATIONS

We are confident in the reported results. The methodology of the study was strong because the underlying assumptions of a crossover design including absence of period by treatment interaction and period effects were met. The results on the 6MW were appropriate for statistical analysis; the learning effect had stabilized and the data was normally distributed. Bias was minimized through the rigorous application of standardized instructions and encouragement, despite the inability to completely blind the participants and assessor to the rollator-style walker intervention. The data collected were appropriate for statistical analysis. Lastly, we combined both quantitative and qualitative measures to reveal a broader perspective towards the interventions.

The study was limited in several ways including several measurement issues with the 6MW. These measurement issues include the clinical relevancy of the 6MW and non-uniform learning effect between walks one through three.

Methodology

Our study disease and intervention met the assumptions of a crossover design. There was no period by treatment interaction or period effect. We were not expecting any treatment by period interaction because of the short-term nature of the interventions and were able to demonstrate this statistically. We also minimized the risk of period effect by excluding participants who had an exacerbation of COPD in the past four weeks. This was further confirmed by asking if anything had happened to the participants between periods one and two that might affect their ability to walk. No one indicated that there had been a change in his or her status. Statistical analysis indicated that we were successful in preventing period effect.

Statistical Properties

The learning effect for distance walked on the 6MW stabilized by the third practice walk test which indicated the improvement seen on the intervention walking test was attributable to the intervention. The assumption of normality was tested for all outcomes under the rollator-style walker and oxygen interventions. The assumption was met for all outcomes except oxygen saturation during the oxygen-assisted walk. One participant who maintained a low saturation despite the application of oxygen skewed the distribution of oxygen saturation. Despite the skewing, we feel confident in using data from both periods in our analysis.

Bias

The introduction of bias is a concern in research. Blinding of the assessor and the participant to the interventions can minimize bias and is an important component of quality in a randomized-controlled trial. Reporting blinding within a publication is one component of quality assessment. Studies of low quality have been shown to overestimate the treatment effect by as much as 34% when compared to high quality studies (76). Unfortunately, the nature of many of the interventions under study in the rehabilitation sciences makes it impossible to blind both the participant and the assessor.

In our study we were able to successfully blind the participant, but not the assessor, to the use of oxygen. The assessor was not blinded for practical reasons, but in this situation it would have been ideal. The taste and smell of oxygen has been reported to be indistinguishable so we wanted to ensure the blind was successful. Participants were not systematically able to distinguish between the two and we were confident that the blind was maintained throughout the study. We were unable to blind both the participants and the assessor to the use of the rollator-style walker for apparent reasons. In order to compensate, we were rigorous in our use of standardized instructions, which minimized the introduction of assessor bias. Unfortunately it did not reduce the possibility of the participants having preconceived notions of effectiveness of the rollator-style walker, which may have altered their effort.

Quantitative and Qualitative Measurements

Much of quantitative clinical epidemiology is related to the comparison of interventions by the mean responses of a group of participants. Often this is further explored by multivariate or stratified analysis in order to adjust for groups of variables that may modify the relationship between the intervention and the outcome. In our case the comparison between rollator-style walkers and oxygen to the outcome of walking ability was primarily measured by total distance walked. Qualitative research can complement the quantitative approach by identifying themes related to the individual's experience of a disease or treatment. Ideally, a combination of both approaches can best enlighten the clinician to the effect of the intervention.

The quantitative components included in this study were distance walked, percent desaturation, perceived exertion, speed and number of rest breaks within the context of the 6MW. The results can show differences in the mean responses between the interventions, the extent of variability in the mean response, and suggests other variables that may modify the relationship. The qualitative component of this study included the both open and closed ended questions about the experience of the participants with the rollator-style walker, whether they would consider purchasing a rollator-style walker, and which (rollator-style walker or oxygen) they would prefer to use. The results of the qualitative component brought out values that may influence the subjects' choices despite the quantitative evidence.

Measurement

Clinical Relevancy

In order to be useful for research, measurement tools require validity, reliability, and relevance within the population of interest. It is also important to define the MCID for a specific population. A less often considered concept is that of clinical relevancy, whether the outcome measures a quality that is important to the clinical population (83).

In this case, the 6MW has been shown to have the qualities of validity and reliability. There is no doubt that the six-minute walk test is a valid measure of exercise capacity, shown by its high correlation with oxygen uptake in individuals with COPD. There is excellent evidence to show, after the initial learning curve is accounted for, that measurements are highly reliable over repeated testing. The MCID has been defined for people with COPD. In addition, the 6MW is well integrated into the clinical setting. Based on these parameters it was the most appropriate walking test for this study.

