Compliance to Different Exercise-Training Protocols in Individuals with Chronic Obstructive Pulmonary Disease

Rima Wardini

A Thesis

In the Department

Of

Exercise Science

Presented in Partial Fulfillment of the Requirements

For the Degree of Master of Science (Exercise Science) at

Concordia University

Montreal, Quebec, Canada

August, 2013

CONCORDIA UNIVERSITY
School of graduate studies

This is to certify that the thesis prepared

By: Rima Wardini

Entitled: Compliance to Different Exercise-Training Protocols in Individuals with Chronic Obstructive Pulmonary Disease

and submitted in partial fulfillment of the requirements for the degree of

Master of Science (Exercise Science)

complies with the regulations of the University and meets the accepted standards

with respect to originality and quality.

Signed by the final examining committee:

_____ Chair
Dr. Richard Courtemanche

_____ Examiner
Dr. Alain Leroux

_____ Supervisor
Dr. Véronique Pepin

Approved by _____
Dr. Simon Bacon
Chair of Department or Graduate Program Director

_____ 20__ _____
Dr. Joanne Locke
Dean of Faculty

ABSTRACT

Compliance to Different Exercise-Training Protocols in Individuals with Chronic Obstructive Pulmonary Disease

Rima Wardini

Rationale: Current guidelines for pulmonary rehabilitation suggest high-intensity exercise training for patients with chronic obstructive pulmonary disease (COPD). However, compliance to this type of training is problematic. Alternative approaches, such as training at the ventilatory threshold and interval training, have been proposed as easier to comply with. The objectives of this study were to: 1) compare patient compliance to three exercise-training protocols: continuous training at high-intensity (CTHI), continuous training at the ventilatory threshold (CTVT), and interval training (IT); 2) determine if a relationship exists between exercise compliance and baseline self-efficacy in COPD patients. **Methods:** Subjects were randomly assigned to one of the protocols and trained on a cycle ergometer three times per week for 12 weeks. Compliance to the training protocol was measured by attendance and compliance rates to the prescribed intensity. Compliance data were obtained through data tracking technology allowing second-by-second recording of exercise-training sessions. Self-efficacy was measured using the Self-Efficacy Scale. **Results:** Thirty-six subjects with moderate to severe COPD participated in the study. Attendance rates did not differ significantly between groups (Mean $\pm$ SD: 70 $\pm$ 33% for CTHI, 82 $\pm$ 17% for CTVT, 63 $\pm$ 35% for IT, $p = 0.229$). Mean compliance rates were 85.6 ± 15.0 % for CTHI, 84.1 ± 15.1 % for CTVT, and 52.0 ± 41.8 % for IT ($p=0.07$). Self-efficacy did not correlate with mean attendance or mean compliance to the prescribed intensity. **Conclusion:** The present study suggests that IT may be associated with lower compliance rates than CTHI and CTVT.

Keywords: COPD, attendance, compliance, exercise-training, self-efficacy.

ACKNOWLEDGEMENTS

I would like to express my deep gratitude to my supervisor, Dr Véronique Pepin, for her patient guidance, enthusiastic encouragement and useful critiques throughout my Master's degree. I would also like to thank Dr. Pepin for giving me the opportunity to be part of a wonderful research project and research team, which greatly helped my personal and professional growth. You are a great source of inspiration.

I would like to extend my thanks and appreciation to my committee members, Dr. Simon Bacon and Dr. Alain Leroux. Your constructive suggestions throughout my Master's degree have permitted the development of my critical thinking in this world of research.

I would also like to thank my amazing research team, Amanda, Emilie and Barbara. Thank you all for being present throughout this hard yet incredible journey. Your support and continuous encouragement have helped me get to my goal. As well, I would like to thank Amélie Forget and Chantal Robitaille for their tremendous help with SPSS. Without you my data collection and analysis would have been a torture.

I would also like to take this opportunity to share my gratitude to my colleague, Esther Dajczman, for her valuable suggestions during the writing of my Master's thesis. Your willingness to give me of your precious time is greatly appreciated. Thank you for being part of this great accomplishment.

I wish to communicate my deep thanks to my mother, brother, sisters and best friends for their constant encouragement without which this accomplishment would not have been possible. Without your love and constant support, I would not be the person I am today.

My unconditional thanks goes also to my step father, Nabil. You are the voice that keeps me focused on the most important things in life. You will forever be in my heart. God bless your soul.

Lastly, I wish to thank my wonderful daughter, Alicia. You give me the strength to strive towards becoming a better and stronger person. I hope to be able to give you in return what you are giving me every single day of my life. You are my sunshine and I love you.

Trust in dreams, for in them is the hidden gate to eternity

-Gibran Khalil Gibran

CONTRIBUTIONS OF AUTHORS

Rima Wardini is the primary author of the manuscript included in this thesis. She is responsible for the literature review and assembly of the manuscript. In addition, she is responsible for the collection of data, and data analysis.

Véronique Pepin is the main supervisor to the primary author and oversaw assembly of the entire research project and manuscript. Dr. Pepin is responsible for the larger randomized control trial. As well, she is the primary editor of the manuscript ensuring its accurateness and completeness. Dr. Pepin has also made significant contributions to the display of results.

Amanda Rizk is responsible for aiding in data collection and ensuring patient safety during the research study and is the coordinator of the larger randomized control trial which included patient recruitment and follow-up.

Emilie Chan-Thim is responsible for aiding in data collection and ensuring patient safety during the research study.

Barbara Trutschnigg is responsible for assessing exercise testing at baseline and follow-up and ensuring patient safety.

Amélie Forget is responsible for aiding in data extraction and cleaning.

Grégory Moullec is responsible for aiding in psychological and quality of life data collection.

Table of Contents

LIST OF FIGURES

LIST OF TABLES

CHAPTER I

1. Theoretical Context

1.1 An Overview of Chronic Obstructive Pulmonary Disease

Individuals with respiratory disease have impaired lung function leading to breathlessness and inactivity which results in disability, a loss of independence, and poor quality of life (Figure 1.1) [1-5]. COPD is comprised of chronic bronchitis and emphysema, and is characterized by chronic airflow limitation, hyperinflation, inflammation, and systemic manifestations such as skeletal muscle wasting and cachexia [2, 4, 6, 7]. It is a chronic illness that is progressive in nature and minimally reversible [6].

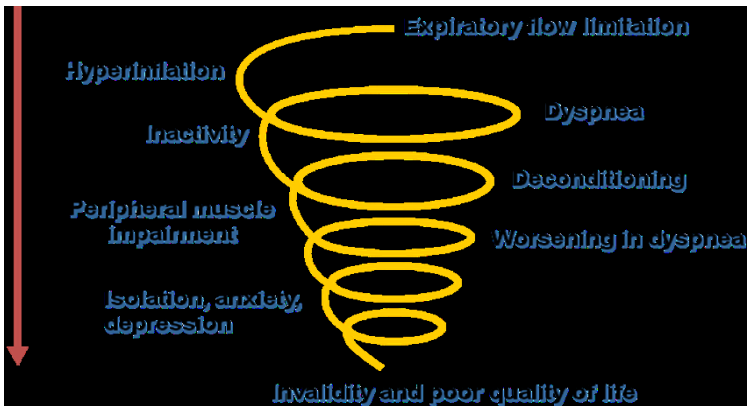


Figure 1.1 COPD downward spiral. Adapted from la Clinique du Souffle la Solane, Osséja, France [8].

Chronic bronchitis is described by the inflammation and swelling of the cells lining the bronchi and bronchioles of the lungs leading to narrowing of the airways. The inflammation stimulates the production of mucus (sputum), which can cause further obstruction of the airways increasing the likelihood of bacterial infections [2, 7]. Clinically, symptoms such as cough and sputum production for at least 3 months in each of 2 consecutive years, serve as a diagnostic criteria for the presence of chronic bronchitis [6].

Emphysema, on the other hand, is a condition of the lungs where the walls of the alveoli, the gas exchanging surfaces of the lungs, are destroyed and loose elasticity hindering the outflow of air during exhalation [2, 6]. Dyspnea represents one of the main symptoms in patients with emphysema [6]. All COPD patients have airflow limitation combining chronic bronchitis and emphysema with the contribution of each varying from one patient to another [6].

1.2 Epidemiology

1.2.1 Prevalence

COPD is the fourth leading cause of mortality in the world and in Canada and represents a major cause of respiratory morbidity [6, 9, 10]. In 2004, COPD was responsible for 9,607 deaths in Canada and it is expected to become the third leading cause of death in the next 20 years [3, 9]. Unlike other major illnesses with either stable or declining mortality rates, COPD is the only disease where mortality continues to rise [11]. More than 750, 000 Canadians are diagnosed with COPD, but the actual prevalence is thought to be higher since only 6-8% of the population have recorded objective criteria fulfilling the diagnosis of this chronic respiratory illness [3, 6, 9, 11]. Up to 60-85% of COPD patients remain undiagnosed, since this illness is often detected at a clinically apparent and advanced stage [1-3, 9, 12]. The prevalence of the disease is expected to increase in the coming years due to continued exposure to COPD risk factors and to aging of the population [1, 6, 9, 10].

1.2.2 Social and Economic Burden

The social and economic burden of COPD is significant [6] and represents a high weight to the Canadian healthcare system [12]. Despite declining smoking rates in

Canada, the number of COPD hospitalizations is still increasing [11]. Not only is COPD the leading cause of hospital admission, it also has a higher readmission rate compared to other chronic diseases such as angina, heart failure, diabetes, or hypertension [11]. In a cohort of 73 106 Canadian patients who have been hospitalized for the first time for severe COPD exacerbation, it was shown that 2 to 3 month [13] following that event represented a period of very-high risk of recurrence. Of the 73 106 COPD patients, 25 290 and 37 935 died at 3.6 and 7.7 years respectively [13]. Other studies have shown that 18% of patients suffering from COPD are readmitted to a hospital once and 14% twice in the same year [12, 14]. In 2008, Mittman et al. reported that the average length of hospital stay for COPD exacerbations was 10 days costing $10 000 per stay [12, 15]. In the same year, it was reported that COPD incurred approximately $1.5 billion in total health care costs in Canada yearly [15]. In addition, COPD mortality rate, within one year of exacerbation hospital admission, is shown to be comparable to myocardial infarction [12, 16]. In their 2012 report, the Conference Board of Canada suggested that an increase of a 140% of direct and indirect costs of COPD would occur by 2030. COPD costs are expected to increase from approximately $4 billion in 2010 to approximately $9.5 billion by 2030 [17].

1.3 Risk Factors

1.3.1 Cigarette Smoking

Cigarette smoking is the principal risk factor contributing to COPD [4, 6]. Indeed, it is believed to be responsible for 80 to 90% of COPD cases [4, 6], and virtually all COPD patients report a smoking history. The risk related to cigarette smoking is dose-dependent, where smoking total dose influences lung function and mortality [2, 6, 18, 19]. Smoking dose can be quantified by total pack years smoked, which is the number of

smoking years multiplied by the number of packs smoked per day [6]. Tobacco smoke induces a specific inflammation process leading to mucus hypersecretion, alveoli destruction, and impairment of the lung defence mechanisms, such as the deterioration of the lung's mucociliary clearance. This in turn creates a susceptibility to infection and COPD exacerbations which can lead to further deterioration of lung function [19]. However, smoking exposure does not systematically lead to the development of COPD [2]. In fact, it has been shown that about 10 to 15 percent of smokers develop this respiratory illness [2]. Other underlying factors have been identified which can likely explain COPD development in non-smokers [6, 20].

1.3.2 Genes

Risk factors for COPD are also believed to be a result of gene-environment interaction [6]. A severe deficiency in alpha-1 antitrypsin, a key inhibitor of serine proteases, is the most important genetic risk factor for COPD [6, 21]. This genetic deficit leads to a precipitated decline in lung function in both smokers and non-smokers [6]. Other mediators, such as transforming growth factor beta 1, microsomal epoxide hydrolase 1, and tumor necrosis factor alpha, have been implicated in COPD genesis [6]. However, their influence on the development of COPD has not yet been fully identified. Alpha-1 antitrypsin deficiency is most commonly seen in individuals originated from Northern Europe and is often found in multiple members of the same family who develop COPD [6, 22].

1.3.3 Occupational Dust and Chemicals

Although the effect of occupational dust and chemicals (i.e. organic and inorganic dust and fumes) are small compared to those of cigarette smoking, it has been shown

that they can contribute to decreased lung function and COPD [2, 6]. An occupational health study focusing on certain specific industries, such as plastics manufacturing, textile mill products, armed forces, construction and trucking demonstrated that high occupational exposure contributed significantly to the cause of COPD [23]. This was estimated at 19.2% among smoker and 31.1 % among non-smokers [23]. This is consistent with Balmes et al. [24], who studied the contribution of occupational risk factors on the burden of COPD, and found that occupational exposures account for 10-20% of COPD cases.

1.3.4 Indoor and Outdoor Air Pollution

Indoor pollution is an important risk factor for COPD. In developing countries, particularly among non-smoking women, exposure to smoke from biomass fuels and heating in poorly ventilated dwellings has been related to increased prevalence of fixed airways disease COPD [2, 6]. Indoor air pollution [25] caused by burning of wood and other biomass fuels is responsible for the death of 2 million women and children every year [6]. The role of outdoor air pollution in COPD is unclear, but high levels of urban air pollution may contribute to accelerated decline in lung function, can exacerbate symptoms and is known to be harmful for individuals with cardio-respiratory diseases [2, 6].

1.3.5 Other Risk Factors

Asthma:

It has been shown that asthmatic adults have a twelve-fold higher risk of developing fixed airways disease similar to what is characteristic of COPD [25]. Although asthma is characterized by spontaneous reversibility of airway limitation, it has been

reported that functional changes of the small airways and alveoli can occur and can lead to accelerated lung function decline and increased exacerbations [26]. These patterns of airway inflammation and structural remodeling can lead to fixed airflow obstruction in some cases of asthma. Studies have shown that the prevalence of fixed airflow obstruction among asthmatic patients vary between 20 and 49% [27, 28].

Lung Development:

Maternal smoking is associated with increased respiratory infections and low birth weight in children, which are both believed to be risk factors for the development of COPD in adulthood [2]. Reduced maximally attained lung function is related to COPD and therefore any factor affecting lung growth during gestation and childhood increases COPD prevalence [2, 6].

Respiratory Infections:

Viral and bacterial respiratory infections are often the precursors to acute exacerbation of COPD and they are believed to contribute to the progression of the disease [6]. Exacerbations are shown to have a significant impact on lung function and quality of life deterioration, as well as increased health care utilization.

Severe childhood infections, which can be explained in some cases by an underlying airway hyper-responsiveness, are shown to decrease lung function and increase respiratory symptoms later in life [6].

Age, Sex and Socioeconomic Status:

Lung function is known to decline with increasing age and may impact on the prevalence of COPD as the population ages [2]. In previous studies, a higher proportion of men were shown to be affected by COPD [6], however, increasing smoking frequencies in women has created sex equality. Today at least 50% of those diagnosed with COPD are women [6]. Furthermore, it has been shown that women are more

susceptible to cigarette smoke and tend to have a faster decline in FEV1 than male smokers [2, 29]. This sex difference could be explained by hormonal factors and by the fact that women are more likely to have smaller lungs and larger airways than men, which could favour women's increased sensitivity to cigarette smoke [29].

Socioeconomic status has been inversely related to COPD development [2, 6]. However, it is unclear whether this correlation is influenced by other factors such as education, nutrition, air pollutants, smoking prevalence, or other social issues [6].

1.4 Pathology, Pathogenesis and Pathophysiology

1.4.1 Pathology

COPD is characterized by an abnormal inflammatory response in the lungs (Figure 1.2), which represents an innate and adaptive response to long term exposure to noxious substances and gases, such as cigarette smoke [6, 30]. COPD comprises pathological changes leading to mucous hypersecretion as seen in chronic bronchitis, and tissue destruction (emphysema), and disturbance of normal defense mechanisms resulting in small airway inflammation and alveolar destruction [30]. These pathological changes lead to the main characteristics found in COPD, which includes increased resistance to airflow in the small airways, increased lung compliance, air trapping, and progressive airflow obstruction [6, 30]. With COPD, the inflammatory and structural changes occur in four distinct areas of the lungs; the proximal (central) airway which includes the trachea and bronchi, the peripheral airways, the lung parenchyma (which include the bronchioles and alveoli), and the pulmonary vasculature which refers to the major vessels [6, 7]. In general, these pathological changes increase with disease severity [6, 30].

1.4.2 Pathogenesis

1.4.2.1 Inflammatory Cells and Mediators:

Noxious stimuli, such as cigarette smoke triggers the activation of inflammatory cells such as lymphocytes (T $CD4^+$, T $CD8^+$), macrophages, and neutrophils [6, 31] (Figure 1.2). These inflammatory cells can then potentially release a variety of cytokines (interleukin-1 beta, interleukin-6, tumor necrosis factor-alpha) and inflammatory mediators such as lipid mediators (leukotriene B4), chemokines (interleukin-8), and growth factors (transforming growth factor-beta) interacting with structural cells in the airways and lung parenchyma [6, 31, 32].

In the proximal airways of COPD patients, an increase in macrophages, lymphocytes and neutrophils occur. In addition, an enlargement of the submucosal bronchial gland and goblet cell cause hypersecretion of mucus. Other structural changes include: airway epithelial squamous metaplasia, ciliary dysfunction, and hypertrophy of smooth muscle and connective tissue [6, 30]. In the peripheral airways, the increased number of inflammatory cells, lymphoid follicles and fibroblasts cause premature bronchiolitis, proliferation of globlet cells and squamous metaplasia as well as peribronchial fibrosis and narrowing of the airways [6, 30]. In the lung parenchyma, the increasing number of macrophages and lymphocytes lead to alveolar wall destruction and loss of epithelial and endothelial cells airway remodelling and parenchymal destruction characteristic of COPD [6, 30]. There is also a loss of epithelial and endothelial cells leading to alveolar wall destruction. With the development of emphysema there is an abnormal enlargement of airspaces distal to terminal bronchioles and dilatation and destruction of bronchioles that occurs in the lung parenchyma [6, 30]. The possible structural changes that occur in the pulmonary vasculature include hypertrophy of smooth muscle, endothelial cell destruction

accompanied by thickening of the intima, which can lead to pulmonary hypertension [6, 30].

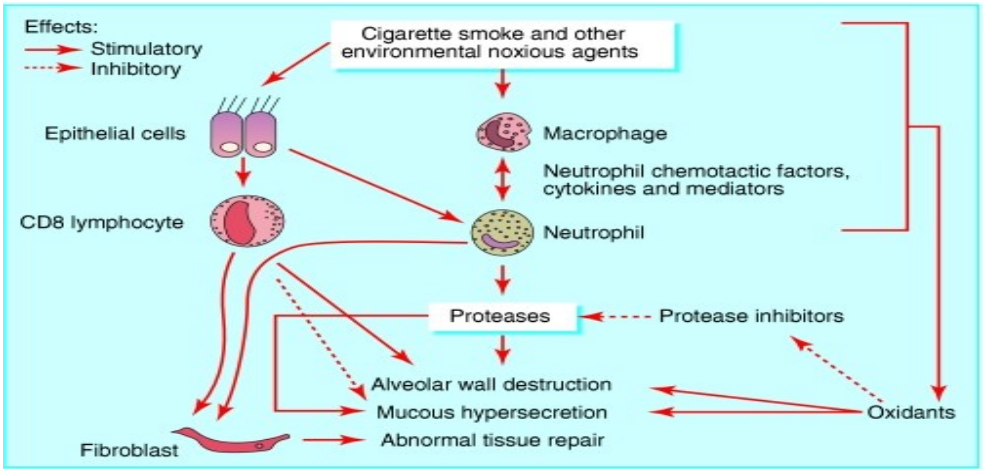


Figure 1.2 Inflammatory mechanisms in COPD [31].

