PHYSICAL ACTIVITY AND SEDENTARY BEHAVIOUR ACROSS THE SPECTRUM OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Doctoral Thesis

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by

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Abstract

Chronic obstructive pulmonary disease (COPD) patients are generally more sedentary and less physically active than healthy adults; putting them at increased risk of hospitalisation and death. For patients with mild-moderate COPD, physical activity appears to be reduced compared with apparently healthy adults but differences in time spent sedentary are less well established. Additionally, there is a need for a greater understanding of the correlates of behaviour in mild-moderate patients with much of the existing literature focusing on more severe or mixed stage patient samples and with many studies lacking objective behavioural monitoring, not adjusting for confounders and a paucity of data on correlates of sedentary time. Despite having mild-moderate airflow obstruction, these patients also report a range of symptom burdens with some individuals reporting severe symptoms. Subsequently, these patients represent a sub-set of individuals who may require lifestyle interventions. Therefore, factors associated with patients reporting more severe symptoms need to be identified to help understand how this phenomenon may manifest and be intervened upon. For patients with more advanced COPD who are admitted to hospital for an acute exacerbation behavioural intervention focussing on less intense movement may be a more suitable approach for reducing the risk of readmissions than more intense physical activity or exercise. To date no studies have specifically targeted reductions in sedentary behaviour in COPD. In addition, wearable self-monitoring technology may facilitate the provision of such interventions, removing important participation barriers such as travel and cost, but this has not been sufficiently examined in COPD.

This thesis investigated: (i) objectively measured physical activity and sedentary time and the correlates of these behaviours for mild-moderate COPD patients and apparently healthy adults (Study One); (ii) factors associated with self-reported symptom severity and exacerbation history in mild-moderate COPD patients (Study Two) and (iii) the feasibility and acceptability of a home-based sedentary behaviour intervention using wearable self-monitoring technology for COPD patients following an acute exacerbation (Study Three).

Methods: Study One: COPD patients were recruited from general practitioners and apparently healthy adults from community advertisements. Objectively measured moderate-to-vigorous physical activity (MVPA), light activity and sedentary time for 109 mild-moderate COPD patients and 135 apparently healthy adults were obtained by wrist-worn accelerometry. Patients with at least four valid days (≥10 waking hours) out of a possible

seven were included in analysis. A range of demographic, social, symptom-based, general health and physical factors were examined in relation to physical activity and sedentary time using correlations and linear regressions controlling for confounders (age, gender, smoking status, employment status and accelerometer waking wear time). **Study Two**: In 107 patients recruited from general practitioners, symptoms were assessed using the COPD Assessment Test (CAT) and Modified Medical Research Council (mMRC) questionnaires. Twelve-month exacerbation history was self-reported. Exercise capacity was assessed via incremental shuttle walk test (ISWT) and self-reported usual walking speed. Physical activity and sedentary time were obtained from a wrist-worn accelerometer. **Study Three:** Patients were randomised in-hospital into a usual care (Control), Education or Education + Feedback group with the intervention lasting 14 days following discharge. The intervention groups received information about reducing prolonged sitting. The Education + Feedback group also received real-time feedback on their sitting time, number of stand-ups and step count at home through an inclinometer linked to a smart device app. The inclinometer also provided vibration prompts to encourage movement when the wearer had been sedentary for too long. Feasibility of recruitment (e.g. uptake and retention) and intervention delivery (e.g. fidelity) were assessed. Acceptability of the intervention technology (e.g. wear compliance, app usage and response to vibration prompts) was also examined.

Results: Study One: COPD patients were more sedentary (592±90 versus 514±93 minutes per day, $p<0.05$) and accrued less MVPA (12±18 versus 33±32 minutes per day, $p<0.05$) than apparently healthy adults. For COPD patients, self-reported dyspnea and percentage body fat were independent correlates of sedentary time and light activity with exercise capacity (incremental shuttle walk test) an independent correlate of MVPA. For apparently healthy adults, percentage body fat and exercise capacity were independent correlates of sedentary time and light activity. Percentage body fat was an independent correlate of MVPA. **Study Two:** ISWT (B=-0.016±0.005, partial R^2=0.117, p=0.004) and years living with COPD (B=0.319±0.122, R^2=0.071, p=0.011) were independently associated with CAT score. ISWT (B=-0.002±0.001, R^2=0.123, $p<0.001$) and vector magnitude counts per minute (VMCPM) (B=0.0001±0.0000, R^2=0.050, p=0.011) were independently associated with mMRC grade. MVPA was independently associated with previous exacerbations (B=-0.034±0.012, R^2=0.081, p=0.005). Patients reporting a CAT score of >20 or an mMRC score of ≥2 had lower VMCPM, were more sedentary and took part in less light activity than patients reporting a CAT score of 0-10 or mMRC of 0, respectively. Patients reporting ≥2

exacerbations took part in less MVPA than patients reporting zero exacerbations. **Study Three:** Study uptake was 31.5% providing a final sample of 33 COPD patients. Retention of patients at two-week follow-up was 51.5% (n=17). Reasons for drop-out were mostly related to being unable to cope with their COPD. Patients wore the inclinometer for 11.8±2.3 days (and charged it 8.4±3.9 times) with at least one vibration prompt occurring on 9.0±3.4 days over the 14 day study period. Overall, 325 vibration prompts occurred with patients responding 106 times (32.6%). 40.6% of responses occurred within 5 minutes of the prompt with patients spending 1.4±0.8 minutes standing and 0.4±0.3 minutes walking, taking 21.2±11.0 steps.

Discussion: Study One: COPD patients were less active and more sedentary than apparently healthy adults; however, factors predicting behaviour were similar between groups. Correlates differed between sedentary time, light activity and MVPA for both groups. Interventions to boost physical activity levels and reduce sedentary time should be offered to patients with mild-moderate COPD, particularly those reporting more severe breathlessness. **Study Two:** Worse exercise capacity, low levels of physical activity and more time spent sedentary are some of the factors associated with patients of the same severity of airflow limitation reporting differing symptom severities. These patients may benefit from both lifestyle and exercise interventions. **Study Three:** Recruitment and retention rates suggest a trial targeting sedentary behaviour in hospitalised COPD patients is feasible. A revised intervention, building on the successful components of the present feasibility study is justified.

Conclusion: The findings from this thesis have contributed a greater understanding of physical activity and sedentary behaviour in COPD and can inform the development of tailored physical activity and sedentary behaviour interventions for patients across the grades of COPD severity.

Keywords: accelerometry, behaviour, breathlessness, COPD-SEAT, exacerbations, PhARaoH Study, symptoms

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"Unity is strength… when there is teamwork and collaboration wonderful things can be achieved"

– Mattie J.T. Stepanek

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Dedication

I dedicate this work to my wonderful family. Mum and Dad, I cannot express the gratitude, love and admiration I have for you.

Maxine, to whom I must offer my deepest thanks for keeping me sane, positive and motivated during my grapples with the beast that is ‘The Thesis’. We have shared the ups and the downs of this journey together and have conquered every challenge set before us. Your calming presence and selflessness have played an invaluable part in this drama and I will be sure to repay this debt of gratitude, with interest.

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List of abbreviations

6MWD	Six Minute Walk Distance
ANCOVA	Analysis of covariance
BMI	Body Mass Index
CAT	Chronic obstructive pulmonary disease Assessment Test
CCG	Clinical Commissioning Group
CONSORT	Consolidation Standards of Reporting Trials
COPD	Chronic Obstructive Pulmonary Disease
COPD-SEAT	Chronic Obstructive Pulmonary Disease-Sitting and ExacerbAtions Trial
FES-I	Falls Efficacy Scale-International
FEV_1	Forced expiratory volume in one second
FVC	Forced Vital Capacity
GOLD	Global Initiative for Obstructive Lung Disease
HADS	Hospital Anxiety and Depression Scale
IMD	Index of Multiple Deprivation
IPAQ	International Physical Activity Questionnaire
ISWT	Incremental Shuttle Walk Test
MECC	Making every contact count
METS	Metabolic equivalents
mMRC	Modified Medical Research Council
MVPA	Moderate-to-Vigorous Physical Activity
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
PCRN	Primary Care Research Network
PhARaoH	Physical Activity and Respiratory Health
QMVC	Quadriceps Maximal Voluntary Contraction
SPPB	Short Physical Performance Battery
VMCPM	Vector Magnitude Counts Per Minute

“Every day you may make progress. Every step may be fruitful. Yet there will stretch out before you an ever-lengthening, ever-ascending, ever-improving path. You know you will never get to the end of the journey. But this, so far from discouraging, only adds to the joy and glory of the climb.”

- Winston Churchill

Thesis contributions

Under the supervision of Dr Lauren Sherar, Dr Dale Esliger and Professor Sally Singh, the work comprising this thesis was carried out by the author. The funding for the observational study, from which Chapter 3 and Chapter 4 data was collected, was obtained prior to the commencement of the author's involvement. This study was led by the author from the development of the study protocol and design, engaging with the collaborators, patient and public involvement, completing the necessary study sponsor and NHS research ethics committee processes, recruitment, data collection, database management and data analysis. Data collection for these chapters was facilitated by a wider research team which included postgraduate and undergraduate students. Reliability testing for the accelerometers was conducted by postgraduate students under the guidance of Dr Dale Esliger. The feasibility intervention, from which Chapter 6 data was collected, was conceived by the author and supervisory team. The author led the study design and protocol, collaborative work, patient and public involvement, study sponsor and NHS ethics processes, recruitment, data collection and data analysis. This study was conducted in collaboration with social science researchers (one postgraduate student and two lecturers) who led the qualitative components of the work which is not reported in this thesis. Intervention fidelity was assessed by two postgraduate students at Loughborough University.

Chapter 1: Introduction and literature review

1.1 Introduction

Following the industrial revolution, the requirement of individuals to be physically active at work, in the home, for travel and for recreation has markedly reduced, resulting in a global pandemic of physical inactivity (Lee et al., 2012). Globally, physical inactivity has been estimated to cost healthcare systems more than $53.8 billion with inactivity-related mortalities attributed to $13.7 billion losses in productivity and 13.4 million disability-adjusted life-years (Ding et al., 2016). In the UK physical inactivity has been found to be responsible for 3% of disability-adjusted life-years; equating to over £1 billion in annual costs (Allender, Foster, Scarborough, & Rayner, 2007). The hypokinetic and obesogenic environments and norms of today's society means that the vast majority of people are at risk of developing a range of illnesses including cardiovascular disease, hypertension and diabetes mellitus by not engaging in physical activity of sufficient intensity, duration and regularity. For example, less than 5% of adults in the UK and the US achieve government recommendations of moderate-to-vigorous physical activity (MVPA) per day (Craig, Mindell, & Hirani, 2009; Troiano et al., 2008). It is estimated that physical inactivity causes 9% of premature mortality worldwide; on par with other risk factors such as smoking and obesity (Lee et al., 2012). Additionally, 67% of older adults (≥60 years of age) spend more than 8.5 hours per day sedentary (Harvey, Chastin, & Skelton, 2013). This pandemic of inactivity and sedentariness has led the Chief of Knowledge Officer of the National Health Service (NHS) to coin this lack of movement as "walking deficiency syndrome" and "excessive sitting syndrome", calling walking the "elixir of life" (Gray, 2009).

Chronic obstructive pulmonary disease (COPD) is a debilitating and progressive condition characterised by persistent airflow obstruction and breathlessness (Global Initiative for Chronic Obstructive Lung Disease., 2014). Whilst COPD primarily affects the respiratory system, it also has significant negative impacts on extra-pulmonary outcomes such as weight loss and muscle wasting (Shrikrishna & Hopkinson, 2012). Together, these abnormalities limit ventilation whilst enhancing the ventilatory requirement during physical activity; contributing to severe breathlessness and fatigue (Troosters et al., 2013). Consequently, engaging in more intense physical activity such as exercise can become an unpleasant experience which many patients actively try to avoid (Troosters et al., 2013). This activity avoidance leads to a downward spiral of muscle deconditioning, reduced fitness and

increased breathlessness causing patients to become trapped in a vicious cycle of physical inactivity and increasing symptom severity (Cooper, 2009; Polkey & Moxham, 2006).

Lower levels of physical activity increase patients' risk of hospitalisation and premature mortality (Vaes et al., 2014). There is evidence that physical activity is reduced and more time is spent sedentary in COPD patients (Pitta et al., 2005) but there is little evidence examining sedentary behaviour in this population. Additionally, understanding the correlates of behaviour in mild-moderate COPD patients is required to inform tailored interventions. To date, much of the focus has been on examining factors related to physical activity in COPD, with a systematic review by Gimeno-Santos (Gimeno-Santos et al., 2014) revealing inconsistent associations with a range of socio-demographic, lifestyle, environmental, clinical and functional factors. The majority of studies included in this review did not adjust associations for potential confounders and only half of the 86 studies used an objective measure of physical activity (e.g. pedometer or accelerometer) (Gimeno-Santos et al., 2014). Moreover, only three (6.7%) studies specifically examined mild-moderate COPD patients. Being sedentary is an independent construct to that of being physically inactive and with the growing interest of its role in COPD (Hill, Gardiner, Cavalheri, Jenkins, & Healy, 2015) it seems pertinent to also explore its correlates. Despite this, there is a severe lack of evidence examining correlates of sedentary behaviour in COPD (Park et al., 2013). Moreover, there is a lack of comparison between behavioural correlates between COPD patients and apparently healthy adults; insights from which will determine the need for specific risk profiling and intervention designs.

Like many chronic diseases, COPD is heterogeneous with patients not only varying in the severity of physiological impairment (airway obstruction) but also the magnitude of symptoms and subsequent impact on their quality of life (Jones, Adamek, Nadeau, & Banik, 2013). With this comes an interesting construct whereby patients with the same physiological progression of COPD report very different symptom burden and impact on their daily life. Reasons for this discordance between disease progression and symptom severity are likely multifaceted but evidence is lacking on what factors contribute to this observation. One possible contributor to this phenomenon may be patients' levels of physical activity and sedentary behaviour; relating to whether patients have started their journey (or how far along they are) on the downward spiral of physical inactivity (Cooper, 2009; Polkey & Moxham, 2006). Patients in the earlier stages of COPD progression (mild-moderate airway obstruction) who report significant burden from their symptoms comprise a particularly noteworthy group

who may benefit from significant risk reductions for premature death and hospitalisation from taking part in behavioural interventions (Lange et al., 2012).

For patients with more severe airway obstruction, physical activity and sedentary behaviour can also play an important role in COPD. Patients with advanced COPD are at high risk of hospitalisation as a result of severe breathlessness (Garcia-Aymerich et al., 2011). When patients return home from hospital, they are not yet fully recovered and their physical activity is significantly lower than pre-hospital levels, putting them at increased risk of readmission (Pitta et al., 2006). Pulmonary rehabilitation is currently offered to patients admitted to hospital but for the minority who take part this does not come until at least four weeks after discharge (Steiner, Holzhauer-Barrie, Lowe, Searle, Skipper, Welham, & Roberts, 2015a). Therefore, interventions promoting the engagement of physical activity are needed earlier to supplement the established benefits of rehabilitation (Spruit et al., 2013). Interventions immediately after discharge have been largely focussed around rehabilitation/exercise with mixed results (Eaton et al., 2009; Greening et al., 2014; Puhan et al., 2012). Little is known as to the feasibility and acceptability of alternative approaches targeting lifestyle; specifically reductions in sedentary behaviour which may be perceived by patients as more suitable or achievable compared with exercise.

The purpose of Study One was to assess the behavioural profiles of mild-moderate COPD patients and identify the correlates of objectively measured physical activity and sedentary time all in comparison to apparently heathy adults. Study Two aimed to identify factors associated with self-reported symptom severities in patients with similar airway obstruction (mild-moderate) using an array of clinical, functional, psycho-social, behavioural and demographic factors. Study Three was a feasibility trial to reduce prolonged periods of sedentary behaviour in COPD patients at home upon discharge following an acute exacerbation. The intervention used wearable self-monitoring technology to provide real-time feedback to patients on their time spent sitting, number of sit-to-stand transitions and step count. Patients were also provided with a vibration prompt when they had been sedentary for too long. The study examines the feasibility of the trial design, recruitment, adherence and procedures and the acceptability of the intervention among patients receiving the intervention.

1.2 Literature review

1.2.1 Background to COPD

Definition and causes of COPD

COPD is a common, preventable and treatable disease, characterised by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and the lung to noxious particles or gases (Global Initiative for Chronic Obstructive Lung Disease., 2014). The chronic airflow limitation which characterises COPD manifests as a combination of obstructive bronchiolitis and emphysema; with the relative contribution of each varying between individuals (Global Initiative for Chronic Obstructive Lung Disease., 2014). COPD is the result of cumulative exposures to noxious gases and/or chemicals over a number of years. Most often, COPD prevalence almost directly relates to the prevalence of tobacco smoking but in many countries, air pollution, from sources such as wood burning and other biomass fuels, is also a major risk factor (Salvi & Barnes, 2009).

The characteristic symptoms of COPD are chronic and burgeoning breathlessness, cough, and sputum production; each with day-to-day variability (Kessler et al., 2011). Airflow limitation can develop after these symptoms as well as advance without the emergence of cough and sputum production. It is recommended that a clinical diagnosis of COPD should be considered in any individual who presents with breathlessness (dyspnea), chronic cough or sputum production, and a history of exposure to risk factors such as tobacco smoke, occupational dusts or chemicals (Global Initiative for Chronic Obstructive Lung Disease., 2014). Spirometry is required to make the diagnosis (Zwar et al., 2011) with the presence of post-bronchodilator forced expiratory volume in one second/forced vital capacity (FEV_1/FVC) ratio <0.70 confirming the presence of chronic airflow obstruction.

Prevalence of COPD

Increases in data quality control (e.g. systematic quality control criteria for spirometry) within large scale studies (e.g. (Menezes et al., 2005); (Buist et al., 2007)) have enabled some conclusions to be drawn regarding COPD prevalence (Global Initiative for Chronic Obstructive Lung Disease., 2014). A systematic review and meta-analysis of studies across 28 countries found the overall prevalence of COPD in adults aged ≥40 years was 9-10% (Halbert et al., 2006). In the UK it has been estimated that 835,000 people are diagnosed with

COPD and an estimated 2.2 million individuals have undiagnosed COPD; equivalent to 13% of the population of England aged 35 and over (Shahab, Jarvis, Britton, & West, 2006). Consequently, health campaigns have been launched in the UK to identify those 'missing millions' (Falzon, Soljak, Elkin, Blake, & Hopkinson, 2013).

COPD morbidity and mortality

It is important to recognise the complex nature of COPD progression which can be characterised by both patient experiences (e.g. psychological wellbeing and ability to perform daily tasks) and clinical outcomes (e.g. hospitalisations and death) (Rothman et al., 2009). Whilst all patients with COPD suffer from chronic airway obstruction, the impact of COPD on symptom perception, activity avoidance and overall quality of life can vary considerable between people.

Measures of morbidity or disease progression for COPD typically include number of physician visits, emergency department visits, and hospitalisations (Global Initiative for Chronic Obstructive Lung Disease., 2014). Morbidity from COPD can be worsened by other conditions such as cardiovascular disease and diabetes mellitus which may impact patients' health and provide additional burdens to existing COPD management (Global Initiative for Chronic Obstructive Lung Disease., 2014). COPD has been estimated to account for approximately one-quarter of all General Practitioner consultations and 2.8 million bed days per year (Respiratory Alliance, Jan 2003).

The under-recognition of COPD as a primary cause of mortality on death certificates and the challenge of under-diagnosis remain important hurdles to overcome in order to accurately establish mortality data (Tálamo et al., 2007). COPD has been found to be more likely to be listed as a contributing factor to death even when it is the primary cause (Jensen, Godtfredsen, Lange, & Vestbo, 2006). Despite this, COPD is now estimated to be the third leading cause of death worldwide (Lozano et al., 2013); representing an important public health challenge that is both preventable and manageable. COPD is the fifth biggest killer disease in the UK causing approximately 25,000 deaths a year in England and Wales (National Statistics, 2008). Unfortunately, the global burden of COPD is projected to increase during the coming decades due to increasing exposure to COPD risk factors (e.g. smoking exposures) in combination with an ageing population and reduced mortality from other conditions (e.g. infectious diseases) (Lopez et al., 2006).

Economic burden of COPD

In the European Union, direct costs from respiratory disease are estimated to be around 6% of the total healthcare budget, with COPD accountable for 56% (€38.6 billion) of this respiratory disease cost (Loddenkemper, 2003). COPD exacerbations constitute the greatest proportion of the total COPD burden on healthcare systems. Concomitantly, there is a strong direct relationship between COPD severity and the cost of care with hospitalisation and ambulatory oxygen costs mounting with disease progression (Global Initiative for Chronic Obstructive Lung Disease., 2014). Moreover, these estimates fail to incorporate the economic value of the care provided to COPD patients by their family and friends. Because healthcare systems are unlikely to provide long term supportive care, COPD may not only force the patient to leave the workplace, but also a family member to provide homecare. Particularly for developing countries where human capital is generally the most important asset, the indirect costs of COPD may represent a serious threat to their economies (Global Initiative for Chronic Obstructive Lung Disease., 2014).

1.2.2 Terminology: Sedentary behaviour, Physical Activity and Exercise

Physical activity definition

Physical activity is a complex and multidimensional construct (LaPorte, Montoye, & Caspersen, 1985) and is typically defined from a physiological perspective as "any bodily movement produced by skeletal muscle which results in caloric expenditure" (Caspersen, Powell, & Christenson, 1985). All human movement can be sub-divided into frequency (e.g. per hour, per day); intensity (e.g. light, moderate, vigorous); duration (e.g. seconds, minutes); mode (e.g. walking, running); and context (e.g. transportation, leisure-time) (Haskell, 2001; Montoye, 2000). It is perhaps the complexity of defining physical activity that has resulted in the misnomer of "exercise". The importance of distinguishing these terms is pivotal to our understanding of how individuals behave and therefore how best we can help them to improve activity behaviours. Most notably the terms exercise and moderate-to-vigorous physical activity (MVPA) are often used interchangeably. MVPA is typically classified as at least three metabolic equivalents (METS), with one MET equivalent to resting metabolic rate (approximately 3.5ml/O_2/kg/min) (Jette, Sidney, & Blumchen, 1990). However, exercise is a subset of physical activity which is planned, structured, repetitive and purposeful to improving or maintaining one or more components of physical fitness (Caspersen et al., 1985). Whilst some exercise is likely to meet the intensity threshold for MVPA, not all

MVPA can be assumed to be exercise (or vice versa). For example, active transport such as cycling to work or running for the bus may also meet the threshold of MVPA but would not be considered exercise.

Physical inactivity versus sedentary

A similar misconstruction has been widely presented as the lower end of movement continuum, between physical inactivity and sedentary behaviour. Physical inactivity is a lack of sufficient physical activity (Hamilton, Healy, Dunstan, Zderic, & Owen, 2008) i.e. a level of MVPA not sufficient to meet physical activity guidelines (Davies, Burns, Jewell, & McBride, 2011). Sedentary behaviour, however, is not a lack of sufficient activity but a distinct construct defined not only by energy expenditure or intensity but also by posture. It is defined as any waking activity characterized by an energy expenditure ≤1.5 METS and a sitting or reclining posture (Sedentary Behaviour Research, 2012). Consequently, physical (in)activity and sedentary behaviour should be considered as independent but interacting constructs both of which require specialised assessment and interpretation.

Active couch potato: putting the definitions in context

The constructs of physical activity and sedentary behaviour are not mutually exclusive. An individual can have high or low levels of MVPA in combination with high or low levels of sedentary behaviour (Marschollek, 2013). Therefore, it is possible for someone to be considered sufficiently physically active (meeting or exceeding guidelines) whilst accruing high amounts of sedentary time e.g. an office worker who goes for a run in the morning before work but then sits at a desk for most of the working day. Conversely, a person may not undertake a lot of MVPA but, at the same time, may not spend a large amount of time sedentary e.g. a waiter/waitress who is on their feet for long periods (low levels of sedentariness) but does not meet MVPA recommendations.

1.2.3 Measurement of physical activity and sedentary behaviour

Overview

The measurement of human movement comprises two constructs: the behaviour (physical activity, sedentary behaviour) and the physiological consequence of the behaviour (energy expenditure) (Lamonte & Ainsworth, 2001). The vast choices of how to measure these constructs faced by researchers vary in feasibility and accuracy (Figure 1.1). Assessments of free-living energy expenditure include calorimetry and doubly-labelled water. Tools for

measuring behaviour include direct observation, diaries, recall questionnaires, pedometers, accelerometers and inclinometers.

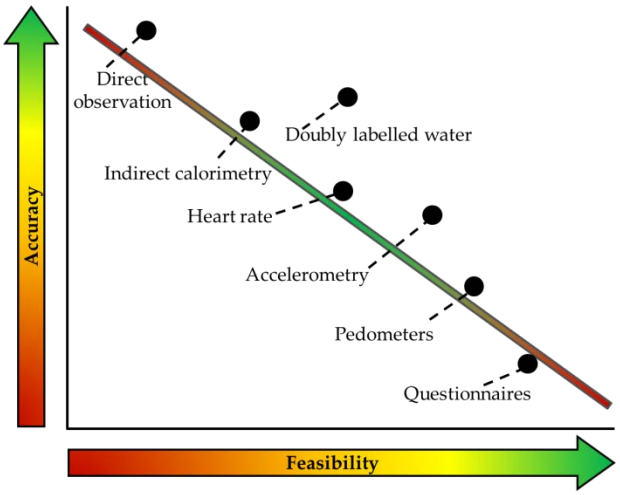

Figure 1.1 Behaviour and energy expenditure measurement options according to accuracy and feasibility (dashed lines indicate recent advances in measurement), adapted from Esliger (Esliger, 2011).

The following sections provide an overview of the methodological approaches for measuring physical activity and sedentary behaviour used in this thesis. The section relating to accelerometry is more detailed as it is primary method pertinent to this thesis.

Self-report

Self-report measures such as recall questionnaires, diaries, logs and surveys remain the most popular method for measuring physical activity levels (particularly in large samples) (Adamo, Prince, Tricco, Connor-Gorber, & Tremblay, 2009) due in part to low cost and minimal participant burden (Dishman, Washburn, & Schoeller, 2001). However, there are significant limitations to self-report approaches which cannot be overlooked. It is reported that up to 15% of adults in the UK are illiterate, with that proportion increasing in elderly populations (Wolf, Gazmararian, & Baker, 2005). Therefore, many individuals may struggle to comprehend questions using more complex language or formatting. Consequently, individuals may ask a friend or relative for assistance, introducing significant bias and inaccuracy. Regardless, self-report measures are open to social desirability bias, with individuals found to greatly over-report levels of physical activity and underestimate time spent sedentary (Adamo et al., 2009). For example, the proportion of US adults found to meet activity guidelines was 62.0% based on self-report and 9.6% for accelerometry (Tucker, Welk, & Beyler, 2011). Similarly, COPD patients have been found to overestimate time spent walking (Pitta, Troosters, Spruit,

Decramer, & Gosselink, 2005). Furthermore, the lack of a conceptual framework underpinning self-reported measures of activity in COPD is an important limitation (Frei et al., 2011; E. Gimeno-Santos et al., 2011). Whilst the absolute numbers obtained from self-report measures may be subject to bias and recall inaccuracies, they can provide useful insight into the context of behaviours e.g. location and type. For example, TV viewing is a highly prevalent sedentary pursuit which has been linked to numerous deleterious health effects (Dunstan et al., 2005; Williams, Raynor, & Ciccolo, 2008). By examining not only the amount but also type of activities (both active and sedentary) a greater understanding of how best to intervene can be gleaned. For example, the PROactive project aims to develop patient reported outcome tools to understand the behavioural adaptation of patients with COPD through the detection of clinically relevant changes in physical activity and symptoms in a way that is easily understood by patients and healthcare providers alike (Gimeno-Santos et al., 2015).

Inclinometers

Inclinometers, or posture sensors, are able to detect the posture of the wearer through in-built algorithms (i.e. lying down, sitting, standing, or stepping). These devices have been purpose built to measure sedentary behaviour but many also provide valid measures of step counts in adults (Dahlgren, Carlsson, Moorhead, Häger-Ross, & McDonough, 2010; Grant, Dall, Mitchell, & Granat, 2008). Unlike many other monitors, these devices are typically worn in contact with the skin to remove extraneous factors such as loose clothing which will contaminate posture allocation. Although this approach improves the accuracy of sedentary behaviour measurement, it can result in compliance issues due to reactions to adhesive pads for thigh-worn sensors and the absorption of sweat into straps for inclinometers worn around the lower back. Despite the emergence of sedentary behaviour as an independent risk factor for developing chronic diseases (Healy et al., 2007; Healy et al., 2008), there are fewer devices available for researchers compared with physical activity monitors. The ActivPAL is the most commonly used inclinometer in behavioural research, worn on the thigh and a well-established valid measure of sedentary behaviour (Kozey-Keadle, Libertine, Lyden, Staudenmayer, & Freedson, 2011). However, placement on the thigh requires adhesive pads to be attached to the skin. Therefore, this approach could be considered intrusive and the adhesive pads can be painful to remove and can induce skin irritation (e.g. rashes) (Mutrie et al., 2012). Additionally, there are a lack of inclinometers that have the capability to provide real-time feedback to the wearer; with most monitors only providing information or prompts

based on periods of inactivity (Sanders et al., 2016). Of the identified inclinometers, a commercial device called a LUMO was found to offer the highest number of feedback attributes, including immediate information on sitting time and stand-ups as well as posture-specific vibration prompts (Sanders et al., 2016). This device has been validated as a measure of both sedentary behaviour (Rosenberger, Buman, Haskell, McConnell, & Carstensen, 2016) and walking (Kooiman et al., 2015). With time, developments in both the research and commercial sectors will increase the options for posture sensing for researchers.

Accelerometers

For many years accelerometry has been a popular method for free-living assessment of physical activity with accelerometers now commonplace in large-scale observational studies such the National Health and Nutrition Examination Survey (Troiano et al., 2008), Health Survey for England (Craig et al., 2009) and more recently a sub-sample of the UK Biobank comprising ~100,000 participants (Allen et al., 2012). Accelerometers are now at the forefront of physical activity measurement in COPD, with extensive validation work concluding that triaxial and multisensory devices are the most accurate for quantifying movement in COPD patients (Rabinovich et al., 2013; Van Remoortel et al., 2012). Although advancements in accelerometry have allowed this technology to become a key player in understanding health and behaviour, there are many options for researchers which can make it difficult to choose the best device and/or model for a given research task.

Accelerometers are most often worn on the waist, hip, wrist or lower limbs and contain a piezoelectric crystal spring-loaded with a test mass in contact with the crystal. When acceleration occurs, the force applied to the crystal generates a voltage equivalent to the acceleration produced. Accelerometers can measure movement in one (uniaxial), two (biaxial) or three (triaxial) planes or combine the three axes to provide vector magnitude (Equation 1.1). Low and high pass frequency filtering are used to remove accelerations outside the range of plausible human movement (0-60 m/s^2 with a frequency response less than 10Hz) (Welk, 2002).

Equation 1.1: $Vector\ magnitude = \sqrt{x^2 + y^2 + z^2}$

Accelerometers are generally set up to collect raw acceleration data at 30-100 Hz but this data is usually integrated upwards to epoch level data (e.g. every 60 seconds); resulting in arbitrary units called activity counts (Figure 1.2). These counts are then used as an objective

assessment of movement intensity with high count values corresponding to greater intensity. It is important to note that these count values are proprietary and manufacturer-specific thus only allow comparisons with data from similar models.

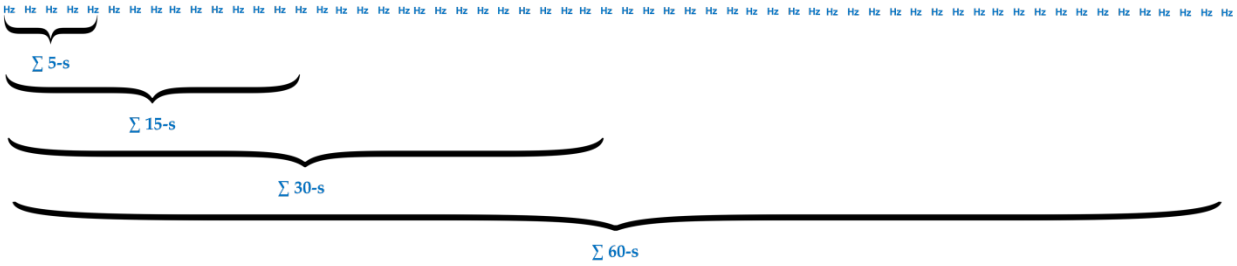

Figure 1.2 Concept of how raw data (Hz) from an accelerometer is summed to epoch data (e.g. 5, 15, 30 or 60-s) in the form of counts, adapted from Esliger (Esliger, 2011). The symbol 'Hz' corresponds to 60 raw data points per second.

In order to facilitate interpretation of these activity counts, calibration studies have converted count data using METS. For adults, light, moderate and vigorous intensity movement is most often classified as 1.50-2.99 METS, 3.00-5.99 METS and ≥6.00 METS, respectively. For these MET ranges, corresponding cut-points have been derived from prediction equations (Freedson, Melanson, & Sirard, 1998) or receiver operator curves (Jago, Zakeri, Baranowski, & Watson, 2007). The use of accelerometric data are complicated by the derivation of multiple cut-points each of which produce different results within the same data (Orme et al., 2014; Strath, Bassett Jr, & Swartz, 2003). Additionally, the decision of which epoch to analyse data in (e.g. 15 versus 60 seconds) has an independent contribution to physical activity results (Orme et al., 2014). Despite these limitations, categorising physical activity (light, moderate, vigorous) per epoch allows the easy calculation of time spent being physically active; arguably the most important variable for health research (Welk, 2002).

Although inclinometers directly measure posture to determine whether the wearer is in sedentary behaviour (sitting or reclining), there has been work to assess sedentary time using accelerometry. The term sedentary time rather than behaviour should be used when reporting accelerometry-derived outcomes due to the lack of postural insight. Similar to the derivation of physical activity cut-points, sedentary equivalents have been produced, corresponding to <1.5 METS. With increasing recognition of the importance of capturing the 24-hour day (Chaput, Carson, Gray, & Tremblay, 2014) the objective quantification of sleep has come to the forefront of the behaviour quantification paradigm.

Within the 24-hour period movement takes place across the intensity spectrum from sleep to vigorous physical activity (Figure 1.3) all of which have important health implications (Schuit, van Loon, A Jeanne M, Tijhuis, & Ocké, 2002). Wrist-worn accelerometry has recently come to the forefront of physical activity monitoring. This emergence is, in part, due to the surge in commercially available devices, with 69% of US adults tracking their behaviour (Fox & Duggan, 2013). Most commercial devices are worn on the wrist; in keeping with user preference (Alley et al., 2014). One of the greatest benefits of placing activity monitors on the wrist is the comfort and convenience for wearers, so much so that they can be worn 24 hours a day (i.e. during both waking and sleeping hours). Inspired from the commercial sector, research-grade accelerometers have now started to move monitors from the waist to the wrist. Consequently, wear compliance (the extent to which people wear a device) is significantly improved (van Hees et al., 2011) which subsequently opens up new analytical opportunities such as the sedentary sphere (Rowlands et al., 2016). The movement towards placing accelerometers on the wrist has gained significant momentum and has now been incorporated into two large epidemiological studies (Allen et al., 2012; Troiano et al., 2008). By improving wear compliance, research studies may benefit from obtaining more representative data, less subject to bias (e.g. devices put on when going for a walk but taken off to watch television in the evening). The greater proportion of participants with 'valid' days will also improve statistical power. 'Valid day' is a term to indicate that an activity monitor was worn for enough time to be representative of the person's day. This concept is important as between-day stability for each participant is needed to obtain a representative picture of their habitual activity, with more valid days equating to increased reliability. A wide range of valid day criteria have been used in COPD literature ranging from six hours to 'all data' (Byrom & Rowe, 2016). Moreover, 47% of studies were found to not report valid day criteria (Byrom & Rowe, 2016).

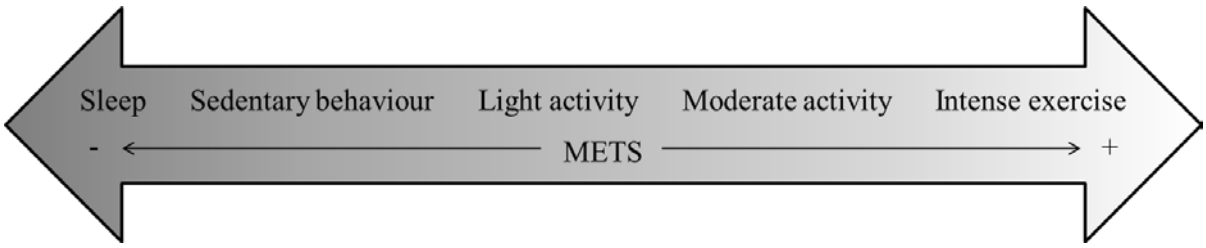

Figure 1.3 The movement continuum for 24-hour behaviour (Tremblay, Colley, Saunders, Healy, & Owen, 2010)

Traditionally, participants are asked to remove activity monitors for sleep, but even within 24-hour protocols there may be other reasons why participants are asked to remove devices. For example, participants are typically asked to remove devices for water-based activities such as showers, baths and swimming to prevent damage to devices and potential loss of data. Additionally, participants may not want to wear devices during social events or might 'want a break' from wearing them. As a result, monitors may be removed and placed on a level surface (e.g. table), detecting a perfect lack of movement (equivalent to an activity count of zero). Regardless of the reason, it is important not to mistake these zeros for sedentary time. Therefore, purpose-built algorithms have been developed to identify biologically implausible runs of consecutive zeros e.g. 60 minutes (Troiano et al., 2008) or 90 minutes (Choi , Liu, Matthews, & Buchowski, 2011; Choi, Ward, Schnelle, & Buchowski, 2012). Not only is wear time important for signifying the representativeness of a person's daily activity but it is an important covariate for statistical analysis. If a person wears an accelerometer longer than someone else, they will automatically accrue more time across the intensity spectrum. Importantly, converting the amount of time in a given intensity into a proportion of wear time does not permit direct comparisons between individuals. This is because having a longer wear time will have a greater impact of sedentary time than for physical activity (particularly MVPA) as this behaviour comprises the majority of most people's waking day. Unfortunately, a recent systematic review found that 87% of studies examining physical activity in COPD did not report how a valid day was defined (Byrom & Rowe, 2016). Therefore, it cannot be assumed that these studies conducted quality assurance or quality control analyses on their data.

In summary, there are a range of methods for quantifying human movement through energy expenditure assessment, posture sensing, accelerometry and self-report. Each approach brings with it varying strengths and weaknesses making it vital that researchers choose the technique most suitable for their research question. Issues such as cost, feasibility (e.g. free-living capabilities), participant burden and reactivity must be considered.

1.2.4 Physical activity, sedentary behaviour and health outcomes

Physical activity provides a vast array of health benefits and protects against a plethora of non-communicable diseases. Protective effects of physical activity against premature mortality, coronary heart disease, stroke, hypertension, type 2 diabetes, cancers of the breast and colon, depression, cognitive impairment, poor sleep, risk of hip fracture and osteoporosis

are established (Physical Activity Guidelines Advisory Committee, 2008). The relationship between the volume of physical activity performed and the size of the subsequent risk reduction for all-cause mortality has demonstrated an inverse, curvilinear relationship (Physical Activity Guidelines Advisory Committee, 2008) (Figure 1.4). Of note, there is no lower threshold for the health benefits of increasing one's physical activity as mortality risk reduces with the first increase in activity beyond baseline behaviour. Therefore, the notion of 'something is better than nothing' (Blair, Kohl, Gordon, & Paffenbarger Jr, 1992) may be a more suitable message than suggesting a particular threshold (e.g. public health guidelines). Importantly, the rate of risk reduction is more pronounced for those individuals who are less physically active to begin with. Given that most people reside in this region of the activity scale (Lee et al., 2012; Tucker et al., 2011) there is much benefit to be gleaned from helping the least active individuals to move more, regardless of whether this increase reaches a predetermined threshold such as MVPA.

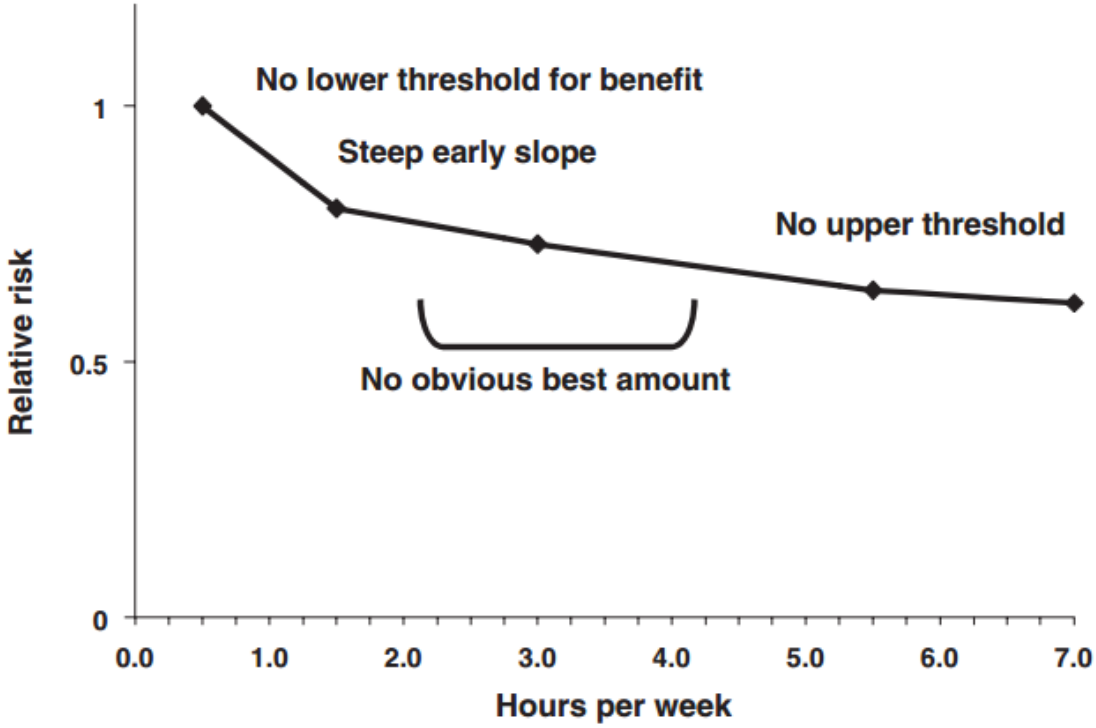

Figure 1.4 Risk of all-cause mortality by hours per week of MVPA (Powell, Paluch, & Blair, 2011)

Spending more time sitting or watching TV (a surrogate measure for leisure-time sedentary behaviour) has been linked to a greater risk of death from all-causes and developing cardiovascular disease and obesity after controlling for time spent engaging in MVPA (Healy et al., 2008; Katzmarzyk, Church, Craig, & Bouchard, 2009). In a recent review, time spent in prolonged sedentary behaviour has been found to be associated with an increased risk of

cardiovascular disease in a dose-response manner (Eijsvogels, George, & Thompson, 2016). In a cross-sectional analysis of 4757 adults, sedentary time was found to be detrimentally associated with waist circumference, high density lipoprotein-cholesterol, C-reactive protein, triglycerides, insulin, beta cell function and insulin sensitivity (Healy, Matthews, Dunstan, Winkler, & Owen, 2011).

Indeed, replacing sedentary behaviour with light activity, even for just a single minute, is beneficial (Healy et al., 2008). In a sample of 168 Australian adults increased breaks in accelerometry-derived sedentary time was associated with lower waist circumference (B=0.16, p=0.026), BMI (B=0.19, p=0.026), triglycerides (B=0.18, p=0.029) and 2-hour plasma glucose (B=0.18, p=0.025), independent of total time spent sedentary and in MVPA (Healy et al., 2008). The association of breaks in sedentary time was also found in a large US cohort with increasing breaks associated with lower waist circumference and C-reactive protein (Healy et al., 2011). The sedentary behaviour profiles of two individuals with a different number of breaks in sedentary time as shown in Figure 1.5. Whilst these individuals share the same total time spent sedentary, the “prolonger” is at increased risk of cardiometabolic disease compared with the “breaker” who regularly breaks up their sedentary behaviour with physical activity (Dunstan, Healy, Sugiyama, & Owen, 2010).

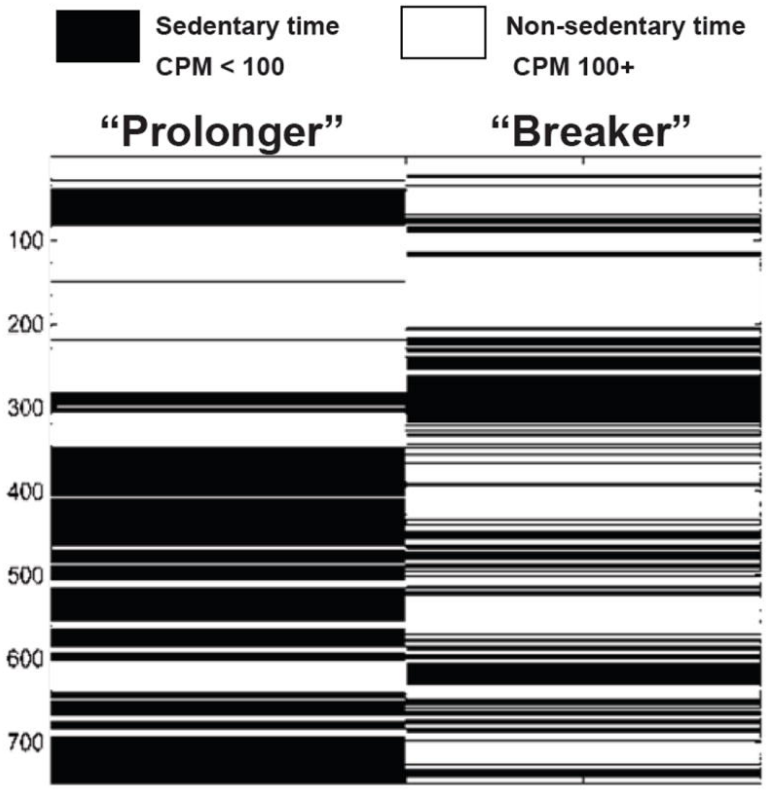

Figure 1.5 Breaks in sedentary time: same amount of sedentary time, but different ways of accumulation. CPM = counts per minute (Dunstan et al., 2010)

Not only do increased sedentary time and less frequent breaks in sedentary behaviour convey an increased risk of detrimental cardio-metabolic health but data from the Canada Fitness Surveys suggests prolonged sitting is related to an increased risk of premature death (Katzmarzyk et al., 2009). Additionally, in a prospective study of TV viewing as a marker of sedentary behaviour, each one-hour increase in time spent watching TV was associated with an 11% increased risk of all-cause mortality and an 18% increased risk of cardiovascular disease mortality (Dunstan et al., 2009). In a study of 7744 men followed-up over 21 years those who reported more than 10 hours a week sitting for transport had an 82% greater risk of dying from cardiovascular disease than those reporting less than four hours a week (Warren et al., 2010). (Dunstan et al., 2009).

With the growing evidence and recognition of the importance of reducing time spent sedentary (particularly prolonged periods) and the benefits of replacing sedentary behaviour with physical activity of any intensity, it has been suggested that population recommendations should be re-conceptualised to account for this (Smith, Ekelund, & Hamer, 2015). Additionally, it has been suggested that interventions may benefit from targeting increases in physical activity through incidental movement such as standing and light

activities (Smith et al., 2015). This may be particularly appropriate for behavioural interventions in the UK and other westernised countries where there are endless opportunities to be sedentary as a result of the abundance of labour-saving technologies, screen-time and environmental constraints which limit the need for people to move (Brownson, Boehmer, & Luke, 2005; Smith et al., 2015). Furthermore, targeting changes in behaviour at the lower end of the movement spectrum may be met with fewer barriers, including lower cognitive effort to increase light intensity activity which in turn produces a less noticeable physiological response (e.g. sweating or increased body temperature) and minimal cost (i.e. no specialist facilities, equipment or memberships compared with MVPA or exercise) (Smith et al., 2015).

Increasing physical activity and reducing sedentary behaviour confer risk reductions for a range of chronic conditions. Individuals who are the least active have the most to gain from small increases in physical activity, regardless of the intensity at which it is performed. Replacing sedentary behaviour with light intensity activity should be encouraged but more intense movement leads to further improved health benefits. Targeting sedentary behaviour and light activity may act as a more palatable conduit for ultimately increasing MVPA.

1.2.5 Physical Activity and Sedentary Behaviour in COPD

Levels of physical activity and sedentariness in COPD

Increasing overall levels of physical activity and reducing time spent in sedentary pursuits are important goals in COPD management. In order to accomplish this, it is vital to understand not only the levels, but also the patterns of these behaviours. Both physical activity and the accumulation of time sedentary are recognised as multi-faceted behaviours involving frequency, intensity (mostly for activity), time and type. By accurately and objectively profiling the nature in which these activities are performed, more appropriate interventions may be implemented.

In a seminal study of 50 COPD patients (64±7 years, FEV_1%pred 43±18) and 25 apparently healthy adults (66±5 years, FEV_1%pred 111±20), Pitta and colleagues (Pitta et al., 2005) objectively assessed the differences in physical activity and sedentary behaviour between groups using the DynaPort activity monitor. Patients with COPD were found to have significantly reduced walking time (44 vs 81 min), standing time (191 vs 295 min) and movement intensity (1.8 vs 2.4 m/s^2, all $p<0.001$) in comparison with apparently healthy adults (Pitta et al., 2005). Moreover, COPD patients spent more time in sitting and lying postures compared with apparently healthy adults (374 v 306 and 87 vs 29 min, respectively,

all $p<0.05$) (Pitta et al., 2005). In 30% of COPD patients, walking time did not reach the recommended 30 minutes of moderate intensity activity per day. Even for patients achieving this threshold, their walking intensity was, on average, 17% lower compared with that of apparently healthy adults (Pitta et al., 2005). Therefore, even the most active COPD patients are unlikely to walk at intensities sufficient to induce the benefits in the form of fitness maintenance.

Donaire-Gonzalez and colleagues (Donaire-Gonzalez et al., 2015) showed that, in a sample of 177 COPD patients (94% male, 71±8 years), patients on average perform over half (57%) of their physical activity in bouts of at least 10 minutes. The observed median number of bouts was 4.4 and 2.6 for overall physical activity and MVPA, respectively, with a mean bout duration of approximately 20 minutes (Donaire-Gonzalez et al., 2015). However, patients with severe or very severe COPD perform physical activity in shorter bouts which are performed less frequently, resulting in significantly fewer steps and less time in physical activity compared with those with mild or moderate COPD (Donaire-Gonzalez et al., 2015). These findings suggest that targeting bouts of activity rather than activity as whole may be more appropriate for patients with more advanced COPD and patients at the milder end of disease progression may be better able to engage with more intense physical activity.

Few studies have objectively examined sedentary behaviours through posture sensors (able to capture specific behaviours such as sitting, standing, stepping and lying down). A study by Kawagoshi and colleagues (Kawagoshi et al., 2013; Kawagoshi et al., 2015) investigated the postural changes of a small sample of COPD patients (n=26) and apparently healthy adults (n=20) using triaxial accelerometers positioned at the mid-thigh and trunk. Patients with COPD were found to have significantly reduced continuous walking time and total times of both slow walking (<2km/hour) and fast walking (≥2km/hour) (Kawagoshi et al., 2013). Furthermore, despite COPD patients having similar time spent standing compared with apparently healthy adults, patients spent more time sitting in total and had a longer average sedentary bout length (Kawagoshi et al., 2013). Consequently, COPD patients accumulated fewer daily breaks in sedentary time than apparently healthy adults (49 vs 84, respectively) (Kawagoshi et al., 2013). These findings have been corroborated by a systematic review of time usage of COPD patients (Hunt, Madigan, Williams, & Olds, 2014). COPD patients were found to spend more time in sedentary behaviours; have limited engagement in physical activities; have higher healthcare requirements (e.g. medical appointments); and experience difficulties performing activities of daily living (e.g. on average, showering 2.5 times per

week and preparing meals 4.7 times per week) (Hunt et al., 2014). These findings raise concerns about not only the inactive lifestyle of patients but also the highly sedentary nature of daily life in this population.

Physical activity in mild-moderate COPD patients

The clinical expression of COPD in its early phase (mild stage) is dependent on numerous factors including, the nature and extent of physiological impairment; the compensatory responses used to maintain sufficient pulmonary gas exchange; and the avoidance of physical activity due to breathlessness (O'Donnell & Gebke, 2014). In the past, mild airway obstruction has been perceived to present with few clinical consequences; not requiring intervention (Guenette et al., 2011). However, there is increasing evidence contradicting such perspectives with findings that exercise capacity and dyspnea severity are important consequences of worsening lung function; even in patients with undiagnosed COPD (Troosters et al., 2010). Over time, these negative health consequences can lead to deconditioning and increased symptom severity, compelling patients to become more sedentary and less physically active.

Van Remoortel and colleagues (Van Remoortel et al., 2013) aimed to investigate the associations between objectively measured physical activity and clinical characteristics in persons newly diagnosed with COPD. One hundred and twenty-four smokers or former smokers were recruited comprising 59 newly diagnosed COPD patients (38 mild, 21 moderate) and 65 matched smoking controls. Physical activity was found to be significantly lower in newly diagnosed COPD patients compared with smoking controls (7986 vs 9765 steps/day and 64 vs 110 min of MVPA, $p<0.05$) (Van Remoortel et al., 2013). These findings highlight that declines in physical activity occur in mild-moderate disease; supporting the guidance from the Centre for Disease Control which lists physical activity as a vital sign for patients with mild COPD (Centers for Disease Control and Prevention, 2010).

In a study of 161 patients with stable COPD and 40 apparently healthy adults, Shrikrishna and colleagues (Shrikrishna et al., 2012) found that patients with mild disease were less physically active than apparently healthy controls (7960±3430 versus 11735±4399 steps per day, $p=0.002$). Physical activity was shown to have a negative linear relationship with lung function (e.g. steps per day r=0.6, $p<0.001$) (Shrikrishna et al., 2012). In a study of 224 physician-diagnosed COPD patients and 1386 age-matched non-smoking controls, using data from National Health and Nutrition Examination Survey 2003-6, patients with COPD were

found to spend a greater proportion of time sedentary (72% vs 68%, $p<0.05$, respectively) (Park et al., 2013). COPD patients also spent less time in light and moderate-to-vigorous physical activity (27% vs 31% and 0.007% vs 0.013%, $p<0.05$, respectively) (Park et al., 2013). These patients also have respiratory constraints when performing activities of daily living (Chin et al., 2013; Van Helvoort, Willems, Dekhuijzen, Van Hees, & Heijdra, 2016).

In a recent study of 39 patients with mild-moderate COPD and 20 apparently healthy adults, significant respiratory impairment was observed in patients during stair climbing, vacuuming and displacing groceries in a cupboard (Van Helvoort et al., 2016). Half of patients developed dynamic hyperinflation compared with 10-35% of apparently healthy adults despite physical activity (average vector magnitude) not being significantly different between groups. Similar findings have been observed during incremental cycle ergometer tests with mild COPD patients reaching their physiological limit at 36% lower peak oxygen uptake and 41% lower ventilation compared with apparently healthy adults (Chin et al., 2013). In more severe COPD or study populations with a range of COPD severities, indicators of respiratory constraint including dynamic hyperinflation and end-expiratory lung volume during exercise have been found to be associated with reduced physical activity levels (Garcia-Rio et al., 2009; Lahaije, van Helvoort, Dekhuijzen, Vercoulen, & Heijdra, 2013).

Physical activity, sedentary behaviour and mortality

Using data from the Copenhagen City Heart Study, a prospective study of 1270 COPD patients and 8734 controls (median follow-up of 17.1 years and 5392 deaths), Vaes and colleagues (Vaes et al., 2014) examined the relationship between self-reported physical activity and mortality. Patients with COPD who reported moderate or high levels of baseline physical activity but reported low physical activity levels at follow-up had the highest hazard ratios of mortality (HR 1.73 and 2.35, respectively, both $p<0.001$) (Vaes et al., 2014). For COPD patients with low baseline physical activity, no differences in risk of mortality were observed between unchanged and increased physical activity at follow-up (Vaes et al., 2014). A higher baseline FEV_1 was associated with a lower risk of reduced physical activity (OR 0.51 and 0.55 for patients with a moderate or high baseline physical activity, respectively, $p<0.001$). Additionally, age (inversely), male sex, not smoking and cohabitating were found to be linked with higher physical activity levels. Smoking for a longer number of years was also associated with a reduction in physical activity in COPD patients. Stimulating physical activity levels at all stages of COPD should be encouraged to help reduce healthcare costs

(Garcia-Aymerich, Lange, Benet, Schnohr, & Anto, 2006) and improve survival rates (Vaes et al., 2014).

In a study of 2295 patients followed up for 12 months after an acute exacerbation of COPD, physical activity was measured using self-reported walking frequency at baseline (retrospective recall) and two months after discharge (Esteban et al., 2016). Multivariate regression models revealed that patients whose physical activity worsened during these two months were more likely to die within one year (OR 2.78 – 6.31) (Esteban et al., 2016). Physical inactivity during this time was a stronger predictor of one year mortality than the presence of comorbidities and long-term domiciliary oxygen therapy or non-invasive mechanical ventilation at home (Esteban et al., 2016). Whilst limitations of this study include recall bias and sample homogeneity (97% male) targeting physical inactivity during the post-exacerbation period may have significant benefits to COPD patients' quality of life.

There is a considerable lack of data exploring the association between a sedentary lifestyle and risk of mortality in COPD patients. It is important to understand if this relationship exists and, if it does, the strength of the relationship. A large prospective cohort study in Japan (33,414 men and 43,274 women) investigated the role of TV viewing and mortality (Ukawa et al., 2015). Over a 19.4 year median follow-up, 278 individuals (88% male) suffered a COPD-related death. Compared with men who reported watching TV for <2 hours/day, those who reported watching >4 hours/day were significantly more likely to die from COPD (HR 1.63 95%CI 1.04 – 2.55) (Ukawa et al., 2015). This relationship was observed independent of age, smoking status, body mass index (BMI), marital status, alcohol consumption and exercise participation. The average time reported for TV viewing was linearly and positively associated with COPD-related mortality (p=0.04) (Ukawa et al., 2015). Interestingly, these findings were only observed in men (Ukawa et al., 2015). Despite the large sample size and long follow-up period, the self-reported assessment of sedentary behaviour is an important limitation as well as the focus only on the leisure-time component of these complex behaviours. Misclassifications which would have arisen from these issues would, however, contribute to a potential underestimation of the true hazard ratios. The mechanism linking sedentary behaviour and increased risk of COPD-related mortality has yet to be fully elucidated. Prolonged sedentary behaviour has been shown to increase inflammatory markers (e.g. IL-6, TNF-α, leptin) (Zhan et al., 2009) which have been found to increase susceptibility to respiratory impairment (Gimeno et al., 2011). Additionally, sedentary behaviour has been found to contribute to metabolic dysfunction (Helmerhorst, Wijndaele, Brage, Wareham, &

Ekelund, 2009) which may lead to hyperinsulinemia which can cause cell differentiation, apoptosis and proliferation (Nandeesha, 2009).