However, the 6MW scores lower relevance to the population under study because the goals of pulmonary rehabilitation differ from what is measured by the 6MW. The 6MW measures a specific body function, exercise capacity, associated with COPD. This has been shown by its strong relationship to maximum oxygen uptake. Function is defined by the World Health Organization (WHO) to include abnormalities of the respiratory system including exercise capacity. The problem of clinical relevancy occurs because rehabilitation teaches the person with COPD to maximize their abilities in spite of impairment in exercise capacity. Abilities, defined as activity or participation by the WHO, includes ability to walk short and long distances. Short distances are considered to be less than one kilometre. The 6MW does not, and was never intended to, measure the ability of walking, but rather an estimate of maximum exercise capacity.

With specific reference to walking this means the patient learns to walk further distances through a variety of mechanisms including the use of a rollator-style walker, oxygen or both. Because of this important difference in the thrust of rehabilitation within COPD populations, improvement of abilities without necessarily improvement of a body function, there is conflict set up in the choice of outcome measure. A clinically relevant outcome measure needs to agree with the goals of the intervention, and in this case the 6MW does not measure the goals of pulmonary rehabilitation of people with moderate to severe COPD.

There is no other walking test available that has been adequately tested for validity and reliability that also meets the requirement of clinical relevancy (84). It may have been more appropriate to choose the 12MW due to its longer time available for walking, because it may have been able to detect differences in the ability to walk versus exercise capacity. Unfortunately, there are no established minimal clinically important differences for this test. It, however, may also be to short to detect the important difference in the improvement in the ability to walk. The development of a new measure of walking disability for COPD is required. Only with a new measure of walking ability or participation, and not pulmonary function, can we truly evaluate the important contributions that both rollator-style walkers and oxygen may play in the management of walking disability related to COPD.

We hypothesize that a longer test of walking endurance may be the most appropriate choice for detecting differences in walking ability. Currently under development is a 20-minute walking test where total distance and consecutive time walked is measured. This will allow change in the total distance and the endurance ability of the patient to be measured. This may have more clinical relevance because most patients with severe impairment in exercise capacity and walking ability understand that they cannot walk quickly in short periods of time like the 6MW requires them to perform.

Learning Effect

Our study suggests the impact of the learning effect on the distance walked on the 6MW is reduced after the second walking test. Our results lend support to the practice of dropping the results of the first two 6MW. This effect has been well documented (59). We were concerned that this relationship might not hold true for our very impaired population. If this were true the implications would be an underestimated treatment effect. Despite no difference in the mean distance walked between the second and third 6MW, the data suggested that the learning curve was not uniform between participants. The standard deviation increased from 83 to 101 metres in each subsequent 6MW. The individuals who fatigued between the second and third walk were similar in respiratory impairment, measured by mean percent-predicted $FEV_{1.0}$ and age. However, there were important differences noted on body mass index. Those who fatigued between walk two and three were heavier compared to those who stabilized. The implications of this may be an underestimation of the true impact of oxygen and rollator-style walkers on the heaviest people in our study population. In addition, this has important implications in clinical practice and for future research; it may be necessary to reduce the number of practice walking tests performed for heavier patients, or to increase the length of rest between practice tests.

CONCLUSIONS

Overall, quantitative and qualitative measures indicate that the rollator-style walker and oxygen perform closely on the 6MW. The distances walked are similar, despite the correction of desaturation and reduction of perceived exertion caused by the oxygen intervention. There were no differences noted in the speed walked. The participants indicated that both interventions improved their ability to walk and were closely split on which one was preferred. Perhaps the open-ended question gave the most insight into the usage of the rollator-style walker. Issues of balance, confidence, embarrassment and environmental accessibility were common themes. Cost was not commented on by any of the participants, perhaps because government programs in Ontario assist in the payment of both therapies. The issue of the choice of outcome measure must be addressed; measuring exercise capacity is not completely appropriate to assess an intervention that impacts walking ability since this ability is impacted by more than just exercise capacity. The true impact of either intervention is not clearly ascertained by this study because of the outcome choice. Overall, like much of the rehabilitation sciences, the art of understanding the person and ensuring patient-directed care suggests both interventions as viable therapies that will depend very much on the individual's circumstances.

