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PAR
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LA DÉPRESSION DANS LA MALADIE PULMONAIRE OBSTRUCTIVE
CHRONIQUE PRÉDIT-ELLE LA FRÉQUENTATION ET LA CONFORMITÉ
À L'EXERCICE PENDANT LA RÉÉDUCATION RÉSPIRATOIRE, ET LE
NIVEAU D'EXERCICE MAINTENU 9 MOIS PLUS TARD ?

DOES DEPRESSION IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE
PREDICT ATTENDANCE AND EXERCISE COMPLIANCE DURING
PULMONARY REHABILITATION, AND EXERCISE LEVELS
MAINTAINED 9 MONTHS LATER

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Sommaire

La maladie pulmonaire obstructive chronique (MPOC) est une maladie respiratoire irréversible, évolutive et très fréquente qui fait peser un lourd fardeau sur le système de santé, les patients et leurs proches. La réadaptation pulmonaire (RP) est efficace pour réduire la dyspnée et l'utilisation des ressources en soins de santé et pour améliorer la capacité physique et la qualité de vie des patients. L'entraînement physique est la pierre angulaire de la RP, mais elle n'est bénéfique que si les patients 1) assistent aux séances d'exercice, 2) se conforment à l'intensité des exercices prescrits et 3) maintiennent l'exercice physique régulier après la RP. La dépression comorbide est disproportionnée dans la MPOC et s'est révélée être un facteur prédictif de « mauvaise » fréquentation de la RP, et d'abandon de la pratique physique régulière après le programme. À notre connaissance, aucune étude ne s'est intéressée aux prédicteurs de conformité à l'intensité d'exercice prescrit pendant la RP et seules quelques études ont explorées les facteurs associés au maintien de l'exercice après la RP. L'objectif principal de cette étude consistait à examiner dans quelle mesure les symptômes dépressifs à l'entrée de la RP permettent de prédire 1) la présence aux séances de RP, 2) le respect de l'intensité (conformité) des exercices d'endurance prescrits pendant la RP, et 3) le niveau d'exercice physique maintenu 9 mois après la RP. Un deuxième objectif consistait à explorer d'autres variables susceptibles d'être associées à ces paramètres. Trente-six patients (64 % de femmes) atteints de la MPOC stable, modérée à sévère, ont été inscrits à un programme de RP de 12 semaines comportant 36 séances d'exercice physique supervisé. À l'entrée du RP les patients ont rempli l'Inventaire de Dépression de Beck (BDI-II, le prédicteur principal) et

le formulaire C de l'Échelle du locus de contrôle sur la santé (LCS), et ont subi des tests de fonction pulmonaire et une épreuve d'effort progressif à vélo (pour déterminer l'intensité de l'exercice pour la RP). Ensuite, ils ont été répartis de façon aléatoire dans trois groupes à intensité d'exercice différente. La fréquentation de la RP était définie comme le pourcentage de séances suivies; la conformité, comme la durée d'entraînement pratiquée à la fréquence cardiaque cible; et le maintien de l'exercice physique régulier comme le niveau d'exercice fait au cours d'une semaine 9 mois après la RP (enregistré dans un journal d'activité physique et calculé en équivalents métaboliques de l'effort [MET] minutes). La médiane (écart interquartile ou IQR) du score au BDI-II était de 8,5 points (6-13), la médiane (IQR) du taux de la fréquentation aux séances était de 83% (67-94), la médiane du taux de compliance à l'intensité d'exercice était de 94% (71-99), et la médiane du nombre de minutes MET après la RP était de 706 (445-1146). Les analyses de régression linéaire ne montrent pas de relation entre les symptômes dépressifs pré-RP et la fréquentation des séances de la RP ($\beta = 0,12$; $p = 0,478$). Par-contre, ils étaient associés à la conformité à l'intensité de l'exercice physique pendant la RP ($\beta = -0,40$; $p = 0,047$), et à la poursuite de la pratique d'un exercice physique régulier après la RP ($\beta = -0,50$; $p = 0,004$). Les analyses étaient ajustées pour des covariables prédéfinies. Les analyses exploratoires ont révélé que certaines variables supplémentaires (y compris LCS) étaient associées aux issues mesurées. Les résultats de cette étude montrent que même les niveaux de dépression sous-cliniques pourraient jouer un rôle important dans la compliance aux programme de réentraînement, et au maintien d'un style de vie actif après la période de réadaptation. Cela a des implications pour améliorer le dépistage des

« mauvais » résultats dans la RP et pour l'élaboration d'interventions ciblées pour améliorer les bénéfices pour la santé découlant de la réadaptation pour la MPOC.

Mots clés : Maladie pulmonaire obstructive chronique, MPOC, réadaptation pulmonaire, dépression, locus de contrôle sur la santé, prédicteurs, conformité, maintien.

Abstract

Chronic obstructive pulmonary disease (COPD) is an irreversible, progressive, and highly prevalent respiratory illness that poses a great burden on the healthcare system, patients, and their families. Pulmonary rehabilitation (PR) is effective in reducing dyspnea and health care resource utilization, and increasing exercise capacity and quality of life. Exercise training is the cornerstone of PR but is only beneficial if patients 1) attend sessions, 2) comply with the prescribed exercise regimen, and 3) maintain regular exercise after supervised PR ends. Comorbid depression is disproportionately high in COPD and has been found to predict poor attendance at PR and low levels of exercise maintained afterwards. To our knowledge, no study has investigated predictors of exercise compliance during PR, and only a few studies have examined predictors of exercise maintenance post PR. The primary objective of this study was to examine how much baseline depressive symptomatology can predict 1) PR attendance, 2) PR exercise compliance, and 3) levels of exercise maintained at 9-months post PR. A secondary, exploratory objective was to identify additional variables that might also have significant associations with these outcomes. Thirty-six patients (64% female) with stable COPD were enrolled in a 12-week 36-session supervised exercise intervention in the context of a PR program. Patients underwent evaluations at entry to PR which included the Beck Depression Inventory (BDI-II, the main predictor), the Multidimensional Health Locus of Control (HLC) Scale Form-C, pulmonary function tests, and an incremental cycling test (to determine the exercise intensity prescription). Patients were randomized to one of three groups of varying exercise intensity. Attendance was defined as the percent of total

sessions attended, compliance as the percent of endurance training time exercising at a prescribed target heart rate, and post-PR exercise as the total exercise performed over a 7-day period recorded in a physical activity diary and calculated as metabolic equivalent of task (MET) minutes. Median (IQR) baseline BDI-II was 8.5 (6-13), median (IQR) percent attendance was 83 (67-94), median (IQR) percent exercise compliance was 94 (71-99), and median (IQR) exercise MET-minutes post PR was 706 (445-1146). In multiple regression analyses, baseline depressive symptomatology did not emerge as a significant independent predictor of PR attendance ($\beta = .12, p = .478$), but was a significant predictor of PR exercise compliance ($\beta = -.40, p = .047$), and of exercise maintained post PR ($\beta = -.50, p = .004$), with adjustment for a-priori defined covariates. Secondary exploratory analyses revealed that certain additional variables (including HLC) had associations with particular outcomes. The findings suggest that even subclinical levels of depression can predict PR exercise compliance and post-PR exercise levels. This has implications for improving screening for, and understanding of, poor outcomes in PR and for developing targeted interventions to optimize the health benefits that can be derived during and after PR for COPD.

Key words: Adherence, chronic obstructive pulmonary disease, COPD, depression, pulmonary rehabilitation, health locus of control, predictors.

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Acronyms

bBDI-II: baseline Beck Depression Inventory, revised

BCa: bias-corrected and accelerated

BDI-II: Beck Depression Inventory, revised

BMI: body mass index

bSmoking: baseline smoking

CI: confidence interval

CO₂: carbon dioxide

COPD: chronic obstructive pulmonary disease

CTHi: constant training at high intensity

CTVT: constant training at the ventilatory threshold

ESWT: endurance shuttle walk test

FEV₁: forced expiratory volume in the first second

FEV₁ %: forced expiratory volume in the first second percent of predicted normal value

FEV₁/FVC: Ratio of forced expiratory volume in the first second divided by forced vital capacity

FVC: forced vital capacity

GOLD: Global Initiative for Chronic Obstructive Lung Disease

HLC: health locus of control

HSCM: Hôpital du Sacré-Coeur de Montréal

IT: interval training

IQR: interquartile range

MET: metabolic equivalent of task

NETT: National Emphysema Treatment Trial

O₂: oxygen

PR: pulmonary rehabilitation

RCT: randomized controlled trial

SD: standard deviation

THR: target heart rate

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Introduction

Decades ago, chronic illnesses surpassed acute medical conditions, such as infectious diseases and injuries, as the major cause of death and disability in developed countries, due mainly to improved living conditions and nutrition and to medical advances such as vaccines and antibiotics (Cohen, 2000). Unfortunately, rates of chronic illness now continue to rise largely as a result of increased longevity and widespread lifestyle and behavioral factors (e.g., smoking, unhealthy diet, and physical inactivity) (OECD, 2011; Ward, Schiller, & Goodman, 2014). It is estimated that 3 out of every 5 Canadians over 20 years old now have at least one chronic medical condition and that these account for 67 % of all direct health care costs (Elmslie, 2012). The effective management of chronic illness is so different from that of acute illness/injury that it has prompted a paradigm shift in health care for both providers and patients: The focus has shifted from *curing* illness to its *management* (Holman & Lorig, 2004). Patients are no longer passive recipients of care provided by experts; instead they work in partnership with healthcare professionals and play an active role in their health care by acquiring knowledge and adopting behaviors that support health and diminish symptoms, and by abandoning other behaviors that are detrimental. As a result, the importance and application of psychology and behavioral science in physical health is evolving to help meet the challenges of adopting and maintaining behaviors that enhance health in chronic illness.

Chronic obstructive pulmonary disease (COPD) is an irreversible and progressive illness characterized by expiratory airflow obstruction, increasing shortness of breath, and respiratory tract infections (O'Donnell et al., 2007), that limits activity levels and reduces quality of life. It is a leading cause of hospitalization and mortality, and its prevalence is increasing (Canadian Institute for Health Information, 2008; World Health Organization, 2008). As such, it poses a tremendous financial and humanistic burden on society, the healthcare system, patients, and their families.

Effective management of COPD involves a multi-faceted approach, which includes early diagnosis, pharmacotherapy, and changes in lifestyle and behavior (e.g., quitting smoking) on the part of the patient, that support health (Celli et al., 2004). However, pulmonary rehabilitation (PR) is firmly established as the most effective therapeutic strategy for decreasing dyspnea, increasing functional capacity, improving quality of life, and reducing healthcare utilization (including hospitalizations) when symptoms persist despite pharmacotherapy (McCarthy et al., 2015). PR is comprised of patient education and the acquisition of self-management skills, but it is the exercise training component that is considered the cornerstone from which most of the above-mentioned benefits are derived (Global Initiative for Chronic Obstructive Lung Disease [GOLD], 2016). Although PR has been shown to be highly beneficial, it can be challenging for patients to engage in due to their COPD symptoms, such as dyspnea and fatigue, as well as the high prevalence of comorbidities (Chatila, Thomashow, Minai, Criner, & Make, 2008).

In this study, exercise “adherence” during PR is comprised of two distinct yet essential components: *attendance* at exercise sessions and *compliance* with prescribed aerobic exercise intensity. Attendance is defined as being present at PR exercise sessions. Exercise compliance is defined as performing physical exercise at a level of intensity sufficient to achieve and sustain a target heart rate that was prescribed for PR for a specific duration. Our measure of PR exercise *adherence* is therefore the product of PR attendance and PR exercise compliance (i.e., percent of total PR sessions attended multiplied by the percent of total exercise time during which exercise was performed at the prescribed target heart rate). Continuing regular exercise after termination of supervised PR is referred to as *maintenance* in this study and is quantified as the total volume of exercise performed over 7 consecutive days at follow-up (9 months post PR).

Levels of uptake and attendance¹ at exercise-based PR, as well as amount of exercise maintained post PR, have been found to be fairly poor (Cindy Ng, Mackney, Jenkins, & Hill, 2012; Hogg et al., 2012; Soicher et al., 2012). This has prompted investigation into their determinants. A wide variety of environmental, demographic, medical, personal, and psychological factors have been identified, but findings are often inconsistent from one study to the next (Cassidy, Turnbull, Gardani, & Kirkwood, 2014; Keating, Lee, & Holland, 2011).

¹ In previous studies, the term “adherence” has been used (perhaps misused) by authors to denote what is in fact attendance only (expressed as a percentage of the total number of PR sessions at which participants are present).

However, depression, both clinical and subclinical,² has emerged repeatedly as a robust predictor of PR attendance and post-PR exercise maintenance (Roshanaei-Moghaddam, Katon, & Russo, 2009; Thorpe, Johnston, & Kumar, 2012). This is particularly relevant because clinically significant symptoms of depression have been found to be disproportionately high in COPD (as much as 40 % prevalence) (Yohannes, Willgoss, Baldwin, & Connolly, 2010) compared to the general population of older community-dwelling adults (15 % prevalence) (Blazer, 2003). Therefore, understanding depression as a potential predictor of attendance and exercise compliance during PR, and of exercise levels maintained post PR may be particularly important for optimizing the treatment and management of COPD.

A weakness of previous studies on predictors of so called exercise “adherence” during PR is that, to our knowledge, they have only measured attendance at PR sessions but not also compliance with the exercise prescribed for PR. This leaves an important gap in the literature. Reporting on attendance at PR exercise sessions is an inadequate measure of adherence, as it does not provide information on the extent to which participants actually meet the exercise targets determined to be associated with health and functional

² *Clinical depression* is defined as meeting the criteria set forth in the DSM-IV-TR (American Psychiatric Association, 2000) for a diagnosis of major depressive disorder, which is the presence of at least five of the following nine symptoms that must include at least one of the first two: depressed mood, loss of interest or pleasure in most activities, significant change in appetite or weight, hypersomnia or insomnia, psychomotor retardation or agitation, loss of energy, feeling worthless or guilty, difficulty concentrating, and recurrent thoughts of death or suicide. *Subclinical* (or *clinically significant symptoms of*) *depression* impacts functioning significantly and causes suffering, but is less severe and does not meet the criteria for clinical depression.

benefits. PR “adherence” studies must assess both attendance *and* exercise compliance during PR, and ideally post-PR exercise, as baseline levels of depressive symptoms may differentially predict each of these outcomes. This study seeks to help fill this gap in the PR literature for COPD.

Given the importance of patients’ active involvement in managing their COPD, health locus of control (HLC) is a variable of interest included in this study’s secondary analyses. Health locus of control is a construct from social cognitive theory (Bandura, 1986) pertaining to people’s beliefs about where the responsibility and control for their health resides. There are two distinct HLC orientations: *internal* is the belief that control and responsibility resides within oneself, and *external* is the belief that factors outside oneself (chance, doctors, or other people) are responsible (Wallston, Stein, & Smith, 1994; Wallston, Wallston, & DeVellis, 1978). Although HLC has been shown to be relevant for a variety of health-related and safety behaviors across a wide range of illnesses and situations that pose risks to one’s health/safety, it has not to our knowledge been studied previously in the context of PR or COPD.

In light of the above, the primary objective of this thesis is to investigate the extent to which baseline depressive symptomatology can predict PR attendance, PR exercise compliance (collectively defined as “adherence”), and levels of exercise maintained 9 months after PR. A secondary exploratory objective is to identify additional potential predictors (such as health locus of control) of each outcome. The results may contribute

to a better understanding of what factors are related to optimally benefitting from an exercise-based PR program for COPD and to developing interventions and resources that effectively target them.

This thesis is divided into five main sections. The first section describes COPD and exercise-based PR as a key component of its management. Suboptimal levels of physical activity/exercise in the general adult population and in the context of PR for COPD specifically are presented and factors found to be linked to these are discussed. The prevalence and importance of depressive symptomatology is highlighted. The first section ends with a presentation of this study's objectives and research hypothesis. Next, the methods section describes the design of this study, its participants, procedure, variables of interest and their measures, and the statistical analyses employed. The results from our statistical analyses are presented in the third section. The fourth section is a discussion of the findings and how they pertain to the objectives, hypotheses, and previous findings reported in the literature. This study's strengths and limitations are described and several suggestions for future research are proposed. In the fifth and final section, the conclusions and clinical implications are presented.

Theoretical Context

COPD: Definition, Causes, Prevalence, and Burden

COPD refers to a combination of respiratory disorders resulting in progressive irreversible airflow obstruction, lung hyperinflation, and increasingly frequent respiratory tract infections O'Donnell et al. (2007). Inflammatory processes cause narrowing of small airways and destruction of alveoli (air sacs in the lining of the lungs) resulting in loss of lung tissue elasticity and chronic expiratory airflow limitation (Celli et al., 2004). Prominent symptoms of COPD include progressive shortness of breath (dyspnea), especially upon physical exertion, coughing, and excessive sputum production. Tobacco smoking is the principle cause, accounting for 80-90 % of cases in North America (Office of the Surgeon General, 2004; Public Health Agency of Canada, 2007). Other risk factors include air pollution, occupational exposure to dust and fumes, respiratory infections, and a genetic deficiency of alpha 1-antitrypsin (Global Initiative for Chronic Obstructive Lung Disease [GOLD], 2016).

COPD is currently the world's (including Canada) fourth leading cause of mortality (Statistics Canada, 2008; World Health Organization, 2008) and as the population ages, morbidity and mortality rates are expected to continue to rise such that by 2020, COPD is expected to become the third leading cause of death (Mittmann et al., 2008; Murray & Lopez, 1997; Public Health Agency of Canada, 2007). Currently a leading cause of hospital admission in Canada, COPD was recently reported to have the highest rate of

readmission of all major chronic illnesses: following a first hospital admission, the 12-month readmission rate was 18 %, while 14 % of patients were admitted three or more times (Canadian Institute for Health Information, 2008). As such, COPD represents a substantial burden on the healthcare system. In a recent systematic review Dang-Tan, Ismaila, Zhang, Zarotsky, and Bernauer (2015) estimated that the total annual cost of COPD in Canada, including costs of healthcare and work/productivity losses, was 5.3 to 9 billion 2012 Canadian dollars. This was based on the estimated prevalence of 1.4 million Canadians with COPD, which most likely underestimates the real prevalence due to under diagnosis (J. Evans, Chen, Camp, Bowie, & McRae, 2014).

Identifying ways to improve treatment for, management of, and quality of life in COPD is vital to reducing its substantial economic and humanistic burden on society, patients, and their families.

Pulmonary Rehabilitation: The Standard of Care for COPD

Effective management of COPD requires a multifaceted approach comprised of medical diagnosis and monitoring, pharmacologic treatment, and lifestyle changes in which patients play an active role in adopting and maintaining health behaviors. Now a consensus among the Canadian and American Thoracic Societies, the European Respiratory Society, and the World Health Organization, pulmonary rehabilitation (PR) is considered a cornerstone in the best management of stable COPD when symptoms persist despite pharmacotherapy (Marciniuk et al., 2010) and is “the most effective

therapeutic strategy for improving dyspnea, exercise endurance and quality of life” (O'Donnell et al., 2007, p. 19B) as well as reducing health care utilization. There is also convincing evidence that undergoing PR soon after an acute exacerbation of COPD improves physical endurance, and reduces hospital readmissions and mortality compared to usual care (Puhan et al., 2011). PR is a grade-A evidence-based treatment whose main goals are to reduce symptoms, increase tolerance for physical activity and engagement in activities of daily living, and enhance quality of life (Nici et al., 2006; Ries et al., 2007). The American Thoracic Society and European Respiratory Society (Spruit et al., 2013) have defined PR as:

A comprehensive intervention based on a thorough patient assessment followed by patient-tailored therapies, which include, but are not limited to, exercise training, education, and behavior change, designed to improve the physical and psychological condition of people with chronic respiratory disease and to promote the long-term adherence of health-enhancing behaviors. (p. e16)

The above-mentioned benefits of PR are strongly established (McCarthy et al., 2015) and are attributed mainly to the physical exercise component (GOLD, 2016), the foundation of which is endurance (aerobic) training, but with additional benefit derived from resistance training (Gosselink et al., 2011; Marciniuk et al., 2010). This is because exercise helps reverse the systemic (extra-pulmonary) effects of COPD – mainly skeletal muscle dysfunction/wasting – which results in loss of strength and endurance (Troosters, Gosselink, Janssens, & Decramer, 2010). Therefore, the Canadian Thoracic Society strongly recommends that all patients with moderate to very severe COPD have access to and undergo PR (Marciniuk et al., 2010), while R. A. Evans, Singh, Collier, Williams,

and Morgan (2009) found that all people with COPD can benefit regardless of disease severity.

Endurance Training in PR: How Often, How Intense, and for How Long?

PR exercise guidelines recommend that participants engage in continuous endurance training (usually walking, cycling, or treadmill) for at least 20 to 30 minutes three to five times per week at a high intensity; i.e., 60–80 % of maximal work rate (Garvey, 2016). This is the amount required to improve cardiac function and produce the anabolic stimulus that can reverse skeletal muscle dysfunction by improving the oxidative capacity of muscle (Vogiatzis et al., 2007), which helps reduce dyspnea and fatigue, and increase functional capacity. However, a large proportion of people with COPD are unable to achieve and sustain high intensity training because of severe symptoms and limited functional capacity (Maltais et al., 1997). Therefore, alternative approaches to exercise, such as interval training (IT) and training at the ventilatory threshold have been recommended and shown to be effective (Beauchamp et al., 2010; Rochester, 2003). Exercising at the ventilatory threshold is a more moderate level of training that is better tolerated, especially by people with more severe COPD, than exercising at higher intensities. The ventilatory threshold is the point above which the rate of respiration starts to increase more rapidly than the level of oxygen consumption. When people exercise above their ventilatory threshold, they usually experience the sensation of not being able to breathe fast or deep enough to satisfy the body's demand for oxygen. IT (interval training) is comprised of segments of high-intensity exercise that alternate with periods of

low intensity or rest, and is also better tolerated than continuous training by people with more advanced COPD. IT has been shown to be as effective as continuous training for improving exercise capacity and health-related quality of life when the total volume of work performed is equal to that recommended for continuous training (Beauchamp et al., 2010; Vogiatzis, Nanas, & Roussos, 2002). The recommended PR program duration is \geq 8 weeks, with some evidence suggesting that longer programs may result in higher levels of physical activity being maintained after PR program termination (Garvey et al., 2016).

The Widespread Problem of Inadequate Physical Activity/Exercise

The terms *physical activity* and *exercise* are often used interchangeably in the literature but actually represent distinct behaviors and objectives. For the present paper, physical activity is defined as “any bodily movement produced by skeletal muscles that results in energy expenditure. . . . Physical activity in daily life can be categorized into occupational, sports, conditioning, household, or other activities” (Casperson, Powell, & Christenson, 1985, p. 126). In contrast, exercise is a “subset of physical activity that is planned, structured, and repetitive and has as a final or an intermediate objective the improvement or maintenance of physical fitness” (Casperson et al., 1985, p. 126).

Achieving and maintaining levels of physical activity and exercise sufficient for the maintenance of good health is a formidable challenge across all age groups, but especially for older adults with chronic illness. A recent survey by Colley et al. (2011) found that only 15.4 % of adults in the general Canadian population were achieving and maintaining

the weekly amount of physical activity recommended by the Canadian Society for Exercise Physiology (2012) and World Health Organization (2010), which is 150-minutes of moderate-intensity aerobic physical activity per week in addition to the normal activities of daily living. The percentage of older adults with COPD meeting this recommendation is likely much lower. For example, a study comparing everyday physical activity levels in patients with COPD to those of healthy age-matched controls found that the patients engaged in 41 % less time walking, 35 % less time standing, and 25 % lower movement intensity when they did walk (Pitta et al., 2005). It follows that the low levels of physical activity, and factors underlying this, impact levels of participation in exercise-based PR.

Rates of PR “Uptake” and Attendance, and Maintenance of Physical Activity Post-PR

Several studies show that many participants do not fully benefit from PR due to absenteeism or dropout during the program, and an even greater proportion do not maintain adequate levels of physical activity afterwards. In a study of seven PR programs, only 73 % of the eligible 1114 COPD patients referred for PR attended assessments, 59 % then started PR, and only 40 % completed the program (Hogg et al., 2012). Garrod, Marshall, Barley, and Jones (2006) reported that among the 69 % of patients who completed a 7-week 14-session PR program, they attended an average of only 71 % of all sessions. In the recent Cochrane review of RCTs of PR by McCarthy et al. (2015), 23 of the 58 studies reporting on dropout had rates of > 20 % (range 21-48 %). In one of the few studies measuring adherence to a PR exercise program for patients who had recently

experienced a COPD exacerbation, S. E. Jones et al. (2014) reported that only 48 % of the patients who had attended initial assessment completed PR. In a longitudinal study, which measured maintenance of exercise over a 9-month period following a PR program, Soicher et al. (2012) found that at 1 month post PR, only 36 % of participants had maintained the minimum weekly level of exercise recommended to them, while at 9 months, the proportion had dropped to just 26 %. A recent systematic review and meta-analysis demonstrated that increases in exercise capacity acquired during PR translated into only small increases of physical activity in daily life. However, these measures were always taken during the last week of – or within 14 days after – PR termination (Cindy Ng et al., 2012). Therefore, this meta-analysis did not demonstrate any lasting changes in physical activity in daily life beyond the time of the PR programs. In an official statement from the European Respiratory Society on physical activity in COPD, Watz et al. (2014) concluded that the 10 studies they indentified that evaluated the impact of PR on physical activity in COPD produced inconsistent results (six showing negative results). Of those showing increases in PA, the increases were all assessed and found immediately at the end of PR, thus providing no evidence that PR is linked to increased physical activity (or exercise) post PR. This lack of sustained exercise is likely a main reason why the gains acquired during PR are frequently lost within 12 months following program termination (Griffiths et al., 2000; Luk, Khan, & Irving, 2015; Moullec, Ninot, Varray, & Prefaut, 2007; Ries, Kaplan, Limberg, & Prewitt, 1995; Ries, Kaplan, Myers, & Prewitt, 2003).

Health Risks Associated with Physical Inactivity

For the general population, physical inactivity is a modifiable risk factor for coronary heart disease, stroke, certain cancers, type 2 diabetes, osteoporosis, cognitive decline and dementia, anxiety, depression, poor quality of life, hospital admission, and all-cause mortality (Garber et al., 2011). In addition to these, the potential consequences of physical inactivity specific to COPD include an increase in acute exacerbations, dyspnea and mortality, and a decrease in exercise capacity and quality of life according to a recent systematic review by Gimeno-Santos et al. (2014). For people with COPD, the consequences of inactivity also frequently manifest in a particular interplay of symptoms and behaviors, which is commonly referred to as the “vicious cycle” or “downward spiral” of COPD (Garvey, 2016; Nici et al., 2006): Dyspnea can cause anxiety and fatigue that may lead to avoidance of physical activity, which results in general deconditioning that can increase dyspnea, foster further inactivity and isolation, and result in poor quality of life (see Figure 1). PR, with its emphasis on exercise, is an intervention that can prevent, delay, and even reverse this downward trajectory by slowing the decline in physical activity and functional capacity.