Patients with moderate-severe COPD are less physically active and spend more time sedentary compared with apparently healthy adults. However, there is a lack of evidence examining the physical activity and sedentary of mild-moderate COPD patients in comparison to apparently healthy adults. Moreover, low levels of physical activity have been consistently linked to an increased risk of all-cause and respiratory disease mortality; highlighting the need for a better understanding of the correlates of these behaviours and whether these correlates differ between patients and apparently healthy individuals.

1.2.7 Correlates and determinants of physical activity in COPD

It is not only important to examine levels of physical activity and sedentary behaviour but understanding the correlates (factors associated with) and determinants (those with a causal relationship to) of these behaviours is needed to inform lifestyle interventions. In a systematic review by Gimeno-Santos and colleagues (Gimeno-Santos et al., 2014) a range of demographic, psycho-social, environmental, clinical and functional factors were examined in relation to physical activity. The review found inconsistent associations with most of the evidence graded as 'very low' or 'low' quality (Gimeno-Santos et al., 2014). The following sections will explore the correlates and determinants of physical activity and sedentary behaviour in COPD, with a primary focus on correlates which are pertinent to this thesis.

Determinants

Studies examining determinants require prospective data through longitudinal or prospective (over time) designs whereby individuals are followed up at at least two time-points or through a randomised controlled trial. In a prospective cohort study of 409 COPD patients followed for five years, physical activity was examined using self-report at baseline and every six months (Yu, Frei, & Puhan, 2015). Multivariate longitudinal analyses found that (in order of strength of association) exercise capacity, age, employment status, smoking pack years, fatigue, gender, education history, taking part in a fitness programme, depressive symptoms, FEV_1, and medication usage to be independent baseline predictors of physical activity (Yu et al., 2015).

Correlation studies are based on cross-sectional data (a single time-point) and are important for a number of reasons, as outlined by Stanovich (Stanovich, 2013). Many scientific

hypotheses are presented in the form of correlations or lack of correlation, making such studies directly relevant to these hypotheses. Although correlation does not infer causality, establishing causation does require correlation. Therefore, whilst correlation studies cannot definitively infer causation, they can rule them out. Additionally, some variables are unable to be manipulated, such as age, sex and ethnicity. Thus, scientific insight into such variables must be made through correlations. Furthermore, evidence obtained from correlation studies can lead to the testing of that evidence under controlled condition (Stanovich, 2013). The following sections will explore correlates of physical activity and sedentary behaviour in COPD.

Correlates

A breakdown of identified cross-sectional studies examining correlates of physical activity in COPD included in the systematic review by Gimenos-Santos and colleagues (Gimeno-Santos et al., 2014) is provided in Table 1.1. Of the 36 studies, two (5.6%) examined mild-moderate COPD patients and 12 studies (33.3%) assessed patients with moderate to very severe disease. The majority of studies used self-report measures of physical activity with 18 (50.0%) studies using accelerometry. Of these 18 studies only four (8.9% of identified studies) also examined sedentary behaviour. Additionally, only seven studies (15.6% of identified studies) included a comparison group (six different criteria) in their analysis (mean n=29±16). It is unclear whether correlates of sedentary behaviour differ between those associated with physical activity.

Table 1.1 Cross-sectional studies examining correlates of physical activity

Reference	N	COPD Severity	Comparison group	PA Method	SB Assessed †
(Altenburg et al., 2013)	155	Mixed	No	Pedometer	No
(Beauchamp et al., 2012)	37	Severe	Yes (n=20) [A]	Self-report (balance)	No
(Berry, Adair, & Rejeski, 2006)	291	Mixed	No	Self-report (ADLs)	No
(Bestall et al., 1999)	100	Severe	No	Self-report (ADLs)	No
(Bon et al., 2011)	190	Mild	No	Self-report	No
(Chao, Ramsdell, Renvall, & Vora, 2011)	21	NP	No	SR (Lifetime)	No
(Eisner et al., 2008)	1202	Mixed	No	Self-report (ADLs)	No
(Eliason, Zakrisson, Piehl-Aulin, & Hurtig-Wennlöf, 2011)	44	Mod-Severe	Yes (n=17) [B]	Accelerometer	Yes
(Garcia-Aymerich et al., 2004)	346	Severe	No	Self-report	No
(Garcia-Aymerich et al., 2009)	341	Mixed	No	Self-report	No
(Garcia-Rio et al., 2009)	110	Mod-Severe	No	Accelerometer	No
(Hartman, Boezen, de Greef, & Nick, 2013)	113	Mixed	No	Accelerometer	Yes
(Inal-Ince, Savci, Coplu, & Arikan, 2005)	30	Severe	Yes (n=30) [C]	Self-report (ADLs)	No
(Jehn et al., 2012)	107	Mixed	No	Accelerometer	No
(Katajisto et al., 2012)	719	Mixed	No	Self-report	No
(Lahaije et al., 2013)	57	Mixed	No	Accelerometer	No
(Lee, Kim, Lim, Jung, & Park, 2011)	131	Mixed	No	Self-report	No
(Lemmens, Nieboer, & Huijsman, 2008)	278	Mixed	No	Self-report	No
(Lores, García-Río, Rojo, Alcolea, & Mediano, 2006)	23	Mod-Severe	Yes (n=12) [B]	Accelerometer	No
(Monteiro et al., 2012)	74	Mod-Severe	No	Accelerometer	No
(Moy, Matthess, Stolzmann, Reilly, & Garshick, 2009)	17	Mixed	No	Accelerometer	No
(Nguyen et al., 2013)	148	Mod-Severe	No	Accelerometer	No
(Pitta et al., 2006)	23	Severe	No	Accelerometer	Yes
(Pitta et al., 2008)	40	Severe	No	Accelerometer	No
(Pitta et al., 2009)	80	Severe	No	Accelerometer	Yes
(Silva et al., 2011)	95	Mixed	No	Self-report	No
(Skumlien, Haave, Morland, Bjortuft, & Ryg, 2006)	110	Mixed	No	Self-report (ADLs)	No
(Troosters et al., 2010)	70	Mixed	Yes (n=30) [D]	Accelerometer	No

(Van Gestel et al., 2012)	154	Mixed	No	Accelerometer	No
(Van Remoortel et al., 2013)	59	Mild-Mod	Yes (n=65) [E]	Accelerometer	No
(Waatevik et al., 2012)	370	NP	No	Self-report	No
(Wakabayashi et al., 2011)	389	Mixed	No	Self-report (ADLs)	No
(Watz et al., 2008)	170	Mixed	No	Accelerometer	No
(Watz et al., 2009)	170	Mixed	Yes (n=30) [F]	Accelerometer	No
(Watz, Waschki, Meyer, & Magnussen, 2009)	163	Mixed	No	Accelerometer	No
(Yeo, Karimova, & Bansal, 2006)	27	Mixed	No	Self-report (ADLs)	No

Abbreviations: ADLs, activities of daily living; Mod, moderate; NP, not provided; PA, physical activity; SB, sedentary behaviour

†, sedentary behaviour assessed using the same method as physical activity

[A], free from respiratory disease and health problems impacting mobility; [B], unable to access full text; [C], sedentary (unspecified) hospital workers; [D], not involved in competitive sport and free from respiratory disease; [E], current smokers free from respiratory disease; [F], chronic bronchitis

COPD is characterised by poor lung function as a result of chronic airflow obstruction. In a study of 163 COPD patients and 29 patients with chronic bronchitis, physical activity was examined in relation to respiratory Global Initiative for Chronic Obstructive Lung Disease (GOLD) classifications (Watz et al., 2009). Daily steps, MVPA and overall physical activity level decreased from chronic bronchitis patients to very severe COPD patients by 69%, 69% and 61%, respectively (Watz et al., 2009). Physical activity was also found to decrease with advancing dyspnea severity with patients reporting a modified MRC (mMRC) score of four averaging less than 2000 steps per day (Watz et al., 2009). mMRC score has been independently associated with physical activity level and step count after controlling for factors including age, gender, BMI, FEV_1%pred, and calf muscle oxidative capacity (Adami, Cao, Porszasz, Casaburi, & Rossiter, 2015). It is important to understand the relationship between breathlessness and physical activity across COPD severities. Regardless of the level of airway obstruction, patients are at risk of falling into the vicious cycle of physical inactivity, putting them at greater risk for an acute exacerbation. Even in mild-moderate patients, breathlessness during exertion may lead to activity-avoidance behaviours which compound symptoms and quality of life.

In COPD patients with moderate to severe airway obstruction, functional exercise capacity, as measured by six-minute walk distance (6MWD), has been found to reflect daily physical activity (Pitta et al., 2005). In a study of 73 COPD patients (67±7 years, 60% female FEV_1%pred 43±16), a multivariate regression revealed that lung function explained the

highest proportion of variance in physical activity level (R^2=0.20) followed by walking speed (R^2=0.18), quadriceps strength (R^2=0.16) and fat-free mass index (R^2=0.08) (Andersson et al., 2013). These findings are supported by Pitta and colleagues (Pitta et al., 2005) which found exercise capacity, as measured by the 6MWD, to be the strongest predictor of walking time (partial R^2 = 0.56), standing time (partial R^2 = 0.35) and movement intensity (partial R^2 = 0.23). Additionally, both quadriceps muscle wasting and 6MWD have been associated with physical activity in mild-moderate COPD patients (Hartman, Boezen, de Greef, & Ten Hacken, 2013; Shrikrishna et al., 2012). Whilst significant associations between physical function and physical activity may exist (van Gestel et al., 2012), the 6MWD, sit-to-stand test and grip strength could not be used to reliably predict physical activity level in COPD (van Gestel et al., 2012). Therefore, exercise capacity and physical activity must be treated as separate constructs requiring specific measurement.

Comorbidities are commonplace in COPD and it has been estimated that 23% of patients have three or more concurrent conditions (Van Manen et al., 2001). The Towards a Revolution in COPD Health study observed that COPD mortalities were more frequently caused by a comorbid condition than from COPD itself (McGarvey et al., 2007). In a study of 228 COPD patients, those with at least one comorbid condition had a significantly lower physical activity level than patients free from comorbidities (Sievi et al., 2015). However, physical activity level did not significantly decline with presence of multiple chronic ailments (Sievi et al., 2015). In a large multicentre observational study of 4574 COPD patients (67.1±10.0 years, 83.8% male, FEV_1%pred 54.0±23.7), level of physical activity was determined by time spent walking; with patients classified as having a high (>60 min/day), medium (30-60 min/day) or low (<30 min/day) physical activity level (Miravitlles, Cantoni, & Naberan, 2014). Compared with patients in the high physical activity group, those in the low physical activity group were found to have a higher mean number of comorbidities (Charlson Index 2.20 vs 1.65, p<0.001) and a higher BMI (28.4 vs 27.9kg/m^2, p=0.034) (Miravitlles et al., 2014).

Specific comorbidities have been associated with physical activity level. Physical comorbidities, classified as a BMI ≥32kg/m^2, musculoskeletal conditions affecting lumbar spine or lower limbs, at least one lower limb joint replacement restricting mobility/range of motion, peripheral vascular disease, or neurological conditions, are highly prevalent in COPD patients (McNamara, McKeough, McKenzie, & Alison, 2014). McNamara and colleagues (McNamara et al., 2014) compared COPD patients with physical comorbidities, patients with

COPD alone, and apparently healthy adults. Patients with COPD and physical comorbidities were found to have reduced levels of physical activity (determined by energy expenditure, steps and activity duration) compared with patients with COPD alone and apparently healthy adults (e.g. 1841 vs 6623 v 10619 steps per day, respectively) (McNamara et al., 2014). It is important to recognise not only the prevalence of comorbidities in COPD but also the consequences of patients having multiple chronic conditions. Targeting physical activity and sedentariness may help to prevent and manage comorbidities in COPD.

Levels of anxiety and depression are highly prevalent in COPD patients (Maurer et al., 2008). Although the association of anxiety and depression has not been extensively examined, evidence has shown negative relationship with self-reported physical activity. For example, the presence of depression has been found to be a significant independent predictor of low walking time, defined as <30 min/day (OR 1.58, 95%CI 1.25-2.01) (Miravitlles et al., 2014). The proportion of patients with anxiety (63.2%) and depression (69.1%) was found to be very high in the low physical activity group (Miravitlles et al., 2014). Additionally, in a longitudinal study of 220 patients, every additional point score on the Hospital Anxiety and Depression Scale (HADS) depression score was associated with 81 fewer steps per day (Duefias-Espin et al., 2016). However, there is conflicting evidence with some studies finding no association with depression (Moy et al., 2009; H. Watz et al., 2008). Anxiety levels have been positively associated with step count after controlling for confounders including dyspnea and exercise capacity (Nguyen et al., 2013). Moreover, anxiety levels were found to negate the inverse relationship between depression and physical activity (Nguyen et al., 2013). Unlike anxiety and depression, levels of self-efficacy have been consistently positively associated with physical activity (Gimeno-Santos et al., 2014); independently predicting daily physical activity when controlling for lung function, exercise capacity and other psychological factors (e.g. anxiety and depression) (Altenburg et al., 2013).

In a study of 224 COPD patients recruited as part of a large population survey in the US (Park et al., 2013), factors associated with mean activity intensity, sedentary time, light intensity physical activity and MVPA were examined. Patients with an education level below high school (approximately equivalent to post-16 education in the UK), who were unemployed, and who reported breathlessness spent more time sedentary. COPD patients who were older, had lower health perception, and had a larger BMI were found to have lower mean activity intensity and spent less time in light intensity physical activity. Patients who

were older, female, reported breathlessness and had lower health perception took part in less MVPA (Park et al., 2013).

In a study of 59 patients and 65 smoking controls, objectively measured physical activity (steps and MVPA) was found to be lower in COPD patients compared to smoking controls (e.g. 7986±2648 versus 9765±3078 steps per day, $p<0.05$) (Van Remoortel et al., 2013). This highlights the importance of intervening on patients in the preclinical stage of COPD progression. Factors associated with physical activity were dyspnea, lower diffusion capacity, poor exercise capacity and low maximal oxygen uptake (Van Remoortel et al., 2013). Physical activity may start to decline in mild-moderate COPD but more evidence is needed to ascertain whether physical activity is lower and sedentary time is greater in mild-moderate patients compared with apparently healthy adults using objective monitoring.

For patients with mild-moderate COPD longer sitting time has been associated with higher fat-free mass, more positive perception of treatment control and 12-month exacerbation history (Hartman et al., 2013). For patients with severe-very severe COPD, longer sitting time has been associated with external regulation in exercise (no choice, others make me do it) and use of long-term oxygen therapy (Hartman et al., 2013); suggesting that symptoms may be the key limiting factor in patients with more advanced COPD. Additionally, sitting time was not significantly impacted by lung function, with no difference observed across respiratory GOLD classifications (Hartman et al., 2013). Therefore, factors associated with physical activity do not necessarily have associations with sedentary behaviour or sedentary time.

In summary, a range of demographic, psycho-social, environmental, clinical and functional factors have been examined in relation to physical activity but there are inconsistent findings with many findings rated as low confidence. Whilst the use of objective monitoring to assess physical activity is improving, more work is needed to refine the accuracy and reliability of processing and utilisation (Byrom & Rowe, 2016). Moreover, even in studies using accelerometry, there is a need to identify factors related to sedentary time in this population. This is important for two main reasons: health risks from sedentary behaviour are independent of levels of MVPA (Healy et al., 2007; Healy et al., 2008) and COPD patients spend most of their day sedentary (Kawagoshi et al., 2013).

1.2.8 COPD symptom severity

Traditional COPD assessment

Traditionally, the severity of a patient's COPD was based solely on airway obstruction, assessed via spirometry. From this, the patient's FEV_1/FVC ratio and FEV_1%pred is used to classify the stage of the disease. However, COPD is a complex and heterogeneous disease and the severity of airflow limitation has been found to be poorly related to many clinically relevant aspects of the disease including dyspnea, quality of life and exacerbation frequency (Hurst et al., 2010; Weatherall et al., 2009). Consequently, in the GOLD 2011 report a combined assessment was proposed to better reflect the complexity of COPD (Rabe et al., 2007) as well as provide a more personalised stratification for improved COPD management (Agusti, Sobradillo, & Celli, 2011).

Combined COPD assessment

The GOLD 2011 assessment includes two dimensions; namely, the impact of the disease as perceived by the patient and the risk of future exacerbations (Figure 1.6) (Vestbo et al., 2013). This classification creates four groups stratifying patients by exacerbation risk (low, high) and symptoms (low, high). Group allocations are as follows: A: low risk, low symptoms; B: low risk, high symptoms; C: high risk, low symptoms; D: high risk, high symptoms (Global Initiative for Chronic Obstructive Lung Disease., 2011).

To classify patients into the "low symptom" or "high symptom" groups, the use of the mMRC dyspnea scale (<2 or ≥2, respectively) or the COPD Assessment Test (CAT) questionnaire (<10 or ≥10, respectively) is recommended. Exacerbation risk can be defined by either exacerbation history in the previous year (<2, low risk and ≥2, high risk) or by airflow limitation as per traditional spirometric classification (FEV_1≥50% predicted, low risk and FEV_1, <50% predicted, high risk) (Global Initiative for Chronic Obstructive Lung Disease., 2011).

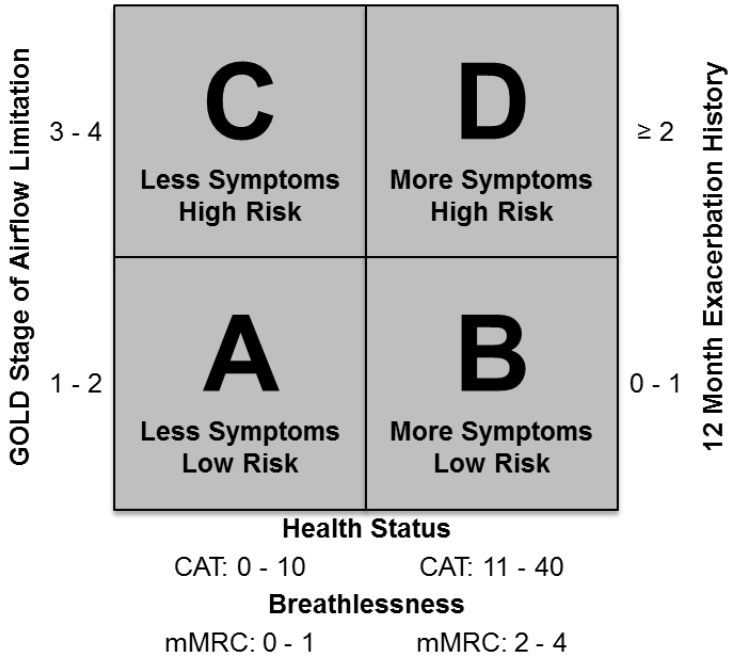

Figure 1.6 The GOLD combined assessment to group patients based on risk of exacerbations (determined by lung function classification or exacerbation history) and symptoms (CAT for health status and mMRC for dyspnea-related disability) (Global Initiative for Chronic Obstructive Lung Disease., 2011)

When there is a discrepancy between the risk categories, as assessed by the FEV_1 and/or exacerbation history, the variable indicating the highest risk should be used (Vestbo et al., 2013). Interestingly, discrepancy criteria are not provided for the variables grouping patients by symptom severity. This means that there is no current guidance for the interpretation of a patient's symptom level if they report an mMRC of 1 (low) and a CAT score of 15 (high), for example. This is an important limitation of the system due to the established discrepancy between the recommended cut-off values for mMRC (<2) and CAT (<10). Using data from European primary-care COPD patients (n=51,810), Jones and colleagues (Jones et al., 2013) suggested that an mMRC cut-point of ≥1 rather than ≥2 had the closest equivalence to a CAT cut-point of ≥10. In a sample of 1659 COPD patients, Price and colleagues (Price et al., 2014) found that 890 (53.65%) patients moved between groups depending on whether the mMRC or CAT score was used. Whilst the incorporation of self-reported symptoms into a risk model is intuitive, strict cut-offs and the assumption that questionnaires can be used interchangeably may limit the utility of this assessment in practice.

Additionally, there is a lack of 'face validity' with the GOLD 2011 A-D groups with patients in group B (high symptoms but low exacerbation risk) more likely to progress to D (high symptoms and high exacerbation risk) rather than progressing to group C (low symptoms but

high exacerbation risk). Furthermore, data from 6628 COPD patients from the Copenhagen Heart Study found GOLD mMRC group B patients to have significantly worse 3 year all-cause hospitalisation rates compared with group C (Lange et al., 2012); despite group B corresponding to mild-moderate COPD and group C equating to severe COPD. This further highlights the importance of understanding what factors are associated with symptom severity; particularly in patients with mild-moderate airflow obstruction who are discordant in their self-reported symptoms (i.e. group B).

Indeed, analysis of 6628 COPD patients followed for more than four years.(Lange et al., 2012) found that mortality rates were 3.8%, 10.6%, 8.2% and 20.1% in groups A, B, C and D, respectively (Lange et al., 2012). Notably, group B and D, both characterised by a high degree of symptom severity had five-to-eight-times higher mortality from cardiovascular disease and cancer than groups A and C (Lange et al., 2012). Agusti and colleagues (Agusti, Calverley, Celli, & et al., 2010) found that group B patients also had higher prevalence of comorbidities and persistent systemic inflammation. These findings are striking and highlight that those patients with mild-moderate disease stage whom report high symptom burden can be at greater risk of premature mortality than some patients with much more advanced COPD.

A similar pattern has been found for physical activity levels between the GOLD 2011 groups. Durheim and colleagues (Durheim et al., 2015) examined accelerometry-derived daily steps in 326 COPD patients. Group A patients were more active (6791±3567 steps) than all other groups and group B patients accumulated significantly fewer steps than group C patients (4216±2729 versus 5456±3132 steps, $p<0.05$) (Durheim et al., 2015). These findings were confirmed by Demeyer and colleagues (Demeyer et al., 2016) across different symptom questionnaires (mMRC dyspnea scale, CAT and Clinical COPD Questionnaire).

Overall, the GOLD 2011 combined assessment groups offer a useful concept for the multidimensional stratification of patients in order to better reflect the multifaceted nature of COPD. However, evidence regarding the utility of this system is inconsistent and the lack of interchangeable measures of symptoms and risk severely limits its utility across studies and in clinical practice. The individual components of the GOLD 2011 groups should still be examined (as continuous variables where possible) when assessing the role of physical activity and sedentary behaviour in COPD.

In a comprehensive assessment of symptoms (including dyspnea, health status, anxiety and depression) over a 24 hour period in 727 patients (67.2±8.8 years, 65.8% male) with stable

COPD (FEV_1%pred 52.8±20.5), Miravitlles and colleagues (Miravitlles et al., 2014b) examined associations with physical activity. For each part of the 24-hour day (early morning, daytime and night-time), significant associations were observed between patient-reported symptoms and physical activity (referred to as sedentary, moderately active or active; $p<0.05$) (Miravitlles et al., 2014b). In this instance, the term 'sedentary' should be replaced with 'inactive' as the definition of 'sedentary' in this study was "does not perform any type of physical activity". Compared with patients who were classified as active, those who were inactive had a higher proportion of symptoms across the whole 24-hour period (64.2% vs 50.4%) (Miravitlles et al., 2014b).

Durr and colleagues (Dürr et al., 2014) investigated the associations between physical activity with physical function and CAT score. Patients were categorised into four groups according to their CAT score: low (0-10), medium (11-20), high (21-30) and very high (31-40) impact on health-related quality of life. Average daily steps (β= -0.31), 6MWD (β= -0.32) and age (β= -0.39) were found to be independent predictors of CAT score (all $p<0.05$) but average daily time spent in physical activity above 3METs (MVPA) was not significant (β 0.08, $p=0.498$) (Dürr et al., 2014). Although not directly measured in this study, the significant independent association between steps taken and health-related quality of life may suggest the beneficial effects of light intensity (or the subsequent reduction in sedentary time) in COPD patients; particularly in light of evidence that for COPD patients walking does not happen at the required intensity to elicit improvements in fitness (Vitorasso et al., 2012). Specifically examining of the role of sedentary time as well as physical activity on symptom severity is required to elucidate the type of intervention(s) required to improve patients' quality of life.

Patient discordance between the severity of their airflow obstruction and their self-reported symptom severity is an interesting phenomenon highlighting not only the limitations of relying solely on lung function as an indicator of disease progression but may also help stratify patients for interventions. GOLD 2011 combined groups B and C, as previously explained, include patients with this discordance. However, discordance can be positive or negative. For example, a patient with severe airflow obstruction who reports a low symptom burden (positive) may be controlling their breathlessness and other symptoms well (e.g. through medication, exercise, physical activity or combinations thereof). On the other hand, a patient with mild-moderate airflow obstruction reporting high levels of symptoms (negative) may require additional self-management advice. In an international survey of 3265 COPD

patients across North America and Europe, this disparity was observed with 35.8% of patients reporting their disease as mild to moderate also reporting that they are too breathless to leave the house (Rennard et al., 2002). Regardless, understanding what factors are associated with this discordance is needed to improve patient stratification and to identify the interventions that will be most beneficial to them. An example of how interventions could be prescribed based on patient characteristics (exercise capacity and physical activity level) has been presented by Singh (Singh, 2014) (Figure 1.7). In this example, patients with acceptable levels of exercise capacity but have a low step count may be provided with an intervention targeting their physical activity levels.

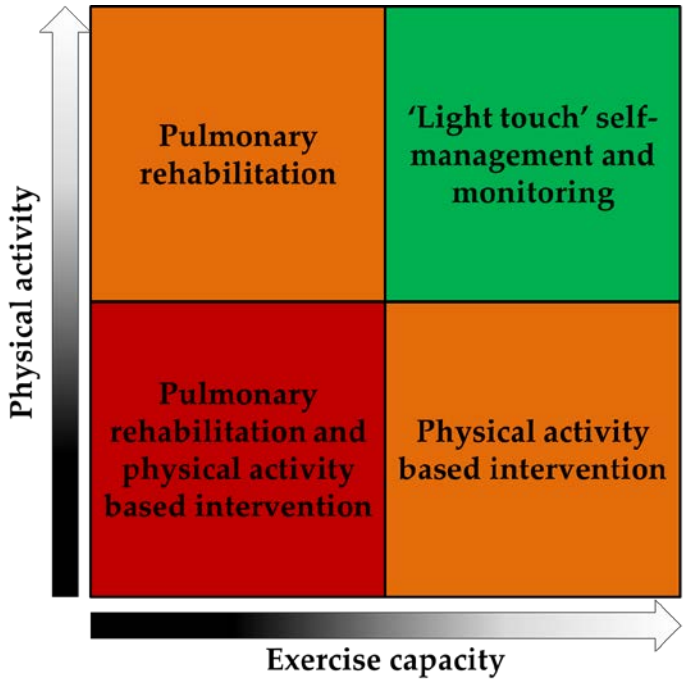

Figure 1.7 Proposed stratification of interventions based on physical activity and exercise capacity (Singh, 2014). The figure is colour coded as follows: red, requires combined intervention; amber, requires one intervention; green, requires maintenance programme.

Revised combined COPD assessment

In November 2016, a revised combined COPD assessment (Global Initiative for Chronic Obstructive Lung Disease., 2017) was produced, following the findings from the 'GOLD rush' publications. Given the GOLD 2011 combined assessment did not perform better than spirometric classifications for the prediction of mortality and other health outcomes, ABCD groups are now to be based only on exacerbation history and symptoms (mMRC and CAT). Criteria for these components have not been altered from the GOLD 2011 criteria (Figure 1.6). Spirometric classification is recommended in conjunction with the revised combined COPD assessment (Global Initiative for Chronic Obstructive Lung Disease., 2017). It is clear

that the GOLD combined COPD assessment will be an ever-evolving criteria. Therefore, it seems pertinent for research to focus more on the understanding of the potential influencers on the components which make up the groups i.e. exacerbation history, dyspnea (mMRC) and symptoms (CAT).

1.2.9 Physical activity, sedentary behaviour and acute exacerbations

Defining an acute exacerbation

An exacerbation of COPD is defined as an acute event characterised by a worsening of the patient's respiratory symptoms that is beyond normal day-to-day variations; leading to a change in medication (Celli & Barnes, 2007). The average annual number of exacerbations experienced by COPD patients is 0.8-2.0 (Hoogendoorn, Hoogenveen, Rutten-van Molken, Vestbo, & Feenstra, 2011; Hurst et al., 2010) but as the disease progresses, exacerbations can become more frequent and/or more severe and the level of dyspnoea can become debilitating (Suter, Hennessey, Florez, & Newton Suter, 2011). It is projected that the number of COPD admissions will rise by at least 150% from 2010 to 2030 with subsequent annual inpatient days increasing by 185% (Khakban et al., 2016). Exacerbations can lower patient quality of life and their ability to perform activities of daily living such as washing, shopping and cleaning (Suter et al., 2011) and it can often take weeks to recover from (Seemungal, Donaldson, Paul, & et al., 1998).

Long-term prognosis following hospitalisation for COPD exacerbation is poor, with a five-year mortality rate of approximately 50% (Hoogendoorn, Feenstra, Hoogenveen, Al, & Molken, 2010). Therefore, patients should now receive a COPD discharge care bundle (including smoking cessation interventions, referral to pulmonary rehabilitation and inhaler technique training) which has been found to reduce readmission rates (Laverty et al., 2015). Patients with more frequent and more severe respiratory symptoms, a lower exercise capacity and worse lung function are also at risk of shorter-term survival following an acute exacerbation (Garcia-Aymerich et al., 2011). Previous admissions to hospital, use of long-term oxygen therapy, poor health-related quality of life and physical inactivity have been found to be predictive of readmissions for an exacerbation (Bahadori & FitzGerald, 2007).

Physical activity and risk of hospitalisation

A study of 340 patients, who were recruited during their hospital stay for an exacerbation and followed-up one year later, investigated the role of modifiable risk factors in reducing

readmission rates (Garcia-Aymerich et al., 2003). After adjusting for significant clinical factors (e.g. ≥3 admission in the previous year and low FEV_1%pred), a high level of physical activity (equivalent to ≥60 minutes a day) was associated with a 46% reduction in the risk of readmission (HR 0.54 95%CI 0.34-0.86) (Garcia-Aymerich et al., 2003). This was the first study to establish a reduced risk of readmission through leading a more physically active lifestyle. The finding of at least one hour a day walking conferring an almost 50% lower risk of readmission is striking. Moreover, this relationship did not diminish when adjusting for COPD severity, nutritional status or pulmonary rehabilitation participation (Garcia-Aymerich et al., 2003). However, the self-reported nature of physical activity assessment and the sample comprising mostly males are important limitations to the generalisability of these findings.

In a large population-based prospective study of 2386 COPD patients (54% male), self-reported physical activity was found to be associated with an increased risk of hospitalisation and mortality (Garcia-Aymerich et al., 2006). When patients were stratified into very low, low, moderate and high physical activity levels, those in the low-to-high groups had significantly reduced odds of hospital admissions (OR 0.72 95%CI 0.53-0.97), all-cause mortality (HR 0.76 95%CI 0.65-0.90) and respiratory mortality (HR 0.70 95%CI 0.48-1.02) compared with the very low group, independent of age, sex, COPD severity and concomitant heart disease (Garcia-Aymerich et al., 2006).

A study by Esteban and colleagues (Esteban et al., 2014), which followed 543 COPD patients for three years, corroborated these findings. COPD patients who maintained a lower level of self-reported physical activity were found to have an increased rate of hospitalisation (OR 1.90 95%CI 1.09-3.32). For patients who began with the highest level of physical activity but who decreased their physical activity in the follow-up period also showed an increased readmission rate (OR 2.13 95%CI 1.15-3.98). In a cohort from the National Emphysema Treatment Trial, physical activity was found to be an independent predictor of hospitalisation with patient-reported activity levels greater than two hours per week associated with significant reductions in hospital admissions (Benzo et al., 2010).

A potential mechanism by which physical activity might prevent or reduce hospitalisations following an acute exacerbation of COPD could be related to the capacity for physical activity to reduce systemic inflammation (as expressed by markers including C-reactive protein) (Pitta et al., 2008). Additionally, physical activity may promote local changes in lung

physiology which can lead to improved pulmonary gas exchange and increased maximal expiratory pressure (Pitta et al., 2008). Maximal expiratory pressure has a positive correlation with maximal voluntary ventilation which reflects the amount of available ventilatory reserve; activated when doing physical activity (Pitta et al., 2008). Furthermore, physical activity more strongly correlates with maximal voluntary ventilation than it does with FEV_1 or inspiratory capacity (Garcia-Rio et al., 2009) supporting the notion that patients would benefit from increasing daily physical activity regardless of disease stage.

There is a paucity of information on changes in physical activity prior, during and after an exacerbation; largely due to the difficulties of obtaining such baseline (pre-exacerbation) physical activity data. In a prospective study of 73 COPD patients, respiratory symptoms and daily step count (measured using a pedometer) were recorded by the patients for 12 months (Alahmari et al., 2014). Patients recorded their step count for a median 198 days (IQR 134-353). Overall days of data for the study were 14,653 in a stable state and 2508 during exacerbation periods. Average self-reported daily step count declined significantly, from 4154±2586 during the week before an exacerbation to 3673±2258 during the initial seven days after experiencing an exacerbation. Moreover, patients who experienced more frequent exacerbations had a greater decline in daily step count but the recovery of step count was faster than that for respiratory symptoms (Alahmari et al., 2014). Whilst the reliance on patients to accurately report their step count is an important limitation, this study highlights well the impact of an exacerbation on activity levels. Moreover, the finding that step count returns to baseline quicker than symptoms suggests that it may be feasible to facilitate this return to baseline during the post-exacerbation period.

Post-discharge physical activity levels

When discharged following an exacerbation, patients are generally less active than during periods of stable symptoms (Pitta et al., 2006). Therefore, behavioural interventions after patients leave the hospital and before starting pulmonary rehabilitation may be important for preventing readmissions and tackling the vicious cycle of inactivity and deconditioning which is often worsened by highly sedentary and lengthy hospital stays (Kortebein, 2009).

In a study of 50 COPD patients (71±10 years) admitted for an acute exacerbation physical activity levels were assessed using the SenseWear Armband MF-SW for three days in-hospital, during the first week following discharge and at six weeks post-discharge (Tsai, Alison, McKenzie, & McKeough, 2016). There was a significant increase in average daily

step count over the time points with a mean (SD) step count of 1385 (1972) in-hospital, 2040 (2680) in the first week and 2328 (2745) at six weeks (p<0.001) (Tsai et al., 2016). Similarly, increases in moderate intensity physical activity (3.0-6.0 METS) were observed over the time points with patients spending 16±27 minutes, 32±46 minutes and 35±58 minutes in-hospital, at one week and six weeks, respectively (Tsai et al., 2016). Additionally, in a study of 54 patients suffering an acute exacerbation, physical activity levels over 30 days for those deemed to participate in 'low levels' of physical activity (average of <60 minutes per day vector magnitude units ≥3000 over the first 7 days) were more likely to have 30-day all-cause readmissions than those with higher activity (OR=6.7, p=0.02) (Chawla, Bulathsinghala, Tejada, Wakefield, & ZuWallack, 2014). These findings highlight the need to intervene in the critical period.

Barriers and enablers of physical activity

Qualitative investigations provide rich contextual insight into patient perceptions. A study by Thorpe and colleagues (Thorpe, Kumar, & Johnston, 2014) conducted semi-structured interviews to examine barriers and enabler of physical activity in patients with COPD following admission to hospital for an acute exacerbation (n=28). A plethora of barriers and enablers were identified and these are summarised in Figure 1.8. The main barriers identified were health-related (e.g. comorbidities, COPD symptoms and illness), environment-related (e.g. weather, transport and finance), and self-related (e.g. age and oxygen therapy). The main enabling factors were access (e.g. to equipment and health professionals), social (e.g. support and routine), and personal (e.g. motivation and goal setting) (Thorpe et al., 2014). It is pivotal for these factors to be adequately addressed in order to help optimise the implementation and success of interventions to promote physical activity following an exacerbation.

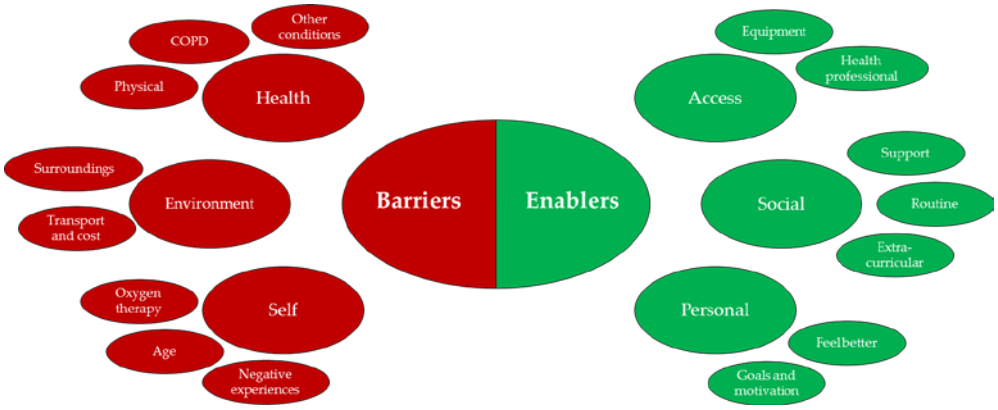

Figure 1.8 Barriers and enablers of physical activity in COPD patients hospitalised following an acute exacerbation (Thorpe et al., 2014)

Critical period for intervention

Pulmonary rehabilitation is a proven treatment for patients with stable COPD and is a well-established central therapy within routine care. Pulmonary rehabilitation facilitates recovery post-exacerbation and it is recommended internationally that eligible patients admitted for an exacerbation should be referred (Rochester et al., 2015; Spruit et al., 2013). Patients who accept pulmonary rehabilitation should be enrolled within one month of discharge (British Thoracic Society, 2014) but only 22% of providers meet this recommendation (Steiner, Holzhauer-Barrie, Lowe, Searle, Skipper, Welham, & Roberts, 2015b). Median (IQR) days from enrolment to initial assessment is 52 (44-65) and from initial assessment to commencing pulmonary rehabilitation is 65 (53-84) (Steiner, Holzhauer-Barrie, Lowe, Searle, Skipper, Welham, & Roberts, 2015b). Given the striking delay from discharge to beginning rehabilitation, some studies have attempted to intervene during this post-exacerbation and pre-rehabilitation period.

In a systematic review and pooled analysis conducted in 2010, nine studies (n=432) of post-exacerbation pulmonary rehabilitation were identified (Puhan et al., 2011). Studies were deemed to be of moderate methodological quality with pooled analysis revealing that pulmonary rehabilitation reduces hospital admissions (pooled OR 0.22 95%CI 0.08-0.58) and mortality (pooled OR 0.28 95%CI 0.10-0.84). Rehabilitation also significantly improved health-related quality of life, respiratory symptoms and exercise capacity above the minimally important differences for COPD patients who have recently experienced an acute exacerbation (Puhan et al., 2011). Post-exacerbation rehabilitation caused no adverse events in the nine identified studies signifying it is both an effective and safe intervention for these patients (Puhan et al., 2011).

In a study of 60 patients admitted for an exacerbation of COPD, Seymour and colleagues (Seymour et al., 2010) found that those receiving post-exacerbation rehabilitation (n=30) had significantly lower readmission rates for an exacerbation at three months (7% versus 33%; OR 0.15, 95%CI 0.03-0.72, p=0.02). Additionally, all unplanned hospital attendance were significantly lower for patients receiving post-exacerbation rehabilitation (27% versus 57%; OR 0.28, 95%CI 0.10-0.82, p=0.02) (Seymour et al., 2010). Whilst the number of patients screened during the study recruitment period (June 2005 to April 2008) is not provided, the recruitment of 60 patients in this period suggests many patients are not willing to participate in pulmonary rehabilitation at this time.

Greening and colleagues (Greening et al., 2014) conducted a study of early rehabilitation in post-exacerbation patients comprising a six week progressive aerobic exercise, resistance training and neuromuscular electrical stimulation starting within 48 hours of admission. Significantly higher one year mortality rates were observed in the early rehabilitation group compared with usual care (OR 1.05 to 2.88, p=0.03) (Greening et al., 2014). Additionally, when offered pulmonary rehabilitation three months after recruitment, uptake in the early rehabilitation group was significantly lower than those randomised to usual care (14% versus 22%, respectively, p=0.04) (Greening et al., 2014). Therefore, it may not be suitable for patients to undergo relatively vigorous activity and exercise at this time. Future studies examining early post-exacerbation rehabilitation or other interventions should routinely capture patient uptake to conventional pulmonary rehabilitation.

Home-based self-monitoring programmes may help to provide additional options for patients who do not feel able to take part in pulmonary rehabilitation. In an effort to increase walking in 30 post-exacerbation patients, Hornikx and colleagues (Hornikx, Demeyer, Camillo, Janssens, & Troosters, 2015) provided physical activity coaching by telephone (three times per week) and a Fitbit Ultra worn around the ankle to provide real-time feedback on step count for one month. Whilst an increase in physical activity was observed over time there was no significant difference between intervention and control (usual care) groups. One potential reason not mentioned by the authors might be the ease of access to the real-time feedback given the self-monitoring device was positioned on the ankle and so difficult to view. With the high levels of breathlessness and limited mobility of patients, feedback from self-monitoring technology needs to be easily accessible and easily understood. Therefore, future research should explore more accessible platforms to provide behavioural information such as those worn on more convenient wear locations like the wrist or providing information on portable devices such as a smart phone. Additional limitations of this study (Hornikx et al., 2015) include its recruitment as it was estimated that a sample size of 62 would be needed to achieve statistical power. However, after one year recruitment was stopped due to difficulty recruiting patients. This highlights the impact of the breathlessness-induced fear and anxiety of patients increasing their daily physical activity levels. Importantly, this should not detract from the value such initiatives could have on those patients willing and eligible to participate. Unfortunately, reasons why patients were refusing the intervention were not examined; invaluable information for future endeavours.

In a study of 42 COPD and 71 Type 2 Diabetes patients (58±8 years of age) recruited from General Practices in The Netherlands, Verwey and colleagues (Verwey et al., 2016) conducted a process evaluation of a self-monitoring intervention using wearable technology. Patients aged 40-75 years who did not take part in regular moderate intensity aerobic physical activity and who had access to the internet were provided real-time information on minutes spent in MVPA via a Smartphone and web application. Goals were mostly set by patients (61%) or in collaboration with a practice nurse (32%). For 20 patients who did not feel they achieved their goals, the most common reasons were physical or psychological symptoms and illness (70%) followed by work commitments (15%) and family issues (15%) (Verwey et al., 2016). Despite the relatively young age of these patients compared with those generally admitted for COPD exacerbations, the impact of symptoms and illness on patients' ability to engage with physical activity is prominent. In this study targeting MVPA may not have been suitable for some patients. Therefore, having an additional component not reliant on activity intensity such as step count or targeting reductions of prolonged sedentary behaviour may also be worth exploring. In addition, 58% of patients experienced problems using the technology or web application (Verwey et al., 2016). Common problems were connection issues between the activity monitor and phone (46% of issues), connection issues between the phone and server (16% of issues) and patients being unable to log in (11%). Other issues included hardware problems with the activity monitor, patients forgetting their password and patients accidentally deleting the app (Verwey et al., 2016). Therefore, future endeavours should attempt to minimise technological barriers to intervention engagement.

A sample of ten COPD patients (61±6 years, 50% female) recruited from a specialised COPD clinic free from any effects of an acute exacerbation were asked to wear a Fitbit One physical activity monitor and feedback device which provided patients with a real-time step count (Caulfield, Kaljo, & Donnelly, 2014). Patients were not required to have home internet access as all participants' received a full installation of both a laptop computer and mobile broadband as part of the study. Patients also received regular calls and texts to remind them to wear the monitor. Compared with baseline activity levels, step counts improved significantly from 310±108 to 370±129 steps on average per hour (p=0.034) (Caulfield et al., 2014). Whilst the sample size for this study was small and the study design is likely unscalable, findings suggest a potential for patients to engage with wearable self-monitoring technology. However, there is currently a lack of information regarding the level of engagement patients have with feedback provided by such devices. Such information will

help to understand what role self-monitoring technology may have in elderly patient populations and identify potential barriers and facilitators to successful engagement with their lifestyle-embedded physical activity levels.

1.2.10 Summary

Patients with COPD are more sedentary and less physically active compared with apparently healthy adults. This inactive lifestyle puts patients at risk of falling into the vicious cycle of inactivity/sedentary behaviour and breathlessness which can subsequently increase their risk of premature mortality and hospitalisation. Identifying correlates of both physical activity and sedentary behaviour in comparison to a large sample of apparently healthy adults is needed to better understand sedentary behaviour in COPD. Sedentary behaviour (both its measurement and understanding) has been too frequently overlooked. Findings from correlation studies may help to inform tailored physical activity and/or sedentary behaviour interventions. Additionally, patients mild-moderate disease who report high levels of symptom severity may represent a particular group of patients requiring lifestyle interventions. Therefore, understanding factors associated with patients with similar airflow obstruction report contrasting symptom burdens are needed to inform the design and implementation of such interventions. At the more severe end of COPD, patients admitted for an acute exacerbation may benefit from a behavioural intervention focussing on less intense movement. Targeting reductions in sedentary behaviour rather than aiming to increase exercise capacity or time spent in MVPA may be more appealing to acutely ill patients. The use of self-monitoring technologies may facilitate the provision of behavioural interventions in this population by bringing such interventions outside the four walls of the NHS and into the lives and homes of the patients. This approach removes important barriers to participation such as travel and financial encumbrance; resulting in an ‘always on’ intervention.

1.2.11 Thesis aims

Study One

1) To compare the objectively measured physical activity and sedentary time between mild-moderate COPD patients and apparently healthy adults.
2) To identify correlates of physical activity and sedentary time for mild-moderate COPD patients and apparently healthy adults.

Study Two

1) To identify factors associated with self-reported symptom severity and exacerbation history in mild-moderate COPD patients
2) To compare physical activity and sedentary time in mild-moderate COPD patients according to their symptom severity (mMRC dyspnea grade and CAT score) and exacerbation history

Study Three

1) Examine the feasibility and acceptability of an at-home sedentary behaviour intervention using wearable self-monitoring technology for COPD patients following an acute exacerbation.

Chapter 2: Physical Activity and Respiratory Health (PhARaoH) Study Methods

2.1 Study design

The Physical Activity and Respiratory Health (PhARaoH) Study is a cross-sectional, observational study of adults with and without a diagnosis of COPD (ISRCTN78843393). Ethical approval was sought and obtained from the National Research Ethics Service Committee East Midlands – Nottingham 2 (13-EM-0389) (Appendix A) and University Hospitals of Leicester NHS Trust acted as study sponsor. Full details of PhARaoH data have been previously published (Orme et al., 2016) (Appendix B) and template informed consent form and participant information sheet can be found in Appendix C and D, respectively. Participants received reimbursement of travel in full.

Recruitment

The Primary Care Research Network (PCRN) invited General Practices across Leicestershire and Rutland, UK to conduct a search on their database to identify COPD patients aged 40-75 years. Fifteen practices sent out invitations to identified patients. Patients who wished to participate were instructed to return the reply form to the Respiratory Biomedical Research Unit, Glenfield Hospital where it was passed to the PhARaoH administrative team. Upon receipt of the reply form, a researcher contacted the interested individual via telephone to confirm eligibility and to schedule an appointment. Fifteen general practices were recruited onto the study for COPD patient recruitment (two from East Leicestershire and Rutland Clinical Commissioning Group (CCG), six from West Leicestershire CCG and seven from Leicester City CCG). Apparently healthy participants were recruited through posters (Appendix E) and leaflets (Appendix F) distributed across Leicestershire in community organisations and facilities (e.g. libraries, community halls, leisure centres).

For the COPD patients, 93 (85.3%) were recruited through general practices. Remaining COPD patients were recruited through an existing research contact database (7; 6.4%), word of mouth (2; 1.8%), leaflet/poster distribution (2; 1.8%) and other recruitment methods (e.g. newspaper advert) (4; 3.7%). Of the apparently healthy adults 40 (29.6%) were recruited through leaflet/poster distribution, 32 (23.7%) through University Hospitals of Leicester intranet adverts, 21 (15.6%) through word of mouth and 42 (31.1%) through other recruitment sources (e.g. community health events).

2.2 Measurements

Data was collected between March and August 2014. Trained researchers collected all data and participants were required to attend the Respiratory Biomedical Research Unit, Glenfield Hospital, Leicestershire, UK on one occasion for approximately 2-3 hours. All participants provided written informed consent before measures were taken.

Anthropometrics and Body Composition

Height was measured using a portable stadiometer and weight and percentage body fat obtained using body composition scales (Tanita MC780MA) with body mass index (BMI) derived. Waist circumference was measured around the mid-point between the lowest rib and iliac crest (World Health Organization, 2008); taken twice using a tape measure with a third measure conducted if the difference between the first two exceeded 3cm.

Spirometry

An objective measure of lung function was conducted using forced spirometry. Spirometric assessment was not used to confirm or reject diagnosis. Daily expiratory calibration was performed with pass/fail criteria set to within 3.5% of a fixed 3L volume. Of the 118 calibrations (one per day of testing), the mean percentage error was 0.45±1.17%. Exclusion criteria for spirometric assessment were: eye surgery in the last 3 months, chest/abdominal surgery in the last three months, participant or household member tuberculosis exposure, history of aneurysm or collapsed lung, history of detached retina, stroke or heart attack in the last six months, glaucoma or history of coughing up blood in the last month. Eligible participants then completed three to eight spirometry readings (MicroLab MK8 spirometer, serial number 68738). Airflow obstruction was defined as an FEV_1/FVC <0.7. COPD severity was determined according to FEV_1%pred with ≥80 as GOLD Stage I (mild), ≥50 to <80 GOLD Stage II (moderate), ≥30 to <50 GOLD Stage III (severe) and <30 as GOLD Stage IV (very severe). Patients with normal spirometry (FEV_1/FVC ≥0.7; GOLD 0) were included in the present analysis, along with GOLD I and GOLD II patients, as these individuals had a diagnosis of COPD. FEV_1 predicted values were derived from European Community for Steel and Coal (Quanjer et al., 1993). Spirometric outputs from all patients were reviewed by a respiratory clinician.

Exercise capacity

The incremental shuttle walk test (ISWT) is a symptom-limited test of exercise capacity requiring participants to walk up and down a 10m course (Singh, Morgan, Scott, Walters, & Hardman, 1992) supervised and instructed by a trained technician. A pre-ISWT suitability to exercise check was conducted using the Physical Activity Readiness Questionnaire (Warburton, Jamnik, Bredin, & Gledhill, 2011) (Appendix G). If the participant answered 'Yes' to any one or more of these questions they were referred to a healthcare professional for sign-off. Walking speed was externally paced using pre-recorded bleep signals provided by an .mp3 file. Walking pace for the test began at 0.5m/s and increased by 0.17m/s at the end of each minute (indicated by a triple bleep). The ISWT was terminated if participants reported symptoms (e.g. muscle pain or breathlessness), were unable to maintain the necessary pace, or completed the test (12 minutes, 1020m). Participants were not permitted to run. The ISWT was repeated by the same operator following at least 30 minutes rest with the best distance achieved used for analysis.

Skeletal muscle strength

For the quadriceps maximal voluntary contraction (QMVC) test, participants sat in a purpose-built chair with an inextensible strap connecting the ankle of their dominant leg to a strain gauge (HURLabs, PR1 force transducer, Finland). Dominant leg was determined by which leg the participant would use to kick a ball. Care was taken to ensure participants' knees were flexed to 90° and that all the strain gauge and couplings were aligned to ensure an isometric contraction (Edwards, Young, Hosking, & Jones, 1977). Participants performed three sustained maximal isometric quadriceps contractions. The force produced was visible to the researcher who provided positive feedback and vigorous encouragement. There was a rest period of 30–60 seconds between each effort. The greatest of the 3 efforts was carried forward for analysis.

Upper body skeletal muscle assessment was obtained by standing grip strength using a hand-held dynamometer (Takeii analogue dynamometer, Niigata, Japan). Three measures of grip strength were taken for both hands. Participants were asked to squeeze the dynamometer with as much force as possible, with their elbow extended down by their side (Parvatikar & Mukkannavar, 2009).

Questionnaires

The full PhARaoH questionnaire is provided in Appendix H. For the purpose of this chapter, self-reported breathlessness was obtained using the mMRC dyspnea scale (graded 0-4) with a score of 0 pertaining to “Not troubled by breathlessness except on strenuous exercise”, 1 “Shortness of breath when hurrying on the level or walking up a slight hill”, 2 “Walks slower than people of the same age on the level because of breathlessness or has to stop for breath when walking at own pace on the level”, 3 “Stops for breath after walking about 100m or after a few minutes on the level” and 4 “Too breathless to leave the house or breathless when dressing or undressing”. The CAT questionnaire was used to examine a range of symptoms and total symptom burden (Jones et al., 2009). The CAT is an 8-item questionnaire comprised of 5-point (0-5) Likert scales for coughing, phlegm, sleep, confidence leaving the home, energy, tight chest and activity limitation with higher scores relating to higher severities (Figure 2.1). Patients were also asked to self-report the number of exacerbations requiring steroids or antibiotics experienced within the last 12 months.The EuroQol EQ-5D-5L was used to assess perceived general health status; comprising Likert scales for problems with mobility, self-care and performing usual activities, pain/discomfort and anxiety/depression and a visual analogue scale (0-100) for self-rated overall health (Herdman et al., 2011). Likert scales were used to form a general health index value (Van Hout et al., 2012). Participants self-reported their usual walking speed as either “slow”, “average”, “fairly brisk” or “brisk”. Postcode greenspace was obtained using physical environment data from http://www.neighbourhood.statistics.gov.uk/dissemination/.

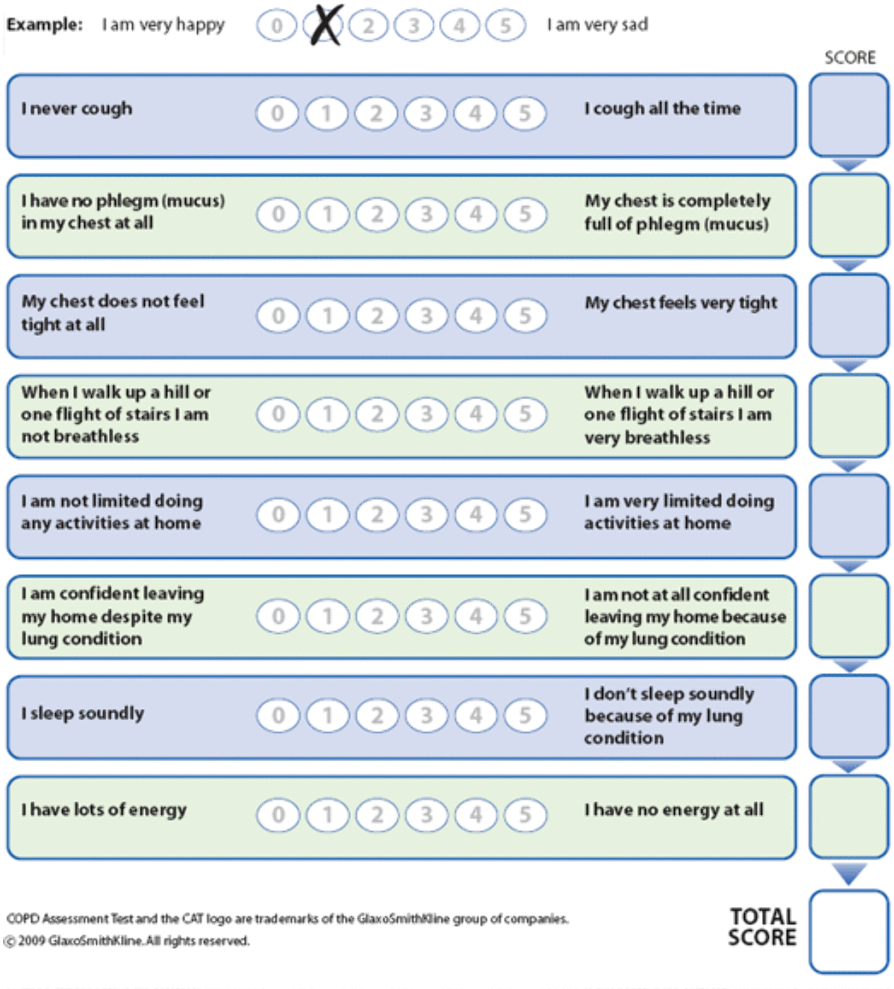

Figure 2.1 The COPD Assessment Test (CAT) questionnaire

2.3 Accelerometry

Reliability testing

Accelerometers are commonplace in the field of physical activity research, in part due to their small size, light weight and ability to measure human movement (acceleration) and store data over many days (Rothney, Apker, Song, & Chen, 2008). The capability of these devices to quantify acceleration with high sensitivity (e.g. acceleration data can be recorded 100 times every second; 100Hz) it is good practice to check that these devices are within an acceptable measurement error before deployment. This is particularly important when a large number of devices are being deployed in a single study due to the increased likelihood of inter-device variability. There are a plethora of examples of studies examining the validity of accelerometers in both controlled and free-living conditions using human participants (Welk, 2005). However, variations in the participants themselves, even when a single person wears multiple devices (Nichols, Morgan, Chabot, Sallis, & Calfas, 2000), introduces inherent

variability in the assessment of monitor accuracy. A more standardised and robust approach for examining the accuracy of accelerometers has been through the use of mechanical shakers (Esliger & Tremblay, 2006; Metcalf, Curnow, Evans, Voss, & Wilkin, 2002). The advantages of using shakers include the large number of accelerations that can be produced, the ability to assess many accelerometers at once, and the reliable and precise oscillations that can be produced (Rothney et al., 2008). For wrist-worn accelerometry, used for Study One and Study Two, the importance of limiting inter-device variation and using devices with acceptable measure errors is pivotal for accurate and reliable behaviour quantification as greater magnitudes of acceleration occur at the wrist compared with near the centre of mass (Kamada, Shiroma, Harris, & Lee, 2016).