1.4.2.2 Oxidative stress and Protease-Antiprotease Imbalance:

In addition to the presence of inflammation, there is an imbalance between proteases and anti-proteases producing or creating oxidative stress in COPD [6, 30, 31]. Oxidants are generated by cigarette smoke and by reactive oxygen and nitrogen species released from inflammatory cells causing an oxidative burden [6, 30]. Oxidative stress biomarkers, such as hydrogen peroxide, are increased in the sputum and systemic circulation and this stress is heightened or increased during respiratory exacerbations. Oxidative stress can lead to the following adverse outcomes; inactivation of anti-proteases, stimulation of mucus secretion, activation of inflammatory enzymes (i.e. nuclear factor-B) and hence gene expression of pro-inflammatory mediators [6, 30].

In addition, an imbalance between proteases (responsible for the connective tissue break down) and anti-proteases (protecting against connective tissue break-down) is seen in COPD. Noxious stimuli lead to oxidative stress which in turn primes several inflammatory cells to release proteases (e.g. Proteinase 3, Cathepsins E, and Matrix metaproteinases-8) and inhibit the activation of anti-proteases (e.g. Alpha-1 antitrypsin,

Elafin and Cystatins) [6, 30]. This imbalance leads to the destruction of the elastin, which is a component of the connective tissue of the lung parenchyma, causing emphysema [6].

1.4.3 Pathophysiology

The above mentioned pathologic changes result in physiologic abnormalities, such as mucous hypersecretion, ciliary dysfunction, airflow obstruction and hyperinflation, and impaired gas exchange. With ongoing disease progression patients may further experience right-sided heart failure, and manifest systemic effects such as metabolic syndrome (hypertension, hperglycemia and obesity) and pulmonary hypertension.

1.4.3.1 Airflow limitation and hyperinflation:

In order to understand the process of airflow limitation and hyperinflation, it is important to present the four basic lung volumes and the four basic lung capacities (Figure 1.3). Lung volumes and lung capacities refer to the volume of air associated with different phases of the breathing cycle, where lung volumes are directly measured and lung capacities are inferred from lung volumes [33]. Tidal volume (V_T) is the amount of air that can be inhaled and exhaled in a regular breathing cycle when at rest. Inspiratory reserve volume (IRV) is the maximum amount of air that can be forcibly inhaled from the end of a tidal inspiration [33]. On the other hand, expiratory reserve volume (ERV) represents the maximal amount of air that can be expired at the end of a tidal expiration. Residual volume (RV) is defined as the amount of air remaining in the lungs after ERV [33].

Lung capacities are subdivisions of total volume that include two or more of the four basic lung volumes. Vital capacity (VC) represents maximal volume of air that can be forcefully exhaled from the lungs following a maximal inspiration (VC = IRV+TV+ERV) [33]. Inspiratory capacity (IC) is defined as the maximal volume of air that can be inspired from end expiration (IC = TV+IRV). The volume of air remaining in the lung at the end of a normal expiration is known as functional residual capacity (FRC) (FRC = RV+ERV) and total lung capacity (TLC) is the volume of air contained in the lungs at the end of a maximal inspiration (TLC = RV+IRV+TV+ERV) [33].

The two main flow rates that are important to measure in COPD are forced expiratory volume in one second (FEV_1) and forced vital capacity (FVC) [6]. The values of these measures in liters and in percent normal predicted, which are determined by spirometry, are central in the evaluation and classification of COPD severity. In addition, FEV_1 to FVC ratio is crucial in the diagnosis of COPD [6].

Air flow limitation occurs mainly in the small airways and is caused by airway remodeling, loss of elastic recoil and destruction of the alveolar matrix [30]. The degree of inflammation, fibrosis and luminal secretions in the small airways is correlated with reduced FEV_1 and FEV_1/FVC ratio [6]. With progressive airway obstruction, air is trapped during expiration leading to lung hyperinflation (increase in the retrosternal air space) [6, 30]. Hyperinflation decreases inspiratory capacity (IC), which in turn causes an increase in functional residual volume [6]. These features are believed to be the main mechanisms leading to exertional dyspnea and limited exercise capacity which characterize COPD [6, 30].

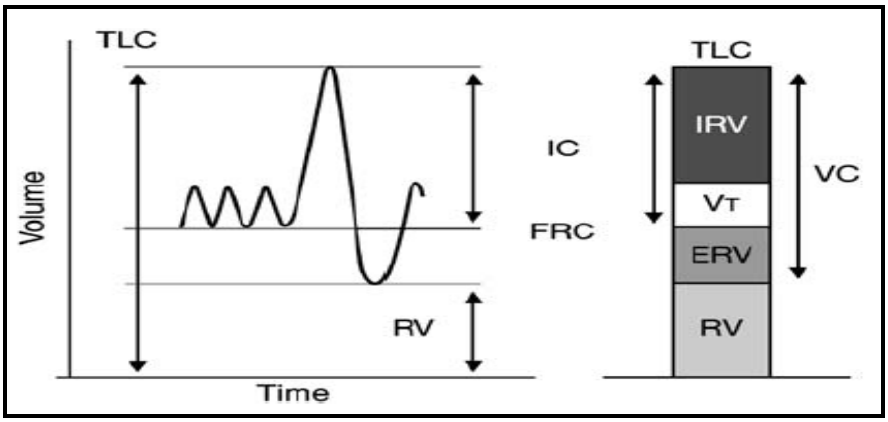


Figure 1.3 Basic lung volumes and capacities. TLC: total lung capacity; IC: inspiratory capacity; FRC: functional residual capacity; RV: residual volume; IRV: inspiratory reserve volume; VT: tidal volume; ERV: expiratory reserve volume; RV: residual volume; VC: vital capacity [33].

1.4.3.2 Impaired gas exchange:

Impaired gas exchange usually occurs in more advanced stages of COPD and is mainly characterized by an uneven distribution of both alveolar ventilation and pulmonary blood flow, known as ventilation-perfusion ratio (V_A/Q) [6, 30, 34]. The destruction of alveoli in COPD reduces entry of oxygen (O_2) into the systemic circulation, and limits carbon dioxide (CO_2) uptake in the alveoli to be expired upon exhalation causing CO_2 trapping in the lungs. This imbalance results in arterial hypoxemia (a decreased partial pressure of O_2 in the blood) with or without hypercapnia (increased levels of CO_2 in the blood) in stable disease and during exacerbation [30, 34].

1.4.3.3 Respiratory and peripheral muscle dysfunction:

In COPD patients, selective wasting of fat-free mass (FFM) coupled with impaired respiratory and peripheral muscle function are common [35]. Wasting generally occurs in COPD as well as other chronic inflammatory diseases and is an important systemic manifestation [35, 36]. The prevalence of tissue depletion (i.e wasting) in COPD patients varies between 20 to 35% and is associated with poor survival [35, 37].

It has also been shown that COPD patients have a higher resting energy expenditure, which is believed to lead to an imbalance of energy intake and expenditure, and thus muscle mass wasting [36]. Possibly as a result of inadequate caloric intake to support the increased metabolic requirements of impaired respiration as well as the burden imposed by frequent infections, there is a breakdown of cell proteins, in particular in the lower muscle extremities, in order to recruit the required amino acids needed for protein synthesis and energy metabolism [35].

1.4.4 Sequela

1.4.4.1 Exercise Intolerance:

Systemic inflammation and skeletal muscle wasting contribute to limiting the exercise capacity in COPD patients [31]. It is of evidence that COPD patients have functional impairment that is attributable to the compromise of respiratory function and to the presence of systemic components [38, 39]. The main pulmonary factors contributing to increased dyspnea and causing exercise limitation is lung hyperinflation. It has been shown that the determination of the exercise level of dyspnea is a better predictor of mortality than the degree of airflow obstruction (FEV_1) [38]. Moreover, the levels of arterial oxygen (O_2) and carbon dioxide (CO_2) have an important influence on COPD patients' exercise capacity. Low levels of arterial O_2 and high levels of CO_2 compromise cardiac function by increasing cardiac load and hyperinflation, which results in increased intra-thoracic pressures and decreased exercise capacity [38].

Skeletal muscle dysfunction has become an important determinant of exercise capacity and a strong predictor of mortality, especially among moderate-to-severe COPD patients [39]. Skeletal muscle dysfunction is characterized by the loss of muscle strength and endurance associated with alteration of muscle fibre-type (I, IIa, IIx) and

leading to decreased oxidative muscle capacity [39]. Moreover, high proportions of COPD patients are inactive and tend to have an inadequate nutrition leading to a significant loss of muscle mass. Physical inactivity has also been shown to induce systemic inflammation mediated by the reduction in the activity of the transcription factor peroxisome proliferator-activated-c coactivator (PGC)-1a, which regulates skeletal muscle morphology and metabolism [38, 39]. These abnormalities, which are associated with loss of muscle strength, are significant determinants of exercise capacity independent of COPD severity [38]. In severe COPD, muscle wasting (protein degradation) has a profound impact on morbidity, hospitalizations, frequency of exacerbations, and mortality [39].

1.4.4.2 Exacerbations:

Exacerbations can be caused by bacterial and viral infections, air pollution, ambient temperature changes and other triggers. It has been hypothesized that during acute exacerbations, a disturbance occurs in the equilibrium between protein breakdown and synthesis [35]. Neutrophilic inflammation and increased number of eosinophils often characterise exacerbations [30]. In mild exacerbations, airflow obstruction is minimally affected. However, in severe exacerbations there is an increased imbalance between ventilation and perfusion due to; airway inflammation, edema, mucous hypersecretion and bronchoconstriction, which lead to pulmonary gas exchange deterioration [30]. Reduced ventilation contributes to hypoxic vasoconstriction of pulmonary arterioles impairing perfusion and subsequently respiratory muscle fatigue [30]. Pulmonary vasoconstriction can result in right ventricle strain, which leads to peripheral edema. Respiratory muscle fatigue contributing to hypoxemia, hypercapnia and respiratory acidosis has been linked to respiratory failure and even death [30].

1.4.4.3 Comorbidities:

The systemic inflammation caused by cigarette smoke may contribute to the development of comorbidities such as cardiovascular diseases, metabolic disorders and some cancers [40]. It has been shown that COPD increases the risk for other diseases because of its extrapulmonary effects leading to weight loss, skeletal muscle dysfunction and malnutrition [6]. Thus, patients with COPD are at higher risk of developing the following; hypertension, diabetes, heart failure, ischaemic heart disease, cancer, osteoporosis, depression and anemia [6, 40]. However, it is difficult to determine whether these comorbidities were coexistent or whether they are a causal association with COPD [40]. COPD patients are believed to often die from other reasons than respiratory failure and it is therefore important to evaluate COPD comorbidities when considering adequate and successful management of the disease [6, 40].

1.4.4.4 Anxiety and Depression:

COPD does not only affect pulmonary function of patients, but it also has an impact on their cognitive functions, which often translate into anxiety and depression disorders [41, 42]. These disorders are markedly enhanced in COPD patients compared to the general population, where the prevalence of anxiety and depression are 33% and 50% respectively [41]. The pathogenesis of these disorders is unclear and the onset can occur at any time in the life of COPD patients [41, 42]. Symptoms related to anxiety and depression are shown to worsen dyspnea, reduce tolerance and compliance to exercise, increase emotional instability, which in turn all lead to increased exacerbations and hospitalizations [41]. A lack of comprehension related to the illness, difficulties adjusting and accepting the illness with its limitations, solitude, and fear of missing air can all lead to anxiety and depression. Therefore, patients affected by COPD should have

psychological support, education and medication if necessary to manage the cognitive sequela caused by this disease [41, 42].

1.5- COPD Assessment and Evaluation

1.5.1 Screening, Diagnosis

Patients with a smoking history presenting with respiratory complaints such as dyspnea, chronic cough or sputum production, and exposure to other COPD risk factors should be screened and evaluated for the presence of obstructive lung disease [6].

Spirometry is recognized as the gold standard for diagnosis and monitoring of COPD [6]. It is necessary to undertake spirometry not only to screen COPD, but also to exclude any other possible diagnosis with similar symptoms [6]. Spirometry should measure FVC, FEV_1, which permits the calculation of the ratio of these measures (FEV_1/FVC) [6]. Since the ratio FEV1/FVC declines with age and in order to avoid over-diagnosis of COPD in the older population, it is important to evaluate spirometry results by comparing them to appropriate reference values based on age, sex, height, and race [6]. However, in order for a true diagnosis to be made, this screening should be performed post-bronchodilator [6]. In fact, the presence of COPD is defined by a post-bronchodilator FEV_1/FVC less than 0.70 [6]. COPD patients have decreased FEV1 and FVC values and the severity of the disease is generally reflected by the degree of flow rate abnormality [6]. Table 1.1 shows the classifications of COPD severity.

Table 1.1 Spirometry classifications of COPD

Stage	FEV_1/FVC	Post-Bronchodilator FEV_1
Stage I: Mild	< 0.70	≥ 80% predicted
Stage II: Moderate	< 0.70	50% to 79% predicted
Stage III: Severe	< 0.70	30% to 49% predicted
Stage IV: Very severe	< 0.70	<30% or <50% plus respiratory failure

Severity based on post-bronchodilator FEV_1. FEV_1: forced expiratory volume in one second; FVC: forced vital capacity. Adapted from GOLD [6].

Pulmonary function tests (PFTs), such as the measurements of flow volume loops, diffusing capacity (D_{LCO}), inspiratory capacity, lung volumes, are not considered routine evaluations [6]. However, these tests are valuable tools to resolve diagnostic uncertainties or to determine patient's condition prior to surgery to assess the risk of complications [6]. More importantly, PFTs reveal the presence of hyperinflation in support of COPD diagnosis.

In addition, the presence of various findings such as hyperinflation, lung hyperlucency and rapid narrowing of the vasculature on chest X-ray (CXR) are important in COPD diagnosis and in detecting the presence of other important comorbidities such as heart failure [6]. Computed tomography (CT) scanning is often used to detect the distribution of bullous emphysema in the lung volume reduction surgery is anticipated [6].

Of great importance is the lack of screening for the disease in patients with a smoking history even when respiratory symptoms are present, which sometimes leads to the prescription of medication without proper disease evaluation and staging. This lack of diagnosis also leads to absence of proper treatment strategies until later stages of the illness. Part of this occurs due to a lack of easily available access to pulmonary function

testing and respiratory specialists. Another problem regarding COPD diagnosis is the misclassification of spirometry results, which are often related to poor coaching, inaccurate spirometer, or inappropriate interpretation of PFTs by primary physicians [43]. Prescription of inhaled medications may help alleviate occasional symptoms, but doing so in the absence of a true diagnosis is not standard of care.

1.5.2 COPD Evaluation: Exercise Testing

Cardiopulmonary exercise testing (CPET) is widely used in COPD for the evaluation of functional capacity and assessment of exercise tolerance and exertional dyspnea, which are the two most important outcomes in COPD patients [44, 45]. CPET typically includes measure of oxygen uptake (VO2), carbon dioxide output (VCO2), minute ventilation (VT) and monitoring of electrocardiography, blood pressure, heart rate, and oxygen saturation [44].

There are various protocols that can be used for exercise testing and they are mainly conducted on a treadmill or a cycle ergometer [44]. Tests conducted on a treadmill permit patients to use larger muscle mass as compared to cycle ergometry, which is revealed through maximal oxygen consumption (VO_2) measurements [46]. However, the cycle ergometer is more cost efficient, requires less space, and puts less physical stress on patients with chronic illnesses [19]. Protocols can be classified as maximal or submaximal, incremental or constant loads, and self-paced or externally-paced [47]. Maximal exercise tests aim to measure maximal oxygen consumption ($VO_{2\,max}$). However, reaching a true physiological maximum, which is challenging for healthy individuals, is almost impossible for COPD patients [48]. Thus, for patients with chronic diseases, symptom-limited or sub-maximal exercise tests (which are stopped at a pre-determined endpoint) are often used [47]. Incremental exercise tests involve a

progressive increase in work rate over time (e.g. maximal incremental cycle ergometry and maximal incremental treadmill), whereas constant-load exercise tests consist of patients exercising at a fixed workload which is mainly determined by a certain percentage of their peak capacity (e.g. endurance shuttle walk test (ESWT) and constant work rate cycling) [47]. A self-paced protocol permits patients to choose their own intensity of exercise and allow them to stop and rest during the test (e.g. 6 minute walking test (6MWT)) [46]. On the other hand, an externally paced exercise test imposes the workload on patients (e.g. ESWT) [46].

The maximal incremental cycle ergometry protocol is the most widely used exercise test in clinical practice [44, 45]. Since work rate is progressively increased during this test, it enables rapid achievement of diagnosis [44]. When considering constant-load tests, the ESWT has become well recognized, since it has shown to be highly responsive to treatment in COPD patients [44]. It has also been shown that ESWT was more likely to detect changes in COPD functional status post-bronchodilator than constant work rate cycling or 6MWT [49]. Since exercise tests do not exhibit the same responsiveness to treatment in COPD patients, it is hard to determine which protocol is best suited to evaluate functional capacity in this patient population [47, 50, 51].

Various factors can affect results obtained from exercise tests such as changes in patient's clinical status, symptoms, and medication(s), which are often seen in progressive diseases (e.g. COPD) [44]. Moreover, instructions, patient motivation, test procedures, equipment calibration errors and time of test conduction can affect the variability of the exercise test values [44]. Thus it is important to control for all these factors in order to minimize inconsistency of results [44].

1.6 Management:

Although there is no cure for COPD, early detection and management are necessary in order to slow the progression of the disease and to improve symptom management [6]. Once a diagnosis is made, there are a number of secondary preventive measures that are important to slow progression of the disease (Figure 1.4). Patients with COPD should ideally be managed in an interdisciplinary environment. Interventions should include; smoking cessation, medication optimization, education and self-management, pulmonary rehabilitation, oxygen therapy and in very rare cases surgery [3].

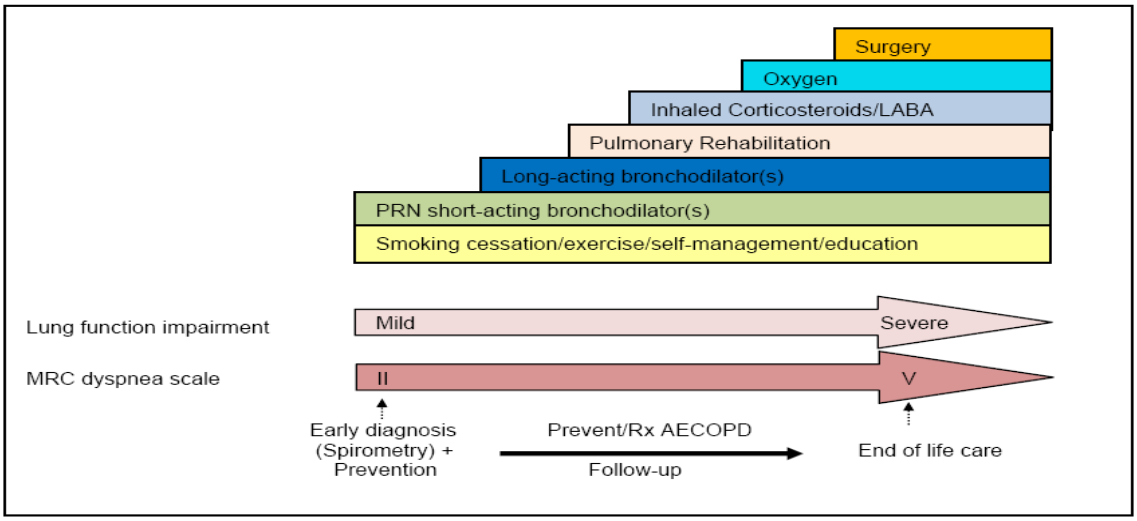


Figure 1.4 A comprehensive approach to the management of chronic obstructive pulmonary disease (COPD). AECOPD Acute exacerbation of COPD; LABA Long-acting beta2-agonist; MRC Medical Research Council; PRN As needed; Rx Treatment [3]

1.6.1 Reducing Risk Factors

Identifying, reducing and controlling COPD risk factors are important steps for the development of adequate prevention and treatment strategies [6]. These factors include cigarette smoking, occupational exposures, and indoor and outdoor air pollutants [6]. Since cigarette smoking is responsible for 80% of COPD cases, it should be regarded as primary and specific intervention [7]. It is of importance to evaluate smoking routinely

and to aid in smoking prevention and cessation at all levels of the disease [6, 7]. In fact, it has been shown that smoking cessation is the single most cost effective approach to prevent or delay airflow limitation progression linked to COPD [3, 6]. Interventions to prevent smoking are effective in both sexes, in all races, and at all ages [6], however a successful smoking cessation strategy requires a multifaceted approach. This highlights the importance for health professionals to offer counselling, support and education to COPD patients throughout the process [6]. In order to reduce exposures to fumes, mineral and biological dusts in the workplace, it is important to implement a legally mandated air control and to educate employees and employers about occupational lung disease in order to encourage reduction of their exposure to these various airborne substances [6]. Individuals exposed to diverse indoor and outdoor environment air pollution should reduce their risk by monitoring public announcements of outdoor air quality and by using adequate ventilation when cooking or heating with various solid fuels [6].