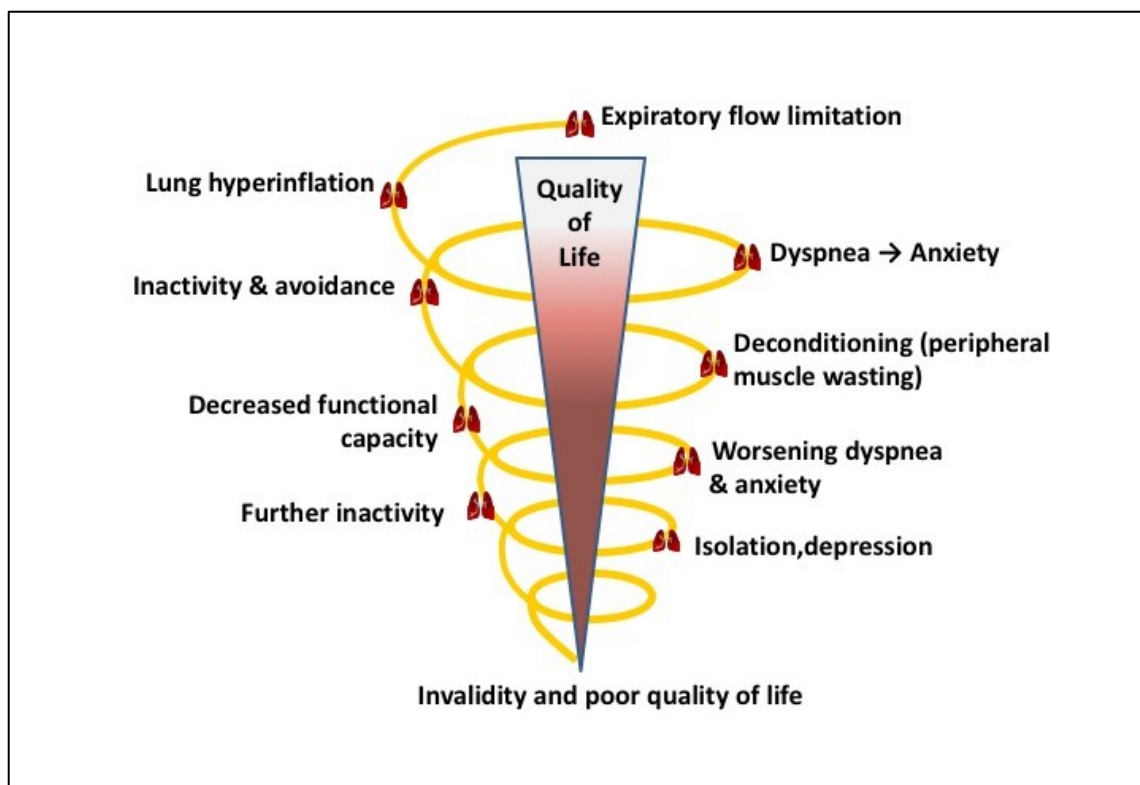


Figure 1. The downward spiral of COPD. This is a common pattern of interplay between disease symptoms and people's responses that can diminish quality of life. Adapted from La Clinique du Souffle la Solane, Osséja, France.

The disparity between the many benefits of being active and the low levels of engagement in regular physical activity and exercise has prompted investigation into their determinants in both healthy and clinical populations with the goal of reducing this evidence-practice gap.

Determinants of Physical Activity and Exercise

Physical activity (including exercise) is a complex behavior whose intensity, duration, frequency, and maintenance are determined not solely by health status and

functional capacity, but by a variety of personal, social, and environmental factors as well. For example, smoking status, exercise history, body mass index, sociodemographic variables (e.g., age, sex, education, marital and economic status), social/family support for exercise, proximity of exercise facilities, type of exercise activity, and the weather have all been linked to levels and frequency of physical activity and exercise (Courneya et al., 2008; Dishman & Sallis, 1994; Martin & Sinden, 2001; Trost, Owen, Bauman, Sallis, & Brown, 2002; White, Ransdell, Vener, & Flohr, 2005). Furthermore, several psychological and social-cognitive factors, such as mood state, self-efficacy, and locus of control for health, have also been implicated (Friis, Nomura, Ma, & Swan, 2003; Gimeno-Santos et al., 2014).

Of these, depression in particular (both subclinical and clinical levels) has repeatedly been linked to lower levels of physical activity and exercise in both the general population and across a range of chronic illnesses. Roshanaei-Moghaddam et al. (2009), for example, conducted a review of 11 studies on the longitudinal relationship between baseline depression and ensuing changes in physical activity levels. Eight studies reported that baseline depression was a significant risk factor for a decline in levels of physical activity, but also for poor adherence to specific physical exercise regimens following a recent coronary event. A ninth study found that emerging (as opposed to baseline) depression was associated with a corresponding shift from being physically active to becoming sedentary. DiMatteo, Lepper, and Croghan (2000) conducted a meta-analysis comprised of 12 studies that investigated associations between depression and adherence

to medical regimens (including exercise) in a variety of chronic conditions such as renal disease, arthritis, angina, and cancer. They found that depression was consistently associated with poorer adherence, with the odds of nonadherence being 3 times higher among depressed versus non-depressed patients. In a 36-session exercise-based cardiac rehabilitation program, Glazer, Emery, Frid, and Banyasz (2002) found that baseline depression symptoms were a significant predictor of lower attendance and higher rates of dropping out altogether. In a systematic review of 20 studies on adherence to physiotherapy treatment (including prescribed exercise) for musculoskeletal problems, Jack, McLean, Moffett, and Gardiner (2010) found “strong” evidence that baseline depression was a barrier to adherence.

What is known about the predictors of attendance and exercise compliance during PR for COPD (i.e., attending sessions and complying with prescribed exercise) and of exercise maintenance after PR? Is depression a significant barrier to participating and benefitting from PR? Answering these questions is a crucial part of gaining a better understanding of how to improve PR outcomes.

Requirements for Obtaining Optimal Benefits from PR

Attaining optimal health benefits from PR is dependent upon participants meeting three fundamental requirements: 1) *Attending* PR sessions, 2) *complying* with the prescribed intensity and duration of aerobic exercise, and 3) *maintaining* regular physical exercise after supervised PR ends. Participants who do not adequately meet these

requirements will not obtain much benefit during PR, or the gains acquired during the program will erode thereafter. Obviously, individuals have to attend PR exercise sessions to avail themselves of what the program offers. When present, participants also have to engage in aerobic exercise with at least some degree of compliance to the recommended intensity and duration to acquire health benefits. Finally, and perhaps most importantly, if regular endurance exercise is not maintained after PR, exercise-related improvements will diminish over time. The findings from studies that examined predictors of PR attendance, exercise compliance, and exercise maintenance are presented below.

Predictors of Attendance at Exercise-Based PR

In the National Emphysema Treatment Trial (Fan, Giardino, Blough, Kaplan, & Ramsey, 2008) multivariate regression analysis revealed that lower socioeconomic status (income) and lung function, greater anxiety, depressive symptoms, and distance to the PR center were all independent predictors of significantly lower PR attendance rates among 1218 COPD patients with severe airflow limitation (forced expiratory volume in the first second [FEV₁] ≤ 45 % predicted). Of note is that even relatively low levels of baseline depressive symptoms were associated with significantly lower odds of completing PR.

In a systematic review of 11 studies (total $N = 2039$) investigating PR uptake and completion, Keating et al. (2011) reported that travel, transport, baseline smoking and depression consistently emerged as predictors of failure to complete exercise based PR for COPD. Cassidy et al. (2014) conducted a study involving 651 respiratory patients (87

% with COPD) on the physiological and psychological predictors of completing a 6-week (12 sessions) PR program. In multiple logistic regression analysis, the strongest predictor of PR completion was currently not smoking, while the second strongest was a component they derived from factor analysis which they labelled “psychological well-being.” This was made up of five factors: The Chronic Respiratory Disease Questionnaire’s fatigue, emotion, and mastery domains; and levels of anxiety and depression from the Hospital Anxiety and Depression Scale. Here again, depression was linked to PR attendance.

A multi-center study conducted in the Netherlands by Fischer et al. (2009), involving 271 COPD patients, found using hierarchical logistic regression analysis that lower fat free mass index and perception of lower treatment effectiveness were independent predictors of significantly lower PR attendance. They did not report on depression in their study.

In a large retrospective study ($N = 711$) recently done in the U.K., Hayton et al. (2013) identified predictors of attendance (defined as attending at least one PR session) and “adherence”³ (present at > 63 % of eight weekly exercise training sessions). Independent predictors of non-attendance, based on a multivariate analysis, were: use of long-term oxygen therapy and living alone. Independent predictors of poor “adherence” (present at < 63 % of PR sessions) were current smoking, shorter incremental shuttle walk test distance, and previous hospital admission. Depression was not included in predictive

³ Adherence” was the term used by the authors, but it actually denotes attendance.

analyses because of missing data, however, patients who dropped out of PR because of acute exacerbations of COPD had Hospital Anxiety and Depression Scale depression scores that were on average 56 % higher than those who completed PR.

In a prospective observational study, Hogg et al. (2012) identified predictors of PR completion rates in a large sample across seven centers (two in hospital and five in the community). Four centers had rolling recruitment (accepting new patients every week) and provided PR sessions twice weekly for 8 weeks, while three centers had cohort recruitment (all patients starting and finishing together) with one PR session per week for 8 weeks. Completion was defined as attending 50 % of sessions (8 out of 16) for the rolling recruitment groups and attending 75 % (6 out of 8) for the cohort recruitment groups. Of 656 patients who started PR, 441 (67 %) completed. Using multivariate logistic regression, independent predictors of lower completion rates were the Hospital Anxiety and Depression Scale *depression* score of ≥ 11 (the caseness threshold), Medical Research Council dyspnea scale score of 4 or 5 (high severity of COPD), greater Index of Multiple Deprivation score (socio-economic deprivation based on geographic area), and referral by a general practitioner (instead of a medical specialist). Depression had a significant effect with an adjusted odds ratio of 0.56 (95 % CI 0.37–0.85) for PR completion. It should be noted however that these variables combined explained only 10 % of the variance in the PR completion rate.

Thorpe et al. (2012) conducted a systematic review to identify both barriers and

enablers of participation in physical activity and exercise-based pulmonary rehabilitation programs. From 11 studies (three quantitative and eight qualitative) that met their inclusion criteria for study quality, six barriers and seven enablers were identified. The *barriers* were: “Personal issues” (fear and uncomfortable feelings regarding exercise, presence of depression), health status (degree of dyspnea, frequency of exacerbations), “external factors” (weather, financial situation, transport, unforeseen events), “lack of support” (living alone, social isolation), “program-related issues” (too long, influence of referral source, lack of perceived benefit), and current smoking. “Personal issues,” which included depression, was the only barrier to emerge in all 11 studies included in this review. The *enablers* of participation that they identified were: “personal drivers” (personal values and motivators that maintain exercise), “personal attributes and perceived benefits” (persistence, positive attitude towards exercise, belief in its benefits), “social support” (giving and receiving emotional support, interacting with and learning from others), “control of condition” (taking an active role engaging in health behaviors that impact health and autonomous functioning), “program-centric enablers” and “professional support” (referral by a trusted medical practitioner, guidance and monitoring by qualified staff), and “goal setting” (improve functional capacity and autonomy, reduce symptoms).

Taken together, these studies show that attendance at PR is associated with a wide range of factors, including different levels of depression (subclinical or clinical).

Predictors of Compliance with Prescribed Exercise During PR

To our knowledge, no studies have been conducted on the predictors of compliance with exercise (specifically, the prescribed intensity and duration) during PR, which represents an important gap in the literature. “Adherence” studies to date have only measured and reported on *attendance* at PR, however, being present at PR sessions does not indicate whether or not participants are exercising to target. One cannot report on the predictors of exercise *adherence* in PR without addressing both attendance at exercise sessions and compliance with the recommended exercise duration and intensity.

Predictors of Maintenance of Physical Activity and Exercise after PR

Only a few studies have examined post-PR maintenance of physical activity/exercise and their predictors in COPD patients. Usually, activity levels decline over time and the improvements in exercise tolerance acquired during PR erode such that by 12-months post PR, these gains are lost. Even when patients participate in a post-PR maintenance program, although they may preserve some gains initially, by the end of the maintenance intervention most patients’ exercise capacity is usually no different from those who received only standard care (Busby, Reese, & Simon, 2014).

In a recent systematic review, Beauchamp, Evans, Janaudis-Ferreira, Goldstein, and Brooks (2013) compared the effect of supervised exercise maintenance programs versus usual care on exercise capacity at 6 and 12 months after PR. The outcomes of seven RCTs involving 619 individuals with moderate to severe COPD showed an average 60 % rate

of attendance to the exercise maintenance program at 1-year post PR. At 6-months post PR, the functional exercise capacity of participants in the maintenance groups was significantly greater than that of usual care. However, this effect was not sustained at 12 months when the exercise capacity of the maintenance and control groups were indistinguishable. Unfortunately, this study did not report on participant characteristics that predicted attendance or dropout.

Heerema-Poelman, Stuive, and Wempe (2013) examined predictors of adherence to an exercise maintenance program of 1-year duration following initial PR. Sixty patients with COPD participated in a maintenance program offered in primary care settings and supervised by physiotherapists trained in PR for COPD. “Adherence” was defined as attending maintenance sessions for the full year, however the authors do not state the number of sessions per week nor if all the exercise sessions took place at a rehabilitation center or partly in the home setting. At 12 months, 63 % of participants were still following the maintenance program. Independent predictors of “nonadherence” (defined as not attending up to 1 year) that emerged from multiple logistic regression analyses were: more severe COPD (indicated by lower forced expiratory volume in the first second [FEV₁]), more depressive symptoms (measured by the Hospital Anxiety and Depression Scale), and shorter duration of the initial PR program.

In a unique longitudinal study investigating the changes in levels of endurance exercise following a 12-week PR program for COPD, Soicher et al. (2012) identified

patterns of endurance exercise levels (based on a self-reported 1-week exercise log) and characterized individuals who did not maintain adequate exercise for health after PR. Endurance exercise levels were measured using a semi-structured telephone interview at 4, 6, 8, and 12 months after the start of a 12-week PR program. Overall, levels of exercise declined following termination of the PR program. Three trajectory classes based on endurance exercise patterns were identified: “low” (mean exercise time of 1.0 hour per week at 1 month post-PR and 0.7 hours per week at 9 months post-PR), “high” (mean of 2.7 hours per week at 1 month post-PR and 3.2 hours at 9 months), and “high/decline” (mean of 3.0 hours per week at 1 month falling to 0.8 hours per week at 9 months post-PR). Stepwise multivariate discriminant analysis yielded three variables that discriminated significantly between the three trajectory classes: exercise history, baseline six-minute walking distance, and number of current barriers to exercising (e.g., too tiring, too costly, too far away, family commitments, working). Although depression was measured at baseline using the Geriatric Depression Scale, and 25 % of the sample was found to have “possible” or “probable” depression (i.e., a score of ≥ 6), the authors did not report on whether depression levels helped characterize participants in the three exercise trajectories.

The above findings demonstrate that maintenance of exercise post-rehabilitation is poor and is associated with a range of factors, among which depression appears to play a significant role.

Prevalence of Depression in COPD

Not only has depression (both subclinical symptoms and clinical disorders) emerged as an important determinant of physical activity/exercise levels, PR attendance and outcomes, it has been established that comorbid depression is highly prevalent in patients with COPD compared to the general population. Several reviews have estimated the prevalence of clinically relevant depression in COPD to be as high as 40 % (K. M. Hynninen, Breivte, Wiborg, Pallesen, & Nordhus, 2005; Mikkelsen, Middelboe, Pisinger, & Stage, 2004; Yohannes, 2005; Yohannes et al., 2010) compared to approximately 11 % in the general population of North American adults \geq age 65 (Blazer, 2003; Fiske, Wetherell, & Gatz, 2009; Pearson, 2013). Furthermore, as much as the physiological symptoms of dyspnea and fatigue can be incapacitating, some findings suggest that comorbid depression in COPD may have an even greater impact on functional capacity (Aydin & Ulusahin, 2001; Kim et al., 2000), treatment adherence (DiMatteo, Haskard, & Williams, 2007; Dowson, Town, Frampton, & Mulder, 2004), quality of life, length of hospital stay (Yellowlees, Alpers, Bowden, Bryant, & Ruffin, 1987), risk of exacerbation (Laurin et al., 2009) and even mortality (de Voogd et al., 2009).

Summary and Gaps in the Literature to be Addressed by the Present Study

In summary, COPD is prevalent and poses a significant economic and social burden. PR is key to optimal management and its benefits derive mainly from attending exercise sessions, complying to the aerobic exercise prescribed, and maintaining regular exercise following completion of supervised PR. Adequate exercise levels are not achieved by a

large majority of the general population, and this is an even greater problem among people living with COPD. Studies have identified a wide range of predictors of daily physical activity and exercise levels in COPD and more specifically, attendance at exercise-based PR. A few studies have investigated predictors of exercise maintenance post PR. An important limitation of previous studies on predictors of “adherence” in COPD is that, to our knowledge, they have only measured and reported on *attendance* at PR exercise sessions. Clearly this does not provide specific information on the degree of compliance with prescribed exercise targets nor on predictors of exercise compliance in PR. This leaves a significant gap in the literature: To what degree do COPD patients comply with prescribed exercise when they attend PR and what predicts this compliance (or non-compliance)? Identifying and understanding the factors that impede and facilitate attending PR, complying with the exercise prescribed in PR, and maintaining regular exercise afterwards is essential to optimizing PR programs and outcomes for COPD. Identifying determinants of exercise compliance is essential for accurately assessing patients at risk for physical inactivity and for developing effective interventions that successfully promote self-managed exercise maintenance, thus reducing the burden that inactivity places on the patient with COPD, their family, and the health-care system.

Primary Objectives

The primary objectives of the present study is to investigate the extent to which baseline levels of depressive symptoms can predict COPD patients’ 1) *attendance* at exercise sessions during a 12-week supervised PR program, 2) *compliance* with the

prescribed duration and intensity of PR endurance exercise regimens, and 3) level of exercise *maintained* 9-months after termination of the supervised PR program.

Primary Hypotheses

Greater baseline depressive symptomatology will predict 1) lower PR exercise session attendance, 2) lower compliance with the prescribed aerobic exercise regimen, and 3) lower levels of exercise maintained 9 months after termination of the PR program.

Secondary Objectives

The secondary objectives of this project are exploratory in nature and are being pursued with the goal of generating hypotheses for further research and confirming or contradicting previous findings. The first secondary objective is to identify variables, in addition to baseline depression, that predict PR attendance, PR exercise compliance, and levels of exercise maintained post PR. We are interested in investigating whether each of these outcomes might have different sets of predictors. Another secondary objective is to identify any significant differences between participants who complete the 1-year study and those who dropout (i.e., do not attend the follow-up evaluation).

Methods

Study Design

This was a prospective observational study which was embedded in a randomized parallel-group clinical trial that compared the effects of three different aerobic exercise training protocols on various outcomes among COPD patients (clinical trial registration number: NCT01933308). The present study included three assessment periods: the first just prior to the start of a 12-week pulmonary rehabilitation program (baseline), the second was over the duration of the PR program, and the third at 9-months post PR (follow-up). The study was approved by the research ethics committee of Hôpital du Sacré-Coeur de Montréal (HSCM, see form in Appendix A) and all participants signed informed consent.

Participants

COPD patients, referred by a pulmonologist for PR, were recruited from the COPD Clinic at HSCM between October 2008 and June 2011. Thirty-six met eligibility requirements, provided informed consent, and were enrolled in this study (see Figure 2). Patients were eligible if they: 1) had a diagnosis of COPD confirmed by their medical record; 2) were clinically stable; 3) were aged ≥ 40 years; 4) had a smoking history of ≥ 10 American pack-years (20 cigarettes per pack); 5) had post-bronchodilation forced expiratory volume in the first second (FEV_1) of $< 80\%$ of the predicted normal value, and an FEV_1 to forced vital capacity (FVC) ratio of < 0.7 . Patients were excluded if they: 1) had experienced an exacerbation of respiratory symptoms in the previous 4 weeks

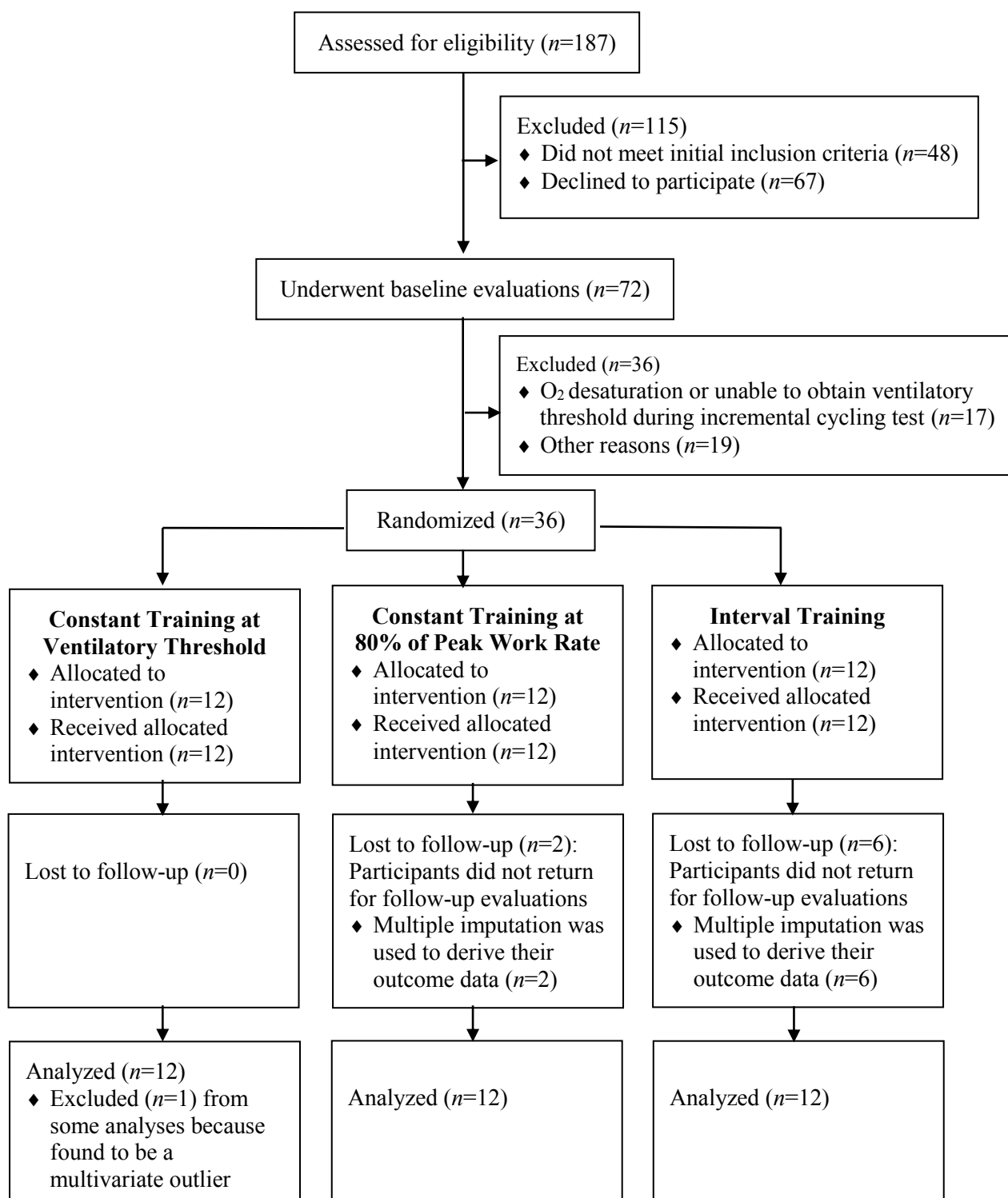


Figure 2. Participant flow.

(defined as change in dyspnea or volume/color of sputum, need for antibiotic treatment, or need for hospitalization); 2) had any contraindication to exercise testing based on American Thoracic Society guidelines (American Thoracic Society & American College of Chest Physicians, 2003); 3) had any active condition other than COPD that could affect their exercise tolerance (e.g., asthma, unstable coronary heart disease, left congestive heart failure, neoplasia, severe claudication, arthritis, etc.); 4) required supplemental oxygen; 5) had participated in a PR program in the previous year; or 6) were unable to complete baseline evaluations (e.g., unable to achieve a ventilatory threshold on the incremental cycling test or to speak/understand English or French adequately). These eligibility criteria were intended to differentiate COPD from other respiratory diseases and to ensure clinical stability and patient safety.

Procedure

As shown in Figure 3, eligible patients underwent baseline assessments, including a sociodemographic and health questionnaire, spirometry, exercise testing, psychological and socio-cognitive measures. Once six patients had completed assessments, they were randomly assigned as a group to one of three aerobic training regimens and enrolled into the PR program, which took place at the Hospital's cardiopulmonary rehabilitation center, *Centre de réadaptation cardio-respiratoire Jean-Jacques-Gauthier*. Six consecutive groups, each comprised of six participants underwent supervised PR at a frequency of three sessions per week over 12 weeks for a total of 36 sessions. Six participants at a time followed the same exercise protocol because of contamination concerns: differential

exercise intensity among participants in the same group could have potentially affected participants' motivation to comply with the demands of their own exercise prescription. Also, it optimized the efficiency of exercise supervision, while respecting the recommended staff to patient ratio of no less than 1 to 8 (Nici et al., 2006). The PR program consisted of endurance exercise training, strength training, stretching, and education about COPD and disease self-management based on the *Living Well With COPD* program (Bourbeau et al., 2006). Once two groups had been randomized to a particular exercise protocol, that protocol was removed from the list to ensure equal allocation of 12 participants to each exercise regimen. During the PR program, attendance and exercise compliance was recorded. At the end of each PR program, participants were instructed to continue exercising autonomously at home and/or in the community at the same level of intensity and duration as during their final week of PR. Follow-up assessments were done 9-months post-PR to measure level of exercise engaged in over a 1-week period. Participants received 50 dollars for each assessment visit.

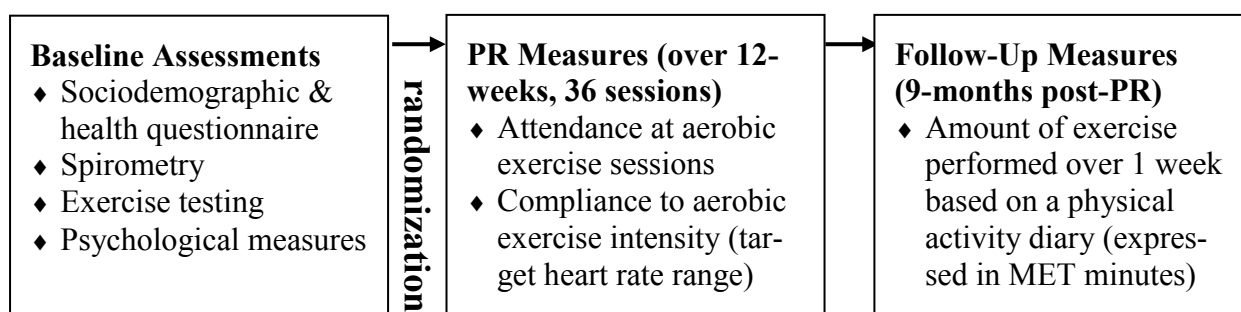


Figure 3. Study overview.