Mechanical shaking and inter-device variability

Before deploying the ActiGraph wGT3x-BT accelerometers (ActiGraph, Pensacola, USA) the reliability of the devices was examined to ensure each unit was measuring acceleration within acceptable limits. 155 units were tested of which 12 (7.7%) were returned and 113 (72.9%) were used as part of the Study One and Study Two. Accelerometers from the pool of reliable units were also used in Study Three.

Accelerometer reliability was assessed using an orbital shaker table (Figure 2.2) to provide the researcher full control of the magnitude of the acceleration and the frequency of the oscillation the devices were exposed to. The five different conditions chosen were selected to produce a range of physiologically relevant accelerometer counts within the confines of the shaker capacity; these were 100, 125, 150, 175 and 200 revolutions per minute (rpm). Each condition was time-stamped and lasted 2.5 minutes with 1.25 minutes between each condition to allow for changes in revolutions per minute.

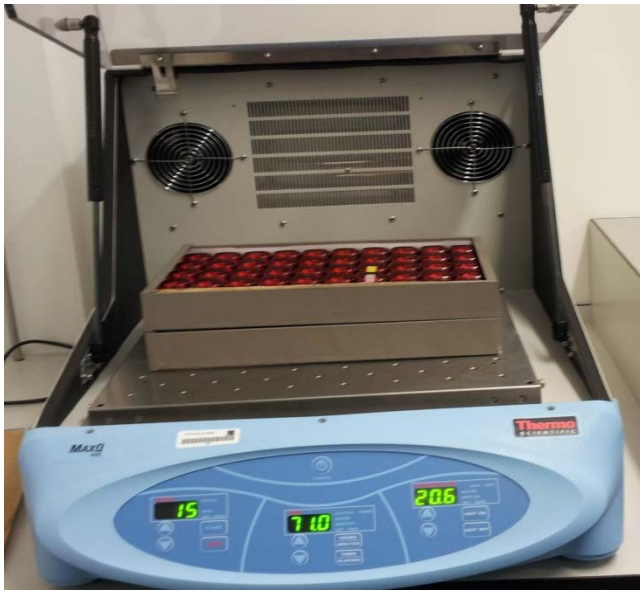

Figure 2.2 Orbital shaker table

Care was taken to secure the monitors were firmly fixed in a vertical position along their sensitive axis in order to maximize and standardize the output (Figure 2.3). Once all accelerometers were in position the orbital shaker was switched on and allowed to warm up in order to facilitate the optimal execution of the conditions.

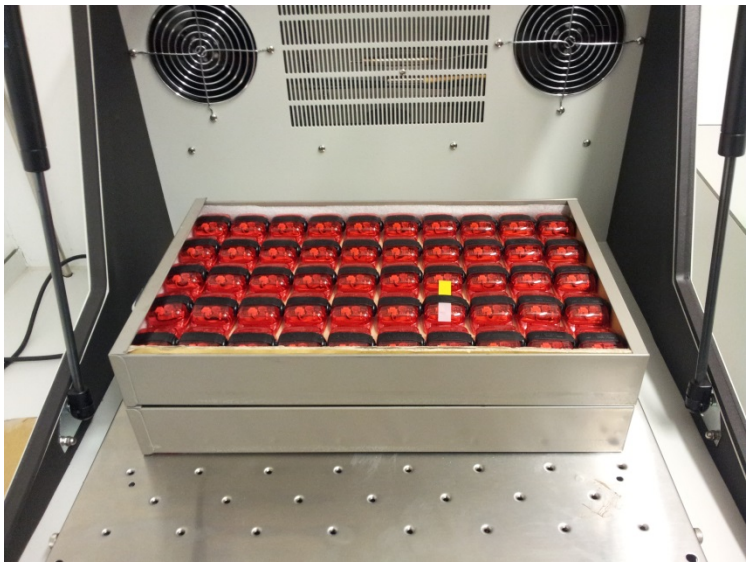

Figure 2.3 Close-up of the positioning of the accelerometers

In order to identify accelerometers working outside acceptable limits i.e. ±10% as per manufacturer guidelines, mean difference percent (Equation 2.1) was calculated for each unit and visualised using Bland-Altman plots for each condition. Units which exceeded this tolerance were deemed “out of calibration” and returned to the manufacturer. A positive mean difference percent means that the unit was high calibrated and a negative mean

difference percent means the unit was low calibrated. Unit serial numbers and corresponding mean difference percent for devices out of calibration are presented in Table 2.1.

Equation 2.1: $Mean\ difference\ percent = \frac{(unit\ specific\ mean - condition\ grand\ mean)}{condition\ grand\ mean} \times 100$

Table 2.1 Accelerometer units out of calibration (mean difference percent > ±10%)

Condition	Serial number	Mean difference percent
100rpm	MOS2A02140347	-13.27
	MOS2A02140519	-10.53
200rpm	MOS2A02140563	33.33
	MOS2A02140636	28.23
	MOS2A02140517	23.53
	MOS2A02140635	21.08
	MOS2A02140523	17.72
	MOS2A02140650	16.24
	MOS2A02140620	14.05
	MOS2A02140544	11.60
	MOS2A02140549	11.15
	MOS2A02140516	11.02

Ten of the 12 units were out of calibration at the higher acceleration (condition 5) with two units out of calibration at the slower acceleration (condition 1). Outputs for all conditions are provided in Figures 2.4-2.8.

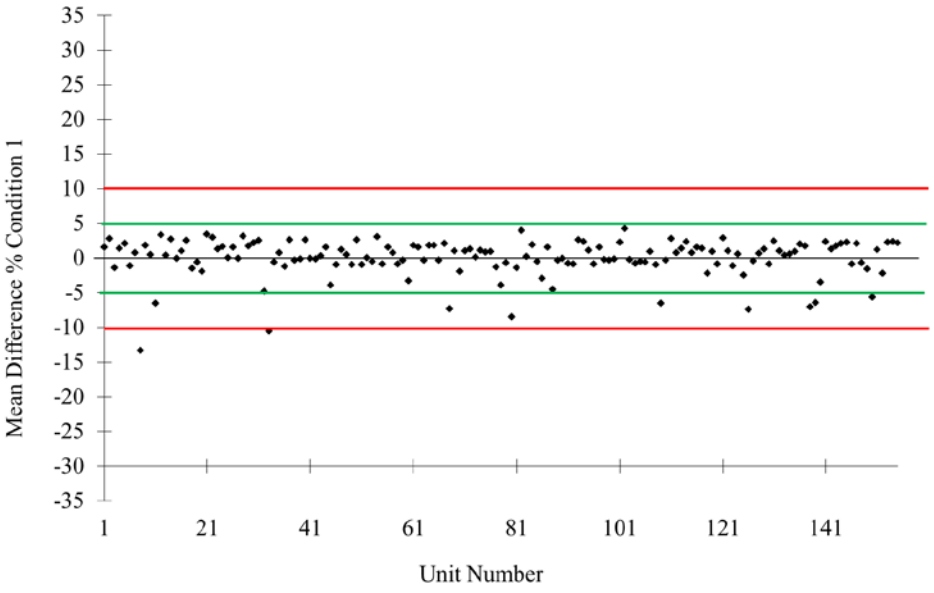

Figure 2.4 Condition 1 (100rpm) resulting in two low calibrated units

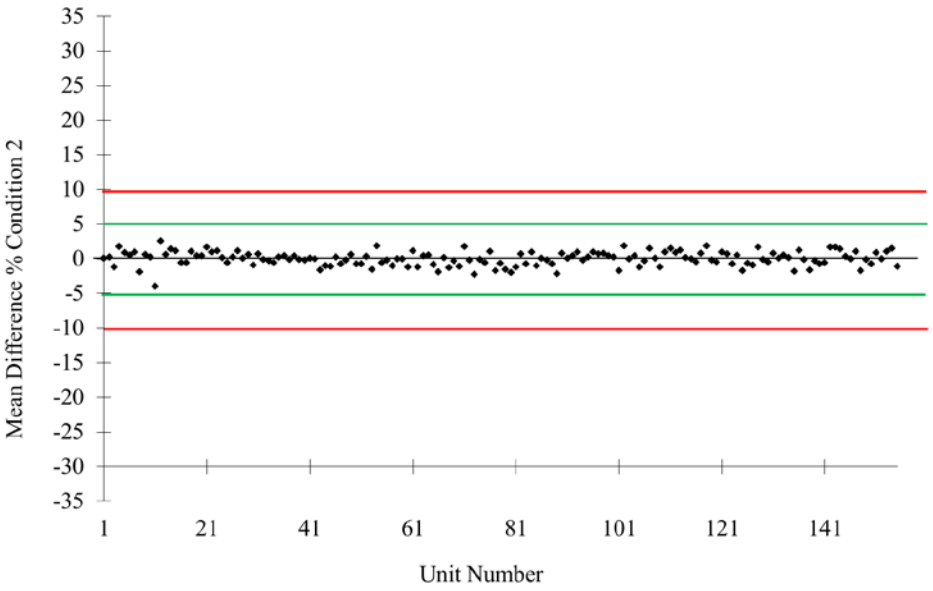

Figure 2.5 Condition 2 (125rpm) resulting in no units out of calibration

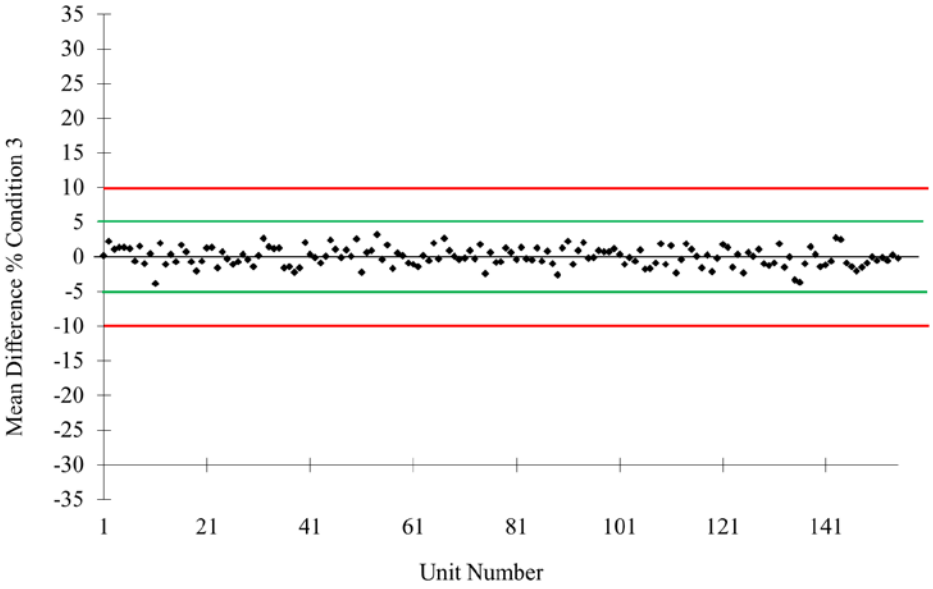

Figure 2.6 Condition 3 (150rpm) resulting in no units out of calibration

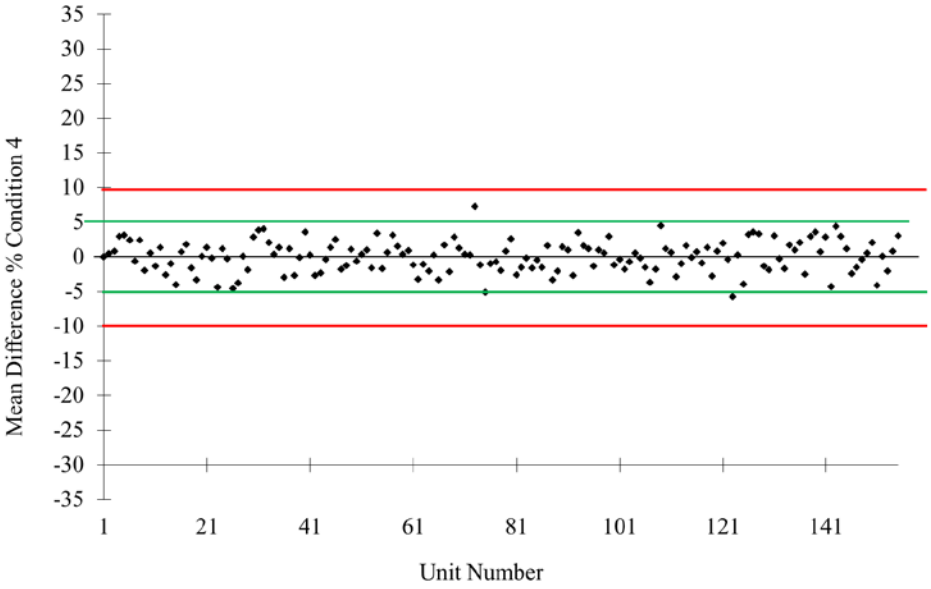

Figure 2.7 Condition 4 (175rpm) resulting in no units out of calibration

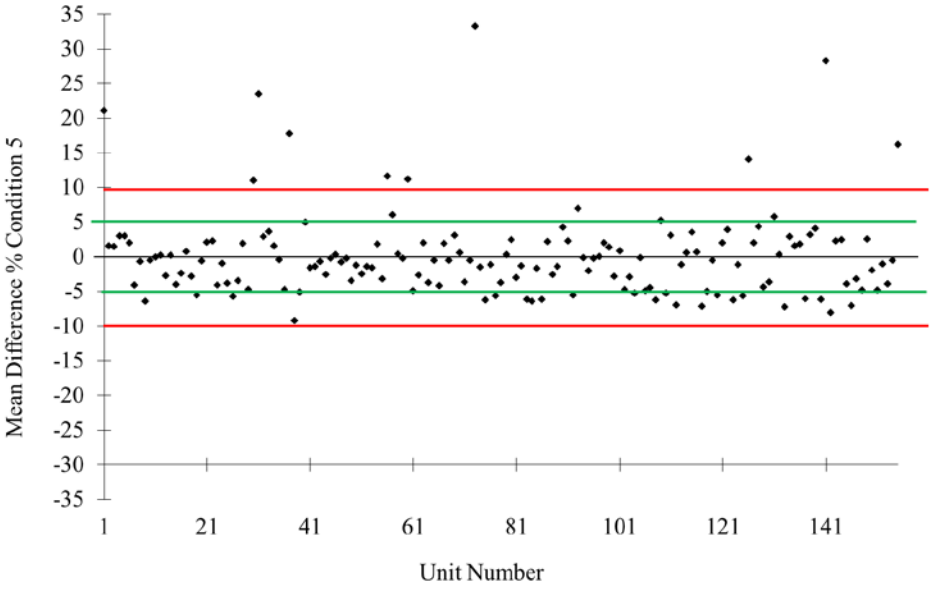

Figure 2.8 Condition 5 (200rpm) resulting in 10 high calibrated units

Data processing

Wrist-worn accelerometry is in its infancy within the field of physical activity and sedentary behaviour measurement but there is general consensus and initial evidence to suggest that this location will permit improvements in wear time compliance (van Hees et al., 2011); a vital advantage for capturing data representative of the wearer's usual activities both within and between days. The main reason for this is the added comfort for the participant which enables them to wear the device during sleep. As a result, participants (for now at least) will only be

asked to take off the monitor for water-based activities such as showering. Therefore, wrist-worn accelerometer protocols permit the capturing of the 24 hour day, limiting the chances or reasons why participants might remove the device. However, with this comes the challenge of differentiating waking and non-waking movement. Traditional approaches have utilised participant diaries whereby individuals record the time they went to bed and time they got up each day but this is thwart with recall inaccuracies and adds to the burden of study participation. Data-driven systematic approaches are needed to objectively identify sleep onset and end without the additional burden to participants.

Location and device set-up

Objectively derived physical activity and sedentary time were collected using the ActiGraph wGT3X-BT accelerometer worn on the non-dominant wrist (non-writing hand) continuously except for water-based activities at a sample rate of 100Hz. Monitors were deployed in delay mode on day 0 and commenced logging on day one at 00:00 with a seven day stop time indicated. Each accelerometer was returned via mail after seven full days of wear. Monitors were initialised and downloaded using ActiLife software (ActiGraph, Pensacola, USA) version 6.13.2 and were analysed using KineSoft (KineSoft, Loughborough, UK) version 3.3.80. Data was processed in 60-second epochs. All pertinent data collection and analytical procedures related to the accelerometry portion of the study are described in Table 2.2.

Pre-processing accelerometry analysis

60-second .agd files were processed through KineSoft using Choi wear-time criteria (Choi et al., 2011; Choi et al., 2012) to identify periods of non-wear. This was conducted in order to avoid coding non-wear as time spent in bed in subsequent analysis. Individual files were exported in 'processed mode' using the File Inspector function in KineSoft. The processed data (i.e. with non-wear coded) was then inserted into the automated sleep algorithm system.

Identifying time in bed and out of bed

Participants were asked to wear the accelerometer 24 hours a day and no sleep diary was provided. Therefore, sleep detection was determined using sustained periods of (in)activity from vector magnitude count values based on the work of Carney and colleagues (Carney, Lajos, & Waters, 2004). To identify the time when participants went to sleep (INBED), the algorithm identified consecutive dips in activity, specifically a 90% reduction from the previous epoch for 15 minutes between the hours of 21:00 and 23:59 (Carney et al., 2004).

Once the INBED criteria were met, the original epoch containing the 90% reduction in counts was used to signify the start of sleep. To identify the time when participants were awake (OUTBED), the algorithm detected consecutive rises in activity level of at least 75% from the previous epoch for 5 minutes between 06:00 and 09:00 (Carney et al., 2004). Once the OUTBED criteria were met, the original epoch containing the 75% increase in counts was used to signify the end of sleep.

Table 2.2 Accelerometry data collection and analytical procedures

Information	**Details**
Accelerometer Model	Actigraph wGT3X-BT (version 6.10.1-6.11.2; firmware 1.0.0-1.2.0)
Serial number range	113 unique devices were used ranging from MOS2A02140336 to MOS2A02140649; averaging four deployments per device
Piezosensor orientation	Triaxial
Mode setup	Mode 29 (x, y, z, steps, lux)
Original sample rate	100 Hz (.gt3x file format)
Deployment method	Fitted in person by researcher (on day 0)
Location worn	Non-dominant wrist via nylon hook and loop strap
Requested days of wear	7 d (10080 epochs) not including day 0
Initialization	Deployed in delay mode on day 0 and commenced logging on day 1 at 00:00 hrs with a 7 d stop time indicated
Wear instructions	Wear continuously except for water based activities
Analytical Processing	
Non-wear appropriation	≥90 min of consecutive 0s with allowance for 2 minutes of interruptions were deemed biologically implausible and coded as non-wear (Choi et al., 2011; Choi et al., 2012)
Valid day criteria	≥10 hours of valid waking wear time (Troiano et al., 2008)
Valid file	At least 4 valid days (Troiano et al., 2008)
Missing data	Data modelling or imputation was not performed
Epoch length	60 seconds
INBED criteria	90% reduction in counts from the previous epoch for 15 minutes (Carney et al., 2004)
OUTBED criteria	75% increase in counts from the previous epoch for 5 minutes (Carney et al., 2004)
Intensity classification	Sedentary time: <1853 vmcpm (Koster et al., 2016) and <2000 vmcpm (Kamada et al., 2016) Light: 2000-7499 vmcpm and 2000-8249 vmcpm (Kamada et al., 2016) MVPA: ≥7500 vmcpm and ≥8250 vmcpm (Kamada et al., 2016)

Window identification

In order to facilitate the aforementioned algorithm, a sub-sample of 80 (18.3%) Physical Activity and Respiratory Health (PhARaoH) study 60-second .agd files (comprising 20 apparently healthy males, 20 apparently healthy females, 20 male COPD patients and 20 female COPD patients) were used to visually inspect the suitability of using the 06:00 to 09:00 and 21:00 to 23:59 windows as part of the sleep detection verification process.

Minute-by-minute vector magnitude was plotted for each of the 7 days of wear and subjected to visual inspection for spikes in activity between 06:00 and 09:00 and dips in activity between 21:00 and 00:00 (Figure 2.9).

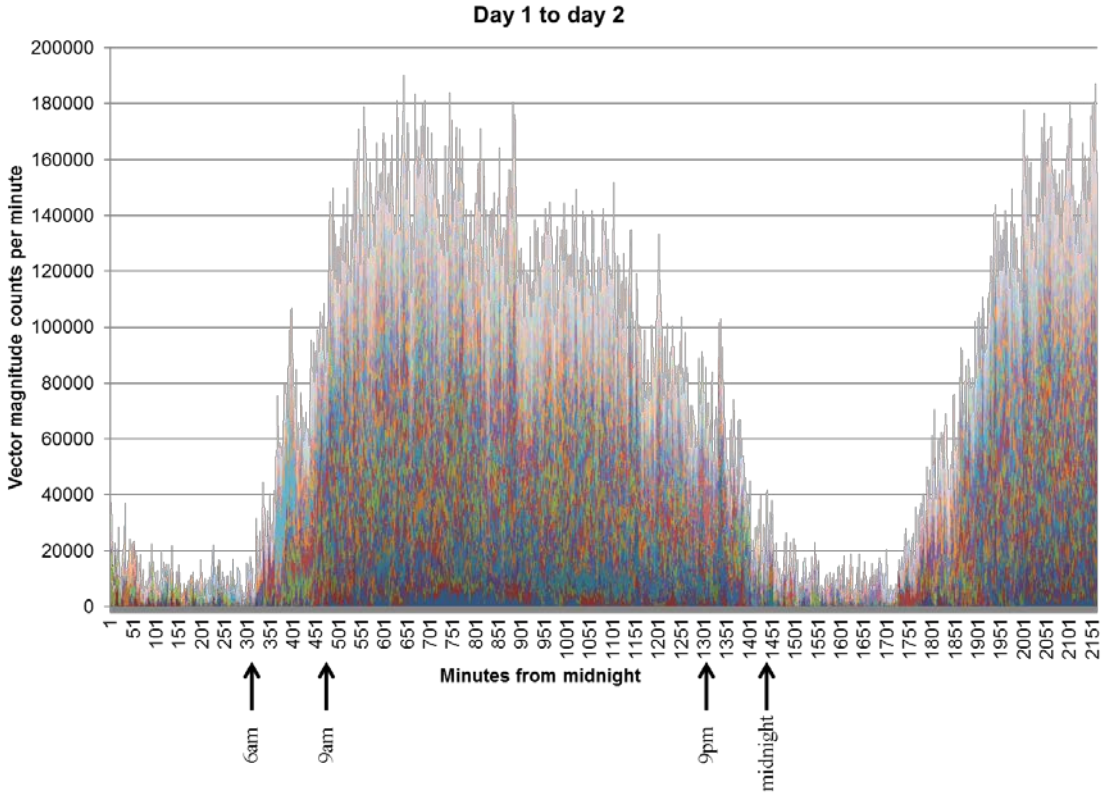

Figure 2.9 Hourly vector magnitude plots for 36 hour periods between days. Data are presented in the form of a stacked frequency bar chart for minute-by-minute vector magnitude counts for 80 participants (20 apparently healthy males, 20 apparently healthy females, 20 male patients and 20 female patients). Higher activity counts relate to more intense movement. Therefore, drops in activity intensity facilitate the identification of sleep and steep rises in activity counts facilitate the detection of waking behaviour.

Whilst these patterns were consistently observed, for the 06:00-09:00 window it was noticed that activity was still relatively high before this window therefore additional criteria were included to identify OUTBED occurrences prior to 06:00 and after 09:00. Similarly, between 21:00-00:00 it was noticed that activity was still relatively high after this window therefore additional criteria were included to identify INBED occurrences after 00:00. Consequently, additional criteria were put in place to account for variation in sleep/wake cycles between participants.

Post-processing data checking

If no INBED occurrence from 21:00-23:59 was identified, the algorithm used a default timestamp of 23:59 and the file was flagged for visual inspection to determine the exact INBED occurrence. An example is provided in Figure 2.10. In these circumstances, participants were awake beyond midnight and the first timestamp after 23:59 was used to determine INBED time. In this case, the first occurrence of an INBED timestamp from midnight of the next day was used; in the example in Figure 2.10 this was 03:12.

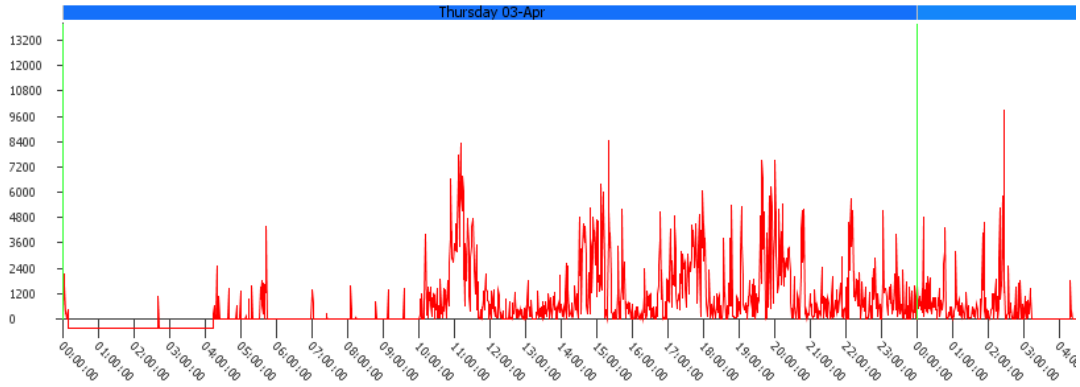

Figure 2.10 Example of algorithm INBED anomaly requiring visual inspection. On this day the wearer did not go to sleep before midnight, as signified by sustained movement detected after this time (vertical green line).

For INBED timestamps that complied with the 21:00 to 23:59 window, visual inspection was required if additional timestamps were present (e.g. 21:05, 21:30 and 22:12) (Figure 2.11). The default timestamp (first occurrence i.e. 21:05) was altered based on visual inspection if subsequent spikes in activity (i.e. at 21:30 and 22:12) lasted at least two minutes at light or moderate intensity (≥2000vmcpm) or five minutes at a sedentary intensity (<2000vmcpm).

For all OUTBED timestamps, an automated time-stamped detection of sustained spikes in vector magnitude was conducted. Files were flagged for visual inspection if a spike in activity occurred within one hour of the algorithm-derived timestamp. An example of when this occurred is provided in Figure 2.12. In this example, the algorithm has detected four spikes in activity of sufficient intensity and duration to signify the wearer is awake. However, as the algorithm was set up to provide a time stamp after 06:00, visual inspection was required to shift the timestamp from 06:01 to 05:33.

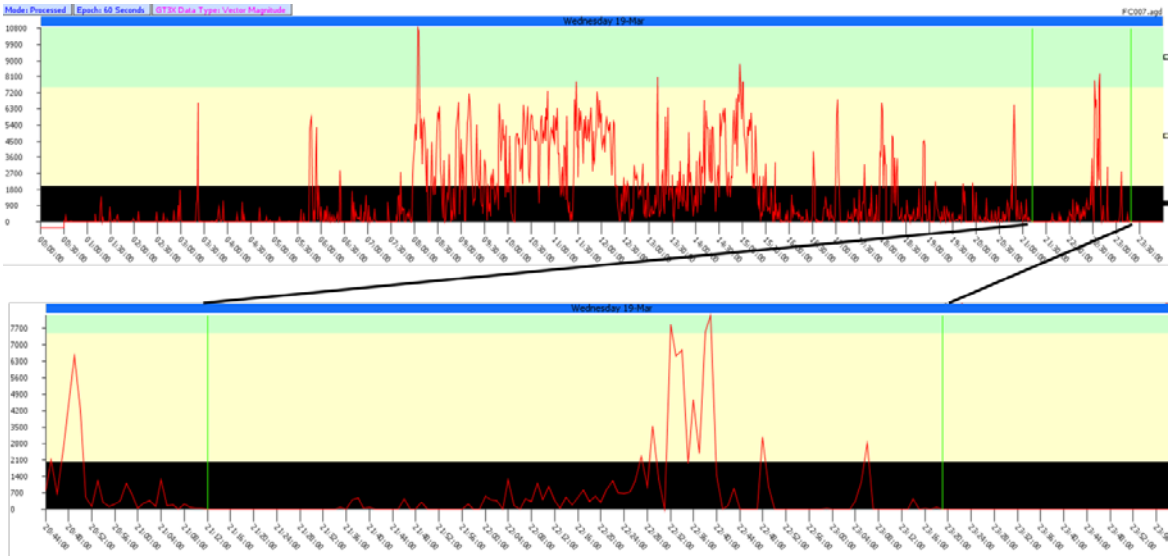

Figure 2.11 Example multiple INBED timestamps between 21:00 and 23:59 requiring visual inspection. On this day, the wearer went to sleep before midnight but likely had a highly sedentary evening. As a result, the algorithm detected two time-points where a sustained drop in activity intensity occurred (vertical green lines). On visual inspection it is clear that the first occurrence was caused by a sustained period of sedentariness. Therefore, the second time-point was used to classify sleep time.

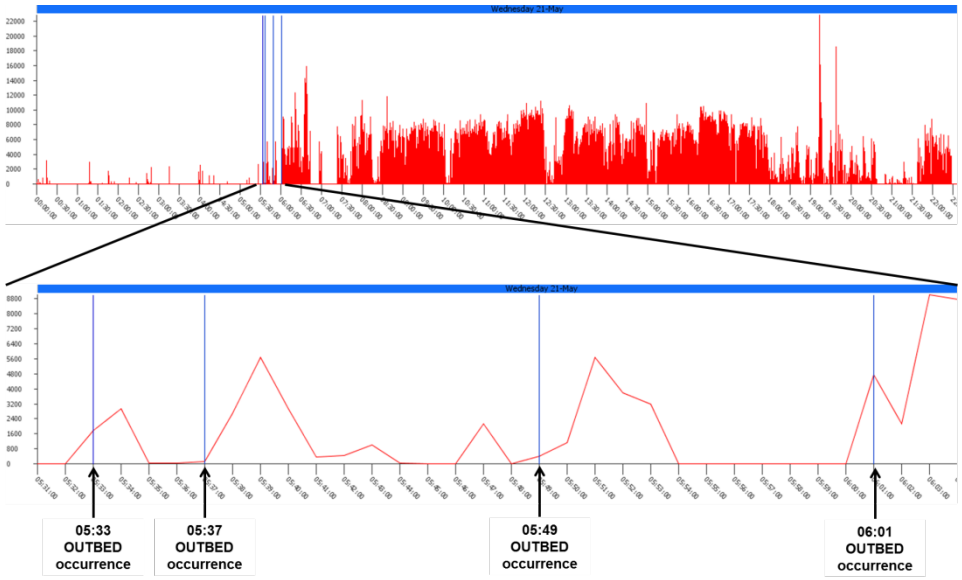

Figure 2.12 Example of OUTBED occurrences before 06:00 detected by the algorithm. On this day, the wearer has woken up before 06:00 and the algorithm has detected three spikes in activity of sufficient intensity and duration to signify the wearer is awake before this time. Visual inspection was required to shift the timestamp from 06:01 to 05:33.

Accelerometry algorithm alterations

Of the 436 total accelerometry files, 435 (99.8%) files were visually inspected for at least one day for either INBED or OUTBED classification. The whole sample of 436 files provided a

total number of 3052 potential days of wear for the PhARaoH participants. Of these, 2437 (79.8%) required visual inspection for INBED detection of which 1515 (62.2%) required an alteration to the algorithm timestamp (originally windowed between 21:00 and 23:59). For OUTBED detection, 694 (22.7%) of days required visual inspection of which 598 (86.0%) required an alteration to the algorithm timestamp (originally windowed after 06:00).

The distribution of the number of days requiring changes to the algorithm-derived timestamps for INBED and OUTBED detections is shown in Figure 2.13. For INBED detection, 25 (5.7%) participants did not require changes to the algorithm-derived timestamps and 17 (3.9%) participants required alterations to all seven days with an average of 3.5 days altered per participant. For OUTBED detection, 207 (47.5%) participants did not require changes to the algorithm-derived timestamps, and 11 (2.5%) participants required alterations to all seven days with an average of 1.4 days changed per participant.

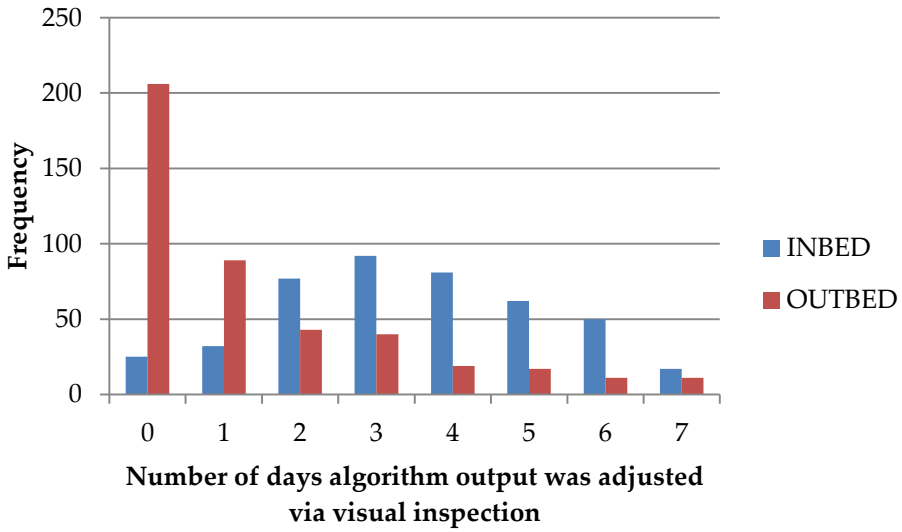

Figure 2.13 Distribution of changes to INBED and OUTBED algorithm-derived timestamps

For the 1515 INBED detections requiring alterations from the original algorithm-derived timestamps, 596 (39.3%) were due to participants going to sleep after midnight, 870 (57.4%) were from adjustments made to the first timestamp after 21:00 and 49 (3.2%) were from visual inspection alone. Of the remaining 922 days the algorithm was not altered with 203 (22.0%) because periods of non-wear were detected, 63 (6.8%) were for day 7 defaulting to 23:59 and 10 (1.1%) were not altered following visual inspection.

For the 598 OUTBED detections requiring amendment from the original algorithm output, 540 (90.3%) were due to participants waking up before 06:00 and 58 (9.7%) were from visual

inspection alone. Of the remaining 96 days the algorithm was not altered with 57 (59.4%) due to periods of non-wear and 39 (40.6%) were not altered following visual inspection.

Corrupt files

During visual inspection, one corrupt file was identified (Figure 2.14), giving a variety of series of consecutive numbers (e.g. 6, 6, 6, 4, 4, 4, 4, 4, 8, 8, 8, 8, 8). This file was included for waking wear time assessment but excluded from activity analysis given the obvious technological fault in the sensor (i.e. such data are biologically implausible).

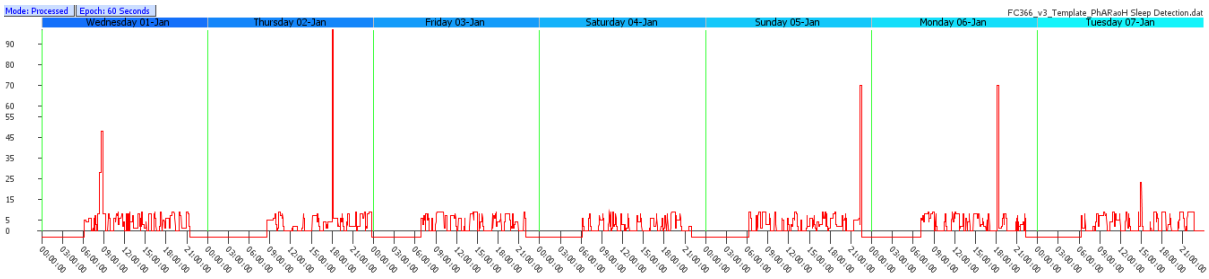

Figure 2.14 Corrupt file FC366 seven day accelerometer plots in processed mode

Accelerometry processing

After establishing the INBED and OUTBED times for each day, sleep was coded as 0 counts (equivalent to non-wear) in order to be removed by non-wear algorithm during data processing. As a result, time spent in activity intensities were derived from waking wear time.

Given the infancy of wrist-worn accelerometry analysis, vector magnitude counts per minute (vmcpm) were used to provide 'raw' indicators of overall movement levels. Counts per minute were calculated by dividing average total counts per day by average waking wear time.

Physical activity intensities were defined according to published cut-points for sedentary time, light intensity activity and MVPA. Sedentary time was defined using cut-points of <1853 vmcpm (Koster et al., 2016) and <2000 vmcpm (Kamada et al., 2016). Two sets of light intensity activity and MVPA cut-points were used. One set defined light activity as 2000-7499vmcpm and MVPA as ≥7500vmcpm and the second defined light activity as 2000-8249vmcpm and MVPA as ≥8250vmcpm (Kamada et al., 2016).

2.4 Waking wear time compliance

Asking participants to wear an activity monitor on the wrist for 24 hours a day (minus water-based activities) is purported to increase overall wear compliance compared to waist-worn

deployments (van Hees et al., 2011). A waking-wear-time-valid-day matrix is provided in Table 2.3. The traditionally used criteria for adults based on waist-worn monitoring, is a minimum of 10 hours of waking activity data per day for at least four days (Troiano et al., 2008). Using this definition, the PhARaoH sample achieved 98.9% compliance.

Table 2.3 Number of participants (maximum n=436) and the percentage of the sample (%) providing a valid day of accelerometry data across a range of minimum waking wear time criteria (6-20 hours). Frequencies are highlighted to facilitate interpretation with green cells showing a high proportion of participants providing valid days and red cells showing a low proportion of participants.

Whole sample (n=436)													
Valid days	**Valid day waking wear time (hours)**												
	≥ 8	**≥ 9**	**≥ 10**	**≥ 11**	**≥ 12**	**≥ 13**	**≥ 14**	**≥ 15**	**≥ 16**	**≥ 17**	**≥ 18**	**≥ 19**	**≥ 20**
≥ 1	434 (99.5)	434 (99.5)	434 (99.5)	434 (99.5)	433 (99.3)	433 (99.3)	430 (98.6)	429 (98.4)	422 (96.8)	348 (79.8)	165 (37.8)	46 (10.6)	19 (4.4)
≥ 2	433 (99.3)	433 (99.3)	433 (99.3)	432 (99.1)	431 (98.9)	430 (98.6)	428 (98.2)	425 (97.5)	396 (90.8)	264 (60.6)	78 (17.9)	17 (3.9)	2 (0.5)
≥ 3	432 (99.1)	432 (99.1)	431 (98.9)	430 (98.6)	429 (98.4)	429 (98.4)	426 (97.7)	419 (96.1)	348 (79.8)	182 (41.7)	46 (10.6)	5 (1.1)	1 (0.2)
≥ 4	432 (99.1)	431 (98.9)	431 (98.9)	429 (98.4)	428 (98.2)	426 (97.7)	421 (96.6)	406 (93.1)	289 (66.3)	118 (27.1)	15 (3.4)	1 (0.2)	0 (0)
≥ 5	428 (98.2)	428 (98.2)	426 (97.7)	425 (97.5)	424 (97.2)	420 (96.3)	411 (94.3)	364 (83.5)	235 (53.9)	59 (13.5)	8 (1.8)	1 (0.2)	0 (0)
≥ 6	422 (96.8)	421 (96.6)	420 (96.3)	417 (95.6)	412 (94.5)	403 (92.4)	379 (86.9)	307 (70.4)	158 (36.2)	22 (5.0)	2 (0.5)	0 (0)	0 (0)
7	401 (92.0)	400 (91.7)	393 (90.1)	386 (88.5)	374 (85.8)	358 (82.1)	296 (67.9)	190 (43.6)	66 (15.1)	10 (2.3)	0 (0)	0 (0)	0 (0)

The pattern of the matrix also provides information on which criteria (waking wear time or number of days required) has the greatest impact on whether a file is deemed valid and how these two factors interact. During the minimum wear-times of 8-16 hours, only a 2.7% (99.5% minus 96.8%) reduction in participants with at least one valid day was observed. During these wear-times, the choice of number of valid days required had a greater weighting on whether files were deemed to be valid (e.g. a 5.7% (99.5% minus 93.8%) and 81.7% (96.8% minus 15.1%) reduction from ≥1 to seven days for ≥8 and ≥16 hours waking wear time, respectively). From ≥16 hours waking wear time, there were large reductions in the number of participants meeting valid day criteria due to the identification of sleep.

A waking-wear-time-valid-day matrix for participants stratified by COPD diagnosis is provided in Table 2.4. Using a minimum of 10 hours per day for at least 4 days (Troiano et al. 2008), COPD patients achieved 98.6% compliance and apparently healthy adults achieved 99.0% compliance. COPD patients exceeded the most compliant group in the National Health

and Nutrition Examination Survey (84% meeting 10 hours on at least 4 days criteria) (Troiano et al., 2008) with a more stringent criterion of at least 13 hours for all seven days whilst the non-COPDs exceeded it with at least 14 hours for at least six days. Therefore, wrist-worn monitor deployment resulted in a greatly improved compliance regardless of COPD diagnosis.

Table 2.4 Number of participants and the percentage of the sample (%) stratified by COPD diagnosis providing a valid day of accelerometry data across a range of minimum waking wear time criteria (6-20 hours). Frequencies are highlighted to facilitate interpretation with green cells showing a high proportion of participants providing valid days and red cells showing a low proportion of participants.

COPD (n=139)													
Valid days	**Valid day waking wear time criteria (hours)**												
	≥ 8	**≥ 9**	**≥ 10**	**≥ 11**	**≥ 12**	**≥ 13**	**≥ 14**	**≥ 15**	**≥ 16**	**≥ 17**	**≥ 18**	**≥ 19**	**≥ 20**
≥ 1	138 (99.3)	138 (99.3)	138 (99.3)	138 (99.3)	138 (99.3)	138 (99.3)	136 (97.8)	135 (97.1)	134 (96.4)	116 (83.5)	71 (51.1)	23 (16.5)	9 (6.5)
≥ 2	138 (99.3)	138 (99.3)	138 (99.3)	138 (99.3)	137 (98.6)	136 (97.8)	136 (97.8)	134 (96.4)	129 (92.8)	93 (66.9)	41 (29.5)	11 (7.9)	1 (0.7)
≥ 3	137 (98.6)	137 (98.6)	137 (98.6)	137 (98.6)	136 (97.8)	136 (97.8)	135 (97.1)	133 (95.7)	115 (82.7)	73 (52.5)	22 (15.8)	3 (2.2)	1 (0.7)
≥ 4	137 (98.6)	137 (98.6)	137 (98.6)	136 (97.8)	136 (97.8)	136 (97.8)	135 (97.1)	132 (95.0)	100 (71.9)	52 (37.4)	8 (5.8)	1 (0.7)	0 (0)
≥ 5	137 (98.6)	137 (98.6)	136 (97.8)	136 (97.8)	136 (97.8)	135 (97.1)	134 (96.4)	121 (87.1)	87 (62.6)	24 (17.3)	4 (2.9)	1 (0.7)	0 (0)
≥ 6	137 (98.6)	136 (97.8)	135 (97.1)	134 (96.4)	133 (95.7)	133 (95.7)	126 (90.6)	108 (77.7)	65 (46.8)	11 (7.9)	2 (1.4)	0 (0)	0 (0)
7	131 (94.2)	131 (95.7)	127 (91.4)	126 (90.6)	122 (87.8)	121 (87.1)	100 (71.9)	73 (52.5)	31 (22.3)	6 (4.3)	0 (0)	0 (0)	0 (0)
Apparently healthy adults (n=297)													
Valid days	**Valid day waking wear time criteria (hours)**												
	≥ 8	**≥ 9**	**≥ 10**	**≥ 11**	**≥ 12**	**≥ 13**	**≥ 14**	**≥ 15**	**≥ 16**	**≥ 17**	**≥ 18**	**≥ 19**	**≥ 20**
≥ 1	296 (99.7)	296 (99.7)	296 (99.7)	296 (99.7)	295 (99.3)	295 (99.3)	294 (99.0)	294 (99.0)	288 (97.0)	232 (78.1)	94 (31.6)	23 (7.7)	10 (3.4)
≥ 2	295 (99.3)	295 (99.3)	295 (99.3)	294 (99.0)	294 (99.0)	294 (99.0)	292 (98.3)	291 (98.0)	267 (89.9)	171 (57.6)	37 (12.5)	6 (2.0)	1 (0.3)
≥ 3	295 (99.3)	295 (99.3)	294 (99.0)	293 (98.7)	293 (98.7)	293 (98.7)	291 (98.0)	286 (96.3)	233 (78.5)	109 (36.7)	24 (8.1)	2 (0.7)	0 (0)
≥ 4	295 (99.3)	294 (99.0)	294 (99.0)	293 (98.7)	292 (98.3)	290 (97.6)	286 (96.3)	274 (92.3)	189 (63.6)	66 (22.2)	7 (2.4)	0 (0)	0 (0)
≥ 5	291 (98.0)	291 (98.0)	290 (97.6)	289 (97.3)	288 (97.0)	285 (96.0)	277 (93.3)	243 (81.8)	148 (49.8)	35 (11.8)	4 (1.3)	0 (0)	0 (0)
≥ 6	285 (96.0)	285 (96.0)	285 (96.0)	283 (95.3)	279 (93.9)	270 (90.9)	253 (85.2)	199 (67.0)	93 (31.3)	11 (3.7)	0 (0)	0 (0)	0 (0)
7	270 (90.9)	269 (90.6)	266 (89.6)	260 (87.5)	252 (84.8)	237 (79.8)	196 (66.0)	117 (39.4)	35 (11.8)	4 (1.3)	0 (0)	0 (0)	0 (0)

2.5 PhARaoH sample characteristics

Table 2.5 shows the overall activity levels of the whole sample and between individuals with and without a diagnosis of COPD. Of the 436 PhARaoH participants, one accelerometer file was corrupt, two COPD patients did not meet valid day criteria and three control participants did not meet valid day criteria. COPD and control groups did not differ for the number of valid days provided (p=0.724) but COPD patients had longer waking wear time (999±73 versus 980±69 minutes, p<0.001). There was no significant difference in waking hours non-wear time between COPD and apparently healthy adults (p=0.888). COPD patients were more sedentary and accrued less time in light intensity activity and MVPA with these differences remaining when accounting for overall waking wear time (p<0.001).

Table 2.5 Accelerometry data for the whole sample and stratified by COPD diagnosis.

	Whole Sample	**COPD patients**	**Apparently healthy adults**
Demographics			
Age (years)	59.7 (9.3)	65.8 (7.0)	56.8 (8.9)
Gender (female, %)	234 (53.7)	47 (33.8)	187 (63.0)
Employment status (%):			
Employed	214 (49.2)	36 (26.1)	178 (59.9)
Unemployed	44 (10.1)	16 (11.6)	28 (9.4)
Retired	177 (40.6)	86 (61.9)	91 (30.6)
Household income β (%):			
<£18,000	124 (28.8)	51 (37.2)	73 (24.8)
£18,000-30,999	113 (26.2)	37 (27.0)	76 (25.9)
£31,000-51,999	79 (18.3)	23 (16.8)	56 (18.9)
£52,000-99,999	60 (13.9)	6 (4.4)	54 (18.2)
≥£100,000	7 (1.6)	0 (0)	7 (2.4)
IMD deprivation score	19.3 (15.0)	22.2 (17.9)	17.9 (13.2)
Postcode percentage green space	44.0 (30.9)	168.8 (9.1)	41.6 (29.9)
Accelerometry			
Number of Valid Days	6.8 (0.8)	6.8 (0.9)	6.8 (0.8)
Valid day frequencies (%, cum%):			
7	392 (91.2)	127 (92.7)	265 (90.4)
6	27 (6.3, 97.5)	8 (5.8, 98.5)	19 (6.5, 96.9)
5	6 (1.4, 98.9)	1 (0.7, 99.2)	5 (1.7, 98.6)
4	5 (1.1, 100)	1 (0.7, 100)	4 (1.4, 100)
Waking Wear Time (min per day)	960.3 (61.4)	968.6 (67.2)	956.4 (58.2) *
Non-wear time (min per day)	30.7 (70.4)	33.0 (87.1)	29.6 (61.3)
Sleep (min per day)	448.3 (54.5)	437.4 (62.3)	453.3 (49.9) *
Sedentary < 1853 vmcpm (min per day)	523.7 (108.1)	579.9 (95.2)	497.7 (104.0) *
Sedentary < 2000 vmcpm (min per day)	541.7 (108.4)	597.9 (94.5)	515.5 (104.5) *
Light 2000-7499vmcpm (min per day)	388.9 (96.4)	356.0 (97.3)	404.3 (92.2) *

Light 2000-8249vmcpm (min per day)	400.8 (102.2)	362.1 (101.6)	418.9 (97.6) *
MVPA ≥7500 (min per day)	30.0 (28.6)	15.9 (15.7)	36.6 (30.8) *
MVPA ≥8250 (min per day)	17.7 (19.2)	8.4 (10.0)	22.0 (20.9) *
Vector magnitude counts per minute	2290.9 (621.4)	1941.5 (489.7)	2454.4 (609.5) *
Respiratory health			
Smoking status (%):			
Current	39 (8.9)	24 (17.3)	15 (5.1)
Former	178 (40.8)	97 (69.8)	81 (27.3)
Never	219 (50.2)	18 (12.9)	201 (67.7)
FEV_1 (L)	2.3 (0.7)	1.9 (0.7)	2.5 (0.7)
FEV_1%pred	87.9 (23.1)	70.2 (21.2)	96.2 (13.9)
FVC (L)	3.5 (1.0)	3.6 (1.0)	3.5 (0.9)
FEV_1/FVC	66.9 (13.1)	53.2 (13.1)	73.3 (6.5)
mMRC score	0.7 (0.8)	1.1 (0.9)	0.5 (0.6)
Body composition			
BMI (kg/m^2)	27.5 (5.4)	28.3 (5.7)	27.2 (5.2)
Percentage body fat	29.7 (8.4)	28.0 (8.8)	30.4 (8.1)
Waist circumference (cm)	93.6 (14.8)	100.2 (14.5)	90.6 (13.9)
Physical function			
ISWT (m)	481.5 (191.0)	381.8 (158.5)	527.4 (187.4)
QMVC (kg)	34.4 (13.5)	34.7 (12.3)	34.2 (14.1)
Grip strength (kg)	34.7 (10.6)	36.2 (10.5)	33.9 (10.6)
Usual walking speed (%):			
Slow	66 (15.1)	40 (28.8)	26 (8.8)
Average	249 (57.1)	77 (55.4)	172 (57.9)
Fairly brisk	111 (25.5)	20 (14.4)	91 (30.6)
Brisk	10 (2.3)	2 (1.4)	8 (2.7)

Abbreviations: cum%, cumulative percentage; MVPA, moderate-to-vigorous physical activity; vmcpm, vector magnitude counts per minute

* $p<0.05$

Chapter 3: Study One

Title: Correlates of objectively measured physical activity and sedentary time in mild-moderate COPD patients: Comparisons with apparently healthy adults

3.1 Introduction

COPD patients with moderate-severe airflow obstruction are typically less physically active and more sedentary compared with apparently healthy adults (Pitta et al., 2005); placing them at increased risk of hospitalisation and premature mortality (Garcia-Aymerich et al., 2003). For these patients with more advanced COPD, severe airflow limitation and more frequent exacerbations likely puts these patient at a greater risk of avoiding physical activity and spending more time sedentary; resulting in a downward spiral of muscle deconditioning, reduced fitness and increased breathlessness (Cooper, 2009; Polkey & Moxham, 2006). However, there is a paucity of data on the physical activity of patients with mild-moderate COPD and whether their behaviour differs from apparently healthy adults (Park et al., 2013; Van Helvoort et al., 2016). Furthermore, a greater understanding of factors associated with behaviour in mild-moderate COPD patients is pivotal for understanding how best to improve patients' lifestyles. Furthermore, research to date has largely focussed on physical activity, rather than examining the full 24 hour day, which includes sedentary behaviour, "defined as any waking activity characterized by an energy expenditure ≤1.5 METS and a sitting or reclining posture" (Sedentary Behaviour Research, 2012).

Identifying correlates of physical activity and sedentary behaviour are an important step in developing tailored interventions. The extent to which physical activity and sedentary behaviour share common correlates has not been sufficiently explored in mild-moderate COPD patients (Park et al., 2013). Understanding the factors influencing patients' physical activity and sedentary behaviour is needed to inform the development of tailored interventions.

A systematic review of 86 studies published in 2014 revealed inconsistent associations for a range of socio-demographic, lifestyle, environmental, clinical and functional factors with physical activity (Gimeno-Santos et al., 2014). Potential reasons for these discrepant findings may be related to most studies failing to adjust associations for potential confounders and only half of the studies used objective measures of behaviour (Gimeno-Santos et al., 2014). Whilst the use of objective monitoring to assess physical activity is improving in studies related to COPD, more work is needed to refine the accuracy and reliability of processing and

utilisation (Byrom & Rowe, 2016). Of the identified cross-sectional studies, only two specifically examined mild-moderate COPD patients compared to 12 studies specifically studying patients with moderate to very severe airflow obstruction. In addition, only seven studies included a control group in their analysis (mean n=29±16) (Gimeno-Santos et al., 2014); limiting comparisons to healthier adults. This is particularly important for mild-moderate COPD patients who may share similar correlates to physical activity as the general adult populations free from respiratory disease.

Exercise capacity, as measured by the 6MWD, has been found to be the strongest correlate of time spent walking (partial R^2=0.56), standing (partial R^2=0.35) and movement intensity (partial R^2=0.23) (Pitta et al., 2005). In a study of 73 COPD patients (67±7 years, 60% female FEV_1%pred 43±16), lung function was found to explain the highest proportion of variance in physical activity (R^2=0.20) followed by walking speed (R^2=0.18), quadriceps strength (R^2=0.16) and fat-free mass index (R^2=0.08) (Andersson et al., 2013). Additionally, quadriceps muscle wasting and poor exercise capacity have been negatively associated with physical activity in mild-moderate COPD patients (Hartman et al., 2013; Shrikrishna et al., 2012). Modified MRC score has also been independently associated with physical activity level and step count (Adami et al., 2015) with patients reporting an mMRC score of four averaging less than 2000 steps per day (Watz et al., 2009).

Factors relating to sedentary behaviour and low intensity activity in this population have been scarcely examined (Park et al., 2013). This is an important knowledge gap given the sedentary lifestyles of many COPD patients (Kawagoshi et al., 2013) and the cardiometabolic health risks from spending too much time sedentary, independent of time spent in MVPA (Healy et al., 2007; Healy et al., 2008). In a US study, correlates of accelerometer assessed sedentary time were found to be different to those of physical activity; highlighting the importance of specifically examining this type of behaviour (Park et al., 2013). Furthermore, as both sedentary behaviour and light intensity activity have been associated with a reduced risk of hospitalisation (Andrzejowski et al., 2015; Donaire-Gonzalez et al., 2015) it seems pertinent to concomitantly explore behavioural correlates across the intensity spectrum.

This study aimed to (i) compare the objectively measured physical activity and sedentary time and (ii) identify correlates of physical activity and sedentary time for mild-moderate patients and apparently healthy adults. It was hypothesised that mild-moderate COPD patients would be less physically active and more sedentary compared with apparently

healthy adults. Also, it was hypothesised that correlates would differ between groups and between physical activity and sedentary time.

3.2 Methods

Data used in this chapter was taken from the PhARaoH Study as described in Chapter 2 and has been previously published (Orme et al., 2016).

Inclusion/exclusion criteria

The original PhARaoH sample comprised 139 COPD patients (31.9%) and 297 apparently healthy adults (68.1%). COPD patients were excluded from the present study due to: being classified as GOLD III or IV (n=21), spirometry not being conducted (n=2), non-white ethnicity (n=5) and less than four valid days of accelerometry (n=2). Apparently healthy adults were excluded from the present study due to: reporting a respiratory condition (n=50), spirometry not being conducted (n=4), non-white ethnicity (n=107) and less than four valid days of accelerometry (n=1). The final sample comprised 109 COPD patients (80.1% of original patient cohort) and 135 apparently healthy adults (45.5% of original non-patient cohort) (Figure 3.1).

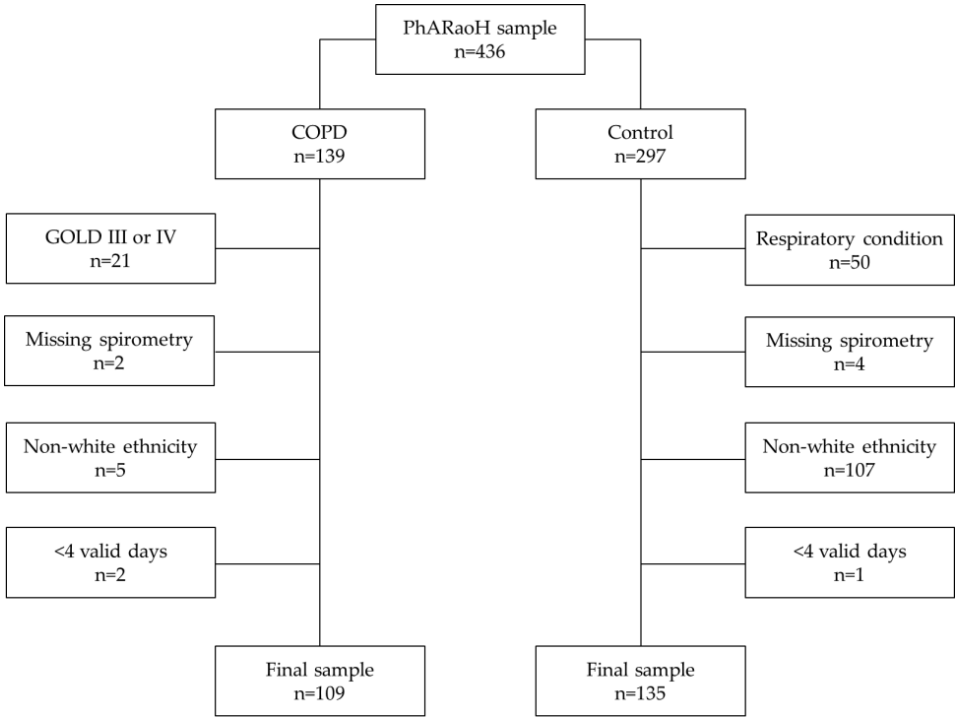

Figure 3.1 Derivation of the present study sample from the original PhARaoH cohort

Statistical analysis

Analyses were conducted using SPSS (version 23.0). Data are reported as mean (SD) with group comparisons performed using independent t-tests. Frequency comparisons between groups were performed using Chi-square (n>5) or Fischer exact test (n≤5). Covariate-adjusted group comparisons for ratio data were performed using analysis of covariance (ANCOVA) controlling for age, gender, smoking status, employment status and accelerometer waking wear time where appropriate.