1.6.2 Pharmacologic Treatment

Pharmacotherapy is used in COPD patients to prevent and control symptoms, to reduce the frequency and severity of exacerbations, and to improve health status and exercise capacity [6]. Pharmacotherapy is optimal when prescribed on an individual basis and by assessing level of COPD severity and frequency of exacerbations [7].

Bronchodilators represent the fundamental pharmacological treatment for the symptomatic management of COPD [6, 7]. They improve expiratory flow rates and decrease hyperinflation by relaxing the airway smooth muscle [6, 7]. There are three common types of bronchodilators, which include β_2-agonists, anticholinergics, and methylxanthines [3, 6]. Bronchodilators can have a rapid or a slow onset. Short-acting

bronchodilators, such as β_2-agonists (e.g. salbutamol) and anticholinergics (e.g. ipratropium bromide) act quickly and are often used as needed, to help relieve dyspnea, increase pulmonary function and exercise capacity in COPD patients [3, 6]. Long-acting bronchodilators (e.g. salmeterol and tiotropium) take longer to act and are shown to be more effective and convenient than short-acting bronchodilators. Side effects associated with bronchodilators include tachycardia, irregular heartbeat, irritability, insomnia, and tremor [3, 6]. Moreover, methylxanthines (e.g. xanthenes and theophyllines), which are slow-onset bronchodilators administered orally, are shown to be less effective than other bronchodilators [6]. Methylxanthines interact with other drugs and are associated with some serious side effects, such as atrial and ventricular arrhythmias and grand mal convulsions [6].

Inhaled and oral corticosteroids are also administered in patients with COPD [6]. Regular treatment with inhaled corticosteroids (ICSs) remains debatable due to its controversial effects regarding lung function, airway inflammation, and frequency of exacerbations [3, 6]. Side effects include ecchymosis, dysphonia, oral candidiasis, cataracts, glaucoma, pneumonia, and a decrease in bone density [3]. Oral corticosteroids can also be prescribed for a short or long periods of time, but there is insufficient evidence of their benefits [3]. Side effects related to oral corticosteroids include muscle weakness, decreased functionality and respiratory failure in advanced COPD [6]. However, combination inhaled corticosteroid/bronchodilator therapy has been shown to be effective in the reduction of exacerbations and in the improvement of pulmonary function and health-status [6].

Influenza vaccines can reduce about 50% of morbidity and mortality in COPD patients and decreases up to 39% of hospitalizations [3, 6]. Vaccines contain killed or live inactive viruses and are usually administered every year [6]. Pneumococal

polysaccharide vaccine is usually administered every 5 to 10 years and is recommended in older patients affected by COPD, since it is shown to decrease pneumonia incidence [3, 6].

Pharmacological treatments do not appear to decrease the rate of decline in lung function in COPD patients and their effect on exercise capacity, peripheral muscle function and quality of life remain modest [2, 3, 7, 52]

1.6.3 Education and self-management

Educating patients and their families about disease specific self-management is important to optimize COPD management [3]. COPD education should preferentially be done individually and should be specific to each patient's disease severity [3]. Integrating self-management as part of the overall management of COPD has been shown to decrease hospital visits. The goal of self-management is to increase patients' skills required to carry out medical procedures specific to their illness, to improve patients' confidence in their ability to follow a self-care regimen, to encourage behavioural change, and to offer patients moral support to control their disease and to have a better health-related quality of life [53, 54]. COPD patients have perceived barriers and factors, which will hinder or facilitate lifestyle modification [54]. Thus, it has been shown that a continuum self-management program promotes self-health behaviours in COPD patients, which reduces use of hospital services [53, 54]. In order for self-management to be successful, a multifaceted approach needs to consist of disease education and implementation of strategies for behavioural change in patients [54].

1.6.4 Exacerbation management

According to the Canadian Thoracic Society recommendations, exacerbations in COPD are defined as 'sustained worsening of dyspnea, cough or sputum production leading to an increase in the use of maintenance medications and/or supplementation with additional medication' [3]. COPD exacerbations worsen disease progression, increase cost and hospitalizations, decrease health-related quality of life and enhance mortality [3, 13]. Exacerbations can also cause tachycardia and tachypnea,insomnia, depression and confusion [6]. It is therefore important to manage and prevent exacerbations in the optimal care of COPD patients [3, 13]. During exacerbations, bacteria have been shown to be present in high concentrations in the lower airway of at least 50% of COPD patients. However, exacerbations can also be caused by viral infections, allergens or irritants, congestive heart failure, and/or pulmonary embolism [3, 6]. Exacerbations can be categorized into simple or complicated based on the presence of risk factors that increase the chances of treatment failure [3].

Management of exacerbations requires a careful medical history, physical examination and laboratory investigation (e.g. arterial blood gas) [3]. To improve functional capacity and to decrease dyspnea during exacerbations, an increase in the dose and/or frequency of short-term acting bronchodilator therapy is often prescribed and is sometimes combined with another bronchodilator or anticholinergic [3]. Oral or inhaled corticosteroids (i.e. prednisone) are often prescribed in acute COPD exacerbations to improve lung function and hypoxemia [6]. Corticosteroids are shown to shorten recovery time, reduce risk of early relapse and treatment failure [3, 6]. Antibiotics are administered when COPD patients experience increase in 2 of the following symptoms; dyspnea, sputum volume, sputum purulence [3, 6].

1.6.5 Oxygen Therapy

Oxygen therapy (OT) is shown to increase survival, improve exercise capacity, and enhance sleep quality and cognitive performance [6, 7]. OT is generally introduced in COPD patients with stage IV severity level and is usually determined by arterial blood gas assessment, which includes acid base information [6, 7]. Arterial oxygen saturation (SpO_2), measured by pulse oximetry, is also a good screening tool [7]. Thus, oxygen therapy is usually prescribed when arterial oxygen pressure (PaO2) is less than 55 mmHg [7]. The primary goal of OT is to increase PaO2 to 60 mmHg at rest and to ensure SpO2 of a minimum of 90% to ensure adequate oxygen delivery to the vital organs [6, 7]. Long-term oxygen therapy (LTOT) should be based on PaO2 values at the patient's waking. If OT is prescribed during exacerbation, reassessment should be done in the following 30 to 90 days [7]. Some COPD patients only require OT during activity. Whatever the patient's need is, OT prescription should include source of supplemental O_2, method, duration, and flow rate at rest, during exercise and during sleep [6]. The combination of LTOT and ventilatory support can also be prescribed in selected patients with prominent day hypercapnia [6].

1.6.6 Surgical Treatment

Surgical treatments in COPD include bullectomy, lung volume reduction surgery, and lung transplantation [6, 7]. Although, COPD patients have increased risk for postoperative pulmonary complications, surgery is not absolutely contraindicated in this patient population [6, 7]. Surgery should be carefully considered and should be based on pre-operative thorough evaluations of pulmonary function tests [7]. In general, the further the surgery procedure is from the diaphragm, the lower the rate of pulmonary complications [7].

Bullectomy can be performed thoracoscopically and consists of removing large bulla to decompress lung parenchyma and alleviate infection or chest pain [6]. Prior to resection of the bulla, it is important to determine its effect on the lung and to evaluate a thoracic CT scan, arterial blood gas measurements and respiratory function tests [6]. Lung volume reduction surgery (LVRS) involves the resection of some parts of the lung to decrease hyperinflation, improve mechanical efficiency of respiratory muscles, increase lung elastic recoil and thus improve expiratory flow rates [6]. LVRS is expensive and should be carefully recommended. Lung transplantation is not only an expensive procedure, but it is also limited due to a lack of donor organs [6]. Many complications are associated with this procedure such as surgery death, acute transplant rejection, bronchiolitis obliterans, fungal and bacterial infections, lymphoproliferative disease, and lymphomas [6].

Although risk is involved with surgery, all aforementioned surgeries aim to improve SpO_2 values, lung volumes, exercise capacity, dyspnea, health-quality of life and survival in appropriately selected COPD patients [7].

1.6.7 Pulmonary Rehabilitation

The benefits attained with Pulmonary Rehabilitation (PR) are significantly greater compared to those obtained with pharmacological treatments [2, 52]. PR has become widely recognized as the best available intervention to impact on the systemic consequences related to COPD [52, 55, 56]. It combines exercise training, patient education, and psychosocial support [57]. These various strategies are integrated into the long-term management of COPD and require a dynamic collaboration among the patient, his/her family and health professionals [56]. The main goals of PR are to increase exercise tolerance, reduce COPD symptoms, improve health-related quality of

life (HRQL), and decrease the economic burden linked to this disease [57]. A meta-analysis of 23 randomized controlled trials, comparing the effects of PR to standard care in patients with COPD, has shown that PR significantly improves HRQL and exercise tolerance and decreases dyspnea compared with conventional care [52, 58]. Studies have also shown the role of PR on psychological benefits in COPD patients, such as improved self-esteem and increased well-being which can contribute to fewer hospital admissions and thus decrease the economic and social burdens related to COPD [3, 59, 60]. Although all components of PR contribute to patient's health, exercise conditioning is considered the key component [2, 3].

1.7- Exercise Training in Pulmonary Rehabilitation

1.7.1 Benefits of Exercise Training in COPD

Although all components of PR contribute to the patient's overall health, exercise conditioning is considered a key component to a successful PR program in COPD [59]. Exercise training has been shown to be responsible for many of the health benefits of PR, such as increased exercise capacity, decreased exertional dyspnea [61], and improved activities of daily living [59, 62].

The main factors limiting exercise capacity in COPD patients are dyspnea and skeletal muscle dysfunction [57, 63, 64]. In this patient population, the ventilatory requirement (or V_E) of any given task is increased compared to healthy individuals due to increased dead space and impaired gas exchange, while ventilatory capacity is reduced because of mechanical constraints inflicted by the lung's pathophysiology [56]. As such, COPD patients often exhaust their ventilatory reserve during incremental exercise and reach a ventilatory limitation, a phenomenon not typically seen in healthy individuals. Furthermore, peripheral muscle dysfunction, muscle wasting and weakness,

typical of COPD patients, all contribute to decreased aerobic capacity and poor muscle endurance [56, 57].

Exercise training has been shown to reduce minute ventilation for any given physical effort [65], to decrease the sensation of dyspnea [61, 64], and to improve peripheral and respiratory muscle strength [66] as well as oxidative capacity [59, 62]. These physiological mechanisms mediated by exercise training lead to improved maximal oxygen consumption (VO_2max), peak work rate, and endurance time to constant-load exercise in this population [66, 67]. It has also been shown that exercise training has a positive effect on motivation, mood, self-esteem, and general well-being [56, 60]. There is also evidence that exercise has a positive acute effect on cognitive performance in COPD patients [68]. These benefits have a great impact on the daily lives of COPD patients' by increasing their ability to perform normal routine tasks and recreational activities [67]. Although physical exercise is a main component of PR and is greatly beneficial, there is an ongoing debate about the type and intensity of exercise that should be prescribed to COPD patients (Table 1.2) [62, 69].

1.7.2 Intensity and Types of Training

1.7.2.1 High-Intensity Exercise:

Current guidelines recommend high-intensity exercise, which was shown to elicit greater physiological adaptation as compared to low-intensity exercise in COPD patients [65]. However, the evidence favouring high-intensity over moderate- or low-intensity training in this patient population is limited. In fact, the guideline encouraging high-intensity training is based on one small (n=19) randomized clinical trial, in which the physiological adaptation to a high training work rate (≈ 80% of peak work rate) was compared to that of a low training work rate (≈ 50% of peak work rate) [65]. At the end of

the program (week 8), the high-intensity exercise was shown to elicit a greater physiological training response (decreased lactate levels and minute ventilation for a given work rate) and higher exercise tolerance and was therefore considered optimal [65]. Moreover, although some studies have shown that high-intensity training can be tolerated by patients with moderate to severe COPD [70, 71], a major concern remains with the ability for patients to remain compliant to this type of intensity [52, 69, 72]. A study by Maltais et al., consisting of a 12-week exercise program, has shown that high-intensity training was only achieved by 0, 3, 5 and 5 patients out of 42 at weeks 2, 4, 10, and 12 respectively [69]. In light of this potential compliance issue related to continuous high-intensity training, other approaches to exercise training have been proposed.

1.7.2.2 Exercise at the Ventilatory Threshold:

The ventilatory threshold is described as the breakpoint during progressive exercise above which minute ventilation increases disproportionately to increments in oxygen consumption [73]. The ventilatory threshold differs for each person and therefore needs to be determined individually with an incremental exercise test. Exercising at the ventilatory threshold is associated with tolerable levels of ventilation and dyspnea, which represent two of the main exercise limiting factors in patients with COPD [73, 74]. The efficacy of training at the ventilatory threshold versus training at a standardized moderate intensity (50% of heart rate reserve) has been studied in 24 patients with moderate COPD [73]. Although the mean training intensity was similar for both groups, training at the ventilatory threshold led to better physiological responses (greater reductions in lactate levels, CO_2 excretion, and minute ventilation for a given workload) than training at 50% of heart rate reserve [73]. This training approach has also been shown to improve peripheral muscle strength and endurance [75]. However, no study

has yet compared the short-term compliance of training at the ventilatory threshold versus training at 80% of peak work rate.

1.7.2.3 Interval Training:

Interval training (IT) has recently been established as an alternative modality to continuous training in PR [55] and consists of alternating bouts of maximal or high-intensity exercise with short periods of rest or active recovery [56, 64, 72, 76, 77]. Interval exercise is most consistent with patterns of activities of daily living in severe COPD patients [55].

The physiological responses to a single IT session were compared to those of continuous training at the same absolute workload (70% of peak workload) in 10 patients with moderate COPD [72]. In this study, IT, which consisted of 1 minute of exercise interspersed with 1 minute of rest, has shown to induced lower levels of ventilation, lung hyperinflation and dyspnea when compared to continuous training and enabled subjects to perform a greater total amount of work [72]. In a randomized non-inferiority trial conducted by Puhan and colleagues [78], which included 98 patients with severe COPD, showed that interval exercise is as beneficial as high-intensity continuous exercise in improving HRQL and exercise capacity. Furthermore, Vogiatzis et al. [77] have demonstrated that high intensity interval training and moderate intensity constant-load exercise caused similar peripheral muscle adaptation (increased oxidative capacity, increased lactate threshold), however interval training was associated with lower dyspnea and leg discomfort levels in COPD patients. Finally, Coppoolse and colleagues [55] compared continuous training with a mixed programme of interval and continuous training and found that peak workload increased only with mixed training while improvement in peak oxygen uptake was observed only with continuous training.

Although, various studies have shown controversial findings, interval training is still considered an adequate alternative for patients who are unable to achieve the prescribed exercise time or intensity [56].

Table 1.2 Overview of studies

Study	Population	Exercise Training	Outcomes
Sabapathy[72]	10 moderate COPD patients	IT: cycling at 70% of P_{peak} (1 min) and rest (1min) (total duration 60min); CT: cycling at 70% P_{peak} (total duration 30min)	IT: ↓ lower levels of ventilation, ↓ lung hyperinflation and ↓ dyspnea and ↑ total amount of work
Puhan[78]	98 severe COPD patients	IT: cycling at 90% of P_{peak} (1min) and 45% of P_{peak} (2min) 3 days/week; CT: cycling at 60% P_{peak} 2 days/week	IT and CTsimilarly ↑HRQL and ↑ exercise capacity
Vogiatzis[77]	19 severe COPD patients	IT: cycling at 100% P_{peak} (30sec) and 45% P_{peak} (30sec) weeks 1-3; at 120% weeks 4-6 and 140% weeks 7-10; CT: Cycling at 60% P_{peak} weeks 1-3 at 70% P_{peak} weeks 4-6 and at 80% weeks 7-10	High intensity IT and CT: ↑ oxidative capacity, ↑ lactate threshold; IT: ↓dyspnea, ↓ leg discomfort levels
Coppoolse[55]	21 severe COPD patients	IT: cycling at 90% of P_{peak} (1min) and 45% of P_{peak} (2min) 3 days/week plus continuous cycling at 60% P_{peak} 2 days/week; CT: cycling at 60% of P_{peak}	Mixed training (IT + CT): ↑ peak workload; CT: ↑peak oxygen uptake

COPD: Chronic Obstructive Pulmonary Disease; IT: Interval training; CT: Continuous training; Ppeak: peak exercise capacity.

1.7.3 What is the Optimal Exercise Prescription?

To date, no controlled study has yet been designed to define optimal duration or frequency of training sessions in PR. Current guidelines regarding session duration are based on evidence obtained in healthy individuals [79], while recommendations for

frequency of training sessions stem from clinical trials of PR versus usual care that were not designed to determine optimal training dose [80, 81]. Thus, the optimal exercise prescription (training mode, intensity, and duration) remains undetermined for patients with COPD, which explains the ambiguity of current guidelines for exercise training in PR. In their 2006 statement on PR [56], the American Thoracic Society and European Thoracic Society made the following recommendations with regards to the exercise dose: "*A minimum of 20 sessions should be given at least three times per week to achieve physiologic benefits; twice-weekly supervised plus one unsupervised home session may also be acceptable. High-intensity exercise produces greater physiologic benefits and should be encouraged; however, low-intensity training is also effective for those patients who cannot achieve this level of intensity. […] The total effective training time should ideally exceed 30 minutes. However, for some patients, it may be difficult to achieve this target training time or intensity, even with close supervision. In this situation, interval training may be a reasonable alternative*". In summary, current guidelines for PR suggest high-intensity exercise training to elicit greater physiological benefit. However, compliance to this type of training has been problematic for COPD patients. Thus, alternative approaches (i.e. ventilatory threshold and interval training) have been proposed as more tolerable, and possibly easier to comply with, but the compliance to these different exercise-training approaches has yet to be examined in COPD patients.

1.8- Compliance to Exercise Training

1.8.1 Definition of compliance

Compliance was first defined by Haynes et al. [82-84] in 1979 as "the extent to which a person's behaviour (in terms of taking medications, following diets, or executing lifestyle changes) coincides with medical or health advice". The term 'compliance' is

exclusive to the conformity of medical goals [85] and is often interpreted as an authoritarian word, suggesting patients' obedience to instructions given by health care professionals [83, 85]. Because of its dictator tone, the term 'compliance' began to be interchangeably used with the term 'adherence' [83]. 'Adherence' characterizes patients as independent and autonomous individuals who voluntarily pursue their goals to follow their medical treatment [85]. The popularity of this term increased with modern era, where patients' rights not to follow medical advice were acknowledged and practitioners' attention to patients' decision-making processes related to their health was recognized [82, 83, 85]. Thus, it is clear that some critical differences between the terms 'compliance' and 'adherence' are present [85]. Hence, for the purpose of this study, we will solely use the term 'compliance'.