Exercise Training Protocols

The endurance exercise training program consisted of cycling on a calibrated cycle ergometer. A 10-minute warm-up phase (5 minutes of unloaded pedaling followed by 5 minutes of pedaling against incremental resistance up to attainment of the target training intensity) preceded the active training phase. For the training phase, participants were instructed to exercise within \pm five beats per minute of their prescribed target heart rate (THR) for the duration of each aerobic exercise session. The THR value was determined by the exercise regimen (constant training at the ventilatory threshold [CTVT], constant training high intensity [CTHi], or interval training [IT]), and was calculated for each participant based on measures from their baseline symptom-limited incremental cycling test which determined their work load at peak effort and at the ventilatory threshold.

Participants in the CTVT group trained at a heart rate corresponding to their ventilatory threshold, which is of moderate intensity and commonly described as the breakpoint in the ventilatory response to incremental exercise above which minute ventilation increases disproportionately in response to increments in oxygen consumption (Beaver, Wasserman, & Whipp, 1986; Vallet et al., 1997). Training at the ventilatory threshold has been associated with tolerable levels of ventilation and dyspnea (Gallagher, 1994; Potter, Olafsson, & Hyatt, 1971). The ventilatory threshold does not occur at the same percentage of peak capacity for all individuals, and was thus determined on an individual basis with the incremental cycling test performed at baseline. Participants in the CTHi group were prescribed a THR equal to that which occurred at 80 % of their peak

wattage during their pre-PR incremental test. The duration for CTHi was 25 minutes. The IT condition was comprised of a 30-second training phase during which participants were instructed to exercise at the heart rate corresponding to 100 % of their peak wattage for 30 seconds, interspersed with 30 second periods of active recovery (unloaded pedaling) for a specified total training duration (Vogiatzis et al., 2002). Training duration for CTVT and IT was adjusted using metabolic equations (American College of Sports Medicine, 2006) such that the total amount of work was equivalent to what each participant would have performed if he/she had been assigned to the CTHi group, thereby isolating the effect of training intensity from that of the total training dose (Casaburi et al., 1991). (These exercise conditions were the exposure for the study (in which the present study was embedded) whose main objective was to determine the optimal aerobic exercise-training regimen for COPD rehabilitation.

Training intensity was ascertained with a heart rate monitor and transmitter (T31 transmitter, Polar®, Finland) that displayed heart rate to participants, thus providing feedback throughout exercise sessions so that participants could constantly monitor and adjust their pedaling speed to maintain their heart rate within the prescribed range (a “beep” sounded when heart rate went below the target range). A 5-minute cool-down phase consisting of unloaded pedaling followed each training phase.

Baseline Measures

Socio-Demographic Data

A research assistant collected socio-demographic information (age, weight, marital status, years of education, smoking status and history, and comorbidities) by interview and from participants' medical chart.

Pulmonary Function Tests

Expiratory flow rates (FEV₁), lung volumes (FVC), were among measures obtained with standard spirometry according to recommended techniques (American Thoracic Society, 1995). Values were compared to predicted normal values from the European Community for Coal and Steel/European Respiratory Society (Quanjer et al., 1993).

Incremental Cycling Test

Patients performed a symptom-limited incremental cycling test to determine their work rate at peak effort and at the ventilatory threshold. These values were used to determine subsequent exercise intensity prescription for PR and to rule out the presence of cardiovascular comorbidities. Participants were seated on an electromagnetically braked cycle ergometer (Ergometrics 800, SensorMedics, Yorba Linda, CA) and were connected to an electrocardiogram and respiratory circuit through a mouthpiece. The respiratory circuit consisted of a pneumotachograph, digital volume sensor, O₂ and CO₂ analyzers, and a mixing chamber (Vmax Encore, Sensor Medics, Yorba Linda, CA). After five minutes of rest and three minutes of unloaded pedaling, 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 participants with a predicted peak work rate < 50 watts; 10-watt increments for those with a predicted peak work rate > 50 watts). This protocol is frequently used in respirology (N. L. Jones, Makrides, Hitchcock, Chypchar, & McCartney, 1985). Gas exchange parameters (minute ventilation, O₂ uptake, CO₂ excretion) and heart rate were measured at rest and during exercise on a breath-by-breath basis. The ventilatory threshold was determined using the V-slope method (Beaver et al., 1986), a computerized approach to identify the breakpoint in the carbon dioxide secretion – oxygen consumption relationship. Peak work rate was defined as the highest work rate the participant could maintain at a pedaling speed of at least 50 revolutions per minute for a minimum of 30 seconds. This test was completed under medical supervision.

Psychological Measures

The Beck Depression Inventory–II. The Beck Depression Inventory–II (BDI-II) is a widely used self-report instrument administered to assess the presence and severity of symptoms of depression (the primary predictor in this study), as described in the *Diagnostic and Statistical Manual of Mental Disorders, fourth edition* (American Psychiatric Association, 1994). Twenty-one items assessing symptoms of depression are rated using descriptors of increasing severity (range 0-3), producing a summary score ranging from 0 (no symptoms) to 63 (maximum symptoms) with cut-off values for distinct levels of severity. A cut-off score of 14 is considered the threshold for “mild” clinical

depression (Beck, Steer, & Brown, 1996) in the general population, with some variation found in specific clinical populations (Wang & Gorenstein, 2013b). The BDI-II has been used across a broad spectrum of psychological and medical conditions and has been found to have very good reliability and validity (Wang & Gorenstein, 2013a). The French translation used in the present study has maintained the sound psychometric properties of the original instrument (Bourque & Beaudette, 1982; Corbiere et al., 2011; Vézina, Landreville, Bourque, & Blanchard, 1990).

The Multidimensional Health Locus of Control Scale – Form C. The Multidimensional Health Locus of Control Scale – Form C (HLC) assesses beliefs about where control and responsibility for one's health lies: internal/personal or external orientation (Wallston et al., 1978). It is an 18-item self-report scale that is adaptable for use with any specific health-related condition (form C), and is comprised of four distinct scales - *Internal*, *Chance*, *Doctors*, and *Other People* - each yielding its own score. Responses are indicated on a 6-point Likert scale that ranges from *strongly disagree* to *strongly agree*. The HLC has shown ample internal consistency reliability for the four scales with Chronbach alphas ranging from 0.70 to 0.82 (Wallston et al., 1994). In a study with 186 asthma patients, Chronbach's alpha coefficients for the four scales ranged from 0.71 to 0.74 (Dupen, Higginbotham, Francis, & Cruickshank, 1996). Each of the four scales of the HLC correlated significantly ($p < .001$) with the same subscales of the Multidimensional HLC Form B, thus supporting its criterion-related validity (Wallston et al., 1994). In arthritis and chronic pain samples, the *Internal Scale* showed a significant

negative correlation to pain and helplessness measures, while the *Chance Scale* showed a significant and positive correlation to measures of depressive symptoms and helplessness, thereby supporting the HLC's construct validity (Wallston et al., 1994). No validated French version of the HLC Form C was found, therefore the English HLC was translated into French and then back translated to English by bilingual members of the study team. As such, only psychometric data available for the English version are presented.

Measures Taken During the PR Program

PR Exercise Attendance

In this study PR *attendance* was recorded was calculated as the ratio of endurance exercise sessions attended to total number of sessions offered (i.e., 36), multiplied by one hundred to produce a percentage value.

PR Exercise Compliance

The measure of *compliance* with the aerobic exercise prescription was calculated as the total time during which each participant exercised within or above their target heart rate range (plus or minus five beats per minute of prescribed target heart rate) divided by the total duration of aerobic exercise sessions prescribed, multiplied by one hundred to produce a percentage value. Each participant's heart rate was measured during every aerobic training session (for which they were present) with continuous data tracking on a second-by-second basis using both hardware (Bike Excite Med 700, Technogym®, Italy; and T31 transmitter, Polar, Finland) and computer software (*CardioMemory*® by Technogym, Italy, 2006). Heart rate (as opposed to watts) was chosen as the measure of

compliance with the exercise prescription because heart rate response at a given submaximal workload decreases as cardiorespiratory fitness increases, therefore this approach ensured that patients would remain at the same *relative* (versus absolute) training intensity throughout the PR program's duration. Compliance for each participant was calculated only from the PR exercise sessions for which he or she was present.

PR Composite Adherence

Finally, because we had both attendance and exercise compliance data, it was possible to calculate a “composite adherence” measure for PR as the product of attendance and compliance with the prescribed exercise target (% attendance \times % compliance). Composite adherence may be useful from a clinical standpoint because it captures in a single measure the two essential aspects of PR exercise adherence. However, it was not a central focus of this study (in terms of predictors), as more valuable information could be gained by investigating the rates and predictors of PR attendance and exercise compliance separately as opposed to if they had just been combined; i.e., composite adherence.

Follow-Up Measure 9-Months Post PR

Nine months post-PR, patients were asked to complete a 7-day physical activity diary at the end of each day, which was based on the Seven-Day Physical Activity Recall (Blair et al., 1985; Garfield et al., 2012; Sallis et al., 1985). They were instructed to document up to three physical activities per day that they had engaged in (continuously for a minimum of 10 minutes each), the duration, and to rate the subjective intensity of

each as “light,” “moderate,” or “high” (see the diary in Appendix E). To obtain the follow-up measure, activities were divided into exercise/sport activities (e.g., walking, cycling), and activities of daily living (e.g., housework, shopping, meal preparation). Only the exercise/sports activities were retained to calculate exercise levels at follow-up because of the inconsistency within and between participants’ recording their activities of daily living (i.e., showering, cooking, and house cleaning were documented by some participants but not by others who presumably had also done some of these activities). The Compendium of Physical Activities (Ainsworth et al., 2011) lists a vast number of highly specific physical exercises and activities and provides ratings on the energy expended for each in Metabolic Equivalent of Task units (METs). One MET is the amount of energy expended by an individual while seated at rest. The MET value while exercising is a ratio of that amount of energy being expended compared to that while seated at rest (1 MET), for example; walking at a moderate pace on level ground has a MET value of 3.5 meaning that the energy being expended is 3.5 times greater than the energy being expended at rest (3.5/1 METs). Using the Compendium, every activity recorded in the 7-day diary was assigned its METs value and was then multiplied by the activity’s duration in minutes to produce a *MET-minutes* value for each (American College of Sports Medicine, 2006; Bushman, 2012) . These were then summed to obtain a MET-minutes total which was the volume of exercise for the week and served as our follow-up outcome.

Adverse Events

COPD exacerbations occurring during the study were noted and participants were

recommended to: 1) follow their action plan; 2) contact a member of the study personnel; 3) refrain from exercising if necessary; and 4) resume exercising as soon as possible. Other medical problems were also noted. No injuries or medical problems resulted from undergoing PR.

Data Screening and Management

Extreme Values

Extreme scores in the dataset were identified and checked against the values in the original source documents to ensure they had been entered correctly. Discrepancies were resolved by retaining the values from the source documents, unless they were outside the possible range, in which case they were entered as missing. When an extreme univariate outlier (extreme value on one variable) or multivariate outlier (unusual score on a combination of two or more variables, such as with correlations or regressions) was identified, statistical analyses were conducted that included the extreme outlier and were then repeated with the outlier winsorized (for univariate outliers) or excluded (for multivariate outliers) (Field, 2013; Lang & Secic, 2006). These results were compared and if an outlier was found to exert substantial influence, results from the analyses in which it had been transformed or excluded were considered to be more valid or representative of our relatively small sample (Appendix C contains normality assessments).

Missing Values

In accordance with intention-to-treat analysis, no cases with missing data were

removed from the data set. Missing baseline and follow-up values were assessed for frequency and patterns (degree of randomness) using SPSS 23 Missing Values Analysis and were then imputed using the SPSS Multiple Imputation Procedure (IBM, 2013), as described in Appendix D and Table 38. Missing exercise compliance data had already been imputed in the larger study's statistical procedures and were retained in the present study for purposes of consistency: when a participant's compliance data were missing for an entire exercise session (due to technical failures to record, store, or retrieve data), values from that participant's previous exercise session were carried forward. When only a segment of a participant's exercise session data was missing, exercise compliance was calculated from the values that had been obtained for that session.

Use of Bootstrapping

Bootstrapping based on 1000 samples employing the bias-corrected and accelerated (BCa) method to construct confidence intervals was used in all regression analyses because of: 1) the modest sample size, 2) the non-normal distribution of some data, and, 3) failure to meet some assumptions for multiple linear regression (e.g., homoscedasticity, normal distribution of residuals). This helped produce robust confidence intervals, standard errors, and p values. All potential IVs for correlation and linear regression analyses were screened for collinearity and multicollinearity and if found, only the variable with the stronger association to the outcome variable was retained in analyses (Tabachnick & Fidell, 2013).

Statistical Analyses

Data were analyzed using the Statistical Package for the Social Sciences version 23.0 software (SPSS 23, Chicago, IL, USA). All tests of significance were two-sided and alpha level was set at $p < .05$.

Descriptive Statistics

Following data screening, descriptive statistics of our sample's characteristics were compiled. Normally distributed quantitative data were described with means and standard deviations (SDs); while data with non-normal distributions were characterized with their medians and interquartile ranges (IQR) in addition to their means and SDs. Categorical data were described with n and percentages.

Univariate Prediction of Outcomes

Pearson correlations were used to characterize the relationship between baseline BDI-II scores and each of the outcome variables (PR attendance, PR exercise compliance, and exercise levels at follow-up). Categorical variables (e.g., exercise protocol, sex) were converted using dummy variable coding so that they could be incorporated into the multiple linear regression analyses (Field, 2013). Pearson correlations were also performed to check levels of collinearity between all independent variables.

Multivariate Prediction of Outcomes

Multivariate prediction using standard linear regressions was carried out for both our primary and secondary (exploratory) analyses. For the *primary* analysis, baseline BDI-II was the predictor of interest for each of our three outcomes: PR attendance, PR exercise compliance, and levels of autonomous exercise maintained at follow-up. Five covariates (IT and CTHi exercise interventions with CTVT chosen as the reference [as it was a constant and stable exercise regimen with the lowest intensity] , sex, baseline FEV₁ %, and baseline smoking status) were selected a priori for inclusion to adjust for their potential confounding effects. Because the present study was embedded in a trial comparing the effects of three exercise interventions, it was decided a priori that these exercise interventions be included as covariates in the analyses to account for possible differential effects on the outcomes. The other covariates were chosen based on their clinical relevance and their emergence in prior research findings. Furthermore, we checked for moderation and mediation in our primary regression analyses by identifying any significant interactions among BDI-II and covariates using *PROCESS procedure* macro for SPSS (Hayes, 2014).

Our secondary analyses were exploratory and sought to construct the regression models that could best predict each outcome by including the strongest (and fewest number of) independent predictors of each outcome (Harrel, 2001). The objective was to identify the sets of variables that could best predict each outcome and to determine whether those sets were different for PR attendance, PR exercise compliance, and levels

of exercised maintained at follow-up. Given the relatively small sample size ($N = 36$) and large number of baseline demographic, clinical, and psychological/socio-cognitive variables, only a few predictors could be included in the regression analyses, otherwise over fitting would occur, thus compromising the validity of the outcomes. It was decided a priori that the ratio of cases to predictors would be no less than seven to one for our exploratory regression analyses. The selection of predictors for each model was based on: strength of Pearson correlations between IVs and each of the three outcomes (see Appendix E, Table 39), significant covariates that emerged in the regressions from our primary analyses, clinical relevance, and findings of previous studies.

Comparison of Study Completers Versus Dropouts

Differences in the characteristics of participants who attended the follow-up evaluations (“completers”) and those who were absent (“dropouts”) were examined using Mann-Whitney U tests (for continuous data) and Pearson chi-square tests (for categorical data). The Mann-Whitney U test was chosen because of: 1) the small sample size, 2) unequal size groups of completers present and dropouts, and 3) some variables (predictors and outcomes) having non-normal data distributions.

Results

Missing Data

Only 0.06 % of all baseline values was missing and this was completely at random (Little's MCAR test: Chi-Square = 15.17, DF = 39, $p = 1.000$). No PR attendance data were missing and only 0.80 % of all the PR exercise compliance data was lost due to exercise equipment or computer problems or human error. This included just two entire exercise sessions out of 899 (0.22 %) for which the values of the previous session were carried forward. For the follow-up data (MET minutes of exercise 9-months post-PR) 11 values (30.56 %) out of 36 were missing: eight participants did not return for follow-up evaluations and for the 28 who did, one did not submit their physical activity diary, while two others submitted diaries lacking information required for scoring. The 11 missing values were imputed using the *Impute Missing Values* procedure in SPSS version 23.0 (see Appendix D for a detailed description and results of this procedure.)

Participants

Baseline characteristics of the 36 study participants are presented in Table 1. The sample had a mean age (SD) of 68 (9) years, tended to be overweight, nearly two thirds were female, and one third (no males) lived alone. The mean (SD) smoking history was 42 (13) American pack-years (20 cigarettes per day), and one third of participants were smoking at baseline. Eighty-six percent of participants had COPD in the moderate (55%) to severe

Table 1

Baseline Characteristics of Participants

<i>Baseline Characteristics of Participants</i>		
Sociodemographic		
Age, years	68 (9)	
Female	23 (64 %)	
BMI, kg/m ²	28 (5)	
Underweight	0 (0 %)	
Normal weight	14 (39 %)	
Overweight	10 (28 %)	
Obese	12 (33 %)	
Cumulative Smoking, pack years ^a	42 (13)	
Smoking at Baseline	12 (33 %)	
Cohabiting ^b	24 (67 %)	
Pulmonary Function		
FEV ₁ , litres	1.4 (0.4)	
FEV ₁ % predicted	59 (17)	
FEV ₁ /FVC %	50 (9)	
GOLD stage (FEV ₁ % predicted)		
1. Mild (≥ 80%)	3 (8 %)	
2. Moderate (50%-79%)	20 (55 %)	
3. Severe (30-49%)	11 (31 %)	
4. Very severe (< 30%)	2 (6 %)	
Psychological		<i>Median (IQR)^c</i>
BDI-II (scale 0-63)	9.4 (6.6)	8.5 (6–13)
HLC Internal orientation		
Internal (0-6)	4.1 (1.2)	4.5 (3.5–5.0)
HLC External orientation		
Chance (scale 0-6)	2.7 (0.9)	
Doctor (scale 0-6)	5.0 (1.4)	5.3 (4.8–6.0)
Other People (scale 0-6)	3.0 (1.4)	

Note. $N = 36$. Data are means (SD) or n (%) unless otherwise indicated. BMI = body mass index; FEV₁ % predicted = forced expiratory volume in 1st second percent of predicted normal value; FVC = forced vital capacity; GOLD = Global Initiative for Chronic Obstructive Lung Disease; IQR = interquartile range; BDI-II = Beck Depression Inventory-II; HLC = Health Locus of Control.

^aU.S. pack years (20 cigarettes per pack). ^bLiving with at least one other person. ^cMedian (IQR) are presented when data distribution is skewed.

(31%) range as per the GOLD classification. Locus of control for health tended to be doctor and internally oriented, while a chance orientation received the lowest rating.

Depression

The sample's median baseline BDI-II score was 8.5 indicating that this sample had generally subclinical levels of depressive symptomatology. Figure 4 shows the distribution of baseline BDI-II scores, which was positively skewed and had one extreme outlying high score (35, $z = 3.85$, $p < .001$; see table 12 in Appendix C for normality assessment). The dashed line marks the threshold score of 14 for clinical depression, and five scores equaled or exceeded this threshold. Winsorizing was used to help reduce the potential impact (bias) of this univariate outlier (Field, 2013; Tabachnick & Fidell, 2013): the outlying value of 35 was brought closer to the center of the distribution by reducing it to 23 ($z = 2.51$, see Table 12), still two units greater than the next highest score and equivalent to the 95th percentile.

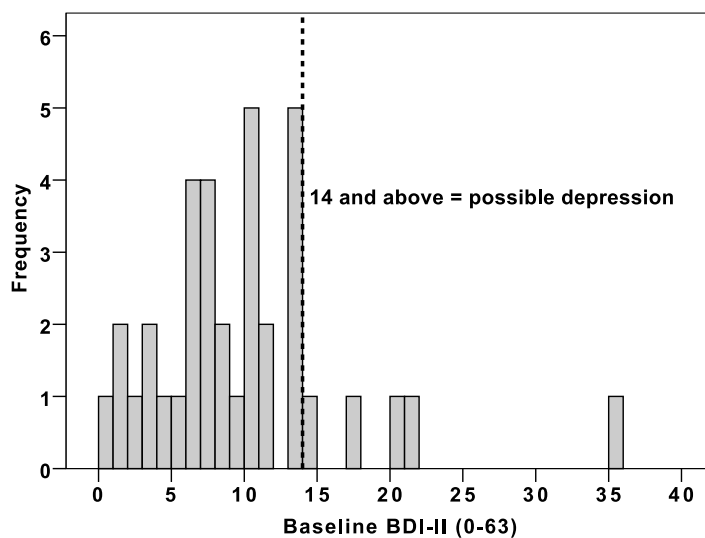


Figure 4. Baseline BDI-II data with threshold for clinical depression.

Outcome Variables

As shown in Table 2, median attendance at PR exercise sessions was generally high, as was median exercise compliance, which was reflected in their negatively skewed data distributions (see Figure 5 and table 13). Median composite adherence was lower, as would be expected given that it is the product of attendance and exercise compliance and as such reflected the deficits of each. Total amounts of exercise for a 1-week period at follow-up had a median of 706 MET-minutes ($N = 36$, 11 missing values imputed). This is equivalent to walking on a level surface at a leisurely pace of 4 KMs hour for about 4 hours (distance of 16 KMs), but it fell short of the median (IQR) prescription of 842 (781–911) MET minutes per week (equivalent to a distance of almost 19 KMs and a duration of almost 5 hours) for ongoing autonomous exercise, which was based on the amount of exercise performed over their last three PR sessions; 58 % of participants failed to meet

their target weekly exercise levels. In contrast to PR attendance and compliance, the follow-up data were positively skewed (see Figure 5 and Appendix C Table 14).

Table 2

Outcome Measures

Outcomes	Median (IQR)	M (SD)
PR Attendance %	83 (67–94)	74 (28)
PR Exercise Compliance %	94 (71–99)	76 (34)
PR Composite Adherence % ^a	72 (29–86)	57 (33)
Exercise Level at Follow-up, MET minutes	706 (445–1146)	919 (739)

Note. $N = 36$. IQR = interquartile range; PR = pulmonary rehabilitation; MET = metabolic equivalents of task; mins. = minutes.

^a PR composite adherence is the product of PR % attendance \times PR % exercise compliance

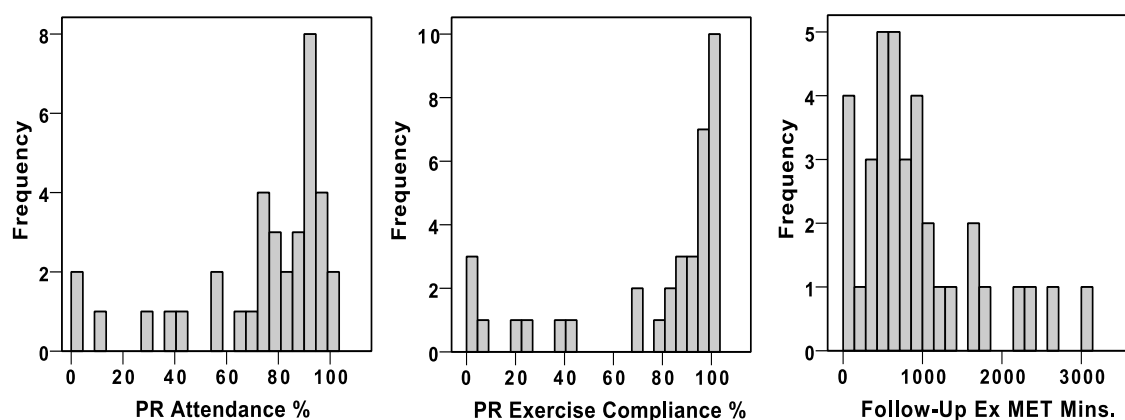


Figure 5. Distributions of PR attendance, PR exercise compliance, and follow-up exercise levels ($N = 36$).

Thirty-six participants were each offered 36 endurance exercise sessions for a grand total of 1296 potential sessions. In all, 34 participants missed a total of 333 PR sessions

(25.7 % of total sessions offered). The reasons for missed PR sessions were documented and are presented in Figure 6 below, as a percentage of the total sessions missed.

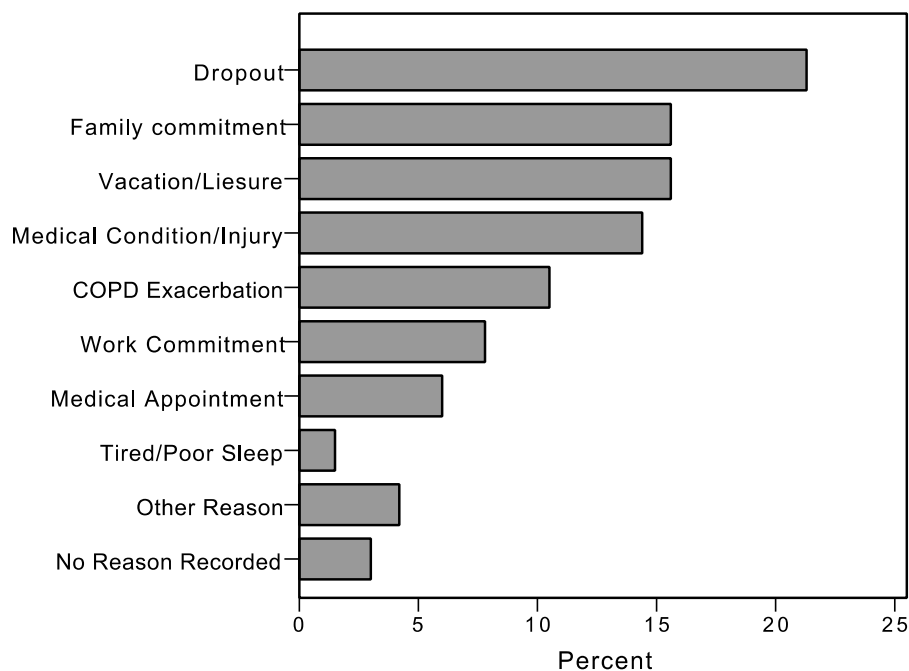


Figure 6. Reasons and their respective proportions for missed PR sessions. “Dropout” values ($n = 71$ of 333) are for two participants who discontinued the PR program shortly after it began.

Correlations

The relationships between baseline depressive symptomatology and each outcome are depicted in Figure 7. Baseline BDI-II and PR attendance had almost no relationship; variation in baseline depressive symptomatology accounted for only 0.04 % of the variation in PR attendance. Figure 7A reveals a high outlying BDI-II score (see Tables 15 and 16 in Appendix C for normality/bias assessments), and when it was winsorized (Field,

2013) from 35 to 23 (reduced to the value corresponding to the 95th percentile), the relationship was found to be even weaker ($r = .00$, BCa CI $[-.26, .24]$, $p = .999$).