Univariate analyses were conducted using partial correlations between predictors (independent variables) and behaviour (dependent variables). Strength of associations (Partial r) were interpreted as follows: Partial r 0.00-0.19 “very weak”; 0.20-0.39 “weak”; 0.40-0.59 “moderate”; 0.60-0.79 “strong” and 0.80-1.00 “very strong” (Evans, 1996). Forced entry linear regressions were used to examine predictors of physical activity and sedentary time, controlling for the above covariates. Variables reaching statistical significance (p<0.05) for either patients or apparently healthy adults were entered into stepwise multivariate linear regression models to identify independent predictors of behaviour. For all models, data were checked for linear relationship, absence of multicollinearity, homoscedasticity and a normal distribution of residuals.

3.3 Results

3.3.1 Sample characteristics

The distribution of GOLD stages for COPD patients were 13 (11.9%) normal spirometry (GOLD 0), 32 (29.4%) mild and 64 (58.7%) moderate. For COPD patients, 26.6% reported an mMRC dyspnea grade of 0 (“Not troubled by breathlessness except on strenuous exercise”), 54.1% reported an mMRC of 1, 12.8% reported an mMRC of 2 and 6.4% reported an mMRC of 3 (“Stops for breath after walking about 100m or after a few minutes on the level”). For apparently healthy adults, 71.9% reported an mMRC of 0, 25.9% reported an mMRC of 1 and 0.7% reported an mMRC of 2. On average, patient had been living with a diagnosis of COPD for a median (IQR) of 5.0 (9.3) years.

Unadjusted sample characteristics are provided in Table 3.1. COPD patients were older, comprised fewer females, were more likely to be retired, had a lower household income, had a higher postcode deprivation score, comprised more current and former smokers, were more breathless, had a higher BMI and larger waist circumference, reported a lower usual walking

speed and achieved a shorter ISWT distance compared with apparently healthy adults. COPD patients had a low perceived general health index; reported more limitations with mobility, performing self-care tasks and usual activities and reported higher levels of pain or discomfort (Appendix I). Despite having a greater average BMI, the prevalence of overweight (41.3 versus 34.8%) or obesity (30.3 versus 25.2%) did not differ significantly between patients and apparently healthy adults.

3.3.2 Physical activity and sedentary time

Overall accelerometer compliance (≥10 waking hours) for seven days was 94.7%, ≥six days was 98.8% and ≥five days was 99.6%. Compliance did not differ significantly between COPD patients and apparently healthy adults. Average accelerometer waking wear time was 957.2±50.6 minutes with COPD patients having longer waking wear time than apparently healthy adults (965.2±50.7 versus 950.6±49.8 minutes).

Accelerometry-derived physical activity and sedentary time analysis revealed COPD patients to be more sedentary (by ~75 minutes/day) and accumulated less time in light activity (by ~43 minutes/day) and MVPA (by ~20 minutes/day) compared with apparently healthy adults (Table 3.1). Average movement intensity (VMCPM) was significantly lower for COPD patients. These observations remained after controlling for confounders (age, gender, smoking status, employment status and accelerometer waking wear time).

Table 3.1 Sample characteristics stratified by COPD status, reported as mean (SD) unless otherwise stated (* $p<0.05$)

	Whole sample (n=244)	**COPD patients (n=109)**	**Apparently healthy adults (n=135)**
Demographics			
Age (years)	61.7 (8.9)	65.7 (7.1)	58.5 (9.0) *
Gender (female, %)	131 (53.7)	42 (38.5)	89 (65.9) *
Employment status (%):			
Employed	100 (41.0)	28 (25.7)	72 (53.3) *
Unemployed	19 (7.8)	12 (11.0)	7 (5.2) *
Retired	125 (51.2)	69 (63.3)	56 (41.5) *
Household income β (%):			
<£18,000	55 (22.5)	40 (36.7)	15 (11.1) *
£18,000-30,999	70 (28.7)	31 (28.4)	39 (28.9)
£31,000-51,999	54 (22.1)	17 (15.6)	37 (27.4) *
£52,000-99,999	40 (16.4)	6 (5.5)	34 (25.2) *
≥£100,000	4 (1.6)	0 (0)	4 (3.0) *
IMD deprivation score	17.2 (15.7)	21.6 (17.8)	13.8 (12.8) *

Postcode percentage green space	50.4 (31.2)	51.4 (31.7)	49.6 (30.9)
24-hour accelerometry-derived behaviour			
Waking wear time (min)	957.2 (50.6)	965.2 (50.7)	950.6 (49.8) *
Sleep (min)	449.7 (53.6)	440.7 (62.8)	456.8 (44.1) *
VMCPM	2245 (573)	1974 (489)	2465 (543) *
Sedentary (min)	549.0 (99.7)	591.7 (90.4)	514.3 (93.4) *
Light activity (min)	379.8 (85.2)	356.3 (96.2)	399.0 (69.8) *
MVPA (min)	28.2 (25.6)	17.1 (16.1)	37.2 (28.3) *
Respiratory health			
Smoking status (%):			
Current	26 (10.7)	18 (16.5)	8 (5.9) *
Former	138 (56.6)	78 (71.6)	60 (44.4) *
Never	79 (32.4)	12 (11.0)	67 (49.6) *
Pack years	30.1 (24.4)	38.8 (25.0)	14.4 (12.8) *
FEV_1 (L)	2.5 (0.7)	2.0 (0.7)	2.8 (0.6) *
FEV_1%pred	93.2 (23.5)	76.2 (17.8)	107.0 (17.9) *
FVC (L)	3.8 (0.9)	3.6 (1.0)	3.9 (0.8) *
FEV_1/FVC	65.3 (12.1)	56.0 (11.2)	72.8 (6.3) *
mMRC score	0.6 (0.7)	1.0 (0.8)	0.3 (0.5) *
Perceived general health			
General health index value	0.840 (0.157)	0.775 (0.181)	0.893 (0.109) *
General health VAS score	82.0 (15.4)	75.0 (18.0)	87.7 (9.9) *
Body composition			
BMI (kg/m^2)	27.7 (5.4)	28.6 (5.6)	26.9 (5.2) *
Percentage body fat	29.3 (8.4)	28.8 (8.6)	29.7 (8.2)
Waist circumference (cm)	94.4 (15.0)	99.9 (13.9)	89.9 (14.4) *
Physical function			
ISWT (m)	495.8 (200.6)	387.4 (158.5)	580.1 (189.5) *
QMVC (kg)	36.8 (14.1)	34.9 (13.2)	38.3 (14.7)
Grip strength (kg)	35.9 (10.7)	35.7 (10.9)	36.0 (10.5)
Usual walking speed (%):			
Slow	32 (13.1)	29 (26.6)	3 (2.2) *
Average	136 (55.7)	63 (57.8)	73 (54.1)
Fairly brisk	71 (29.1)	15 (13.8)	56 (41.5) *
Brisk	5 (2.0)	2 (1.8)	3 (2.2)

Abbreviations: BMI, body mass index; FEV_1, forced expiratory volume in one second; FEV_1%pred, forced expiratory volume in one second percentage predicted; FVC, forced vital capacity; IMD, index of multiple deprivation; ISWT, incremental shuttle walk test; LPA, light physical activity; mMRC, modified Medical Research Council; MVPA, moderate-to-vigorous physical activity; QMVC, quadriceps maximal voluntary contraction; VAS, visual analogue scale; VMCPM, vector magnitude counts per minute

β, 15 (13.7%) COPD patients and 6 (4.5%) apparently healthy adults did not provide an answer

Figure 3.2 shows the proportion of time spent sleeping, sedentary, in light activity and in MVPA for COPD patients (Panel A) and apparently healthy adults (Panel B). COPD patients spent 42% of their day sedentary (equating to almost 66% of the waking day) compared with 37% for apparently healthy adults (equating to just over 50% of their waking day).

Apparently healthy adults accumulated almost three times the amount of MVPA per day compared to COPD patients.

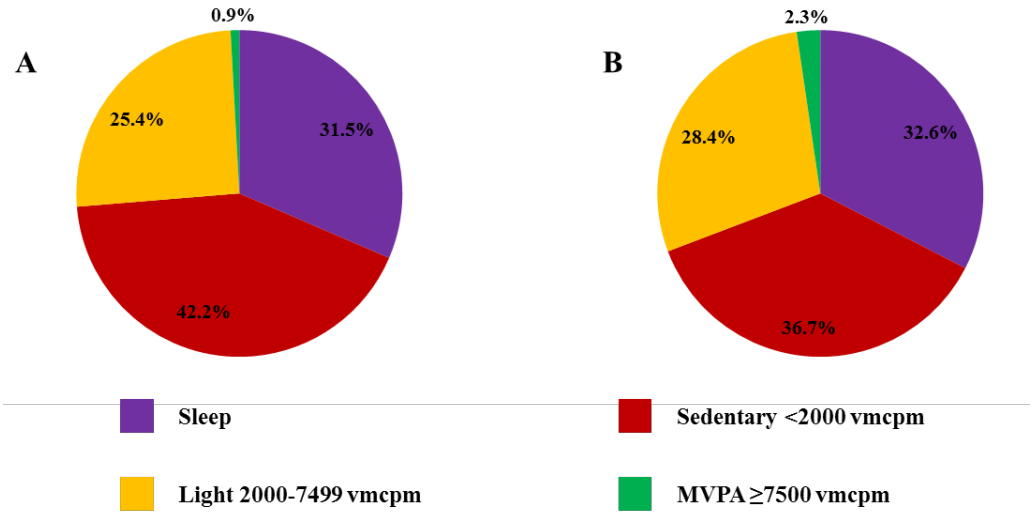

Figure 3.2 Physical activity, sedentary time and sleep as a percentage of an average 24-hour day for COPD patients (Panel A) and apparently healthy adults (Panel B)

3.3.3 Univariate correlates of behaviour

COPD patients

Partial correlations (controlling for accelerometer waking wear time) showed that being male, mMRC score, problems with mobility, problems performing usual activities, BMI and waist circumference were positively associated with sedentary time (Table 3.2). General health index value, general health score, usual walking speed and ISWT were significantly negatively associated with sedentary time. The same variables (except for general health score and index) value were associated with light activity, but in the opposite direction. For MVPA, significant positive associations were observed for general health score, usual walking speed and ISWT. Significant negative associations were found for age, mMRC score, problems with self-care (e.g. washing, getting dressed) and waist circumference. The strength of associations for all variables were either “weak” or “very weak”. Retired COPD patients had significantly lower levels of MVPA than employed patients, after controlling for accelerometer waking wear time (13.4±1.8 versus 25.2±2.3 min, p=0.002).

Apparently healthy adults

Factors significantly positively associated with sedentary time in apparently healthy adults based on partial correlations were age, postcode deprivation, mMRC score, BMI, percentage body fat and waist circumference (Table 3.3). Usual walking speed and ISWT were significantly negatively correlated with sedentary time. The same variables (except for age), in the opposite direction, were associated with light activity. Factors significantly positively associated with MVPA were usual walking speed and ISWT. Age and waist circumference were significantly negatively associated with MVPA. The strength of associations for all variables were either "weak" or "very weak". Retired apparently healthy adults had significantly lower levels of MVPA than employed apparently healthy adults controlling for accelerometer waking wear time (28.4±3.7 versus 45.1±3.2 min, p=0.002).

3.3.4 Independent correlates of behaviour

Factors significantly correlated with each activity variable (VMCPM, sedentary time, light activity and MVPA) were entered into linear regression models, controlling for age, gender, smoking status, employment status and accelerometer waking wear time (Table 3.3). Separately for the two samples (COPD patients and apparently healthy adults), factors associated with behavioural variables were then included in stepwise multiple linear regression models to identify independent correlates of physical activity and sedentary time (Table 3.4). When multiple measures of the same construct were present, only one measure was entered into the models. For perceived general health the index value was preferentially entered, for body composition percentage body fat was preferentially entered and for physical function ISWT was preferentially entered.

COPD patients

Regression analyses revealed that modified MRC score, problems with mobility, problems with self-care, problems performing usual activities, general health score, BMI, percentage body fat and waist circumference and ISWT were correlates of VMCPM. Modified mMRC score, problems with mobility, BMI, percentage body fat, waist circumference and ISWT were correlates of sedentary time and light intensity activity in COPD patients. Problems with self-care and ISWT were correlates of MVPA. Partial regression plots for factors independently associated with sedentary time (percentage body fat (Panel A) and mMRC (Panel B)) and MVPA (ISWT distance (Panel C)) are provided in Appendix J.

Apparently healthy adults

Regression analyses revealed that modified MRC score, BMI, percentage body fat, waist circumference and ISWT were correlates of VMCPM, sedentary time and light intensity physical activity. Percentage body fat and ISWT were correlates of MVPA. Partial regression plots for factors independently associated with sedentary time (ISWT distance (Panel A) and percentage body fat (Panel B)) and MVPA (percentage body fat (Panel C)) are provided in Appendix K.

Table 3.2 Partial correlations between correlates and time spent sedentary and in physical activity, after controlling for accelerometer waking wear time (**bold**, $p<0.05$). For significantly correlated variables, partial r is colour-coded according to strength of associations: Dark orange "very weak" and amber "weak".

	VMCPM		Sedentary		Light		MVPA	
	COPD	**AHA**	**COPD**	**AHA**	**COPD**	**AHA**	**COPD**	**AHA**
Demographics								
Age	**-0.253**	**-0.284**	0.109	**0.173**	-0.047	-0.073	**-0.378**	**-0.330**
Gender [A]	-0.168	-0.137	**0.233**	0.120	**-0.214**	-0.110	-0.181	-0.083
Income [B]	0.061	0.109	0.024	-0.123	-0.023	0.092	-0.011	0.135
IMD deprivation	0.031	**-0.221**	0.047	0.109	-0.065	-0.103	0.089	-0.067
Postcode green space	**-0.193**	0.014	0.100	0.009	-0.076	-0.010	-0.167	-0.003
Respiratory health								
Smoking status [C]	-0.064	0.111	0.026	-0.150	-0.021	0.130	-0.038	0.123
Pack years	0.024	0.014	0.032	0.008	-0.028	-0.024	-0.035	0.038
FEV_1	-0.025	0.006	0.090	0.048	-0.117	-0.082	0.123	0.059
FEV_1%pred	0.002	0.086	-0.019	-0.010	-0.006	0.001	0.144	0.027
mMRC score	**-0.301**	**-0.219**	**0.301**	**0.240**	**-0.296**	**-0.226**	-0.123	-0.156
Perceived general health								
Index value	**0.258**	0.103	**-0.207**	0.020	0.190	-0.049	0.163	0.068
Mobility [D]	**-0.287**	-0.107	**0.268**	0.075	**-0.252**	-0.047	-0.174	-0.105
Self-care [D]	**-0.189**	-0.031	0.146	-0.028	-0.119	0.061	**-0.197**	-0.068
Usual activities [D]	**-0.245**	-0.098	**0.202**	0.027	-0.181	-0.004	-0.178	-0.071
Pain/discomfort [D]	-0.178	-0.130	0.145	0.029	-0.127	0.027	-0.143	-0.150
Anxiety/depression [D]	0.001	0.005	-0.018	-0.046	0.015	0.033	0.022	0.055
Health scale	**0.198**	**0.189**	**-0.190**	-0.144	0.166	0.121	**0.191**	0.127
Body composition								
BMI	**-0.239**	**-0.296**	**0.199**	**0.337**	**-0.193**	**-0.357**	-0.099	-0.118
Percentage body fat	-0.119	**-0.210**	0.069	**0.241**	-0.076	**-0.239**	0.018	-0.125
Waist circumference	**-0.318**	**-0.324**	**0.306**	**0.350**	**-0.285**	**-0.341**	**-0.211**	**-0.195**
Physical function								
ISWT	**0.326**	**0.301**	**-0.270**	**-0.314**	**0.225**	**0.286**	**0.331**	**0.263**
QMVC	0.052	0.065	-0.002	-0.013	0.009	-0.028	-0.039	0.108
Grip strength	-0.117	-0.030	0.154	0.037	-0.148	-0.051	-0.084	0.016
Usual walking speed [E]	**0.277**	**0.292**	**-0.219**	**-0.241**	**0.191**	**0.182**	**0.228**	**0.264**

Abbreviations: AHA, apparently healthy adults; BMI, body mass index; FEV_1, forced expiratory volume in one second; FEV_1%pred, forced expiratory volume in one second percentage predicted; IMD, index of multiple deprivation; ISWT, incremental shuttle walk test; LPA, light intensity physical activity; mMRC, modified Medical Research Council; MVPA, moderate-to-vigorous physical activity; QMVC, quadriceps maximal voluntary contraction; vmcpm, vector magnitude counts per minute

[A], 0=female, 1=male; [B], 1= less than £18,000, 2=£18,000-30,999, 3=£31,000-51,999, 4=£52,000-99,999, 5=£100,000+; [C], 1=current, 2=former, 3=never; [D], 1=no, 2=slight, 3=moderate, 4=severe, 5=unable/extreme (problems/pain/anxiety); [E], 1=slow, 2= average, 3=fairly brisk, 4= brisk

Table 3.3 Linear regression analysis, controlling for age, gender, smoking status, employment status and accelerometer waking wear time, with VMCPM, sedentary time, light activity and MVPA as the dependent variables for COPD patients and apparently healthy adults (**bold**, $p<0.05$)

	VMCPM				**Sedentary time**				**Light activity**				**MVPA**			
	COPD		**AHA**		**COPD**		**AHA**		**COPD**		**AHA**		**COPD**		**AHA**	
Variables	**B (SE)**	**Partial R^2**	**B (SE)**	**Partial R^2**	**B (SE)**	**Partial R^2**	**B (SE)**	**Partial R^2**	**B (SE)**	**Partial R^2**	**B (SE)**	**Partial R^2**	**B (SE)**	**Partial R^2**	**B (SE)**	**Partial R^2**
Respiratory health																
mMRC score	**-222.78 (53.84)**	**0.144**	**-228.50 (96.32)**	**0.043**	**35.98 (10.81)**	**0.099**	**39.780 (15.062)**	**0.053**	**-33.334 (10.367)**	**0.093**	**-32.234 (12.629)**	**0.050**	-2.642 (1.794)	0.021	-7.543 (5.080)	0.017
Perceived general health																
Index Value	**581.10 (261.21)**	**0.047**	54.90 (428.98)	<0.001	-79.43 (50.43)	0.024	56.227 (70.328)	0.005	69.976 (48.357)	0.021	-49.161 (60.545)	0.005	9.458 (8.102)	0.014	-7.123 (21.865)	0.001
Mobility [A]	**-131.35 (50.74)**	**0.062**	-84.08 (127.77)	0.003	**23.71 (9.58)**	**0.057**	6.560 (20.192)	0.001	**-21.746 (9.177)**	**0.052**	-5.366 (17.095)	0.001	-1.971 (1.558)	0.016	-1.192 (6.661)	<0.001
Self-care [A]	**-202.05 (95.27)**	**0.042**	68.31 (375.19)	<0.001	19.47 (18.75)	0.011	-40.162 (58.975)	0.004	-13.265 (17.972)	0.005	45.160 (49.856)	0.006	**-6.204 (2.937)**	**0.042**	-5.018 (19.481)	0.001
Usual activities [A]	**-153.21 (58.79)**	**0.064**	-146.15 (158.32)	0.007	22.38 (11.35)	0.038	2.563 (25.738)	<0.001	-19.907 (10.879)	0.033	1.364 (22.160)	<0.001	-2.484 (1.830)	0.018	-3.928 (7.977)	0.002
Health scale	**5.31 (2.57)**	**0.040**	8.92 (4.60)	0.029	-0.77 (0.49)	0.024	-1.017 (0.733)	0.015	0.631 (0.467)	0.018	0.678 (0.622)	0.009	0.137 (0.077)	0.030	0.340 (0.240)	0.016
Body composition																
BMI	**-19.81 (8.01)**	**0.057**	**-33.73 (8.63)**	**0.107**	**3.54 (1.51)**	**0.052**	**5.737 (1.351)**	**0.125**	**-3.217 (1.446)**	**0.047**	**-4.845 (1.143)**	**0.124**	-0.319 (0.245)	0.017	-0.891 (0.466)	0.028
Percentage body fat	**-25.88 (7.07)**	**0.116**	**-25.62 (6.17)**	**0.120**	**4.61 (1.36)**	**0.103**	**4.195 (0.973)**	**0.130**	**-4.313 (1.298)**	**0.099**	**-3.355 (0.830)**	**0.116**	-0.297 (0.226)	0.017	**-0.839 (0.328)**	**0.050**
Waist Circ.	**-9.77 (3.28)**	**0.080**	**-12.00 (3.42)**	**0.088**	**1.67 (0.62)**	**0.067**	**2.065 (0.534)**	**0.106**	**-1.485 (0.596)**	**0.058**	**-1.705 (0.453)**	**0.100**	-0.182 (0.101)	0.031	-0.359 (0.182)	0.030
Physical function																
ISWT	**1.22 (0.30)**	**0.149**	**1.02 (0.25)**	**0.120**	**-0.19 (0.06)**	**0.099**	**-0.164 (0.039)**	**0.125**	**0.155 (0.056)**	**0.074**	**0.130 (0.033)**	**0.110**	**0.033 (0.009)**	**0.116**	**0.034 (0.013)**	**0.049**
Usual walking speed [B]	**200.71 (65.02)**	**0.085**	**222.21 (77.69)**	**0.060**	**-27.92 (12.60)**	**0.046**	**-30.392 (12.357)**	**0.045**	22.181 (12.132)	0.032	**20.714 (10.543)**	**0.030**	**5.739 (1.973)**	**0.077**	**9.698 (4.051)**	**0.043**

Abbreviations: AHA, apparently healthy adults; BMI, body mass index; ISWT, incremental shuttle walk test; mMRC, modified Medical Research Council; vmcpm, vector magnitude counts per minute

[A], 1=no, 2=slight, 3=moderate, 4=severe, 5=unable/extreme problems; [B], 1=slow, 2= average, 3=fairly brisk, 4= brisk

Table 3.4 Stepwise multiple linear regression analysis identifying variables associated with physical activity and sedentary time; controlling for age, gender, smoking status, employment status and accelerometer waking wear time

	VMCPM		
	B (SE)	**Partial R^2**	***p***
COPD (R^2=0.283)			
mMRC score	-179.363 (54.682)	0.096	0.001
Percentage body fat	-19.054 (7.070)	0.067	0.008
AHA (R^2=0.243)			
Percentage body fat	-16.904 (7.406)	0.041	0.024
ISWT	0.637 (0.294)	0.037	0.032
	Sedentary time		
	B (SE)	**Partial R^2**	***p***
COPD (R^2=0.229)			
Percentage body fat	3.754 (1.374)	0.072	0.008
mMRC score	29.567 (11.258)	0.067	0.010
AHA (R^2=0.363)			
ISWT	-0.105 (0.046)	0.041	0.024
Percentage body fat	2.566 (1.164)	0.038	0.029
	Light activity		
	B (SE)	**Partial R^2**	***p***
COPD (R^2=0.230)			
Percentage body fat	-3.555 (1.322)	0.070	0.008
mMRC score	-27.135 (10.833)	0.062	0.014
AHA (R^2=0.170)			
ISWT	0.128 (0.033)	0.108	<0.001
	MVPA		
	B (SE)	**Partial R^2**	***p***
COPD (R^2=0.358)			
ISWT	0.033 (0.009)	0.116	0.001
AHA (R^2=0.173)			
Percentage body fat	-0.839 (0.328)	0.050	0.012

Abbreviations: AHA, apparently healthy adults; BMI, body mass index; ISWT, incremental shuttle walk test; mMRC, modified Medical Research Council; vmcpm, vector magnitude counts per minute

3.4 Discussion

Correlates of objectively measured physical activity and sedentary time have not been sufficiently explored in mild-moderate COPD patients. Understanding the factors associated with lifestyle behaviours are important for the successful development of early, tailored interventions in COPD. In this study, mild-moderate COPD patients were found to be less physically active and more sedentary than apparently healthy adults but had similar behavioural correlates. However, different correlates were identified for objectively measured physical activity and sedentary time in both groups. For COPD patients, exercise capacity (ISWT) was an independent correlate of MVPA whilst self-reported breathlessness and percentage body fat were independent correlates of sedentary time and light intensity activity.

Although patients in this study had mild-moderate COPD, they were still found to be less physically active (17 versus 37 minutes of MVPA per day) and spend more time sedentary (592 versus 514 minutes per day) compared with apparently healthy adults. Even when patients were physically active, most of their time was spent in light activity (97% of total activity time). Whilst direct comparisons cannot be made between wrist and waist accelerometry locations, this finding is consistent with previous work which found patients to spend 34 minutes more sedentary per day compared to apparently healthy adults in the US (Park et al., 2013). These patients were also found to spend only 0.007% of their day in MVPA (Park et al., 2013). Equally concerning is the high amount of total sedentary time accumulated each day (~62% of their waking day) given the independent health risks of being sedentary on cardiometabolic health (Healy et al., 2007; Healy et al., 2008). This is particularly important as over one-quarter of COPD patient deaths are primarily caused by cardiovascular disease (McGarvey et al., 2007). Overall these observations support existing work demonstrating lower levels of physical activity (Park et al., 2013; H. Van Remoortel et al., 2013) and more time spent sedentary (Park et al., 2013) in mild-moderate COPD compared with apparently healthy adults. Together, findings suggest that mild-moderate patients require interventions targeting increases in MVPA *and* reductions in sedentary time. Correlates identified in the present study can help inform tailored interventions for these patients.

Dyspnea is the characteristic symptom of COPD and both the present study and previous work (Park et al., 2013) has found breathlessness to be related to more time sedentary. However, it is important to note that low explained variance (6-10%) was observed. Therefore, assessing patients' breathlessness is not sufficient to infer levels of physical activity or sedentariness. Similar observations (Watz et al., 2009) support the notion that mild-moderate patients reporting a high breathlessness burden may require interventions targeting the displacement of sedentary time with light activity. However, other work has found longer sitting time to be associated with external regulation in exercise (no choice, "others make me do it") and use of long-term oxygen therapy; suggesting symptoms may be more limiting in more advanced COPD rather than in mild disease (Hartman et al., 2013). Patients with mild-moderate COPD reporting high levels of dyspnea have been found to have worse 3-year all-cause hospitalisation rates compared to patients with severe airflow limitation reporting low levels of breathlessness (Lange et al., 2012). With a one unit change in mMRC score (e.g. from mMRC 0 to 1) associated with ~30 more minutes spent sedentary,

the present study clearly highlights that breathlessness and behaviour are associated even in the milder COPD.

Body fat percentage was independently positively associated with sedentary time and negatively associated with light intensity activity in COPD patients. Whilst there is support for the impact of body composition on behaviour in COPD (Park et al., 2013), conflicting evidence in this population also exists (McGlone, Venn, Walters, & Wood-Baker, 2006; Moy et al., 2009). COPD patients reporting more severe symptoms have been found to have five-to-eight-times higher mortality rates from cardiovascular disease than patients reporting low symptom burden, regardless of the level of airflow obstruction (Lange et al., 2012); supporting the need to help patients achieve a healthier body composition. However, percentage body fat could only explain a small amount of variance for behaviour (4-7%). Results from the present study suggest weight loss for general health may be an important target for these patients. Therefore, pulmonary rehabilitation may need to broaden outcomes beyond exercise capacity and respiratory health for milder stage patients and incorporate regular objective measures of body composition.

Correlates of MVPA were found to differ from those of sedentary time and light activity in the present study; consistent with previous work (Park et al., 2013). Walking capacity, as measured by the ISWT, was independently associated with MVPA for COPD patients whereas body composition was found to be associated with MVPA for apparently healthy adults. Pitta and colleagues (Pitta et al., 2005) found exercise capacity (6MWD) to be the strongest predictor of walking time, standing time and movement intensity. COPD patients achieved shorter distances on the ISWT compared with apparently healthy adults, highlighting not only reduced levels of accelerometry-derived physical activity but also worse exercise capacity. Pulmonary rehabilitation has been found to be equally beneficial to patients with mild COPD compared with more severe patients (Jacome & Marques, 2016) supporting the need to refer patients before symptoms become too debilitating. Increased exercise capacity has been consistently positively associated with objectively assessed physical activity but improvements in physical functioning have failed to translate into subsequent increases in daily physical activity in COPD patients ranging in the severity of airflow obstruction (Egan et al., 2012). Therefore, it is not only important to improve exercise capacity but also to facilitate patients to make the most of these improvements in everyday life (through increasing their physical activity such as walking more).

The present study found that COPD patients in employment took part in more MVPA than those who were retired after controlling for age and other confounders. This is in contrast to previous work which found employment to be associated with lower sedentary time rather than more physical activity for COPD patients (Park et al., 2013). Together, these findings suggest that the transition from employment to retirement may be an important period for lifestyle interventions to reduce sedentary time and/or increase participation in MVPA in mild-moderate COPD patients. In future interventions and existing programmes such as pulmonary rehabilitation, employment status should not only be obtained for demographic descriptive data but should be used to help design tailored behaviour change strategies.

Findings from the present study suggest that patients with higher percentage body fat and those reporting more severe breathlessness may benefit from lifestyle interventions focussing on replacing sedentary time with light activity. However, it is only breathlessness that is a unique correlate of sedentary time and light activity for COPD patients when compared to apparently healthy adults. Exercise capacity was a unique correlate of MVPA for COPD patients compared with apparently healthy adults, for which body composition was independently associated. Therefore tailored interventions for mild-moderate COPD patients must recognise the unique correlates of behaviour and account for differences in identified correlates between behaviours of differing intensities. Overall, the results of the present study support the idea that pulmonary rehabilitation (despite ~81% of patients reporting mMRC of 0 or 1), physical activity promotion and reductions in sedentary time should be encouraged within the primary care setting (Chakravarthy, Joyner, & Booth, 2002) and that these initiatives need to be tailored for mild-moderate COPD patients.

Overall explained variances in physical activity and sedentary time were similar to previous work in mild-moderate COPD patients. The present study explained 23% (sedentary time and light activity) to 36% (MVPA) of the variance in behaviour for patients. In a study of mild-moderate patients recruited from primary care in the US, Park and colleagues (Park et al., 2013) explained 21.7% of the variance in sedentary time, 29.4% for light intensity activity and 30.5% for MVPA as determined by waist-worn accelerometry. Similarly, Hartman and colleagues (Hartman et al., 2013) were able to explain 25% of the variance in time spent walking in mild-moderate COPD patients.

Major strengths of the study include the recruitment of patients from primary care in which facilitated the recruitment of mild-moderate COPD patients who do not have the access to

research participation compared with patients attending rehabilitation or admitted to hospital. The comprehensive list of predictors and the use of objectively measured physical activity and sedentary time, the high accelerometer compliance and comparison to apparently healthy adults must also be noted. Recruitment bias may have occurred. For example, those patients concerned about their health, more able to complete the range of measures as part of the study or patients who are more physically active may have preferentially responded to the study invitation. The cross-sectional design of the study means causality cannot be inferred. Whilst the present sample was ethnically homogenous due to an insufficient sample of non-White COPD patients recruited, the lower occurrence of smoking (10% for Indian South Asians and 26% for White British) translates into fewer South Asian COPD patients and lower COPD admission rates in Leicestershire (Director of Public Health., 2010). As data from this study relates to mild-moderate COPD patients, stronger associations between physical activity and some related variables may have existed had more severe patients from the study been included. Whilst findings were materially unchanged when additional cut-point thresholds for sedentary time (<1853 vmcpm) (Koster et al., 2016), light activity (2000-8249 vmcpm) and MVPA (≥8250 vmcpm) (Kamada et al., 2016) no cut-points have yet been developed against criterion methods such as indirect calorimetry. Sedentary time was unable to discriminate between sitting and standing. Further advancements in the objective measurement of behaviour will provide richer insights into the role of physical activity and sedentary time in COPD.

3.5 Conclusion

Despite the early disease progression, mild-moderate COPD patients were less physically active and more sedentary than apparently healthy adults. Whilst factors predicting behaviour were similar between patients and apparently healthy adults, correlates differed for sedentary time and light activity compared to those of MVPA for patients. Patients with mild-moderate COPD reporting more severe breathlessness, with higher body fat percentage and poor exercise capacity would benefit from interventions targeted at increasing physical activity levels and/or reducing sedentary time. In established interventions such as pulmonary rehabilitation the addition of body composition as a key outcome for patients with mild-moderate COPD should be explored.

Chapter 4: Study Two

Title: Associations between physical activity and sedentary behaviour and symptom severity in mild-moderate COPD

4.1 Introduction

Determining the grade of a patient's COPD has traditionally been based solely on the degree of airflow limitation as determined by spirometry. More recently evidence has shown that due to the heterogeneous nature of COPD lung function alone does not sufficiently account for numerous extrapulmonary aspects of the disease such as breathlessness, muscle wasting and quality of life (Cooper, 2009; Hurst et al., 2010; Weatherall et al., 2009). Whilst breathlessness is the primary characteristic of COPD other symptoms include coughing, phlegm production and chest tightness with the severity of these symptoms fluctuating on a daily basis (Kessler et al., 2011). However, when these symptoms worsen beyond that of normal day-to-day variations patients can experience an exacerbation of their COPD (Celli & Barnes, 2007). Exacerbations are responsible for the majority of the economic burden of COPD; becoming more frequent and more severe as the disease progresses (Suter et al., 2011).

Commonly used measures of COPD symptom severity are the mMRC (Bestall et al., 1999) and CAT (Jones et al., 2009) questionnaires; both recommended for use by GOLD (Global Initiative for Chronic Obstructive Lung Disease., 2017). In an attempt to better reflect the complexity of COPD, the GOLD 2011 report created a combined assessment for improved patient stratification based on exacerbation risk (lung function or exacerbation history) and symptoms (CAT or mMRC) (Global Initiative for Chronic Obstructive Lung Disease., 2011). The combined assessment is provided in Figure 1.6 and its conception resulted in a 'GOLD rush' of research into its utility (Soriano, 2013). Following the subsequent findings a revised combined COPD assessment has been produced based only from exacerbation history and symptoms (mMRC and CAT) with spirometry now recommended in conjunction with the revised combined COPD assessment (Global Initiative for Chronic Obstructive Lung Disease., 2017).

For all patients with COPD, symptom severity can vary greatly but it has generally been considered that patients with mild-moderate disease are less burdened by their symptoms compared with more advanced patients (Guenette et al., 2011). However, it is now recognised that considerable reductions in exercise capacity and increases in dyspnea can occur in mild-

moderate patients and/or those with undiagnosed COPD (Troosters et al., 2010). Moreover, data from the Copenhagen Heart Study found that patients with mild-moderate COPD reporting high levels of dyspnea had significantly worse 3-year all-cause hospitalisation rates compared with severe COPD patients reporting low levels of breathlessness (Lange et al., 2012). Indeed, patients reporting high symptom severity had five-to-eight-times higher mortality rates from cardiovascular disease and cancer than patients reporting low symptom burden, regardless of the level of airflow obstruction (Lange et al., 2012). Notably, an international survey across Europe and North America found that over a third of mild-moderate patients reported sometimes being too breathless to leave the house (Rennard et al., 2002).

Patients with mild-moderate COPD reporting a high degree of symptom burden likely require additional self-management programmes. These individuals may be a particularly important sub-group of patients who may benefit from behavioural or exercise-based interventions. Despite this, pulmonary rehabilitation is scarcely prescribed to mild-moderate COPD patients (Steiner, Holzhauer-Barrie, Lowe, Searle, Skipper, Welham, & Roberts, 2015b). Therefore, understanding what factors are associated with patients reporting higher levels of symptom burden is needed in order to improve patient stratification and to identify the interventions that will be most beneficial to them. Exercise programmes are established interventions to improve patient wellbeing (Lacasse, Goldstein, Lasserson, & Martin, 2006) but there is increasing recognition of the importance of targeting increases in physical activity (Garcia-Aymerich et al., 2006; Troosters et al., 2013) and reductions in sedentary behaviour (Hill et al., 2015). Much of the literature has focussed on evaluating patients' symptoms in the context of the GOLD 2011 combined assessment and attempting to calibrate the range of questionnaires assessing symptoms but little is known about the factors associated with perceptions of more severe symptoms in patients with mild-moderate COPD.

The aims of the present study on mild-moderate COPD patients were to (i) identify factors associated with self-reported symptom severity and exacerbation history and (ii) compare physical activity and sedentary time in patients according to their symptom severity and exacerbation history. It was hypothesised that better exercise capacity, more time being physically active and spending less time sedentary would be associated with lower self-reported symptom severity and fewer exacerbations in the preceding year.

4.2 Methods

Data used in this chapter was taken from the PhARaoH Study as described in Chapter 2 and has been previously published (Orme et al., 2016).

Inclusion/exclusion criteria

From the original PhARaoH sample (n=436), all participants aged 40-75 with a diagnosis of COPD according to their general practitioner were included (n=139). COPD patients were excluded from the present study if they were classified as GOLD III or IV (n=21), spirometry had not being conducted (n=2), if they reported a 'non-white' ethnicity (due to insufficient sample, n=5), if they had missing CAT score (n=2) and if they had less than four valid days of accelerometry (n=2). The final sample comprised 107 COPD patients.

Statistical analysis

Analyses were conducted using SPSS (version 23.0). Normal distribution for all variables was conducted using the Kolmogorov-Smirnov test with $p<0.05$ signifying non-normal distribution. Data were reported as mean (SD). Unadjusted comparisons between two groups for parametric data were performed using an independent t-test. Unadjusted frequency comparisons between groups were performed using Chi-square ($n>5$) or Fischer exact test ($n\leq5$). Covariate-adjusted (age, gender, smoking status, employment status and accelerometer waking wear time where appropriate) group comparisons for ratio data were performed using ANCOVA.

The level of agreement between symptoms scores for the components of the CAT questionnaire and between CAT score and mMRC grade were examined using the Kappa statistic (Landis & Koch, 1977) and were interpreted according to McHugh (McHugh, 2012) (Table 4.1). Univariate analyses were conducted using bivariate correlations. Pearson's r was used for data meeting parametric assumptions and Spearman's Rho was used for non-parametric data. Correlation coefficients were interpreted according to Evans (Evans, 1996) (Table 4.1).

Table 4.1 Interpretation of the Kappa statistic (McHugh, 2012) and correlation coefficients (Evans, 1996)

Kappa statistic	Level of agreement	Correlation coefficient	Strength of association
0.00-0.20	None	0.00-0.19	Very weak
0.21-0.39	Minimal	0.20-0.39	Weak
0.40-0.59	Weak	0.40-0.59	Moderate
0.60-0.79	Moderate	0.60-0.79	Strong
0.80-0.90	Strong	0.80-1.00	Very strong
0.91-1.00	Almost perfect		

Forced entry multiple linear regressions were used to examine predictors of CAT (and components), mMRC and exacerbation history; controlling for the above covariates. Variables reaching statistical significance ($p<0.05$) were entered into stepwise multivariate linear regression models to identify independent predictors of symptoms and unique explained variance (partial R^2). All models were checked for linear relationship, absence of multicollinearity, homoscedasticity and a normal distribution of residuals.

4.3 Results

4.3.1 Sample characteristics

Patient characteristics are provided in Table 4.2. No patients reported mMRC 4 ("Too breathless to leave the house or breathless when dressing or undressing") with 26.2% of patients reporting mMRC grade 0, 54.2% reporting mMRC 1 and 19.6% reporting mMRC ≥2. The majority of patients (56.1%) reported no exacerbations requiring steroids or antibiotics in the last 12 months. Using BMI, 30.8% of patients were classified as obese, 41.1% were overweight, 27.1% had a normal BMI and 0.9% of patients were classed as underweight.

Table 4.2 Sample characteristics, reported as mean (SD) unless otherwise stated (* $p<0.05$)

Sample characteristics	Whole sample (n=107)
Demographics	
Age (years)	65.8 (7.1)
Employment status: employed/unemployed/retired	28/11/68
IMD deprivation score	21.8 (17.9)
Respiratory health	
Smoking status: current/former/never	18/77/11
Pack years	38.7 (25.2)
FEV_1 (L)	2.0 (0.7)
FEV_1%pred	76.4 (17.9)
FVC (L)	3.7 (1.0)
FEV_1/FVC	55.0 (16.0)
Years since COPD diagnosis	7.6 (7.7)
Body composition	
BMI (kg/m^2)	28.7 (5.7)
Percentage body fat	28.7 (8.7)
Waist circumference (cm)	100.2 (13.8)
Physical function	
ISWT (m)	387.0 (159.7)
QMVC (kg)	35.0 (13.3)
Grip strength (kg)	36.0 (19.1)
Usual walking speed: slow/average/fairly brisk/brisk	28/63/14/2
24-hour accelerometry-derived behaviour	
Waking wear time (min)	965.7 (50.9)
Sleep (min)	440.7 (63.3)
VMCPM	1975 (493)
Sedentary (min)	591.4 (91.2)
Light activity (min)	357.2 (96.9)
MVPA (min)	17.0 (16.1)
Symptoms	
CAT score (0-40)	13.0 (7.5)
CAT score: 0-9/10-19/20-29/≥30	38/47/20/2
mMRC grade (0-4)	1.0 (0.8)
mMRC grade: 0/1/2/3	28/58/14/7
Exacerbations in the last 12 months	1.2 (1.8)
Exacerbations: 0/1/≥2	60/20/27

Abbreviations: BMI, body mass index; CAT, COPD Assessment Test; FEV_1, forced expiratory volume in one second; FEV_1%pred, forced expiratory volume in one second percentage predicted; FVC, forced vital capacity; ISWT, incremental shuttle walk test; LPA, light intensity physical activity; mMRC, modified Medical Research Council; MVPA, moderate-to-vigorous physical activity; QMVC, quadriceps maximal voluntary contraction; vmcpm, vector magnitude counts per minute

4.3.2 Comparison of CAT symptom components

The components of the CAT questionnaire cover a range of COPD-related symptoms, to which patients assign a score 0-5 with a higher score indicating greater severity/burden. Large variability in the proportion of scores for each component were observed (Figure 4.2) with almost a third (30%) of patients reporting a score of ≥4 for breathlessness and 88% of patients scoring ≤1 for confidence leaving the home. Agreement between CAT components was rated as either "none" or "minimal" (Appendix L) and associations between CAT components ranged from "very weak" to "strong" (Appendix M).

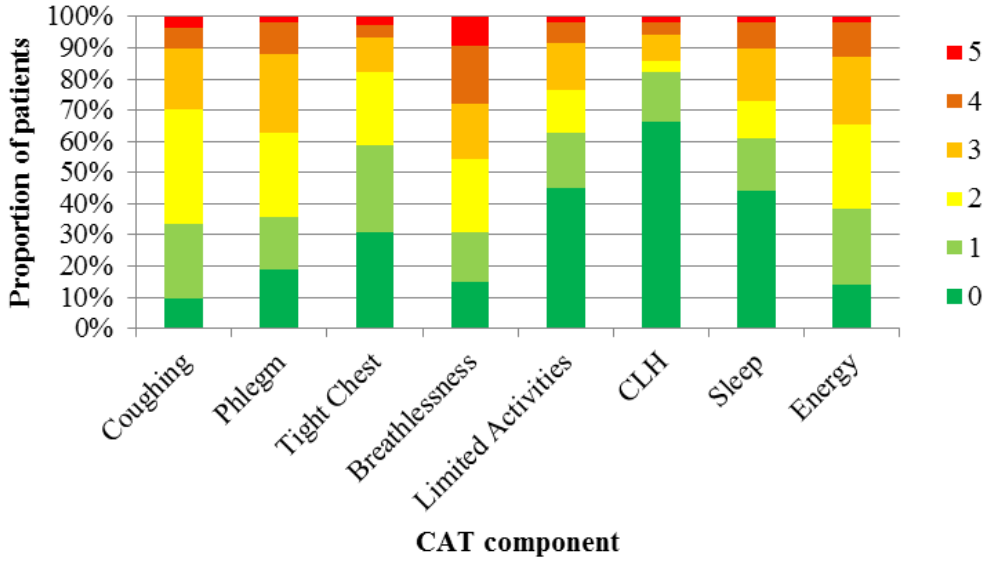

Figure 4.1 Proportion of patient scoring (0-5) the components of the CAT questionnaire. Abbreviation: CLH, confidence leaving the home

4.3.3 Factors associated with symptom severity

Linear regression analyses of factors associated with CAT score, mMRC grade and exacerbations (controlling for age, gender, smoking status, employment status and accelerometer waking wear time) are presented in Table 4.3. Factors associated with CAT score were gender, ISWT distance, usual walking speed, average movement intensity (VMCPM), sedentary time and light activity. Retired patients reported a significantly higher CAT score compared with employed patients after controlling for covariates (14.6±1.0 versus 9.0±1.5, p=0.016). Factors associated with mMRC grade were BMI, percentage body fat, waist circumference, ISWT distance, usual walking speed, average movement intensity, sedentary time and light activity. Unemployed patients reported a significantly higher mMRC score compared with employed patients (1.5±0.3 versus 0.7±0.2, p=0.006). Factors associated

with exacerbations were age, ISWT distance, usual walking speed, sedentary time and MVPA.

Sedentary time was significantly positively associated with mMRC independent of time spent in MVPA but produced a very small coefficient i.e. not clinically/behaviourally meaningful (B=0.003, *p*=0.003). MVPA was significantly negatively associated with exacerbation history independent of sedentary time (B=-0.031, *p*=0.014); equating to ~1 (0.93) less exacerbation in the last year with a 30 minute increase in MVPA per day. When sedentary time and MVPA were both entered into a multivariate regression model, significance was lost for both intensities for CAT score.

Table 4.3 Linear regression analysis, controlling for age, gender, smoking status, employment status and accelerometer waking wear time, to predict CAT score, mMRC grade and exacerbations (**bold**, $p<0.05$)

	CAT score		mMRC grade		Exacerbations	
Variables	**B (SE)**	**Partial R^2**	**B (SE)**	**Partial R^2**	**B (SE)**	**Partial R^2**
Demographics						
Age	-0.227 (0.127)	0.031	-0.017 (0.014)	0.014	**-0.082 (0.030)**	**0.068**
Gender [A]	**-2.981 (1.449)**	**0.040**	-0.075 (0.163)	0.002	-0.421 (0.344)	0.015
Respiratory health						
Years with COPD	**0.311 (0.115)**	**0.091**	0.023 (0.013)	0.042	-0.009 (0.029)	0.001
Body composition						
BMI	0.135 (0.126)	0.011	**0.040 (0.014)**	**0.077**	-0.009 (0.030)	0.001
Percentage body fat	0.101 (0.114)	0.008	**0.037 (0.012)**	**0.084**	-0.006 (0.027)	<0.001
Waist circumference	0.074 (0.052)	0.020	**0.018 (0.006)**	**0.097**	-0.004 (0.012)	0.001
Exercise capacity						
ISWT	**-0.015 (0.005)**	**0.093**	**-0.002 (0.000)**	**0.200**	**-0.003 (0.001)**	**0.052**
Usual walking speed [B]	**-3.774 (0.986)**	**0.127**	**-0.476 (0.109)**	**0.161**	**-0.535 (0.245)**	**0.045**
Accelerometer-derived behaviour						
VMCPM	**-0.004 (0.001)**	**0.066**	**-0.001 (0.000)**	**0.147**	-0.001 (0.000)	0.030
Sedentary †	**0.018 (0.008)**	**0.051**	**0.003 (0.001)**	**0.106**	**0.004 (0.002)**	**0.040**
Light activity †	**-0.018 (0.008)**	**0.044**	**-0.003 (0.001)**	**0.100**	-0.003 (0.002)	0.026
MVPA †	-0.078 (0.051)	0.023	-0.008 (0.005)	0.019	**-0.036 (0.012)**	**0.088**

Abbreviations: BMI, body mass index; CAT, COPD Assessment Test; ISWT, incremental shuttle walk test; mMRC, modified Medical Research Council; vmcpm, vector magnitude counts per minute
[A], 0=female, 1=male; [B], 1=slow, 2=average, 3=fairly brisk, 4=brisk

Factors that were significantly associated with symptom variables were included in stepwise multiple linear regression models to identify independent associations with symptom severity. When multiple measures of the same construct are present, only one measure was entered into the models. For body composition percentage body fat was preferentially entered (followed by BMI) and for exercise capacity the ISWT was preferentially entered. For behaviour VMCPM was preferentially entered when significant. Sedentary time and MVPA were both entered for exacerbations.

ISWT (B=-0.016±0.005, p=0.004) and years with COPD (B=0.319±0.122, p=0.011) were independently associated with CAT score uniquely explaining 11.7% and 7.1% of the variance, respectively. ISWT (B=-0.002±0.001, p<0.001) and VMCPM (B=0.0001±0.0000, p=0.011) were independently associated with mMRC grade uniquely explaining 12.3% and 5.0% of the variance, respectively. MVPA was independently associated with exacerbations (B=-0.034±0.012, p=0.005) uniquely explaining 8.1% of the variance.

4.3.4 Factors associated with CAT components

Analyses of factors associated with CAT components (controlling for age, gender, smoking status, employment status and accelerometer waking wear time) are presented in Table 4.4. Only deprivation score was associated with Coughing with no factors examined associated with Tight Chest.

Retired patients reported significantly higher Phlegm compared with employed patients (2.3±0.2 versus 1.4±0.3, p=0.022). Factors associated with Breathlessness were gender, waist circumference, ISWT distance, usual walking speed, average movement intensity, sedentary time, light activity and MVPA. Factors associated with Limited Activities were ISWT distance, usual walking speed average movement intensity, sedentary time, light activity and MVPA. Unemployed patients reported significantly higher Limited Activities compared with employed patients (2.1±0.5 versus 0.7±0.3, p=0.019). Factors associated with Confidence Leaving the Home were gender, BMI, percentage body fat, waist circumference, ISWT distance, usual walking speed average movement intensity and sedentary time. Retired patients reported significantly higher Confidence Leaving the Home scores compared with employed patients (1.0±0.2 versus 0.1±0.3, p=0.034). Factors associated with Sleep were gender and smoking status. Factors associated with Energy were gender, FEV_1%pred, ISWT, usual walking speed, average movement intensity, sedentary time and light activity.

When sedentary time and MVPA were both entered into a multivariate regression model, significance was lost for both intensities for Limited Activities. Sedentary time was significantly positively associated with Breathlessness (B=0.004, p=0.014) and Energy (B=0.003, p=0.026) independent of time spent in MVPA.

Deprivation score uniquely explained 5.9% of Coughing. VMCPM (B=-0.001±0.000, p<0.001) was independently associated with Breathlessness uniquely explaining 12.5% of the variance. ISWT (B=-0.004±0.001, p<0.001) was independently associated with Limited Activities uniquely explaining 15.6% of the variance. ISWT was independently associated

with Confidence Leaving the Home (B=-0.002±0.001, p=0.002) uniquely explaining 9.2% of the variance. ISWT was independently associated with Energy (B=-0.003±0.001, p<0.001) uniquely explaining 16.2% of the variance.

Table 4.4 Linear regression analysis (controlling for age, gender, smoking status, employment status, accelerometer waking wear time) to predict CAT components (**bold**, $p<0.05$)

	Coughing		Phlegm		Tight chest		Breathless		Limited activities		CLH		Sleep		Energy	
Variables	**B (SE)**	**Partial R^2**	**B (SE)**	**Partial R^2**	**B (SE)**	**Partial R^2**	**B (SE)**	**Partial R^2**	**B (SE)**	**Partial R^2**	**B (SE)**	**Partial R^2**	**B (SE)**	**Partial R^2**	**B (SE)**	**Partial R^2**
Demographics																
Gender [A]	-0.011 (0.243)	<0.001	0.116 (0.260)	0.002	-0.024 (0.262)	<0.001	**0.394 (0.207)**	**0.051**	-0.337 (0.192)	0.014	-0.166 (0.242)	0.005	**-0.710 (0.279)**	**0.044**	**-0.493 (0.169)**	**0.037**
Smoking status [B]	-0.124 (0.245)	0.003	0.001 (0.263)	<0.001	0.029 (0.264)	<0.001	0.099 (0.309)	0.001	-0.202 (0.287)	0.005	**-0.806 (0.240)**	**0.100**	**-0.609 (0.282)**	**0.060**	-0.296 (0.252)	0.013
Postcode deprivation	**-0.017 (0.007)**	**0.060**	-0.014 (0.007)	0.034	-0.001 (0.008)	<0.001	-0.009 (0.009)	0.011	-0.002 (0.008)	0.001	0.000 (0.007)	<0.001	0.001 (0.008)	<0.001	0.001 (0.007)	<0.001
Respiratory health																
FEV_1%pred	-0.007 (0.007)	0.013	-0.001 (0.007)	<0.001	0.003 (0.007)	0.001	-0.004 (0.008)	0.003	0.001 (0.008)	<0.001	0.007 (0.007)	0.011	0.008 (0.008)	0.011	**-0.014 (0.007)**	**0.043**
Body composition																
BMI	-0.028 (0.021)	0.017	-0.010 (0.023)	0.002	0.009 (0.023)	0.001	0.044 (0.027)	0.027	0.031 (0.025)	0.015	**0.050 (0.020)**	**0.056**	0.021 (0.024)	0.007	0.019 (0.022)	0.008
Waist circumference	-0.005 (0.009)	0.003	0.000 (0.009)	<0.001	0.002 (0.009)	<0.001	0.020 (0.011)	0.034	0.017 (0.010)	0.026	**0.019 (0.008)**	**0.049**	0.007 (0.010)	0.004	0.014 (0.009)	0.024
Exercise capacity																
ISWT	-0.001 (0.001)	0.008	0.000 (0.001)	<0.001	0.000 (0.001)	<0.001	**-0.003 (0.001)**	**0.092**	**-0.004 (0.001)**	**0.169**	**-0.002 (0.001)**	**0.093**	-0.001 (0.001)	0.016	**-0.003 (0.001)**	**0.165**
Usual walking speed [C]	-0.328 (0.174)	0.035	-0.063 (0.190)	0.001	-0.154 (0.190)	0.007	**-0.832 (0.207)**	**0.138**	**-0.939 (0.185)**	**0.205**	**-0.596 (0.164)**	**0.116**	-0.272 (0.202)	0.018	**-0.591 (0.172)**	**0.105**
Accelerometer-derived behaviour																
VMCPM	0.000 (0.000)	0.007	0.000 (0.000)	0.003	0.000 (0.000)	<0.001	**-0.001 (0.000)**	**0.136**	**-0.001 (0.000)**	**0.125**	**-0.001 (0.000)**	**0.047**	0.000 (0.000)	0.001	**-0.001 (0.000)**	**0.061**
Sedentary	0.001 (0.001)	0.009	0.001 (0.001)	0.005	0.000 (0.001)	0.001	**0.005 (0.002)**	**0.097**	**0.004 (0.001)**	**0.061**	**0.003 (0.001)**	**0.045**	0.001 (0.002)	0.003	**0.004 (0.001)**	**0.064**
Light	-0.001 (0.001)	0.007	0.001 (0.002)	0.008	0.000 (0.002)	0.001	**-0.005 (0.002)**	**0.081**	**-0.003 (0.002)**	**0.047**	**-0.003 (0.001)**	**0.041**	-0.001 (0.002)	0.002	**-0.004 (0.001)**	**0.059**
MVPA	0.008 (0.009)	0.008	0.006 (0.009)	0.004	0.000 (0.009)	<0.001	**-0.026 (0.010)**	**0.062**	**-0.025 (0.009)**	**0.068**	-0.011 (0.008)	0.015	-0.003 (0.010)	0.001	-0.012 (0.009)	0.017

Abbreviations: BMI, body mass index; CAT, COPD Assessment Test; CLH, confidence leaving the home; FEV_1%pred, forced expiratory volume in one second percentage predicted; ISWT, incremental shuttle walk test; mMRC, modified Medical Research Council; vmcpm, vector magnitude counts per minute

[A], 0=female, 1=male; [B], 1=current, 2=former, 3=never ; [C], 1=slow, 2=average, 3=fairly brisk, 4=brisk

4.3.5 Physical activity and sedentary time across symptom severities

For CAT, mMRC and exacerbation history, patients were grouped using pragmatic cut-offs to permit more equal sample sizes. Using the CAT score patients were put into three groups: CAT of 0-9 (n=38), 10-19 (n=47) and ≥20 (n=22). Using the mMRC patients were put into three groups: mMRC of 0 (n=28), 1 (n=58) and ≥2 (n=21). Using previous exacerbations patients were put into three groups: 0 (n=60), 1 (n=20) and ≥2 (n=27) exacerbations in the last year.

Patients reporting a CAT score of >20 had lower average movement intensity (VMCPM) (2120±77 versus 1700±101vmcpm, p=0.005), were more sedentary and took part in less light activity than patients reporting a CAT score of 0-10 (Figure 4.3). Patients reporting an mMRC score of ≥2 had lower average movement intensity (VMCPM) (2208±86 versus 1703±101vmcpm, p=0.001), were more sedentary and took part in less light activity than patients reporting an mMRC of 0 (Figure 4.4). Agreement between CAT and mMRC group classification was minimal (k=0.376). Half of patients classified as low CAT (0-10) also classified as low mMRC (grade 0) and 64% of patients classified as high CAT (>20) also classified as high mMRC (grade ≥2) (Appendix N). Patients reporting ≥2 exacerbations took part in less MVPA than patients reporting zero exacerbations (Figure 4.5).

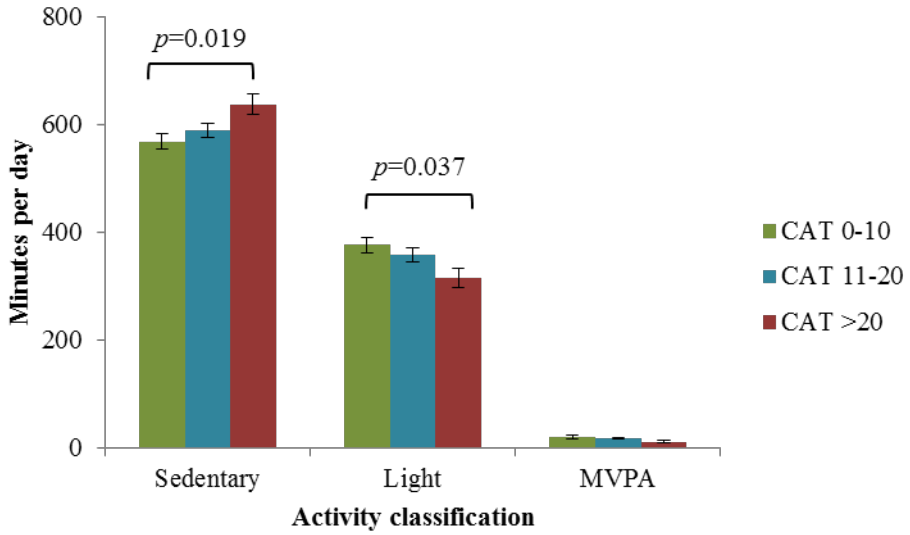

Figure 4.2 Comparison of sedentary time, light activity and MVPA across COPD patients grouped by CAT score. Higher the CAT score the greater the symptom severity.