APPENDIX A: PICTURE OF ROLLATOR-STYLE WALKER

Features

- Lightweight aluminium frame
- 3 seat heights
- Patented brake system with adjustable tension
- Seat flips up for greater reach access and for gait training
- Adjustable back support provides comfort and safety
- Stepless handle height adjustment
- Curb climber and basket included

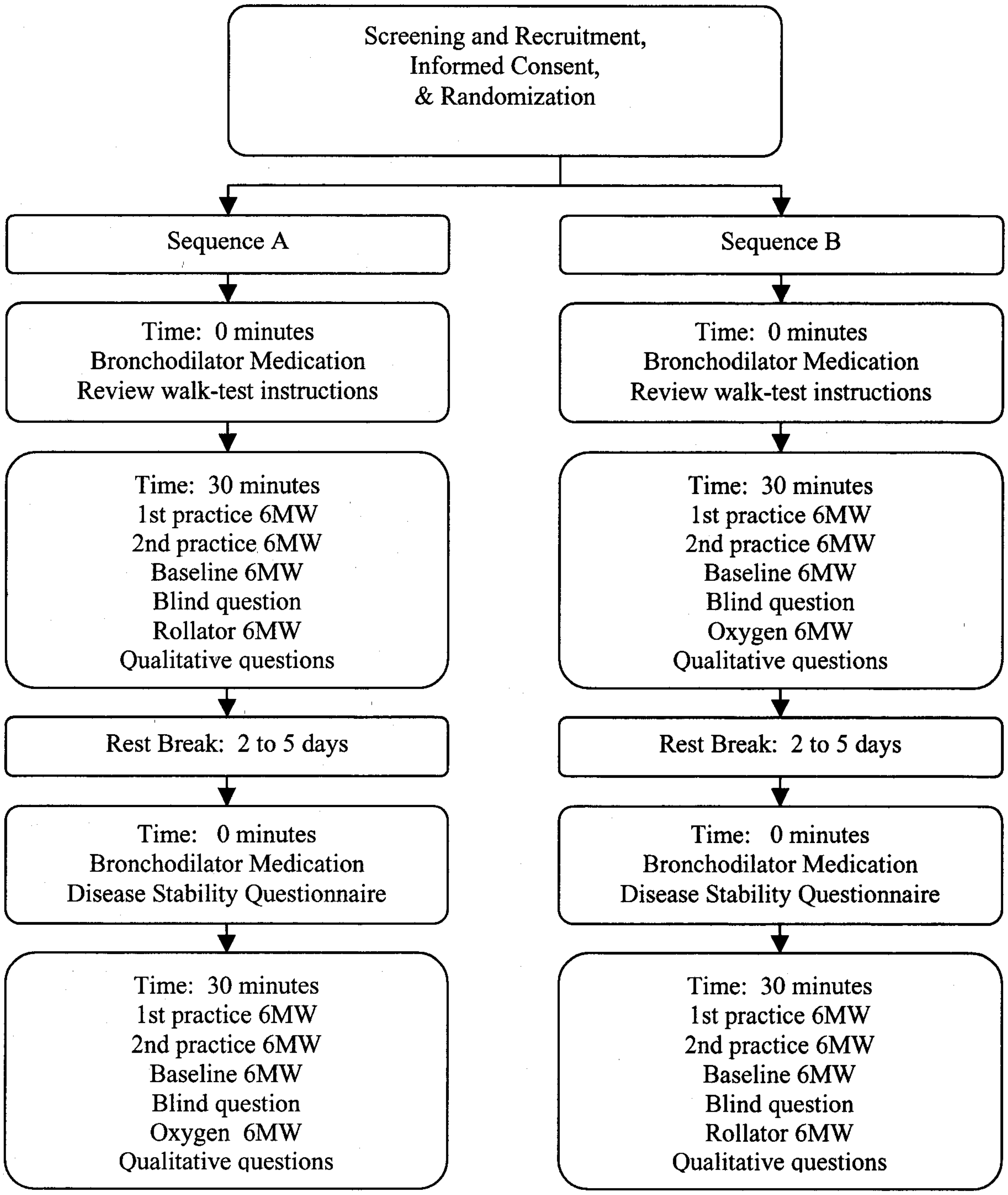
Weight capacity: 275 lbs.
Color: Silver

APPENDIX B: MODIFIED BORG SCALE

Instructions: "How short of breath are you right now?"

MAXIMAL	10
VERY, VERY SEVERE	9
	8
VERY SEVERE	7
	6
SEVERE	5
SOMEWHAT SEVERE	4
MODERATE	3
SLIGHT	2
VERY SLIGHT	1
VERY, VERY SLIGHT	0.5
NOTHING AT ALL	0

APPENDIX C: STUDY PROTOCOL



APPENDIX D: INSTRUCTIONS FOR THE SIX MINUTE WALK

This is a six-minute walk test. We are measuring the distance walked in this time frame. You are encouraged to cover as much distance as you can in the six-minute time frame. Should you feel the need to stop, please do so. The time will continue to count down. Start walking again when you are ready. Resume your walk with the objective of covering as much distance as possible until the six minutes are up.

Minute Two: You are doing fine.

Minute Four: You are doing fine.

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