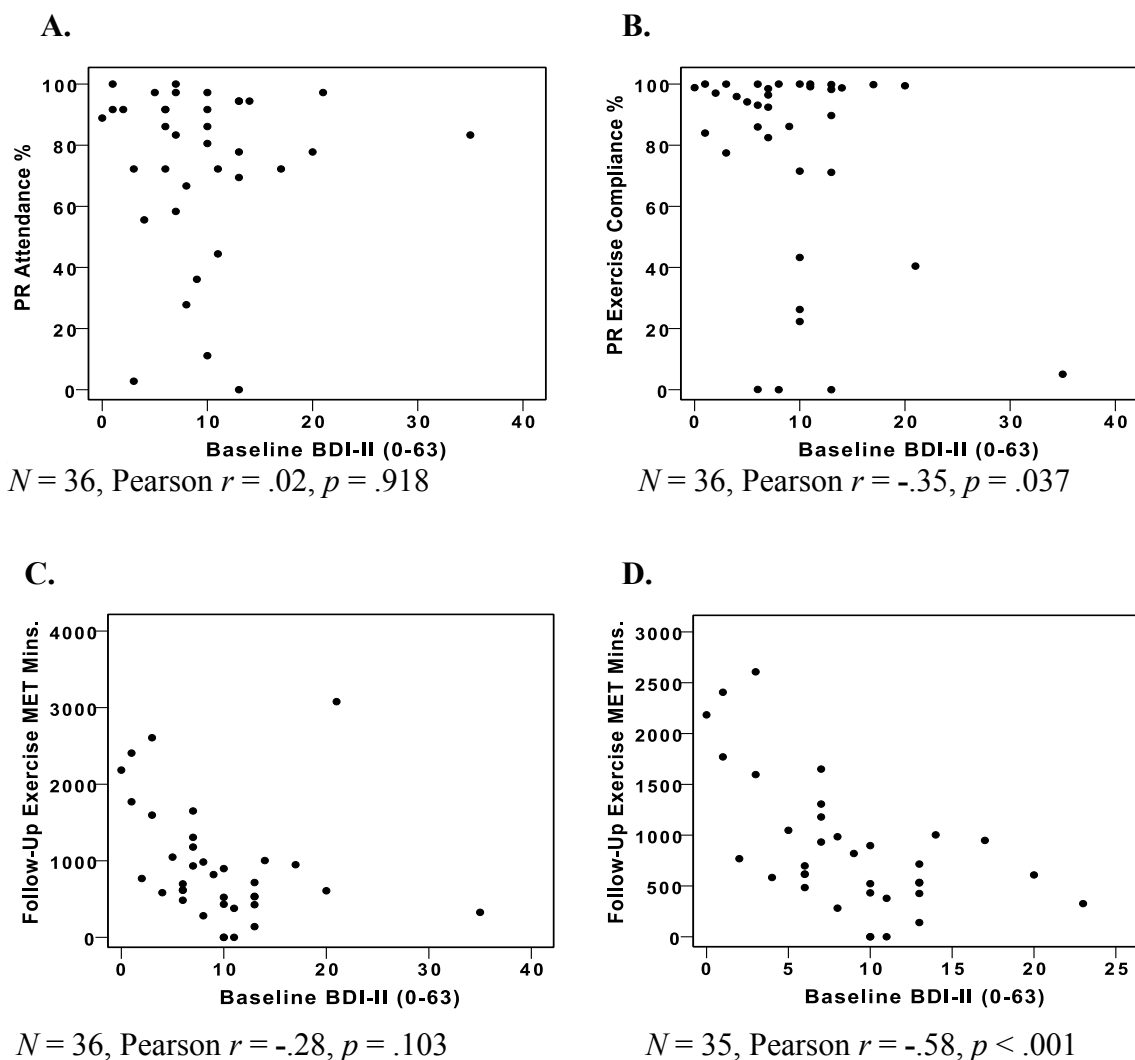


Figure 7. Relationships between baseline depression and each outcome: (A) PR attendance, (B) PR exercise compliance, (C) exercise levels at follow-up with the high outlying BDI-II score and multivariate outlier included and, (D) exercise levels at follow-up with the high BDI-II winsorized (from 35 to 23) and the multivariate outlier removed.

Baseline BDI-II and PR exercise compliance were weakly negatively associated, with variation in the former accounting for 12.3 % of the variation in the latter. Again, the

impact of the outlying high baseline BDI-II score was assessed by winsorizing it and repeating the correlation, which then yielded a Pearson r of $-.29$ ($p = .086$) where variation of baseline BDI-II scores accounted for 8.4% of the variation in PR exercise compliance. This was a weaker and statistically non-significant negative association compared to that which included the outlying BDI-II score, suggesting that the outlier exerted substantial influence over the r statistic (see bias assessments in Appendix C Tables 17 and 18). Therefore, the r value based on the less extreme BDI-II score (23 instead of 35), more accurately portrayed the relationship between baseline depressive symptomatology and PR exercise compliance for the majority of this sample, was less likely to produce a type I error, and was likely a more generalizable result (Field, 2013; Tabachnick & Fidell, 2013).

Only a weak and statistically non-significant negative correlation emerged between baseline BDI-II and composite PR adherence, and this was the case whether the BDI-II outlier winsorized or not (more details are presented in Appendix F, Figures F1 and F2).

The scatterplot depicting the relationship between baseline BDI-II scores and participants' exercise levels at follow-up is shown in Figure 7C above. It reveals an influential bivariate outlier with high discrepancy and leverage (standardized residual = 3.49, see normality assessments in Appendix C Table 19) who had the second highest baseline BDI-II score and the highest exercise level of all participants at 9-months post PR. This profile is contrary to the trend displayed by the other participants and had a

disproportionate impact on the Pearson correlation coefficient. With this outlier in the analysis, the sample's baseline depressive symptomatology (BDI-II) had a weak and statistically non-significant negative association with exercise levels at follow-up, with variation in baseline depressive symptomatology accounting for only 7.6 % of the variation in exercise levels at follow-up. However, when the analysis was conducted with the bivariate outlier removed and the high (outlying) BDI-II score winsorized, the negative relationship was moderately strong ($r = -.58, p < .001$), indicating that as baseline depressive symptomatology increased, exercise levels at follow-up decreased. Variation in baseline BDI-II accounted for 33.6 % of the variation in exercise levels making BDI-II the strongest single predictor among all baseline variables of exercise levels at follow-up. This more accurately represents the baseline BDI-II – follow-up exercise relationship for 35 of 36 participants in this sample, as removing the bivariate outlier substantially reduced bias and improved the normality and generalizability of the model (see Tables 20 - 22 in Appendix C).

Primary Multivariate Analyses

Standard multiple regression analyses were performed to test the hypotheses that higher baseline BDI-II scores (depressive symptomatology), within the context of the five selected covariates, predicted 1) lower PR attendance, 2) lower PR exercise compliance, and 3) lower levels of exercise sustained at follow-up. For all regression analyses, the extreme high outlying BDI-II score was winsorized (reduced to a value two units greater than the next highest score, and at the 95th percentile), as the outlier introduced substantial

bias, reduced generalizability, and increased the likelihood of type I errors. Bootstrapping was used because assumptions of normality and homogeneity of variance for residuals were violated (see Appendix C Tables 23 – 30).

First, regression analysis was performed with PR attendance as the outcome, baseline BDI-II as the main predictor and the five covariates. As can be seen in Table 3, the full regression model did not predict PR attendance significantly better than if its mean alone had been used; $F(6, 29) = 1.96, p = .105$.

Table 3
*Multiple Regression Model for Prediction of PR Attendance
by Baseline BDI-II with Covariates*

Variable	<i>B</i>	β	Bootstrap ^a		
			<i>SE B</i>	<i>p</i>	95 % CI for <i>B</i> ^b
Constant	33.20		23.34	.174	[-11.48, 85.39]
bBDI-II	0.59	.12	0.87	.478	[-1.37, 1.85]
IT	-4.02	-.07	13.24	.764	[-29.79, 17.51]
CTHi	2.79	.05	11.23	.803	[-19.74, 28.72]
Sex (F)	-17.88	-.32	8.57	.051	[-34.88, -3.41]
bFEV ₁ %	0.79	.49	0.30	.018	[0.20, 1.30]
bSmoking	1.90	.03	10.34	.851	[-18.87, 23.91]
Regression Model	$R = .54$	Adjusted $R^2 = .14$	$F(6, 29) = 1.96, p = .105$		

Note. $N = 36$. CI = confidence interval; bBDI-II = baseline Beck Depression Inventory-II; IT = interval training; CTHi = constant training high intensity; bFEV₁ % = baseline forced expiratory volume in the first second percent of predicted normal value; bSmoking = smoking at baseline.
^aBootstrap results are based on 1000 bootstrap samples. ^bConfidence intervals are bias-corrected and accelerated.

Baseline BDI-II did not emerge as a significant independent predictor of PR attendance. FEV₁ % was the only covariate that had a statistically significant positive association to PR attendance, while sex reached borderline significance (female sex was associated with lower PR attendance).

Standard multiple regression was next performed on PR exercise compliance as the outcome, baseline BDI-II as the predictor of interest, with the same covariates as above. Table 4 below reveals that the full model was effective at predicting compliance, $F(6, 29) = 6.34, p < .001$. Baseline BDI-II emerged as a significant independent predictor when effects of the covariates were held constant: higher baseline depressive symptomatology predicted lower compliance with exercise intensity in PR. Covariates significantly associated with lower exercise compliance were the IT exercise protocol, higher FEV₁ % predicted, and Sex (male). Because exercise compliance scores were calculated only from the sessions attended, we realized that this may have introduced bias; i.e., what if exercise compliance measured over many exercise sessions (say > 30) tended to be lower (or higher) than that measured over fewer (say < 10) sessions simply because it was more likely over many exercise sessions to fall below the target intensity? In order to verify this possibility, a correlation was performed between PR attendance and PR exercise compliance. This yielded a Pearson r of .11 ($p = .51$) which showed that PR attendance accounted for only 1.2% of the variance in exercise compliance and showed that the number of exercise sessions upon which exercise compliance scores were based had virtually no influence on participants' compliance scores.

Table 4
*Multiple Regression Model for Prediction of PR Exercise Compliance
 by Baseline BDI-II with Covariates*

Variable	<i>B</i>	β	Bootstrap ^a		
			<i>SE B</i>	<i>p</i>	95 % CI for <i>B</i> ^b
Constant	141.94		20.13	.001	[101.50, 181.17]
bBDI-II	-2.49	-.40	1.05	.047	[-4.76, -0.18]
IT	-54.89	-.77	12.56	.004	[-79.57, -27.20]
CTHi	-10.27	-.14	10.43	.332	[-30.55, 7.53]
Sex (F)	26.65	.38	11.36	.034	[1.36, 47.78]
bFEV ₁ %	-0.66	-.33	0.29	.039	[-1.13, -0.04]
bSmoking	1.12	.02	10.07	.910	[-18.18, 23.07]
Regression Model	<i>R</i> = .74	Adjusted <i>R</i> ² = .46	<i>F</i> (6, 29) = 5.90, <i>p</i> < .001		

Note. *N* = 36. CI = confidence interval; bBDI-II = baseline Beck Depression Inventory-II; IT = interval training; CTHi = constant training high intensity; bFEV₁ % = baseline forced expiratory volume in the first second percent of predicted normal value; bSmoking = smoking at baseline. ^aBootstrap results are based on 1000 bootstrap samples. ^bConfidence intervals are bias-corrected and accelerated.

A moderation model was tested using the method described by Hayes (2013) to determine if the relationship between baseline BDI-II (the predictor) and PR exercise compliance changed as a function of exercise intervention (the moderator) while adjusting for baseline smoking status, FEV₁% predicted, and sex. This was done using the *PROCESS procedure* macro for SPSS developed by Hayes (2014). A significant interaction effect between baseline BDI-II and exercise intervention was found (*b* = -2.16, 95 % CI [-3.30, -1.01], *t* = -3.86, *p* < .001) indicating that the relationship between baseline

depressive symptomatology and PR exercise compliance was moderated by exercise intervention (see Figure 8 below). When the exercise intervention was CTHi, there was a

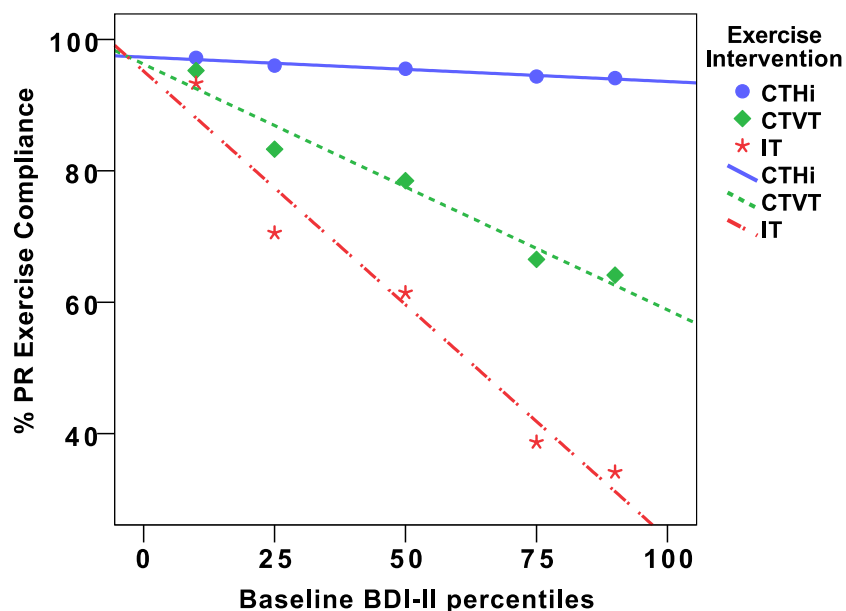


Figure 8. Baseline depression symptomatology predicting PR exercise compliance moderated by PR aerobic exercise intervention (adjusting for baseline smoking status, FEV₁ % predicted, and sex).

non-significant negative relationship between baseline depression symptomatology and PR exercise compliance, $b = -0.61$, 95 % CI [-2.16, 0.95], $t = 0.80$, $p = .430$. With CTVT, there was a significant negative relationship between baseline depression symptomatology and PR exercise compliance, $b = -2.40$, 95 % CI [-3.74, -1.05], $t = -3.63$, $p = .001$. The IT exercise intervention had the strongest negative relationship between baseline depression symptomatology and PR exercise compliance, $b = -4.18$, 95 % CI [-5.92, -2.45], $t = -4.93$, $p < .001$. (The variability of BDI scores was similar within the three exercise groups, thus

confirming it was the type of exercise, not BDI variability, that caused the moderation.)

Next, composite PR adherence was regressed against baseline BDI-II and covariates. BDI-II was not found to be a significant independent predictor of lower composite adherence (see table 40 in Appendix F). Combining PR attendance and exercise compliance into *composite* adherence (outcome) resulted in the significant relationship between BDI-II and exercise compliance being masked by the weak relationship between BDI-II and PR attendance in our sample. IT exercise was the only covariate to emerge as a significant independent predictor of poorer composite adherence (see Table 40), but this was driven mainly by the exercise compliance component (see Appendix F for more PR composite adherence results).

Finally, exercise levels at follow-up were regressed against baseline BDI-II and our five covariates. Verification of data revealed an extreme multivariate outlier (standardized residual = 3.29) that exerted substantial influence on the model (biased the parameter estimates and dramatically affected the sum of squared errors – see assessment of bias and normality in Appendix C, table 29). We therefore ran the regression analysis both with and without the multivariate outlier in the data set, as recommended by Field (2013) and Tabachnick and Fidell (2013). We believed excluding the multivariate outlier would produce a less biased result more representative of our sample. Table 5 displays results derived from data which included the outlier. It shows that the regression model accounted for only 19 % (adjusted R^2) of the variation of follow-up exercise levels and did not predict significantly better than using the outcome's mean. Baseline BDI-II did not emerge as a

significant predictor. Baseline smoking status had the only statistically significant (negative) association with post-PR exercise levels.

Table 5

Multiple Regression Model for Prediction of Exercise Levels at Follow-Up by Baseline BDI-II with Covariates (Multivariate Outlier Included)

Variable	<i>B</i>	β	Bootstrap ^a		
			<i>SE B</i>	<i>p</i>	95 % CI for <i>B</i> ^b
Constant	1742.89		607.51	.014	[475.32, 3065.67]
bBDI-II	-27.30	-.20	35.07	.513	[-87.55, 30.93]
IT	-175.46	.11	352.03	.623	[-1075.30, 512.86]
CTHi	-242.30	.16	344.48	.523	[-959.65, 416.89]
Sex (F)	-111.35	-.07	236.37	.635	[-663.36, 335.54]
bFEV ₁ %	-2.37	-.06	6.88	.716	[-16.13, 10.26]
bSmoking	-678.88	-.44	211.10	.011	[-1208.45, -199.70]
Regression Model	<i>R</i> = .58	Adjusted <i>R</i> ² = .19	<i>F</i> (6, 29) = 2.39, <i>p</i> = .053		

Note. *N* = 36. CI = confidence interval; bBDI-II = baseline Beck Depression Inventory-II; IT = interval training; CTHi = constant training high intensity; bFEV₁ % = baseline forced expiratory volume in the first second percent of predicted normal value; bSmoking = smoking at baseline. ^aBootstrap results are based on 1000 bootstrap samples. ^bConfidence intervals are bias-corrected and accelerated.

The analysis was repeated with the multivariate outlier removed (see Table 6 below). The full model then accounted for 46 % (adjusted *R*²) of the variation of exercise levels at follow-up. Within the context of this model, baseline BDI-II emerged as the strongest independent predictor of exercise levels at follow-up. Baseline Smoking was the only significant covariate to emerge and predicted lower exercise levels at follow-up.

These results, derived from data with the multivariate outlier excluded, are less biased and more representative of this sample (see Appendix C, Tables 29 and 30).

Table 6

Multiple Regression Model for Prediction of Exercise Levels at Follow-Up by Baseline BDI-II with Covariates (Multivariate Outlier Removed)

Variable	<i>B</i>	β	Bootstrap ^a		
			<i>SE B</i>	<i>p</i>	95 % CI for <i>B</i> ^b
Constant	1923.64		527.47	.004	[1033.71, 3005.76]
bBDI-II	-62.06	-.50	18.67	.004	[-106.02, -30.55]
IT	41.85	.03	267.19	.882	[-438.50, 557.68]
CTHi	41.88	.03	244.09	.868	[-471.41, 539.28]
Sex (F)	-188.55	-.14	210.40	.351	[-603.64, 113.50]
bFEV ₁ %	-4.15	-.11	6.13	.487	[-18.55, 8.23]
bSmoking	-557.23	-.41	174.16	.008	[-899.97, -118.53]
Regression Model	<i>R</i> = .75	Adjusted <i>R</i> ² = .46	<i>F</i> (6, 28) = 5.84, <i>p</i> < .001		

Note. *N* = 35. CI = confidence interval; bBDI-II = baseline Beck Depression Inventory-II; IT = interval training; CTHi = constant training high intensity; bFEV₁ % = baseline forced expiratory volume in the first second percent of predicted normal value; bSmoking = smoking at baseline. ^aBootstrap results are based on 1000 bootstrap samples. ^bConfidence intervals are bias-corrected and accelerated.

A moderation model was tested, again using the method by Hayes (2013), to determine if the relationship between baseline BDI-II (the predictor) and exercise levels at follow-up (the outcome) changed as a function of sex (the moderator) while adjusting for baseline exercise intervention, FEV₁ % predicted, and smoking status. A significant interaction effect was found between baseline BDI-II and Sex (*b* = 116.22, 95 % CI [22.33, 209.96], *t* = 2.54, *p* = .017), indicating that the relationship between baseline BDI-II scores

and MET minutes of exercise at 9 months post-PR was indeed moderated by the sex of the participants (see Figure 9). With female participants, there was a non-significant negative relationship between baseline depression symptomatology and follow-up exercise levels, $b = -29.30$, 95 % CI $[-66.05, 7.44]$, $t = -1.64$, $p = .113$. However, with male participants, there was a stronger and statistically significant negative relationship between baseline depression symptomatology and follow-up exercise levels, $b = -145.45$, 95 % CI $[-235.45, -55.45]$, $t = -3.32$, $p = .003$. (This occurred despite the lower variability of male BDI scores compared to that of females, thus confirming that the moderation was indeed due to sex, not the differences in variability of BDI scores).

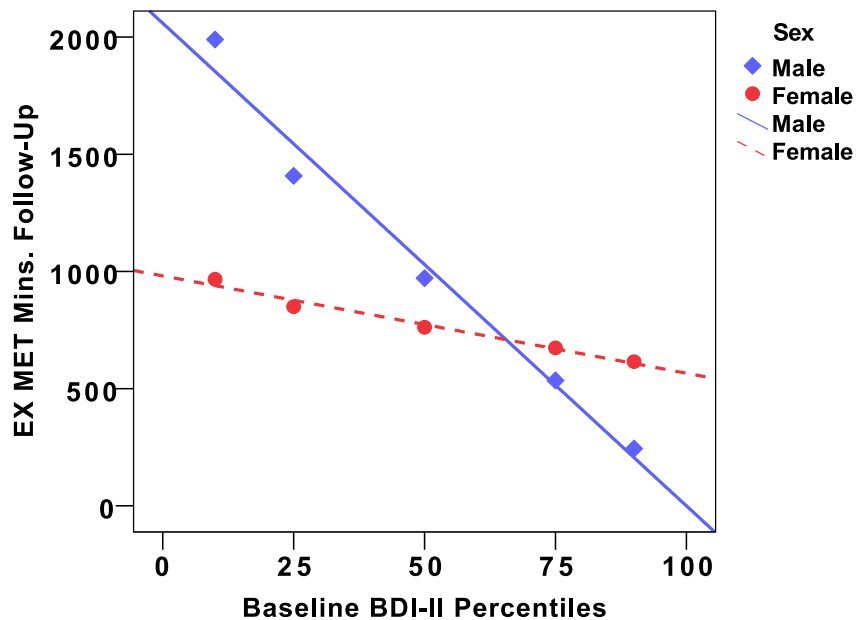


Figure 9. Baseline depression predicting exercise levels at follow-up moderated by sex (adjusting for PR exercise intervention, baseline FEV₁% predicted, and smoking status; multivariate outlier removed, $N = 35$).

Mediation models were also tested and no variables were found to mediate the relationship between baseline BDI-II and PR attendance, PR exercise compliance, or levels of exercise maintained at follow-up.

Secondary Multivariate Analyses

Secondary analyses, exploratory in nature, were run with the objective of developing linear regression models with the fewest IVs that could best predict each outcome: PR attendance, PR exercise compliance, and exercise levels at follow-up. Predictors were selected based on their Pearson correlations with each outcome (see Appendix B, Table 39), their emergence as significant covariates in the primary analyses, findings of previous studies, and theory. It was decided a priori that the ratio of predictors to number of participants would be no larger than 1/6 due to the relatively small N of our sample. For all analyses, the univariate BDI-II extreme outlier was winsorized to reduce bias (see Appendix C Tables 31 to 37 for assessments of bias and normality justifying winsorizing the high BDI-II score). Bootstrapping (using 1000 samples) was again performed because of the relatively small sample size and violation of some assumptions for linear regression.

A standard linear regression with PR attendance as the outcome and baseline FEV₁% predicted, cohabiting (or not), and HLC Other People scale, as predictor variables was found to account for 36% (adjusted R^2) of the variation in PR attendance, which predicted the outcome significantly better than using its mean. As can be seen in Table 7, higher FEV₁% and cohabiting were significant predictors of higher PR attendance. HLC

“Other People” strengthened the model somewhat, though it did not reach statistical significance.

Table 7

Multiple Regression Model with Strongest Predictors of PR Attendance

Variable	<i>B</i>	β	Bootstrap ^a		
			<i>SE B</i>	<i>p</i>	95 % CI for <i>B</i> ^b
Constant	-9.20		23.55	.716	[-52.59, 42.05]
bFEV ₁ %	0.92	.57	0.26	.004	[0.43, 1.34]
Cohabiting	24.04	.42	9.44	.026	[5.78, 43.21]
HLC other people	4.27	.22	2.83	.144	[-1.02, 9.95]
Regression Model	<i>R</i> = .65	Adjusted <i>R</i> ² = .36	<i>F</i> (3, 32) = 7.64, <i>p</i> = .001		

Note. *N* = 36. CI = confidence interval; FEV₁ % = forced expiratory volume in the first second percent of predicted normal value; HLC = health locus of control scale.

^aBootstrap results are based on 1000 bootstrap samples. ^bConfidence intervals are bias-corrected and accelerated.

Next, it was found that a multiple regression model comprised of the IT and CTHi exercise protocols (CTVT as the reference), sex, FEV₁ % predicted, and baseline BDI-II accounted for 47 % (adjusted *R*²) of the variation in PR exercise compliance. Each predictor’s contribution, except for CTHi, was statistically significant. The IT exercise intervention, higher baseline BDI-II scores, and higher baseline FEV₁ % were predictive of lower PR exercise compliance, while being female predicted higher exercise compliance (see table 8 below).

Table 8

Multiple Regression Model with Strongest Predictors of PR Exercise Compliance

Variable	<i>B</i>	β	Bootstrap ^a		
			<i>SE B</i>	<i>p</i>	95 % CI for <i>B</i> ^b
Constant	141.85		19.31	.001	[100.75, 181.61]
BDI-II	-2.48	-.40	0.97	.031	[-4.41, -0.58]
IT	-54.49	-.77	11.23	.003	[-76.87, -28.48]
CTHi	-10.10	-.14	9.72	.322	[-28.18, 5.89]
Sex (F)	26.75	.38	11.00	.027	[3.40, 47.94]
FEV ₁ %	-0.57	-.33	0.28	.029	[-1.10, -0.09]
Regression Model	<i>R</i> = .74	Adjusted <i>R</i> ² = .47	<i>F</i> (5, 30) = 7.32, <i>p</i> < .001		

Note. *N* = 36. CI = confidence interval; BDI-II = Beck Depression Inventory-II; IT = interval training; CTHi = constant training high intensity; FEV₁ % = forced expiratory volume in the first second, percent of predicted normal value.

^aBootstrap results are based on 1000 bootstrap samples. ^bConfidence intervals are bias-corrected and accelerated.

Next, a multiple regression analysis was run on the outcome of exercise levels at follow-up with baseline BDI-II, smoking status, and health locus of control (HLC) *chance* scale as predictors. Examination of residuals revealed an extreme *multivariate* outlier (standardized residual = 3.79), which exerted substantial influence on the model as a whole (see Appendix C, Tables 34 to 37). Regression results are therefore presented for analyses that included the outlier followed by those for which the outlier was removed, as suggested by Field (2013) and Tabachnick and Fidell (2013). Table 9 below presents results, which included the outlier. The model predicted the outcome significantly better than the outcome's mean accounting for 33 % (adjusted *R*²) of the variation in exercise

levels at follow-up. Baseline smoking status and higher HLC Chance scores were statistically significant predictors of lower levels of exercise at follow-up. Baseline BDI-II's contribution was weak and not statistically significant.

Table 9

Multiple Regression Model with Strongest Predictors of Exercise Levels at Follow-Up (Multivariate Outlier Included)

Variable	<i>B</i>	β	Bootstrap ^a		
			<i>SE B</i>	<i>p</i>	95 % CI for <i>B</i> ^b
Constant	2178.21		361.40	.001	[1216.11, 2830.27]
BDI-II	-23.95	-.18	31.69	.542	[-73.21, 29.93]
bSmoking	-800.41	-.52	197.14	.006	[-1262.08, -386.56]
HLC chance	-292.28	-.35	95.25	.009	[-503.91, -73.36]
Regression Model	<i>R</i> = .65	Adjusted <i>R</i> ² = .37	<i>F</i> (3, 32) = 7.71, <i>p</i> = .001		

Note. *N* = 36. CI = confidence interval; BDI-II = Beck Depression Inventory-II; bSmoking = smoking at baseline; HLC = health locus of control.