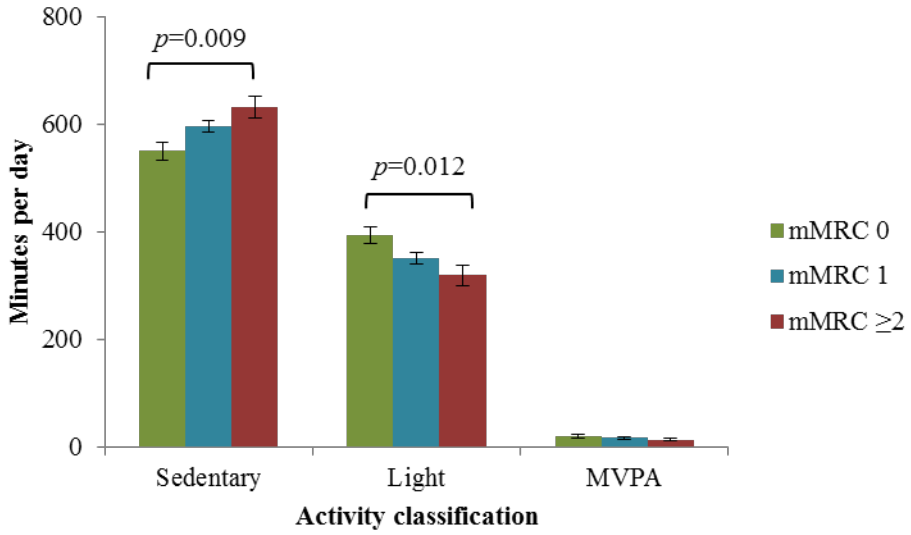

Figure 4.3 Comparison of sedentary time, light activity and MVPA across COPD patients grouped by mMRC grade. Higher the mMRC score the greater the dyspnea severity.

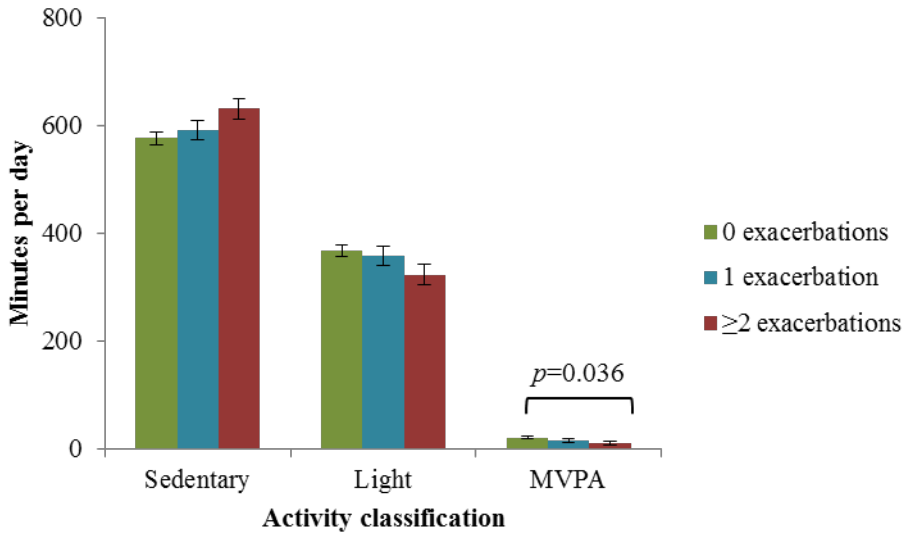

Figure 4.4 Comparison of sedentary time, light activity and MVPA across COPD patients grouped by the number of self-reported exacerbations in the last year.

4.3.6 Exercise capacity across symptom severities

After controlling for age, gender, smoking status and employment status, patients reporting a CAT score of >20 had a lower ISWT than patients reporting a CAT score of 0-10 (327.5±34.5 versus 433.6±24.6m, p=0.048). Patients reporting an mMRC score of 1 (382.8±18.3 versus 462.1±26.4m, p=0.045) or an mMRC score of ≥2 (267.8±34.1 versus 462.1±26.4m, p<0.001) had a lower ISWT than patients reporting an mMRC of 0. Patients reporting ≥2 exacerbations had a lower ISWT than patients reporting zero exacerbations (312.6±33.5 versus 414.5±19.6m, p=0.034).

4.4 Discussion

Patients with mild-moderate COPD who report severe symptoms are an important sub-group of patients who may require lifestyle and exercise interventions. The present study examined the relationships between measures of symptoms and previous exacerbations; identified factors associated with patient-reported symptom severity; and assessed how physical activity and sedentary time differ across degrees of symptom severity in mild-moderate COPD patients.

CAT and mMRC questionnaires shared common correlates including lower exercise capacity, less light intensity physical activity and more time spent sedentary. The role of physical activity in the management of COPD has become increasingly recognised but sustained behaviour change remains one of the biggest challenges in this population. Whilst sedentary behaviour has been recommended as a more suitable conduit for behaviour change than exercise (Cavalheri, Straker, Gucciardi, Gardiner, & Hill, 2015; Hill et al., 2015) few studies have specifically examined this behaviour (Orme et al., 2016). The present study highlights the importance of sedentary time in COPD; advocating that future studies not only target physical activity and exercise but also movement at the lower end of the intensity continuum (Chaput et al., 2014); even for more mild stage COPD patients.

Physical activity and exercise capacity should be interpreted as separate entities (Mitchell et al., 2016). In support of this was the finding in the present study that performance on the ISWT was associated with CAT score and mMRC grade after controlling for physical activity. However, the ISWT was only able to explain 12% of the variance for CAT and mMRC questionnaires. Physical activity (VMCPM for mMRC grade and MVPA for exacerbation history) was found to be independently associated with symptoms but explained less than 10% of symptom variance. That being said, patients reporting more severe symptoms (CAT score >20 or mMRC ≥2) spent 69-81 more minutes sedentary each day compared with patients reporting less severe symptoms (CAT score ≤10 or mMRC 0). Therefore, exercise capacity, physical activity and sedentary time partly explained some of the differences between mild-moderate patients reporting low and high symptom burdens. Whilst findings from the present study are in support of the National Institute for Health and Care Excellence (NICE) guidelines which state that pulmonary rehabilitation should be offered to patients who consider themselves functionally disabled by their COPD (usually mMRC ≥2) (National Institute for Health and Care Excellence (NICE)., 2010), exercise

capacity was found to be significantly lower in mMRC 1 patients compared to mMRC 0 patients. Therefore, mild-moderate patients may benefit from pulmonary rehabilitation even if they do not report severe dyspnea-related disability (mMRC ≥2). However, more work is needed to explore factors that could not be addressed in the present study which may be associated with patients of similar airflow obstruction reporting contrasting symptom burdens. Such factors may include dynamic hyperinflation (Van Helvoort et al., 2016), diet quality and medication adherence (Rabe, 2006).

Whilst the composite CAT score has been associated with hospitalisation (Papaioannou et al., 2014) and recovery after an acute exacerbation (Feliz-Rodriguez et al., 2013), by breaking the score down into its constituent parts a more detailed understanding of the inter-relationships between COPD symptoms can be gleaned. In the present study, agreement in the scoring of the component symptoms was poor; with coughing, phlegm, breathlessness and lack of energy contributing more to the composite CAT score than other symptoms. Strong associations between only coughing and phlegm scores and breathlessness and limited activities scores suggest that the CAT questionnaire comprises largely distinct entities. Therefore, the CAT questionnaire can not only identify mild-moderate patients reporting severe symptom burden but can also be used to identify particular symptoms that need to be targeted; providing a more personalised approach to symptom management. For example, seven day coughing history has been independently associated with health-related quality of life (Deslee, Burgel, Escamilla, & Chanez, 2016) and breathlessness and phlegm components have been predictive of COPD diagnosis (Raghavan et al., 2012).

Breaking down the CAT into its individual symptom components also provided additional insight into the role of physical activity, sedentary time and exercise capacity in patients of the same degree of airflow limitation reporting varying levels of symptom severity. Associations between behaviour and exercise capacity with breathlessness, limitations performing daily activities, confidence leaving the home and energy levels are supported by existing work. In a large international study conducting telephone interviews with over 1000 patients, the most frequent complaint from patients was shortness of breath and an inability to take part or complete activities they used to enjoy (Miravitlles, Anzueto, Legnani, Forstmeier, & Fargel, 2007). Therefore, physical activity is an important construct to patients to which COPD has a markedly negative impact (Miravitlles et al., 2007). Additionally, patients have reported that climbing the stairs and walking uphill are the first activities to be impacted by their COPD (Dobbels et al., 2014), with the present study demonstrating that significant

impacts of COPD can occur even in patients with mild-moderate respiratory impairment. Therefore, interventions are suggested targeting patients with mild-moderate COPD reporting severe symptoms before patients transition from adapting their behaviour (e.g. pacing themselves or slowing down, using aids and resting longer) to avoiding many activities altogether (Dobbels et al., 2014).

Strengths of the present study include the recruitment of patients from primary care in which facilitated the recruitment of mild-moderate COPD patients who do not have the access to research participation compared with patients attending rehabilitation or admitted to hospital. Additionally, the use of multiple measures of symptom severity, the examination of the component symptoms of the CAT questionnaire and the objective quantification of exercise capacity, physical activity and sedentary time with very high accelerometry compliance are also important strengths. However, the cross-sectional design of the study limits causal inference and the array of measures investigated may have led to some chance findings due to no correction for multiple comparisons The pragmatic analyses of individual CAT items when the questionnaire's validation was based on the composite score must be noted. Whilst mild-moderate patients reporting severe symptoms the present study was unable to examine patients with severe COPD reporting low symptoms. Future studies should explore reasons why these patients are less burdened by their COPD despite having more advanced disease. Whilst findings were consistent between additional cut-point thresholds for sedentary time (<1853 vmcpm) (Koster et al., 2016), light activity (2000-8249 vmcpm) and MVPA (≥8250 vmcpm) (Kamada et al., 2016) no cut-points have yet been developed against criterion methods such as indirect calorimetry. Sedentary time was unable to discriminate between sitting and standing. As the advancement of wrist-worn accelerometry continues, further behavioural insights into the role of physical activity and sedentary time in COPD will be obtained.

4.5 Conclusion

This study showed that measures of COPD symptoms should not be used interchangeably and exploring the individual components of the CAT questionnaire provides valuable additional insight into patients' perceptions of their symptoms and the factors associated with them. Patients with mild-moderate COPD vary considerably in the severity of their symptoms; with exercise capacity, low levels of physical activity and spending more time sedentary independently associated with greater symptom burden. Patients with mild-moderate COPD

reporting severe symptoms would benefit from lifestyle and exercise interventions. Patients should be stratified by exercise capacity and behaviour to inform personalised intervention designs.

Chapter 5: Study Three Rationale and Methods

Title: Study protocol for Chronic Obstructive Pulmonary Disease-Sitting and ExacerbAtions Trial (COPD-SEAT): a randomised controlled feasibility trial of a home-based self-monitoring sedentary behaviour intervention

5.1 Introduction

Targeting increases in physical activity in COPD patients has been the emphasis of a large number of exercise training and behaviour change interventions for over a decade (Watz et al., 2014). Despite these considerable efforts, there has been limited success (Cindy Ng, Mackney, Jenkins, & Hill, 2012; H. Watz et al., 2014). The lower levels of physical activity coupled with the often fragile physical and psychological health (e.g. low exercise capacity and low self-esteem) among COPD patients may make reducing sedentary behaviour a more suitable conduit for behaviour change (Cavalheri et al., 2015; Hill et al., 2015). Sedentary behaviour is defined as 'any waking behaviour characterised by an energy expenditure ≤1.5 metabolic equivalents while in a sitting or reclining posture' (Sedentary Behaviour Research, 2012). Patients with COPD demonstrate significantly higher levels of sedentary behaviour compared with apparently healthy adults (Pitta et al., 2005).

An acute exacerbation of COPD marks a critical life-event, characterised by a worsening of symptoms beyond normal day-to-day variation; bringing with it a plethora of negative impacts affecting both physical and psychological health (Celli & Barnes, 2007). For example, exacerbations contribute to reductions in patients' abilities to perform activities of daily living (Suter et al., 2011). For patients hospitalised for an acute exacerbation of COPD, there is amplitude attention at the initial phase of admission followed by approximately seven days of monitored inactivity and sedentariness (Morgan, 2003). Consequently, patients may be discharged less well equipped to manage their 'usual routine' than when they were admitted (Morgan, 2003). Interventions for COPD patients in close temporal proximity to hospital admissions are promising, with pulmonary rehabilitation within four weeks post-discharge, found to reduce re-hospitalisation in the preceding three months (Puhan et al., 2011). Despite this, post-discharge pulmonary rehabilitation is sparsely taken up by patients who are offered it at the point of discharge (Jones et al., 2014). A stepping stone approach which does not emphasise exercise and does not require travel and additional time/appointments may serve to facilitate the physical and psychological well-being required for patients to invest in pulmonary rehabilitation. To date, few studies have specifically

targeted non-rehabilitation physical activity or sedentary behaviour immediately after discharge. There is a need to determine the feasibility and acceptance of such programmes. Such an approach may even offer as an alternative for those patients unable to exercise at sufficient capacity to reduce readmission risk (Greening et al., 2014).

The time between hospital discharge and the commencement of pulmonary rehabilitation (for those who attend) marks an important period for patients. Pitta and colleagues (Pitta et al., 2006) highlighted that patients with low activity levels at one month after discharge were more likely to be readmitted within the following year. Therefore, there is a need for behavioural interventions for patients upon leaving the hospital in order to prevent further decline in quality of life, functional capacity and potentially encourage uptake of pulmonary rehabilitation. Due to the impact of an acute exacerbation (e.g. dyspnea and fatigue) interventions requiring large amounts of effort or time may be impracticable (Jones et al., 2014). Consequently, targeting sedentary behaviour (e.g. long periods of consecutive sitting) during the early stages of post-discharge recovery may act as a catalyst to encourage patients to sit less and move more; equipping them with the ethos and habits to better engage in pulmonary rehabilitation when the time comes. Furthermore, increasing light activity such as low intensity walking has been found to help to reduce the risk of readmissions (Donaire-Gonzalez et al., 2015). Indeed, physical inactivity is widely regarded as the strongest predictor of all-cause mortality in COPD (Waschki et al., 2011) and preliminary evidence has suggested that a reduction in sedentary time from discharge to six weeks will also help reduce the risk of readmissions (Andrzejowski et al., 2015).

Wearable technologies such as pedometers, which provide a basis for self-monitoring and real-time feedback, have been shown to elicit increases in physical activity in COPD patients (Kawagoshi et al., 2015; Mendoza et al., 2015). Patient-driven healthcare, facilitated by behavioural feedback and/or prompting, may empower patients to improve and track their health outcomes (Wicks, Vaughan, & Heywood, 2014). In a meta-regression to identify the active ingredients in activity promotion research, Michie (Michie, Abraham, Whittington, McAteer, & Gupta, 2009) found self-monitoring and feedback to be among the most potent behaviour change techniques. Coupling behaviour change strategies such as self-monitoring and feedback, which are grounded in Control Theory (Carver & Scheier, 1982), tend to have an impact greater than the sum of their independent effects (Michie et al., 2009). As supported by a comprehensive review of sedentary behaviour change strategies (Gardner, Smith, Lorencatto, Hamer, & Biddle, 2015), providing patients with education, self-

monitoring, real-time feedback and behaviour prompts may yield promising results. However, in post-exacerbation care for COPD patients the use of wearable technology for behaviour change has not been widely explored. Technology competency and psychosocial issues in this population, particularly during phases of acute illness, makes examining the uptake and engagement with such interventions fundamental to future success. The 'Chronic Obstructive Pulmonary Disease Sitting and ExacerbAtions Trial' ('COPD-SEAT') focussed on the feasibility of delivering a home-based sedentary behaviour self-monitoring intervention in patients following hospital discharge for an acute exacerbation.

The objectives of the trial were to:

1. Examine the feasibility of the 'COPD-SEAT' intervention including the trial design, recruitment, adherence and procedures.
2. Assess the acceptability of the intervention among patients receiving the intervention.
3. Reduce prolonged periods of sedentary behaviour at home in COPD patients admitted for an acute exacerbation.

5.2 Methods

Trial design and registration

The feasibility study was a three-armed randomised controlled trial with 1:1:1 individual allocation comparing usual care (Control) with usual care plus education (Education Intervention) and usual care with education plus feedback (Education + Feedback Intervention) (Orme et al., 2016) (Appendix O). Testing the feasibility of the randomisation process, patients responses to being randomised (e.g. drop-out before discharge) and comparing retention rates between groups was important to assess in order to inform a future larger trial. The design of the study and flow of participants is presented in Figure 5.1.

This study was conducted, analysed and reported according to the CONSORT statement for parallel group RCTs (Schulz, Altman, & Moher, 2010). Ethical approval was obtained from the Research Ethics Committee East Midlands Leicester Central (15-EM-0433) (Appendix P) and University Hospitals of Leicester acted as study sponsor. The trial was prospectively registered on the ISRCTN website (ISRCTN13790881). Template informed consent form and participant information sheet are provided in Appendix Q and R, respectively.

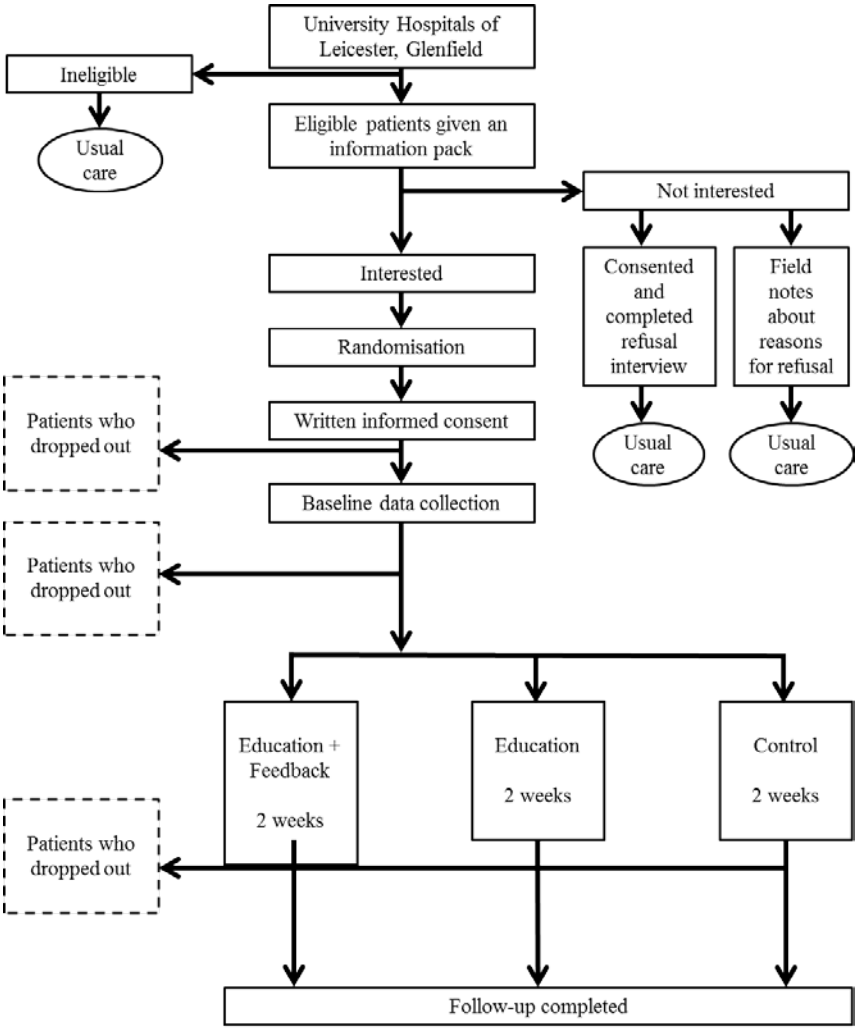

Figure 5.1 Patient flow through the study

Eligibility criteria for patients

Patients eligible for inclusion in the study were: aged between 40 and 85 years; a confirmed diagnosis of COPD; fewer than 4 exacerbations requiring hospital admission in the previous 12 months (as a marker for increased mortality risk (Soler-Cataluna et al., 2005)); a confirmed acute exacerbation as the reason for current hospitalisation; willingness and ability to comply with the trial protocol; ability to participate in light intensity physical activity (i.e. walking with an aid); and ability to provide informed consent (e.g. read and understand English).

Patients were not eligible if the COPD specialist nurses or clinicians considered them unsuitable for any reason: for example, patients with severe mental impairment or terminally ill; patients with an injury or additional health condition that precluded their ability to take part in light intensity physical activity; patients with an overlying medical disorder that

interfered with provision of consent, completion of measurements, intervention, or follow-up; and/or were taking part in concomitant research studies.

Sample size estimation and recruitment target

The study aimed to recruit as many patients as are admitted to hospital for an acute COPD exacerbation within the operational period. One of the main objectives of this feasibility study was to provide data on eligibility and recruitment and to enable an accurate estimation of the required sample size for a future trial based on a realistic recruitment plan. The number of hospital admissions for an acute exacerbation of COPD is approximately 80-100 patients per month and in a previous in-hospital early rehabilitation trial conducted in part at Glenfield Hospital, overall recruitment uptake was 32.3% (Greening et al., 2014). Therefore, a similar admissions rate and uptake (~1 in 3) was expected for COPD-SEAT.

Setting

Participants were recruited from patients admitted to Glenfield Hospital, University Hospitals of Leicester NHS Trust for an acute exacerbation of COPD and were screened for eligibility by COPD specialist nurses.

Procedure

Eligible patients were given a verbal description of the study, participant information sheet and expression of interest form by a researcher after they had received usual care from a COPD specialist nurse. A researcher revisited the patients at the bedside at an agreed time to collect the expression of interest form. For those patients who were not interested in taking part in the trial, reasons for this (if offered freely) were taken as field notes. For patients wishing to take part in the study, informed consent was obtained before patients were informed of their group allocation. If allocated to the Education or Education + Feedback group, patients then received the respective intervention. Questionnaires and activity monitor deployment were then completed prior to discharge (where possible). The timing of these procedures varied based on expected discharge. Upon discharge, patients were asked to wear the activity monitors for 14 days before returning for their follow-up appointment.

Control group

Although there are some variations in practice, ‘usual care’ offered to COPD patients admitted to hospital for an acute exacerbation typically comprised brief advice to take part in

regular exercise, information about pulmonary rehabilitation, and a referral to a follow-up clinic if the patient was eligible and did not decline pulmonary rehabilitation during their admission. No in-hospital rehabilitation was conducted as part of usual care. Patients also received brief discussions and advice regarding smoking cessation (if appropriate), medication and inhaler techniques, and oxygen therapy (if appropriate); generally lasting 15-30 minutes. All patients received a phone call during the first week of discharge, as per usual care.

Education group

Written information was provided by an educational booklet, four pages in length, adapted for COPD patients from 'On Your Feet to Earn Your Seat' (Gardner et al., 2014). The 'On Your Feet to Earn Your Seat' booklet was originally developed in accordance with the habit formation model (Gardner, Lally, & Wardle, 2012; Lally, Van Jaarsveld, Potts, & Wardle, 2010) and designed using a 'small changes' approach as detailed by Gardner and colleagues (Gardner et al., 2014). This booklet (Gardner et al., 2014) was modified to emphasise simpler behaviours, in this case standing up from a chair, which may be more appealing and attainable to COPD patients post-exacerbation compared with more daunting behaviours such as stair climbing (Lally et al., 2010).

The researcher read through the revised booklet, entitled 'Sit Less, Move More, Live Healthier' (Appendix S), with the patient at the bed-side outlining the importance of breaking up long periods of sitting and discussing individualised strategies and opportunities for the patient to do this at home. This booklet contained seven suggestions: leave the house daily; make ad breaks active; stand-ups (e.g. when waiting for a bus); tiptoe through the queue; increase your steps, sit to stand with no hands, and treat the seat as a treat. For each of these tips, 'handy-hints' were provided to facilitate the adoption of these small changes (e.g. offering ways to incorporate them into everyday life). The components of the education delivery are presented in Table 1. In addition to the extensive focus groups and interviews for the original booklet (Gardner et al., 2014), the 'Sit Less, Move More, Live Healthier' booklet was put through a Pulmonary and Cardiac Rehabilitation Patient and Public Involvement Advisory group who provided feedback on content, readability and design.

Education + Feedback group

Patients randomised into the Education + Feedback group received the above education intervention (i.e. 'Sit Less, Move More, Live Healthier' booklet) plus a wearable device to

self-monitor their sedentary behaviour and physical activity as well as provide a behavioural nudge in the form of a vibration prompt. The wearable device provided real-time, visual and numeric feedback on time spent sitting, standing and lying down, number of sit-to-stand transitions and step count. It also allowed the user to look back at previous days, providing day-to-day comparisons in the form of a bar chart.

Patients were shown how to wear the device at the bedside and fitted the monitor themselves to ensure the device is correctly adjusted to ensure a secure and snug fit. The device, LUMO (Lumo Bodytech, Palo Alto, CA), is a small (4.15 x 10 x 0.8cm; 25g) and flexible sensor (Figure 5.2) which was worn around the lower back on a belt. The sensor connects wirelessly via low energy Bluetooth to a mobile application on a Smart Device provided to patients. The embedded inertial sensors of the LUMO continuously tracked the amount of time spent lying down, slouching, sitting, standing and transitioning from sitting to standing providing the patients with up-to-date information of their behaviour whenever they wanted it.

Figure 5.2 LUMO sensor

Patients were trained whilst in hospital on how to navigate the app (touch screen). Real-time feedback was provided on a mobile app with panels displaying time spent sitting (including proportions of time spend standing and stepping) (Figure 5.3 Panel A), sit-to-stand transitions (Figure 5.3 Panel B) and step count (Figure 5.3 Panel C) using low cognitive load graphics and data presented on a daily, weekly and monthly format. Patients were also provided with written instructions on how to navigate the mobile app (Appendix T)

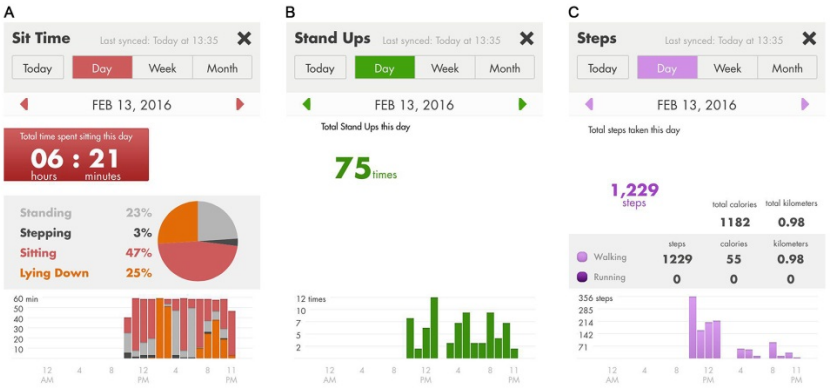

Figure 5.3 LUMO app panels showing: a) proportion of the day spent standing, stepping, sitting and lying down; b) daily number of sit-to-stand transitions; and c) daily step count

Additionally, the LUMO alerted the patient to break up their sitting time when they had been sitting for 'too long' via gentle vibration. After a full explanation of the LUMO and app patients were asked how much consecutive sitting they would want to accumulate before being prompted (e.g. every hour of continuous sitting). The vibration frequency was fixed for the 2 week duration. The components of the LUMO app and vibration prompt delivery are shown in Table 5.1. Patients in all groups were provided with a 24 hour number to call if they had any questions during the course of their involvement in the trial.

Feasibility

Measures for assessing feasibility are provided in Table 5.2. Feasibility was assessed using information on patient recruitment and retention, whether patients wore and charged the study devices (LUMO and/or smart device) and missing data. Feasibility of the trial was assessed on patient recruitment and retention. In an audit of early pulmonary rehabilitation referral and uptake for 448 COPD patients admitted for an acute exacerbation, 286 (63.8%) patients were eligible for rehabilitation. 90 (31.5%) of these patients were referred to rehabilitation. 60 (66.6%) of these patients started the programme and 43 (65.2%) of these patients completed rehabilitation (Jones et al., 2014). Feasibility thresholds for eligibility, uptake and retention in the present study were 66.6%, 33.3% and 50.0%, respectively as involvement in research may not be as appealing compared to an established clinical service.

Patients were asked to wear the LUMO for 14 days with discharge date considered day 0 and follow-up visit as day 15. Therefore, patients were asked to charge the device overnight 13 times (between days 1 and 14) during the study period. Thirteen charging occurrences (one per day/overnight period for at least 15 uninterrupted minutes) were considered 100%

compliance. The feasibility threshold for charging the LUMO was set to 50% (every other day). Charging was automatically detected by the LUMO and coded as "NW" (non-wear). If the LUMO was worn and the period of charging starting after midnight (00:00:00) but before the first occurrence of physical activity (e.g. standing or walking) the charging period was considered as belonging to the previous day.

Missing data from the LUMO can be caused by the battery dying or from being manually turned off by the patient. If missing data started at 15:00 and the next data point was at 16:00 there was an hour of missing data. If the data point at 16:00 was coded as "NW" (put on charge) then the LUMO battery died. If the data point at 16:00 was coded as a behaviour (e.g. sitting, standing or walking) the LUMO was turned off by the patient.

Acceptability

Acceptability to the patients was assessed according to the:

a) Proportion of patients who stopped wearing the device during the 2 weeks of follow-up; when they did this (e.g. number of days into the follow-up).
b) Proportion of patients who attended the follow-up appointment.
c) Patients' response to the vibration prompts, as examined by LUMO data (e.g. number of vibrations; average response time from vibration to stand-up; number of times the vibration prompt resulted in behaviour change).

For patients in the Feedback group, engagement with the LUMO prompts (i.e. did the patient stand-up after the vibration prompt occurred?) was quantified using the LUMO inclinometer. Vibration prompt identification was based on periods of consecutive time spent sedentary (lying down or sitting) based on patients' choice of vibration setting (e.g. after 30 minutes of consecutive sedentary behaviour). For each day the LUMO was worn, bouts of consecutive sedentariness were identified to determine the time of vibration prompt. LUMO data was in five minute (300 second) epochs. Six consecutive epochs of 300 seconds sedentary with 0 seconds sedentary in the preceding epoch signified that the prompt occurred at the end of a five minute epoch. For example, if a period of sitting began at 12:00:00 and lasted until 12:30:00, the vibration would have occurred at 12:30:00.

After time-stamped vibration prompts were identified, the subsequent 15 minutes (three 300 second epochs) were analysed to examine whether patients responded to the vibration prompt and, if they did, how long it took and what they decided to do (e.g. time spent standing and/or

stepping). For each vibration prompt responses were coded as one of the following: no response (patient remained sedentary for 15 minutes after the prompt occurred); response (patient stood up) within 5 minutes of the prompt; response 5-10 minutes after the prompt occurred; or response 10-15 minutes after the prompt occurred. For the three response timings (0-5, 5-10 and 10-15 minutes), time spent sedentary, standing and walking were analysed along with step count.

Table 5.1 COPD-SEAT intervention components

Education Booklet: Components to cover during intervention delivery
It was explained that the booklet will provide information to help them to sit less and move more
It was explained that sitting for too long can be harmful to their health
It was explained that breaking up long periods of sitting can help reduce joint stiffness and pain
The principle of 'use it or lose it' was explained in relation to deconditioning
If deemed appropriate, other tailored examples of benefits to be had was explained
The patient was directed to the 7 suggestions for an active recovery
If deemed appropriate the first suggestion(Leave the house daily) was discussed
If deemed appropriate the second suggestion (Make TV advert breaks active) was discussed
If deemed appropriate the third suggestion (Stand up when waiting for something) was discussed
If deemed appropriate the fourth suggestion (Tiptoe when waiting in a queue) was discussed
If deemed appropriate the fifth suggestion (Increase your steps) was discussed
If deemed appropriate the sixth suggestion (Sit to stand with no hands) was discussed
If deemed appropriate the seventh suggestion (Treat the seat as a treat) was discussed
If deemed appropriate additional tailored top tip examples was discussed
Smart Device: Components to cover during intervention delivery
It was explained that the LUMO and Smart Device communicate with each other automatically
Patients were taught how to lock and unlock the Smart Device
LUMO App: Components to cover during intervention delivery
It was explained that the app provides the patient with information on sitting, standing and stepping
Patients were shown where to find their time spent sitting 'today' on the app home screen
Patients were shown where to find how many time they have stood up 'today' on the app home screen
Patients were shown where to find their step count 'today' on the app home screen
Sit Time Panel: Components to cover during intervention delivery
Patients were shown how to access the pie chart for time sitting, standing, stepping and lying down
Patients were shown the hourly bar chart for all behaviours
Patients were shown how to look back at previous days
Patients were shown how to return to 'today's' information
Patients were shown how to return to the home screen
Stand Ups Panel: Components to cover during intervention delivery
Patients were shown the hourly bar chart for all behaviours
Patients were shown how to look back at previous days
Patients were shown how to return to 'today's' information
Patients were shown how to return to the home screen
Steps Panel: Components to cover during intervention delivery
Patients were shown the hourly bar chart for all behaviours

Patients were shown how to look back at previous days
Patients were shown how to return to ‘today's’ information
Patients were shown how to return to the home screen
Vibration Prompt: Components to cover during intervention delivery
It was explained that the LUMO device provides a vibration prompt when they have sat for 'too long'
It was explained that the vibration will only go off once then the timer will reset
Patients chose the duration of consecutive sitting before the vibration occurs

Intervention fidelity

Examining intervention fidelity may help to explain variance in outcomes (e.g. wearing the activity monitors) related to non-adherence or partial adherence to the intervention (Bellg et al., 2004). Intervention deliveries for patients in the Education and Education + Feedback groups were audio recorded using TapMedia Voice Recorder (TapMedia, London, UK). Each component was coded separately by two trained, independent assessors using dichotomous scales (present or absent) to determine consistency and ordinal scales to determine quality (none, adequate or excellent) of the delivery. Quality definitions for Education components were: ‘Poor’, mentioned without examples; ‘Adequate’, explained without examples; ‘Excellent’, explained with examples. Quality definitions for Feedback components were: ‘Poor’, mentioned without patient performing task; ‘Adequate’, explained without patient performing task; ‘Excellent’, explained with patients performing task. All recordings were analysed by both assessors for quality control and quality assurance purposes. When scores for each component did not match between assessors, a third independent reviewer was consulted.

Table 5.2 Outline of feasibility indicators

Indicators	Data sources	Timing
Recruitment		
Feasibility of patient screening and recruitment	Project records (e.g. number of eligible patients missed)	Ongoing throughout the study
Number of eligible patients, number of patients screened, number of patients invited to take part, actual number of patients who consent to take part	Medical records and project records	Ongoing throughout the study
Number of patients who refuse, drop out or opt out	Patient requests, field notes	
Intervention delivery		
Duration of intervention sessions (education and/or device training); patient engagement in the content.	Audio recordings of the intervention sessions	Ongoing throughout the study
Description of unintended events		
It is important to note whether there were any unintended side effects or outcomes from the intervention.	Medical notes	2 week follow-up appointment
Hospital readmissions related to the study. For example, trying to move more resulting in a fall.	Medical notes	Ongoing throughout the study
Potential sustainability		
The number of telephone contacts and duration of telephone conversations with patients during follow-up beyond usual care.	Project records	Ongoing throughout the study

Data collection

Data was collected January-August 2016 by trained researchers, following standard operating procedures. Researchers were not blinded to treatment allocation for study measurements. Baseline data were collected during patients' hospital stay. The timing of baseline data collection could not be standardised due to variation in the timing of patients receiving usual care from COPD Specialist Nurses, screening and length of stay.

Sample characteristics

Baseline only

Usual dyspnea severity

In order to examine patients' usual breathlessness severity i.e. when not acutely ill, the mMRC dyspnea scale (single item) (Mahler & Weels, 1988) was completed.

Baseline and follow-up

Questionnaires

The full COPD-SEAT questionnaire is provided in Appendix U. During hospital stay and at follow-up a range of health/psychosocial measures were taken. COPD-specific health status was examined using the CAT (8 items) (Jones et al., 2009). Overall health status was assessed using the EuroQol EQ-5D-5L (5 items) (Herdman et al., 2011). Additional symptom burdens were assessed by the Functional Assessment of Chronic Illness Therapy-Fatigue (40 items) with a score <30 indicating severe fatigue (Webster, Cella, & Yost, 2003)and the Hospital Anxiety and Depression Scale (HADS) (14 items) (Zigmond & Snaith, 1983) with normal anxiety/depression levels classified as a score 0-7, borderline abnormal levels classified as a score of 8-10 and abnormal levels considered a score of 11-21 (Snaith, 2003). Fear of falling was assessed using the Falls Efficacy Scale-International (FES-I) (16 items) (Yardley et al., 2005). Patients self-reported information on the ownership and usage of technology (computer and smart phone) relating to browsing the internet, emails, entertainment (e.g. listening to music), online shopping and social networking. Deprivation levels were examined using patients' home postcodes using the IMD 2015 explorer (http://dclgapps.communities.gov.uk/imd/idmap.html).

Self-reported physical activity and sitting

During hospital stay patients' usual time spent sitting in domain-specific activities (TV, transport, work, computer and other) during weekdays and weekend days was self-reported using an adapted version of the Marshall Sitting Time Survey (10 items) (Marshall, Miller, Burton, & Brown, 2010). Patients were asked to complete an adapted version of the International Physical Activity Questionnaire (IPAQ) Short Form (3 items) (Craig et al., 2003) to assess usual physical activity levels.

Follow-up only

Body composition and physical function

At follow-up height, weight and waist circumference were measured to the nearest 0.1cm, 0.1 kg and 0.1 cm, respectively. Waist circumference was measured twice, with a third conducted if the difference between the first two was greater than 3cm. Patients were also asked to complete the Short Physical Performance Battery (SPPB) which comprised repeated chair stands; balance tests and a 4m walk (Puthoff, 2004). Upper limb skeletal muscle

strength was assessed using a hand-held dynamometer (Takeii analogue dynamometer, Niigata, Japan) (Parvatikar & Mukkannavar, 2009).

Pulmonary rehabilitation

Past and present pulmonary rehabilitation referral and attendance information was obtained through the Hospital Information Support System by senior pulmonary rehabilitation physiotherapists on-site at Glenfield Hospital, UK. Present pulmonary rehabilitation attendance was established based on the referral during the hospital stay related to their participation in this trial. Attendance was defined as completing at least one class and completion was defined as finishing the six week programme.

Continuous measurement

Objectively measured physical activity and sedentary behaviour

Following hospital discharge (day 0), patients were asked to wear two monitors, one posture sensor (gyroscope) and one triaxial accelerometer, for 14 days and returned the devices at the follow-up appointment (day 15). An ActiGraph wGT3X-BT triaxial accelerometer was worn on a waistband (on the right anterior axillary line) for 2 weeks to measure time spent in physical activity (i.e. sedentary, light, moderate, and vigorous) using common cut-points and step count. Patients were asked to wear the device during waking hours and to only remove it during that period for water-based activities.

Accelerometers recorded data at 100Hz and were initialised, downloaded and converted to 60-second epoch files using ActiLife version 6.13.2 (Pensacola, FL). Non-wear was defined as 60 minutes of consecutive zeros with allowance for two minutes of interruptions and a valid day was defined as at least 600 minutes of wear during waking hours (Troiano et al., 2008). Accelerometer processing was conducted using KineSoft version 3.3.80 (Loughborough, UK). A summary of accelerometry methodology is provided in Table 5.3.

Table 5.3 Accelerometry data collection and analytical procedures

Information	Details
Accelerometer Model	Actigraph wGT3X-BT (version 6.13.2; firmware 1.6.1)
Serial number range	Sixteen unique devices were used ranging from MOS2A02140493 to MOS2A02140631; averaging two deployments per device
Piezosensor orientation	Triaxial
Mode setup	Mode 29 (x, y, z, steps, lux)
Original sample rate	100 Hz (.gt3x file format)
Deployment method	Fitted by patient (on day 1) and after demonstration and practice (on day 0)
Location worn	Anterior hip adjacent to the mid-line of the thigh
Requested days of wear	14 d (20160 epochs) not including day 0
Initialization	Deployed in delay mode on day 0 (during admission) and commenced logging on day 1(first full day after discharge) at 00:00 hrs with no stop time (estimated date of discharge not reliable)
Wear instructions	Wear continuously except for sleep and water based activities
Analytical Processing	
Non-wear appropriation	≥60 min of consecutive 0s with allowance for 2 minutes of interruptions were deemed biologically implausible and coded as non-wear (Troiano et al., 2008)
Valid day criteria	≥10 hours of valid waking wear time (Troiano et al., 2008)
Valid file	At least 4 valid days (Troiano et al., 2008)
Missing data	Data modelling or imputation was not performed
Epoch length	60 seconds
Intensity classification	Uniaxial (x-axis) cut-points as follows: Sedentary time: <100 cpm (Troiano et al., 2008) Light: 100-2019 cpm (Troiano et al., 2008) MVPA: ≥2020 cpm (Troiano et al., 2008)

The LUMO posture sensor served to objectively quantify sedentary behaviour in all groups (Control, Education and Education + Feedback). Therefore, it acted as both the measurement and intervention device for the Education + Feedback Group. In addition to physical activity intensity data collected by the ActiGraph accelerometer, the LUMO provided information on sitting, driving, lying, standing, sit-to-stand transitions and stepping. The device was worn on the lower back (in contact with skin) for 2 weeks post-discharge. Patients were asked to wear the monitor during waking hours and to remove it for water-based activities. The LUMO has been found to produce valid measurements of free-living sedentary behaviour (mean error of 9.5%) (Rosenberger et al., 2016) and step count (mean absolute percentage error 0.4%) (Kooiman et al., 2015) compared with the ActivPAL (PAL Technologies Ltd, Glasgow, UK). Whilst no validation study to date has specifically examined LUMO stand-ups, valid free-living sedentary behaviour against the ActivPAL supports accurate detection of sit-to-stand transitions. LUMO data was analysed in five minute epochs with behaviours summarised as a proportion of each five minute epoch (e.g. 50% sitting will be converted to 2.5 minutes sitting).

Patients were asked to wear for the ActiGraph and LUMO monitors concomitantly for two main reasons. Firstly, as noted above, the LUMO monitor was a relatively new device and had not yet been subject to multiple validation studies across different populations (e.g. ages, disease states and habitual activity levels). Therefore, the ActiGraph provided a well-established measurement of physical activity and sedentary time in COPD and general populations. Secondly, it was unclear whether patients would dislike the nudge/vibration feature of the LUMO and thus remove it. Consequently there was a need for an independent evaluation and intervention sensor.

Randomisation

Block randomisation (1:1:1) was used to ensure a balance in sample size between the three study groups. Balanced combinations of group allocations within blocks were conducted by a researcher at Loughborough University independent of the research team. This ensured study team researchers were blinded to group allocation prior to patients deciding whether to take part in the study. Due to limited study team members and logistical barriers study team researchers were made aware of group allocation before consent. However, study team members were not aware of prospective group allocation when approaching patients to provide the information sheet. Patients were only informed of their group allocation after providing informed consent. Baseline measures were conducted after group allocation.

Quantitative data analysis

All participant information collected as part of the research was kept strictly confidential. With permission, patients' general practitioner was informed of their participation in the study. Any information regarding patients which left the hospital had their name and address removed.

Data were entered and housed on a secure web-based database system, Research Electronic Data Capture (REDCap), which has discrepancy management capabilities. Data were transferred from REDCap to the Statistical Package for the Social Sciences (SPSS) for statistical analysis.

Comparisons between study groups (Control, Education and Feedback) were conducted using analysis of variance (ANOVA) with Bonferroni post-hoc tests. Changes in characteristics from baseline to follow-up were examined using paired t-test. Comparisons between patients who did or did not complete the study were performed using independent t-tests. Categorical

data was analysed using Fischer exact test for frequencies of less than five patients and Chi-squared for frequencies of at least five patients. Analysis was conducted using SPSS version 22.0 for Windows (SPSS Inc, Chicago, IL) with alpha set to 0.05.

Adverse events

To monitor intervention safety, adverse events including readmissions, deaths and falls during each patient's study involvement were recorded.

Chapter 6: Study Three Results and Discussion

Title: A feasibility study of a home-based self-monitoring sedentary behaviour intervention in COPD patients suffering from an acute exacerbation: Trial results

6.1 Results

6.1.1 Feasibility of recruitment and retention

Patient screening

Of the 346 patients admitted during the study period 300 (86.7%) were screened for inclusion in this study, comprising 164 females (54.7%, 69.9±9.6 years) and 136 males (45.3%, 71.0±8.4 years). The remaining 46 (13.3%) patients were seen by the COPD specialist nurses but were not entered on the screening log. Gender and age distributions of the screened patients are presented in Figure 6.1. Two (0.7%) patients had missing age data.

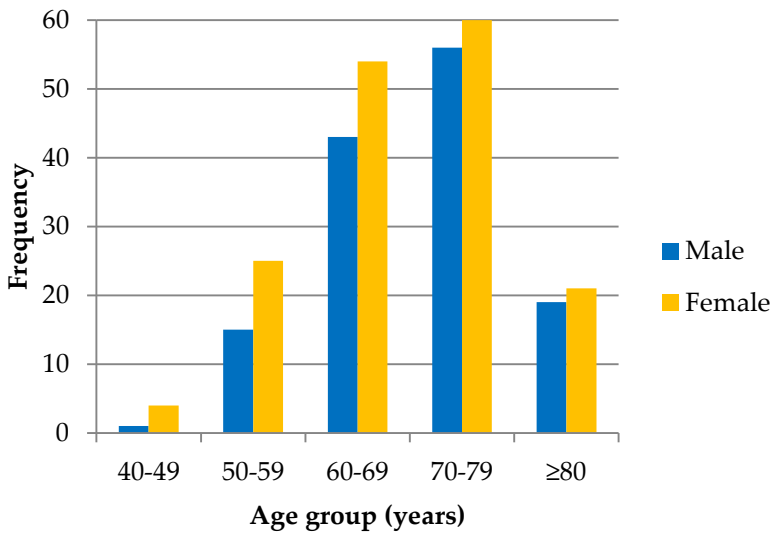

Figure 6.1 Age and gender distribution for screened patients

Patient flow

Participant flow through the trial is presented in Figure 6.2. Of the 300 patients screened, 212 (70.7%) were eligible to take part in the study (69.6±8.6years, 52.4% female). Of these, 100 (47.2%) were discharged before the researcher could approach them (69.3±9.0 years, 52% female) and for 1 (0.4%) male patient, the ward nurses advised the researcher not to approach due to an unspecified complicated social situation. Therefore 111 (52.4%) were approached

to take part in the study with 35 (31.5%) consenting to participate. Of these, 2 patients (1 Control and 1 Education) were identified as having early stage dementia after consent and randomisation. These patients were withdrawn from the study leaving 33 patients (11 Control, 10 Education and 12 Education+Feedback). 17 patients (51.2%; 6 Control, 3 Education and 8 Education+Feedback) attended the follow-up appointment.

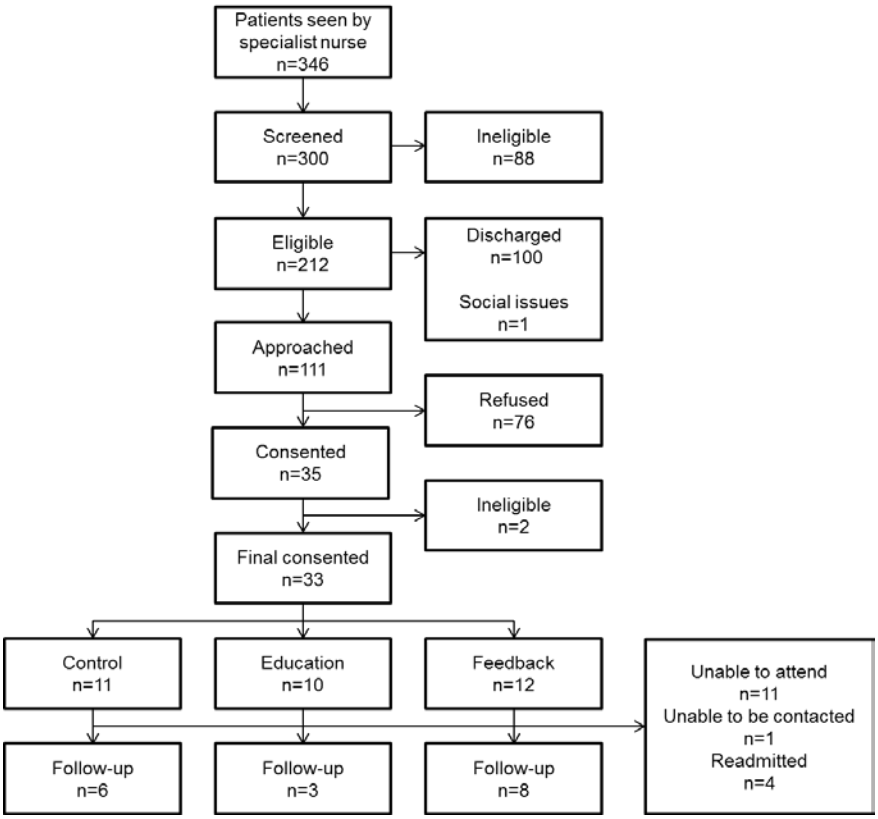

Figure 6.2 CONSORT diagram for COPD-SEAT

Reasons for ineligibility

Of the 88 ineligible patients, the mean age was 72.2 years comprising 53 (60.2%) females. The most cited reasons for exclusion by COPD specialist nurses were: too severe comorbidities (25.0%), more than 4 exacerbations in the previous year (20.5%), taking part in other research (14.8%) and physically incapable (11.4%). No patient screened was under the age of 40 years whilst 8 patients (9.1%) were older than 85 years. A diagnosis of COPD could not be confirmed in 7 (8.0%) patients screened.

Of the 22 patients excluded because of comorbidities, 8 (36.4%) had a psychological condition (e.g. bipolar or schizophrenia), 3 (13.6%) had dementia, 3 (13.6%) had poor eyesight (e.g. macular degeneration), 4 (18.2%) had additional lung conditions (e.g. cancer)

and 4 (18.2%) suffered from neurological or skeletal ailments severely impairing mobility (e.g. multiple sclerosis or spinal stenosis).

Patients approached

Of the 111 patients (70.1±8.3 years, 52.3% female) approached for the study, 92 (82.9%) accepted and read the patient information sheet. There were 2 (1.8%) patients aged 40-49 years, 17 (15.3%) patients aged 50-59 years, 30 (27.0%) patients aged 60-69 years, 46 (41.4%) patients aged 70-79 years and 16 (14.4%) patients aged at least 80 years. There were 9 (8.1%) patients admitted to the clinical decisions unit, 23 (20.7%) to a short-term stay ward and 79 (71.2%) to long-term stay wards.

Reasons for refusal

Of the 111 patients approached, 76 (68.5%) refused to take part in the study. More than one main reason for refusal was reported for 9 (8.1%) patients. The most common reasons were: feeling too unwell or having too many health-related issues/commitments (40.0%) and considering themselves sufficiently active (12.9%). Other reasons for refusal included being a carer for their partner (7.1%), not wanting to commit to the time (5.9%) or travel commitments (1.2%), and being content with taking part in pulmonary rehabilitation (5.9%). Two (2.4%) patients were put off by wearing the activity monitors.

Length of hospital stay

The average length of hospital stay was 5.6±3.2 days with an average of 3.6±1.7 days from admission to consent and 2.0±3.2 days from consent to discharge. No significant differences were observed between groups. Time from admission to consent ranged between 1-7 days with 12.1% of patients consented the day after their admission date. Over one-third (36.4%) of patients were discharged the same day as they were consented, 30.3% were discharged the day after consent and 20.1% of patients were discharged more than 3 days after consenting.

Adverse events

Four patients (12%) (1 Control, 3 Education + Feedback) were readmitted for an acute exacerbation of COPD during the 2 week follow-up. Two patients (6%) (2 Education) were admitted to hospital for at least one overnight stay for bronchoscopy or undiagnosed stomach pains. No hospital admissions were as a result of the trial and no deaths occurred to patients during their trial involvement.

6.1.2 Patient characteristics

Baseline characteristics

Sample characteristics are presented in Table 6.2 and comprise 33 patients (69.7% female) aged 71±20 years. No differences in baseline characteristics were observed between study groups. Two-thirds of patients were former smokers and one-third current smokers at the time of admission with a combined pack year history of 46.7±25.6 years. Patients reported a median mMRC dyspnea grade of 3 when stable (pre-hospitalisation) and 9.1% of patients required ambulatory oxygen upon discharge. For self-reported general health using EQ-5D-5L, 82.6% of patients reported at least moderate problems with mobility, 39.1% for self-care, 73.9% for performing their usual activities and 47.7% for pain or discomfort. 30.3% of patients were classified as having abnormal (high) depression levels, 39.4% of patients had abnormal (high) anxiety and 81.8% reported severe fatigue. There were no significant differences in comorbidity prevalence between study groups.

Follow-up characteristics

For the 17 patients who completed the trial, mobility limitation (SPPB <10 points) was observed in 95.7% of patients. The prevalence of overweight or obesity based on BMI was 64.7% with one patient (5.9%) classified as underweight. Control group patients had significantly greater BMI and waist circumference values compared with Education and Education + Feedback groups.

Pulmonary rehabilitation

Of the 33 patients who took part in the trial, 14 (42.4%) attended the pulmonary rehabilitation clinic appointment as part of usual post-exacerbation care. Seven (21.2%) patients agreed to attend pulmonary rehabilitation of which four (12.1%) did attend. Overall pulmonary rehabilitation uptake was 12.1%. Ten (30.3%) patients had previously completed pulmonary rehabilitation with one (9.1%) patient attending within 12 months of admission, another (9.1%) patient attending within 12-24 months of admission, nine (27.3%) attending more than two years ago and the remaining 22 (66.7%) never attending. No significant differences were observed between study groups.

Table 6.1 Baseline patient characteristics for the whole sample and group allocations, reported as mean (SD) unless otherwise stated

	Whole Sample (n=33)	Control (n=11)	Education (n=10)	Education + Feedback (n=12)
Demographics				
Age	71.0 (20.0)	65.3 (13.0)	66.2 (9.2)	72.0 (7.9)
Female gender (%)	23 (69.7)	7 (63.6)	9 (90.0)	7 (58.3)
IMD decile	4.5 (3.2)	3.8 (2.9)	3.7 (3.4)	5.7 (3.1)
Employment status (%):				
Retired	25 (75.8)	6 (54.5)	8 (80.0)	11 (91.7)
Unemployed	5 (15.1)	3 (27.3)	1 (10.0)	1 (8.3)
Employed	3 (9.1)	2 (18.2)	1 (10.0)	0 (0)
Lung health and comorbidities				
Smoking status (%):				
Current	11 (33.3)	5 (50.0)	5 (50.0)	1 (8.3)
Former	21 (63.6)	5 (50.0)	5 (50.0)	11 (91.7)
Pack years	46.7 (25.6)	40.2 (27.6)	53.2 (28.2)	47.4 (22.2)
Usual mMRC grade	2.6 (1.2)	2.3 (0.9)	3.1 (1.4)	2.6 (1.2)
Home oxygen (%)	3 (9.1)	0 (0)	1 (10.0)	2 (16.7)
12 month all-cause admissions	1.7 (1.8)	1.7 (2.0)	0.9 (0.9)	2.3 (2.1)
12 month AECOPD admissions	0.9 (1.2)	1.2 (1.5)	0.5 (0.9)	1.0 (1.1)
New diagnosis of COPD (%)	3 (9.1)	1 (9.1)	1 (10.0)	1 (8.3)
Number of comorbidities	3 (3)	3 (5)	4 (3)	3 (3)
Self-reported health				
EQ-VAS	40.8 (20.4)	43.6 (18.7)	31.4 (22.5)	43.3 (21.7)
CAT score	24.9 (7.5)	23.6 (7.2)	27.9 (8.5)	23.7 (6.7)
Fatigue score	19.8 (11.8)	22.6 (8.2)	11.4 (9.4)	22.1 (13.8)
HADS depression score	8.2 (4.7)	9.2 (3.1)	10.4 (6.0)	5.9 (4.2)
HADS anxiety score	9.2 (5.8)	10.6 (6.0)	12.5 (12.0)	6.8 (4.5)
FESI score	33.4 (13.7)	34.7 (1.1)	35.0 (15.0)	31.0 (15.4)
Self-reported physical activity				
Daily walking time (min)	12.9 (15.8)	16.1 (14.8)	9.0 (20.1)	12.2 (15.6)
Daily moderate PA (min)	2.2 (7.7)	7.0 (12.9)	0.0 (0.0	0.0 (0.0)
Daily vigorous PA (min)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)
Self-reported sitting time β				
Daily TV sitting time (min)	354.4 (246.9)	362.9 (260.2)	382.3 (288.0)	333.7 (242.0)
Daily travel sitting time (min)	56.0 (67.2)	51.2 (50.4)	17.0 (25.4)	79.4 (85.5)
Daily computer sitting time (min)	40.2 (59.3)	38.6 (46.9)	44.0 (77.0)	39.7 (65.1)
Daily other sitting time (min)	102.4 (130.4)	115.2 (67.8)	150.0 (256.3)	68.4 (78.0)
Daily total sitting time (min)	553.0 (253.6)	567.8 (198.1)	593.3 (223.0)	521.1 (319.9)
Pulmonary rehabilitation				
Attended clinic appointment (%)	14 (42.4)	8 (72.7)	3 (30.0)	3 (25.0)
PR accepted (%)	7 (21.2)	3 (27.3)	2 (20.0)	2 (16.7)
PR attended (%)	4 (12.1)	1 (9.1)	1 (10.0)	2 (16.7)
Previously completed PR (%):				
Within 12 months	1 (3.0)	1 (9.1)	0 (0)	0 (0)
Within 24 months	1 (3.0)	0 (0)	0 (0)	1 (8.3)
More than 24 months ago	9 (27.3)	4 (36.4)	1 (10.0)	4 (33.3)
Never	22 (66.7)	6 (54.5)	9 (90.0)	7 (58.3)

Abbreviations: AECOPD, acute exacerbation of chronic obstructive pulmonary disease; CAT, COPD assessment test; EQ-VAS, EuroQol visual analogue scale; FESI, falls efficacy scale international; HADS,

hospital anxiety and depression scale; IMD, Index of Multiple Deprivation; mMRC, modified Medical Research Council; PA, physical activity; TV, television
β, daily work sitting is missing for the three patients in employment

Table 6.2 Follow-up patient characteristics for the whole sample and group allocations, reported as mean (SD) unless otherwise stated

	Whole Sample (n=33)	**Control (n=11)**	**Education (n=10)**	**Education + Feedback (n=12)**
Body composition				
Height (cm) †	163.1 (8.4)	164.8 (8.5)	160.2 (6.5)	163.5 (9.4)
Weight (kg) †	73.4 (16.6)	59.2 (9.1) [A, B]	90.4 (17.6)	77.7 (12.8)
BMI (kg/m^2) †	27.6 (7.4)	21.3 (3.2) [B]	37.3 (9.7)	28.8 (3.8)
BMI category † (%):				
Underweight	1 (5.9)	1 (16.7)	0 (0)	0 (0)
Normal weight	5 (29.4)	4 (66.7)	0 (0)	1 (12.5)
Overweight	7 (41.2)	1 (16.7)	1 (33.3)	5 (62.5)
Obesity	4 (23.5)	0 (0)	2 (66.7)	2 (25.0)
Waist circumference (cm) †	99.1 (13.8)	86.7 (11.1) [A, B]	106.5 (15.3)	106.6 (8.5)
Lung health and comorbidities				
FEV_1 †	1.2 (0.6)	1.2 (0.8)	1.7 (0.4)	1.1 (0.5)
FEV_1%predicted †	57.3 (29.9)	52.3 (34.9)	84.7 (26.6)	50.8 (24.1)
FVC †	2.6 (1.0)	2.4 (0.7)	2.5 (0.6)	2.6 (0.7)
FEV_1/FVC ratio †	45.0 (19.1)	45.0 (20.5)	67.0 (3.0)	42.0 (18.2)
Physical function				
Grip strength (kg) †	27.9 (7.5)	29.2 (5.0)	23.7 (1.5)	28.5 (10.0)
SPPB points †	7.4 (1.9)	8.2 (1.9)	5.3 (2.1)	7.6 (1.4)

Abbreviations: BMI, body mass index; FEV_1, forced expiratory volume in one second; FVC, forced vital capacity; SPPB, short physical performance battery
BMI categories: underweight <18.5kg/m^2; normal, ≥18.5 and <25.0kg/m^2; overweight, ≥25.0 kg/m^2 and obesity, <30.0kg/m^2 (World Health Organization, 2000)
SPPB: mobility limitation defined as <10 points (Bernabeu-Mora et al., 2015)
[A], different to Education + Feedback group; [B], different to Education group

Technology ownership and usage

Given the use of wearable self-monitoring technology in the present study it is important to examine the potential for adoption of technology in this population (Table 6.3). Twenty (60.6%) patients reported owning a computer (desktop, laptop or tablet). Eight (24.2%) patients reported owning a Smart phone (e.g. iPhone or Android). Seven (21.2%) patients reported owning both a computer and Smart phone. No significant differences in the ownership of a computer or Smart phone were observed between study group allocations. A significantly larger proportion of patients in the Education group used a computer or Smart phone for entertainment compared with Control and Education + Feedback groups.