1.8.2 Factors affecting Exercise Compliance

Despite the increased knowledge and proven benefits of exercise training, only about 15% of Canadian adults meet the new physical activity guidelines [86, 87]. To achieve health benefits, the World Health Organization and Canadian guidelines recommend that adults accumulate a minimum of 150 minutes of moderate-to high-intensity aerobic exercise per week [87]. In Canada, the proportion of adults over 65 years of age is growing rapidly and represents the most sedentary portion of the population [86]. Research suggests that 49% of older adults who enrol in community exercise programs will drop out within one-year of starting the program [86]. Hence, the importance for health professionals to be aware of and to understand the various variables influencing the initial adoption and long-term maintenance of exercise training patterns [88]. In fact, factors such as behavioral, personal, environmental, program-

related, and self-efficacy elements need to be taken into consideration when looking at exercise compliance rates and success of therapeutic regimens [88].

1.8.2.1 Behavioural factors :

Behavioural factors, such as behavioural shaping, goal setting, enjoyment, intrinsic and extrinsic reinforcement, social support, behavioural success, self-monitoring, and self-management, are considered important when eliciting initial adoption of exercise. Gradual shaping or progression of the exercise-training program towards the individual's goal is a key consideration [88]. Shaping behavioural success is influenced by realistic goal settings and based on principles that are specific, measurable, realistic, and time specific [88]. Thus, individuals are more likely to successfully achieve their goals if they are realistic and motivationally challenging [88]. Moreover, the individual's motivation to continue exercise training and adopt a healthy lifestyle depends on the rewards and the degree of enjoyment coming from the new behaviour [88]. Enjoyment and perceived improvement of any activity play a significant role for patients PR maintenance [89]. On the other hand, longer periods of inactivity are negatively associated to intrinsic reinforcements [88]. In fact, the more unfit the individual is or becomes, the more time it will take before any exercise training becomes reinforced (e.g. feels good to exercise) [88]. It is therefore important for patients to receive extrinsic rewards (motivation, encouragement) and social support (e.g. from health professionals and family members) to help ensure their behavioural change success and their compliance to exercise [88, 89]. Other ways of establishing behavioural success include: monitoring attendance and adherence, engagement and performance in exercise training programs, and integration of exercise habits [88]. In addition, behavioural factors incorporate the skills to carry out and comply with physical activity to facilitate health

benefits while avoiding injury or boredom. In summary, patient exercise compliance can be achieved by setting realistic goals, engaging in enjoyable activity, and encouraging and motivating good health behaviours [88].

1.8.2.2 Personal factors :

Personal health factors have been shown to be directly related to levels of physical activity [88]. In fact, older individuals with medical disabilities, such as COPD, have a higher risk of adopting a sedentary lifestyle [88]. Cognitive and experiential variables, such as bad experiences, a low level of enjoyment with physical activity, and degree of self-motivation can all negatively influence exercise initiation and participation [88]. Certain life events such as recurrent exacerbations, admission to hospital, and family health problems [90] can make exercise compliance very challenging. Another key factor affecting patients' willingness to partake in exercise programs is the level of understanding regarding their illnesses and the personal benefits that they could achieve with physical activity [82, 88]. Thus, COPD patients having the internal desire for achievement may increase their readiness to start and pursue exercise regimens [88]. Self-motivation can be achieved when individuals are capable of identifying self-related rewards for their behaviour [88]. Finally, targeting each person's interests and goals, stressing the beneficial outcomes of exercise training, and exploring perceived barriers can all positively influence exercise habits [88].

1.8.2.3 Environmental factors :

Several environmental factors have an impact on the initiation and maintenance of an exercise program, such as proximity and affordability of facilities, time constraints, weather, social (family support), and physical environment (sidewalks, street-lights) [88].

A study conducted in the UK has shown that poor attendance is associated to the distance between the patient's home and PR location and is often related to transportation difficulties [90]. It is, therefore, important to carefully evaluate the proximity of exercise programs in order to minimize the negative factors leading to exercise non-compliance [88].

1.8.2.4 Program-related factors:

Adequate attendance and compliance are necessary to gain benefits from PR programs [90] and it has been shown that the type, intensity, duration, and frequency of the exercise programs are important factors influencing the levels of participation [88]. It is therefore important to consider program-related factors to prevent risks of aversive sensory and physiologic consequences [88] and to reduce their negative effect on exercise compliance.

Compliance to the type of exercise:

In relation to program-related factors, Mador et al. [91] have shown that it is easier for elderly patients with COPD to perform high-intensity training on a cycle ergometer than on a treadmill. In fact, this study revealed that this patient population had a lower compliance rate to high-intensity training on a treadmill when compared to a cycle ergometer, due to the difficulty in maintaining the required speed. Additionally it was shown that there was a higher risk of fall [91]. There is also evidence supporting interval training over continuous training [72], where interval training has been associated with reduced breathlessness, longer periods of exercise, and greater total amount of work in COPD patients [52, 72, 92]. In Puhan et al.'s study, where IT was compared to high-intensity CT, tolerance to the protocol was compared by looking at the number of unintended breaks of ≥ 1 minute and at the proportion of patients achieving the target

intensity, as assessed via continuous data tracking technology [78]. Interval training was found to be associated with significantly fewer unintended breaks and with better compliance to the IT protocol than continuous high-intensity training (48% versus 24%, respectively) [78]. Interval training is believed to lead to an increased compliance to the exercise regimen compared to continuous training [52, 72], hence the importance of prescribing the adequate type of exercise training to specific populations.

Compliance to the intensity of exercise: (high versus low)

When individuals, especially sedentary ones, are initiated to exercise programs that are often too high in intensity, there is an increased chance for non-compliance due to aversive sensory and physiologic consequences [88]. In fact, high-intensity exercise regimens have been associated with decreased exercise compliance rates, since this exercise intensity is often linked to increased cardiovascular and orthopedic problems in elderly patients [79, 88]. Moreover, although high-intensity (80% of peak work rate) exercise regimens are shown to be feasible in some COPD patients [65], the majority of moderate to severe COPD patients can hardly tolerate this exercise intensity [56, 69].

Compliance to the duration and frequency of sessions:

Several studies have compared exercise compliance rates in COPD patients between a short-term (3 or 6 weeks) and a long-term (18 weeks) exercise rehabilitation program [90, 93]. A study comparing short and long-term effects of outpatient rehabilitation has shown that 31% of participants have dropped out of the study by 6-months and that this drop-out rate increased to 36% by 18-months of the program [66]. Another study has shown that mean exercise frequency is greatest in the early weeks of rehabilitation programs and decreased linearly throughout a 12 month home-walking exercise prescription in COPD patients [94]. These findings were similar to that of Soicher et al. who found a decrease in adherence to physical exercise following PR [95].

In fact, at 1 and 12 months following completion of PR, patients' adherence rate to endurance training was 61% and 46% respectively [95]. These studies have shown that mean attendance tended to be higher in short-term compared to long-term programs [90, 93]. This may be explained by the patients' loss of motivation, failure to develop a group identity and increasing likelihood to develop exacerbations and hospitalization over time when attending longer duration PR programs [90, 94]. Supervision is however vital as the duration (expressed in minutes) of activity is shown to increase with time in patients that are supervised during their exercise sessions and decrease in those who exercise without supervision [94].

1.8.2.5 Self-Efficacy :

In 1970s, Bandura developed the Social Cognitive Theory (SCT), which is also known as the Social Learning Theory [96]. This theory states that behaviour change is influenced by complex interactions between the individual, the environment, and the behaviour [97]. One of the main components of Bandura's SCT is self-efficacy [98]. The SCT construct of self-efficacy explains how individual perceptions of ability affect behaviour, level of motivation, thoughts, and emotional reactions [99]. Self-Efficacy investigates an individual's emotional function and coping skills required to deal with a particular situation [100, 101]. Self efficacy is developed from four primary experiences: performance accomplishments (achieving mastery over a task through personal experience), verbal persuasion (using strong verbal encouragement regarding the behaviour benefits and individual's progress), social modelling (observing success of others), and emotional arousal (reassuring individual's response to the effects of the behaviour) [99, 102].

COPD results in dyspnea and patients develop a lack of confidence in their capacity to perform certain tasks, which leads to decreased activity of daily living and quality of life [101]. Some of the important aims of PR are to increase confidence, improve physical capacity, and enhance self-management ability in patients suffering from COPD [100]. Self-efficacy has been shown to be a determinant of exercise adherence and it has been identified as being a fundamental aspect in patients' ability to manage their own disease [97, 100]. This highlights the importance of focusing on self-efficacy in the treatment of COPD [100]. A recent study by Bentsen et al. [101], has shown that higher levels of self-efficacy in COPD patients at baseline is a good predictor of increased health status and quality of life, and improved psychosocial function after completion of PR. Moreover, it has been shown that increasing self-efficacy positively influences health behaviors, which in turn impacts the effects of PR on clinical and functional outcomes [97, 100]. In fact, higher self-efficacy levels have been related to PR completion and success, and exercise compliance and maintenance [97, 100-102]. It has also been shown that participation in a PR program could in turn enhance self-efficacy levels regarding self-management and control of dyspnea in COPD patients [102]. Studies have shown that multifaceted PR programs have a great impact on patients' self-efficacy by incorporating performance accomplishment, vicarious experiences, verbal persuasion and control of emotional/physical arousal [98, 102]. In addition, increase in compliance with an exercise program was associated with enhanced expectations to perform this type of exercise in the future [98]. Thus, self-efficacy plays an important role in exercise compliance and has the advantage of making specific predictions about the relationships between behaviour and cognitive changes [98].

CHAPTER II

Rational and Clinical Significance

PR is currently considered the best available intervention to impact the systemic consequences of COPD. Current PR guidelines advocate high-intensity exercise training (at ≈ 60-80% of peak work rate) for COPD patients. However, the compliance to this type of training has been problematic in this patient population. Alternative approaches to exercise training in COPD patients, including training at the ventilatory threshold and interval training, have been proposed as more tolerable, less unpleasant, and thus possibly easier to comply with, but this assumption remains to be verified. To our knowledge, no study to date has directly compared these three different exercise-training protocols (high-intensity training, ventilatory threshold training, and interval training) to determine which one, if any, best ensures patient compliance.

The general aim of the present randomized clinical trial [103] was thus to compare patient compliance between these three exercise-training protocols in individuals with COPD. Clinically, this research project will improve our understanding of exercise compliance in COPD and the main role that it plays in the optimization of the benefits derived from a PR program. Given that exercise compliance is essential to the effectiveness of PR and that, without it, no therapeutic goal can be achieved, findings from this study are expected to contribute significantly to future PR clinical practice guidelines [83, 93, 104].

CHAPTER III

Research Objectives and Hypotheses

The purpose of the present study was to compare the 12-week compliance rates to the following three exercise-training protocols: 1) continuous training at high-intensity (CTHI), 2) continuous training at the ventilatory threshold (CTVT), and 3) interval training (IT) in patients with moderate to severe COPD. More specifically, the primary objective of this research was to compare compliance to the three training protocols by measuring the attendance rate and the compliance rate to the prescribed intensity during the 12-week program. The secondary objective was to examine the relationship between exercise compliance and baseline self-efficacy scores in patients with COPD.

The research hypotheses were as follows: 1) patient compliance will be highest in the CTVT group, followed respectively by the IT group and the CTHI group; and 2) a significant direct relationship will be found between compliance rates and baseline self-efficacy scores.

CHAPTER IV

Compliance to Different Exercise-Training Protocols in Individuals with Chronic Obstructive Pulmonary Disease: A Randomized Controlled Trial

Primary Author

Rima Wardini, B.Sc., rimawardini@gmail.com

Co-Authors

Amanda K. Rizk, ak_rizk@gmail.com

Emilie Chan-Thim, e.chanthim@gmail.com

Barbara Trutschnigg,b.trutsc@gmail.com

Amélie Forget, amelie.forget@umontreal.ca

Grégory Moullec, gregory.moullec@crhsc.rtss.qc.ca

Véronique Pepin, v-pepin@crhsc.rtss.qc.ca

Institution

Axe de recherche en maladies chroniques, Hôpital du Sacré-Coeur de Montréal

Rima Wardini, B.Sc. (Kinesiology) Hôpital du Sacré-Coeur de Montréal, master's student, Department of Exercise Science, Concordia University.

Amanda K. Rizk, M.Sc. (Kinesiology) Montreal Behavioural Medicine Centre, Hôpital du Sacré-Coeur de Montréal, PhD student, Department of Exercise Science, Concordia University.

Emilie Chan-Thim, M.Sc. (Kinesiology) Hôpital du Sacré-Coeur de Montréal, PhD student, Department of Exercise Science, Concordia University.

Barbara Trutschnigg, M.Sc. (Kinesiology) Hôpital du Sacré-Coeur de Montréal.

Amélie Forget, (Research assistant) Hôpital du Sacré-Coeur de Montréal

Grégory Moullec, Ph.D. (Health Psychology) Hôpital du Sacré-Coeur de Montréal.

Véronique Pepin, Ph.D. (Kinesiology), Montreal Behavioural Medicine Centre, Hôpital du Sacré-Coeur de Montréal, Assistant Professor, Department of Exercise Science, Concordia University.

ABSTRACT

Rationale: Current guidelines for pulmonary rehabilitation suggest high-intensity exercise training for patients with chronic obstructive pulmonary disease (COPD). However, compliance to this type of training is problematic. Alternative approaches, such as training at the ventilatory threshold and interval training, have been proposed as easier to comply with. The objectives of this study were to: 1) compare patient compliance to three exercise-training protocols: continuous training at high-intensity (CTHI), continuous training at the ventilatory threshold (CTVT), and interval training (IT); 2) determine if a relationship exists between exercise compliance and baseline self-efficacy in COPD patients. **Methods:** Subjects were randomly assigned to one of the protocols and trained on a cycle ergometer three times per week for 12 weeks. Compliance to the training protocol was measured by attendance and compliance rates to the prescribed intensity. Compliance data were obtained through data tracking technology allowing second-by-second recording of exercise-training sessions. Self-efficacy was measured using the Self-Efficacy Scale. **Results:** Thirty-six subjects with moderate to severe COPD participated in the study. Attendance rates did not differ significantly between groups (Mean $\pm$ SD: 70 $\pm$ 33% for CTHI, 82 $\pm$ 17% for CTVT, 63 $\pm$ 35% for IT, p= 0.229). Mean compliance rates were 85.6 ± 15.0 % for CTHI, 84.1 ± 15.1 % for CTVT, and 52.0 ± 41.8 % for IT (p=0.07). Self-efficacy did not correlate with mean attendance or mean compliance to the prescribed intensity. **Conclusion:** The present study suggests that IT may be associated with lower compliance rates than CTHI and CTVT.

Keywords: COPD, attendance, compliance, exercise-training, self-efficacy.

Introduction

COPD is the fourth leading cause of mortality in the world and in Canada and it represents a major cause of respiratory morbidity [6, 9, 10]. COPD is characterized by chronic airflow limitation, chronic respiratory symptoms and declining functional status and quality of life [2, 6, 9]. In 2004, COPD was responsible for 9,607 deaths in Canada [3, 9]. More then 750, 000 Canadians are diagnosed with COPD, but the actual prevalence is thought to be higher [3, 9] as COPD is often under diagnosed [2, 3, 9]. The prevalence of the disease is likely to increase due to continued exposure to cigarette smoke and other potential COPD risk factors and to the aging of the population [6, 9, 10]. COPD is a major respiratory illness exerting serious economic and social burden in Canada accounting for approximately $4 billion of total health care costs in 2010 [17] The rise in this chronic illness necessitates the expansion of existing services (primary care, hospital) as well as a comprehensive approach to its management [6].

PR has become widely recognized as the best available strategy to tackle the systemic consequences of COPD [52, 55, 56]. It combines exercise training, patient education, and psychosocial support [57]. These various approaches are integral to the long-term management of COPD and require a dynamic collaboration among the patient, his/her family and the health care team [56]. Although all components of PR contribute to benefit patients' overall psychological and physical health, exercise conditioning is considered the key element [2, 3].

Exercise training is a mandatory component to a successful PR program in patients with COPD [59]. In fact, exercise training is responsible for many of the health benefits related to respiratory rehabilitation, such as increased exercise capacity, decreased exertional dyspnea [61], and improved activities of daily living [59, 78]. The optimal exercise-training prescription (mode, intensity, and duration) remains

undetermined for patients with COPD. Current PR guidelines suggest high-intensity exercise training to elicit greater physiological adaptation [65]. However, it has been shown that although high-intensity exercise regimens can be feasible in some COPD patients [65], the majority of moderate to severe COPD patients can hardly tolerate this exercise intensity [56, 69]. Therefore, alternative approaches have been proposed, such as training at the ventilatory threshold and interval training. The ventilatory threshold is described as the breakpoint during progressive exercise above which minute ventilation increases disproportionately to increments in oxygen consumption [73]. The ventilatory threshold typically occurs at 50 to 60 % of VO_2 peak in the elderly, but it remains a parameter that needs to be determined on an individual basis [105]. Exercising at the ventilatory threshold is associated with tolerable levels of ventilation and dyspnea, which represent two of the main exercise-limiting factors in patients with COPD [73, 74]. Interval training consists of alternating bouts of maximal or high-intensity exercise with short periods of rest or active recovery [56]. There is evidence supporting interval training over continuous training in COPD patients [72], where interval training has been associated with reduced breathlessness and lung hyperinflation, longer periods of exercise, and greater total amount of work [52, 72, 92]. For the above mentioned reasons, training at the ventilator threshold and interval training have been proposed as more tolerable and thus easier to comply with for this patient population [73, 74]. Yet, this assumption needs to be verified.

Many factors, including behavioural, personal, environmental, and program-related factors, are important to consider when studying compliance to exercise training. Self-efficacy, a behavioural factor [97, 100], has been identified as a fundamental aspect in patients' ability to manage their own disease and as a determinant of exercise adherence [97, 100]. Self-Efficacy investigates an individual's emotional functioning and

coping skills to deal with a particular situation [100, 101]. A recent study by Bentsen et al. [101] has shown that higher levels of exercise self-efficacy at baseline was a good predictor of improved health status, quality of life, and psychosocial function after completion of PR in COPD patients. This highlights the importance of considering self-efficacy in the treatment of COPD [100]. Moreover, it has been shown that increasing self-efficacy with disease management programmes positively influences health behaviours [97], which in turn is likely to further impact the effects of PR on clinical and functional outcomes [97, 100]. Higher self-efficacy levels in COPD patients have been found to be a good predictor of improved exercise capacity and psychosocial function in relation to PR [101] and is a key component in translating PR completion and success [100, 102].

The general aim of the present study was to determine the optimal exercise-training program to tackle the compliance issue often seen in COPD patients. More specifically, the primary objective was to compare, in individuals with COPD, the 12-week compliance to the following three exercise-training protocols: continuous training at high-intensity (CTHI), continuous training at the ventilatory threshold (CTVT), and interval training (IT). The secondary objective was to examine the relationship between exercise compliance and baseline self-efficacy scores in patients with COPD. The research hypotheses were the following: 1) patient compliance will be highest in the CTVT group, followed respectively by the IT group and the CTHI group; and 2) a significant direct relationship will be found between compliance rates and baseline self-efficacy scores.

Methods

Study Design and Procedure

The present study was a sub-study to a larger randomized, parallel-group, clinical trial (RCT) comparing the short-and long-term effects of different exercise training protocols on various PR program outcomes in COPD. As part of the larger RCT, patients who met the eligibility criteria and accepted to participate completed a thorough baseline evaluation and were then randomly assigned to one of three exercise training protocols: continuous training at high-intensity (CTHI), continuous training at the ventilatory threshold (CTVT), and interval training (IT). Subjects from the three subgroups trained three times per week for 12 weeks, for a total of 36 exercise sessions. Session duration was adjusted such that the total amount of work performed per session was comparable across the three protocols (Figure 4.1). Outcome assessors were blinded as to subjects' group assignment.