^aBootstrap results are based on 1000 bootstrap samples. ^bConfidence intervals are bias-corrected and accelerated.

However, this changed markedly when the multivariate outlier was removed. Table 10 presents results from the analysis with the multivariate outlier removed (*n* = 35).

(Removing the multivariate outlier reduced bias and improved the generalizability of the model, but bootstrapping was still used because of heterogeneity of variance, see Table 37 in Appendix C). The regression model was significantly better at predicting post-PR exercise levels than using its mean. The three predictors combined accounted for 62 % (adjusted *R*²) of the variation in exercise levels 9-months post-PR. Higher baseline BDI,

smoking at baseline, and lower HLC Chance all emerged as statistically significant independent predictors of lower exercise levels at follow-up.

Table 10

Multiple Regression Model with Strongest Predictors of Exercise Levels at Follow-Up (Multivariate Outlier Removed)

Variable	<i>B</i>	β	Bootstrap ^a		
			<i>SE B</i>	<i>p</i>	95 % CI for <i>B</i> ^b
Constant	2249.03		295.11	.001	[1608.14, 2845.93]
BDI-II	-56.33	-.45	14.02	.002	[-86.73, -31.24]
bSmoking	-643.34	-.48	131.78	.001	[-923.54, -374.90]
HLC chance	-273.16	-.38	79.22	.002	[-427.81, -106.10]
Regression Model	<i>R</i> = .81	Adjusted <i>R</i> ² = .62	<i>F</i> (3, 31) = 19.38, <i>p</i> < .001		

Note. *N* = 35. CI = confidence interval; BDI-II = Beck Depression Inventory-II; bSmoking = smoking at baseline; HLC = health locus of control.

^aBootstrap results are based on 1000 bootstrap samples. ^bConfidence intervals are bias-corrected and accelerated.

Differences Between Study Completers and Dropouts

Differences in baseline characteristics, PR attendance and PR exercise compliance levels between participants who attended the follow-up evaluations (completers) and those who did not (dropouts) were examined. Boxplots and Mann-Whitney U tests were used for continuous variables, while bar graphs and Pearson chi-square tests were used for categorical data. Twenty-eight (78 % of the total) participants attended the follow-up evaluation 9 months post-PR, while eight (22 %, all females) did not. Mann-Whitney U tests (see Table 11) revealed that dropouts (participants who did not attend follow-up

Table 11

Differences Between Study Completers and Dropouts Assessed with Mann-Whitney U

Baseline Characteristics & PR Data	Median for Completers (n = 28)	Median for Dropouts (n = 8)	U Statistic	z (Stand. Test Statistic)	P ^a (2-tailed)	Effect Size ^b
Age	69.0	64.0	86.0	-0.99	.333	-.16
BMI	27.3	25.2	92.0	-0.76	.466	-.13
Smk Hx p-yrs	42.5	37.5	93.5	-0.71	.492	-.12
HLC internal	4.7	4.0	83.5	-1.09	.287	-.18
HLC chance	2.5	2.8	106.0	-0.23	.830	-.04
HLC doctor	5.5	5.0	89.0	-0.91	.374	-.15
HLC other people	3.0	2.8	87.5	-0.94	.361	-.16
BDI-II	7.0	11.5	56.5	-2.12	.033	-.35
FEV ₁ %	64.9	44.9	54.0	-2.21	.027	-.37
FEV ₁ /FVC %	52.1	42.2	45.0	-2.55	.009	-.42
ESWT seconds	380.5	281.5	65.5	-1.77	.078	-.29
PR Attend %	87.5	52.8	55.0	-2.18	.028	-.36
PR Exercise Compliance %	96.7	71.3	59.0	-2.02	.043	-.34

Note. BMI = body mass index, Smk Hx p-yrs = smoking history in pack-years, HLC = Health Locus of Control scale (0-6), BDI-II = Beck Depression Inventory (0-63), FEV₁ % = forced expiratory volume in 1 second percent of predicted normal value, FEV₁/FVC = ratio of forced expiratory volume in one second to forced vital capacity, ESWT = endurance shuttle walking test, PR Attend % = percent of pulmonary rehabilitation classes attended, PR Exercise Compliance % = percent of total pulmonary rehabilitation exercise session time during which participant was exercising within or above their target heart rate range.

^aThe *exact* method was used to calculate *p*.

^bThe effect size was calculated by dividing *z* (standardized test statistic) by the square root of *N* (Field, 2013).

evaluations) had statistically significant higher baseline depression scores, lower FEV₁ % predicted and FEV₁/FVC values, and lower rates of both PR attendance and PR exercise compliance.

Bar graphs illustrate differences in baseline nominal variables between study completers and dropouts (see Figure 10 below). Pearson's chi-square tests of independence were also conducted to determine whether sex, smoking status, cohabiting status (living alone vs. with someone), or the prescribed exercise training regimen for PR were each associated with completing the study or dropping out. There was a significant association between sex and attendance at the follow-up evaluations: $\chi^2 (1) = 5.81$, p (Fisher's exact sig.) = .032: Females tended to drop out whereas males tended to complete the follow-up evaluation. The association between baseline smoking status and completing the study was not statistically significant: $\chi^2 (1) = 3.94$, p (Fisher's exact sig.) = .086. However, there was a trend of participants smoking at baseline being more likely to drop out. There was virtually no association between cohabiting status and attendance at follow-up evaluation: $\chi^2 (1) = .080$, p (Fisher's exact sig.) = 1.000. The association between PR exercise intervention and follow-up attendance was significant: $\chi^2 (2) = 9.0$, p (Fisher's exact sig.) = .014, Cramer's V = .500, p (exact significance) = .014. Participants undergoing IT exercise during PR had the highest drop-out rate with 75 % not attending follow-up, followed by 25 % dropout rate for CTHi, and 0 % for CTVT.

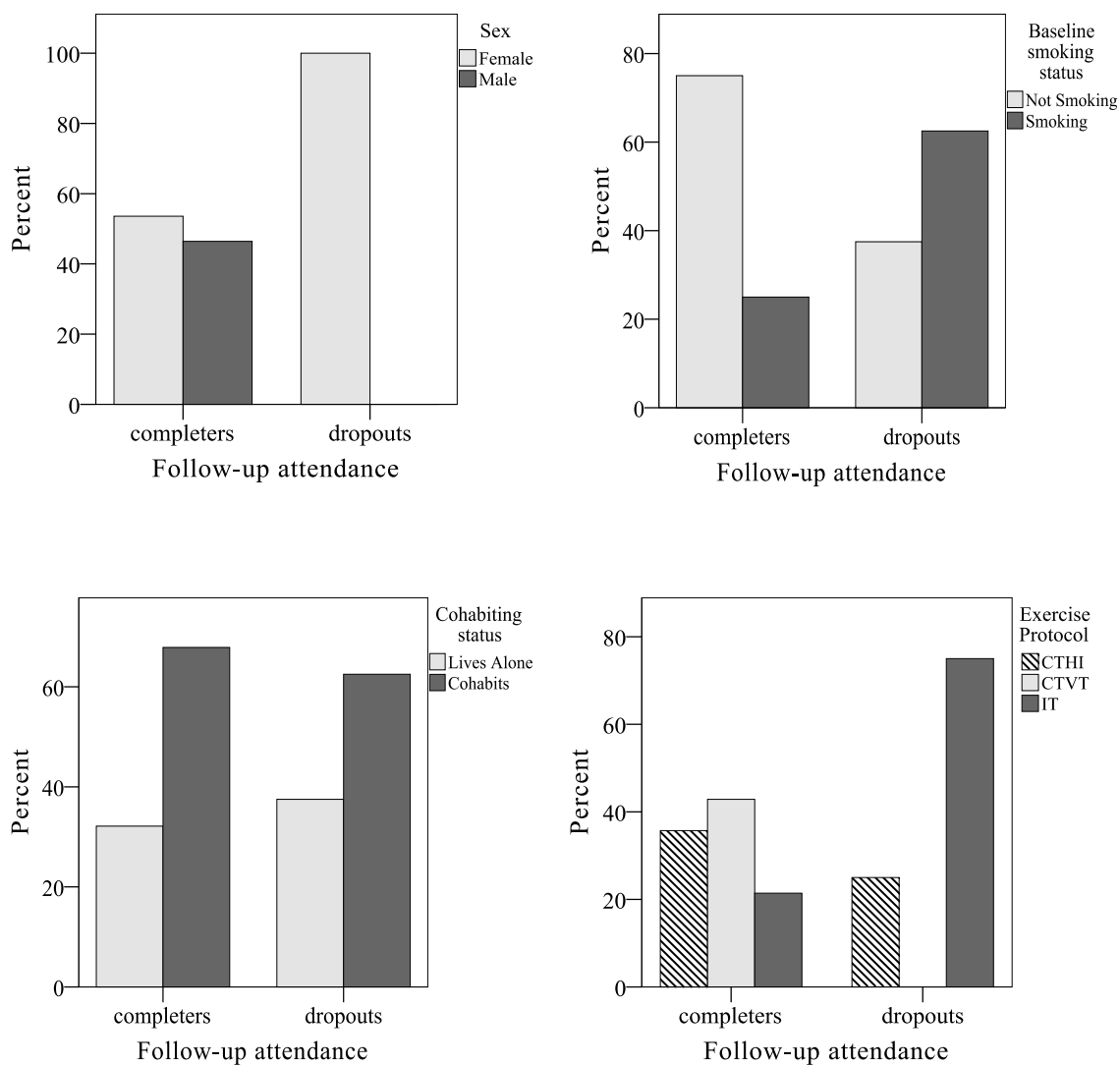


Figure 10. Differences between study completers (did attend follow-up evaluation, $n = 28$) and dropouts (did not attend, $n = 8$).

Discussion

Primary Findings

This study investigated baseline depressive symptoms as a predictor of: 1) attendance at PR exercise sessions, 2) compliance with endurance exercise intensity targets prescribed for PR, and 3) level of exercise maintained 9-months post-PR in a sample of patients with moderate to severe COPD. After adjusting for covariates, we found that while greater baseline depressive symptomatology did not predict PR attendance, it did predict lower compliance with exercise targets during PR as well as lower levels of exercise maintained at 9-months post-PR. This indicates that depressive symptoms at entry to PR may be more predictive of exercise compliance than attendance during PR, and predict the maintenance of physical exercise after termination of PR.

Depressive Symptoms

Depression symptomatology at baseline (entry to PR) was generally low in our sample (median = 8.5, IQR = 6-13), with only 14 % of participants having symptoms at or above the “caseness” threshold, as measured by the BDI-II. This is lower than levels generally reported in the COPD population (K. M. Hynninen et al., 2005; Mikkelsen et al., 2004) and may be due to self-selection for participating in this intervention study; patients who consented to undergo the 36 exercise sessions over 12 weeks may have had less depression than those who declined, as has been documented for patient uptake in PR following initial assessment (Cassidy et al., 2014; Johnston & Grimmer-Somers, 2010).

Depression and PR Exercise Session Attendance

PR attendance levels, defined as the percentage of total number of sessions attended, were generally high (median = 84 %, IQR = 67-94), a rate similar to those found in a review of RCTs on PR (Bjoernshave, Korsgaard, & Nielsen, 2010). Contrary to our hypothesis, baseline depressive symptoms did not predict PR attendance in our sample, in both univariate and multivariate analyses. This may have been due to the generally low levels of depressive symptoms, which may not have interfered with attendance. Furthermore, the close supervision, attention, and support afforded by the high ratio of two supervisors (trained exercise physiologists) per six participants may have helped overcome the potential impact of depressive symptoms on attendance.

Our finding conflicts with many previous studies which found an association between baseline depressive symptoms and PR attendance; however, this discrepancy may be due to different participant characteristics, larger sample sizes, and the timing of attendance measures. For example, Fan et al. (2008) in the National Emphysema Treatment Trial (NETT), who observed similar mean baseline depression scores on the original version of the BDI, found that greater baseline depressive symptomatology did predict lower attendance at PR exercise sessions. However, they measured attendance at 10 PR exercise sessions delivered over a 9 to 10-week period that followed an initial 16 to 20 mandatory exercise sessions that were performed over a 6 to 10-week period prior to randomization. It was only during the post-randomization phase consisting of 10 exercise sessions that an association between baseline depression symptoms and attendance was

measured and found. It has been documented that attendance diminishes as the length of a PR program increases (Sabit et al., 2008), which may be why an association between baseline depression levels and attendance was found in the NETT study but not in ours: our study measured attendance from week 0 to 12 of PR, whereas attendance was measured starting sometime between the 7th to the 11th week of exercise and ending sometime between the 16th and 19th week in the NETT trial. Another possible explanation for the discrepancy in findings between our study and the NETT is that patients' COPD was much more severe in the NETT (mean FEV₁ % = 27, *SD* = 7) compared to our sample (mean FEV₁ % = 59, *SD* = 17). COPD severity might have moderated the relationship between depressive symptoms and attendance such that an association might only have emerged in the context of more severe COPD than was present in our sample. Of note, a moderation model was tested in our study, but no interaction was found between baseline depressive symptoms and FEV₁ % predicted (as a measure of COPD severity).

Our results are also inconsistent with those of Garrod et al. (2006), who also found that depression predicted attendance at PR exercise sessions. Patients who completed < 10 out of 14 PR sessions were defined as dropouts. The authors stratified baseline and outcome measures according to Medical Research Council dyspnea grades and reported that 46 % of dropouts had a Medical Research Council dyspnea grade of 5 or "severe." Unfortunately, the authors presented no scores for depression despite listing it as one of their primary outcomes and reporting that it independently discriminated PR completers from PR drop-outs. Once again, it is possible that the association between depression and

attendance found in that study emerged in the context of greater COPD severity than was present in our study, and that this could account for the discrepant findings.

Yet another study reporting that baseline depression levels predicted PR attendance was conducted by Hogg et al. (2012). They reported higher levels of baseline depression in their sample relative to ours (31 % at or above the “caseness” threshold, as measured by the Hospital Anxiety and Depression Scale, versus 14 % in ours, as measured by the BDI-II). Furthermore, their sample was comprised of a larger proportion of patients whose COPD was more severe: 52 % with GOLD stages III & IV versus only 37 % in our sample. The higher levels of baseline depression and more severe COPD within a much larger sample (n = 656) than ours may have resulted in the emergence of depression as a statistically significant independent predictor of PR attendance in their analysis. Greater severity in both COPD and depression, and larger sample sizes, may explain why an association between baseline depression and PR attendance emerged in these studies but not in ours.

Depression and PR Exercise Compliance

To our knowledge, this was the first study to examine baseline depressive symptomatology as a predictor of compliance with the aerobic exercise intensity prescribed in PR. Previous “adherence” studies have only reported levels of PR uptake and attendance. We used continuous data tracking technology that measured heart rate during each and every exercise training session to determine the percentage of time

participants were exercising within or above their target heart rate range. Levels of compliance were high overall: the median proportion of time that participants exercised within or above the target heart rate zone was 94 % (IQR = 71-99 %). Univariate correlational analyses revealed a negative association between baseline depressive symptomatology and compliance with prescribed exercise intensity. Multivariate analyses also found that greater depressive symptomatology predicted lower compliance ($\beta = -.40$), after adjusting for exercise protocol, sex, baseline FEV₁ % and smoking status. Finding this significant relationship in the context of generally low levels of depressive symptoms, high levels of compliance, and a relatively small sample size, suggests that baseline depressive symptoms may be a fairly robust predictor of exercise compliance. This finding is similar to those of related studies which have investigated the impact of depression on compliance with a variety of health behaviors (other than exercising at specified intensities) prescribed across a range of medical conditions (DiMatteo et al., 2000; Grenard et al., 2011).

To our knowledge, only one other study (Lavoie et al., 2004) has ever investigated the association between depressive symptoms and compliance with a target exercise intensity, but this was with a sample of patients with coronary artery disease as opposed to COPD. Lavoie et al. investigated this association in the context of an exercise stress test, and assessed performance of patients undergoing electrocardiography or single-photon-emission-computer-tomography for the detection of myocardial ischemia. Baseline depressive symptoms were measured with an earlier version of the Beck

Depression Inventory (BDI) and the Primary Care Evaluation of Mental Disorders (PRIME-MD). They measured exercise stress test performance using total exercise METs, duration, and, as in our study, they recorded the percent of maximum predicted heart rate as an indicator of exercise intensity. Consistent with our findings, they reported a significant negative association between meeting criteria for a baseline depression (both major depressive disorder and subthreshold symptom levels) and their three measures of exercise performance. Patients with higher levels of depression performed more poorly on their exercise stress tests to the extent that some were unable to achieve the minimum level of intensity required for a valid stress test outcome in detecting myocardial ischemia (which increased the risk for false negative tests).

Our findings also correspond to the manifestation and impact of depressive symptoms in daily life: both cognitive and somatic symptoms of depression can make initiating and sustaining even moderate levels of exercise (and other health behaviors) too difficult to engage in (Detweiler-Bedell, Friedman, Leventhal, Miller, & Leventhal, 2008; Roshanaei-Moghaddam et al., 2009). For example, a lack of pleasure, interest and motivation; feeling hopeless; difficulty concentrating, possibly combined with insomnia, fatigue, and psychomotor retardation are all potential obstacles to reaching exercise targets, even when patients do attend PR sessions.

Exercise protocol as a moderator. We found a significant interaction between baseline BDI-II score and type of endurance exercise (i.e., CTVT, CTHi, and IT),

indicating that exercise protocol moderated the relationship between baseline depressive symptomatology and exercise compliance during the PR program. The strength of the inverse relationship between baseline depressive symptomatology and exercise compliance was greatest for the IT exercise protocol, followed by CTVT, and weakest for CTHi. Physiological and respiratory response measures taken during exercise, previously reported by Rizk (2014), indicate that IT was the most demanding in terms of metabolic strain (followed by CTHi and CTVT) and was therefore the most difficult for our participants to comply with. The moderation model suggests that the negative impact of baseline depressive symptomatology on exercise compliance increased with the demands of the exercise protocol, a finding supported by some previous studies, though not in the context of COPD (Callaghan, Khalil, Morres, & Carter, 2011; Khalil, Callaghan, Carter, & Morres, 2012; Morgan, 2001). It is interesting that in the moderation model, baseline depressive symptomatology had a greater (negative) impact on CTVT compliance than on CTHi because CTVT was of a lower intensity (i.e., easier for participants) than CTHi. One possible explanation is that CTVT's duration was on average 5 minutes and 40 seconds longer than CTHi's and that the association between baseline depression and compliance may have been driven by the longer duration of CTVT rather than the difference in exercise intensity between CTVT and CTHi: the difference between CTVT and CTHi target exercise intensity was relatively small (on average 7.6 heart beats per minute) compared to the difference between CTHi and IT (16.1 heart beats per minute). A second possible explanation, presented by Rizk et al. (2015) is that the greatest drop in global positive affect (the degree of pleasure experienced) occurred in participants

undergoing the CTVT exercise regimen halfway through their exercise session. This suggests that they may have experienced a state of boredom due to under arousal, compared to participants in the CTHi and IT interventions (Rizk, 2014). To summarize, baseline depressive symptomatology may have had a greater negative impact on compliance within the CTVT than on the CTHi group because of CTVT's longer duration and the lower levels of arousal it produced. It has been reported that better exercise participation is achieved when participants with depression choose their own levels of exercise intensity (Callaghan et al., 2011); this may also apply in PR for COPD.

Depression and Post-PR Exercise Levels

In contrast to the overall high rates of PR attendance and exercise compliance, the median volume of exercise that participants reported engaging in at 9-months post PR was fairly low (706 MET minutes) when compared to the level recommended (842 MET minutes), which was based on the amount of exercise performed during participants' final three PR sessions. In fact, 58 % of participants fell short of meeting their prescribed weekly target, a finding consistent with previous reports on post-PR levels of exercise and physical activity (Cindy Ng et al., 2012; Soicher et al., 2012).

In support of our hypothesis, greater baseline depressive symptomatology predicted lower levels of exercise maintained at follow-up in both univariate and multivariate analyses ($\beta = -.50$), again adjusting for exercise protocol, sex, baseline FEV₁ % and smoking status. This is consistent with the findings of Heerema-Poelman et al. (2013) and

Roshanaei-Moghaddam et al. (2009), who also found that higher depressive symptomatology was associated with a longitudinal decline in the levels of exercise maintained. Of note in our study is that baseline depression, compared to all other variables, emerged as the strongest predictor of post-PR exercise behavior in the context of our covariates. It is not surprising that after termination of the PR program, with the loss of the support, guidance, assurances, and structure it provided, that many participants did not autonomously maintain the levels of exercise they were engaging in during the program, especially those who had higher levels of depressive symptoms at the start of PR.

Interestingly one remarkable exception to this pattern emerged (a multivariate outlier) who had the second highest baseline BDI-II score and yet reported engaging in the highest level of exercise post-PR. This single case represents the ideal PR outcome for a patient with COPD and comorbid depressive symptoms. Closer examination revealed that this 65-year old female with moderate COPD had a history of regular walking for exercise, had quit smoking 3 months before starting PR, had hypothyroidism (with symptoms of fatigue, dizziness, hot flashes indicating a possible hormone imbalance during the period of PR), and was experiencing some stress related to her elderly parent's and her own living arrangements. Post-PR, she had resumed walking 5 days per week, remained a non-smoker, had settled her living arrangements, and had received an increased dose of thyroid medication. Her post-PR BDI score was 6, down from her baseline of 21. It is not known whether she received treatment for her depressive

symptoms per se, however it is well known that inadequately treated hypothyroidism can manifest with symptoms similar to depression. This case illustrates how adequate treatment may help alleviate the negative impact that clinically significant depressive symptoms can have on PR outcomes.

Sex as a moderator. We determined that sex moderated the relationship between baseline depressive symptomatology and exercise levels maintained 9 months after PR: the negative association between baseline depressive symptoms and post-PR exercise levels was significantly stronger for men than for women. This suggests that the women in our sample were less impacted by the presence of baseline depressive symptoms than the men with regards to continuing to exercise after PR. This finding emerged despite a trend of higher baseline depressive symptoms in women (mean = 10, *SD* = 5.8) compared to men (mean = 7, *SD* = 4.4) in our sample, which is consistent with the higher rates of depression (subclinical and clinical) reported in women in the general adult population (Nolen-Hoeksema, 2001; Weissman et al., 1996). This might be explained by some of the gender differences in the way depression is experienced, responded to, reported, and impacts daily functioning. For example, one study (Poutanen, Koivisto, Mattila, Joukamaa, & Salokangas, 2009) found that significantly more depressed men than women reported that “everything was an effort,” which may result in poorer maintenance of regular exercise, which requires some (physical) effort. Another possible explanation is that perhaps many women in our sample were, as homemakers, more accustomed to engaging regularly in physical activity at home over the years than men, whose physical

activity was linked more to their work outside the home, and who became more sedentary after retiring (Nolen-Hoeksema, 1990). This, however, is only speculative: the literature on sex differences in depression is vast, complex, and inconclusive and we cannot provide any definitive explanation for sex moderating the relationship between baseline depressive symptoms and exercise levels post-PR, though it might merit further investigation.

In summary, finding a negative association between baseline depressive symptomatology and exercise intensity compliance, but not attendance in this sample, suggests that baseline depressive symptomatology may have had a greater impact on these patients' ability to achieve and sustain target exercise intensities than it did on attending PR sessions. However, given that patients had to volunteer to participate in the study, it is likely there was some degree of selection bias, with patients with severe depression being less likely to volunteer for a demanding PR trial such as this. Further, for those who did participate in the study, once the structure and support of supervised PR ended, baseline depression appeared to exert its greatest impact on levels of exercise maintained autonomously (an example of a substantial behavior change challenge).

Secondary Findings

Our secondary objectives were exploratory and conducted in order to generate hypotheses to be tested in future research. One objective was to identify baseline variables, in addition to depressive symptomatology, that were predictive of outcomes in our sample. These emerged as significant variables in correlational analyses or as significant

covariates in our primary regression analyses. Using these baseline variables, we derived three separate regression models composed of the fewest number of variables that accounted for the greatest variance in each of our three outcomes. Our hypothesis was supported: The sets of baseline variables that predicted PR attendance, PR exercise compliance, and level of exercise maintained post PR were different for each outcome. Findings must be interpreted with caution due to the limited sample size and study design: they only signal possible relationships and, as such, suggest topics for further research.

Strongest Predictors of PR Attendance

In bivariate analyses, baseline FEV₁ % predicted had a positive and significant correlation with PR attendance. In multivariate analyses, independent predictors of higher PR attendance were: higher FEV₁% ($\beta = .57$), cohabiting ($\beta = .42$), and stronger “other people” health locus of control orientation ($\beta = .22$), with the latter not reaching statistical significance but contributing nevertheless to the regression model, which overall accounted for 36 % of the attendance variance (see Table 7). FEV₁ % predicted is a measure of COPD severity and the positive association with PR attendance found in this study is consistent with previous reports from studies with much larger sample sizes (Fan et al., 2008; Hayton et al., 2013). Though a causal relationship cannot be drawn from the present (or previous) studies, it is likely that participants with more severe COPD (poorer lung function) experience greater symptoms of dyspnea and fatigue, more frequent COPD exacerbations (O'Donnell et al., 2007), and may therefore attend fewer PR sessions than those whose disease is less severe. Living alone also emerged as a significant independent

predictor or lower PR attendance, a finding consistent with those reported in the review by Keating et al. (2011). This association may be due to the fact that participants who live by themselves bear more or all of the responsibility for tasks of daily living (such as shopping and other errands, preparing meals, maintaining their home, travel and transportation), which may sometimes not leave them adequate time and energy needed to attend PR sessions. Another possibility is that people living alone may not receive as much support or encouragement for attending an exercise program, which has been linked to poorer attendance or dropout (Hayton et al., 2013; Keating et al., 2011). Having a stronger *other people* health locus of control orientation was a third independent predictor of greater attendance. It refers to a belief that other people play a role in or can impact one's own health. Although an *other people* locus of control as a predictor of PR attendance did not reach statistical significance, we retained it because, to our knowledge, this is the first study to investigate health locus of control in COPD and it did contribute somewhat to the regression model. In contrast to participants with an internal HLC orientation, those with a more external *other people* health locus may respond more favorably to sources of motivation outside themselves, such as the support of trainers and interactions/discussion with a group of peers (integral to PR), resulting in higher attendance. Normally, an external locus of control orientation was believed to be associated with poor engagement in health-related behaviors (Norman, Bennett, Smith, & Murphy, 1998). However, our finding along with those others (Burk & Kimiecik, 1994; Janowski, Kurpas, Kusz, Mroczek, & Jedynak, 2013) suggest that an *other people* orientation may be linked to greater engagement in certain health behaviors, depending

perhaps on the specific context, such as learning and adopting new health management behaviors in a group rehabilitation setting. Although inconclusive here, locus of control may merit further investigation to determine if it helps drive PR attendance.