Table 6.3 Technology usage in patients stratified by group allocation

	Control (n=11)	Education (n=10)	Education + Feedback (n=12)
Computer usage			
Computer ownership (%)	5 (45.5)	6 (60.0)	9 (75.0)
Computer usage (%):			
Go on the internet	4 (80.0)	4 (66.7)	6 (66.7)
Emails	3 (60.0)	3 (50.0)	4 (44.4)
Entertainment	1 (20.0)	5 (83.3) [A]	3 (33.3)
Shopping	2 (40.0)	3 (50.0)	4 (44.4)
Social networking	0 (0)	3 (50.0) [A]	0 (0)
Smart phone ownership			
Smart phone ownership (%)	3 (27.3)	3 (30.0)	2 (16.7)
Smart phone usage (%):			
Go on the internet	1 (33.3)	2 (66.7)	1 (50.0)
Emails	0 (0)	1 (33.3)	1 (50.0)
Entertainment	0 (0)	3 (100) [A]	0 (0)
Shopping	0 (0)	1 (33.3)	0 (0)
Social networking	2 (66.7)	2 (66.7)	1 (50.0)

[A], significantly different to other two groups

Physical activity and sedentary time

Patients who completed the study provided significantly more valid days (≥600 minutes) compared with those who did not attend the follow-up appointment (5.3±3.4 versus 1.6±2.0 days, p=0.005). Ten patients (38.5%) provided at least four valid days with an average wear time of 731±78 minutes. Patients spent 559±115 minutes sedentary, 169±87 minutes in light activity and 2±3 minutes in moderate intensity activity; accruing 2272±1712 steps per day.

6.1.3 Feasibility of intervention delivery

Intervention fidelity

Twenty-one (95%) of interventions were delivered; comprising 9 (90%) for Education and 12 (100%) for Education + Feedback. For one patient, who was randomised to the Education group, the intervention was not delivered verbally because the patient had been discharged before it could be delivered. The patient only received the educational booklet to take home. A full breakdown of intervention fidelity is provided in Table 6.4. Overall consistency of the intervention delivery was 77.3% with “poor”, “good” and “excellent” quality ratings for 0.2%, 9.4% and 90.4% of all occurrences, respectively.

For the Education component, the overall consistency score was 188 out of a possible 273 highlighting moderate adherence (68.9%). Two factors had very poor adherence; “tiptoe

when waiting in a queue" (0%) and "sit to stand with no hands" (10%). Removal of the two factors increased overall consistency to 186 out of 231 (80.5%). Of the 188 occurrences, overall quality scores for "poor", "good" and "excellent" were 1 (0.5%), 3 (1.6%) and 184 (97.9%), respectively, indicating excellent quality in delivery.

For the feedback component, the overall consistency score was 227 out of a possible 264 highlighting overall good adherence (86.0%). Of the 227 occurrences, overall quality scores for "good" and "excellent" were 36 (15.9%) and 191 (84.1%), respectively, indicating excellent quality in delivery.

Table 6.4 Intervention fidelity for education and feedback components

	Consistency (%)		**Quality (%)**		
	Present	**Absent**	**Poor**	**Adequate**	**Excellent**
Education Booklet (n=21)					
The booklet is designed to help you to sit less and move more	21 (100)	0 (0)	0 (0)	0 (0)	21 (100)
Sitting for too long can be harmful to your health	21 (100)	0 (0)	0 (0)	1 (5)	20 (95)
Use it or lose it - Keep muscles active to help prevent deconditioning	19 (90)	2 (10)	1 (5)	0 (0)	18 (95)
Other examples of benefits to be had	20 (95)	1 (5)	0 (0)	0 (0)	20 (100)
Directed to 7 suggestions for an active recovery	21 (100)	0 (0)	0 (0)	0 (0)	21 (100)
1 - Leave the house daily	14 (67)	7 (33)	0 (0)	0 (0)	14 (100)
2 - Make TV advert breaks active	21 (100)	0 (0)	0 (0)	0 (0)	21 (100)
3 - Stand up when waiting for something (e.g. bus, kettle)	7 (33)	14 (67)	0 (0)	0 (0)	7 (100)
4 - Tiptoe when waiting in a queue	0 (0)	21 (100)	N/A	N/A	N/A
5 - Increase your steps	18 (86)	3 (14)	0 (0)	0 (0)	18 (100)
6 - Sit to stand with no hands	2 (10)	19 (90)	0 (0)	0 (0)	2 (100)
7 - Treat the seat as a treat	7 (33)	14 (67)	0 (0)	2 (29)	5 (71)
Additional tailored top tip examples	17 (81)	4 (19)	0 (0)	0 (0)	17 (100)
Total score	**188 (68.9)**	**85 (31.1)**	**1 (0.5)**	**3 (1.6)**	**184 (97.9)**
Smart Device (n=12)					
LUMO and Smart Device communicate with each other	12 (100)	0 (0)	0 (0)	0 (0)	12 (100)
Patient shown how to lock and unlock the Smart Device	9 (75)	3 (15)	0 (0)	0 (0)	9 (100)
Total score	**21 (87.5)**	**3 (12.5)**	**0 (0)**	**0 (0)**	**21 (100)**
LUMO App (n=12)					
App provides you with information on sitting, standing and stepping	12 (100)	0 (0)	0 (0)	0 (0)	12 (100)
Patient shown where to find time spent sitting	12 (100)	0 (0)	0 (0)	0 (0)	12 (100)
Patient shown where to find how many times they have stood up	12 (100)	0 (0)	0 (0)	1 (8)	11 (92)
Patient shown where to find their step count	12 (100)	0 (0)	0 (0)	0 (0)	12 (100)
Total score	**48 (100)**	**0 (0)**	**0 (0)**	**1 (2.1)**	**47 (97.9)**
Sit Time Panel (n=12)					
Patient shown the pie chart for sitting,	12 (100)	0 (0)	0 (0)	0 (0)	12 (100)

standing, stepping, lying down					
Patient shown the hourly bar chart for all behaviours	12 (100)	0 (0)	0 (0)	1 (8)	11 (92)
Patient shown how to look back at previous days	10 (83)	2 (17)	0 (0)	5 (50)	5 (50)
Patient shown how to return to today's information	5 (42)	7 (58)	0 (0)	0 (0)	5 (100)
Patient shown how to return to the home screen	12 (100)	0 (0)	0 (0)	1 (8)	11 (92)
Total score	**51 (85.0)**	**9 (15.0)**	**0 (0)**	**7 (13.7)**	**44 (86.3)**
Stand Ups Panel (n=12)					
Patient shown the hourly bar chart for all behaviours	10 (83)	2 (17)	0 (0)	3 (30)	7 (70)
Patient shown how to look back at previous days	10 (83)	2 (17)	0 (0)	5 (50)	5 (50)
Patient shown how to return to today's information	7 (58)	5 (42)	0 (0)	2 (29)	5 (71)
Patient shown how to return to the home screen	9 (75)	3 (15)	0 (0)	0 (0)	9 (100)
Total score	**36 (75.0)**	**12 (25.0)**	**0 (0)**	**10 (27.8)**	**26 (72.2)**
Steps Panel (n=12)					
Patient shown the hourly bar chart for all behaviours	10 (83)	2 (17)	0 (0)	2 (20)	8 (80)
Patient shown how to look back at previous days	11 (92)	1 (8)	0 (0)	7 (64)	4 (36)
Patient shown how to return to today's information	7 (58)	5 (42)	0 (0)	4 (57)	3 (43)
Patient shown how to return to the home screen	11 (92)	1 (8)	0 (0)	1 (9)	10 (91)
Total score	**39 (81.3)**	**9 (18.8)**	**0 (0)**	**14 (35.9)**	**25 (64.1)**
Vibration Prompt (n=12)					
LUMO provides a vibration prompt when patient sits for 'too long'	12 (100)	0 (0)	0 (0)	1 (8)	11 (92)
Vibration will only go off once then the timer will reset	8 (67)	4 (33)	0 (0)	1 (12)	7 (88)
Patient chooses the duration of sitting before vibration occurs	12 (100)	0 (0)	0 (0)	2 (17)	10 (83)
Total score	**32 (88.9)**	**4 (11.1)**	**0 (0)**	**4 (12.5)**	**28 (87.5)**

Duration of intervention deliveries

On average, the educational component (n=21) delivery took 6.9±3.5 minutes and the feedback component (n=12) took 10.0±6.0 minutes. Individual timings of intervention deliveries are provided in Figure 6.3.

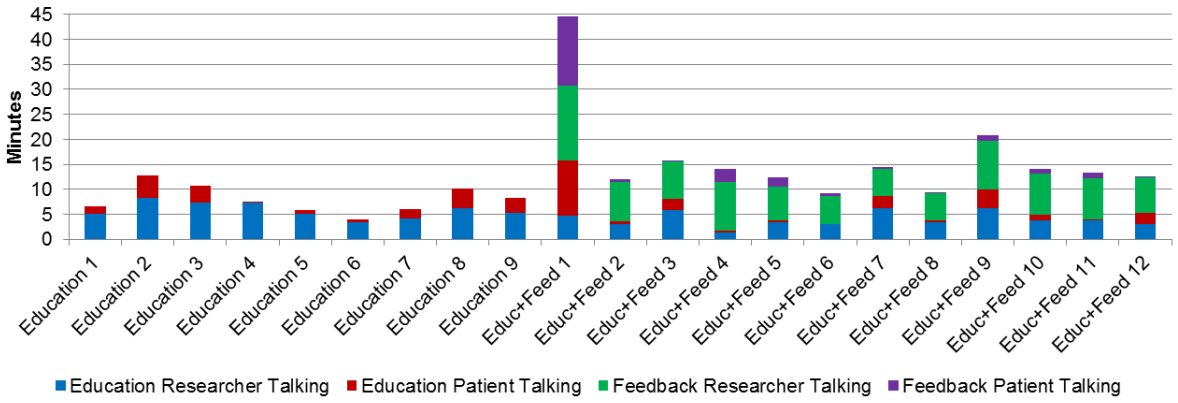

Figure 6.3 Individual durations of intervention deliveries stratified by intervention component (education and feedback) and person speaking (researcher or patient)

6.1.4 Feasibility of intervention technology

Device malfunctions

Three patients (25%) experienced a device malfunction. For two patients, the smart device malfunctioned which meant patients were unable to look at the LUMO app. For the other patient, it was reported that the step count was not updating even though the patient was stepping (day 5). There was a delay in communication between the LUMO and smart device but the problem did not persistent and no replacement device was required. Five phone calls were required to resolve the issues (2.80±0.75minutes per phone call).

Missing data

Missing data occurred for three patients (20%) with one patient having one missing day (patient turned the LUMO off), one patient having eight missing days (battery died for 5 days and patients turned LUMO off for 3 days) and one patient having 12 missing days (patient turned LUMO off).

6.1.5 Acceptability of activity monitors

Choice of vibration frequency

Of the 12 patients (58.3% female) randomised to the Education + Feedback group, 6 (50%; 66.7% female) chose for the vibration to occur after 30 minutes, 1 (8.3%; 0% female) after 45 minutes and 5 (41.7%; 60% female) after 60 minutes of consecutive sitting.

LUMO wear compliance

Patients wore the LUMO for 11.8±2.3 days over the 14 day period with 9.0±3.4 days having at least one vibration prompt occurring. Individual compliance with the LUMO and days prompted are presented in Figure 6.4. Two patients (25%) wore the LUMO for the full 14 days with wear compliance ranging 8-14 days. The number of days prompted ranged 2-12 with patients selecting a vibration setting of 30 minutes averaging 8.3±4.4 days prompted compared with 9.8±2.6 for patients selecting a vibration setting >30 minutes of consecutive sedentary behaviour (p=0.414).

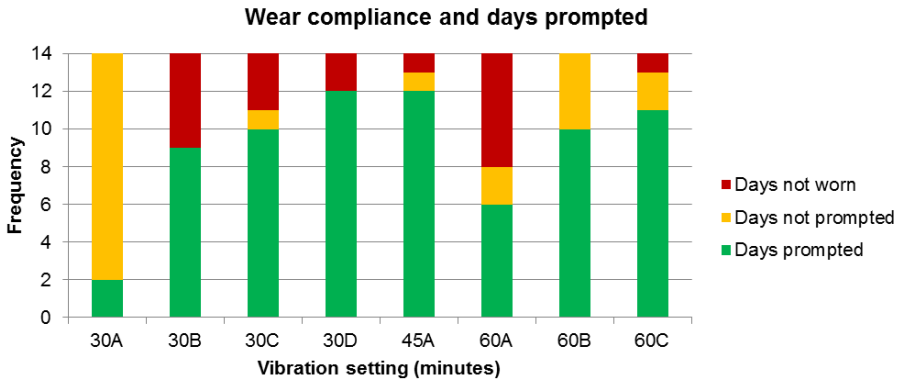

Figure 6.4 Wear compliance for the LUMO and number of days prompted

The day-by-day wear compliance and prompt occurrence over the 14 days is shown in Figure 6.5. The LUMO was worn on days 2-5 by all patients with day 14 having the lowest compliance (50%). Out of a total of 94 days the LUMO was worn, at least one vibration prompts occurred on 72 days (76.6%) with an average of five prompts per day.

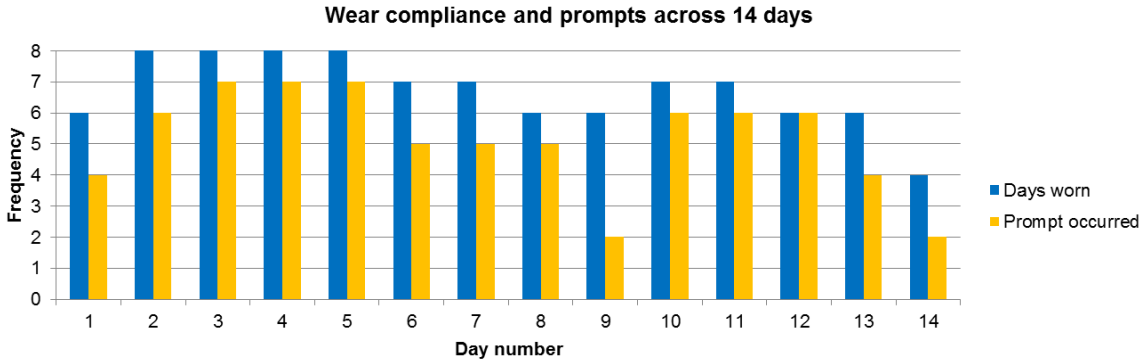

Figure 6.5 Wear compliance for the LUMO and number of days prompted over the 14 day period

Charging compliance

Charging compliance for 15 patients (88.2% of patients who completed the study) was examined, with a maximum 13 overnight occurrence where patients were asked to charge the LUMO. Thirteen charging occurrence (one per day/overnight) was considered 100% compliance. On average, patients charged the LUMO 8.4±3.9 times lasting 617±320 minutes over the 14 days. Ten patients (66.6%) had more than 50% charging compliance (≥7 days) and seven patients (46.6%) had greater than 75% charging compliance (≥10 days).

6.1.6 Acceptability: Comparison of completers and non-completers

Characteristics of patients by study completion

Examining differences between patients who did and did not complete the trial may help to identify potential reasons for this (Table 6.5). Patients who did not complete the study had higher postcode deprivation and had more comorbidities than patients who completed the study.

Table 6.5 Baseline characteristics of patients stratified by trial completion, reported as mean (SD) unless otherwise stated

	Not Completed (n=16)	**Completed (n=17)**
Demographics		
Age	69.5 (11.2)	66.6 (9.6)
Female gender (%)	11 (68.8)	12 (70.6)
IMD decile	3.0 (2.6)	5.8 (3.1) *
Income decile	2.9 (2.4)	5.3 (2.8) *
Employment decile	3.1 (2.7)	5.7 (2.8) *
Education and skills decile	2.3 (1.8)	4.4 (2.6) *
Health and disability decile	3.4 (2.8)	6.1 (3.0) *
Crime decile	3.5 (2.4)	5.3 (2.3) *
Barriers to housing and services decile	5.9 (2.4)	7.2 (2.5)
Living environment decile	5.4 (2.4)	6.4 (1.8)
IDACI decile	2.3 (2.1)	5.4 (2.9) *
IDAOPI decile	3.0 (2.2)	5.7 (2.7) *
Distance to travel for appointment (miles)	9.3 (6.9)	7.2 (3.7)
Employment status (%):		
Retired	13 (81.3)	12 (70.6)
Unemployed / Unable to work	1 (6.3)	4 (23.6)
Employed	2 (12.5)	1 (5.9)
Lung health and comorbidities		
Smoking status (%):		
Current	7 (43.8)	4 (23.5)
Former	9 (56.3)	12 (70.6)

Pack years	49.5 (25.1)	44.3 (26.5)
Usual mMRC grade	2.6 (1.3)	2.7 (1.1)
Home oxygen (%)	1 (6.3)	2 (11.8)
12 month all-cause admissions	1.6 (1.2)	1.7 (2.3)
12 month AECOPD admissions	1.2 (1.3)	0.7 (1.1)
New diagnosis of COPD (%)	0 (0)	3 (17.6)
Number of comorbidities	4 (3)	2 (3) *
Hospital stay		
Time from admission to consent (days)	3.3 (1.9)	3.7 (1.6)
Time from consent to discharge (days)	2.1 (3.8)	2.1 (2.5)
Time from admission to discharge (days)	5.4 (3.7)	5.8 (2.8)
AECOPD readmissions (%)	4 (25.0)	0 (0) *
Self-reported symptoms		
EQ-VAS	40.5 (22.4)	41.2 (19.3)
CAT score	25.4 (7.8)	24.5 (7.4)
Fatigue score	18.1 (11.7)	21.0 (12.2)
HADS depression score	9.3 (3.9)	7.4 (5.2)
HADS anxiety score	9.6 (6.2)	8.9 (5.5)
FESI score	35.4 (14.2)	31.5 (13.5)
Self-reported physical activity		
Daily walking time (minutes)	19.3 (19.4)	6.5 (7.7)
Daily moderate PA (minutes)	2.5 (8.7)	2.0 (7.1)
Daily vigorous PA (minutes)	0.0 (0.0)	0.0 (0.0)
Self-reported sitting time β		
Daily TV sitting time (minutes)	378.0 (267.5)	336.3 (239.4)
Daily travel sitting time (minutes)	28.0 (35.1)	77.5 (78.7)
Daily computer sitting time (minutes)	30.0 (58.3)	48.1 (61.2)
Daily other sitting time (minutes)	51.9 (50.6)	141.2 (159.7)
Daily sitting time (minutes)	487.9 (245.9)	603.1 (257.4)
Pulmonary rehabilitation		
Attended clinic appointment (%)	6 (37.5)	8 (47.1)
PR accepted (%)	2 (12.5)	5 (29.4)
PR attended (%)	2 (12.5)	2 (11.8)
Previously attended PR (%):		
Within 12 months	0 (0)	1 (5.9)
Within 24 months	0 (0)	1 (5.9)
More than 24 months ago	3 (18.8)	6 (35.3)
Never	13 (81.3)	8 (47.1)

Abbreviations: AECOPD, acute exacerbation of chronic obstructive pulmonary disease; BMI, body mass index; CAT, COPD assessment test; EQ-VAS, EuroQol visual analogue scale; COPD, chronic obstructive pulmonary disease; FESI, falls efficacy scale international; FEV_1, forced expiratory volume in one second; FVC, forced vital capacity; HADS, hospital anxiety and depression scale; IDACI, income deprivation affecting children index; IDAOPI, income deprivation affecting older people index; IMD, Index of Multiple Deprivation; mMRC, modified Medical Research Council; PA, physical activity; PR, pulmonary rehabilitation; SPPB, short physical performance battery; TV, television

β, daily work sitting is missing for the three patients in employment

6.1.7 Indicators of intervention efficacy

Vibration prompt occurrences and response timings

Overall, 325 vibration prompts occurred with patients not responding 219 times (67.4%) (Figure 6.6). Of the 106 responses, 43 (40.6%) occurred within 5 minutes, 25 (23.6%) occurred 5-10 minutes after the prompt and 38 (35.8%) occurred 10-15 minutes after the prompt.

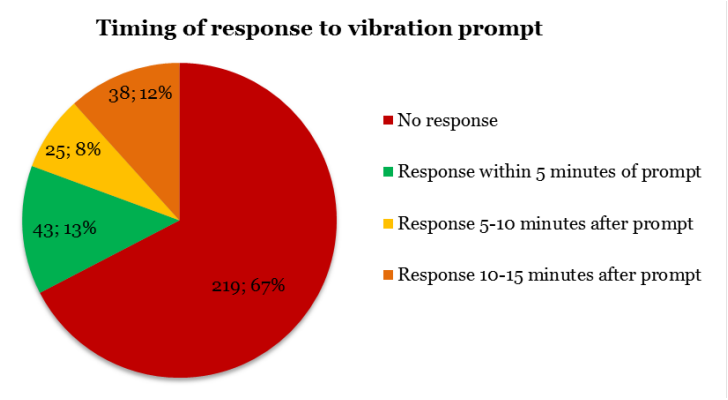

Figure 6.6 Overall responses to vibration prompts

Behavioural response to vibration prompts

Behavioural responses (sedentary, standing and walking) to the vibration prompts within five minutes of the prompt occurring are provided in Figure 6.7. When patients responded to the prompt, they spent 1.4±0.8 minutes standing and 0.4±0.3 minutes walking, taking 21.2±11.0 steps. Time standing ranged 0.3-3.0 minutes and time walking ranged 0.2-1.2 minutes (Figure 6.8).

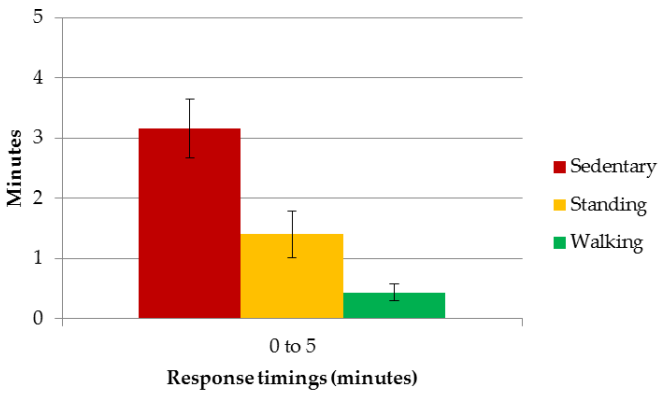

Figure 6.7 Behavioural responses to the LUMO vibration prompt as a group within five minutes of the prompt occurring

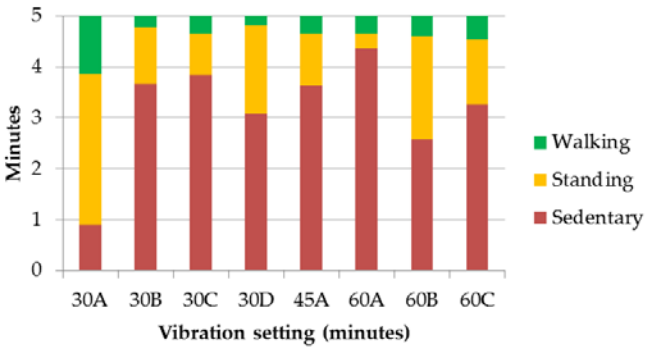

Figure 6.8 Behavioural responses to LUMO vibration prompts for individual patients within five minutes of the prompt occurring

6.2 Discussion

This study examined the feasibility of conducting an education and self-monitoring intervention using wearable technology to reduce sedentary behaviour in COPD patients admitted for an acute exacerbation. Almost one-third of patients offered the study took part or which around half attended their follow-up appointment. Reasons for not attending were predominantly around to being unable to cope or being readmitted. Patients responded to approximately one-third of the vibration prompts of which ~40% occurred within 5 minutes.

The proportion of eligible patients (70.7%) exceeded the threshold of feasibility set for the trial (66.6%). Patient uptake to the trial (31.5%) approached the specified threshold for feasibility (33.3%). Study uptake was similar to that of a peri-exacerbation pulmonary rehabilitation study (32.3%) conducted in the same hospital (Greening et al., 2014) with the rate of recruitment faster than a physical activity intervention using wearable technology (Fitbit Ultra) at a similar time point (average of 2.2 versus 0.6 patients per week) (Hornikx et al., 2015). Main reasons for refusing the intervention in-hospital were feeling too unwell or having concomitant ailments. Retention of patients to the two week follow-up appointment (51.2%) met the feasibility threshold (50.0%). The screening method in the present study failed to capture ~13% of patients and ~47% of admitted patients were discharged before they could be offered the study. The main reasons for this were: 1) patients received usual care before being entered onto the screening log, 2) usual care may have occurred close to discharge, and 3) only one researcher recruited patients. This has important implications for the feasibility of service implementation as well as future trials.

For patients receiving the education and self-monitoring interventions 75% of patients completed the trial; comparable to previous behavioural interventions in this population (Tabak, Brusse-Keizer, van der Valk, Hermens, & Vollenbroek-Hutten, 2014). Given the greater flexibility of at-home self-monitoring interventions with regard to facility requirements and travel commitments, offering such interventions at multiple time-points when symptoms are more stable may improve uptake. Whilst this 'light-touch' (i.e. no study-specific contacts with patients until a telephone call on day 12 (out of 14) to confirm attendance to the follow-up appointment) approach may be more scalable and better implemented into routine care, study-specific contacts may need to be better tailored depending on patients' circumstances. For example, patients burdened by more comorbidities and those living in more deprived areas were found to be less likely not to attend the follow-up visit. Therefore, more 'touches' may be needed for these individuals.

The accelerometer wear compliance was poor (38.5%) when evaluated using traditional wear time criteria of at least 10 waking hours. For example, older US adults have been found to achieve 84% compliance based on this criterion (Troiano et al., 2008). This may have been attributable, at least in part, to the dual monitor deployment. With advancements in activity monitoring technology and increasing recognition of the importance of capturing the 24 hour day for understanding behaviour and health outcomes (Chaput et al., 2014) there is a need to shift the traditional form-factors (e.g. wear location and attachment mechanism) for activity monitoring. Wrist-worn activity monitoring appears to be the most popular location for commercially available activity trackers with 53% of adults preferring to wear such devices at this location (Alley et al., 2015). Moreover, consumer devices are becoming increasingly sophisticated with many devices able to measure multiple health indices (Piwek, Ellis, Andrews, & Joinson, 2016). Therefore, the future RCT should consider moving activity monitors to a more desirable location to improve compliance (van Hees et al., 2011).

Despite patients not responding to the vibration prompt two-thirds of the time, positive responses within 5 minutes of the vibration prompts involved an additional 18-23 steps (~1% increase in total daily step count) and 1.1-1.9 minutes less sedentary time each time a patient responded. It is perhaps unrealistic to expect patients to respond to all vibration prompts as even in apparently healthy office workers barriers such concentrating on work tasks prevent behaviour change from occurring (Geleijnse, Van Halteren, & Diekhoff, 2011). Furthermore, some of the unheeded nudges may have been the result of poor timing as the technology was not 'context aware'. For example, prompts could have gone off whilst driving. Due to usage

restrictions placed on the smart device the choice of vibration setting could not be changed during the 14 days. As patients report considerable variations in day-to-day symptoms (Miravitlles et al., 2014a) additional flexibility permitting patients to easily alter the frequency of the haptic feedback may facilitate greater engagement with the intervention.

Whilst the post-discharge period is a critical time for intervention, additional opportunities for patients to engage with programmes to reduce sedentary behaviour and promote increases in physical activity may also be warranted. For example, reducing prolonged sedentary behaviour during patients' hospital stay has been advocated (Lazarus, Murphy, Coletta, McQuade, & Culpepper, 1991) as prolonged bed rest has been associated with complications which may negate recovery including disuse muscle atrophy, joint deformity and rigidity, and thromboembolic disease (Brower, 2009). Important barriers to the adoption of physical activity or sedentary behaviour programmes in-hospital include the misconception that activity is only a preventative measure, lack of time, lack of structural support and lack of high quality studies testing the approach (Börjesson, 2013). Additionally, patients generally have short-stays when admitted, creating logistical barriers (Börjesson, 2013). However, implementation of an intervention that begins in-hospital and continues after discharge may help overcome some of these issues. Objective quantification of in-hospital physical activity and sedentary behaviour in COPD patients is lacking but observations from hospital staff found to be lying in bed for 51% of the day, sitting out of bed for 43%, standing for 1% and walking for 5% of the day (Cattanach, Sheedy, Gill, & Hughes, 2014).

Previous physical activity or sedentary behaviour self-monitoring studies in COPD seldom report on the fidelity of the intervention. In the present study, intervention fidelity was good, indicating that the education and feedback components were consistently delivered at a sufficient quality. However, inter-rater variation could not be examined in the present study as only one person delivered the education and feedback components. Therefore, no inferences can be made on how multiple delivers may vary in the provision of the interventions. For the education component, two suggestions were deemed unsuitable for most patients and were therefore not suggested verbally to them; these were "tiptoe when waiting in a queue" and "sit to stand with no hands". Future designs of the educational booklet should explore more attainable and less daunting alternatives for patients.

The study eligibility criteria, uptake and retention were deemed to be feasible overall and acceptable by some of the patients and most hospital staff. Several modifications are

proposed: (a) to offer the interventions at multiple time-points along the care pathway; (b) improve the targeting of patients who may need more contacts to comply with the intervention; (c) explore alternative form-factors (e.g. wear location and attachment mechanism) for objective physical activity and sedentary behaviour monitoring; (d) focus on the haptic feedback aspect of the self-monitoring technology; (e) increase the flexibility of patients' ability to engage with the intervention tool (e.g. changing the vibration frequency); (f) use data from the present study to inform flexible goal setting; and (g) adjust the education booklet to ensure suggestions resonate with all patients.

Key strengths of the present study include the successful recruitment of older, multi-morbid and acutely ill patients to a lifestyle behaviour change intervention using wearable self-monitoring technology during hospital admission; the rich information collected to thoroughly examine the feasibility and acceptability of trial and the objective quantification of physical activity and sedentary behaviour. However, retention rates and activity monitor wear time compliance of this 'low-touch' trial require improvement in order to sufficiently assess the efficacy of a full trial. Additionally, health economic analyses are needed to ensure the intervention is cost-effective before incorporation into routine care.

6.3 Conclusion

Eligibility, recruitment and retention rates suggest a trial targeting sedentary behaviour in hospitalised COPD patients is feasible. Strategies to improve overall activity monitor compliance are needed in order for a full-scale trial to obtain reliable primary outcome data. The vibration prompts were acceptable to patients and resulted in meaningful increases in time spent standing and step count. A revised intervention, building on the successful components of the present feasibility study is justified.

Chapter 7: General discussion

In the UK an estimated 3.7 million adults have a diagnosis of COPD (Shahab et al., 2006) and it is the second most common reason for emergency hospital admission (Healthcare Commission, 2006); costing the NHS approximately £500 million each year (Pauwels & Rabe, 2004). Physically inactive and sedentary lifestyles put patients at risk of falling into the vicious cycle of inactivity-breathlessness, in turn increasing their risk of hospitalisation (Donaire-Gonzalez et al., 2015; Garcia-Aymerich et al., 2006). Whilst it is suspected that COPD impacts physical activity in milder disease, there has been little focus on the role of sedentary behaviour and understanding the drivers of this deleterious health behaviour. Equally, it has been postulated that sedentary behaviour may be successful conduit for lifestyle behaviour change in COPD patients (Hill et al., 2015) but no studies have addressed this idea to date.

The approach taken in this three study thesis was to examine the role of physical activity and sedentary behaviour across the spectrum of COPD severities, using objective quantification of behaviour to better understand the need for lifestyle interventions in this population. The work comprising this thesis has explored the factors associated with lifestyle behaviours in mild-moderate COPD patients (Study One), assessed the role of these behaviours in mild-moderate COPD patients reporting severe symptoms (Study Two) and examined the feasibility of an intervention in patients with severe COPD admitted for an exacerbation to reduce their sedentary behaviour using wearable self-monitoring technology (Study Three). The individual findings, strength and limitations of these studies have been provided in the respective chapters. This chapter will discuss the findings of the thesis as a whole and how these findings add to existing literature in the context of proposed directions for future research.

Gaps identified for Study One were:

a. Need for the examination of correlates of physical activity in mild-moderate COPD using objective monitoring and comparisons to apparently healthy adults
b. Paucity of evidence assessing correlates of sedentary time in COPD and whether these correlates differ with those of physical activity

Gaps identified for Study Two were:

c. Need to understand factors associated with mild-moderate COPD patients reporting severe symptom burden
d. Need to explore the potential role of physical activity and sedentary time in patients reporting more severe symptoms

Gaps identified for Study Three were:

e. Lack of behavioural interventions for patients after an acute exacerbation
f. No studies have specifically targeted reductions in sedentary behaviour in COPD

7.1 Key findings from the thesis

In Study One mild-moderate COPD patients were found to be more sedentary and less physically active than apparently healthy adults. Breathlessness and percentage body fat were independently positively associated with sedentary time and negatively associated with light activity. Exercise capacity was independently positively associated with MVPA for COPD patients. Factors associated with behaviour were similar to apparently healthy adults. Although cross-sectional, these findings demonstrate that even in patients with milder COPD interventions to boost physical activity levels and reduce sedentary time are required; particularly for patients reporting more severe breathlessness and/or who are overweight or obese. Study Two found that physical activity and sedentary time were associated with more severe breathlessness, physical limitations performing activities of daily living, confidence leaving the home, energy levels and previous exacerbations in mild-moderate COPD patients. Study Three was the first intervention in COPD specifically targeting reductions in sedentary behaviour. This randomised controlled feasibility trial provided evidence that targeting reductions in sedentary behaviour is a feasible and suitable conduit for advanced patients and supports the conduct of a revised intervention, building on the successful components of this trial. Together, this work highlights the importance of examining lifestyle behaviours across the intensity spectrum, from time spent sedentary to engaging in MVPA, regardless of the grade of patients' COPD.

7.1.1 The timing of behavioural interventions

This thesis has explored physical activity and sedentary behaviour across the spectrum of disease severity, from mild-moderate patients to those with more advanced disease admitted for an acute exacerbation. It is clear that patients with COPD would benefit from lifestyle

and/or exercise interventions regardless of the severity of airflow limitation and symptom burden. For patients with mild-moderate COPD, Study One identified breathlessness, body composition and exercise capacity to be important factors associated with behaviour. Study Two found physical activity, sedentary time and exercise capacity to be related to patients reporting more severe symptoms. These are important findings given the milder stage of the disease. As a result, interventions to prevent patients falling into the vicious cycle of physical inactivity and increased dyspnea are needed within existing care pathways.

The benefits of leading a physically active lifestyle follow the law of diminishing returns whereby those individuals leading highly inactive and sedentary lifestyles have the most to gain from small improvements to their daily routine (Sparling, Howard, Dunstan, & Owen, 2015). Therefore, achieving small changes in the lifestyle activity of COPD patients are likely to have significant impacts on health. Pulmonary rehabilitation is an established intervention for COPD patients in order to improve exercise capacity and health-related quality of life (Lacasse et al., 2006). Whilst rehabilitation plays a pivotal role in patient recovery and the prevention of readmissions lifestyle-embedded physical activity must also be addressed in order to reduce the risk of hospitalisation and mortality (Garcia-Aymerich et al., 2006). In a meta-analysis (Cindy Ng et al., 2012), pulmonary rehabilitation was found to have only a small effect on physical activity beyond that of the structured exercise classes. Moreover, when patients complete pulmonary rehabilitation improvements in fitness are lost, suggesting that patients do not take part in sufficient physical activity to maintain the benefits gained from the supervised sessions (Egan et al., 2012). Consequently, physical activity requires its own module within the multidisciplinary system of pulmonary rehabilitation. Objective monitoring of patients' physical activity and sedentary behaviour inside and outside of pulmonary rehabilitation will be fundamental to the successful integration of behaviour change programmes.

Whilst specific physical activity and sedentary behaviour modules are needed within pulmonary rehabilitation, Study One and Study Two have highlighted the need to address these issues sooner i.e. before patients present to hospital. One avenue may be through primary care. For example, 'making every contact count' (MECC) initiatives such as general practitioners offering advice on increasing physical activity has shown signs of potential based on self-reported behavioural outcomes (Orrow, Kinmonth, Sanderson, & Sutton, 2012). However, data is lacking on whether this approach is feasible or effective for COPD patients. Given the rigorous time constraints placed on primary care consultations, the coupling of

these appointments with objective data (e.g. physical activity, inhaler compliance) from sensors providing data prior to the appointment (e.g. through a secure cloud-based system) may facilitate such MECC schemes. Another approach, specific to COPD, has been the Self-management Programme of Activity, Coping and Education for Chronic Obstructive Pulmonary Disease (SPACE for COPD) trial which has shown positive results in patients recruited from primary care (Steiner, 2013). Patients engaging with the SPACE for COPD manual, which includes help and advice on staying fit and active, managing symptoms, improving diet, resistance training and dealing with setbacks was found to improve anxiety, disease knowledge and exercise capacity in a sample of 184 patients (Mitchell et al., 2014).

Study Three found that a self-monitoring intervention targeting sedentary behaviour using wearable technology is feasible for COPD patients post-discharge following an exacerbation. Therefore, future research should continue to explore the use of low intensity movement prescription as a conduit for increases in physical activity and reductions in sedentary time. Few devices are currently available to allow patients to specifically monitor their sedentary behaviour (Sanders et al., 2016) but results from this thesis support the potential for such devices to positively impact patients' lifestyles. As highlighted in previous chapters, the post-exacerbation period marks a critical period for intervention but it has received little attention as a potential opportunity to influence behaviour.

Whilst there have been efforts to increase physical activity (Mantoani, Rubio, McKinstry, MacNee, & Rabinovich, 2016), including during the post-discharge period (Hornikx et al., 2015) and after pulmonary rehabilitation (Vorrink, Kort, Troosters, Zanen, & Lammers, 2016), Study Three was the first to target reductions in sedentary behaviour for COPD patients. Whilst there is more evidence for the benefits of increasing physical activity on reduced risk of hospitalisation and premature mortality (Donaire-Gonzalez et al., 2015; Esteban et al., 2016; Garcia-Aymerich et al., 2006), the sedentary lifestyles led by more severe patients, although well recognised (Pitta et al., 2005), have not been extensively examined. Perhaps one reason for the lack of attention for sedentary behaviour has been confusion over its distinction with physical inactivity. Physical inactivity is considered to be a level of MVPA not sufficient to meet physical activity guidelines (Davies et al., 2011) whereas sedentary behaviour is defined as any waking activity characterized by an energy expenditure $\leq$1.5 METS in a sitting or reclining posture (Sedentary Behaviour Research, 2012). For example, in a systematic review of studies using objective monitors for behavioural assessment, only nine out of 76 identified studies were found to have assessment

sedentary behaviour. However, one of these nine studies defined sedentary behaviour as 1.0-1.9 METS and three of these studies used <3.0 METS which incorporates light intensity physical activity (Byrom & Rowe, 2016). Therefore, before interventions can be designed, the knowledge and measurement of sedentary behaviour in COPD must be improved and its distinction from physical inactivity understood.

7.1.2 Patient stratification

This thesis has shown that a patient's physical activity, sedentary time and exercise capacity are associated with the severity of their COPD symptoms. Therefore, these baseline characteristics should be accounted for when designing interventions. It is important to highlight that exercise and/or physical activity centred approaches may be too unrealistic for many COPD patients; particularly those recently admitted for an acute exacerbation. Study Three found that for many of these individuals, targeting reductions in their sedentary time was appealing and feasible to conduct during the post-exacerbation period. Therefore, an additional component to the stratification model proposed by Singh (Singh, 2014) (Figure 1.7). A modified version is provided in Figure 7.1. The polar groups by this stratification are coded green (e.g. similar exercise capacity to healthy adults and meets recommended levels of MVPA and sedentary behaviour) and red (e.g. poor exercise capacity, does not meet recommended levels of MVPA and exceeds the recommended time sedentary). A particularly important group to target would be the "S&P" group who, despite being physically capable (i.e. similar exercise capacity to healthy adults), do not participate in sufficient physical activity and spend too much time being sedentary. By stratifying patients based on their functional capacity and their behaviour (activity and sedentariness) existing and future interventions may better tailor their content and delivery to suit the needs and preferences of patients. For example, patients attending pulmonary rehabilitation do not necessarily share the same end goal. For example, there are a range of baseline levels of fitness, symptoms, airflow limitation, exacerbation history and activity levels which makes a 'one size fits all' approach very difficult and can result in an inefficient use of both patient and staff resources. Having multiple options within a single programme may not only improve the relevance and quality of delivery for individual patients but it may also encourage more patients to attend, engage with and complete such interventions.

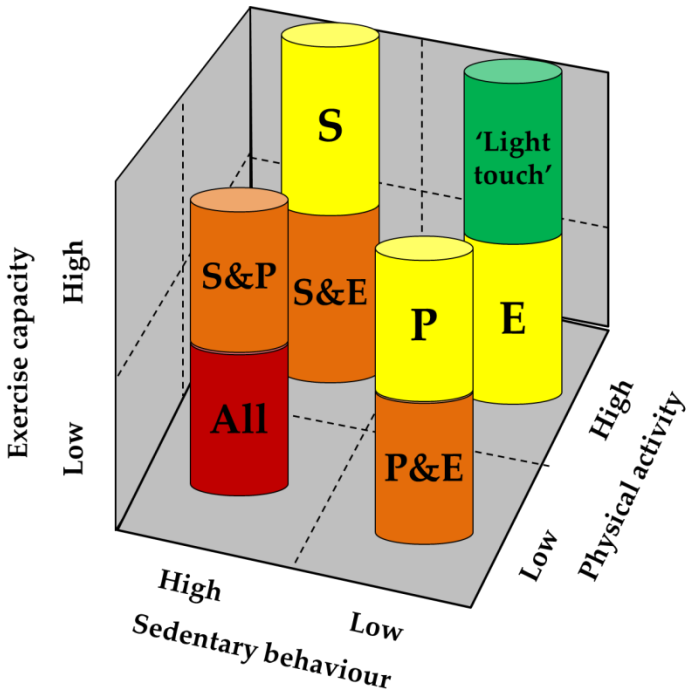

Figure 7.1 The potential stratification of interventions based on physical activity, exercise capacity and sedentary behaviour. The figure is colour coded as follows: red, requires three-component intervention; amber, requires two-component intervention; yellow, requires single-component intervention; green, requires maintenance programme. Abbreviations are as follows: E, requires exercise capacity intervention; P, requires physical activity intervention; S, requires sedentary behaviour intervention.

Interventions aiming to increase physical activity and reduce sedentary behaviour must not only take into account baseline levels and patient ambitions relating to these constructs but also extraneous factors such as social circumstances and frequency of hospital or General Practice visits. Figure 7.2 presents the three C's: Capability, Context and Category which should also be considered for patient stratification. The focus of an intervention should be related to the *context* in which a patients lives and the context in which the intervention will be set. For example, patients in the earlier stages of the disease may have more regular contact with their general practitioner compared with more severe patients who likely spend more time in hospital. For patients with a strong social support, interventions may need to engage family members as well as the patient themselves. The *capability* (i.e. what type of intervention is most suited to the patients physical or mental state) and *category* (i.e. which mode of intervention delivery is most appealing to the patient) should also be considered. For example, exercise capacity is routinely examined prior to a patient starting pulmonary rehabilitation but patients are not yet asked to wear an activity monitor to capture baseline

physical activity and sedentary behaviour. Future research to optimise patient stratification approaches to intervention development is needed.

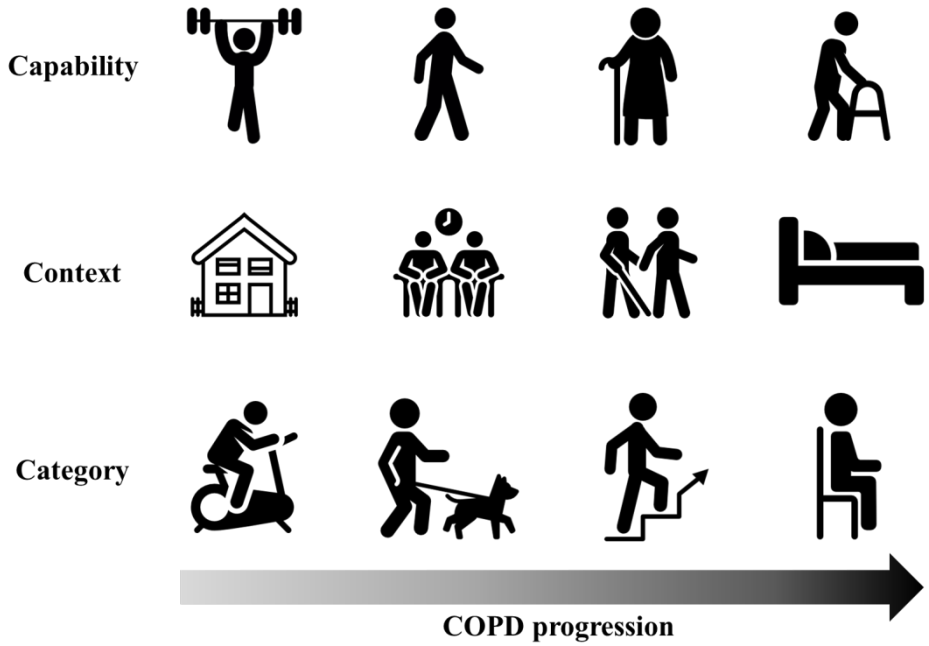

Figure 7.2 The three C's of patient considerations for interventions

7.1.3 The "Quantified Patient"

COPD patients were found to be highly compliant wearing a wrist-worn physical activity monitor in the PhARaoH Study (Study One and Study Two) with findings from COPD-SEAT (Study Three) supporting the potential for patients to use wearable self-monitoring technology; even when recovering from an exacerbation at home. Moreover, as time goes on the level of technology competency and adoption in elderly populations will increase as technology as a whole becomes ever-present in daily life. Consequently, efforts to engage patient populations with technology-based intervention will become increasingly important and more feasible. With recent technological advancements in wearable self-monitoring technology has emerged the Quantified Self movement (Swan, 2013) which aims to empower individuals to improve their health through the reviewing of data related to their own physiology and lifestyle. The movement began in the management of diabetes, notably the self-management of blood sugar levels through capillary sample analysis at home. However, health markers fluctuate invariably every second in response to environmental changes, stresses, sickness, emotional states and physical activity (or lack of). Thus, technology to monitor health must adapt just as quickly in order to adequately account for the severity, frequency, duration and regularity of these occurrences.

In respiratory disease, patients typically rely on the use of peak flow meters and inhalers to manage their breathlessness; with some inhalers acting as 'preventers' with others used as 'responders' i.e. prevent symptoms occurring or respond when symptoms become severe. However, adherence to inhalers is poor (Corden, Bosley, Rees, & Cochrane, 1997) and many patients struggle to management their symptoms on a daily basis (Bourbeau & Bartlett, 2008). It is clear from Study One and Study Two that even patients with mild COPD can report severe symptom burden such as severe breathlessness. Consequently, the next steps in improving the management of COPD symptoms is to further empower patients to understand their disease and how best to manage it in the context of its inevitable fluctuations and in relation to their own body and behaviour. Advances in commercial technology now mean that the real-time unobtrusive and non-invasive measure of a range of health markers (e.g. behaviour, medication adherence, and physiology) is paving the way for more long-term and sophisticated monitoring. As advances in health technology continue, both patients and healthcare providers will have the potential to have a veritable armoury of self-monitoring tools to improve the daily management of disease for patients with COPD and other ailments.

Results from Study Two revealed consistent associations of physical activity and sedentary time with symptom severity; demonstrating the importance of targeting behaviour in the context of symptom management. A potential avenue for future research and a potential use of the advancing technologies is bio-behavioural feedback whereby both the behaviour and the physiological consequence of the behaviour are provided to the user. For example, many patients experiencing an exacerbation are particularly fearful of pushing themselves to be physically active, thereby entering the vicious inactivity-breathlessness cycle (Polkey & Moxham, 2006). However, if patients could see in real-time their breathing rate, depth and oxygen levels, for example, whilst engaging in physical activity also quantified in real-time they could see first-hand when their body needs to rest/recover. This concept is used as standard stopping criteria for field walking tests (Holland, Spruit, & Singh, 2015), supporting the need for research to transition this principle from the confines of a controlled setting to patients' homes. Over time, patients can learn how much they can push themselves in accordance with their own physiological response rather than the premature fear of becoming too breathless or becoming too desaturated. By facilitating patients to understand their body's response to physical activity and sedentary behaviour we may be able to empower them to move more and sit less, safely, informed by their own physiological response to movement. Future research should first explore this concept during pulmonary rehabilitation and/or

during hospital admission where patients can be educated by trained healthcare staff in a safe and structured environment.

7.2 Strengths and limitations

7.2.1 Strengths

"The NHS belongs to the people. It is there to improve our health and wellbeing, supporting us to keep mentally and physically well, to get better when we are ill, and when we cannot fully recover, to stay as well as we can to the end of our lives"

- The NHS constitution

We cannot hope to conduct impactful research without consulting those we are trying to impact. A strength of this thesis was the genuine and early PPI. For the PhARaoH Study (Study One and Study Two), feedback from PPI members included advice and suggestions on the order of tests performed in order to provide frequent rest periods for patients (e.g. using the questionnaire between spirometry efforts) as well as the types of physical tests conducted as part of the 2-3 hour visit and the length/suitability/language of the questionnaire and study documentation. For COPD-SEAT (Study Three), PPI members provided extensive input into the design and content of the educational booklet and the suitability of the self-monitoring technology (e.g. app designs and patient-driven vibration frequency). PPI members also provided valuable insight into study documentation and offered advice and input on how to make the study more appealing in the context of experiencing an acute exacerbation of COPD.

Much of the published research and clinical focus on COPD has been on patients in the more severe stages of the disease; notably patients classified as GOLD 1 (mild) comprise a small proportion of referrals to pulmonary rehabilitation across England and Wales (Steiner, Holzhauer-Barrie, Lowe, Searle, Skipper, Welham, & Roberts, 2015b). A key strength of this thesis is the recruitment from primary care (Study One and Study Two) in order to reach patients who do not necessarily meet the entry criteria for pulmonary rehabilitation or get admitted to hospital often and therefore are not provided with clear opportunities to engage with research. Consequently, it was possible to understand the physical activity and sedentary behaviour of patients who may be less burdened by their COPD. It is understandable that patients with more advanced disease require more intensive and more frequent healthcare services, resulting in an estimated annual cost of £149 for a patient with mild COPD compared with £1307 for a patient with severe COPD (PEARSON, 2004). However, by

better understanding the role of behaviour in COPD the three studies in this thesis were able to provide valuable insight into the types of interventions which may be more suitable and yield improvements in symptom management; potentially reducing or delaying subsequent healthcare costs.

Unlike many other measures which are obtained in controlled settings under ideal conditions (e.g. walking tests or anthropometry), the deployment of activity monitors often relies on the participant to wear the device each day and for a sufficient duration to be considered representative. An important strength of the wrist-worn deployment used in the PhARaoH Study (Study One and Study Two) was the high compliance obtained over the seven day wear period. During a one week monitoring period, 4-7 days of data are considered a reliable measure of physical activity (Janz, Witt, & Mahoney, 1995; Trost, Pate, Freedson, Sallis, & Taylor, 2000). In the original sample used for these thesis studies (i.e. the PhARaoH Study sample), 98.9% of participants met the minimum four days of at least 10 waking hours criteria. Much of this high compliance was likely due to the placement of the monitor on the wrist rather than traditional locations such as the waist (van Hees et al., 2011) which permitted participants to wear the monitor during sleep. As a result of this, participants did not need to remember to put the monitor on in the morning or remove it at bedtime, limiting the opportunities for human error and increasing the comfort of wearing the device.

The transparency and rigour of the behavioural measurement in this thesis is a strength; allowing fully reproducible deployment, processing and analysis for both wrist-worn and waist-worn accelerometer locations. The reporting of information pertaining to data collection parameters, data cleaning and the identification of valid accelerometer data is lacking in existing COPD literature (Byrom & Rowe, 2016) which limits data pooling capabilities and comparisons between studies. Of note is the omission of four processing criteria that should be reported as standard: 36% of studies were found not to report the number of days patients were instructed to wear the device; 70% of studies did not state how many days were required from patients to be included in analysis; 87% of studies did not report criteria for determining non-wear; and 47% of studies did not report how a valid day of accelerometer data was defined (Byrom & Rowe, 2016). In addition 11% of studies included days where the activity monitor was worn for 22-24 hours each day (Byrom & Rowe, 2016) which is likely to contain a large amount of sleep which may have been misclassified as sedentary. Therefore, whilst methodological transparency should be standard, the detail provided in the present thesis goes well beyond what has been observed to date.

7.2.2 Limitations

Whilst the use of accelerometry is an important strength of this thesis, accelerometers are not without their limitations. Accelerometers used were not waterproof which meant participants were asked to take them off for shower, baths and swimming. Ideally, wearable devices should be able to capture every second of the day regardless of the types of activities being performed by the wearer. In addition, the accuracy of measurement from these devices (particularly when worn on the waist, Study Three) is directly related to proper placement of the devices by study participants (i.e. correct orientation). Therefore, the quality of the resulting data can be negatively impacted by deviations from proper placement which can arise by participant error, waist circumference and clothing. For waist-worn accelerometer placements (Study Three), accelerometry would be unable to capture activities such as cycling and resistance training due to the body (centre of mass) remaining still during performance (Montoye, Kemper, Saris, & Washburn, 1996). Wrist-worn accelerometry may be able to detect these types of activities in the future (e.g. through pattern recognition and machine learning) (Mannini, Intille, Rosenberger, Sabatini, & Haskell, 2013). However, this is not currently possible without extensive controlled calibration; limiting utility for observation studies requiring intense data collection periods. Given the location on the extremities, wrist-worn accelerometry has not yet been calibrated using criterion measures such as indirect calorimetry. Therefore, the cut-points used in this thesis (Study One and Study Two) were derived from concurrent validity studies against established waist-worn accelerometry criteria for sedentary time, light activity and MVPA (Kamada et al., 2016) and a thigh-worn inclinometer for sedentary time (Koster et al., 2016).

It would have been preferable for apparently healthy adults and COPD patients taking part in the PhARaoH Study (Study One) to have been better matched for age and gender (these factors were instead controlled for statistically as covariates). Unfortunately, matching was difficult to achieve in part due to the recruitment strategy for patients i.e. mostly from General Practice invitations through the Primary Care Research Network. It was largely unknown the timescales for invitation and how receptive both General Practices and the patients would be to taking part in a study comprising a large battery of measures. The final samples of apparently healthy adults and COPD patients did not permit matching on age and gender. One potential solution may have been to actively encourage spouse participation for the COPD patients who took part in the study as well as the apparently healthy controls meeting similar age ranges of the completed patients.