Subjects and Eligibility

Subjects were recruited from l'Hôpital du Sacré-Coeur de Montréal and participated to this pilot study between May 2009 and November 2011. Inclusion/exclusion criteria were as follows. Inclusion: 1) clinically stable COPD; 2) age 40 years or older; 3) smoking history of at least 10 American pack-years (20 cigarettes per pack); 4) post-bronchodilation forced expiratory volume in one second (FEV_1) less than 80% of the predicted normal value; and 5) FEV_1 to forced vital capacity (FVC) ratio less than 0.7. Exclusion: 1) exacerbation of respiratory symptoms in the past 4 weeks (change in dyspnea or volume/colour of sputum, need for antibiotic treatment, or need for hospitalization); 2) any contraindication to exercise based on guidelines from the American Thoracic Society (Appendix C) [106]; 3) any active condition other than COPD

that can influence exercise tolerance (asthma, unstable coronary heart disease, congestive heart failure, neoplasia, severe intermittent claudication, severe arthritis, etc.); 4) the need for oxygen therapy; 5) participation in a PR program in the past year; and 6) inability to complete baseline evaluations (including the achievement of a ventilatory threshold on the incremental cycling exercise test). These eligibility criteria were meant to differentiate COPD from other respiratory diseases and ensure clinical stability and patient safety.

Randomization

Patients were randomized to CTHI, CTVT, or IT in groups of six. Randomization by group (rather than individually) was selected for feasibility and contamination concerns. Subjects from the same group trained in the same room at the same time; this approach enabled us to optimize the human resources needed for supervision, while respecting the staff/patient ratio recommended (1/8). Randomizing subjects who trained together into the same intervention arm ensured that no contamination occurs between more demanding and less demanding protocols. Randomization of groups of six subjects was achieved in block, once all six subjects completed baseline assessments. The randomization process consisted of a computer-generated random listing of the three treatment allocations blocked by groups of six.

Exercise Training Intervention

The exercise training bouts were performed on calibrated cycle ergometers (Bike Med, TechnoGym, Italy) at the hospital's cardiopulmonary rehabilitation center (Centre de réadaptation cardio-respiratoire Jean-Jacques-Gauthier). Patients trained at a prescribed intensity and duration and at a frequency of three sessions per week for a total of 12 weeks. Sessions included a 10-minute warm-up, a training phase at the target intensity, and a 5-minute cool-down. CTHI consisted of pedalling for 25 minutes at the

HR reached at 80% of peak workload during the symptom-limited test; CTVT consisted of training at the HR reached at the ventilator threshold; and IT consisted of 30-second intervals at the HR reached at 100% of peak workload interspersed with 30-second of unloaded pedalling IT was based on Vogiatzis and colleagues [64] method in a reasonable sample (n = 36) and was shown to be as effective as continuous exercise training at a moderate intensity. Session duration for CTVT and IT was adjusted for each subject using metabolic equations, such that the total amount of work performed was comparable to 25 minutes of CTHI. This approach has been used successfully in the past to isolate the effect of training intensity from that of total training dose [65].

Patients were asked to train within $\pm$ 5 beats/min of their target heart rate, which was detected continuously throughout their workout by a HR transmitter (T31, Polar, Finland). Since heart rate response at a given submaximal workload decreases as cardiorespiratory fitness increases, this approach ensures that patients remain at the same *relative* (versus *absolute*) training intensity throughout the program. Patients also performed upper and lower-extremity strength training, stretching, and relaxation exercises. These components were standardized and identical for all groups. Overall, exercise sessions lasted 2-2.5 hours, including cycling (45-60 min), strength training (30 min), stretching (10 min), and relaxation exercises (20 min).

Supervision was provided by trained clinical exercise physiologists (CEPs) at a ratio of 2 healthcare practitioners per 6 patients, which exceeds the minimum ratio of 1:8 recommended by current guidelines [56]. Patient instructions and encouragements were standardized throughout the exercise training intervention since encouragement to the patient has been shown to have a significant effect on exercise performance [107]. CEPs all had basic cardiopulmonary resuscitation (CPR) training and followed the emergency procedures outlined for the building (YMCA-Cartierville) and those for the PR

program. As per current exercise training guidelines [79], patients were asked to follow a list of recommendations before each exercise session, including no smoking within the previous 2 hours, no drinking of caffeinated beverages and alcohol 2 hours before exercising, avoiding food for one hour or less prior to the exercise session, and taking their medications as prescribed.

Measurements

Baseline Measurements

The following baseline measurements were used to characterize the sample and to examine potential associations with exercise compliance: demographic and clinical information, pulmonary function, exercise capacity, and exercise self-efficacy. Details regarding these measurements are provided below.

Demographic and Clinical Information

Basic demographic and clinical information were collected at baseline and include age, sex, ethnicity, and measured height and weight (for body mass index calculation).

Pulmonary Function

Spirometry, lung volumes, and lung diffusion capacity for carbon monoxide (D_LCO) obtained at the time of enrolment. Pulmonary function tests were performed according to recommended techniques [106] and values were compared to predicted normal values from the European Community for Coal and Steel/European Respiratory Society [108].

Exercise Capacity

Exercise capacity was obtained from a symptom-limited incremental cycling exercise test. This test was performed at baseline to rule out the presence of

cardiovascular co-morbidities and to determine the work rate at peak effort and at the ventilatory threshold for subsequent exercise prescription. Subjects were seated on an electromagnetically braked cycle ergometer (Ergoselect 200P, Ergoline, Germany) and connected to a 12-lead electrocardiogram (Jaeger Oxycon Pro, CareFusion, Germany) and to a respiratory circuit through a mouthpiece. The respiratory circuit consisted of a digital volume sensor (TripleV), O_2 and CO_2 analyzers, and a mixing chamber. After five minutes of rest and three minutes of unloaded pedalling, the workload was increased in a stepwise manner up to the individual's maximal capacity. Each step lasted one minute and increments of 5-10 watts were used (5-watt increments for subjects with a predicted work rate < 50 watts; 10-watt increments for those with a predicted peak work rate > 50 watts). This protocol is frequently used in standard practice [109]. Gas exchange parameters (minute ventilation, O_2 uptake, CO_2 excretion) and heart rate were measured at rest and during exercise on a breath-by-breath basis. Dyspnea and leg fatigue were evaluated at rest and every other minute during the test with the modified 10-point Borg scale [110]. The ventilatory threshold was determined using the V-slope method [111], an approach to identify the breakpoint in the VCO_2-VO_2 relationship. Exercise capacity was defined as the highest work rate maintained at a pedalling speed of at least 50 revolutions per minute for a minimum of 30 seconds. Laboratory temperature (22.2 ± 0.6ºC) and humidity (37.6 ± 14.6%) were maintained within recommended ranges for all tests. Instructions given to participants followed ACSM guidelines (ref), encouragement during the test was standardized, and all tests were conducted by the same 2 CEPs.

Exercise Compliance and Adherence Measurements

In the present study, the term 'compliance' was used to refer to the degree to which a patient's behaviour concurs with instructions from a health care practitioner.

As such, in the present study, exercise compliance was assessed by measuring i) attendance to the 12-week PR program and ii) compliance to the prescribed training intensity from baseline to week 12.

Attendance

Patients' attendance was taken at the beginning of every training session by one of the healthcare practitioner supervising the session. Attendance rate was computed as the percentage of sessions attended over the possible total of 36 sessions. If a patient missed a session, the data was not imputed

Compliance to the prescribed intensity

Compliance to the prescribed intensity was measured through new technology from Technogym (Italy), which is composed of special hardware (Bike Med 700 CE-R LED, Polar heart rate monitor, and computer) and software (CardioMemory software package) and allows second by second tracking of each individual exercise session [112]. More specifically, the CardioMemory software package records level of intensity (1-30), workload (Watts), pedalling speed (revolutions/minute), distance (km), pace (mm:ss/km), heart rate (beats/minute), estimated oxygen consumption (VO_2) (ml/min/kg), metabolic equivalent of physical effort (METs), estimated energy expenditure (kcal/hour), and estimated energy consumed (kcal) on a second by second basis [112]. The details regarding this methodology have been described in a previous manuscript [113]. As mentioned previously, patients were asked to train within $\pm$ 5 beats/min of their target heart rate. As such, patient compliance to the prescribed intensity was determined by assessing the percent time spent within the target heart rate (THR) range (target heart rate $\pm$ 5 beats/min) during the training phase of each cycling session. Since patients in the IT group were expected to spend only 50% of their time at their THR (during the high interval), the mean compliance to the THR of all patients

randomized to that group was obtained for the entire intensity phase and then multiplied by two. This was performed due to the inability to precisely identify interval changes on the data tracking software. Mean compliance rate was then computed for each subject as the average compliance rate maintained throughout the 12-week program. If a session was lost due to technical problems, the value from the last available exercise session was imputed to replace the lost values (bring the last value forward approach). It is important to note that compliance to the prescribed THR was measured only for attended sessions.

Other Measurements

Self-Efficacy Measures

As part of the larger RCT, subjects completed a series of psychosocial questionnaires, which measured variables associated with quality of life and known to change with exercise training [114]. For the present sub-study, baseline exercise self-efficacy, as measured with the Self-Efficacy Scale (SES) [95, 115]was used to describe patients' confidence in their ability to successfully perform exercise training at entry into the program. This questionnaire was self-administered before the start of the 12-week pulmonary rehabilitation program. The self-efficacy questionnaire includes the following four sections: an exercise compliance sections (8 questions), an exercise endurance section (5 questions), an exercise muscle strength section (5 questions), and an exercise barriers section (13 questions). The questions in the exercise compliance section evaluate how confident patients feel in complying with a pulmonary rehabilitation program. For the purpose of the study, questions 5 and 7 of the exercise compliance section targeting 6- and 8-week PR programs were removed. Questions regarding exercise endurance evaluate the level of confidence that patients have in their capacity to endure various exercise durations. Questions in the exercise muscle strength section

aim at evaluating patient's ability to complete resistance training and questions concerning exercise barriers assess patient's confidence in overcoming obstacles that could affect exercising 3 times weekly as part of a PR program. Finally, the scores in the self-efficacy questionnaire go from 0 to 100% by increments of 10%, where 0% represents not at all confident, 50% represents moderately confident and 100% represents highly confident (Appendix D).

Exercise Measures

Additional exercise measures, such as heart rate (HR) and exercise workload (Watts) achieved during each session attended, were computed for each subject in order to have a better idea of the effort accomplished throughout the 12-week program.

Additional Information gathering

Information pertaining to subjects' reasons for absence to the exercise sessions, such as respiratory exacerbations, COPD hospitalization, other health reasons and personal reasons were recorded throughout the study.

Statistical Analyses

Mean compliance from week 0 to week 12 was compared between the three treatment groups (CTHI, CTV, IT) and was analyzed as mean percent attendance and mean percent time patients spent at their target heart rate during the 12-week program. Double entry and extraction of the data were performed and only 3 participants out of 36 had an error and the error was less than 5% in all 3 cases. To evaluate the distribution of our results, the skewness (degree to which a variable's score fall at one, or the other ends of the variable's scale) and Kurtosis (relative frequency of scores in both extremes) of variables were evaluated. Levene's test was conducted to evaluate the homogeneity-of-variances assumption. If this assumption was met, then one-way repeated-measures

analyses of variance (ANOVA), with treatment group as the between-subjects factors with three levels (CTHI, CTVT, IT) was executed. If a significant treatment effect was obtained, pairwise comparisons were conducted using Tukey's honestly significant difference (HSD) test to locate between which groups the differences occurred. If on the other hand, the Levene's test rejected the assumption of homogeneity of variances, the Welch's ANOVA was used instead of the usual ANOVA to test between-group differences. If a significant treatment effect was obtained, the Games-Howell post-hoc test was performed to locate where the difference had occurred.

To examine the relationship between exercise compliance and each subscale of the Self-Efficacy Scale, Pearson's correlations were conducted. Moreover, interactions between the intervention and the SES subscales on compliance rate were analyzed by conducting General Linear Model Univariate procedures. All analyses were conducted at the 5% level of significance and performed with SPSS version 16.0 (Chicago, IL).

Power Calculation

The primary objective of this study was to compare, in individuals with COPD, the 12-week compliance to three different exercise-training protocols (CTHI, CTVT, IT). The sample size for this project was estimated at 36 participants (12 in each group) and the primary outcome measure (percent time spent within the target heart rate range) was used for the power calculation. Based upon previously reported data [69, 78, 116], the total sample of 36 subjects would achieve 80% power to detect differences among the means with a 0.05 significance level. The size of the variation in the means is represented by their standard deviation of 2.71.

Results

Thirty-six subjects (13 males; 23 females) with a mean age of 68 ± 9 years were recruited from the outpatient COPD clinic at the Hôpital du Sacré-Coeur de Montréal between spring 2009 and fall 2011, and were randomized into the study. The majority of our patient sample was Caucasian (97%) and had a mean FEV_1 of 1.41 ± 0.42 L with a mean percent predicted value of 58.6 ± 17 %, indicating moderate to severe COPD (GOLD stage II – III) [6]. At time of study entry, patients had a mean BMI of 27.6 ± 5.1 $Kg.m^{-2}$, indicative of an overweight population sample. Subjects randomized to the different exercise-training protocols (CTHI, CTVT, and IT) did not differ significantly with regards to overall demographic measures, such as age, BMI, FEV_1 (in liters and percent predicted), and DLCO (Table 4.1). A trend towards a lower FEV_1 represented as percent predicted was observed in the IT group (Table 4.1).

Mean peak work rate and mean peak VO_2 on the symptom-limited incremental cycling test were 68.2 ± 22.8 Watts and 1.05 ± 0.33 $L.min^{-1}$ respectively (Table 4.1). These measurements did not differ significantly between the three exercise-training groups.

Exercise Attendance and Compliance

Attendance and compliance rates were both normally distributed, but their variance was not homogeneous across the three treatment groups, which led to the use of Welch's ANOVA and Games-Howell post-hoc test.

The mean attendance rate was 70 ± 33% (range: 2.8 – 100.0%) for CTHI, 82 ± 17% for CTVT (range: 44.4 – 97.2%), and 63 ± 35% for IT (range: 11.1 -100.0%), with no significant difference identified between groups (p= 0.229) (Figure 4.2). As mentioned previously, data was not imputed for any missed session. Thus considering the sessions that were missed (266 out of 1030 sessions) and by excluding the warm-up and cool-

down phases (15 min of total exercise-training session), the number of data points included in our analysis was approximately 1 545 000. Reasons for lack of attendance to training included acute exacerbation of COPD (6.8%), hospitalization due to exacerbation (8.6%), other health reasons (doctor appointment, surgery, feeling tired) (24.8%) and personal reasons (vacation, work, family problems) (59.8%) (Figure 4.3). Eight out of 36 patients (22%) experienced at least 1 exacerbation and the average length of symptoms was 5 days. Out of those patients, three were hospitalized for 45, 10, and 6 days respectively.

The mean compliance rate, i.e. the mean percent time spent at the prescribed THR, was 85.6 ± 15.0% (range: 44.4 - 96.1%) for CTHI, 84.1 ± 15.1% (range: 40.2 - 96.4%) for CTVT, and 52.0 ± 41.8% (range: 0.0 -100.0%) for IT (Figure 4.4). The difference in compliance rate between exercise-training groups did not reach statistical significance (p=0.067), but a trend towards a lower compliance rate in the IT group compared to the other two groups was observed. The average heart rate achieved by patients throughout the program was 107.9 ± 16.6 bpm, 101.0 ± 11.0 bpm and 112.8 ± 12.5 bpm for CTHI, CTVT and IT respectively. The watts achieved throughout the 36 sessions by patients were 37.5 ± 11.9 W (CTHI), 41.6 ± 23.6 W (CTVT) and 46.2 ± 22.4 (IT). Of note, there were a number of sessions where technical problems caused a loss of data. This occurred in 2% of CTHI, 0.9% of CTVT, and 7.5% of IT sessions. This was felt to be minor in view of the amount of data collected.

Exercise Self-Efficacy

The association between self-efficacy, mean attendance and mean compliance scores for CTHI, CTVT, and IT are shown in table 4.2 and partial self-efficacy correlations with mean attendance and mean compliance correcting for intervention are shown in table 4.3. No significant correlation between self-efficacy subscale scores and

compliance (mean attendance and mean time spent at THR) were found. Finally, no significant interaction between the intervention and SES subscales on compliance rate were found in our study.

Adverse Events

No adverse events occurred during the exercise sessions throughout the study.

Discussion

The present study compared exercise compliance, using both attendance rate and percent time spent at the prescribed training intensity, between three exercise regimens in COPD patients: continuous training at high-intensity (CTHI), continuous training at the ventilatory threshold (CTVT), and interval training (IT). To our knowledge, this is the second study only to use continuous data tracking technology to precisely assess exercise compliance in COPD patients and the first original trial to compare compliance to these three commonly used exercise-training approaches. Our results did not show any significant differences in compliance between the three approaches, but a trend towards a lower percent time spent at the target intensity was observed in the group undergoing IT.

In a previous prospective observational study from Maltais et al. [69], 42 patients with moderate to severe COPD completed a 12-week aerobic exercise-training program similar to the CTHI approach used in our study. The training program consisted of 3 weekly sessions of stationary cycling for a target duration of 25-30 minutes and a target intensity of 80% of baseline peak work rate (Wpeak). The average attendance rate was 86 ± 10% and the prescribed training intensity was achieved by 0 (0%), 3 (7%), 5 (12%), and 5 (12%) patients at weeks 2, 4, 10, and 12 respectively [69]. In our study, a lower attendance rate of 70 ± 33% was observed for the CTHI group but, contrary to Maltais et

al's [69] findings, a majority of patients were able to achieve the target intensity, with a mean percent time spent at the THR of 86 ± 15% throughout the 12-week program. Patients who underwent CTHI in our trial had less severe airflow obstruction and a better exercise tolerance than those who completed Maltais et al's study, which may explain the higher compliance rate in our group. Moreover, although the targeted intensity was 80% of peak work rate in both studies, the methodology used to ascertain achieved intensity was different. In fact, the actual work rate achieved on calibrated ergocycles at a fixed pedalling speed was recorded in Maltais et al's study, while the percent time spent at the THR (± 5 beats from the heart rate reached at 80% of peak work rate on the incremental cycle test) was extracted in our study. According to the average wattage recorded throughout the 12-week program in the CTHI group (37.5 ± 11.9 W) compared to their average peak wattage at baseline (65.4 ± 16.2 W), our methodology resulted in an intensity closer to 60% of peak work rate. Together with the differences in disease severity and exercise tolerance likely explains the much higher compliance rate observed in our CTHI patients compared to those who completed Maltais et al's study.

In a clinical trial conducted by Puhan and colleagues [78] , patients with severe COPD were randomly assigned to either continuous high-intensity or interval training. The high-intensity training protocol consisted of pedalling at a target workload of ≥ 70% of Wpeak. The interval training protocol involved high-intensity intervals of 20 seconds alternated with low-intensity intervals of 40 seconds; the target work rate for the high- and low-intensity intervals was, respectively, 50% and 10% of short-term maximum exercise capacity, as determined from a previously completed steep ramp test [78]. According to the authors, 50% of short-term maximum exercise capacity is equivalent, on average, to 90-100% of Wpeak, thus suggesting similar intensities as in our IT protocol, but shorter high-intensity intervals (20 seconds versus 30 seconds in our trial),

longer low-intensity intervals (40 seconds versus 30 seconds in our trial), and smaller work-recovery ratio (1:2 versus 1:1 in our trial). Protocol tolerance was compared by looking at the number of unintended breaks of ≥ 1 minute and at the proportion of patients achieving the target intensity, as assessed via continuous data tracking technology [78]. Interval training was found to be associated with significantly fewer unintended breaks and, in contrast to our findings, with better adherence to the planned protocol than continuous high-intensity training (48% versus 24%, respectively) [78].In our study, a similar compliance rate of 52% was recorded in the IT group, but the 86% adherence rate observed in our CTHI group is markedly greater than the 24% reported in that study. Although the targeted intensity for continuous high-intensity training was theoretically higher in our trial (80% of Wpeak versus 70% of Wpeak in Puhan et al's study), the actual achieved wattage corresponded to approximately 60% of Wpeak in both studies. Once again, patients who underwent CTHI in our trial had less severe airflow obstruction than those who completed Puhan et al's study, possibly explaining the differences in findings.