Strongest Predictors of PR Exercise Compliance

Correlational analyses indicated significant and borderline significant associations respectively between both the IT exercise protocol, baseline BDI-II, and PR exercise compliance. In multivariate analyses, IT ($\beta = -.68$), higher baseline BDI-II ($\beta = -.41$), male sex ($\beta = -.35$), and higher FEV₁ % pred ($\beta = .30$) were the strongest predictors of lower PR exercise compliance and together accounted for 48 % of its variance. All four variables were significant independent predictors. Surprisingly, IT was associated the lowest levels of exercise compliance (median of 49 %), compared to the CTVT and CTHi (medians of 98 % and 95 %, respectively), and emerged as the strongest independent predictor of poor exercise compliance. Physiological and respiratory measures (i.e., heart rate, respiratory rate, minute ventilation) previously reported by (Rizk, 2014) indicated that IT was the most demanding exercise regimen, compared to CTHi and CTVT. This is contrary to previous reports where IT was recommended and offered as an exercise option because it was better tolerated by patients with more severe COPD (Sabapathy, Kingsley, Schneider, Adams, & Morris, 2004; Vogiatzis et al., 2004). As explained by Rizk et al. (2015), the disparity between our finding and that of Sabapathy et al. (2004) can be attributed to our IT intervals being shorter (30 versus 60 seconds), higher in relative intensity (100 % versus 70 % peak wattage), and our recovery being an active one (unloaded pedaling intervals)

versus complete rest. These factors may not have allowed for sufficient rest to repeatedly attain the target heart rate that was prescribed for the exercise interval. Other findings, such as those of Vogiatzis et al. (2004), conflict with ours possibly because their continuous training protocol was of higher intensity than our CTHi, which resulted in their IT being relatively easier and better tolerated compared to IT (see Rizk et al., 2015). Furthermore, IT, which required repeatedly alternating between recovery and maximal intensity every 30 seconds throughout the whole training duration, may have demanded levels of alertness and motivation which surpassed those of many participants, especially those with higher baseline depressive symptomatology.

As with the primary multivariate analyses, higher baseline depressive symptomatology (BDI-II score) remained a significant independent predictor of lower exercise compliance ($\beta = -.41$) in our exploratory analysis. Again, depressive symptoms may limit participants' capacity to achieve and sustain target intensities prescribed for PR. Female sex was a significant independent predictor of greater endurance exercise compliance. This suggests that women with COPD may better tolerate endurance exercise than men and therefore sustain their target intensity during training, but this hypothesis remains speculative. It is possible that the women in our sample were more accustomed than the men to meeting the physical demands of daily activities and continuing to function despite fatigue, physical discomfort, and even symptoms of depression; 40 years ago women were traditionally the primary caretakers of their children (Nolen-Hoeksema,

2002), and 42 % were also working outside the home in 1976 (Statistics Canada, 2015). This may have increased their tolerance for physical activity generally.

Another unexpected finding was that *lower* FEV₁ % was a significant independent predictor of *greater* PR exercise compliance in our sample. One would have thought that worse lung function (indicating more severe COPD) would be associated with poorer, not better, PR exercise compliance. We are not aware of any other studies that have specifically examined the association between baseline FEV₁ % and exercise compliance with which to compare our findings. A possible explanation for this negative association is that the target exercise intensities for patients with more severe disease were lower than those of patients with better lung functions, such that healthier patients had to reach and sustain higher target exercise intensities throughout every one of their PR sessions. This may have proven to be more difficult. Secondly, it is possible that patients with more severe disease were more motivated to comply with their training targets than those with milder COPD if they believed in, or actually experienced, greater improvements in terms of functional capacity, dyspnea, fatigue, and quality of life from PR. This may have motivated them to reach their exercise targets when in attendance. In support of this hypothesis, several studies have found that milder COPD (greater FEV₁ %) is linked to dropout among some patients because they do not feel they are benefitting from PR enough to continue (Fischer et al., 2009; Harrison et al., 2012; Hayton et al., 2013). Similarly, Di Meo et al. (2008) found, in a sample of older patients, that those with worse COPD achieved greater benefit (increase in their 6MWT distance) relative to their

baseline values than patients whose COPD was less severe. The authors, however, do not report on patients' levels of attendance at or compliance to their exercise program during PR. In another study conducted by Spruit et al. (2015), patients were clustered into categories reflecting their responses to PR. The "very good responders" had poorer physical and mental health status and worse dyspnea at baseline. Interestingly, this negative association between FEV₁ % and exercise compliance is in direct contrast to the positive one we found between FEV₁ % and PR attendance. This clearly illustrates how PR attendance and compliance are differentially predicted – they appear to have different facilitators and barriers.

Strongest Predictors of Post-PR Exercise Levels

In correlational analyses, baseline smoking status, baseline BDI-II, and having a chance locus of control orientation for one's health all had significant negative correlations with levels of exercise maintained at 9-months post PR. In multivariate analysis, baseline smoking ($\beta = -.48$), higher baseline BDI-II scores ($\beta = -.45$), and greater chance locus of control orientation for health ($\beta = -.38$) all remained independent predictors of engaging in less exercise post-PR and accounted for 62 % of this outcome's variance. In our sample, even low levels of baseline depression represented an important impediment for long-term exercise maintenance. This is consistent with the findings of Heerema-Poelman et al. (2013) who reported that baseline depressive symptomatology was an independent predictor of poor attendance at a supervised maintenance program for exercise that followed a PR program. It is also consistent with the findings of eight

longitudinal studies reviewed by Roshanaei-Moghaddam et al. (2009) in which baseline depression was a significant risk factor for decline in physical activity levels.

Baseline smoking also emerged as a robust independent predictor of lower levels of exercise maintained at follow-up in our study. It is possible that *baseline* smoking was indicative of *continued* smoking, which may have limited exercise capacity at follow-up. This is consistent with previous studies that have reported a negative association between current smoking and maintenance of health promoting behaviors, including exercise (Hansen, Johnsen, & Molsted, 2016; Trost et al., 2002).

To our knowledge, our study was the first to examine HLC as a predictor of exercise levels maintained after PR in COPD. We found that a higher *chance* locus of control orientation for health was a significant independent predictor of lower levels of exercise at follow-up. A *chance* locus of control for health indicates the belief that fate, luck, genetics, or other forces over which one has no control, are responsible for the state and evolution of one's health. It is plausible that people who think their health is a matter of chance do not believe that their actions would have much impact, and therefore, would not be very motivated to pursue regular exercise or other health enhancing behaviors. This has been documented in multiple studies on the impact of health locus of control in a range of health-related behaviors. Steptoe and Wardle (2001) found that the odds of engaging in all 10 health-related behaviors that they examined were reduced by 20-35 % for participants with high *chance* locus of control scores.

Differences Between Study Completers and Dropouts

Another secondary objective was to examine the differences between study completers (participants who attended the follow-up evaluations 9-months post PR) and dropouts (those who did not attend follow-up evaluations). Eight participants (22 %) dropped out. They had significantly higher levels of baseline depressive symptomatology than completers, more severe COPD (as reflected by significantly lower FEV₁ % predicted values and FEV₁/FVC ratios), significantly lower PR attendance and PR exercise compliance levels, were significantly more likely to be female, to have undergone the IT exercise intervention (as opposed to CTVT or CTHi) during PR, and were more likely to be smoking at baseline.

Strengths and Limitations

Several limitations of this study should be noted and the findings interpreted with them in mind. The sample size was fairly small and homogeneous: 1) all participants were recruited from a single hospital center clinic through which they had all been referred for PR, 2) patients with more severe COPD who could not achieve a ventilatory threshold on baseline exercise tests, or who desaturated while exercising, were excluded, 3) self-selection for study participation may have biased our sample towards individuals who were less depressed and more motivated than those who refused. Therefore, one should be cautious about the extent to which the present findings can generalize to the larger and more varied COPD population. Another consideration is that the level of supervision and support provided to participants during PR in this study, as with many clinical trials, was

likely much greater than in most PR programs and probably resulted in higher attendance and compliance levels than those normally seen. All this may have resulted in the limited variance and skewed results in some of our data, which could limit the generalizability of findings. Another potential limitation was reliance on self-report measures for several independent variables (e.g., depressive symptomatology, health locus of control orientation) and for our outcome of exercise level at post-PR follow-up (based on a 7-day physical activity diary). Data based on self-reported may not be entirely valid and was not verified with more objective measures. However, the selected self-report measures have been used widely in the health literature and their sound psychometric properties are well established.

Despite some limitations, this study also had a number of notable strengths. It was the first, to our knowledge, to investigate the role of baseline symptoms of depression in predicting both attendance *and* exercise compliance (a true measure of PR adherence) during exercise-based PR, and levels of exercise maintained post-PR. All three outcomes are essential for understanding the extent to which participants benefit (or not) from PR and the variables that can predict this. The use of several objective measures was another strength of this investigation: rigorous standardized procedures were used to measure respiratory functions, determine exercise capacity and exercise prescriptions, and measure compliance with prescribed exercise intensity. It was also the first study to explore the possible role of HLC in the context of PR for COPD.

Future Research

Further research is needed to confirm our findings and to better understand the differential impact of baseline depression (both clinical and subclinical) on PR attendance, but especially on PR exercise compliance and ongoing exercise post PR, as knowledge is especially lacking in these last two areas. Each of these aspects is a distinct component essential to the success of PR and a better understanding of their determinants could result in better screening and intervention to optimize the health benefits of PR. In light of our findings, HLC merits further investigation as a potentially important variable for successful self-management of health in COPD. RCTs of adjunct treatments during PR that specifically target comorbid depression in COPD (and possibly HLC), are also needed to determine if improvements in depression result in better PR health outcomes via better PR attendance and exercise compliance, and improved maintenance of exercise afterwards.

From a broader perspective, there is a need to develop theoretical models (such as the downward spiral of COPD presented above) to help elucidate the interplay of the physical, neurobiological, cognitive, affective, and behavioral aspects of COPD and depression to understand how depression develops (or worsens) in COPD. For example, episodes of dyspnea in COPD are often trigger a response of heightened anxiety even panic, which can quickly result in sustained anticipatory anxiety about many activities and situations. Is it possible that repeated episodes of dyspnea (accompanied by heightened anxiety or panic) over time precipitate abnormalities of the monoaminergic systems like

the hypothalamic-pituitary-adrenal axis, and could this be partly why levels of depression are disproportionately high in COPD? Until such theoretical models are proposed and tested, it will be difficult to fully understand comorbid depression in COPD and to develop sound interventions targeting specific factors to improve health outcomes.

Conclusion

In conclusion, we found in our sample of 36 participants with moderate-to-severe COPD, that attendance and exercise compliance during supervised PR were generally high, while levels of autonomous exercise maintained post-PR were relatively low (compared to levels prescribed). Baseline depressive symptomatology did not predict PR attendance, but did predict compliance to prescribed exercise intensity during PR and levels of exercise maintained 9-months post PR (with adjustment for covariates). This indicates that baseline levels of depression may differentially impact each. To our knowledge, this is the first study to examine depressive symptomatology at entrance to PR as a predictor of exercise compliance during PR for COPD. Endurance exercise training is the cornerstone of PR for COPD and complying with the prescribed exercise targets is crucial for obtaining optimal benefits. If the presence of even subclinical depressive symptomatology (let alone clinical depression) is associated with noncompliance with exercise targets during PR and lower levels of exercise maintained after PR ends, then its diagnosis and treatment may be key for improving PR outcomes. Depression is especially relevant because it is highly prevalent in COPD. Our findings support our argument that while measuring PR attendance is necessary for reporting on PR exercise adherence, it is not sufficient: compliance to exercise targets must also be assessed and reported.

We found that the type of endurance exercise intervention (CTVT, CTHi, or IT) moderated the relationship between baseline depressive symptoms and exercise compliance. We also found that sex moderated the relationship between baseline depressive symptoms and level of exercise maintained at 9-months post PR.

Exploratory analyses identified several variables in addition to baseline depressive symptomatology that were independent predictors of each outcome. Interestingly, different variables predicted PR attendance, PR exercise compliance, and post-PR exercise levels in multivariate analyses, demonstrating that optimally benefitting from exercise-based PR is associated with a number of patient and exercise program characteristics which need to be considered for attainment of optimal PR outcomes. A HLC “other people” orientation may be positively associated with increased PR attendance, possibly due to a greater response to guidance and support from others, while high “chance” HLC orientation at baseline may be a significant predictor of lower exercise levels maintained 9-months post PR in this study.

Clinical recommendations

In light of these findings, we suggest that the assessment of both subclinical and clinical depression be incorporated into standard intake for PR and that treatment of depression be provided during (and if necessary following) PR programs as an essential component for helping patients with COPD obtain (and maintain) optimal benefits from PR. When both attendance and PR exercise compliance are measured, a composite

measure of PR exercise *adherence* can be calculated (i.e., percent attendance multiplied by percent exercise compliance) that can provide a comprehensive score of overall exercise adherence during PR. This could be useful for flagging participants during or at completion of PR who are not likely to benefit. Then, having distinct measures of PR attendance and compliance makes it possible to identify specifically where a participant's difficulty in adhering to PR lies (with attendance, adherence, or both). This may also be useful for PR program quality assessment and improvement.

The finding that the exercise regimen's intensity moderated the relationship between baseline depression levels and PR exercise compliance may have implications for exercise prescription: participants with greater depression may comply better with moderate (as opposed to low or high) intensity exercise or self-selected intensities. Our finding that sex moderated the relationship between baseline depression levels and levels of exercise maintained post-PR suggests that men with depressive symptoms may require more support than women with similar symptoms to maintain regular exercise.

Relatively brief and focused cognitive-behavioral interventions' effectiveness have begun to be investigated and some promising results have emerged (Coventry & Gellatly, 2008; Health Quality Ontario, 2015; M. J. Hynninen, Bjerke, Pallesen, Bakke, & Nordhus, 2010; Panagioti, Scott, Blakemore, & Coventry, 2014). Based on this study's findings and the latest definition of PR (Spruit et al., 2013) these kinds of interventions should now be integrated into PR for COPD by qualified professionals.

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Appendix A
Research Ethics Committee Approval



APPROBATION D'UN PROJET DE RECHERCHE

NO DE DOSSIER DU CÉR : 2008-01-107

TITRE : «Optimisation d'un programme de réadaptation respiratoire »
- *Protocole, en date du 1^{er} février 2008 incluant les annexes A et B*
- *Questionnaires : CRQ pré-réadaptation, version du 23 juin 2004, CRQ post-réadaptation, version du 23 juin 2004, Beck Depression Inventory, Anxiety Sensitivity Index, Questionnaire d'auto-efficacité, Multidimensional Health Locus of Control, General Health Questionnaire, questionnaire de somnolence d'Epworth, Index de qualité du sommeil de Pittsburgh*
- *Formulaire d'information et de consentement*

LIEU : Hôpital du Sacré-Cœur de Montréal, 5400 boul. Gouin Ouest, Montréal (Québec) H4J 1C5

CHERCHEUR(S) : **Véronique Pepin, Ph. D.**, Simon L. Bacon, Ph. D., Kim Lavoie, Ph. D., Manon Labrecque, M.D., Simon Parenteau, M.D. Jean-François Gagnon, Ph. D., Catherine Lemièrre, M.D., Simon Parenteau, M.D., et François Beaucage, M.D., collaborateurs

PROVENANCE DES FONDS : Fonds de la recherche en santé du Québec et Association pulmonaire du Canada

PROBLÉMATIQUE et OBJECTIF DE L'ÉTUDE : L'objectif général de l'étude présente est de comparer la réponse physique, psychologique, neuropsychologique et comportementale d'individus atteints de MPOC à différents protocoles d'entraînement physique. Les objectifs sont de 1) comparer l'impact à court terme de trois différents protocoles d'entraînement sur la tolérance à l'effort, la capacité fonctionnelle, la dyspnée, la qualité de vie, la santé psychologique et la fonction cognitive; 2) comparer l'observance des patients aux trois protocoles d'entraînement; 3) comparer le maintien à long terme (1 an) des gains physiques, psychologiques et neuropsychologiques entre les 3 groupes; et 4) comparer l'adhérence à long terme des sujets aux niveaux d'exercices recommandés entre les 3 groupes.

TYPE DE RECHERCHE : Essai clinique

ADMISSIBILITÉ DES SUJETS : Sujets 1) MPOC stable 2) 40 ans ou plus 3) histoire tabagique de 10 paquets-année ou plus 4) VEMS post-bronchodilatation inférieur à 80 % de la prédite 5) VEMS/CVF inférieur à 0,7

CONSÉQUENCES ÉTHIQUES : Liberté de participer : oui Consentement éclairé : oui
Confidentialité : oui Liberté d'en sortir sans contrainte : oui

FORMULAIRE DE CONSENTEMENT :

Requis : oui (version initiale du 7 février 2008)
Approuvé : oui 8 février 2008

DATE DE L'ÉTUDE PAR LE COMITÉ : 28 janvier 2008 (séance plénière)

- 17 septembre 2008 (Modification au protocole, en date du 15 août 2008, au formulaire d'information et de consentement, en date du 15 août 2008, modification et ajout de questionnaires (CRQ pré et post-réadaptation, SF-36 Générique V2, Module spécifique (B), questionnaire CFQ, Broadbent et al, Montreal cognitive assessment (MOCA), Index de sévérité de l'insomnie, Panas)
- 6 janvier 2009 (renouvellement)
- 8 janvier 2010 (renouvellement accepté rétroactivement au 6 janvier 2010 jusqu'au 8 janvier 2011)
- 7 juin 2010 (modification au formulaire d'information et de consentement, en date du 7 juin 2010)
- 15 février 2011 (renouvellement accepté rétroactivement au 8 janvier 2011 jusqu'au 15 février 2012)

MEMBRES DU COMITÉ D'ÉTHIQUE DE LA RECHERCHE ET DE L'ÉVALUATION DES TECHNOLOGIES DE LA SANTÉ

AVIS FAVORABLE : Dre Chantal Lambert, scientifique non-médecin, présidente
Mme Marie-France Thibaudeau, scientifique non-médecin, vice-présidente
M. Guy Beauregard, personne spécialisée en éthique
Me Marie Boivin, juriste
M. Jean Caillé, membre non affilié représentant la collectivité
Mme Henriette Bourassa, membre non affilié représentant la collectivité
Dr Roberto Castaño, scientifique médecin
Mme Isabelle Larouche, scientifique non-médecin
Dre Jadranka Spahija, scientifique non-médecin
Dr Marcio Stürmer, scientifique médecin
Dr Colin Verdant, scientifique médecin

Marie-France Thibaudeau

N.B. : Le Comité d'éthique de la recherche de l'HSCM poursuit ses activités en accord avec *Les bonnes pratiques cliniques (Santé Canada) et tous les règlements applicables*
Cette approbation est valable pour une période d'un an seulement. Une demande de renouvellement doit être faite après cette période.

Appendix B
Physical Activity Diary



Quelques consignes pour remplir votre journal:

! Pendant **7 jours consécutifs**, nous vous demandons d'inscrire les activités physiques que vous pratiquez pendant la journée. Chacune de ces activités physiques doit être exercée pendant **un minimum de 10 minutes de façon continue ou soutenue**. Vous indiquerez la durée de l'activité dans la case appropriée.

! Voici des **exemples de types d'activités physiques**: marche, vélo, baignade, jardinage, exercices de renforcement, golf, yoga, danse, quilles, pétanque, ski, etc. **Soyez précis**, par exemple: épicerie en poussant le panier à roulettes.

! Pour chacune des activités, veuillez indiquer l'intensité à laquelle vous l'avez pratiquée. Voici des **exemples**:

I d'activités légères: vélo stationnaire sans résistance, vitesse confortable; marche de magasinage; danser un «slow»;

I d'activités modérées: danse sociale; racler des feuilles; peinturer; vélo sur route, pour le plaisir, à une vitesse inférieure à 10 mph ou 16 kmh;

I d'activités intenses: vélo stationnaire, effort modéré, avec une résistance de 150 watts; vélo sur route, effort modéré, à une vitesse d'au moins 12 mph ou 19 kmh; marche rapide militaire à 5mph ou 8kmh; pelleter.

Questions:

Est-ce que la semaine qui vient de se terminer était « typique » en ce qui a trait à votre pratique d'activités physiques?

OUI NON

Si NON, pour quelle raison?

Vacances

Exacerbation de ma maladie

Autre maladie

Autre raison: expliquez _____

De quelle façon la semaine qui vient de passer était-elle atypique?

plus d'activités physiques que dans une semaine typique

moins d'activités physiques que dans une semaine typique

aucune activité physique

Nom: _____

Étude «Optimisation d'un programme de réadaptation respiratoire»

Journal d'activités physiques

Veuillez s.v.p. consulter les instructions à l'endos de la feuille avant de remplir le journal.

	Dimanche	Lundi	Mardi	Mercredi	Jeudi	Vendredi	Samedi
Dates (j-m-a)							
Activité #1 (type)							
Intensité (légère, modérée ou élevée)							
Durée (min)							
Activité #2 (type)							
Intensité (légère, modérée ou élevée)							
Durée (min)							
Activité #3 (type)							
Intensité (légère, modérée ou élevée)							
Durée (min)							

Appendix C
Assessment of Bias, Normality, and Generalizability of Data

For univariate data, normality and homoscedasticity were assessed by examining histograms, boxplots, and P-P plots, as well as z -scores, standardized measures of skewness and kurtosis, and Kolmogorov-Smirnov and Shapiro-Wilk tests. For bivariate (i.e., correlations) and multivariate data (i.e., multiple regression analyses), normality, linearity, and homoscedasticity were assessed by examination of standardized residual scatterplots, histograms, P-P plots, and other assessments of normality available in SPSS 23 linear regression (Cook's distance, Mahalanobis distance, average leverage, standardized DFBeta and DFFit). When a multivariate outlier exerting disproportionate effects on the results of a regression analysis was identified, regression analyses were performed and presented with and without that case (Lang & Secic, 2006; Tabachnick & Fidell, 2013). All potential IVs to be included in the linear regression analyses were screened for collinearity and multicollinearity and if found, only the variable with the stronger association to the outcome variable was retained in the final regression model (Tabachnick & Fidell, 2013).

One extremely high univariate outlier was found among the baseline BDI-II scores. When this high score was winsorized (reduced from 35 to 23) it resulted in an acceptable z score and more normal data distribution (see Table 12 below).

Normality Assessments for Primary Analyses

Table 12

Assessments of Bias and Normality for Baseline BDI and Covariates Included in Regression Models

Predictors	Histogram shows	Boxplot shows	High/low z-scores (<i>p</i> , 2-tailed)	P-P plot (Skewness/ Kurtosis)	Skewness <i>z</i> (<i>p</i> , 2-tailed)	Kurtosis <i>z</i> (<i>p</i> , 2-tailed)	Kolmog-S (<i>p</i> , 2-tailed)	Shapiro-W (<i>p</i> , 2-tailed)
BDI-II (With high score =35)	1 outlier CL029, + skewed [X]	Positive skew, 1 Extreme outlier [X]	CL029 = 3.85 (< .001) outlier [X]	Some skew & kurtosis [X]	4.4 (< .001) very significant [X]	6.85 (< .001) [X]	.157 (.025) [X]	.872 (.001) [X]
BDI-II (High score winsorized* to 23)	Appears normal, no outliers [√]	Slight + skew, No outliers [√]	CL029 = 2.51 (.012) Acceptable [√]	Appears normal [√]	1.63 (.103) [√]	0.44 (.660) [√]	.103 (.200) [√]	.956 (.166) [√]
FEV ₁ % (n = 36)	Quite normal [√]	Quite normal [√]	-2.19 not extreme [√]	Slight skew [√]	-0.33 (.741) [√]	-1.02 (.308) [√]	.091 (.200) [√]	.974 (.538) [√]
HLC-op (n = 36)	Some + skew [√]	Some + skew, No outliers [√]	2.05 not extreme [√]	Quite normal [√]	1.02 (.308) [√]	-0.84 (.401) [√]	.094 (.200) [√]	.948 (.089) [√]
HLC-c (n = 36)	Looks normal [√]	Very normal [√]	1.92 not extreme [√]	Very normal [√]	0.21 (.834) [√]	-0.82 (.412) [√]	.083 (.200) [√]	.978 (.666) [√]

Note. N = 36. Assessments are presented for baseline BDI scores including extreme outlier and with that score winsorized. Kolmog-S = Kolmogorov-Smirnov test; Shapiro-W = Shapiro Wilk test; + = positively; BDI-II = Beck Depression Inventory; *Assigned CL029 a BDI score value of 23 instead of 35 (2 units higher than the next highest score, so less extreme); [√] Normal, not cause for concern; [X] Non-normal, cause for concern.

Assessments of bias and normality for PR attendance and Compliance data are presented in Table 13 below. Bootstrapping is indicated for analyses involving this outcome because of the non-normal negatively skewed data distributions and several outlying scores.

Table 13

Assessments of Bias and Normality for Univariate PR Program Data

PR Program Outcomes	Histogram	Boxplot	High/low z-scores	P-P plot (Skewness/ Kurtosis)	Skewness z (p, 2-tailed)	Kurtosis z (p, 2-tailed)	Kolmog-S (p, 2-tailed)	Shapiro-W z(p, 2-tailed)
Attend PR (n = 36)	Neg skew Outliers not obvious [X] ∴ bootstrap	Neg skew, 4 outliers [X] ∴ bootstrap	-2.67, -2.57, 02.27: abnormal [X] ∴ bootstrap	Shows skew ("S" shape) [X] ∴ bootstrap	-3.79 (< .001) [X]	1.89 (.059) [√]	.200 (.001) [X] ∴ bootstrap	.807 (< .001) [X] ∴ bootstrap
Comply PR (n = 36)	Neg skew, possible outliers [X] ∴ bootstrap	Neg skew, 6 non-extreme outliers [X] ∴ bootstrap	-2.24 x 3, -2.10 not normal [X] ∴ bootstrap	Shows skew ("S" Shape) [X] ∴ bootstrap	-3.61 (< .001) [X]	0.69 (.490) [√]	.267 (< .001) [X] ∴ bootstrap	.705 (< .001) [X] ∴ bootstrap

Note. N = 36. Kolmog-S = Kolmogorov-Smirnov test; Shapiro-W = Shapiro-Wilk test; Attend PR = Attendance at pulmonary rehabilitation; Comply PR = Compliance at pulmonary rehabilitation; Neg = negative; [√] Normal, not cause for concern; [X] Non-normal, cause for concern.

The assessments of bias and normality for the follow-up exercise level data (Table 14 below) reveal a positively skewed distribution and justify using bootstrapping in analyses.

Table 14

Assessments of Bias and Normality for Follow-Up Exercise Levels Data

Follow-Up post-PR Outcome	Histogram	Boxplot	High/low z-scores	P-P plot (Skewness/ Kurtosis)	Skewness z (<i>p</i> , 2-tailed)	Kurtosis z (<i>p</i> , 2-tailed)	Kolmog-S z (<i>p</i> , 2-tailed)	Shapiro-W z (<i>p</i> , 2-tailed)
Exercise in METmins (n = 36)	+ skew, one possible outlier [X] ∴ bootstrap	+ skew LD008 is extreme outlier [X] ∴ bootstrap	LD008 = 2.92 (<i>p</i> = .004) is an outlier [X]	Some skew, “S” shape Abnormal [X] ∴ bootstrap	3.35 (< .001) sig. skew [X] ∴ bootstrap	1.88 (.060) [√]	.181 (.004) [X] ∴ bootstrap	.878 (.001) [X] ∴ bootstrap

Note. *N* = 36. Kolmog-S = Kolmogorov-Smirnov test; Shapiro-W = Shapiro Wilk test; METmins = Metabolic Equivalent of Task minutes (measure of amount of exercise performed); [√] Normal, not cause for concern; [X] Non-normal, cause for concern.