Although not unique to the studies conducted as part of this thesis, participation bias, whereby the individuals taking part in research disproportionally possess particular characteristics which prevent a representative sample being obtained, may have occurred in PhARaoH (Study One and Study Two) and COPD-SEAT (Study Three). For example, the array of measures taken as part of the PhARaoH Study may have attracted individuals who may be concerned about their health (e.g. someone may have a family history of asthma or heart disease). Equally, the COPD patients who took part in the study may be those individuals who felt able to complete the large battery of tests. In COPD-SEAT, the study information sheet given to eligible patients clearly identifies sedentary behaviour and wearable technology as important components of the study; thereby potentially attracting patients with a greater understanding or interest in these areas. However, much like for pulmonary rehabilitation, those individuals finding the method of delivery or target outcome more appealing will naturally be more likely to participate. Just as the self-monitoring technology and subsequent study designs will continue to advance so will the level of technology competency and experience of the patients who may benefit. Despite this, it should be noted that a technology-based intervention will never be acceptable for some people.

A limitation of the COPD-SEAT intervention (Study Three) was the assumption of patients' motivation to reduce their sedentary behaviour and/or motivation to be active. The LUMO was designed to support the volitional phase of behaviour change (Schwarzer, 2008) by nudging/prompting the wearer and providing information on activity and sitting. However, the information and behavioural prompts could not be set up to adjust for established fluctuations in people's motivation levels (Conroy, Elavsky, Doerksen, & Maher, 2013) as well as symptom severity (Kessler et al., 2011). Assessing patients' motivation and precise intentions at the start of the intervention may facilitate their engagement with the programme and produce tailored goals to assist with maintenance.

Practical barriers, primarily concomitant research studies and training commitments, meant that COPD-SEAT (Study Three) was not delivered by healthcare staff in routine contact with patients i.e. COPD Specialist Nurses or physiotherapists. However, the intervention delivery was designed in line with current routine practice (e.g. within comparable timeframes as smoking cessation advice or inhaler technique training). Nevertheless, future iterations should explore whether the status/role of the intervention deliverer plays a significant role in the uptake, retention or engagement levels of patients with the intervention.

Chapter 8: Future directions and conclusions

8.1 Future directions

There has been an exponential rise in the volume of research into physical activity in COPD, but as with research into public health, the holy grail of behaviour change remains hidden. In addition, the recognition of sedentary behaviour as a key target for intervention has appeared late on the scene and as such a large gap in the evidence base exists. Much like the field of physical activity and public health, the primary challenge faced by researchers is to find ways to evoke sustainable and sufficient behaviour change to ameliorate symptoms, reduce admissions and prevent premature mortality. This thesis supports the following areas for future research:

1. The potential impact of sedentary behaviour in COPD, including symptom severity, using prospective study designs.
2. Personalised behavioural and exercise interventions based on baseline characteristics e.g. participation in MVPA, time spent sedentary and walking capacity.
3. Behavioural interventions for patients with mild disease (particular those reporting high symptom burden) before they present to hospital in order to prevent patients falling into the vicious cycle of inactivity and breathlessness.
4. Exploring the use of targeting reductions in sedentary behaviour as a conduit for behaviour change; particularly for patients with more advanced COPD or for whom more intense activity may be unrealistic or unsuitable.
5. Incorporating significant advancements in technology such as non-invasive, unobtrusive physiological and behavioural devices into existing care pathways (e.g. pulmonary rehabilitation and during admission) to facilitate positive behaviour change and improved self-management.

As the objective measurement of physical activity and sedentary behaviour is likely to remain a prominent feature in COPD research, improvements in the quality and transparency of deployment, processing and analysis are urgently required. Future research endeavours should continue to meld expertise across disciplines, including measurement experts in the field of physical activity and sedentary behaviour. The incorporation of objective behaviour quantification for patients is an important area for future research; from informing general practitioners about the lifestyles of their patients, to evaluating activity levels inside and away

from pulmonary rehabilitation, to in-hospital monitoring as a potential marker of readiness for discharge.

8.2 Conclusions

Mild-moderate COPD patients were less physically active and spent more time sedentary then apparently healthy adults. However, factors predicting behaviour were similar between groups. Correlates were different between sedentary time, light activity and MVPA for both groups. Lower exercise capacity, less time spent being physically active and spending more time sedentary are associated with patients of the same severity of airflow limitation reporting contrasting symptom severities. These findings support the need for interventions to boost exercise capacity, physical activity and reduce sedentary time to be offered to patients with mild-moderate COPD, particularly those reporting more severe symptoms. In the first intervention targeting sedentary behaviour in COPD, the use of wearable self-monitoring technology was feasible and acceptable to patients following an acute exacerbation. Evidence from this thesis has contributed a greater understanding of physical activity and sedentary behaviour in COPD patients across the spectrum of disease severity, from understanding the correlates of behaviour in mild-moderate COPD patients to intervening during periods of acute illness in patients with advanced COPD.

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Appendices

Appendix A

PhARaoH Study research ethics committee approval letter

Health Research Authority

NRES Committee East Midlands - Nottingham 2

The Old Chapel Royal Standard Place
Nottingham NG1 6FS
Telephone : 0115 8839695

11 November 2013

Professor Mike Morgan
National Clinical Director for respiratory
disease University Hospitals of Leicester
Glenfield Hospital
Groby Road
Leicester
LE39QP

Dear Professor Morgan,

Study title:	**Physical Activity and Respiratory Health (PhARaoH) Study**
REC reference:	**13/EM/0389**
IRAS project ID:	**127506**

The Research Ethics Committee reviewed the above application at the meeting held on 28 October 2013.

We plan to publish your research summary wording for the above study on the NRES website, together with your contact details, unless you expressly withhold permission to do so. Publication will be no earlier than three months from the date of this favourable opinion letter. Should you wish to provide a substitute contact point, require further information, or wish to withhold permission to publish, please contact the REC Manager - Liza Selway 0115 8839695

Ethical opinion

- The chair introduced himself and the committee and welcomed the researchers to the meeting
- The committee asked what will happen to the audio recordings at the end of the study and the researchers advised the once transcribed then all audio tapes will be destroyed
- The committee asked what is the role of the undergraduates and the researchers advised that they will not be taking any blood samples or analysing participants personal data. Both undergraduates are studying sport science
- The committee asked how the early stages of recruitment of participants would occur. The researchers advised that participants will be identified through Clinical Care Groups that will contact GP surgeries within their area by using a database of patients. Participants will also self-refer through advertisement in GP surgeries. The GP practices will then send out Patient Information Sheets to different patient groups who have previously given spirometry readings

Guidance on applying for NHS permission for research is available in the Integrated Research Application System or at http://www.rdforum .nhs.uk.

Where a NHS organisation 's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre'}, guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of approvals from host organisations

Registration of Clinical Trials

All clinical trials (defined as the first four categories on the IRAS filter page) must be registered on a publically accessible database within 6 weeks of recruitment of the first participant (for medical device studies, within the timeline determined by the current registration and publication trees).

There is no requirement to separately notify the REC but you should do so at the earliest opportunity e.g when submitting an amendment. We will audit the registration details as part of the annual progress reporting process.

To ensure transparency in research, we strongly recommend that all research is registered but for non clinical trials this is not currently mandatory.

If a sponsor wishes to contest the need for registration they should contact Catherine Blewett (catherineblewett@nhs.net), the HRA does not, however, expect exceptions to be made.

Guidance on where to register is provided within IRAS.

It is responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

Approved documents

The documents reviewed and approved at the meeting were:

Document	*Version*	*Date*
Advertisement	Website Advert V1	30 September
Advertisement	Radio Advert	30 September
Advertisement	1	30 September
Covering Letter		01 October 2013
GP/Consultant Information Sheets	1	30 September
Interview Schedules/Topic Guides	Sub study interview	30 September 2013
Investigator CV	Professor Morgan	

Adding new sites and investigators

- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

The NRES website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

Feedback

You are invited to give your view of the service that you have received from the National Research Ethics Service and the application procedure. If you wish to make your views known please use the feedback form available on the website.

Further information is available at National Research Ethics Service website > After Review

13/EM/0389 **Please quote this number on all correspondence**

We are pleased to welcome researchers and R & D staff at our NRES committee members' training days – see details at http://www.hra.nhs.uk/hra-training/

With the Committee's best wishes for the success of this project.

Yours sincerely
Dr Martin Hewitt Chair

Email: NRESCommittee.EastMidlands-Nottingham2@nhs.net

Enclosures: *List of names and professions of members who were present at the meeting and those who submitted written comments*

"After ethical review - guidance for researchers" SL-AR2

Copy to: *Mrs Carolyn Maloney, Research and Development Manager University Hospitals of Leicester*

Mrs Carolyn Maloney, Research and Development Manager University Hospitals of Leicester

Appendix B

PhARaoH Study methods and database publication

open health data

Orme, M W et al 2016 Physical Activity and Respiratory Health (PhARaoH): Data from a Cross-Sectional Study. *Open Health Data*, X: eX, DOI: http://dx.doi.org/10.5334/ohd.28

DATA PAPER

Physical Activity and Respiratory Health (PhARaoH): Data from a Cross-Sectional Study

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Corresponding author: Mark W. Orme (m.w.orme@lboro.ac.uk)

The dataset consists of a densely phenotyped sample of adults collected from March to August 2014. The dataset captures behavioural, physical, physiological and psychosocial characteristics of individuals with and without a General Practitioner diagnosis of chronic obstructive pulmonary disease (COPD). Data were collected at Glenfield Hospital on 436 individuals (139 COPD patients and 297 apparently healthy adults) aged 40–75 years, residing in Leicestershire and Rutland, United Kingdom. The dataset includes seven days of raw wrist-worn accelerometry, venous blood biomarkers, non-invasive point-of-care cardio-metabolic risk profiles, physical measures and questionnaire data.

Keywords: Physical activity; respiratory; accelerometry; health
Funding statement: NHS England facilitation funds.

1. Overview

Introduction/Study Description

The Physical Activity and Respiratory Health (PhARaoH) study is a cross-sectional study funded by research facilitation funds from National Health Service (NHS) England. The study was devised, managed and conducted in collaboration between Loughborough University, University Hospitals of Leicester NHS Trust and the Respiratory Biomedical Research Unit at Glenfield Hospital.

The aims of the study were: (i) to examine the role of physical activity and sedentary behaviour on respiratory health with an emphasis on its associations with chronic obstructive pulmonary disease (COPD) and (ii) to investigate associations between behavioural, physical, psychosocial, clinical and demographic information with self-reported symptom severity in COPD patients recruited from primary care.

2. Context

Spatial coverage

The study recruited participants residing in Leicestershire and Rutland and appointments were conducted at the Respiratory Biomedical Research Unit, Glenfield Hospital, Leicester, United Kingdom.

Temporal coverage

10th March 2014–31st August 2014.

Species

Homo sapiens.

3. Methods

Steps

The Primary Care Research Network (PCRN) invited General Practices across Leicestershire and Rutland, United Kingdom to conduct a search on their databases to identify patients with a diagnosis of COPD of any respiratory stage, aged 40–75 years. Fifteen practices (two from East Leicestershire and Rutland Clinical Commissioning Group (CCG), six from West Leicestershire CCG and seven from Leicester City CCG) sent out invitations to identified patients. Patients wishing to participate were instructed to return the reply form to the Respiratory Biomedical Research Unit, Glenfield Hospital. Upon receipt of the reply form, a researcher from the PhARaoH team contacted the interested individual via telephone to confirm eligibility and to book the visit.

Apparently healthy adults were recruited through posters and leaflets distributed across Leicestershire and Rutland in community organisations and facilities (e.g. libraries, community halls, leisure centres). Targeted recruitment of apparently healthy South Asians was conducted through a Gujarat Hindu Association Health and Wellbeing event and by a radio show and advertisements aired in English and Sikh Punjab (Kohinoor Radio 97.3 FM).

Appendix C

PhARaoH Study consent form

CONSENT FORM

Physical Activity and Respiratory Health (PhARaoH) Study

Chief Investigator: Professor Mike Morgan

Contact Investigator: Dr Lauren Sherar

Contact: Dr Lauren Sherar, +44 (0)1509 223285

Participant Study ID Label: ☐

PLEASE INITIAL EACH BOX

1. I confirm that I have read and understood the Participant Information Sheet version 3, dated 7th January 2014 and have had the opportunity to ask questions. ☐
2. I understand that my consent and participation are voluntary and that I am free to withdraw from the study at any time without my medical care or legal rights being affected. ☐
3. I agree to undertake the investigations as described in the information sheet. ☐
4. I agree to my GP being informed about my participation in the study. ☐
5. My GP can be informed of the results obtained from my participation in the study. ☐
6. I understand that my data may be used by, shared and stored with other ethically approved research, and with academic or industry partners, if it is anonymised, now and in the future. ☐ Yes ☐ No
7. I understand that relevant sections of my medical notes and/or study data may be looked at by responsible individuals from the study team, the sponsor, NHS Trust or from regulatory authorities where it is relevant to my taking part in the research. I give permission for these individuals to access my records. ☐
8. I agree to take part in the study. ☐
9. I wish to be contacted regarding the one-to-one interviews (sub-study). ☐ Yes ☐ No
10. I wish to be contacted regarding other studies ☐

Appendix D

PhARaoH Study participant information sheet

PATIENT INFORMATION SHEET

Physical Activity and Respiratory Health

(PhARaoH) Study

An observational study investigating the roles of physical activity and sedentary behaviours, and psychological and social factors in chronic obstructive pulmonary disease (COPD) patients in order to inform strategies to delay COPD development or progression.

TO TAKE PART IN THE STUDY PLEASE CALL

01509 228225

Chief Investigator: **Professor Mike Morgan**

Co- Researchers: Professor Stuart Biddle, Dr Dale Esliger, Dr Dominic Malcolm, Professor Myra Nimmo, Dr Lauren Sherar, Professor Sally Singh, Dr Michael Steiner

You may contact:: **Dr Lauren Sherar**

+44 (0)1509 228225

If you have any questions regarding your health please contact your GP.

Invitation

You are being invited to take part in an observational study looking at the associations among physical activity and sedentary behaviours, and psychological and social factors in the development of chronic obstructive pulmonary disease (COPD). The information obtained from this study will be used to inform strategies to delay COPD progression or development. Before you decide whether or not you want to take part, you should understand what the purpose of the study is and how you will be involved. Please take time to read this information sheet and discuss it with family and friends if you wish. Please ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

What is the purpose of the study?

The purpose of this study is to examine the physical, psychological and social factors that are related to physical activity and sedentary behaviours (such as watching television) on respiratory health in patients diagnosed and not diagnosed with COPD. We hope that the findings of this study will enable a greater understanding of COPD and will inform strategies to improve respiratory health.

Why have I been chosen?

You have been identified as potentially eligible for the study because you are between the age of 40 and 75 years, registered with a GP practice in Leicestershire and Rutland

Do I have to take part?

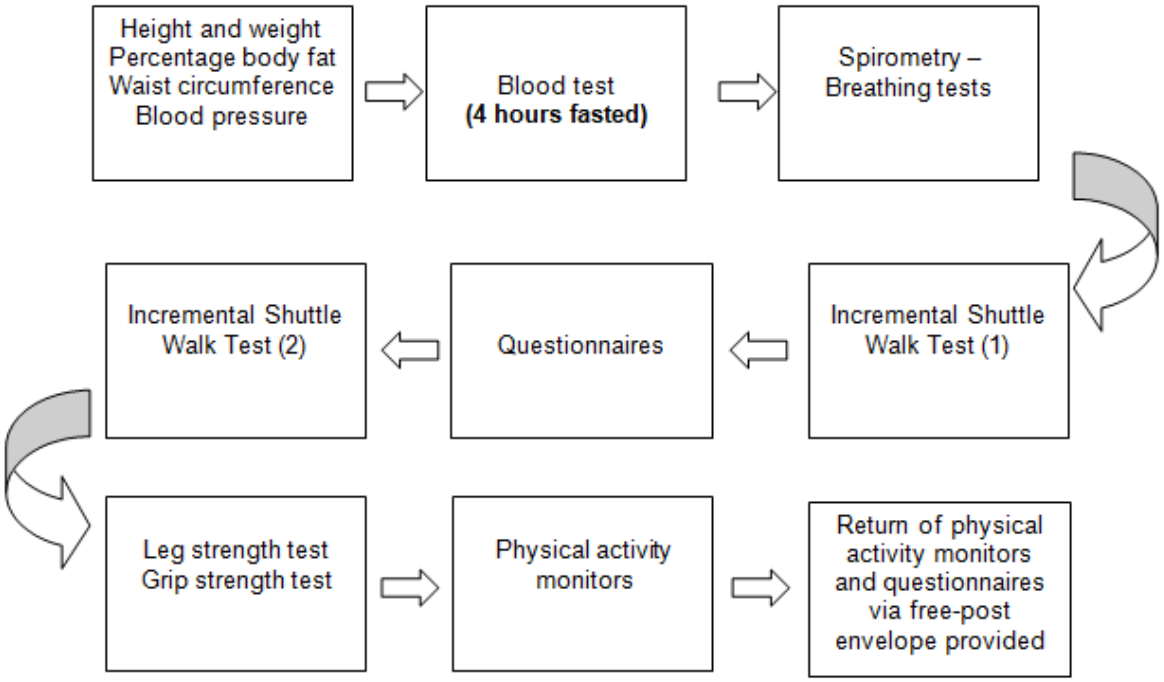
It is up to you to decide to join the study. We will describe the study and go through the information sheet with you. If you agree to take part, we will ask you to sign a consent form. You are free to withdraw at any time, without giving a reason. If you decide not to participate or withdraw from the study, your NHS care will **not be affected** in any way. If you do decide to withdraw we may still use the data and samples collected up until the point you withdraw from the study.

What will happen to me if I take part?

We ask that you arrive to your appointment having fasted for 4 hours(not eaten or drank anything except water) and, if possible, refrain from smoking and being exposed to second-hand smoke for 24 hours prior to your appointment. We also ask that you do not take part in exercise on the day of your visit.

You will be asked to participate in a one-off visit to the Respiratory Biomedical Research Unit at Glenfield Hospital in Leicester for approximately 2 hours.

Assessment Visit Flow Chart



Description of the investigations

Height, weight, waist circumference, percentage body fat, blood pressure

Measurements of height and weight will be used to calculate your body mass index. You will be asked to remove your shoes, socks and personal belongings during the measurements. Weight and percentage body fat will involve standing on a weighing scale device. Waist circumference is measured using a tape measure and is an important indicator of abdominal or central obesity. Blood pressure will be measured whilst you are seated at rest. Immediate feedback of these results will be provided to you.

Blood sample

We kindly ask that you do not eat or drink (except water) 4 hours prior to your appointment time as blood samples will need to obtained with you in a fasted state. A small blood sample will be taken by a trained health professional in order to examine your cardiovascular and metabolic health status including blood sugar and blood cholesterol levels. These results will be sent to your GP if consented, who will contact you directly if the results suggest that you may require treatment or advice.

Breathing Tests

We kindly ask that, if possible, you do not smoke and avoid second-hand smoke for 24 hours prior to your appointment time. An opportunity to have a cigarette will be provided during the visit. These will involve several breathing tests on different machines by breathing out as hard as you can several times separated by recovery periods. These breathing tests may cause some temporary light headedness, and coughing.

Incremental Shuttle Walk Test (ISWT)

The ISWT is a fitness test requiring you to walk only. You will walk up and down a 10meter (11 yard) course in an empty corridor with the speed of the walk dictated by a CD player. The time limit to walk the 10m course will be signalled by bleeps, with the time between bleeps shortening as the test progresses. You will be asked to continue walking until you feel unable to maintain the necessary speed without becoming unduly breathless. A researcher will help with pacing by walking alongside you at the beginning of the walk. This test will be performed twice, with a 30 minute rest period in between. Portable oxygen or walking aids can be used if this is what you are used to. You will also be asked to wear a chest strap which monitors heart and breathing rate during the test.

Questionnaires

The rest period between the shuttle walk tests provides the ideal time to complete the questionnaires. The questionnaires cover a variety of factors important for understanding the effects of lifestyle (e.g. physical activity and smoking); psychological factors (e.g. anxiety and perceived health); social factors (e.g. demographics); and physical influences (e.g. breathlessness) on respiratory health. Researchers will be on hand to answer any questions you may have whilst filling them in.

Leg and Grip Strength Tests

We will measure the strength of your leg muscles by asking you to sit on a specially designed strength testing machine and push with your leg as hard as you can against a pad, while we measure the force you produce. The grip strength test involves you squeezing a measuring device with maximal force on three occasions with a rest period in between.

Cardiovascular Health

These quick, non-invasive measurements will be taken whilst you are seated at rest in order to measure the function and health of your blood vessels (arteries). The first involves a sensor being placed on your finger for a few seconds. The second involves resting your forearm on a device which assesses, using light, blood vessel heath.

Physical activity

You will be given a wrist-worn activity monitor and a waist-worn activity monitor to take home after the assessment. These are to measure your physical activity and sitting time over an 8 day period. You are asked to take the waist-worn device off during water-based activities e.g. bath, swimming, etc. and overnight. The wrist-worn monitor can be kept on continuously. We do not wish you to change your normal day- to-day routine. These devices will be returned after the 8 days using the free-post envelope we provide you with. An information sheet about the monitors and verbal instructions will be provided at the visit. **We ask that you do not change your usual activity habits.**

Interview Sub-study

In addition to the visit conducted at Glenfield Hospital, approximately 50 COPD patients will take part in a smaller-scale qualitative study which will involve one-on- one interviews, at the participant's chosen location, to obtain responses to developing COPD; particularly regarding physical activity. Evidence will be used to inform tailored interventions to increase physical activity in an effort to reduce the rate of decline in lung function and improve health-related quality-of-life. Each participant will complete one

interview lasting no longer than 1 hour. Participation in this sub-study is also entirely voluntary with interviews scheduled to suit you. As only a sub-sample of individuals will be recruited, consenting to be contacted does not mean you will definitely be asked to take part. More information can be found in the enclosed information sheet.

Expenses
We will reimburse you for your travel expenses (petrol and parking) from home to Glenfield Hospital and if required we can arrange taxis for you. Refreshments will also be provided during study visits.

What will I have to do?

We kindly ask that you do not eat or drink (except water) 4 hours prior to your appointment time.

If you are a smoker, we kindly ask that you do not smoke for 24 hours or as long as possible prior to your appointment time.

We also ask that you do not take part in exercise on the day of your visit.

If you currently take prescription medication, please bring a copy of your prescription or medication packaging with you to the visit.

Please wear light clothing for the visit. A snack will be provided after your blood sample has been taken. We **do not** ask that you make any other changes to your lifestyle.

What are the possible benefits of taking part?
By taking part in this study, you will receive a comprehensive health check sent to both yourself and your GP as well as written information and explanation of your physical activity levels. Any clinically important results will be passed on to your GP. Ultimately, taking part in the research will help to facilitate better care for COPD patients and those at risk of developing COPD.

What are the possible disadvantages and risks of taking part?

As with all physical activity, there is a very small risk of accident or injury during the exercise tests (walking and strength tests). All the exercise will be supervised by trained research staff and will take place on NHS premises with resuscitation equipment available and trained staff on hand to use it. Taking blood samples from your arm may cause slight pain or bruising afterwards. There are no specific disadvantages other than the time commitment for the visit.

What will happen to the samples that I have donated?
The blood samples will be processed at Glenfield Hospital by the research team. If you do not complete the whole study we will still use the samples that you have donated up until the point you withdrew unless you request otherwise.

What happens when the research study ends?
The results of this study will be circulated in medical journals, professional publications and presentations made at relevant conferences. Results will be reported in

such a way that you or your information will not be identifiable. You will receive a summary of the results and will be invited to a presentation of the findings.

What if there is a problem?

If you are harmed by taking part in this research project, there are no special compensation arrangements. If you are harmed due to someone's negligence, then you may have grounds for a legal action but you may have to pay for it. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been approached or treated during the course of this study, the normal National Health Service complaints mechanisms would be available to you. Advice can also be sought from the Patient Information and Liaison Service, contact 0808 178 8337 (free number).

Will my taking part in this study be kept confidential?

When you enter this study you will be given a unique study number. This number will be used in place of any identifiable information, such as your name. All information which is collected about you during the course of the research will be kept strictly confidential. Any information about you which leaves the hospital, for example for data analysis or monitoring, will have your name and address removed so that you cannot be recognised from it. Your medical records may also be looked at by the regulatory authorities, the sponsor or the NHS Trust to check that the study is being carried out correctly. All information resulting from you taking part in the study will be stored both in paper and computerised form, and will be treated confidentially.

Who is organising and funding the research?

The study is sponsored by University Hospitals of Leicester NHS Trust. The study is being funded by the Department of Health, UK after thorough review by leading scientists in this field. The study is supported by NIHR Leicester Respiratory Biomedical Research Unit.

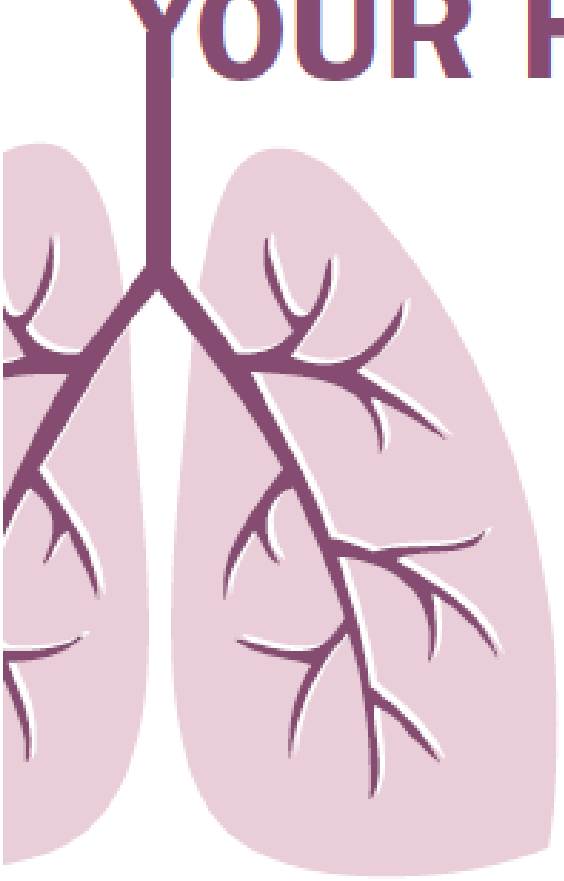
Who has reviewed the study?

All research that involves NHS patients or staff, information from NHS medical records or uses NHS premises or facilities must be reviewed by an NHS Research Ethics Committee before it goes ahead. Approval does not guarantee that you will not come to any harm if you take part. However, approval means that the committee is satisfied that your rights will be respected, that any risks have been reduced to a minimum and balanced against possible benefits and that you have been given sufficient information on which to make an informed decision. The NHS Research Ethics Committee(East Midlands Nottingham 2) approved the study on (11th November 2013).The UHL Trust Research Management Governance team has also reviewed and given permission for the study to be carried out.

Appendix E

PhARaoH Study recruitment poster

DO YOU WANT TO KNOW MORE ABOUT YOUR HEALTH?



ARE YOU AGED BETWEEN 40 AND 75 LIVING IN LEICESTERSHIRE?

The Respiratory BRU at Glenfield Hospital and Loughborough University are conducting a research study looking at the effect of physical activity on respiratory health.

CONTACT US

Text your name or call us for free on

01509 228225

or visit us at

www.pharaohstudy.com

Feedback includes your ...

- Blood Pressure
- Lung Function
- Physical Activity Level
- Grip Strength

DH Department of Health

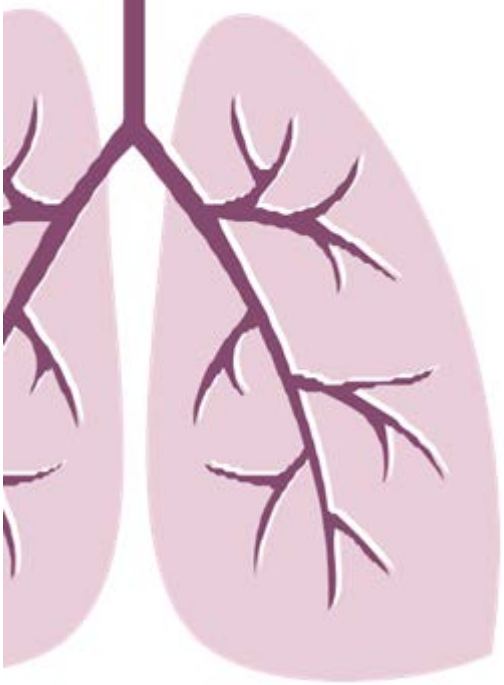
University Hospitals of Leicester NHS

Loughborough University

Appendix F

PhARaoH Study recruitment leaflet

DO YOU WANT TO KNOW MORE ABOUT YOUR HEALTH?



ARE YOU AGED BETWEEN **40 AND 75** LIVING IN LEICESTERSHIRE?

The Respiratory BRU at Glenfield Hospital and Loughborough University are conducting a research study looking at the role of physical activity behaviours in the development of lung disease. Findings from this study will be used to inform strategies to delay lung disease progression and development.

Testing will be from **January 2014**

You be asked to attend one visit lasting approximately 2 hours at the Respiratory Biomedical Research Unit (BRU) at Glenfield Hospital, Leicester.

You will be asked to attend your appointment, having fasted (not eat or drink anything other than water) for 4 hours. A snack will be provided during your visit.

All travel expenses will be reimbursed.

Interested in taking part?

Text your name or call us on

01509 228225

or visit us at

www.pharaohstudy.com

MEASUREMENTS INCLUDE:

- Body mass index
- Waist circumference
- Percentage body fat
- Blood pressure
- Lung function
- Grip strength
- Leg strength
- Aerobic fitness (submaximal)
- Blood cholesterol and sugar levels
- Physical activity level

Version 1, 7-Jan-14, ISRC TM78843393

DH Department of Health

University Hospitals of Leicester NHS

Loughborough University

Appendix G

Physical Activity Readiness Questionnaire (PAR-Q)

PAR-Q+

The Physical Activity Readiness Questionnaire for Everyone

Regular physical activity is fun and healthy, and more people should become more physically active every day of the week. Being more physically active is very safe for MOST people. This questionnaire will tell you whether it is necessary for you to seek further advice from your doctor OR a qualified exercise professional before becoming more physically active.

SECTION 1 - GENERAL HEALTH

	Please read the 7 questions below carefully and answer each one honestly: check YES or NO.	YE	NO
1.	Has your doctor ever said that you have a heart condition OR high blood pressure?	☐	☐
2.	Do you feel pain in your chest at rest, during your daily activities of living, OR when you do physical activity?	☐	☐
3.	Do you lose balance because of dizziness OR have you lost consciousness in the last 12 months? Please answer NO if your dizziness was associated with over-breathing (including	☐	☐
4.	Have you ever been diagnosed with another chronic medical condition (other than heart disease or high blood pressure)?	☐	☐
5.	Are you currently taking prescribed medications for a chronic medical condition?	☐	☐
6.	Do you have a bone or joint problem that could be made worse by becoming more physically active? Please answer NO if you had a joint problem in the past, but it does not limit your current ability to be physically active. For example, knee, ankle, shoulder or other.	☐	☐
7.	Has your doctor ever said that you should only do medically supervised physical activity?	☐	☐

If you answered NO to all of the questions above, you are cleared for physical activity. Go to Section 3 to sign the form. You do not need to complete Section 2.

- Start becoming much more physically active – start slowly and build up gradually.
- Follow the Canadian Physical Activity Guidelines for your age (www.csep.ca/guidelines).
- You may take part in a health and fitness appraisal.
  - If you have any further questions, contact a qualified exercise professional such as a CSEP Certified Exercise Physiologist® (CSEP-CEP) or CSEP Certified Personal Trainer® (CSEP-CPT).
  - If you are over the age of 45 yrs. and NOT accustomed to regular vigorous physical activity, please consult a qualified exercise professional (CSEP-CEP) before engaging in maximal effort exercise.

If you answered YES to one or more of the questions above, please GO TO SECTION 2.

Delay becoming more active if:

- You are not feeling well because of a temporary illness such as a cold or fever – wait until you feel better
- You are pregnant – talk to your health care practitioner, your physician, a qualified exercise professional, and/or complete the PARmed-X for Pregnancy before becoming more physically active OR
- Your health changes – please answer the questions on Section 2 of this document and/or talk to your doctor or qualified exercise professional (CSEP-CEP or CSEP-CPT) before continuing with any physical activity programme.

SECTION 2 - CHRONIC MEDICAL CONDITIONS

Please read the questions below carefully and answer each one honestly: check YES or NO.			YES	NO
1.	Do you have Arthritis, Osteoporosis, or Back Problems?		☐ If yes, answer questions 1a-1c	☐ If no, go to question 2
	1a.	Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer NO if you are not currently taking medications or other treatments)	☐	☐
	1b.	Do you have joint problems causing pain, a recent fracture or fracture caused by osteoporosis or cancer, displaced vertebra (e.g., spondylolisthesis), and/ or spondylolysis/pars defect (a crack in the bony ring on the back of the	☐	☐
	1c.	Have you had steroid injections or taken steroid tablets regularly for more than 3 months?	☐	☐
2.	Do you have Cancer of any kind?		☐ If yes, answer questions 2a-2b	☐ If no, go to question 3
	2a.	Does your cancer diagnosis include any of the following types: lung/bronchogenic, multiple myeloma (cancer of plasma cells), head, and	☐	☐
	2b.	Are you currently receiving cancer therapy (such as chemotherapy or radiotherapy)?	☐	☐
3.	Do you have Heart Disease or Cardiovascular Disease? This includes Coronary Artery Disease, High Blood Pressure, Heart Failure, Diagnosed Abnormality of Heart Rhythm		☐ If yes, answer questions 3a-3e	☐ If no, go to question 4
	3a.	Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer NO if you are not currently taking medications or other treatments)	☐	☐
	3b.	Do you have an irregular heart beat that requires medical management? (e.g. atrial fibrillation, premature ventricular	☐	☐
	3c.	Do you have chronic heart failure?	☐	☐
	3d.	Do you have a resting blood pressure equal to or greater than 160/90 mmHg with or without medication? (Answer YES if you do not know your resting	☐	☐
	3e.	Do you have diagnosed coronary artery (cardiovascular) disease and have not participated in regular physical activity in the last 2 months?	☐	☐
4.	Do you have any Metabolic Conditions? This includes Type 1 Diabetes, Type 2 Diabetes, Pre-Diabetes		☐ If yes, answer questions 4a-4c	☐ If no, go to question 5
	4a.	Is your blood sugar often above 13.0 mmol/L? (Answer YES if you are not sure)	☐	☐
	4b.	Do you have any signs or symptoms of diabetes complications such as heart or vascular disease and/or complications affecting your eyes, kidneys, and the sensation in your toes and feet?	☐	☐
	4c.	Do you have other metabolic conditions (such as thyroid disorders, pregnancy- related diabetes, chronic kidney disease, liver problems)?	☐	☐
5.	Do you have any Mental Health Problems or Learning Difficulties? This includes Alzheimer's, Dementia, Depression, Anxiety Disorder, Eating Disorder, Psychotic Disorder, Intellectual Disability, Down Syndrome)		☐ If yes, answer questions 5a-5b	☐ If no, go to question 6
	5a.	Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer NO if you are not currently taking medications or other treatments)	☐	☐
	5b.	Do you also have back problems affecting nerves or muscles?	☐	☐
Please read the questions below carefully and answer each one honestly: check YES or NO.			YES	NO

6.	Do you have a Respiratory Disease? This includes Chronic Obstructive Pulmonary Disease, Asthma, Pulmonary High Blood Pressure		☐ If yes, answer questions 6a-6d	☐ If no, go to question 7
	6a.	Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer NO if you are not currently taking medications or other treatments)	☐	☐
	6b.	Has your doctor ever said your blood oxygen level is low at rest or during exercise and/or that you require supplemental oxygen	☐	☐
	6c.	If asthmatic, do you currently have symptoms of chest tightness, wheezing, laboured breathing, consistent cough (more than 2 days/week), or have you used your rescue medication more than twice	☐	☐
	6d.	Has your doctor ever said you have high blood pressure in the blood vessels of your lungs?	☐	☐
7.	Do you have a Spinal Cord Injury? This includes Tetraplegia and Paraplegia		☐ If yes, answer questions 7a-7c	☐ If no, go to question 8
	7a.	Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer NO if you are not currently taking medications or other treatments)	☐	☐
	7b.	Do you commonly exhibit low resting blood pressure significant enough to cause dizziness, light-headedness, and/or fainting?	☐	☐
	7c.	Has your physician indicated that you exhibit sudden bouts of high blood pressure (known as Autonomic Dysreflexia)?	☐	☐
8.	Have you had a Stroke? This includes Transient Ischemic Attack (TIA) or Cerebrovascular Event		☐ If yes, answer questions 8a-c	☐ If no, go to question 9
	8a.	Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer NO if you are not currently taking medications or other treatments)	☐	☐
	8b.	Do you have any impairment in walking or mobility?	☐	☐
	8c.	Have you experienced a stroke or impairment in nerves or muscles in the past 6 months?	☐	☐
9.	Do you have any other medical condition not listed above or do you live with two chronic conditions?		☐ If yes, answer questions 9a-c	☐ If no, read the advice on page 4
	9a.	Have you experienced a blackout, fainted, or lost consciousness as a result of a head injury within the last 12 months OR have you had a diagnosed concussion within the last 12 months?	☐	☐
	9b.	Do you have a medical condition that is not listed (such as epilepsy, neurological conditions, kidney problems)?	☐	☐
	9c.	Do you currently live with two chronic conditions?	☐	☐

Please proceed to Page 4 for recommendations for your current medical condition and sign this document.

If you answered NO to all of the follow-up questions about your medical condition, you are ready to become more physically active:

› It is advised that you consult a qualified exercise professional (e.g., a CSEP-CEP or CSEP-CPT) to help you develop a safe and effective physical activity plan to meet your health needs.

› You are encouraged to start slowly and build up gradually – 20-60 min. of low- to moderate-intensity exercise, 3-5 days per week including aerobic and muscle strengthening exercises.

› As you progress, you should aim to accumulate 150 minutes or more of moderate-intensity physical activity per week.

- If you are over the age of 45 yrs. and NOT accustomed to regular vigorous physical activity, please consult a qualified exercise professional (CSEP-CEP) before engaging in maximal effort exercise.

If you answered YES to one or more of the follow-up questions about your medical condition:

- You should seek further information from a licensed health care professional before becoming more physically active or engaging in a fitness appraisal and/or visit a or qualified exercise professional (CSEP-CEP) for further information.

Delay becoming more active if:

- You are not feeling well because of a temporary illness such as a cold or fever – wait until you feel better
- You are pregnant - talk to your health care practitioner, your physician, a qualified exercise profesional, and/or complete the PARmed-X for Pregnancy before becoming more physically active OR
- Your health changes - please talk to your doctor or qualified exercise professional (CSEP-CEP) before continuing with any physical activity programme.

SECTION 3 - DECLARATION

- You are encouraged to photocopy the PAR-Q+. You must use the entire questionnaire and NO changes are permitted.
- The Canadian Society for Exercise Physiology, the PAR-Q+ Collaboration, and their agents assume no liability for persons who undertake physical activity. If in doubt after completing the questionnaire, consult your doctor prior to physical activity.
- If you are less than the legal age required for consent or require the assent of a care provider, your parent, guardian or care provider must also sign this form.
- Please read and sign the declaration below:

I, the undersigned, have read, understood to my full satisfaction and completed this questionnaire. I acknowledge that this physical activity clearance is valid for a maximum of 12 months from the date it is completed and becomes invalid if my condition changes. I also acknowledge that a Trustee (such as my employer, community/fitness centre, health care provider, or other designate) may retain a copy of this form for their records. In these instances, the Trustee will be required to adhere to local, national, and international guidelines regarding the storage of personal health information ensuring that they maintain the privacy of the information and do not misuse or wrongfully disclose such information.

NAME___DATE _____

SIGNATURE_____WITNESS _____

SIGNATURE OF PARENT/GUARDIAN/CARE PROVIDER _____

Appendix H

PhARaoH Study Questionnaire

Physical Activity and Respiratory Health

PhARaoH study

Questionnaire

Participant ID:

To be completed by study staff only: **D1 –**   **S1 –**

This questionnaire is made up of modules that ask you about a specific aspect of your life. Your answers will be treated as **strictly confidential** and will only be used for research purposes.

Please complete the questionnaire by **checking** answers or **enter** a response in the boxes provided next to or below the question. Try to answer every question, except when there is a specific request to skip a section.

Section A – Demographics

D1 - To which of the groups do you consider you belong?

- ☐ White – British
- ☐ White – Irish
- ☐ Any other white background
- ☐ Mixed – White and Black Caribbean
- ☐ Mixed – White and Black African
- ☐ Mixed – White and Asian
- ☐ Asian or Asian British – Indian
- ☐ Asian or Asian British – Pakistani
- ☐ Asian or Asian British – Bangladeshi
- ☐ Any other Asian/Asian British Background
- ☐ Black or Black British – Caribbean
- ☐ Black or Black British – African
- ☐ Any other Black/Black British background
- ☐ Chinese
- ☐ Any other (please specify) ☐

D2 - Where were you born?

Select **one** from:

- ☐ England
- ☐ Wales
- ☐ Scotland
- ☐ Northern Ireland
- ☐ Republic of Ireland
- ☐ Elsewhere (please specify) ☐
- ☐ Do not know

D3 - What year did you first come to live in the UK?

☐

- ☐ From birth
- ☐ Do not know

D4 - Do you own or rent the accommodation that you live in?

- ☐ Own outright
- ☐ Own with a mortgage
- ☐ Rent – from local authority, local council, housing association
- ☐ Rent – from private landlord or letting agency
- ☐ Pay part rent and part mortgage
- ☐ Live in accommodation rent free
- ☐ None of the above

D5 - Including yourself, how many people are living together in your household? (Include those who usually live in the house such as students living away from home during term, partners in the armed forces or professions such as pilots)

D6 - At what age did you finish your continuous full-time education at school or college?

- ☐ Never went to school
- ☐ 14 or under
- ☐ 15
- ☐ 16
- ☐ 17
- ☐ 18
- ☐ 19 or over

D7 - What is the highest education you have completed?

- ☐ Primary school
- ☐ Some secondary school
- ☐ Completed secondary school
- ☐ Some additional training (e.g. apprenticeship, GNVQ)
- ☐ Undergraduate university
- ☐ Postgraduate university

Section B – Childhood

Please answer the following questions in relation to your childhood **(i.e. when you were less than 18 years of age**).

CH1 - What was the highest education completed by your father?

- ☐ Primary school
- ☐ Some secondary school
- ☐ Completed secondary school
- ☐ Some additional training (e.g. apprenticeship, GNVQ)
- ☐ Undergraduate university
- ☐ Postgraduate university

CH2 - What was the highest education completed by either your mother?

- ☐ Primary school
- ☐ Some secondary school
- ☐ Completed secondary school
- ☐ Some additional training (e.g. apprenticeship, GNVQ)
- ☐ Undergraduate university
- ☐ Postgraduate university

CH3 - What was the employment status of your father?

- ☐ Unemployed
- ☐ Employed
- ☐ Self-employed

CH4 - What was the employment status of your mother?

- ☐ Unemployed
- ☐ Employed
- ☐ Self-employed

CH5 – What was the highest income range your father earned per year?

- ☐ £0 - £5,000
- ☐ £5,000 - £10,000
- ☐ £10,000 - £15,000
- ☐ £15,000 - £20,000
- ☐ £20,000 - £25,000
- ☐ £25,000 - £30,000
- ☐ £30,000 - £35,000
- ☐ £35,000 - £40,000
- ☐ £40,000 - £45,000
- ☐ £45,000 - £50,000
- ☐ £50,000 +
- ☐ Do not know

CH6 - What was the highest income range your mother earned per year?

- ☐ £0 - £5,000
- ☐ £5,000 - £10,000
- ☐ £10,000 - £15,000
- ☐ £15,000 - £20,000
- ☐ £20,000 - £25,000
- ☐ £25,000 - £30,000
- ☐ £30,000 - £35,000
- ☐ £35,000 - £40,000
- ☐ £40,000 - £45,000
- ☐ £45,000 - £50,000
- ☐ £50,000 +
- ☐ Do not know

CH7 - Please tick which of the following were present inside your childhood home.

- ☐ Bathroom
- ☐ Toilet
- ☐ Bath
- ☐ Hot water

CH8 - Did you have access to a car during your childhood?

☐ Yes

☐ No

CH9 - Did you have a shared bedroom for most of your childhood?

☐ Yes

☐ No

CH10 - Do you recall the presence of damp or mould inside the home?

☐ Yes

☐ No

Section C – Work

W1 - Which of the following best describes your current situation? (Please tick only one)

- ☐ In paid employment or self-employed
- ☐ Retired
- ☐ Looking after home and/or family
- ☐ Unable to work because of sickness or disability
- ☐ Unemployed
- ☐ Doing unpaid or voluntary work
- ☐ Full-time or part-time student
- ☐ None of the above

IF NOT "PAID EMPLOYMENT" OR "SELF-EMPLOYED" PLEASE GO TO W5

W2 - How many years have you worked in your current job? (If you have more than one job please answer this, and the following questions on work, for your MAIN job only)

☐

W3 - Over the last 12 months, for how many months did you work full-time?

☐

W4 - In a typical week, how many hours do you spend at work? (Do not include hours travelling to and from work)

☐

- ☐ Do not know

W5 - What is the average total income before tax received by your household?

- ☐ Less than £18,000
- ☐ £18,000 - £30,999
- ☐ £31,000 – £51,999
- ☐ £52,000 - £100,000
- ☐ Greater than £100,000
- ☐ Do not know

Section D1 – General Health – Part 1

GH1 - How is your health in general? Would you say it was (select from the following)

- ☐ Very good
- ☐ Good
- ☐ Fair
- ☐ Bad
- ☐ Very bad

GH2 - Do you have any long-standing illness, disability or infirmity? By long-standing I mean anything that has troubled you over a period of time, or that is likely to affect you over a period of time?

- ☐ Yes
- ☐ No

GH3 - Do you have an impairment or health problem that limits your ability to walk or run?

- ☐ Yes
- ☐ No

IF "NO" PLEASE GO TO GH5

GH4 - Is this an impairment or health problem that has lasted, or is expected to last 12 months or longer?

- ☐ Yes
- ☐ No

GH5 - Because of a health problem, do you have difficulty walking without using any special equipment?

- ☐ Yes
- ☐ No

GH6 - Do you get short of breath walking with people of your own age on level ground?

- ☐ Yes
- ☐ No
- ☐ Do not know

GH7 - Do you use private healthcare?

- ☐ Yes, all of the time
- ☐ Yes, most of the time
- ☐ Yes, sometimes
- ☐ No, never

GH8 - How often do you visit friends or family or have them visit you?

- ☐ Almost daily
- ☐ 2 – 4 times a week
- ☐ About once a week
- ☐ About once a month
- ☐ Once every few months
- ☐ Never or almost never
- ☐ No friends/family outside household
- ☐ Do not know

Section D2 – General Health – Part 2

Under each heading, please tick the ONE box that best describes your health TODAY

MOBILITY

I have no problems in walking about ..... ❑
I have slight problems in walking about ..... ❑
I have moderate problems in walking about ..... ❑
I have severe problems in walking about ..... ❑
I am unable to walk about ..... ❑

SELF-CARE

I have no problems washing or dressing myself ..... ❑
I have slight problems washing or dressing myself ..... ❑
I have moderate problems washing or dressing myself ..... ❑
I have severe problems washing or dressing myself ..... ❑
I am unable to wash or dress myself ..... ❑

USUAL ACTIVITES *(e.g. work, study, housework, family or leisure activities)*

I have no problems doing my usual activities ..... ❑
I have slight problems doing my usual activities ..... ❑
I have moderate problems doing my usual activities ..... ❑
I have severe problems doing my usual activities ..... ❑
I am unable to do my usual activities ..... ❑

PAIN / DISCOMFORT

I have no pain or discomfort ..... ❑
I have slight pain or discomfort ..... ❑
I have moderate pain or discomfort ..... ❑
I have severe pain or discomfort ..... ❑
I have extreme pain or discomfort ..... ❑

ANXIETY / DEPRESSION

I am not anxious or depressed ..... ❑
I am slightly anxious or depressed ..... ❑
I am moderately anxious or depressed ..... ❑
I am severely anxious or depressed ..... ❑
I am extremely anxious or depressed ..... ❑

Section D2 – General Health – Part 3

- We would like to know how good or bad your health is TODAY.

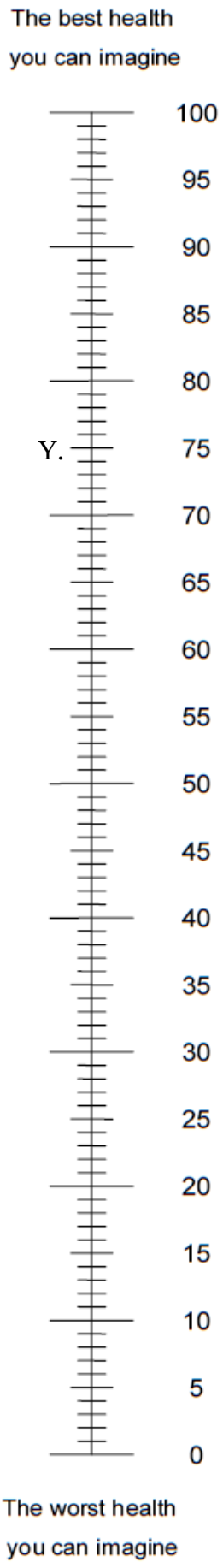
- This scale is numbered from 0 to 100

- 100 means the best health you can imagine
- 0 means the worst health you can imagine

- Mark an X on the scale to indicate how your health is TODAY.

- Now, please write the number you marked on the scale in the box below.

YOUR HEALTH TODAY = ☐



Section E – Family History

FH1 - Has/did your father ever suffer from? (You can select more than one answer)

Select from:

- ☐ Heart disease
- ☐ Stroke
- ☐ High blood pressure
- ☐ Diabetes
- ☐ Chronic bronchitis/emphysema/COPD
- ☐ Alzheimer's disease/dementia
- ☐ None of the above
- ☐ Do not know

FH2 - Has/did your mother ever suffer from? (You can select more than one answer)

Select from:

- ☐ Heart disease
- ☐ Stroke
- ☐ High blood pressure
- ☐ Diabetes
- ☐ Chronic bronchitis/emphysema/COPD
- ☐ Alzheimer's disease/dementia
- ☐ None of the above
- ☐ Do not know

FH3 - How many brothers and sisters do you have? (Please include those who have died. Do not include half, step or adopted sibling(s))

☐

IF "0" PLEASE GO TO (SECTION F)

FH4 - Have any of your brothers or sisters suffered from any of the following illnesses? (You can select more than one answer)

Select from:

- ☐ Heart disease
- ☐ Stroke
- ☐ High blood pressure
- ☐ Diabetes
- ☐ Chronic bronchitis/emphysema
- ☐ Alzheimer's disease/dementia
- ☐ None of the above
- ☐ Do not know

Section F – Medication, Blood Pressure and Diabetes

MBD1 - Do you regularly take any of the following medications? (You can select more than one answer)

Select from:

- ☐ Cholesterol lowering medication
- ☐ Blood pressure medication
- ☐ Insulin
- ☐ None of the above
- ☐ Do not know

MBD2 - Do you now have, or have you ever had high blood pressure (sometimes called hypertension)?

- ☐ Yes
- ☐ No

IF "NO" PLEASE GO TO MBD5

MBD3 - Were you told by a doctor or nurse that you had high blood pressure?

- ☐ Yes
- ☐ No

MBD4 - How old were you when you were first told by a (doctor/nurse) that you had high blood pressure?

☐

MBD5 - Do you now have, or have you ever had diabetes?

- ☐ Yes
- ☐ No

IF "NO" PLEASE GO TO MBD11

MBD6 - Were you told by a doctor or nurse that you had diabetes?

- ☐ Yes
- ☐ No

IF FEMALE:
MBD7 - Can I just check, were you pregnant when you were told that you had diabetes?

☐ Yes

☐ No

IF "YES"**:**

MBD8 - Have you ever had diabetes apart from when you were pregnant?

☐ Yes

☐ No

IF "NO" PLEASE GO TO DB11

MBD9 - Apart from when you were pregnant, approximately how old were you when you were first told by a doctor that you had diabetes?

☐

MBD10 - Do you currently inject insulin for diabetes?

☐ Yes

☐ No

MBD11 - Have you ever been told by a doctor or other health professional that you have health conditions or a medical or family history that increases your risk for diabetes?

☐ Yes

☐ No

☐ Don't know

Section G – Smoking

S1 - Have you ever smoked cigarettes?

- ☐ Yes
- ☐ No

IF "NO" PLEASE GO TO S11

S2 - Do you currently smoke cigarettes?

- ☐ Yes
- ☐ No

IF "YES" PLEASE GO TO S5

S3 - How long ago did you stop smoking cigarettes?

☐

S4 - How old were you when you last smoked cigarettes on most days?

☐

S5 - How old were you when you started to smoke cigarettes regularly?

☐

S6 - About how many cigarettes a day do you usually smoke on weekdays?

☐

S7 - About how many cigarettes a day do you usually smoke on weekend days?

☐

S8 - How soon after waking do you usually smoke your first cigarette of the day?

- ☐ Less than 5 minutes
- ☐ 5 – 14 minutes
- ☐ 15 – 29 minutes
- ☐ 30 minutes – 1 hour
- ☐ 1 – 2 hours
- ☐ 2 hours or more

S9 - Has a medical person, for example a doctor or nurse ever advised you to stop smoking altogether because of your health?

☐ Yes

☐ No

S10 - How long ago was that?

☐ Within the last 12 months

☐ Over 12 months ago

S11 - Does anyone in your household smoke?

☐ Yes, one household member smokes

☐ Yes, more than one household member smokes

☐ No

S12 - Now, in most weeks, how many hours a week are you exposed to other people's tobacco smoke?

S13 - Did your father ever smoke regularly when you were a child?

☐ Yes

☐ No

S14 - Did your mother ever smoke regularly when you were a child?

☐ Yes

☐ No

Section H1 – Lung Health

LH1 - Did a doctor ever tell you that you had chronic bronchitis, emphysema or COPD (Chronic Obstructive Pulmonary Disease)?

☐ Yes

☐ No

IF "NO" PLEASE GO TO LH4

LH2 - Which of the following did the doctor tell you that you had?

☐ COPD

☐ Chronic bronchitis

☐ Emphysema

LH3 - How old were you when you were first told by a doctor that you had COPD/chronic bronchitis/emphysema?

☐

LH4 - Did a doctor ever tell you that you had asthma?

☐ Yes

☐ No

IF "NO" PLEASE GO TO LH6

LH5 - How old were you when you were first told by a doctor or nurse that you had asthma?

☐

LH6 - Over the last 12 months, have you used an inhaler, puffer or nebuliser prescribed by a doctor to treat asthma, wheezing or whistling, or difficulty in breathing?

☐ Yes

☐ No

LH7 – Over the last 12 months, have you had or taken any treatment or medication for asthma, wheezing or whistling, or difficulty breathing?

☐ Yes

☐ No

IF "NO" PLEASE GO TO LH10

LH8 - What treatment or medication, *if any*, are you taking every day for asthma, wheezing or whistling, or difficulty breathing?

- ☐ Steroid tablets
- ☐ Theophylline tablets (e.g. Nuelin, Slo-Phyllin, Uniphylline, Phylocontin)
- ☐ Antibiotics
- ☐ Tablets, capsule or other liquid medicine to help bring up phlegm – Carbocisteine, Erdotin, Visclair
- ☐ Other tablets or granules (e.g. montelukast/Singulair; zafirlukast/Accolate)
- ☐ Inhalers
- ☐ Oxygen
- ☐ Other treatment of mediation
- ☐ None

IF "None" PLEASE GO TO LH10

LH9 - How many courses of steroids or antibiotics have you received for exacerbations / chest infections in the last 12 months?

☐

LH10 - On average, during the past week, how limited were you in activities because of breathing problems for strenuous physical activities (such as climbing stairs, hurrying, doing sports)?

- ☐ Not limited at all
- ☐ Very slightly limited
- ☐ Slightly limited
- ☐ Moderately limited
- ☐ Very limited
- ☐ Extremely limited
- ☐ Totally limited/can't do these activities

LH11 - On average during the past week, how limited were you because of your breathing problems for moderate physical activities (such as walking, housework, carrying things)?

- ☐ Not limited at all
- ☐ Very slightly limited
- ☐ Slightly limited
- ☐ Moderately limited
- ☐ Very limited
- ☐ Extremely limited
- ☐ Totally limited/can't do these activities

LH12 - On average during the past week, how limited were you because of your breathing problems for daily activities at home (such as dressing, washing)?

- ☐ Not limited at all
- ☐ Very slightly limited
- ☐ Slightly limited
- ☐ Moderately limited
- ☐ Very limited
- ☐ Extremely limited
- ☐ Totally limited/can't do these activities

LH13 - On average during the past week, how limited were you because of your breathing problems for social activities (such as talking, being with children, visiting friends/relatives)?

- ☐ Not limited at all
- ☐ Very slightly limited
- ☐ Slightly limited
- ☐ Moderately limited
- ☐ Very limited
- ☐ Extremely limited
- ☐ Totally limited/can't do these activities

LH14 - Have you ever been told by a doctor that you also have heart failure?

- ☐ Yes
- ☐ No

Section H2 – Breathlessness

B1 - Are you ever too breathless to leave the house?

☐ Yes

☐ No

IF "NO" PLEASE GO TO B3

B2 - Is that all or most days, at least once a week, or less often than that?

☐ All or most days

☐ At least once a week

☐ Less often

B3 - Please choose the **one** best response to describe your shortness of breath.