Lastly, in a randomized controlled trial by Vogiatzis et al. [64], COPD patients were either assigned to continuous moderate-intensity or interval training. Patients from both groups were asked to perform their exercise sessions on a cycle ergometer, for a period of 40 minutes per session and at a frequency of 2 days weekly. The continuous training protocol consisted of pedalling at 50% of peak work rate (Wpeak), while the interval protocol involved, as in the present study, intervals of 30 seconds at 100% of Wpeak alternated with 30 seconds of rest [64]. As in our trial, attendance did not differ between both protocols (88 ± 4% in patients undergoing continuous training and 90 ± 4% in patients undergoing interval training), but the attendance rates were higher than those recorded in our subjects, especially those who underwent IT (63%) in our study. This

can likely be explained by the lower training frequency in Vogiatzis et al.'s study, done in an attempt to reduce problems with compliance and to ensure greater attendance rates. In summary, attendance to CTHI and IT was slightly lower in the present trial than what was previously reported [64]. Compliance to IT was similar than what was found in one prior randomized study [78]. Lastly, compliance to CTHI was particularly high in the present investigation when compared to prior studies [69, 78], possibly because patients assigned to CTHI in our trial had less severe disease.

An additional aim of the present study was to examine the relationship between exercise compliance and baseline self-efficacy scores. No significant correlation was found between the four components of self-efficacy (adherence, exercise, strength, and obstacle) and mean attendance or mean compliance rates. Contrary to our findings, various studies have found a significant relation between self-efficacy and exercise behaviour (exercise adoption, adherence and maintenance) [101, 117, 118]. Kaplan and Atkins [98] have found that a higher level of self-efficacy was associated with increased compliance to exercise prescription. Other studies have found that COPD patients with greater self-efficacy feel more confident to perform physical and psychosocial activities [54, 101]. However, a study conducted by Vincent et al. [100] found similar results as in the present study. Indeed, these investigators used the Pulmonary Rehabilitation Adapted Index of Self-efficacy (PRAISE) on 225 patients prior to and on completion of a 7-week PR program and found no relationship between PRAISE score and completion of PR [100]. There could be a few reasons explaining the lack of correlation between self-efficacy and attendance and compliance to the THR. Several factors other than self-efficacy, such as personal factors, can influence attendance and compliance to the PR program. These factors could have had a bigger impact on compliance than the baseline level of self-efficacy. In addition, a bigger sample size might be needed to reveal a

significant correlation between self-efficacy and attendance and compliance to the exercise-training programs.

Limitations and Strengths:

There were a number of technical challenges in the current study that could have affected the reliability of the results. Computer problems occurred causing the loss of data during several sessions. To compensate for this technical problem, the last exercise session was imputed to replace the lost values. The percentage of lost sessions to the overall study was, however, minor in relation to the data accrued and likely did not affect the overall results of the study. Another limitation was that patients were required to be cued to change intervals every 30 seconds in the IT group. This short interval was difficult from both the patient and health care practitioners supervising the exercise sessions. Patients sometimes missed their cue and health care practitioners may have missed the exact time to prompt the patient to change their intensity. This may have caused an over or under estimation of the compliance rate to the prescribed target heart rate in the IT group. This problem may have been overcome by identifying the exact moment of interval changes on the CardioMemory tracing. However, by not identifying the occurrence of interval change and by expecting patients in the IT group to spend only 50% of their time at the prescribed THR for the high interval, we were able to account for the delay in the physiologic response that occurs during the change between high and low intensities. Lastly, the small number of patients per group and the generally low level of disease severity may have affected our findings regarding compliance to the different exercise prescriptions and the correlation with baseline self-efficacy.

The present study also has a number of strengths. It took into consideration both attendance rates and compliance to the prescribed training intensity, which permitted a

broader and more thorough evaluation of overall exercise compliance. The second-by-second tracking of each individual exercise session allowed for more specific monitoring of patients' ability to comply with the prescribed exercise intensity. In an attempt to determine the optimal prescription in COPD, our study, which was a randomized trial, compared compliance to three different-exercise training protocols, contrary to previous work which has compared compliance to two different exercise regimens at a time.

Conclusions:

Results from this pilot study showed no significant difference in attendance and compliance rates between different exercise-training protocols in patients with moderate to severe COPD. However, a trend towards poorer compliance in patients undergoing IT compared to those assigned to CTHI and CTVT was observed. Moreover, baseline self-efficacy scores did not correlate significantly with mean attendance and percent time spent at prescribed THR. Although these findings need to be confirmed in a larger sample size, to our knowledge, this study is the first to compare compliance to three different exercise-training protocols in COPD. Exercise compliance is essential to the effectiveness of PR and without it no therapeutic goal can be achieved [83, 93, 104]. This study highlights the benefit of using an innovative and a precise way to track adhrence measurements.

Clinical implications and future directions:

This study emphasizes the important role of exercise compliance in order to optimize the benefits of PR in COPD. Further studies should focus on factors that influence exercise compliance and on interventions that can motivate behavioural change in this population.

LEGEND FOR FIGURES

TABLES

Table 4.1 Characteristics of the study group

	CTHI	CTVT	IT	p-value
Male/Female, n	3/9	6/6	4/8	
Age, years	66.3 ± 7.0	69.3 ± 8.8	66.9 ± 10.3	0.670
BMI, $kg.m^{-2}$	28.3 ± 5.1	27.1 ± 5.4	27.5 ± 5.3	0.852
FEV_1, L	1.37 ± 0.30	1.60 ± 0.42	1.25 ± 0.48	0.110
FEV_1, % predicted	59.5 ± 15.1	66.2 ± 16.7	50.0 ± 16.6	0.061
FEV1/FVC, %	51.8 ± 11,5	50.4 ± 9.4	47.4 ± 7.0	0.508
TLC, %	107.5 ± 22.9	113.0 ± 18.6	112.4 ± 20.9	0.781
FRC, %	130.7 ± 36.0	136.3 ± 27.5	139.1 ± 26.6	0.792
RV, %	134.9 ± 44.0	135.8 ± 41.0	146.2 ± 35.6	0.749
DLCO, ml/CO/mmHg	2.47 ± 0.77	2.12 ± 0.57	2.21 ± 0.80	0.470
Peak Work Rate, Watts	65.4 ± 16.2	72.1 ± 24.8	67.1 ± 27.4	0.768
VO_2peak, $L.min^{-1}$	1.01 ± 0.18	1.07 ± 0.40	1.08 ± 0.38	0.856
VO2peak, $mL.(kg.min)^{-1}$	13.54 ± 3.11	14.03 ± 3.75	14.67 ± 3.04	0.618

Values are presented as Mean ± SD.
BMI, Body Mass Index; FEV_1, Forced Expiratory Volume in 1 second; FVC, Force Vital Capacity; VO_2peak, peak O_2 Uptake.

*$p < 0.05$

Table 4.2 Association between self-efficacy, mean attendance and mean compliance.

Self-Efficacy Subscales	Mean Attendance		Mean Compliance	
	r	p	r	p
Adherence Subscale	0.074	0.466	0.164	0.370
Exercise Subscale	0.255	0.230	-0.106	0.551
Strength Subscale	-0.190	0.969	0.013	0.942
Obstacle Subscale	0.228	0.902	-0.246	0.154

*$p < 0.05$

Table 4.3 Partial self-efficacy correlations with mean attendance and mean compliance correcting for intervention.

Self-Efficacy Subscales	Mean Attendance		Mean Compliance	
	r	p	r	p
Adherence Subscale	0.136	0.683	0.203	0.274
Exercise Subscale	0.222	0.140	-0.018	0.923
Strength Subscale	-0.007	0.914	0.026	0.891
Obstacle Subscale	-0.023	0.182	-0.246	0.183

*$p < 0.05$

FIGURES

Figure 4.1

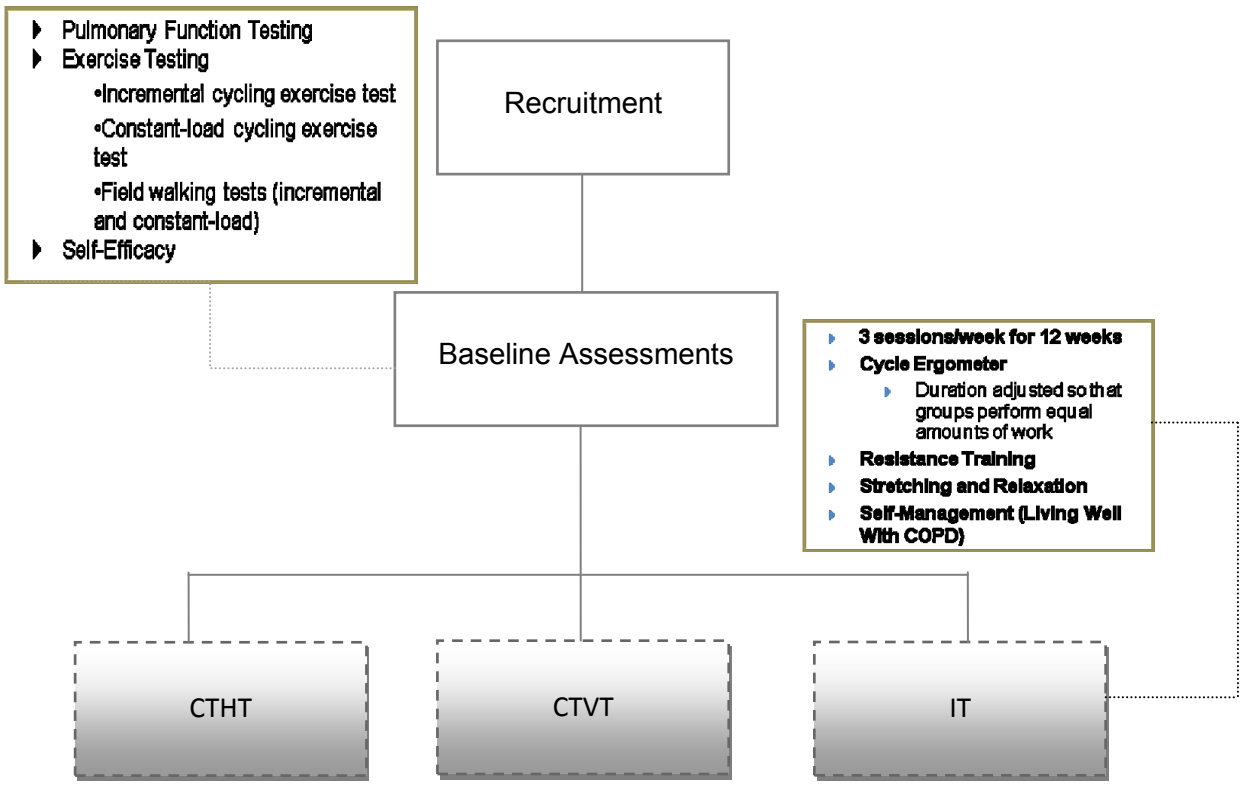
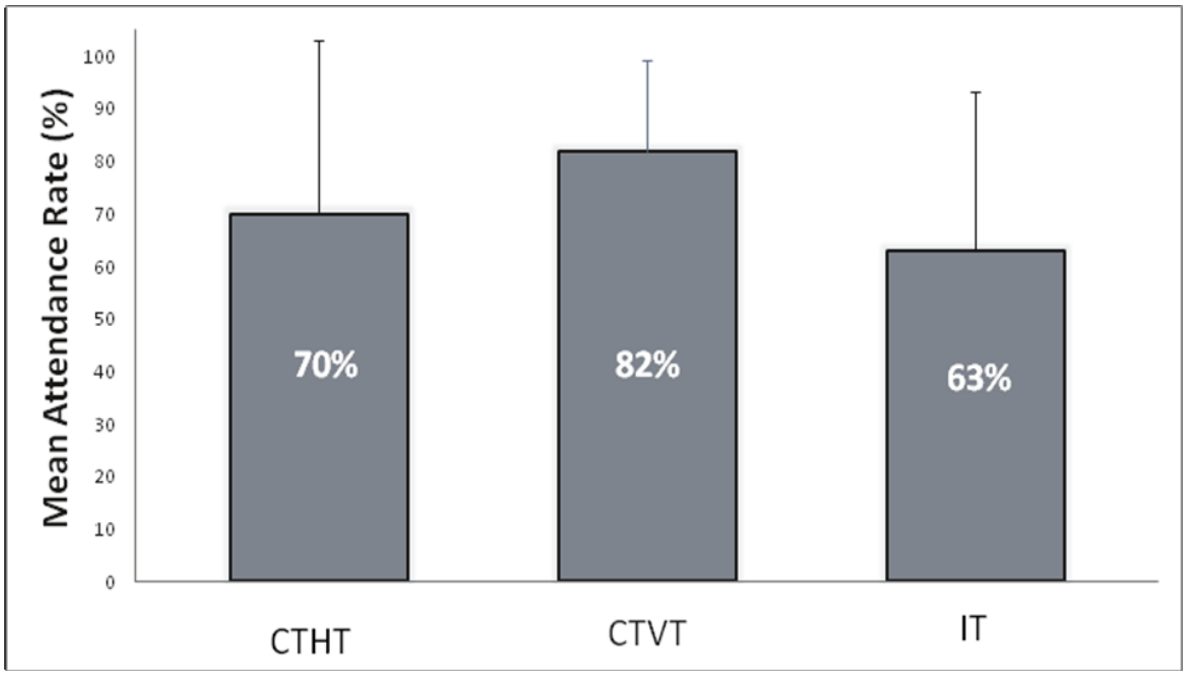


Figure 4.2



Mean ± SD
*p < 0.05

Figure 4.3

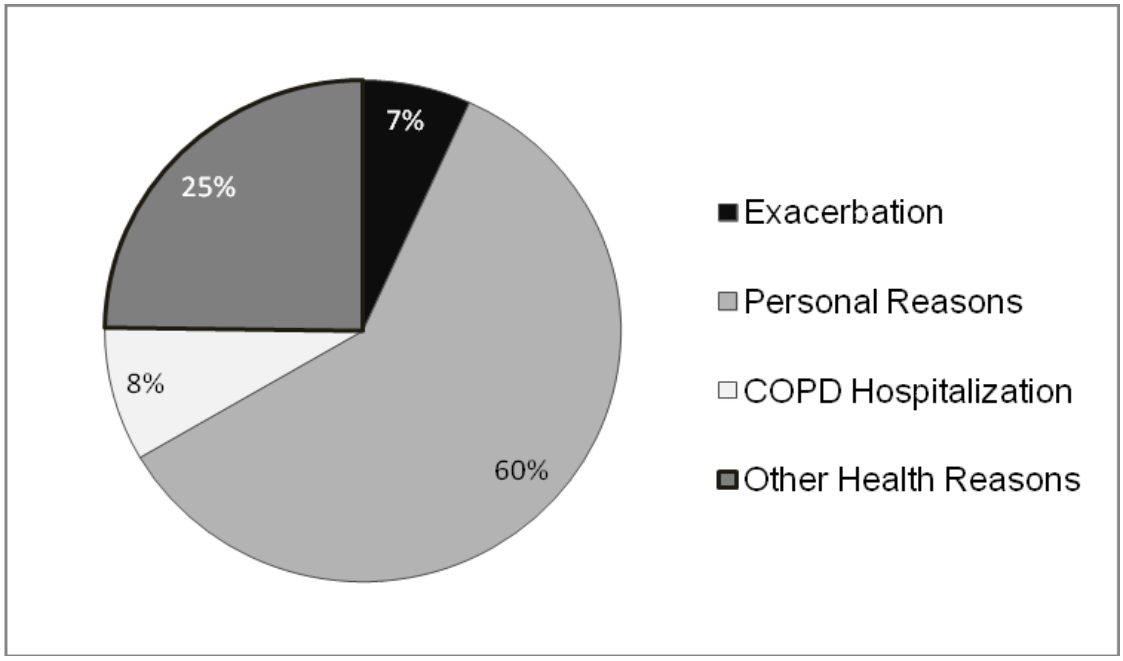
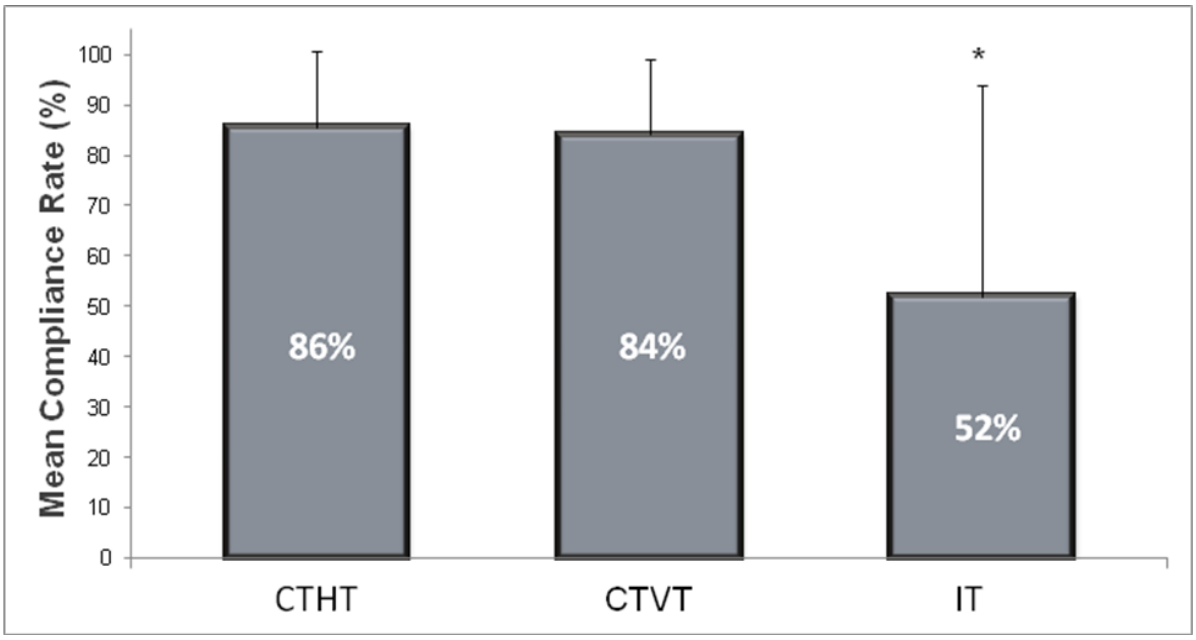

7%
25%
8%
60%
Exacerbation
Personal Reasons
COPD Hospitalization
Other Health Reasons

Figure 4.4



Mean ± SD
*p = 0.07

REFERENCES

1. Pauwels RA, Rabe KF, *Burden and clinical features of chronic obstructive pulmonary disease (COPD).* Lancet, 2004. **364**(9434): p. 613-620.
2. Shapiro SD, *Chronic Bronchitis and Emphysema* in *Textbook of Respiratory Medicine* C.V. Broaddus, Mason, R.J., Murray, J.F. and Nadel, J.A., Editor. 2005, Elseiver Saunders: Pennsylvania.
3. O'Donnell DE, Hernandez P, Kaplan A, et al., *Canadian Thoracic Society recommendations for management of chronic obstructive pulmonary disease - 2008 update - highlights for primary care.* Can Respir J, 2008. **15 Suppl A**: p. 1A-8A.
4. *Chronic Obstructive Pulmonary Disease*. Public Health Agency Canada 2008 [cited 2010 28-01]; Available from: http://www.phacaspc.gc.ca/cd-mc/crd-mrc/copd-mpoc-eng.
5. Halpin DM, Tashkin D, *Defining disease modification in chronic obstructive pulmonary disease.* COPD, 2009. **6**(3): p. 211-225.
6. *Global Initiative For Chronic Obstructive Lung Disease. Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease: Updated 2010.* 2010.
7. Celli BR, MacNee W, Agusti A, et al., *Standards for the diagnosis and treatment of patients with COPD: a summary of the ATS/ERS position paper.* Eur Respir J, 2004. **23**(6): p. 932-946.
8. Clinique du Souffle la Solane, *COPD downward spiral*: Osséja, France.
9. *Life and Breath: Respiratory Disease in Canada* 2007 Januray, 2010 [cited.
10. Maltais F, Bourbeau J, Shapiro S, et al., *Effects of home-based pulmonary rehabilitation in patients with chronic obstructive pulmonary disease: a randomized trial.* Ann Intern Med, 2008. **149**(12): p. 869-78.
11. *Largest-Ever COPD Study Reveals Alarming Gaps in Care*. The Lung Association 2005 [cited 2013 08-02-2013].
12. Benady S, *The Human and Economic Burden of COPD: A Leading Cause of Hospital Admission in Canada*. Canadian Thoracic Society 2010 [cited 2013].
13. Suissa S, Dell' Aniello S, Ernst P, *Long-term natural history of chronic obstructive pulmonary disease: severe exacerbations and mortality.* Thorax, 2012. **67**: p. 957-963.
14. *C.I.O.H. Health Indicators 2008*. 2008 [cited 2008.
15. Mittmann N, Kuramoto L, Seung SJ, Haddon JM, Bradley-Kennedy C, Fitzgerald JM. and *The cost of moderate and severe COPD exacerbations to the Canadian healthcare system.* Respiratory Medicine 2008. **102**.
16. Nie JX, Wang L, Upshur RE., *Mortality of elderly patients in Ontario after hospital admission for chronic obstructive pulmonary disease.* Can Respir J 2007. **14**(8): p. 485-489.
17. Hermus G, Stonebridge C, Goldfarb D, Thériault L, and Bounajm F, *Cost Risk Analysis for Chronic Lung Disease in Canada*, in *The Conference Board of Canada*. 2012. p. 1-52.
18. Halbert RJ, Natoli J, Gano A, Badamgarav E, Buist AS, Mannino DM. , *Global burden of COPD: sysemic review and meta-analysis.* Eur Respir J 2006. **28**: p. 523-532.