Bias, normality, and generalizability of assessments of PR attendance regressed on baseline BDI-II (see Table 15 below) justify winsorizing one extreme baseline BDI-II high score (35) which would otherwise exert substantial influence on analyses.

Table 15

Assessment of Bias, Normality, and Generalizability for the Simple Regression of Baseline BDI-II (High BDI-II Outlier in Data Set) Predicting PR Attendance

Standardized Residuals	Cook's Distance	Mahalanobis Distance	Centered Leverage	Standardized DFBetas	Standardized DFFit	Covariance Ratio (Little influence = close to 1.0)
CM034 = -2.64 ($p = .008$) Outlier, but not extreme [X]	LD012 = .19 highest, but < 1 OK [✓]	CL029 = 14.83 > Cutoff = 6.64, $df=1$, $p = .01$ Outlier [X]	CL029 = .42, (> .11, critical value) Outlier [X]	All values < 2 [✓]	All values < 2 [✓]	CL029 = 1.92 (0.83 to 1.17 is ideal) so undue influence [X]

Durban-Watson Test (for independent errors)	Residuals Analyses (for stand regression analysis)	Multicollinearity (Doesn't apply because bivariate)
2.27 (values between 1 to 3 acceptable, so OK) [✓]	Histogram: very - skew [X] P-P Plot: abnormal [X], Zpred Zresid heteroscedastic , CL029 outlier [X] ∴ bootstrap	Greatest Pearson r among predictors [✓] Tolerance: lowest value = 1.0 VIF: largest value = 1.0 [✓] Each predictor's variance proportion is distributed across diff dimensions [✓]

Note. $N = 36$. [✓] = Normal, not cause for concern; [X] = Non-normal, cause for concern; VIF = variable inflation factor.

Table 16 shows that winsorizing the outlying high baseline BDI-II score from 35 to 23 reduces bias and improves generalizability of the simple regression of PR attendance (outcome) regressed on baseline BDI-II.

Table 16

Assessment of Bias, Normality, and Generalizability for the Simple Regression of Baseline BDI-II (High Outlier Winsorized) Predicting PR Attendance

Standardized Residuals	Cook's Distance	Mahalanobis Distance	Centered Leverage	Standardized DFBetas	Standardized DFFit	Covariance Ratio (Little influence = close to 1.0)
CM034 = -2.63 ($p = .009$) Outlier, but not extreme [X]	LD012 = .23 highest, but < 1 OK [✓]	CL029 = 6.32 < Cutoff = 6.64, $df=1$, $p = .01$ Outlier [✓]	CL029 = .18, (> .11, critical value) Outlier [X]	All values < 2 [✓]	All values < 2 [✓]	CL029 = 1.33 (0.83 to 1.17 is ideal) slight influence, but OK [✓]

Durban-Watson Test (for independent errors)	Residuals Analyses (for stand regression analysis)	Multicollinearity (Doesn't apply because bivariate)
2.26 (values between 1 to 3 acceptable, so OK) [✓]	Histogram: very - skew [X] P-P Plot: abnormal [X], Zpred Zresid heteroscedastic , but no outlier [X] ∴ bootstrap	Greatest Pearson r among predictors [✓] Tolerance: lowest value = 1.0 VIF: largest value = 1.0 [✓] Each predictor's variance proportion is distributed across diff dimensions [✓]

Note. $N = 36$. [✓] = Normal, not cause for concern; [X] = Non-normal, cause for concern; VIF = variable inflation factor.

Bias, normality, and generalizability of assessments of PR exercise compliance regressed on baseline BDI-II (see Table 17 below) show that winsorizing one extreme baseline BDI-II high score of 35 is justified to reduce its exerting substantial influence on bivariate analyses.

Table 17

Assessment of Bias, Normality, and Generalizability for the Simple Regression of Baseline BDI-II (High Outlier in Data Set) Predicting PR Exercise Compliance

Standardized Residuals	Cook's Distance	Mahalanobis Distance	Centered Leverage	Standardized DFBetas	Standardized DFFit	Covariance Ratio (Little influence = close to 1.0)
GC036 = -2.55 ($p = .011$) Acceptable [X]	CL029 = .47 highest, but < 1 OK [√]	CL029 = 14.83 > (Cutoff = 6.64, $df=1, p = .01$) Extreme Outlier [X]	CL029 = .42, (> .11, critical value) Outlier [X]	All values < 2 CL029 = -0.94 [√]	All values < 2 CL029 = -0.97 [√]	CL029 = 1.81 (0.83 to 1.17 is ideal) Very influential [X]

Durban-Watson Test (for independent errors)	Residuals Analyses (for stand regression analysis)	Multicollinearity (Doesn't apply because bivariate)
1.35 (values between 1 to 3 acceptable, so OK) [√]	Histogram: very - skewed [X] P-P Plot: abnormal [X], Zpred Zresid heteroscedastic , CL029 outlier [X] ∴ bootstrap	Greatest Pearson r among predictors [√] Tolerance: lowest value = 1.0 VIF: largest value = 1.0 [√] Each predictor's variance proportion is distributed across diff dimensions [√]

Note. $N = 36$. [√] = Normal, not cause for concern; [X] = Non-normal, cause for concern; VIF = variable inflation factor.

Table 18 shows that winsorizing the outlying high baseline BDI-II score (from 35 to 23) reduces bias and improves generalizability of the simple regression of PR exercise compliance regressed on baseline BDI-II.

Table 18

Assessment of Bias, Normality, and Generalizability for the Simple Regression of Baseline BDI-II (With Outlier Winsorized) Predicting PR Exercise Compliance

Standardized Residuals	Cook's Distance	Mahalanobis Distance	Centered Leverage	Standardized DFBetas	Standardized DFFit	Covariance Ratio (Little influence = close to 1.0)
GC036 = -2.55 ($p = .011$) Acceptable [X]	CL029 = .33 highest, but < 1 OK [✓]	CL029 = 6.32 < (Cutoff = 6.64, $df=1, p = .01$) [✓]	CL029 = .18, (> .11, critical value) Slight outlier [X]	All values < 2 CL029 = -0.77 [✓]	All values < 2 CL029 = -0.83 [✓]	CL029 = 1.15 (0.83 to 1.17 is ideal) [✓]

Durban-Watson Test (for independent errors)	Residuals Analyses (for stand regression analysis)	Multicollinearity (Doesn't apply because bivariate)
1.39 (values between 1 to 3 acceptable, so OK) [✓]	Histogram: - skewed [X] P-P Plot: abnormal [X], Zpred Zresid heteroscedastic , but no outlier [X] ∴ bootstrap	Greatest Pearson r among predictors [✓] Tolerance: lowest value = 1.0 VIF: largest value = 1.0 [✓] Each predictor's variance proportion is distributed across diff dimensions [✓]

Note. $N = 36$. [✓] = Normal, not cause for concern; [X] = Non-normal, cause for concern; VIF = variable inflation factor.

Table 19 presents results of bias, normality, and generalizability assessments for follow-up exercise levels regressed on baseline BDI-II scores. An extreme bivariate outlier exerting substantial influence is revealed.

Table 19

*Assessment of Bias, Normality, and Generalizability for Simple Regression of Baseline BDI-II (High Outlier in Data Set)
Predicting Exercise Levels at Follow-Up (With bivariate Outlier in Data Set)*

Standardized Residuals	Cook's Distance	Mahalanobis Distance	Centered Leverage	Standardized DFBetas	Standardized DFFit	Covariance Ratio (Little influence = close to 1.0)
LD008 = 3.49 ($p < .001$) Extreme Outlier [X]	LD008 = .89 < 1, influential, but acceptable [√]	CL029 = 14.83 > Cutoff = 6.64 ($df=1$) $p = .01$) [X]	CL029 = .42, (lot > .11, critical value) [X]	LD008 = 1.48 > 1 Some influence [X]	LD008 = 1.70 > 1 Some influence [X]	LD008 = 0.43 CL029 = 1.92 (.083 to 1.17 ideal) so much influence [X]

Durban-Watson Test (for independent errors)	Residuals Analyses (for stand regression analysis)	Multicollinearity (Doesn't apply because bivariate)
1.96 (values between 1 to 3 acceptable, so OK) [√]	Histogram: looks + skew, outlier [X] P-P Plot: abnormal [X], Zpred Zresid heteroscedastic , LD008 outlier [X] ∴ bootstrap	Greatest Pearson r among predictors [√] Tolerance: lowest value = 1.0 VIF: largest value = 1.0 [√] Each predictor's variance proportion is distributed across diff dimensions [√]

Note. $N = 36$. [√] = Normal, not cause for concern; [X] = Non-normal, cause for concern; + = positive VIF = variable inflation factor.

Table 20 presents results of bias, normality, and generalizability assessments for follow-up exercise levels regressed on baseline BDI-II scores with the high BDI-II score winsorized (from 35 to 23), however the extreme bivariate outlier remains influential.

Table 20

Assessment of Bias, Normality, and Generalizability for the Simple Regression of Baseline BDI-II Predicting Exercise Levels at Follow-Up (Bivariate Outlier in Data Set and the High BDI-II Score Winsorized)

Standardized Residuals	Cook's Distance	Mahalanobis Distance	Centered Leverage	Standardized DFBetas	Standardized DFFit	Covariance Ratio (Little influence = close to 1.0)
LD008 = 3.63 ($p < .001$) Extreme Outlier [X]	LD008 = 1.49 > 1, much influence [X]	LD008 = 4.63 < Cutoff = 6.64 ($df=1$) $p = .01$ [√]	LD008 = .13, CL029 = .18 (>.11 critical value) [X]	LD008 = 2.11 > 2 (much influence [X]	LD008 = 2.11 > 2 much influence [X]	LD008 = 0.37 CL029 = 1.34 (0.83 to 1.17 ideal) so much influence [X]
Durban-Watson Test (for independent errors)	Residuals Analyses (for stand regression analysis)		Multicollinearity (Doesn't apply because bivariate)			
2.00 (values between 1 to 3 acceptable, so OK) [√]	Histogram: looks + skewd, outlier [X] P-P Plot: abnormal [X], Zpred Zresid heteroscedastic , LD008 outlier [X] ∴ bootstrap		Greatest Pearson r among predictors [√] Tolerance: lowest value = 1.0 VIF: largest value = 1.0 [√] Each predictor's variance proportion is distributed across diff dimensions [√]			

Note. $N = 36$. [√] = Normal, not cause for concern; [X] = Non-normal, cause for concern; + = positive; VIF = variable inflation factor.

Table 21 presents results of bias, normality, and generalizability assessments for follow-up exercise levels regressed on baseline BDI-II scores with the extreme bivariate outlier removed, but with the high outlying baseline BDI-II score not winsorized. The level of bias and non-normality is problematic and again justifies winsorizing the outlying high baseline BDI-II score.

Table 21

Assessment of Bias, Normality, and Generalizability for the Simple Regression of Baseline BDI-II Predicting Exercise Level at Follow-Up (Bivariate Outlier Removed and High BDI-II Outlier in the Data Set)

Standardized Residuals	Cook's Distance	Mahalanobis Distance	Centered Leverage	Standardized DFBetas	Standardized DFFit	Covariance Ratio (Little influence = close to 1.0)
JV069 = 2.54 ($p = .011$) Not too unusual [√]	JV069 = 2.17 is highest, Much > 1 So very great influence [X]	CL029 = 16.23 Cutoff = 6.64 ($df=1, p=.01$) Very distant [X]	CL029 = .48 is highest (> .11, critical value) [X]	CL029 highest = 2.13 > 2 Influential [X]	CL029 highest = 2.2 > 2 [X]	CL029 = 1.64 (0.83 to 1.17 is ideal) [X]

Durban-Watson Test (for independent errors)	Residuals Analyses (for stand regression analysis)	Multicollinearity (Doesn't apply because bivariate)
1.46 (values between 1 to 3 acceptable, so OK) [√]	Histogram: slight + skew [X] P-P Plot: not normal [X] Zpred Zresid heteroscedastic [X] ∴ bootstrap	Greatest Pearson r among predictors [√] Tolerance: lowest value = 1.0 VIF: largest value = 1.0 [√] Each predictor's variance proportion is distributed across diff dimensions [√]

Note. $N = 35$. [√] = Normal, not cause for concern; [X] = Non-normal, cause for concern; + = positive; VIF = variable inflation factor.

Removal of the bivariate outlier and winsorizing the high baseline BDI-II score reveals improvement in bias, normality, and generalizability of the simple regression of baseline BDI-II predicting exercise level at follow-up, though bootstrapping is still indicated (see Table 22 below).

Table 22

Assessment of Bias, Normality, and Generalizability for the Simple Regression of Baseline BDI-II Predicting Exercise Level at Follow-Up (Bivariate Outlier Removed and High BDI-II Outlier Winsorized)

Standardized Residuals	Cook's Distance	Mahalanobis Distance	Centered Leverage	Standardized DFBetas	Standardized DFFit	Covariance Ratio (Little influence = close to 1.0)
JV069 = 2.48 ($p = .013$) Not too unusual [√]	JV069 = 0.23 is highest, Much < 1 OK [√]	CL029 = 7.46 Cutoff = 6.64 ($df=1, p=.01$) [X]	CL029 = .22 is highest (.11, critical value) [X]	CL029 highest = 0.58 < 2, OK [√]	JV069 highest = 0.73 < 2, OK [√]	JV069 = 0.73 (0.83 to 1.17 is ideal), OK [√]

Durban-Watson Test (for independent errors)	Residuals Analyses (for stand regression analysis)	Multicollinearity (Doesn't apply because bivariate)
1.56 (values between 1 to 3 acceptable, so OK) [√]	Histogram: slight + skew [X] P-P Plot: quite normal [√] Zpred Zresid heteroscedastic [X] ∴ bootstrap	Greatest Pearson r among predictors [√] Tolerance: lowest value = 1.0 VIF: largest value = 1.0 [√] Each predictor's variance proportion is distributed across diff dimensions [√]

Note. $N = 35$. [√] = Normal, not cause for concern; [X] = Non-normal, cause for concern; + = positive; VIF = variable inflation factor.

Bias, normality, and generalizability assessments for the regression of baseline BDI-II and covariates predicting PR attendance reveal that the outlying high BDI-II score of 35 exerts substantial influence on the model (see table 23), which justified it being winsorized from 35 to 23.

Table 23

Assessment of Bias, Normality, and Generalizability for the Multiple Regression Model of BDI-II (Extreme High Score in Data) and Covariates Predicting PR Attendance

Standardized Residuals	Cook's Distance	Mahalanobis Distance	Centered Leverage	Standardized DFBetas	Standardized DFFit	Covariance Ratio (Little influence = close to 1.0)
LD012 = -2.28 ($p = .023$) Not too unlikely [√]	0.32 is highest < 1 [√]	CL029 = 17.53 Cutoff = 16.8 ($df=6$, $p=.01$), high leverage [X]	CL029 = .50 is highest (< .58, critical value) OK [√]	LD012 = 1.1 absolute value < 2 for (highest value) [√]	LD012 = -1.69 < 2 acceptable [√]	LD012 = .25 CL029 = 2.22 (0.42 to 1.6 ideal) [X]

Durban-Watson Test (for independent errors)	Residuals Analyses (for stand regression analysis)	Multicollinearity
2.0 (values between 1 to 3 acceptable, so OK) [√]	Histogram: some skew [√] P-P Plot: skew [X], Zpred Zresid heteroscedastic , no outlier [X] ∴ bootstrap	Greatest Pearson r among predictors (FEV ₁ % & IT) = -.362 ($p = .031$) [√] Tolerance: lowest value = 0.548 VIF: largest value = 1.824 [√] Each predictor's variance proportion is distributed across diff dimensions [√]

Note. $N = 36$. [√] = Normal, not cause for concern; [X] = Non-normal, cause for concern; VIF = variable inflation factor.

Table 24 shows that winsorizing the extreme outlying baseline BDI-II score from 35 to 23 helps reduce bias and produces a model that is more representative of the sample.

Table 24

Assessment of Bias, Normality, and Generalizability for the Multiple Regression Model of BDI-II (High Score Winsorized) and Covariates predicting PR Attendance

Standardized Residuals	Cook's Distance	Mahalanobis Distance	Centered Leverage	Standardized DFBetas	Standardized DFFit	Covariance Ratio (Little influence = close to 1.0)
LD012 = -2.23 ($p = .026$) Not too unlikely [√]	LD012 is highest = 0.34 < 1, OK [√]	CL029 = 10.13 Cutoff=16.81 ($df=6, p=.01$), OK [√]	CL029 = .29 is highest (< .39, critical value) OK [√]	LD012 = .57 highest, absolute value < 2 [√]	LD012 = -1.75, absolute value < 2, OK [√]	LD012 = .25 CL029 = 1.36 (0.42 to 1.6 ideal) [X]

Durban-Watson Test (for independent errors)	Residuals Analyses (for stand regression analysis)	Multicollinearity
1.97 (values between 1 to 3 acceptable, so OK) [√]	Histogram: some neg. skew [√] P-P Plot: skew [X], Zpred Zresid heteroscedastic , no outlier [X] ∴ bootstrap	Greatest Pearson r among predictors (FEV ₁ % & IT) = -.361 ($p = .031$) [√] Tolerance: lowest value = 0.546 VIF: largest value = 1.831 [√] Each predictor's variance proportion is distributed across diff dimensions [√]

Note. $N = 36$. [√] = Normal, not cause for concern; [X] = Non-normal, cause for concern; neg. = negative; VIF = variable inflation factor.

Table 25 reveals that the high outlying baseline BDI-II score exerts substantial influence on the regression model predicting PR exercise compliance and justifies winsorizing it from 35 to 23 to reduce its substantial influence.

Table 25

Assessment of Bias, Normality, and Generalizability for the Multiple Regression Model of BDI-II (High Score in Data) and Covariates Predicting PR Exercise Compliance

Standardized Residuals	Cook's Distance	Mahalanobis Distance	Centered Leverage	Standardized DFBetas	Standardized DFFit	Covariance Ratio (Little influence = close to 1.0)
CM034 = -2.41 ($p = .016$) somewhat unlikely but OK [✓]	CM034 = .18 highest (all < 1 so OK) [✓]	CL029 = 17.53 > Cutoff = 16.8 ($df = 6, p = .01$): cause for concern [X]	CL029 = .50 (> .38, critical value) exerts undue influence [X]	All values < 2 so no case exerts undue influence on model parameters [✓]	All values < 2 [✓]	CM034 = .23, CL029 = 2.68 (0.42 to 1.6 ideal) Some influence [X]

Durban-Watson Test (for independent errors)	Residuals Analyses	Multicollinearity
2.01 (values between 1 to 3 acceptable, so OK) [✓]	Histog shows near normal distrib [✓] P-P Plot std residual some skew [X] Zpred Zresid some heteroscedast [X] ∴ bootstrap	Greatest Pearson r among predictors (IT & FEV ₁ %) = -.36 ($p = .031$) [✓] Tolerance: lowest value = 0.79 VIF: largest value = 1.26 [✓] Each predictor's variance proportion distributed across diff dimensions [✓]

Note. $N = 36$. [✓] = Normal, not cause for concern; [X] = Non-normal, cause for concern; std = standardized; VIF = variable inflation factor.

Table 26 shows that bias, normality, and generalizability of the regression analysis of baseline BDI-II and covariates predicting PR exercise compliance are improved when the BDI-II outlying high score is winsorized from 35 to 23.

Table 26

Assessment of Bias, Normality, and Generalizability for the Multiple Regression Model of BDI-II (High Score Winsorized) and Covariates Predicting PR Exercise Compliance

Standardized Residuals	Cook's Distance	Mahalanobis Distance	Centered Leverage	Standardized DFBetas	Standardized DFFit	Covariance Ratio (Little influence = close to 1.0)
CM034 = -2.17 ($p = .030$) somewhat unlikely [√]	CM034 = .15, highest (all < 1 so OK) [√]	CL029 = 10.13 < Cutoff = 16.8 ($df = 6$, $p = .01$) [√]	CL029 = .29 (< .38, critical value) OK [√]	All values < 2 so no case exerts undue influence [√]	All values < 2 [√]	CM034 = .34, CL029 = 1.39 (0.42 to 1.58 ideal) [X]

Durban-Watson Test (for independent errors)	Residuals Analyses	Multicollinearity
2.06 (values between 1 to 3 acceptable, so OK) [√]	Histog shows near normal distrib [√] P-P Plot std residual some skew [X] Zpred Zresid some heteroscedast [X] ∴ bootstrap	Greatest Pearson r among predictors (IT & FEV ₁ %) = -.36 ($p = .031$) [√] Tolerance: lowest value = 0.79 VIF: largest value = 1.26 [√] Each predictor's variance proportion distributed across diff dimensions [√]

Note. $N = 36$. [√] = Normal, not cause for concern; [X] = Non-normal, cause for concern; std = standardized; VIF = variable inflation factor.

Table 27 reveals a multivariate outlier exerting substantial influence on the regression model of baseline BDI-II (extreme high score in) and covariates predicting exercise levels at follow-up, thus justifying repeating the regression with the multivariate outlier removed.

Table 27

Assessment of Bias, Normality, and Generalizability for the Regression Model of BDI-II (High Score Included) and Covariates Predicting Exercise Levels at Follow-Up

Standardized Residuals	Cook's Distance	Mahalanobis Distance	Centered Leverage	Standardized DFBetas	Standardized DFFit	Covariance Ratio (Little influence = close to 1.0)
LD008 = 3.26 ($p = .001$) Unlikely [X]	LD008 = .5, < 1 but is greatest [√]	CL029 = 17.53 Cutoff = 16.8, ($df=6, p=.01$) [X]	CL029 = .50 is highest (> critical value of .38) [X]	LD008=1.61, high Substantial influence [X]	LD008 = 2.51 > 2, Influential case [X]	LD008 = .02, low (< 0.41 considered problematic) [X]

Durban-Watson Test (for independent errors)	Residuals Analyses (for stand regression analysis)	Multicollinearity
2.14 (values between 1 to 3 acceptable, so OK) [√]	Histogram: positively skewed [X] P-P Plot: skew [X] Zpred Zresid heteroscedastic [X] ∴ bootstrap	Greatest Pearson r among predictors (FEV ₁ % pred & IT) = -.36 ($p = .031$) [√] Tolerance: lowest value = 0.55 VIF: largest value = 1.82 [√] Distribution of variance proportions across dimensions [√]

Note. $N = 36$. [√] = Normal, not cause for concern; [X] = Non-normal, cause for concern; VIF = variable inflation factor.

Table 28 reveals there is still considerable bias remaining, despite removal of the influential multivariate outlier. This bias is due to the presence of the extreme high outlying baseline BDI-II score and justifies winsorizing it from 35 to 23.

Table 28

Assessment of Bias, Normality, and Generalizability for the Multiple Regression Model of BDI-II (High Score Included) and Covariates Predicting Exercise Levels at Follow-up (Influential Mutivariate Outlier Removed)

Standardized Residuals	Cook's Distance	Mahalanobis Distance	Centered Leverage	Standardized DFBetas	Standardized DFFit	Covariance Ratio (Little influence = close to 1.0)
JV069 = 2.25 ($p = .024$) Acceptable [√]	CL029 = .38 is greatest, but < 1.0 [√]	CL029 = 19.05 Cutoff = 16.8, ($df = 6, p = .01$) [X]	CL029 = .56 is highest (> critical value of .38) [X]	CL029=1.43 for BDI [√]	CL029 = 1.65 < 2, [√]	JV069=.28, lowest (< 0.4 considered problematic) [X]

Durban-Watson Test (for independent errors)	Residuals Analyses (for stand regression analysis)	Multicollinearity
1.69 (values between 1 to 3 acceptable, so OK) [√]	Histogram: Appears normal [√] P-P Plot: Some skew [X] Zpred Zresid heteroscedastic [X] ∴ bootstrap	Greatest Pearson r among predictors (FEV ₁ % pred & IT) = -.35 ($p = .038$) [√] Tolerance: lowest value = 0.54 VIF: largest value = 1.87 [√] Distribution of variance proportions across dimensions [√]

Note. $N = 35$. [√] = Normal, not cause for concern; [X] = Non-normal, cause for concern; VIF = variable inflation factor.

Table 29 reveals considerable bias for the multiple regression model of BDI-II (high score winsorized) and covariates predicting exercise levels at follow-up, with the multivariate outlier in the data set.

Table 29

Assessment of Bias, Normality, and Generalizability for the Multiple Regression Model of BDI-II (High Score Winsorized) and Covariates Predicting Exercise Levels at Follow-up (Influential Multivariate Outlier in Data Set)

Standardized Residuals	Cook's Distance	Mahalanobis Distance	Centered Leverage	Standardized DFBetas	Standardized DFFit	Covariance Ratio (Little influence = close to 1.0)
LD008 = 3.29 ($p = .001$) Not acceptable [X]	LD008 = .72 is greatest, but < 1.0 [√]	CL029 = 10.13 LD008 = 8.00, Cut-off = 16.8, ($df = 6$, $p = .01$) [X]	LD008 = .23 is highest (< critical value of .38) [√]	LD008 = 2.25 for BDI (> critical 2) [X]	LD008 = 3.12 Much > 2 [X]	LD008=.01, lowest (< 0.4 considered problematic) [X]

Durban-Watson Test (for independent errors)	Residuals Analyses (for stand regression analysis)	Multicollinearity
2.12 (values between 1 to 3 acceptable, so OK) [√]	Histogram: Appears + skewed [X] P-P Plot: skewed [X] Zpred Zresid heteros, outlier [X] ∴ bootstrap	Greatest Pearson r among predictors (FEV ₁ % pred & IT) = -.35 ($p = .038$) [√] Tolerance: lowest value = 0.55 VIF: largest value = 1.83 [√] Distribution of variance proportions across dimensions [√]

Note. $N = 35$. [√] = Normal, not cause for concern; [X] = Non-normal, cause for concern; + = positive; VIF = variable inflation factor.

Removing the multivariate outlier and winsorizing the extreme high baseline BDI-II score greatly reduces the bias and helps produce a regression model that is more accurate and representative of out sample, as can be seen from Table 30 below.

Table 30

Assessment of Bias, Normality, and Generalizability for the Multiple Regression Model of BDI-II (High Score Winsorized) and Covariates Predicting Exercise Levels at Follow-Up (Multivariate Outlier Removed)

Standardized Residuals	Cook's Distance	Mahalanobis Distance	Centered Leverage	Standardized DFBetas	Standardized DFFit	Covariance Ratio (Little influence = close to 1.0)
JV069 = 2.21 ($p = .027$) Acceptable [√]	JV069 = .18 is greatest, but < 1.0 [√]	CL029 = 11.45 Cutoff = 16.8, ($df = 6, p = .01$) [√]	CL029 = .34 is highest (< critical value of .6) [√]	JV069=1.1 for Intercept [√]	CL029 = 1.25 < 2, [√]	JV069=.30, lowest (< 0.4 considered problematic) [X]

Durban-Watson Test (for independent errors)	Residuals Analyses (for stand regression analysis)	Multicollinearity
1.73 (values between 1 to 3 acceptable, so OK) [√]	Histogram: Appears not normal [X] P-P Plot: Some skew [X] Zpred Zresid heteroscedastic [X] ∴ bootstrap	Greatest Pearson r among predictors (FEV ₁ % pred & IT) = -.35 ($p = .038$) [√] Tolerance: lowest value = 0.54 VIF: largest value = 1.86 [√] Distribution of variance proportions across dimensions [√]

Note. $N = 35$. [√] = Normal, not cause for concern; [X] = Non-normal, cause for concern; VIF = variable inflation factor.

Normality Assessments for Exploratory/Secondary Analyses:

Below are tables presenting assessments of bias, normality, and generalizability for data in the regression models made up of the strongest baseline predictors of PR attendance, PR compliance, and exercise levels at follow-up. Table 31 shows only slight bias not requiring any transformation of values, but that bootstrapping should be used to as assumptions of normally distributed residuals appear to have not been satisfied.

Table 31

Assessment of Bias, Normality, and Generalizability for Regression Model Predicting PR attendance from Baseline FEV₁ %, Cohabiting Status, and HLC Other People

Standardized Residuals	Cook's Distance	Mahalanobis Distance	Centered Leverage	Standardized DFBetas	Standardized DFFit	Covariance Ratio (Little influence = close to 1.0)
LD012 = -2.11 (<i>p</i> = .035) Normal enough [√]	LD012 = .21, highest (all < 1 so OK) [√]	FB007 = 9.49 Cutoff = 11.34 (<i>df</i> = 3, <i>p</i> = .01): not extreme outlier [√]	FB007 = .27 (> .22, critical value) slight influence [√]	All absolute values < 1 [√]	All absolute values < 1 [√]	FB007 = 1.61 LD012 = 0.65 (0.67 – 1.33 is OK) acceptable [√]

Durban-Watson Test (for independent errors)	Residuals Analyses	Multicollinearity
1.75 (values between 1 to 3 acceptable, so OK) [√]	Histogram: little skew [√] P-P Plot std residual skewed [X] Zpred Zresid: some hetercedast [X] ∴ bootstrap	Greatest Pearson <i>r</i> among predictors (FEV ₁ % & cohabiting) = -.3 (<i>p</i> = .08) [√] Tolerance: lowest value = 0.90 VIF: largest value = 1.11 [√] Each predictor's variance proportion distributed across diff dimensions [√]

Note. *N* = 36. [√] = Normal, not cause for concern; [X] = Non-normal, cause for concern; VIF = variable inflation factor.

Data used in the best regression predicting PR exercise compliance were assessed for bias and normality (see Table 32 below). An influential case with an outlying high baseline BDI-II score was revealed that justified repeating the regression with that score winsorized from 35 to 23.

Table 32

Assessment of Bias, Normality, and Generalizability for the Regression Model Predicting PR Exercise Compliance from Baseline BDI-II (High Score in Data), IT and CTHi Protocols, Sex, and FEV₁ %

Standardized Residuals	Cook's Distance	Mahalanobis Distance	Centered Leverage	Standardized DFBetas	Standardized DFFit	Covariance Ratio (Little influence = close to 1.0)
CM034 = -2.43 ($p = .015$) Normal, expected [√]	CM034 = .15 is highest (all < 1 so OK) [√]	CL029 = 16.24 > Cutoff = 15.09 ($df = 5, p = .01$): cause for concern [X]	CL029 = .464 (> .333, critical value) may exert undue influence [X]	All values < 2 [√]	All values < 2 [√]	CL029 = 2.39 is cause for concern (0.5 – 1.5 is OK) [X]

Durban-Watson Test (for independent errors)	Residuals Analyses	Multicollinearity
2.02 (values between 1 to 3 acceptable, so OK) [√]	Histog shows near normal distrib [√] P-P Plot std residual fairly normal [√] Zpred Zresid some heteroscedast [X] ∴ bootstrap	Greatest Pearson r among predictors (IT & CTHi) = -.50 ($p = .002$) [√] Tolerance: lowest value = 0.59 VIF: largest value = 1.69 [√] Each predictor's variance proportion distributed across diff dimensions [√]

Note. $N = 36$. [√] = Normal, not cause for concern; [X] = Non-normal, cause for concern; std = standardized; VIF = variable inflation factor.

As can be seen from results of the bias and normality assessments in Table 33 below, winsorizing the outlying high baseline BDI-II score from 35 to 23 resulted in substantially reducing the substantial influence and producing a regression model that is more representative of our sample.

Table 33

Assessment of Bias, Normality, and Generalizability for the Regression Model Predicting PR Exercise Compliance from Baseline BDI-II (High Score Winsorized), IT and CTHi Protocols, Sex, and FEV₁ %

Standardized Residuals	Cook's Distance	Mahalanobis Distance	Centered Leverage	Standardized DFBetas	Standardized DFFit	Covariance Ratio (Little influence = close to 1.0)
CM034 = -2.23 ($p = .026$) Normal, expected [√]	MP060 = .15, highest (all < 1 so OK) [√]	CL029 = 8.38 < Cutoff = 15.09 ($df = 5, p = .01$) [√]	CL029 = .24 (< .333, critical value) [√]	All values < 1 so no case exerts undue influence on model parameters [√]	MP060 = 0.99 has highest absolute value: < 2 [√]	CL029 = 1.30 (0.5 – 1.5 is OK) [√]

Durban-Watson Test (for independent errors)	Residuals Analyses	Multicollinearity
2.04 (values between 1 to 3 acceptable, so OK) [√]	Histog shows near normal distrib [√] P-P Plot std residual fairly normal [√] Zpred Zresid some heteroscedast [X] ∴ bootstrap	Greatest Pearson r among predictors (IT & CTHi) = -.50 ($p = .002$) [√] Tolerance: lowest value = 0.59 VIF: largest value = 1.69 [√] Each predictor's variance proportion distributed across diff dimensions [√]

Note. $N = 36$. [√] = Normal, not cause for concern; [X] = Non-normal, cause for concern; std = standardized; VIF = variable inflation factor.

Table 34 presents bias and normality assessments of data for the strongest regression model predicting exercise levels at follow-up. Clearly, there is a problem with bias, the source of which appears to be two cases: One is the outlying high baseline BDI-II score of 35, the other was previously identified as a multivariate outlier.

Table 34

Assessment of Bias, Normality, and Generalizability for the Regression Model Predicting Exercise Levels at Follow-Up from BDI-II (High Score in), Smoking Status, HLC Chance (With Multivariate Outlier in Data Set)

Standardized Residuals	Cook's Distance	Mahalanobis Distance	Centered Leverage	Standardized DFBetas	Standardized DFFit	Covariance Ratio (Little influence = close to 1.0)
LD008 = 3.79 ($p < .001$) Very unlikely [X]	LD008 = .63 highest but < 1 [√]	CL029 = 15.93 is furthest case from centroid. Cutoff = 11.34 ($df=3, p=.01$) [X]	CL029 = .46 is highest (.33 is critical value), so big influence [X]	LD008 = 1.9 highest for BDI, big influence on model parameters [X]	LD008 = 2.25 much > 1, suggests is influential case [X]	LD008 = .07 Much < cutoff (0.67 to 1.33 ideal) CL029 = 2.09 [X]

Durban-Watson Test (for independent errors)	Residuals Analyses	Multicollinearity
2.18 (values between 1 to 3 acceptable, so OK) [√]	Histogram: looks + skewed [X] P-P Plot: abnormal [X] Zpred Zresid heteroscedastic , LD008 outlier [X] ∴ bootstrap	Greatest Pearson r among predictors (BDI & HLC chance) = .12 ($p = .49$) [√] Tolerance: lowest value = 0.97 VIF: largest value = 1.03 [√] Each predictor's variance proportion is distributed across diff dimensions [√]

Note. $N = 36$. [√] = Normal, not cause for concern; [X] = Non-normal, cause for concern; + = positive; VIF = variable inflation factor.

Table 35 presents bias and normality assessments for the regression analysis predicting exercise levels at follow-up, but with the high baseline BDI-II outlier winsorized from 35 to 23. This appears to have done little to reduce bias and the non-normal distribution of residuals. Removing the multivariate outlier is therefore justified to reduce substantial bias.

Table 35

Assessment of Bias, Normality, and Generalizability for the Regression Model Predicting Exercise Levels at Follow-Up from BD-II (High Score Winsorized), Smoking Status, and HLC Chance (With Multivariate Outlier in Data Set)

Standardized Residuals	Cook's Distance	Mahalanobis Distance	Centered Leverage	Standardized DFBetas	Standardized DFFit	Covariance Ratio (Little influence = close to 1.0)
LD008 = 3.79 ($p < .001$) Very unlikely [X]	LD008 = 1.01 > 1 is highest [X]	CA065 = 6.03 is furthest case from centroid. Cutoff = 11.34 ($df=3, p=.01$) So OK [✓]	CA065 = .17 is highest (.33 is critical value), so OK [X]	LD008 = 2.59 highest for BDI, big influence on model parameters [X]	LD008 = 2.95 much > 1, suggests is influential case [X]	LD008 = .06 Much < cutoff (0.67 to 1.33 ideal) JH067 = 1.34 [X]

Durban-Watson Test (for independent errors)	Residuals Analyses	Multicollinearity
2.17 (values between 1 to 3 acceptable, so OK) [✓]	Histogram: looks + skewed [X] P-P Plot: abnormal [X] Zpred Zresid heteroscedastic , LD008 outlier [X] ∴ bootstrap	Greatest Pearson r among predictors (BDI & HLC chance) = .14 ($p = .41$) [✓] Tolerance: lowest value = 0.97 VIF: largest value = 1.04 [✓] Each predictor's variance proportion is distributed across diff dimensions [✓]

Note. $N = 36$ [✓] = Normal, not cause for concern; [X] = Non-normal, cause for concern; + = positive; VIF = variable inflation factor.

The bias and normality assessments are presented in Table 36 for the “best” regression model predicting exercise levels at follow-up. Here, the case of the multivariate outlier was removed from the analysis, but the univariate high baseline BDI-II score was left in and continued to exert substantial influence on the regression model. Therefore, winsorizing it would seem justified.

Table 36

Assessment of Bias, Normality, and Generalizability for the Regression Model Predicting Exercise Levels at Follow-Up from BDI-II (High Score in), Smoking Status, and HLC Chance (Multivariate Outlier Removed)

Standardized Residuals	Cook’s Distance	Mahalanobis Distance	Centered Leverage	Standardized DFBetas	Standardized DFFit	Covariance Ratio (Little influence = close to 1.0)
JV069 = 2.59 (.010) CT018 = -2.43 (.015) Acceptable [✓]	CL029 = .48 < 1 is highest [✓]	CL029 = 17.72 is furthest case from centroid. Cutoff = 11.34 ($df=3, p=.01$) So NOT OK [X]	CL029 = .52 is highest (.33 is critical value), so much influence [X]	CL029 = 1.35 highest for BDI, influence on model parameters [X]	CL029 = 1.40 > 1, suggests is influential case [X]	CL029 = 2.05 > cutoff (0.66 to 1.34 ideal) [X]

Durban-Watson Test (for independent errors)	Residuals Analyses	Multicollinearity
2.01 (values between 1 to 3 acceptable, so OK) [✓]	Histogram: looks - skewed [X] P-P Plot: abnormal [X] Zpred Zresid [X] heteroscedastic ∴ bootstrap	Greatest Pearson r among predictors (BDI & HLC chance) = .11 ($p = .52$) [✓] Tolerance: lowest value = 0.98 VIF: largest value = 1.02 [✓] Each predictor’s variance proportion is distributed across diff dimensions [✓]

Note. $N = 35$. [✓] = Normal, not cause for concern; [X] = Non-normal, cause for concern; - = negative; VIF = variable inflation factor.

Table 37 clearly illustrates that the substantial bias was only improved by both winsorizing the high baseline BDI-II score from 35 to 23 and removing the multivariate outlier from the data on which the regression analysis for “best” prediction of exercise level at follow-up was performed.

Table 37

Assessment of Bias, Normality, and Generalizability for the Regression Model Predicting Exercise Levels at Follow-Up from BDI-II (High Score Winsorized), Smoking Status, and HLC Chance (With Multivariate Outlier Removed)

Standardized Residuals	Cook’s Distance	Mahalanobis Distance	Centered Leverage	Standardized DFBetas	Standardized DFFit	Covariance Ratio (Little influence = close to 1.0)
JV069 = 2.57 (.010) CT018 = -2.33 (.020) Acceptable [✓]	CT018 = .22 < 1 is highest [✓]	CL029 = 9.08 is furthest case from centroid. Cutoff = 11.34 ($df=3, p=.01$) So OK [✓]	CL029 = .27 is highest (.33 is critical value) [✓]	CT018 = 0.82 highest for HLCc, influence on model parameters [✓]	CL029 = 1.04 ~ 1, Not too influential a case [✓]	JV069 = .43 < cutoff (0.66 to 1.34 ideal) [X]

Durban-Watson Test (for independent errors)	Residuals Analyses	Multicollinearity
2.03 (values between 1 to 3 acceptable, so OK) [✓]	Histogram: looks neg skewed [X] P-P Plot: abnormal [X] Zpred Zresid bit heteroscedastic [X] ∴ bootstrap	Greatest Pearson r among predictors (BDI & bSmoking) = .16 ($p = .355$) [✓] Tolerance: lowest value = 0.95 VIF: largest value = 1.05 [✓] Each predictor’s variance proportion is distributed across diff dimensions [✓]

Note. $N = 35$. [✓] = Normal, not cause for concern; [X] = Non-normal, cause for concern; neg = negative; VIF = variable inflation factor.

Appendix D
Multiple Imputation Procedure for Missing Values at Follow-Up

Eleven out of 36 values (30.56%) for exercise levels at follow-up were missing due to participant dropout ($n = 8$), physical activity diaries that were missing key information ($n = 2$) or diary not submitted ($n = 1$). SPSS Multiple Imputation procedure was used to impute these missing values. The imputation was performed using data that did not include the extreme multivariate outlier, as this would have introduced substantial bias. The following eight baseline variables were selected to inform the imputation: sex, age, smoking status, FEV₁/FVC ratio, ESWT distance, BDI-II score, Anxiety Sensitivity Index score, MHL Chance scale score. These were chosen based on their relevance as predictors of the missing follow-up data and their being key participant characteristics (i.e., age, sex). The imputation option we chose was “automatic,” which let SPSS select the imputation method best suited for the degree of randomness in the pattern of the missing data. The imputation method selected by SPSS was the monotone method, suggesting the data was not missing completely at random. (However a missing values analysis including all of the variables listed above suggested the data was missing completely at random, as Little’s MCAR test was: Chi Square = 9.393, df = 6, $p = .153$.) Fifteen imputations with a maximum of 55 case draws and a maximum of 2 parameter draws were requested. Constraints of 0 minimum to 2700 maximum were specified for the follow-up exercise levels (MET minute values) to prevent SPSS from producing negative values of MET minutes, which would have fallen outside the range of what is possible for level of exercise. The maximum value of 2700 was greater than the existing MET minute values in the data set. This procedure successfully produced complete follow-up exercise data ($N = 36$). Table 38 below shows the means and standard deviations, and medians and

interquartile ranges for the follow-up exercise level data before missing values were imputed ($n = 25$) and after missing values were imputed ($N = 36$).

Table 38

Follow-Up Exercise Level Values Before and After Multiple Imputation of Missing Values

Statistic	Mean (SD)	Median (IQR)
Before MI ($n = 25$)	1062 (838)	933 (510-1623)
After MI ($n = 36$)	919 (739)	706 (445-1146)

Note. SD = standard deviation; IQR = interquartile range; MI = multiple imputation.

The mean and median values were substantially lower after imputation of the 11 missing values. This was expected given that the 8 participants absent at follow-up had higher baseline BDI-II scores than those who were present, and tended more to be baseline smokers, both of which predicted lower exercise levels at follow-up.

Histograms (Figures 11 and 12) show that the distributions of data before and after missing data were imputed are quite similar, thus confirming that imputation did introduce much bias.

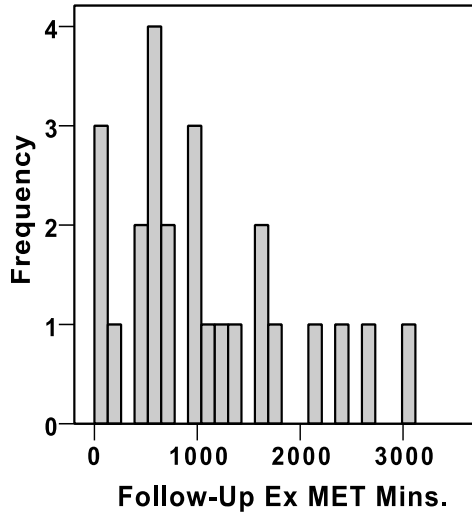


Figure 11. Distribution of follow-up exercise levels before imputation of missing data ($n = 25$).

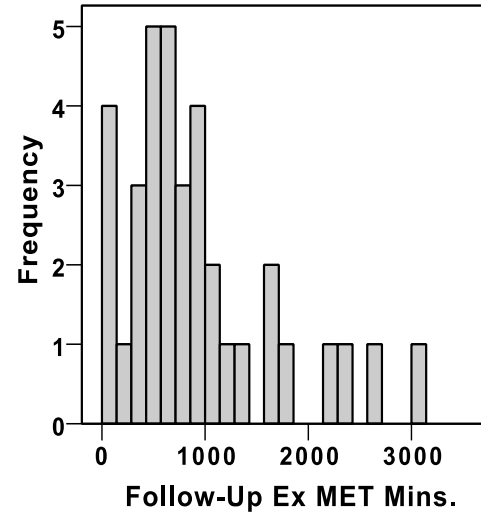


Figure 12. Distribution of follow-up exercise levels after imputation of missing data ($N = 36$).

Appendix E
Pearson Correlation Table

Table 39

Correlation Matrix of Baseline and Outcome Variables

Variables	IT N=36	Age N=36	Sex N=36	BMI N=36	Pk/yr N=36	Smoking N=36	Cohabit N=36	FEV ₁ % N=36	ESWT Time N=36	BDI N=36	HLC-I N=36	HLC-C N=36	HLC-D N=36	HLC-OP N=36	Attend N=36	Comply N=36	Maint N=36	Maint N=35 ^a
IT <i>r</i>	1.00	-.048	.041	-.025	-.264	.250	.000	-.361*	-.025	.078	-.160	-.032	-.162	.050	-.274	-.563***	-.130	-.081
Age <i>r</i>		1.00	-.125	-.193	.176	-.296	-.393*	.331*	-.123	-.159	.063	.280	.101	.176	.154	-.044	-.039	-.016
Sex (F) <i>r</i>			1.00	.095	-.121	.164	-.532**	.220	.067	.272	-.118	.220	-.071	-.116	-.164	.143	-.245	-.359*
BMI <i>r</i>				1.00	.045	.075	.026	.309	-.237	-.063	-.068	.038	-.429**	.146	.109	-.018	-.161	-.045
Pack/yr <i>r</i>					1.00	.014	.023	-.043	-.484**	.013	.074	-.104	-.293	.065	.032	.077	-.082	-.078
Smoking <i>r</i>						1.00	.250	-.021	-.027	.051	.082	-.106	-.162	-.032	-.034	-.150	-.500**	-.512**
Cohabit <i>r</i>							1.00	-.299	.007	.039	.086	-.229	-.073	.101	.268	-.104	-.038	.098
FEV ₁ % <i>r</i>								1.00	.235	-.106	.089	.115	-.023	-.032	.439**	.054	-.012	-.083
ESWT, time <i>r</i>									1.00	-.119	-.193	-.094	.153	-.207	.267	.011	.446**	.331
BDI-II <i>r</i>										1.00	-.127	.118	.104	.026	.018	-.350*	-.276	-.515**
HLC-I <i>r</i>											1.00	-.058	.549***	.519***	-.012	.090	-.052	-.021
HLC-C <i>r</i>												1.00	.006	.182	-.007	-.062	-.318	-.388*
HLC-D <i>r</i>													1.00	.189	-.087	.079	.066	.054
HLC-OP <i>r</i>														1.00	.247	-.045	-.094	-.083
Attend <i>r</i>															1.00	.113	.139	.077
Comply <i>r</i>																1.00	.100	.224
Maintain 36 <i>r</i>																	1.00	.
Maintain 35 <i>r</i>																		1.00

Note. IT = interval training, *r* = Pearson correlation coefficient, BMI = body mass index, Pk/yr = U.S. pack years, FEV₁ % = forced expiratory volume in 1 second percent of predicted normal, ESWT = endurance shuttle walking test, BDI = Beck Depression Inventory, HLC-I = health locus on control internal scale, HLC-C = health locus of control chance scale, HLC-D = health locus of control doctor scale, HLC-OP = health locus of control other people scale, Attend = PR attendance, Comply = PR exercise compliance, Maintain = exercise levels 9 months post-PR. ^aOutlier removed.

Appendix F
PR Composite Adherence Data and Analyses

Pulmonary rehabilitation (PR) “Composite adherence” refers to a measure comprised of attendance at PR exercise sessions *and* compliance with target intensity prescribed for endurance exercise during PR. This measure is the product of PR attendance and PR exercise compliance, both equally weighted (percent of total sessions attended × percent of total endurance training time exercising to target) for each participant. We would argue that attendance alone, the measure consistently reported in the literature on PR “adherence” and its predictors, is an inadequate metric of PR adherence, as being present does not reflect the extent to which endurance exercise is being performed, which is the key component of PR. As mentioned in the main text of this thesis, compliance with exercise, to our knowledge, has not been measured or reported in any previous study investigating predictors of engagement in exercise-based PR.

In the present study, PR attendance and PR exercise compliance were both equally weighted, however differential weightings could be assigned to each aspect to reflect their respective importance. Although determining and then applying differential weightings is beyond the scope of the present study, we believe PR *attendance* takes precedence over PR exercise compliance because compliance (in PR) is conditional upon attending. Furthermore, if a participant was attending PR but not initially engaging in the physical exercise component, their motivation and self-confidence to do so might increase over the course of the sessions such that they might begin to engage in exercise. (This would be even more likely if the PR program were to include interventions that targeted motivation and self-efficacy for exercise.)

Composite adherence may have some use in a clinical context in terms of predicting or evaluating PR outcomes (i.e., improvements in exercise capacity, dyspnea, health-related quality of life, and frequency/severity of COPD exacerbations), but it was not a main focus in meeting this study's objectives, as more information could be gleaned from examining PR attendance and exercise compliance (and their distinct predictors) separately. The composite measure alone does not allow for an analyses or appreciation of its component parts or their distinct predictor variables and therefore does not inform with which aspect of PR a participant may be having difficulty (i.e., attendance or exercise compliance or both) nor what the focus of an intervention to help improve PR adherence should be. Nevertheless, we present in this appendix the correlation and multiple regression analyses conducted on baseline depression symptoms (our predictor of interest) and composite adherence in the context of the same selected covariates included in the regressions conducted on the separate outcomes to show what emerges.

The median percent (IQR) PR composite adherence score for our sample is 72 (29–86) and the mean percent (SD) was 57 (33). The distribution of PR composite adherence scores for our sample is presented in Figure 13 below and reveals a somewhat bimodal pattern with grouping of several participants with low adherence and others with high adherence. Figure 14 illustrates the relationship between baseline BDI-II and PR composite adherence. Baseline depressive symptomatology does not predict composite adherence (at least not significantly). The Pearson correlation is negative and weak when the outlying high BDI-II score is retained in the data set ($r = -.27, p = .116$) and weaker

when it is winsorized from 35 to 23 ($r = -.22, p = .196$). When the outlying BDI-II score is kept in, variation in BDI-II accounts for only 7.3 % of variation in composite adherence and this decreases to 4.8 % when the outlier is winsorized. We know from the correlation analyses run on each separate component of composite adherence that it is the negative association between baseline depression and PR exercise compliance that drives the weak association between baseline BDI-II and composite adherence.

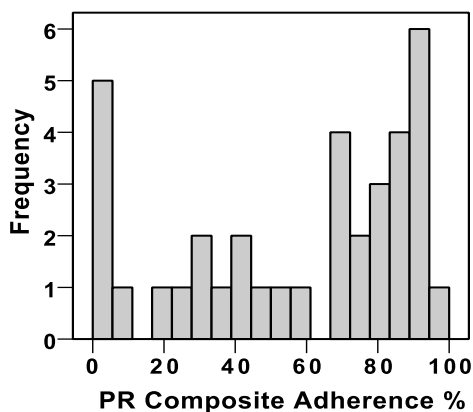


Figure 13. Distribution of PR composite adherence ($N = 36$).

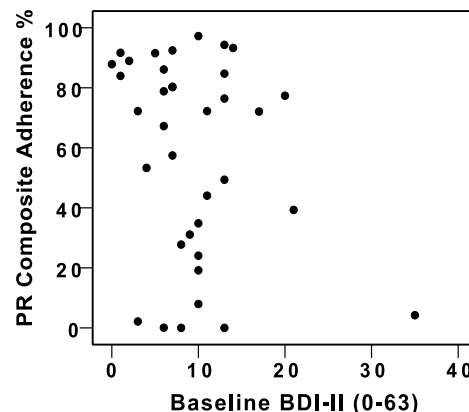


Figure 14. Relationship between baseline depression and PR composite adherence ($N = 36$, Pearson $r = -.27, p = .116$).

Table 40 below presents the results of the multiple linear regression analysis with baseline BDI-II as the predictor of interest and PR composite adherence as the outcome in the context of selected covariates. Interval training is the only variable that emerged as a significant predictor of lower composite adherence (IT was the hardest and most demanding for participants). We know from the regression analyses performed on each component of composite adherence that IT was not a significant predictor of PR

attendance (though there was a weak negative signal there), but was a strong predictor of poor PR exercise compliance. So its emergence as a predictor of composite adherence is driven mainly by the correlation between IT and PR exercise compliance, not PR attendance.

Table 40

Multiple Linear Regression Model for Prediction of PR Composite Adherence from Baseline BDI-II and Selected Covariates

Variable	<i>B</i>	β	Bootstrap ^a		
			<i>SE B</i>	<i>p</i>	95 % CI for <i>B</i> ^b
Constant	80.43		27.30	.008	[26.85, 140.92]
bBDI-II	-1.45	-.24	0.98	.162	[-3.27, 0.35]
IT	-41.52	-.60	14.40	.014	[-68.14, -15.44]
CTHi	-4.55	-.07	11.99	.727	[-30.11, 18.92]
Sex (F)	9.96	.15	11.43	.401	[-10.51, 29.81]
bFEV ₁ %	0.02	.01	0.35	.953	[-0.59, 0.66]
bSmoking	-6.08	-.09	10.26	.561	[-27.92, 15.23]
Regression Model	<i>R</i> = .65	Adjusted <i>R</i> ² = .30	<i>F</i> (6, 29) = 3.47, <i>p</i> = .011		

Note. *N* = 36. CI = confidence interval; bBDI-II = baseline Beck Depression Inventory-II; IT = interval training; CTHi = constant training high intensity; bFEV₁ % = baseline forced expiratory volume in the first second percent of predicted normal value; bSmoking = smoking at baseline. ^aBootstrap results are based on 1000 bootstrap samples. ^bConfidence intervals are bias-corrected and accelerated.

Interval training is the only variable that emerged as a significant predictor of lower composite adherence (IT was the hardest and most demanding for participants). We know from the regression analyses performed on each component of composite adherence that

IT was not a significant predictor of PR attendance (though there was a weak negative signal there), but was a strong predictor of poor PR exercise compliance. So its emergence as a predictor of composite adherence is driven mainly by the correlation between IT and PR exercise compliance, not PR attendance.