19. Bartal M, *COPD and tobacco smoke.* Monaldi Arch Chest Dis, 2005. **63**(4): p. 213-225.
20. Klaus FR, et al., *Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease: Gold Executive Summary.* Am J Respir Crit Care Med 2007. **176**: p. 532-555.
21. Stoller JK, Aboussouan L, *Alpha1-antitrypsin deficiency in European countries.* Eur Respir J, 2005. **365**: p. 2225-2236.
22. Blanco I, DeSerres F, Fernandez Bustillo E, Lara B, Miravitlles M. , *Estimated numbers and prevalence of PI*S and PI*Z alleles of alpha1-antitrypsin deficiency in European countries.* Eur Respir J, 2006. **27**(1): p. 77-84.
23. Hnizdo E, Sullivan P, Bang KM, Wagner G. , *Association between chronic obstructive pulmonary disease and employment by industry and occupation in the US population: astudy of data from the Third National Health and Nutrition Examination Survey, .* Am J Epidemiol, 2002. **156**(8): p. 738-746.
24. Balmes J, Becklake M, Blanc P, et al., *American Thoraci Society Statement: occupational contribution to the burden of airway disease.* Am J Respir Crit Care Med, 2003. **167**(5): p. 787-797.
25. Silva GE, Sherrill D, Gerra S, Barbee RA. , *Asthma as a risk factor for COPD in a Longitudinal study.* CHEST, 2004. **126**(1): p. 59-65.
26. Wagner EM, Liu MC, Weinmann GG, et al., *Peripheral lung resistance in normal and asthmatique subjects.* Am Rev Respir Dis, 1990. **141**: p. 584-588.
27. Ulrik CS, Backer V, *Nonreversible airflow obstruction in life-long nonsmokers with moderate to severe asthma.* Eur Respir J, 1999. **14**: p. 892-896.
28. Brinke A, Zwinderman A, Sterk PJ, Rabe KF, Bel EH. , *Factors associated with persistent airflow limitation in severe asthma* Am J Respir Crit Care Med, 2001. **164**: p. 744-748.
29. Xu X, Weiss ST, Rijcken B, Schouten JP. , *Smoking, changes in smoking habits, and rate of decline in FEV1: new insight into gender differences.* Eur Respir J, 1994. **7**: p. 1056-1061.
30. McNee W, *ABC of chronic obstructive pulmonary disease. Pathology, pathogenesis, and pathophysiology.* BMJ, 2006. **332**(7551): p. 1202-1204.
31. Barnes PJ, *Mediators of Chronic Obstructive Pulmonary Disease.* Pharmacological Reviews, 2004. **56**(4): p. 515-548.
32. Barnes PJ, *The Cytokine Network in Chronic Obstructive Pulmonray Disease.* Am J Respir Cell Mol Bio, 2009. **41**: p. 631-638.
33. Ferguson GT, *Why does the lung hyperinflate? .* Proc Am Thorac Soc, 2006. **3**(2): p. 176-179.
34. Rodriguez-Roisin R, Drakulovic M., Rodriguez DA, Roca J, Barbera AJ, Wagner PD. , *Ventilation-perfusion imbalance and chronic obstruction pulmonary disease staging severity.* J Appl Physiol, 2009. **106**: p. 1902-1908.
35. Wouters EFM, Creutzberg EC, Schols AMW. , *Systemic Effects in COPD.* CHEST, 2002. **121**: p. 127-130.
36. Debigaré R, Côté C, Maltais F, *Peripheral Muscle Wasting in Chronic Obstructive Pulmonary Disease.* Am J Respir Crit Care Med, 2001. **164**: p. 1712-1717.
37. Schols AMWJ, Broekhuizen R, Welling-Scheepers CA, Wouters EF, *Body composition and mortality in chronic obstructive pulmonary disease.* Am J Clin Nutr, 2005. **82**: p. 53-59.
38. Barnes PJ, Celli B, *Systemic manifestations and comorbidities of COPD.* Eur Respir J, 2009. **33**: p. 1165-1185.

39. Remels AH , Schrauwen P, Broekhuizen R, Willems J, Kersten S, Gosker HR, AM Schols., *Peroxisome proliferator-activated receptor expression is reduced in skeletal muscle in COPD.* Eur Respir J, 2007. **30**: p. 245-252.
40. Bakakos P, Kostikas K, Loukides S, , *COPD and Comorbidities.* PNEUMON, 2010. **23**(1): p. 24-27.
41. Ninot G, *Anxiety and depression in COPD: A review.* Rev Mal Respir, 2011. **28**(6): p. 739-748.
42. Mikkelsen RL, Middleboe T, Pisinger C, Bjerregaard K, *Anxiety and depression in patients with chronic obstructive pulmonary disease (COPD). A review.* 2004. **58**(1): p. 65-70.
43. Enright P, *The use and abuse of office spirometry.* Primary Care Respiratory Journal, 2008. **17**(4): p. 238-242.
44. *ATS/ACCP Statement on cardiopulmonary exercise testing.* Am J Respir Crit Care Med, 2003. **167**(2): p. 211-77.
45. Pepin V, Laviolette L, Brouillard C, et al., *Significance of changes in endurance shuttle walking performance.* Thorax, 2010: p. 1-6.
46. *ATS statement: guidelines for the six-minute walk test.* Am J Respir Crit Care Med, 2002. **166**(1): p. 111-7.
47. Pepin V, Maltais F, Lacasse Y, *Goals of Treatments and Measurement of Their Efficacy: From Clinical Trials to Real World Practice, in Clinical Management of Chronic Obstructive Pulmonary Disease*. 2007, Taylor & Francis Group: New York. p. 239-261.
48. Noonan V, Dean E, *Submaximal Exercise Testing: Clinical Application and Interpretatio.* Physical Therapy 2000. **80**(8): p. 782-807.
49. Pepin V, Brodeur J, Lacasse Y, Milot J, Leblanc P, Whittom F, Maltais F, *Six-minute walking versus shuttle walking: responsiveness to bronchodilation in chronic obstructive pulmonary disease.* Thorax, 2007. **62**(4): p. 291-8.
50. Pepin V, Saey D, Whittom F, LeBlanc P, Maltais F, *Walking versus cycling: sensitivity to bronchodilation in chronic obstructive pulmonary disease.* Am J Respir Crit Care Med, 2005. **172**(12): p. 1517-22.
51. Revill SM, Morgan MD, Singh SJ, Williams J, Hardman AE., *The endurance shuttle walk: a new field test for the assessment of endurance capacity in chronic obstructive pulmonary disease.* Thorax, 1999. **54**(3): p. 213-22.
52. Troosters T, Casaburi R, Gosselink R, Decramer M., *Pulmonary rehabilitation in chronic obstructive pulmonary disease.* Am J Respir Crit Care Med, 2005. **172**(1): p. 19-38.
53. Bourbeau J, Julien M, Maltais F, et al., *Reduction of Hospital Utilization in Patients With Chronic Obstructive Pulmonary Disease.* Arch. Intern. Med., 2003. **163**: p. 585-591.
54. Bourbeau J, Nault D, Dang-Tan T, *Self-management and behaviour modification in COPD.* Patient education and couseling, 2004. **52**: p. 271-277.
55. Coppoolse R, Schols A, Baarends EM, Mostert R, Akkermans MA, Janssen PP, Wouters EF, *Interval versus continuous training in patients with severe COPD: a randomized clinical trial.* Eur Respir J, 1999. **14**(2): p. 258-63.
56. Nici L, Donner C, Wouters E, et al., *American Thoracic Society/European Respiratory Society statement on pulmonary rehabilitation.* Am J Respir Crit Care Med, 2006. **173**(12): p. 1390-1413.
57. Lacasse Y, Maltais F, Goldstein RS, *Pulmonary rehabilitation: an integral part of the long-term management of COPD.* Swiss Med Wkly, 2004. **134**(41-42): p. 601-5.

58. Lacasse Y, Goldstein R, Lasserson TJ, Martin S, *Pulmonary rehabilitation for chronic obstructive pulmonary disease.* Cochrane Database Syst Rev, 2006(4): p. CD003793.
59. Maltais F, LeBlanc P, Simard C, et al., *Skeletal muscle adaptation to endurance training in patients with chronic obstructive pulmonary disease.* Am J Respir Crit Care Med, 1996. **154**(2 Pt 1): p. 442-7.
60. Bendstrup KE, Ingemann Jensen J, Holm S, Bengtsson B, *Out-patient rehabilitation improves activities of daily living, quality of life and exercise tolerance in chronic obstructive pulmonary disease.* Eur Respir J, 1997. **10**(12): p. 2801-6.
61. Gigliotti F, Coli C, Bianchi R, Romagnoli I, Lanini B, Binazzi B, Scano G, *Exercise training improves exertional dyspnea in patients with COPD: evidence of the role of mechanical factors.* Chest, 2003. **123**(6): p. 1794-802.
62. Puhan MA, Busching G, Schunemann HJ, VanOort E, Zaugg C, Frey M, *Interval exercise versus continuous exercise in patients with moderate to severe chronic obstructive pulmonary disease--study protocol for a randomised controlled trial [ISRCTN11611768].* BMC Pulm Med, 2004. **4**: p. 5.
63. Laviolette L, Bourbeau J, Bernard S, et al., *Assessing the impact of pulmonary rehabilitation on functional status in COPD.* Thorax, 2008. **63**(2): p. 115-21.
64. Vogiatzis I, Nanas S, Roussos C, *Interval training as an alternative modality to continuous exercise in patients with COPD.* Eur Respir J, 2002. **20**: p. 12-19.
65. Casaburi R, Patessio A, Loli F, Zanaboni S, Donner CF, Wasserman K., *Reductions in exercise lactic acidosis and ventilation as a result of exercise training in patients with obstructive lung disease.* Am Rev Respir Dis, 1991. **143**(1): p. 9-18.
66. Troosters T, Gosselink R, Decramer M, *Short- and long-term effects of outpatient rehabilitation in patients with chronic obstructive pulmonary disease: a randomized trial.* Am J Med, 2000. **109**(3): p. 207-12.
67. Rochester CL, *Exercise training in chronic obstructive pulmonary disease.* J Rehabil Res Dev, 2003. **40**(5 Suppl 2): p. 59-80.
68. Emery CF, Honn V, Frid DJ, Lebowitz KR, Diaz PT, *Acute effects of exercise on cognition in patients with chronic obstructive pulmonary disease.* Am J Respir Crit Care Med, 2001. **164**(9): p. 1624-7.
69. Maltais F, LeBlanc P, Jobin J, et al., *Intensity of training and physiologic adaptation in patients with chronic obstructive pulmonary disease.* Am J Respir Crit Care Med, 1997. **155**(2): p. 555-61.
70. Ries AL, Kaplan R, Limberg TM, Prewitt LM, *Effects of pulmonary rehabilitation on physiologic and psychosocial outcomes in patients with chronic obstructive pulmonary disease.* Ann Intern Med, 1995. **122**(11): p. 823-32.
71. Punzal PA, Ries AL, Kaplan RM, Prewitt L. , *Effects of pulmonary rehabilitation on physiologic and psychosocial outcomes in patients with chronic obstructive pulmonart disease.* Ann Inter Med, 1995. **122**: p. 823-832.
72. Sabapathy S, Kingsley RA, Schneider DA, Adams L, Morris NR, *Continuous and intermittent exercise responses in individuals with chronic obstructive pulmonary disease.* Thorax, 2004. **59**(12): p. 1026-31.
73. Vallet G, Ahmaidy S, Serres I, et al., *Comparison of two training programmes in chronic airway limitation patients: standardized versus individualized protocols.* Eur Respir J, 1997. **10**(1): p. 114-22.

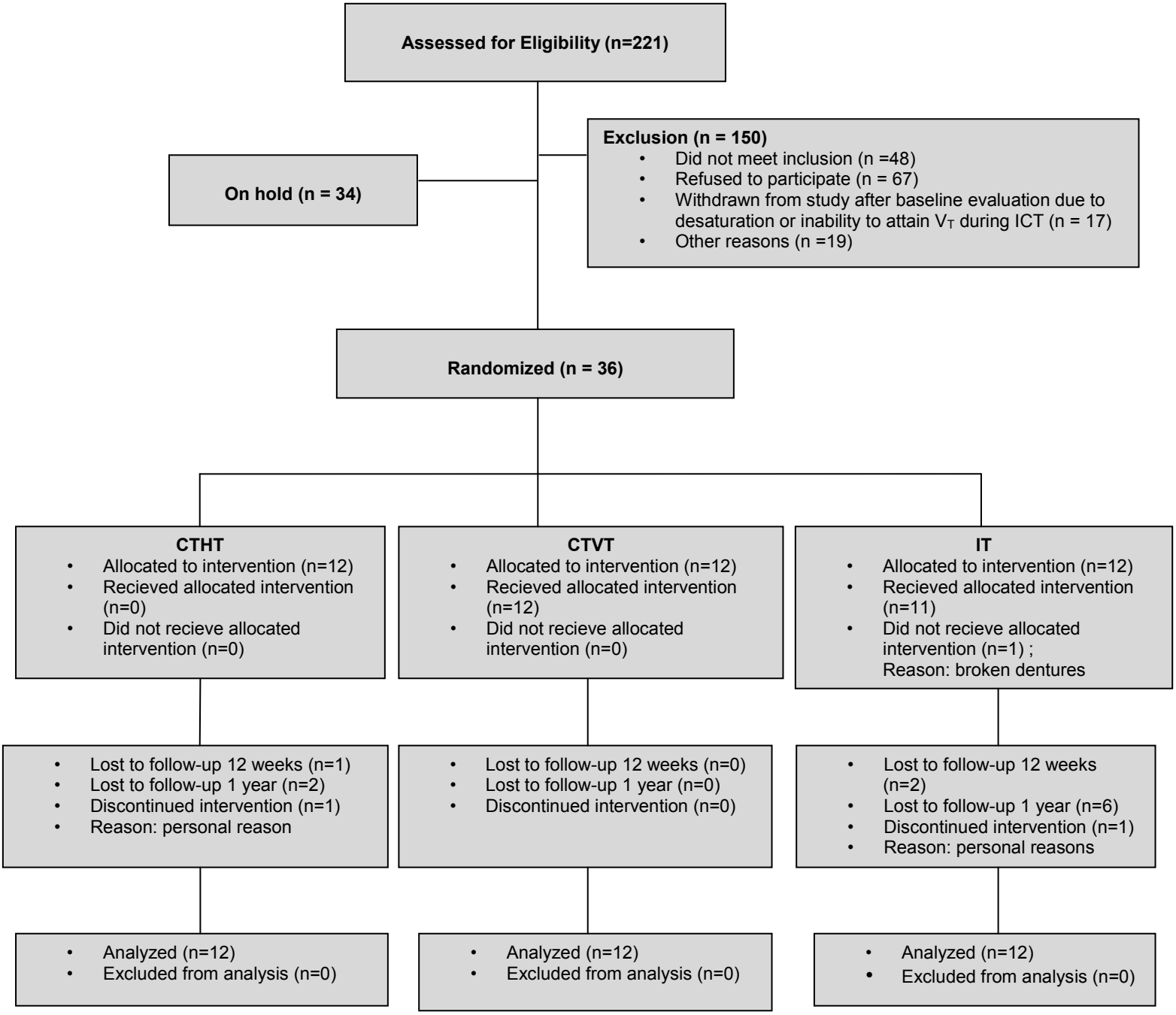
74. Potter WA, Olafsson S, Hyatt RE., *Ventilatory mechanics and expiratory flow limitation during exercise in patients with obstructive lung disease.* J Clin Invest, 1971. **50**(4): p. 910-9.
75. Serres I, Varray A, Vallet G, Micallef JP, Prefaut C, *Improved skeletal muscle performance after individualized exercise training in patients with chronic obstructive pulmonary disease.* J Cardiopulm Rehabil, 1997. **17**(4): p. 232-8.
76. Gimenez M, Servera E, Vergara P, Bach JR, Polu JM, *Endurance training in patients with chronic obstructive pulmonary disease: a comparison of high versus moderate intensity.* Arch Phys Med Rehabil, 2000. **81**(1): p. 102-9.
77. Vogiatzis I, Terzis G, Nanas S, et al., *Skeletal muscle adaptations to interval training in patients with advanced COPD.* Chest, 2005. **128**(6): p. 3838-45.
78. Puhan MA, Busching G., Schunemann HJ, VanOort E, Zaugg C, Frey M, *Interval versus continuous high-intensity exercise in chronic obstructive pulmonary disease: a randomized trial.* Annals of Internal Medicine, 2006. **145**: p. 816-825.
79. *American College of Sports Medicine Position Stand. The recommended quantity and quality of exercise for developing and maintaining cardiorespiratory and muscular fitness, and flexibility in healthy adults.* Med Sci Sports Exerc, 1998. **30**(6): p. 975-91.
80. Ringbaek TJ, Broendum E, Hemmingsen L, Lybeck K, Nielsen D, Andersen C, Lange P., *Rehabilitation of patients with chronic obstructive pulmonary disease. Exercise twice a week is not sufficient!* Respir Med, 2000. **94**(2): p. 150-4.
81. Engstrom CP, Persson LO, Larsson S, Sullivan M., *Long-term effects of a pulmonary rehabilitation programme in outpatients with chronic obstructive pulmonary disease: a randomized controlled study.* Scand J Rehabil Med, 1999. **31**(4): p. 207-13.
82. George J, Kong DC, Stewart K, *Adherence to disease management programs in patients with COPD.* Int J Chron Obstruct Pulmon Dis, 2007. **2**(3): p. 253-62.
83. Cameron C, *Patient compliance: recognition of factors involved and suggestions for promoting compliance with therapeutic regimens.* J Adv Nurs, 1996. **24**(2): p. 244-50.
84. Jay S, Litt IF, Durant RH, *Compliance with therapeutic regimens.* J Adolesc Health Care, 1984. **5**(2): p. 124-36.
85. Lutfey KE, Wishner WJ, *Beyond "compliance" is "adherence". Improving the prospect of diabetes care.* Diabetes Care, 1999. **22**(4): p. 635-9.
86. Gareth, *Canadian Centre for Activity and Aging's Get Fit for Active Living Program*, G.H. Living, Editor. 2004: Ontario.
87. *Physical activity levels of Canadian adults, 2007 to 2009*. Statistics Canada 2012 [cited 2012 August 5].
88. *ACSM's Resource Manual for Guidelines for Exercise Testing and Prescription*. Sixth edition ed. 2010: Lippincott Williams & Wilkins.
89. Arnold, *Adherence to pulmonary rehabilitation.* Respiratory Medicine, 2006. **100**: p. 1716-1723.
90. Sabit R, Griffith TL, Watkins AJ, Evans W, Bolton CE, Shale DJ, Lewis KE., *Predictors of poor attendance at an outpatient pulmonary rehabilitation programme.* Respir Med, 2008. **102**(6): p. 819-24.
91. Mador MJ, Krawza M, Alhajhusian A, Khan AI, Shaffer M, Kufel TJ., *Interval training versus continuous training in patients with chronic obstructive pulmonary disease.* Journal of Cardiopulmonary Rehabilitation and Prevention, 2009. **29**: p. 126-132.

92. Beauchamp MK, Nonoyama M, Goldstein RS, et al., *Interval versus continuous training in individuals with chronic obstructive pulmonary disease-a systemic review.* Thorax, 2009. **65**: p. 157-164.
93. Berry MJ, Rejeski W, Adair NE, Ettinger WH, Zaccaro DJ, Sevick MA, *A randomized, controlled trial comparing long-term and short-term exercise in patients with chronic obstructive pulmonary disease.* J Cardiopulm Rehabil, 2003. **23**(1): p. 60-8.
94. Donesky-Cuenco, *Adherence to a home-walking prescription in patients with chronic obstructive pulmonary disease.* Heart Lung, 2007. **36**: p. 348-363.
95. Soicher JE, Mayo NE, Gauvin L, Hanley JA, Bernard S, Maltais F, Bourbeau J, *Trajectories of endurance activity following pulmonary rehabilitation in COPD patients.* European Respiratory Journal, 2012. **39**(2): p. 272-278.
96. Nieuwenhuijsen ER, Zemper E, Miner KR, Epstein M, *Health behavior change models and theories: contributions to rehabilitation.* Disabil Rehabil, 2006. **28**(5): p. 245-56.
97. Lemmens KMM, Nieboer A, Huijsman R. , *Designing patient-related interventions in COPD care: Empirical test of a theoretical model.* Patient Education and Counseling, 2008. **72**: p. 223-231.
98. Kaplan RM, Atkins CJ, Reinsch S, *Specific efficacy expectations mediate exercise compliance in patients with COPD.* Health Psychology, 1984. **3**(3): p. 223-242.
99. Keller C, Fleury J, Gregor-Holt N, Thompson T, *Predictive ability of social cognitive theory in exercise research: an integrated literature review.* Online J Knowl Synth Nurs, 1999. **6**: p. 2.
100. Vincent E, Sewell L, Wagg K, Deacon S, Williams J, Singh S, *Measuring a Change in Self-Efficacy Following Pulmonary Rehabilitation* CHEST, 2011. **140**(6): p. 1534-1539.
101. Bentsen SB, Wentzel-Larsen T, Henrikson AH, Rokne B, Wahl AK, *Self-efficacy as a predictor of improvement in health status and overall quality of life in pulmonary rehabilitation - An exploratory study.* Patient education and couseling 2010. **81**: p. 5-13.
102. Scherer YK, Schmieder L, *The role of self-efficacy in assisting patients with chronic obstructive pulmonary disease to manage breathing difficulty.* Clin Nurs Res, 1996. **5**(3): p. 343-55.
103. Boutron I, Moher D, Altman DG, Schulz KF, Ravaud P, *Extending the CONSORT Statement to Randomized Trials of NOnpharmacologic Treatment: Explanantion and Elaboration.* Annal of Internal Medicine 2008. **148**: p. 295-309.
104. Mertens DJ, Shephard RJ, Kavanagh T., *Long-term exercise therapy for chronic obstructive lung disease.* Respiration, 1978. **35**(2): p. 96-107.
105. Wait J, *Cardiopulmonary Stress Testing A Review of Noninvasive Approaches.* CHEST, 1984. **90**: p. 504-510.
106. *Standards for the diagnosis and care of patients with chronic obstructive pulmonary disease. American Thoracic Society.* Am J Respir Crit Care Med, 1995. **152**(5 Pt 2): p. S77-121.
107. Guyatt GH, Pugsley SO, Sullivan MJ, et al., *Effect of encouragement on walking test performance.* Thorax, 1984. **39**(11): p. 818-22.
108. Quanjer PH, Tammeling GJ, Cotes JE, Pedersen OF, Peslin R, Yernault JC., *Lung volumes and forced ventilatory flows. Report Working Party Standardization of Lung Function Tests, European Community for Steel and Coal. Official*

Statement of the European Respiratory Society. Eur Respir J Suppl, 1993. **16**: p. 5-40.
109. Jones NL, Makrides L, Hitchcock C, Chypchar T, McCartney N., *Normal standards for an incremental progressive cycle ergometer test.* Am Rev Respir Dis, 1985. **131**(5): p. 700-8.
110. Borg GA, *Psychophysical bases of perceived exertion.* Med Sci Sports Exerc, 1982. **14**(5): p. 377-81.
111. Beaver WL, Wasserman K, Whipp BJ., *A new method for detecting anaerobic threshold by gas exchange.* J Appl Physiol, 1986. **60**(6): p. 2020-7.
112. *TechnoGym*. Wellness System [cited 01 March 2010]; Available from: http://www.technogymusa.com/_vti_g7_plsystem.aspx?rpstry=11902_.
113. Rizk AK, Wardini R, Chan-Thim E, Trutschnigg B, Forget A, Pepin V., *Using Continuous Data Tracking Technology to Study Exercise Adherence in Pulmonary Rhabilitation.* Journal of Visualized Experiments, 2013.
114. Guell R, Resqueti V, Sangenis M, Morante F, Martorell B, Casan P, Guyatt GH., *Impact of pulmonary rehabilitation on psychosocial morbidity in patients with severe COPD.* Chest, 2006. **129**(4): p. 899-904.
115. McAuley E, Jerome GJ, Marquez DX, Elavsky S, *Exercise SElf-Efficacy in Older Adults: Social, Affective, and Behavioral Influences.* Ann Behav Med, 2003. **25**(1): p. 1-7.
116. Stephens S, Feldman BM, Bradley N, et al. , *Feasibility and effectiveness of an aerobic exercise program in children with fibromyalgia: results of a randomized controlled pilot trial.* Arthritis Rheum, 2008. **59**(10): p. 1399-406.
117. Calfas KJ, Sallis JF, Olbenburg B, French M, *Mediators of change in physical activity following an intervention in primary care :Pace* Prevention Medicine, 1997. **26**(3): p. 297-304.
118. Fontaine KR, Shaw DF, *Effects of self-efficacy and dispositional optimism on adherence to step aerobic exercise classes.* Perceptual and Motor Skills 1995. **81**(1): p. 251-255.

APPENDIX

Appendix A. **Flow of participants through each stage**



Appendix B. Checklist of Items for Reporting Trials of Nonpharmacologic Treatments*

Section	Item	Standard Consort Description	Extension for Nonpharmacologic Trials	Page
Title and Abstract	1	How participants were allocated to interventions	In the abstract, description of the experimental treatment, comparator, care providers, centers, and blinding status	46, 47
Introduction				
Background	2	Scientific background and explanation of rationale		48-50
Methods				
Participants	3	Eligibility criteria for participants and the settings and locations where the data were collected	When applicable, eligibility criteria for centers and those performing the interventions	51-52
Intervention	4	Precise details of the interventions intended for each group and how and when they were actually administered	Precise details of both the experimental treatment and comparator	52-54
	4A		Description of the different components of the interventions and, when applicable, descriptions of the procedure for tailoring the interventions to individual participants	53, 54
	4B		Details of how the interventions were standardized	53, 54
	4C		Details of how adherence of care providers with the protocol was assessed or enhanced	53, 54
Objectives	5	Specific objectives and hypotheses		50
Outcomes	6	Clearly defined primary and secondary outcome measures and, when applicable, any methods used to enhance the quality of measurements		53-57
Sample size	7	How sample size was determined and, when applicable, explanation of any interim analyses and stopping rules	When applicable, details of whether and how the clustering by care providers or centers was addressed	59
Randomization-sequence generation	8	Method used to generate the random allocation sequence, including details of any restriction (e.g., blocking, stratification)	When applicable, how care providers were allocated to each trial group	52
Allocation concealment	9	Method used to implement the random allocation sequence (e.g., numbered containers or central telephone), clarifying whether the sequence was concealed until interventions were assigned		52
Implementation	10	Who generated the allocation sequence, who enrolled participants, and who assigned participants to their groups		52
Blinding (masking)	11	Whether or not participants, those administering the interventions, and those assessing the outcomes were blinded to group assignment	Whether or not those administering co-interventions were blinded to group assignment	51
Statistical methods	12	Statistical methods used to compare groups for primary outcome(s); methods for additional analyses, such as subgroup analyses and adjusted analyses	When applicable, details of whether and how the clustering by care providers or centers was addressed	58, 59

Results				
Participant flow	13	Flow of participants through each stage (a diagram is strongly recommended) specifically, for each group, report the numbers of participants randomly assigned, receiving intended treatment, completing the study protocol, and analyzed for the primary outcome; describe protocol deviations from study as planned, together with reasons	The number of care providers or centers performing the intervention in each group and the number of patients treated by each care provider or in each center	85 Appendix A
Implementation of intervention	New item		Details of the experimental treatment and comparator as they were implemented	53
Recruitment	14	Dates defining the periods of recruitment and follow-up		60
Baseline data	15	Baseline demographic and clinical characteristics of each group	When applicable, a description of care providers (case volume, qualification, expertise, etc.) and centers (volume) in each group	60, 61
Numbers analyzed	16	Number of participants (denominator) in each group included in each analysis and whether analysis was by "intention-to-treat"; state the results in absolute numbers when feasible (e.g., 10/20, not 50%)		85 Appendix A
Outcomes and estimation	17	For each primary and secondary outcome, a summary of results for each group and the estimated effect size and its precision (e.g., 95% confidence interval)		60-62
Ancillary analyses	18	Address multiplicity by reporting any other analyses performed, including subgroup analyses and adjusted analyses, indicating those prespecified and those exploratory		61, 62
Adverse events	19	All important adverse events or side effects in each intervention group		62

Discussion				
Interpretation	20	Interpretation of the results, taking into account study hypotheses, sources of potential bias or imprecision, and the dangers associated with multiplicity of analyses and outcomes	In addition, take into account the choice of the comparator, lack of or partial blinding, and unequal expertise of care providers or centers in each group	66, 67
Generalizability	21	Generalizability (external validity) of the trial findings	Generalizability (external validity) of the trial findings according to the intervention, comparators, patients, and care providers and centers involved in the trial	62
Overall evidence	22	General interpretation of the results in the context of current evidence		62-66

* Additions or modifications to the CONSORT checklist. CONSORT Consolidated Standards of Reporting Trials. † This item anticipates a planned revision in the next version of the standard CONSORT checklist.

Appendix C. Contraindications for Cardiopulmonary Exercise Testing Based on the American Thoracic Society

TABLE 8. ABSOLUTE AND RELATIVE CONTRAINDICATIONS FOR CARDIOPULMONARY EXERCISE TESTING

Absolute	Relative
Acute myocardial infarction (3–5 days)	Left main coronary stenosis or its equivalent
Unstable angina	Moderate stenotic valvular heart disease
Uncontrolled arrhythmias causing symptoms or hemodynamic compromise	Severe untreated arterial hypertension at rest (> 200 mm Hg systolic, > 120 mm Hg diastolic)
Syncope	Tachyarrhythmias or bradyarrhythmias
Active endocarditis	High-degree atrioventricular block
Acute myocarditis or pericarditis	Hypertrophic cardiomyopathy
Symptomatic severe aortic stenosis	Significant pulmonary hypertension
Uncontrolled heart failure	Advanced or complicated pregnancy
Acute pulmonary embolus or pulmonary infarction	Electrolyte abnormalities
Thrombosis of lower extremities	Orthopedic impairment that compromises exercise performance
Suspected dissecting aneurysm	
Uncontrolled asthma	
Pulmonary edema	
Room air desaturation at rest ≤ 85%*	
Respiratory failure	
Acute noncardiopulmonary disorder that may affect exercise performance or be aggravated by exercise (i.e. infection, renal failure, thyrotoxicosis)	
Mental impairment leading to inability to cooperate	

Adapted by permission from References 10, 43, and 295.
* Exercise patient with supplemental O_2.

HRN Health Respiratory Network of the FRSQ

Pulmonary Rehabilitation Research Infrastructure
COPD Reseach Axis

EXERCISE SELF-EFFICACY QUESTIONNAIRE
(pre-rehabilitation)

Centre [ ] Project [ ] Subject [ ][ ] Visit [1]

Date [ ][ ][ ] yyyy-mmm-dd Time at the beginning of the questionnaire [:] on 24:00

Current or recent exacerbation

The subject currently has or had an exacerbation in the past 4 weeks? No ☐ Yes ☐

This questionnaire assesses your confidence or belief in your ability to perform a specific activity, using the scale below from 0 % to 100 % in intervals of 10 %.

For example, if you have complete confidence that you could exercise three times per week without quitting for the next 2 weeks, you would choose 100 %. However, if you had no confidence at all that you could exercise without quitting for the next 2 weeks, you would choose 0 %.

Please remember to answer honestly and accurately. There are no right or wrong answers.
MARK YOUR ANSWER BY INDICATING A PERCENTAGE (%) WITH A CHECK MARK (√)

Exercise - Compliance

	Not at all confident					Moderately confident					Highly confident
	0 %	10 %	20 %	30 %	40 %	50 %	60 %	70 %	80 %	90 %	100 %
1. I am able to exercise 3 times per week in the pulmonary rehabilitation program, without quitting, for the ***first week*** of the exercise program.											
2. I am able to exercise 3 times per week in the pulmonary rehabilitation program, without quitting, for the first ***2 weeks*** of the exercise program.											
3. I am able to exercise 3 times per week in the pulmonary rehabilitation program, without quitting, for the first ***4 weeks*** of the exercise program.											
4. I am able to exercise 3 times per week in the pulmonary rehabilitation program, without quitting, for the first ***6 weeks*** of the exercise program.											
5. I am able to exercise 3 times per week in the pulmonary rehabilitation program, without quitting, for the ***full 6 weeks*** of the exercise program. **(For a 6-week exercise program)**											

EXERCISE SELF-EFFICACY QUESTIONNAIRE
(pre-rehabilitation)

Centre [ ] [ ] [ ] Project [ ] [ ] [ ] Subject [ ] [ ] [ ] [ ] [ ] [ ] Visit [1]

	Not at all confident					Moderately confident					Highly confident
	0 %	10 %	20 %	30 %	40 %	50 %	60 %	70 %	80 %	90 %	100 %
6. I am able to exercise 3 times per week in the pulmonary rehabilitation program, without quitting, for the first ***8 weeks*** of the exercise program. **(For a 12-week exercise program)**											
7. I am able to exercise 3 times per week in the pulmonary rehabilitation program, without quitting, for the ***full 8 weeks*** of the exercise program. **(For an 8-week exercise program)**											
8. I am able to exercise 3 times per week in the pulmonary rehabilitation program, without quitting, for the ***full 12 weeks*** of the exercise program. **(For a 12-week exercise program)**											

Exercise - Endurance

	Not at all confident					Moderately confident					Highly confident
	0 %	10 %	20 %	30 %	40 %	50 %	60 %	70 %	80 %	90 %	100 %
1. I am able to do exercise for endurance (stationary bicycle or treadmill) at moderate intensity for ***5*** **minutes** without stopping.											
2. I am able to do exercise for endurance (stationary bicycle or treadmill) at moderate intensity for ***10*** **minutes** without stopping.											
3. I am able to do exercise for endurance (stationary bicycle or treadmill) at moderate intensity for ***20*** **minutes** without stopping.											
4. I am able to do exercise for endurance (stationary bicycle or treadmill) at moderate intensity for ***30*** **minutes** without stopping.											
5. I am able to do exercise for endurance (stationary bicycle or treadmill) at moderate intensity for ***40*** **minutes** without stopping.											

EXERCISE SELF-EFFICACY QUESTIONNAIRE

(pre-rehabilitation)

Centre |__|__| Project |__|__| Subject |__|__|__|__| Visit |1|

Exercise – Muscle Strength

	Not at all confident					Moderately confident					Highly confident
	0 %	10 %	20 %	30 %	40 %	50 %	60 %	70 %	80 %	90 %	100 %
1. I am able to do exercise for muscle strength (weights or Theraband) at moderate intensity for ***5 repetitions***.											
2. I am able to do exercise for muscle strength (weights or Theraband) at moderate intensity for ***10 repetitions***.											
3. I am able to do exercise for muscle strength (weights or Theraband) at moderate intensity for ***15 repetitions***.											
4. I am able to do exercise for muscle strength (weights or Theraband) at moderate intensity for ***20 repetitions***.											
5. I am able to do exercise for muscle strength (weights or Theraband) at moderate intensity for ***30 repetitions***.											

Please indicate <u>the degree to which you are confident that you could exercise 3 times per week in the pulmonary rehabilitation program</u> during the coming months in the event that any of the following circumstances were to occur. For example, in question number 1 if you have <u>complete confidence</u> that you could exercise even if « the weather was very bad », you would circle 100 %. If , however, you had <u>no confidence at all</u> that you could exercise, you would circle 0 %.

Exercise - Barriers

I believe that I could exercise 3 times per week in the pulmonary rehabilitation program <u>even if</u> :	Not at all confident					Moderately confident					Highly confident
	0 %	10 %	20 %	30 %	40 %	50 %	60 %	70 %	80 %	90 %	100 %
1. The weather was very bad (hot, humid, rainy, cold).											
2. I was bored by the program or activity.											
3. I was on vacation.											

EXERCISE SELF-EFFICACY QUESTIONNAIRE

(pre-rehabilitation)

Centre |__|__|__| Project |__|__|__| Subject |__|__|__|__|__|__| Visit 1

I believe that I could exercise 3 times per week in the pulmonary rehabilitation program **even if** :	Not at all confident 0 %	10 %	20 %	30 %	40 %	Moderately confident 50 %	60 %	70 %	80 %	90 %	Highly confident 100 %
4. I was not interested in the activity.											
5. I felt pain or discomfort when exercising.											
6. I experienced shortness of breath when exercising.											
7. I did not feel compatible with the exercise instructor or the other program participants.											
8. It was not fun or enjoyable.											
9. It became difficult to get to the exercise location.											
10. I didn't like the particular activity program that I was involved in.											
11. I was the caregiver for a sick family member.											
12. I had work or family obligations.											
13. I had an exacerbation of my lung disease, or I had another illness.											

Time at the end of the questionnaire |__|__| : |__|__| on 24:00