Grade

0 "I only get breathless with strenuous exercise"

1 "I get short of breath when hurrying on the level or walking up a slight hill"

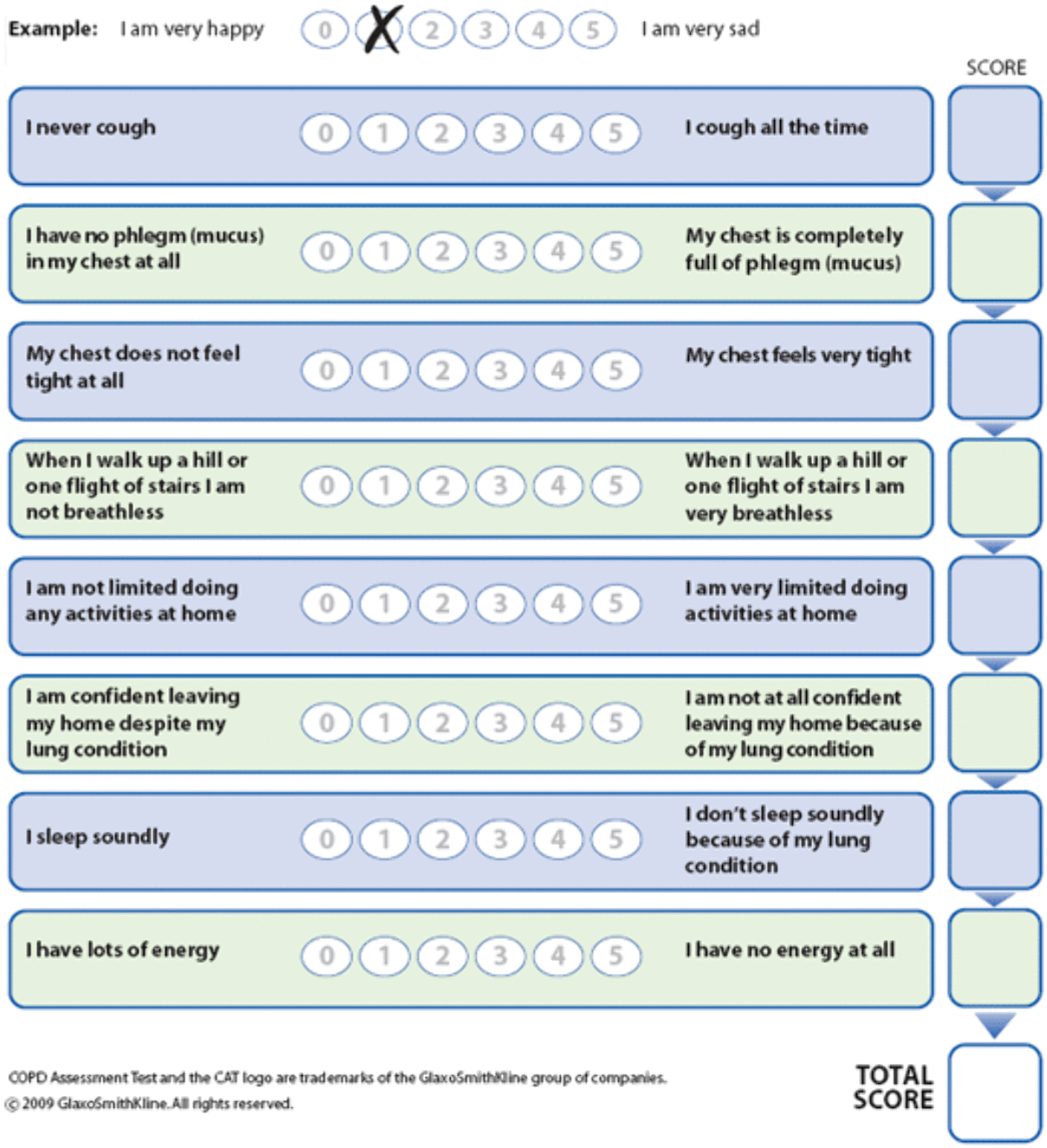
2 "I walk slower than people of the same age on the level because of breathlessness or have to stop for breath when walking at my own pace on the level"

3 "I stop for breath after walking about 100 yards or after a few minutes on the level"

4 "I am too breathless to leave the house" or "I am breathless when dressing"

Grade ☐

Section I – COPD Health – Part 1



Section I – COPD Health – Part 2

Below is a list of statements that other people with your illness have said are important**. Please circle or mark one number per line to indicate your response as it applies to the <u>past 7 days</u>.**

	PHYSICAL WELL-BEING	Not	A little	Some-	Quite	Very
GP1	I have a lack of energy	0	1	2	3	4
GP2	I have nausea	0	1	2	3	4
GP3	Because of my physical condition, I have trouble meeting the needs of my family	0	1	2	3	4
GP4	I have pain	0	1	2	3	4
GP5	I am bothered by side effects of treatment	0	1	2	3	4
GP6	I feel ill	0	1	2	3	4
GP7	I am forced to spend time in bed	0	1	2	3	4

.....

	SOCIAL/FAMILY WELL-BEING	Not at all	A little bit	Some-what	Quite a bit	Very much
GS1	I feel close to my friends	0	1	2	3	4
GS2	I get emotional support from my family	0	1	2	3	4
GS3	I get support from my friends.....	0	1	2	3	4
GS4	My family has accepted my illness	0	1	2	3	4
GS5	I am satisfied with family communication about my illness.....	0	1	2	3	4
GS6	I feel close to my partner (or the person who is my main support)	0	1	2	3	4
Q1	*Regardless of your current level of sexual activity, please answer the following question. If you prefer not to answer please mark this box and go to the next section.*					
GS7	I am satisfied with my sex life	0	1	2	3	4

EMOTIONAL WELL-BEING

		Not at all	A little bit	Some-what	Quite a bit	Very much
GE1	I feel sad	0	1	2	3	4
GE2	I am satisfied with how I am coping with my illness.....	0	1	2	3	4
GE3	I am losing hope in the fight against my illness.....	0	1	2	3	4
GE4	I feel nervous.....	0	1	2	3	4
GE5	I worry about dying.....	0	1	2	3	4
GE6	I worry that my condition will get worse	0	1	2	3	4

FUNCTIONAL WELL-BEING

		Not at all	A little bit	Some-what	Quite a bit	Very much
GF1	I am able to work (include work at home)	0	1	2	3	4
GF2	My work (include work at home) is fulfilling.....	0	1	2	3	4
GF3	I am able to enjoy life.....	0	1	2	3	4
GF4	I have accepted my illness.....	0	1	2	3	4
GF5	I am sleeping well	0	1	2	3	4
GF6	I am enjoying the things I usually do for fun	0	1	2	3	4
GF7	I am content with the quality of my life right now.....	0	1	2	3	4

ADDITIONAL CONCERNS

		Not at all	A little bit	Some-what	Quite a bit	Very much
HI7	I feel fatigued	0	1	2	3	4
HI12	I feel weak all over	0	1	2	3	4
An1	I feel listless ("washed out")	0	1	2	3	4
An2	I feel tired	0	1	2	3	4
An3	I have trouble starting things because I am tired.....	0	1	2	3	4
An4	I have trouble finishing things because I am tired	0	1	2	3	4
An5	I have energy	0	1	2	3	4
An7	I am able to do my usual activities.....	0	1	2	3	4
An8	I need to sleep during the day	0	1	2	3	4
An12	I am too tired to eat	0	1	2	3	4
An14	I need help doing my usual activities	0	1	2	3	4
An15	I am frustrated by being too tired to do the things I want to do.....	0	1	2	3	4
An16	I have to limit my social activity because I am tired.....	0	1	2	3	4

Section I – COPD Health – Part 3

We are now going to ask you about your ability to cope with your COPD condition. Please circle where you feel you are now.

Statement	Score			
I can always manage to solve difficult problems if I try hard enough.	1	2	3	4
If someone opposes me, I can find the means and ways to get what I want.	1	2	3	4
It is easy for me to stick to my aims and accomplish my goals.	1	2	3	4
I am confident that I can walk for a good distance, at my own pace, despite it making me breathless.	1	2	3	4
I am confident that I could deal efficiently with unexpected events.	1	2	3	4
Thanks to my resourcefulness, I know how to handle unforeseen situations.	1	2	3	4
I feel confident that I will be able to perform the exercises asked of me during the course of rehabilitation, even if I find them difficult.	1	2	3	4
I can solve most problems if I invest the necessary effort.	1	2	3	4
I feel that I have an adequate amount of knowledge about my lung disease, despite it being a complex condition.	1	2	3	4
I can remain calm when facing difficulties because I can rely on my coping abilities.	1	2	3	4
When I am confronted with a problem, I can usually find several solutions.	1	2	3	4
I feel positive that I will be able to complete the exercises at home, despite there being no supervision from a health professional.	1	2	3	4
If I am in trouble, I can usually think of a solution.	1	2	3	4
I can handle whatever comes my way.	1	2	3	4
On a day to day basis I feel in control of my lung disease and how that affects my lifestyle, even when my symptoms become distressing.	1	2	3	4

Response Format.

1= Not at all true **2**= Hardly true **3**= Moderately true **4**= Exactly true

Section J – Physical Activity and Sitting

PA1 - In the last 4 weeks, which form of transport have you used most often to get about? (Not including any journeys to and from work; please only select the most frequent mode of transport used)

- ☐ Car/motor vehicle
- ☐ Walk
- ☐ Public transport
- ☐ Cycle
- ☐ None of the above

PA2 - How many times in the last 4 weeks did you do swimming?

- ☐ None
- ☐ Once in the last 4 weeks
- ☐ 2 – 3 times in the last 4 weeks
- ☐ Once a week
- ☐ 2 – 3 times a week
- ☐ 4 – 5 times a week
- ☐ Every day
- ☐ Do not know

PA3 - How many times in the last 4 weeks did you do cycling?

- ☐ None
- ☐ Once in the last 4 weeks
- ☐ 2 – 3 times in the last 4 weeks
- ☐ Once a week
- ☐ 2 – 3 times a week
- ☐ 4 – 5 times a week
- ☐ Every day
- ☐ Do not know

PA4 - Which of the following do you attend once a week or more often? (you can select more than one)

- ☐ Sports club or gym
- ☐ Pub or social club
- ☐ Religious group
- ☐ Adult education class
- ☐ Other group activity
- ☐ None of the above

PA5 - Which of the following best describes your usual walking pace?

- ☐ A slow pace
- ☐ An average pace
- ☐ A fairly brisk pace
- ☐ A fast pace

PA6 - We are interested in finding out about the kinds of physical activities that people do as part of their everyday lives. The questions will ask you about the time you spent being physically active in the **last 7 days**. Please answer each question even if you do not consider yourself to be an active person. Please think about the activities you do at work, as part of your house and gardening, to get from place to place, and in your spare time for recreation, exercise or sport.

Think about all the **vigorous** activities that you did in the **last 7 days**. **Vigorous** physical activities refer to activities that take hard physical effort and make you breathe much harder than normal. Think *only* about those physical activities that you did for at least 10 minutes at a time.

1. During the **last 7 days**, on how many days did you do **vigorous** physical activities like heavy lifting, digging, aerobics, or fast bicycling?

_____days per week

☐ No vigorous physical activities → ***Skip to question 3***

2. How much time did you usually spend doing **vigorous** physical activities on one of those days?

_____hours per day

_____minutes per day

Think about all the **moderate** activities that you did in the **last 7 days**. **Moderate** activities refer to activities that take moderate physical effort and make you breathe somewhat harder than normal. Think only about those physical activities that you did for at least 10 minutes at a time.

3. During the **last 7 days**, on how many days did you do **moderate** physical activities like carrying light loads, bicycling at a regular pace, or doubles tennis? Do not include walking.

_____days per week

☐ No moderate physical activities → ***Skip to question 5***

4. How much time did you usually spend doing **moderate** physical activities on one of those days?

_____hours per day

_____minutes per day

Think about the time you spent **walking** in the **last 7 days**. This includes at work and at home, walking to travel from place to place, and any other walking that you might do solely for recreation, sport, exercise, or leisure.

5. During the **last 7 days**, on how many days did you **walk** for at least 10 minutes at a time?

days per week

☐ No walking → ***Go to next section***

6. How much time did you usually spend **walking** on one of those days?

hours per day

_____minutes per day

I have already asked you about walking and cycling. I would now like to ask you about other types of sport, exercise, and recreational physical activity. Please think about all the activities whether for competition, training or receiving tuition, socially, casually or for health and fitness.

In the questions below 'sporty' refers to actively participating in sports rather than following/watching sport.

PA7 – Do you consider yourself to have been a 'sporty' child?

☐ Yes

☐ No

PA8 - Do you consider yourself a 'sporty' adult relative to your peers?

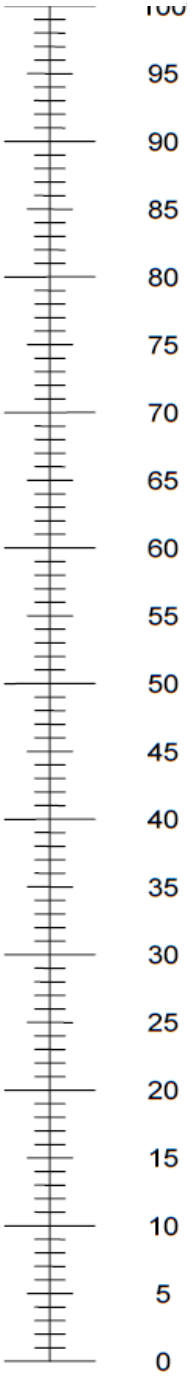
☐ Yes

☐ No

PA9 - We would like to know how sporty you consider yourself as an adult. The scale is numbered 0 to 100. 100 means you participate in sports/recreation regularly (i.e., on most days).
0 means you never participate in sports/recreation Mark
an X on the scale to indicate your sportiness.

Sporty

Y OUR SPORTINESS =



Not Sporty

PA10 - Please think about how much time you spend sitting on a **typical** week day and weekend day.

When filling in the table below, if you take part in more than one of the activities at the same time, e.g. watching television whilst using a laptop computer, please record time spent taking part in the activity you mainly focus on e.g. it may be you watch television and only use the laptop when you get an email. In this case you would record time spent watching television.

Please estimate how many hours you spend SITTING EACH DAY in the following situations: ***(please write your answer)***

	On a WEEK Day		**On a WEEKEND Day**	
	Hours	**Minutes**	**Hours**	**Minutes**
While travelling to and from places				
While at work				
While watching television				
While using a computer at home				
In your leisure time, NOT including television (e.g. visiting friends, movies, dining out, etc)				

Section K – Sport Inventory

Now we are going to ask you about the types of activities you have previously completed or would like to complete in the future.

Please only **tick** those activities you have completed **outside of physical education (PE) lessons**.

Please state additional activities in the spaces provided at the end of the activity list.

Ages < 18	Ages 18 - 29	Ages 30 - 39	Ages 40 - 75	Doing regularly	Could see yourself doing in the next year	
☐	☐	☑	☐	☑	☐	**EXAMPLE**
☐	☐	☐	☐	☐	☐	Aerobics / Exercise-to-music
☐	☐	☐	☐	☐	☐	Archery
☐	☐	☐	☐	☐	☐	Athletics
☐	☐	☐	☐	☐	☐	Badminton
☐	☐	☐	☐	☐	☐	Baseball / Softball
☐	☐	☐	☐	☐	☐	Basketball
☐	☐	☐	☐	☐	☐	Bicycling
☐	☐	☐	☐	☐	☐	Bowling
☐	☐	☐	☐	☐	☐	Canoeing / Kayaking
☐	☐	☐	☐	☐	☐	Climbing
☐	☐	☐	☐	☐	☐	Cricket
☐	☐	☐	☐	☐	☐	Dancing
☐	☐	☐	☐	☐	☐	Fencing
☐	☐	☐	☐	☐	☐	Football
☐	☐	☐	☐	☐	☐	Gardening
☐	☐	☐	☐	☐	☐	Golf
☐	☐	☐	☐	☐	☐	Handball
☐	☐	☐	☐	☐	☐	Hiking
☐	☐	☐	☐	☐	☐	Hockey

☐	☐	☐	☐	☐	☐	Horse riding
☐	☐	☐	☐	☐	☐	Ice skating
☐	☐	☐	☐	☐	☐	Martial arts
☐	☐	☐	☐	☐	☐	Netball
☐	☐	☐	☐	☐	☐	Orienteering
☐	☐	☐	☐	☐	☐	Press-ups, sit-ups, lunges, etc.
☐	☐	☐	☐	☐	☐	Racquetball
☐	☐	☐	☐	☐	☐	Rowing
☐	☐	☐	☐	☐	☐	Rugby
☐	☐	☐	☐	☐	☐	Running / Jogging
☐	☐	☐	☐	☐	☐	Sailing
☐	☐	☐	☐	☐	☐	Skateboarding
☐	☐	☐	☐	☐	☐	Skiing
☐	☐	☐	☐	☐	☐	Snooker / Pool
☐	☐	☐	☐	☐	☐	Squash
☐	☐	☐	☐	☐	☐	Swimming
☐	☐	☐	☐	☐	☐	Table tennis
☐	☐	☐	☐	☐	☐	Tennis
☐	☐	☐	☐	☐	☐	Volleyball
☐	☐	☐	☐	☐	☐	Walking for exercise
☐	☐	☐	☐	☐	☐	Weight training
☐	☐	☐	☐	☐	☐	Wind surfing
☐	☐	☐	☐	☐	☐	Yoga / Thai Chi
☐	☐	☐	☐	☐	☐	_____
☐	☐	☐	☐	☐	☐	_____
☐	☐	☐	☐	☐	☐	_____

Appendix I

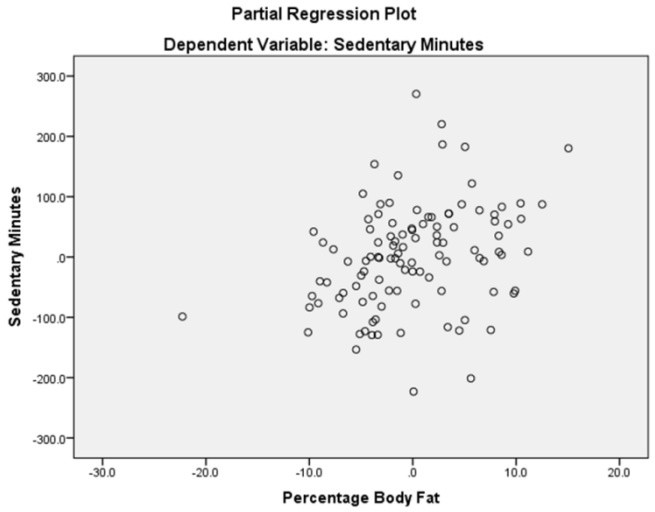
Comparison of self-reported general health index value components between COPD patients and apparently healthy controls

	Whole sample (n=244)	COPD (n=109)	Control (n=135)
General health			
Mobility (%):			
No problems	174 (71.3)	54 (49.5)	120 (88.9) *
Slight problems	38 (15.6)	26 (23.9)	12 (8.9) *
Moderate problems	26 (10.7)	24 (22.0)	2 (1.5) *
Severe problems	5 (2.0)	5 (4.6)	0 (0) *
Unable to	0 (0)	0 (0)	0 (0)
Self-care (%):			
No problems	223 (91.4)	91 (83.5)	132 (97.8)
Slight problems	16 (6.6)	14 (12.8)	2 (1.5)
Moderate problems	4 (1.6)	4 (3.7)	0 (0)
Severe problems	0 (0)	0 (0)	0 (0)
Unable to	0 (0)	0 (0)	0 (0)
Usual activities (%):			
No problems	183 (75.0)	59 (54.1)	124 (91.9) *
Slight problems	37 (15.2)	30 (27.5)	7 (5.2) *
Moderate problems	17 (7.0)	16 (14.7)	1 (0.7) *
Severe problems	2 (0.8)	2 (1.8)	0 (0)
Unable to	0 (0)	0 (0)	0 (0)
Pain discomfort (%):			
None	123 (50.4)	45 (41.3)	78 (57.8) *
Slight	87 (35.7)	35 (32.1)	52 (38.5) *
Moderate	27 (11.1)	23 (21.1)	4 (3.0) *
Severe	6 (2.5)	6 (5.5)	0 (0) *
Extreme	0 (0)	0 (0)	0 (0)
Anxiety/depression (%):			
None	176 (72.1)	75 (68.8)	101 (74.8)
Slight	49 (20.1)	22 (20.2)	27 (20.0)
Moderate	14 (5.7)	9 (8.3)	5 (3.7)
Severe	3 (1.2)	2 (1.8)	1 (0.7)
Extreme	1 (0.4)	1 (0.9)	0 (0)

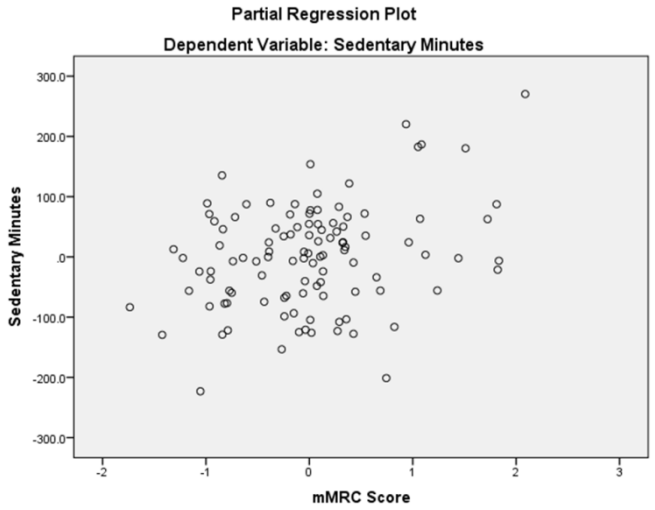
Appendix J

Partial regression plots for factors independently associated with sedentary time (percentage body fat (Panel A) and mMRC (Panel B)) and MVPA (ISWT distance (Panel C)) in COPD.

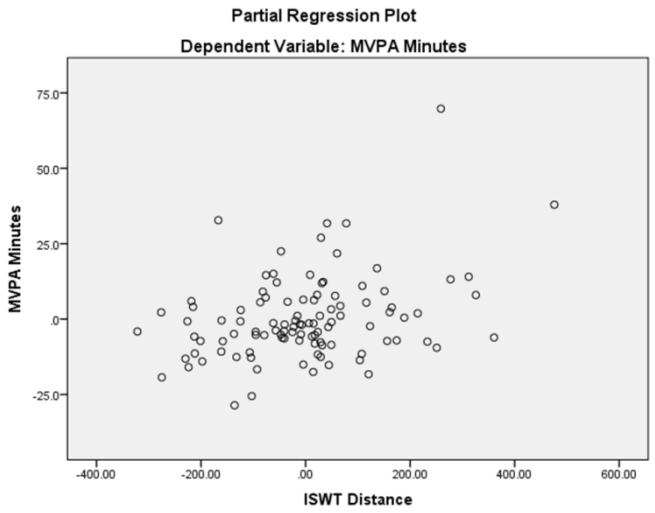
A



B



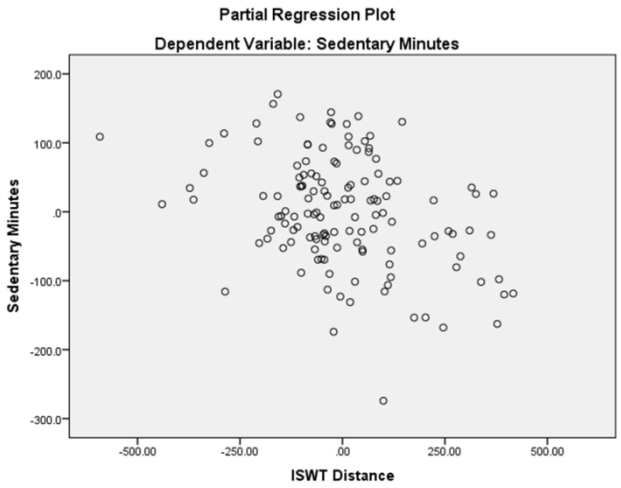
C



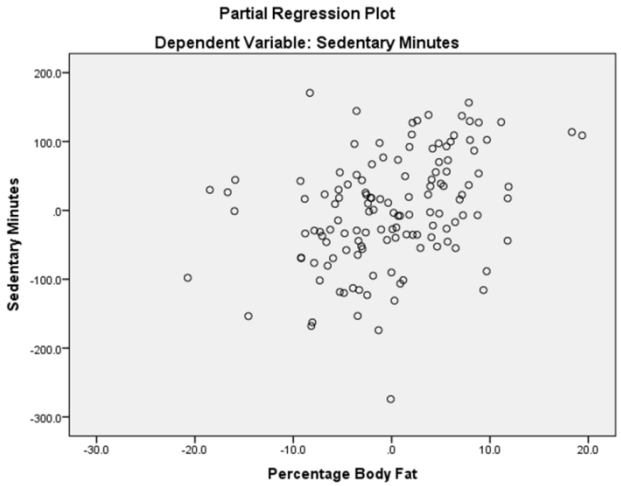
Appendix K

Partial regression plots for factors independently associated with sedentary time (ISWT distance (Panel A) and percentage body fat (Panel B)) and MVPA (percentage body fat (Panel C)) in apparently healthy adults.

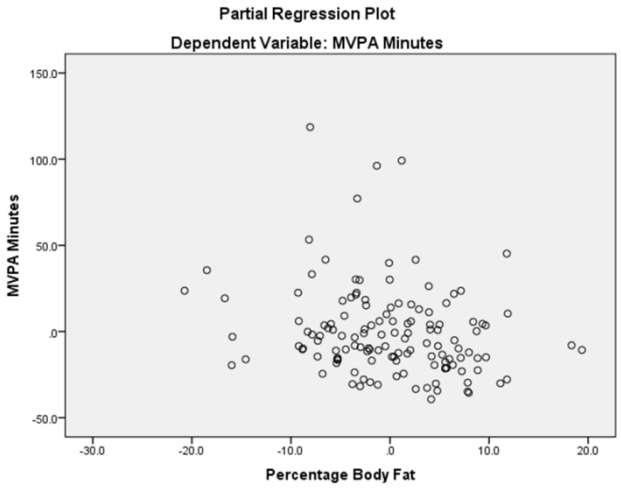
A



B



C



Appendix L

Agreement (Kappa statistic) between CAT components (* $p<0.05$); cells are coded as follows: Dark orange, “none”; amber, “minimal”

CAT Component	Phlegm	Tight Chest	Breathless	Limited Activities	CLH	Sleep	Energy
Coughing	0.334 *	0.115 *	0.183 *	0.132 *	0.007	0.115 *	0.232 *
Phlegm		0.228 *	0.050	0.104 *	0.047	0.095 *	0.199 *
Tight Chest			0.117 *	0.102 *	0.117 *	0.098 *	0.108 *
Breathless				0.157 *	0.080 *	0.157 *	0.164 *
Limited Activities					0.228 *	0.330 *	0.153 *
CLH						0.306 *	0.027
Sleep							0.235 *

Abbreviations: CAT, COPD Assessment Test; CLH, confidence leaving the home

Appendix M

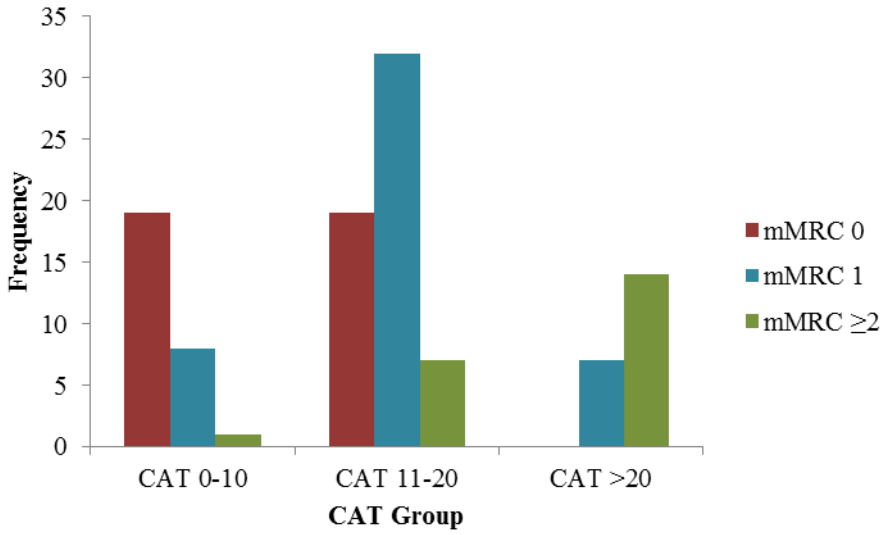
Correlation coefficient between CAT components (* $p<0.05$); cells are coded as follows: Dark orange, “very weak”; amber, “weak”; yellow, “moderate”; green, “strong”

CAT Component	Phlegm	Tight Chest	Breathless	Limited Activities	CLH	Sleep	Energy
Coughing	0.629 *	0.398 *	0.412 *	0.284 *	0.301 *	0.327 *	0.432 *
Phlegm		0.435 *	0.322 *	0.139	0.169	0.234 *	0.388 *
Tight Chest			0.295 *	0.367 *	0.339 *	0.371 *	0.358 *
Breathless				0.644 *	0.436 *	0.396 *	0.525 *
Limited Activities					0.597 *	0.463 *	0.583 *
CLH						0.569 *	0.473 *
Sleep							0.525 *

Abbreviations: CAT, COPD Assessment Test; CLH, confidence leaving the home

Appendix N

Comparison of patient classification into symptom severity groups between CAT score and mMRC grade



Appendix O

COPD-SEAT protocol publication

BMJ Open

Study protocol for Chronic Obstructive Pulmonary Disease-Sitting and ExacerbAtions Trial (COPD-SEAT): a randomised controlled feasibility trial of a home-based self-monitoring sedentary behaviour intervention

Mark Orme,[1] Amie Weedon,[2] Dale Esliger,[1,3] Paula Saukko,[2] Mike Morgan,[4] Michael Steiner,[1,4] John Downey,[3] Sally Singh,[1,4] Lauren Sherar[1,2]

To cite: Orme M, Weedon A, Esliger D, *et al*. Study protocol for Chronic Obstructive Pulmonary Disease-Sitting and ExacerbAtions Trial (COPD-SEAT): a randomised controlled feasibility trial of a home-based self-monitoring sedentary behaviour intervention. *BMJ Open* 2016;**6**:e013014. doi:10.1136/bmjopen-2016-013014

► Prepublication history for this paper is available online. To view these files please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2016-013014).

SS and LS are joint last authors.

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For numbered affiliations see end of article.

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ABSTRACT

Introduction: An acute exacerbation of chronic obstructive pulmonary disease (COPD) marks a critical life event, which can lower patient quality of life and ability to perform daily activities. Patients with COPD tend to lead inactive and highly sedentary lifestyles, which may contribute to reductions in functional capacity. Targeting sedentary behaviour (SB) may be more attainable than exercise (at a moderate-to-vigorous intensity) for behaviour change in patients following an exacerbation. This study aims to evaluate the feasibility and acceptability of a 2-week at-home intervention providing education and self-monitoring to reduce prolonged periods of SB in patients with COPD discharged following an acute exacerbation.

Methods and analysis: Patients will be randomised into 1 of 3 conditions: usual care (control), education or education+feedback. The education group will receive information and suggestions about reducing long periods of sitting. The education+feedback group will receive real-time feedback on their sitting time, stand-ups and step count at home through an inclinometer linked to a smart device app. The inclinometer will also provide vibration prompts to encourage movement when the wearer has been sedentary for too long. Data will be collected during hospital admission and 2 weeks after discharge. Qualitative interviews will be conducted with patients in the intervention groups to explore patient experiences. Interviews with healthcare staff will also be conducted. All data will be collected January to August 2016. The primary outcomes are feasibility and acceptability, which will be assessed by qualitative interviews, uptake and drop-out rates, reasons for refusing the intervention, compliance, app usage and response to vibration prompts.

Ethics and dissemination: The research ethics committee East Midlands Leicester-Central has provided ethical approval for the conduct of this study. The results of the study will be disseminated through appropriate conference proceedings and peer-reviewed journals.

Strengths and limitations of this study

- The study will target a critical period for behaviour change in a clinical population admitted to hospital.
- Important insights into the suitability of focussing on sedentary behaviour (SB) using novel wearable technology will be obtained.
- Given the timing of the intervention, it will not be possible to obtain an objective assessment of habitual physical activity or SB prior to hospital admission.

Trial registration number: ISRCTN13790881; Pre-results.

INTRODUCTION

Targeting increases in physical activity in patients with chronic obstructive pulmonary disease (COPD) has been the emphasis of a large number of exercise training and behaviour change interventions for over a decade.[1] Despite these considerable efforts, there has been limited success.[1 2] The lower levels of physical activity coupled with the often fragile physical and psychological health (eg, low exercise capacity and low self-esteem) among patients with COPD may make reducing sedentary behaviour (SB) a more suitable conduit for behaviour change.[3 4] SB is defined as 'any waking behaviour characterised by an energy expenditure ≤1.5 metabolic equivalents while in a sitting or reclining posture'.[5] Patients with COPD demonstrate significantly higher levels of SB compared with healthy controls.[6]

Appendix P

COPD-SEAT research ethics committee approval letter

East Midlands - Leicester Central Research Ethics Committee
The Old Chapel Royal Standard Place
Nottingham NG1 6FS
Telephone: 0115 883 9275

27 October 2015

Professor Sally Singh
Head of Pulmonary and Cardiac Rehabilitation University Hospitals of Leicester NHS Trust Centre for Exercise and Rehabilitation Science
Glenfield Hospital
Leicester LE3 9QP

Dear Professor Singh

Study title:	**The feasibility of a home-based sedentary behaviour intervention for hospitalised chronic obstructive pulmonary disease (COPD) patients following an acute exacerbation: Sitting and ExacerbAtions Trial (COPD-SEAT)**
REC reference:	**15/EM/0433**
IRAS project ID:	**181453**

Thank you for your letter responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Chair.

We plan to publish your research summary wording for the above study on the HRA website, together with your contact details. Publication will be no earlier than three months from the date of this opinion letter. Should you wish to provide a substitute contact point, require further information, or wish to make a request to postpone publication, please contact the REC Manager, Ellen Swainston, nrescommittee.eastmidlands-leicester@nhs.net.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Conditions of the favourable opinion

The favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission ("R&D approval") should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements.

Guidance on applying for NHS permission for research is available in the Integrated Research Application System or at http://www.rdforum.nhs.uk.

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.
For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.
Sponsors are not required to notify the Committee of approvals from host organisations

Registration of Clinical Trials

All clinical trials (defined as the first four categories on the IRAS filter page) must be registered on a publically accessible database within 6 weeks of recruitment of the first participant (for medical device studies, within the timeline determined by the current registration and publication trees).

There is no requirement to separately notify the REC but you should do so at the earliest opportunity e.g. when submitting an amendment. We will audit the registration details as part of the annual progress reporting process.

To ensure transparency in research, we strongly recommend that all research is registered but for non clinical trials this is not currently mandatory.

If a sponsor wishes to contest the need for registration they should contact Catherine Blewett (catherineblewett@nhs.net), the HRA does not, however, expect exceptions to be made. Guidance on where to register is provided within IRAS.

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

Ethical review of research sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).
Non-NHS sites
The Committee has not yet completed any site-specific assessment (SSA) for the non-NHS research site(s) taking part in this study. The favourable opinion does not therefore apply to any non-NHS site at present. We will write to you again as soon as an SSA application(s) has been reviewed. In the meantime no study procedures should be initiated at non-NHS sites.

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document	*Version*	*Date*
Interview schedules or topic guides for participants [Baseline Interview Education]	1.0	30 July 2015
Interview schedules or topic guides for participants [Baseline Interview Feedback]	1.0	30 July 2015
Interview schedules or topic guides for participants [Follow Up Interview Education]	1.0	30 July 2015
Interview schedules or topic guides for participants [Follow Up Interview Feedback]	1.0	30 July 2015
Interview schedules or topic guides for participants [Nonparticipation Interview]	1.0	30 July 2015
Interview schedules or topic guides for participants [Focus Groups Schedules]	1.0	30 July 2015
IRAS Checklist XML [Checklist_26102015]		26 October 2015
Other [Education Booklet]	1.0	30 July 2015
Other [Nonparticipation Consent Form]	1.0	30 July 2015
Other [Monitor Instruction Manual]		
Other [App Instruction Manual]		
Other [Respiratory Discharge Letter]		
Other [Measurement Form]	1.0	30 July 2015
Other [Agreement and Undertaking]	1.0	30 July 2015
Other [Non Intervention Interview Consent Form]	1.1	24 October 2015
Other [Expression of Interest]	1.1	24 October 2015
Other [Letter to REC]		
Participant consent form [Main Consent Form]	1.1	24 October 2015
Participant information sheet (PIS) [Participant Information Sheet]	1.1	24 October 2015
REC Application Form [REC_Form_09092015]		09 September 2015
Research protocol or project proposal [Protocol]	1.0	30 July 2015
Summary CV for Chief Investigator (CI) [CI Curriculum vitae]	1.0	30 July 2015
Validated questionnaire [Follow Up]		
Validated questionnaire [Montreal Cognitive Assessment]		
Validated questionnaire [Trail Making Test]		
Validated questionnaire [Baseline]	1.1	24 October 2015

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

Reporting requirements

The attached document *"After ethical review – guidance for researchers"* gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

The HRA website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

User Feedback

The Health Research Authority is continually striving to provide a high quality service to all applicants and sponsors. You are invited to give your view of the service you have received and the application procedure. If you wish to make your views known please use the feedback form available on the HRA website:
http://www.hra.nhs.uk/about-the-hra/governance/quality-assurance/

HRA Training

We are pleased to welcome researchers and R&D staff at our training days – see details at http://www.hra.nhs.uk/hra-training/

15/EM/0433	**Please quote this number on all correspondence**

With the Committee's best wishes for the success of this project.
Yours sincerely

pp. G. Sroczyńska

Mr Ken
Willis Chair

Email: nrescommittee.eastmidlands-leicestercentral@nhs.net

Enclosures:
"After ethical review – guidance for researchers"

Mark Orme
Carolyn Maloney

Appendix Q

COPD-SEAT consent form

Main Trial Consent Form

Final Version 2.1, 05-March-2016, REC Ref: 15-EM-0433

The feasibility of a sedentary behaviour intervention for hospitalised chronic obstructive pulmonary disease patients following an acute exacerbation: Sitting and ExacerbAtions Trial (COPD-SEAT)

Please Initial

1. I confirm that I have read and understood the participant information sheet [Version 2.1, 05-March-2016] for the above study and have had the opportunity to ask questions ☐

2. I understand that my participation is voluntary and that I am free to withdraw from the study at any time, without providing a reason, and without my medical care and legal rights being affected. I understand that should I withdraw from the study, the information collected so far cannot be erased and that this information may still be used in the study analysis. ☐

3. I understand that relevant sections of my medical notes and data collected as part of this study may be looked at by authorised individuals from the sponsor, Loughborough University, the research group and regulatory authorities where it is relevant to my taking part in this study. I give permission for these individuals to have access to these records and to collect, store, analyse and publish information obtained from my participation in this study. I understand that my details will be kept confidential. ☐

4. I understand that I will be asked to complete physical measurements, questionnaires and interviews, as detailed in the participant information sheet [Version 2.1, 05-March-2016]. ☐

5. I understand that the interviews will be recorded and that anonymous direct quotes from the interviews may be used in the study reports. ☐

6. I agree that all contact with the research team will be audio recorded for the purposes detailed in the participant information sheet [Version 2.1, 05-March-2016]. ☐ ☐

7. I agree my General Practitioner (GP) being informed of my participation in the study. ☐ ☐

8. I would like the Respiratory Discharge Service to be informed of my participation in the study and results obtained from the study measurements to be entered into my medical notes. ☐ ☐

9. I agree for identifiable information to be securely transferred to Loughborough University. ☐

10. I understand that information about me recorded during the study will be kept in a secure database. If the data is transferred it will be made anonymous. Data will be retained for 10 years after the end of the study and made anonymous and archived at secure archive facilities. ☐

11. I agree to take reasonable care of the loaned equipment and I agree to return all equipment once my involvement in the study has ended. ☐

12. I am happy to be contacted regarding other research studies being conducting by Loughborough University or the University Hospitals of Leicester. ☐ ☐

13. I agree to take part in the study. ☐

Name of Participant	**Date**	**Signature**
Name of Researcher	**Date**	**Signature**

3 Copies: 1 for participant, 1 for medical notes & 1 original for study notes.

Appendix R

COPD-SEAT participant information sheet

Participant Information Sheet

Final Version 2.1 05-March-2016, REC Ref: 15-EM-0433

The feasibility of a sedentary behaviour intervention for hospitalised chronic obstructive pulmonary disease patients following an acute exacerbation: Sitting and ExacerbAtions Trial (COPD-SEAT)

You have been invited to take part in a research study. Before you decide whether to take part it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with friends and relatives if you wish to.

Please take time to decide whether you wish to take part or not. Do not hesitate to contact a member of the usual care team and/or research team if you have any questions or would like more information. Thank you.

Background

In this research, we want to test an intervention targeting people's sitting time following admission to hospital for an exacerbation of chronic obstructive pulmonary disease (COPD). The research programme is called COPD-SEAT (Sitting and ExacerbAtions Trial) and we want to see how well an intervention aimed at reducing sitting time can be conducted in this setting. Information from this study will contribute towards PhD qualifications.

It is important for everyone to try to limit the amount of sitting in daily life. Following an exacerbation of COPD, sitting time can often increase and this may not help individuals to maintain or improve their physical capabilities and quality of life. It is therefore important to find effective ways for some people to sit less after being discharged from hospital.

Why have you been chosen?

You have been chosen because you are aged between 40 and 85 years, have a clinical diagnosis of COPD and have had fewer than 4 exacerbations requiring hospital admission. You will be amongst up to 60 patients admitted to Glenfield Hospital taking part in this research.

Do you have to take part?

No. This research is entirely voluntary. You will choose whether or not to take part. If you agree to take part, then you will be asked to sign a Consent Form, which states that you are happy to participate. You can change your mind about taking part at any time without giving a reason. Your usual care will not be affected if you decide to withdraw from the study.

If you would like any further information to help you make your decision, please do not hesitate to speak to Mark Orme or a member of the REDs team at your convenience.

What does the study involve?

Participation in the study will last for ~3 weeks, from the time a member of the research team meets you following your expression of interest to the end of the follow-up visit.

If you agree to take part, you will be randomly assigned to one of three groups. Two groups will take part in a COPD-SEAT intervention and one group will receive usual care.

You will not be told which group you will be assigned to before agreeing to take part. Whether you are in one of the COPD-SEAT interventions or the usual care group will be decided at random (a bit like picking names out of a hat). If you agree to take part, you will then be given an envelope that will tell you which group you are in. Nobody knows which group they will be in until they open their envelope.

The reason for selecting at random is so that every individual has an equal chance of being offered a COPD-SEAT programme. It also means that the groups should have an equal mix of different ages, gender, length of COPD diagnosis, and exacerbation history.

If your envelope shows that you are not in the group that receives a COPD-SEAT intervention, we will ask you to complete the baseline measures and questionnaires and take part in one interview before your discharge. We would then like you to carry out your normal daily activities after discharge and we will see you again 4 weeks later for follow-up measures and questionnaire completion. **You will have the option to receive the educational materials at the 2 week visit.**

What happens next?

We ask that you please complete the Expression of Interest form that came with this information pack indicating whether you do or do not wish to take part. Sending back this form does not mean you agree to take part in the study - it just means we can meet you to tell you more about it.

When we meet you, we will ask you to fill in a Consent Form which states that you are happy to take part in the study. We will then ask you to fill in some questionnaires and perform the following physical measurements:

Interview One

Those Wanting to Take Part

We would like to speak to you before your discharge to talk about your COPD diagnosis, exacerbation history and how physical activity and sedentary behaviours fit into your daily life and COPD management. This information will help us to understand the role that lifestyle plays in COPD and how best we can facilitate better care. Your participation in this interview is entirely voluntary and, with your permission, we would like to audio record the conversations so they can be used as part of our research.

Those NOT Wanting to Take Part

We would like to speak to you before your discharge to talk about your reasons for not wanting to take part in the COPD-SEAT programme. We want to learn as much as we can about how best to put in place a programme to reduce sedentary behaviour after an exacerbation. Understanding why people did not want to take part will provide invaluable information and help us to design and implement better ideas in the future. Taking part in this interview is entirely voluntary and, with your permission, we would like to audio record the conversations so they can be used as part of our research.
If you agree to take part:

Please Note:
You are not required to complete any or all measurements as part of the study if you feel unable to do so. You will be asked throughout the completion of measurements if you are happy to do them or if you require rest. These measures do not have to be completed together and can be spaced apart as much as you like.

Questionnaires

We kindly ask you to complete a questionnaire covering topics such as employment status, smoking history, symptoms, anxiety, depression, physical activity levels and sitting time.

Cognitive Function

A cognitive function test will be undertaken (paper-pen and verbally) with a member of the research team upon consenting to take part in the study.

Body Composition

Measurements of height and weight will be used to calculate your body mass index. You will be asked to remove your shoes, socks and personal belongings during the measurements. Weight will involve standing on a weighing scale device. Waist circumference will be measured using a tape measure and is an important indicator of abdominal body composition.

Lung Function

Spirometry will be conducted at the follow-up appointment only and will involve breathing out as hard as you can several times with recovery periods of at least a few minutes between each effort. These breathing tests may cause some temporary light headedness and coughing.

Physical Function

Please Note:

You are not required to complete any or all measurements in this section if you feel unable to do so. You will be asked throughout the completion of measurements if you are happy to do them or if you require rest. The measures do not have to be completed together and can be spaced apart as much as you like.

We will measure the strength of your upper body by performing a grip strength test which will involve you squeezing a measuring device with maximal force on three occasions with a rest period in between.

To measure your ability to rise from a chair, we will ask you to perform a five repetition sit-to-stand test. This will involve rising from a chair with your arms folded across your chest.

To look at your balance, we will ask you to complete a tandem stance test which will involve you trying to hold your balance with one foot directly in front of the other and arms out sideways for 30 seconds.

During the above physical function tests we will ask you to wear a sensor called a Physilog on your chest as well as around each foot. These sensors will not interfere with the performance of each test and will provide very detailed analysis of your physical function levels.

Physical Activity and Sedentary Behaviour

You will be given a device called a LUMO which will measure your posture (i.e. sitting, lying down and standing) and an activity monitor, both will be worn on a belt around your lower back and waist. These will be worn during some of your hospital admission and for the 2 weeks leading up to the follow-up visit. You are asked to take the monitors off during water-based activities and overnight. These devices will be returned to us during your follow-up visit 2 weeks after you are discharged from hospital. We will ask you to charge the LUMO overnight. We will also provide you with disinfectant wipes so you can clean the straps as often as you like during the 2 weeks.

An information sheet about the monitors and verbal instructions will be provided before your discharge.

These devices **do not** transmit or receive information (e.g. GPS, video). They are each a 'black box' storing information about movement, activity and posture.

Participant-Researcher Interactions

In order to assess the quality of delivery and information regarding the study, we will ask your permission to audio record interactions/conversations between yourself and the researcher (Mark Orme). This information will be kept strictly confidential and destroyed following transcription. It will be used to examine the consistency and accuracy of the delivered information. You will be asked if it is okay to record at the beginning of each interaction with the researcher and saying no will not impact on your participation in the study or your usual care.

What happens in the COPD-SEAT intervention groups?

Education Group

Before you are discharged we will spend time with you, providing one-to-one education and information on what sedentary behaviour is and why it is important to reduce it after being in hospital. Ideas about how to best achieve these reductions will be discussed. You will be provided with our 'top tips' booklet and, together we will discuss ways to reduce your time spent sedentary which might work best for you. We will be contacting you during your first week to see how you are getting on, to answer any questions you might have, and to provide support and advice as needed.

Please Note:

Both the Usual Care and Education groups will receive feedback on their sedentary behaviour and walking at the end of the follow-up visit. This will include information about time spent sitting and number of steps taken.

Education plus Feedback Group

Individuals in this group will receive the exact same intervention as described in the Education Group section above but will also receive feedback and prompts (gentle vibrations) by the waist worn LUMO device which will act as a reminder for you to try to break up your sitting time if you wish to do so. After talking to you about reducing your sitting time, together, we will decide how often you would like to be reminded to try to break up your sitting time. A full tutorial on the device will be provided as well as written information for you to take home.

Interview Two

We would like to speak to you about what you thought of the COPD-SEAT programme. This will be a short interview with one of the researchers. It will take place during your follow-up visit at the end of the study. These interviews are entirely voluntary, and if you are happy with it, we would like to audio record our conversations so they can be used as part of the research evaluation. These interviews will shed light on what aspects of the programme worked well, which parts require improvement to ultimately lead to improved intervention designs in the future.

What happens at the end of the study?

We will arrange for participants in all COPD-SEAT groups to meet us 2 weeks after discharge to complete physical measures and fill in some questionnaires. Those individuals in one of the two intervention groups will also have an interview.

If you did not receive an intervention as part of COPD-SEAT, you will be provided with the educational materials for reducing sitting time at the end of your 2 week visit. You will also receive feedback on their sedentary behaviour and walking at the end of the follow-up visit.

Those of you in the Feedback Group will also be offered the chance to continue wearing the LUMO and receive feedback for an additional 2 weeks. This is entirely optional and your decision will not affect your usual care.

What are the possible risks of taking part?

When individuals with COPD reduce their sitting time, the increased time that could be spent being more physically active may cause breathlessness and other symptoms. Planning ahead with your daily activities can help. Please do not hesitate to talk to the research team of members of REDS if you want to find out more.
Please note. This intervention will not prescribe or advise on any aspect of medication, provide information or guidance on smoking cessation, or refer individuals to pulmonary rehabilitation. These will be covered by the REDS team and clinicians as routine practice and will not affect your potential involvement in this study.

What are the possible benefits of taking part?

We cannot promise the study will have direct benefits for you, but we hope you will engage with the study and the information we get will help us to improve COPD care in the future. If you consent for us to do so, we will inform the Respiratory Discharge Service of your involvement in the study and the results of the measures will be entered into your medical records.

What if something goes wrong?

It is unlikely that anything will go wrong during this study. But if you have a complaint about anything as you go through the study, then please tell Mark or a member of the REDS team immediately. If you have reason to complain about this study, complaints should be addressed in the first instance to Prof Sally Singh whose details are at the end of this document.

If you remain unhappy and wish to complain formally, you can do this by contacting Patient Information and Liaison Service, contact 0808 178 8337 (free number).

Expenses

Travel expenses will be offered for when you travel to and from the follow-up visit to Glenfield Hospital. Expenses will cover parking and petrol or travel by bus or train. Travel by taxi will be reimbursed in full.

Will taking part in this study be kept confidential?

We will follow ethical and legal practice and all information about you will be handled in confidence.
If you join the study, some parts of your medical records (e.g. exacerbation and medication history) and the data collected for the study will be looked at by authorised persons from Loughborough University who are organising the research. They may also be looked at by regulatory authorities to check that the research is being conducted correctly. All will have a duty of confidentiality to you as research participants and we will do our best to meet this duty.
Personal data (e.g. address, telephone number) will be kept for 3-6 months after the end of the study so that we are able to contact you about the findings of the study and possible follow-up studies (unless you advise us that you do not wish to be contacted). All other data (research data) will be kept securely for 7 years. After this time your data will be disposed of securely. During this time all precautions will be taken by all those involved to maintain confidentiality. Only members of the research team will have access to personal data.

Whilst everything about you is kept confidential, confidentiality will have to be broken if something is mentioned that we believe puts you or someone else in danger. If we believe this to incur immediate danger, we will have to contact the police without any delay. Any non-immediate cause for concern will be discussed in confidence with the research team.

What will happen if I don't want to carry on with the study?

Your participation is voluntary and you are free to withdraw at any time, without giving a reason, and without your legal rights and usual care being affected. The treatment you receive from the REDS team and clinicians will not be affected. You should know, however, that if you withdraw then the information collected so far cannot be erased and this information may still be used in the research analysis. If you are happy to do so, we will ask you for a short interview over the phone at your convenience so we can learn more about some of the reasons people might not wish to continue their participation in the study.

What will happen to the results of the research study?

Results from this study will be used to help us understand whether the COPD-SEAT programme is acceptable for individuals with COPD following admission to hospital for an exacerbation. The findings will be written up and presented as research publications and presentations (2016/2017) and as part of PhD theses. In the future, the COPD-SEAT programme might be used in a much larger study. The researchers will make sure all participant data is made anonymous and any identifying features will be removed before publication.

Who is organising and funding the research?

The research is organised and funded by Loughborough University and University Hospitals of Leicester.

Who has reviewed the study?

All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and approved by Research Ethics Committee East Midland-Leicester(15-EM-0433). Study design and content has been reviewed by individuals diagnosed with COPD and members of the REDS team.

Contact for Further Information

If you would like to know more about the research, then please talk to me in the clinic or inform a member of the REDS team who will inform me of your request. My name is Mark Orme and you can contact me by phone via the Rehabilitation Office on 0116 2502535 or 0116 2583181. You will see me around the Ward as well so please do not hesitate to ask me anything about the study.

Thank you for taking the time to read this.

NHS
National Institute for Health Research

Appendix S

COPD-SEAT education booklet

SIT LESS MOVE MORE LIVE HEALTHIER

This booklet offers some Top Tips to Tweak your Week. Read more inside...

Loughborough University

University Hospitals of Leicester NHS
NHS Trust

Sit Less, Move More, Live Better

This booklet offers some tips for small changes you can make to sit for shorter periods and move more often.

Did you know?

- Breaking up long periods of sitting can help to reduce joint stiffness and pain
- Even if you are physically active, sitting for too long can be harmful to your health
- Sitting for long periods is thought to increase the risk of hospital readmission
- Keeping as active as possible can improve the quality of everyday life and reduce symptoms of depression

Use it or lose it

Whilst it is important to rest, it is also vital to maintain an active lifestyle to keep you independent and improve your quality of life. This can be done by reducing prolonged periods of sitting and also breaking up your sitting time with small amounts of physical activity.

Physical activity doesn't always mean exercising or walking. Breaking up your sitting with stretching or balancing can help prevent falls and keep you mobile and more mentally alert.

TOP TIPS for healthy habits

Adding small portions of physical activity into your everyday routine is a great way to keep active and break up prolonged sitting. Start developing a new habit by:

- Choosing a specific activity
- Doing the specific activity repeatedly
- Doing the specific activity at the same point in your routine

This booklet shows some simple activity tips for you to try. Some will get your heart pumping a little more and others will help you stretch and strengthen your body and maintain your balance. Try to do as many of them as you can.

Seven suggestions for an active recovery

1. Leave the house daily

Try to go out at least once a day. Going out reduces time spent inactive indoors. Go out with a friend or relative if possible and make sure you feel comfortable with the outside conditions such as the weather.

TOP TIP Use a stick or walking aid if you need to. It will help your balance and allow you to walk further, keeping you active for longer.

2. Make ad breaks active

When you watch TV, stand up or walk around during advert breaks. This will stop your joints becoming stiff and will keep your muscles active.

TOP TIP Try to watch TV for no more than one hour at a time, including two active ad breaks.

TOP TIP Leave the remote control by the TV or out of reach so that you have to get up to change the channel.

3. Stand-ups

Stand up when waiting, whether it be for a bus, train or the kettle. Stay standing as long as possible. This will help to maintain balance.

TOP TIP Ask yourself if you really need to sit down when you are waiting for something.

4. Tiptoe through the queue

When waiting in a queue, use the time to increase your leg strength with this simple exercise. Stand on your tip toes and then drop back down to your heels with a gentle bounce. This will also help maintain bone density and reduce the likelihood of falls. Use support if you need to.

TOP TIP Tiptoe on the spot anywhere you are standing and waiting, including at home.

5. Increase your steps

Try to build up the number of steps you do each day. The more steps you do, the healthier you will be. Remember, when you are stepping, you are not sitting.

TOP TIP Look for opportunities to increase your steps each day. For example:

- Walk to the shop or if you do drive, park further away from the entrance
- Get off the bus a stop or two early
- Walk around your home when on the phone
- Take the lift to one floor below your destination and walk up the last staircase
- When meeting friends, go for a walk together rather than sitting down

6. Sit to stand with no hands

Each time you stand up, try doing it without using your hands. Make sure your feet are flat on the floor and your chair is sturdy. This helps to maintain your balance and leg power.

TOP TIP When you get up from your chair, try holding your position a few inches above the chair and count to ten.

TOP TIP As a seated exercise, try standing up and then sitting back down again, gradually doing more as they becomes easier.

7. Treat the seat as a treat

It is important for you to rest during your recovery. Moving during prolonged sitting periods will provide you with the ability to be independent and improve the quality of everyday life.

TOP TIP Put notes on your fridge, cupboard or wall to remind yourself to do your chosen activities.

Get in the habit

You will find it easier to form habits if you:

- **Plan ahead:** Spend some time now thinking about how, when and where you will fit these tips into your current routines.
- **Start early:** If a tip seems too hard, then build up to it gradually until you are comfortable doing it.
- **Keep going:** Doing the activity repeatedly in your routine will make it easier to form a habit. If you forget to do your chosen activity, don't worry. Just keep going and do it next time as part of your routine.

Watch for improvements

By doing the activities in this booklet, you will find that, over time, your breathing, stamina and strength improve and everyday tasks become more manageable. You'll also find that more intensive activities, such as fast walking and climbing stairs, become easier.

Appendix T

COPD-SEAT LUMO mobile app instructions

LUMO App

Instruction Manual

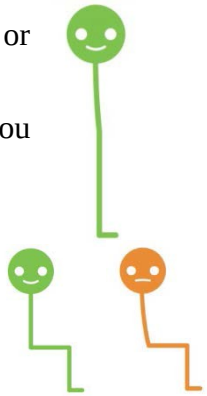
Please read this document carefully for instructions on how to navigate the LUMO app during the 2 weeks of wearing the monitors.

If you have any **questions** or **concerns** regarding any aspect of the study, please do not hesitate to contact **Mark Orme** on **07772810402** or email at **m.w.orme@lboro.ac.uk**.

1. How do I open the app on the phone?

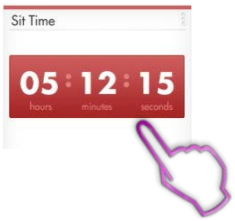
- Touch the button on the top right corner of the device or the round button at the bottom
- The app will then appear, taking up the full screen
- You will then be able to navigate the app to look at the different feedback options

2. How do I interpret the avatar?

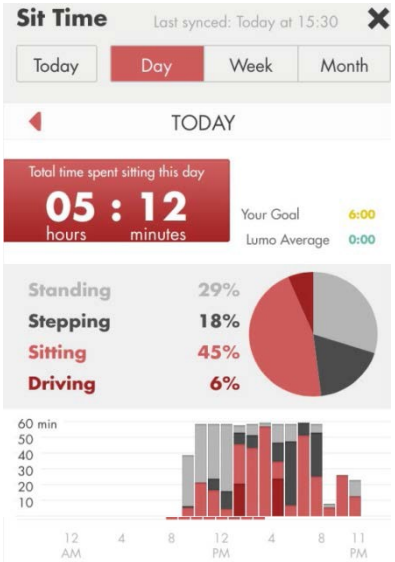


- The avatar represents your current posture (sitting, standing or walking)
- The avatar does not provide any other function than showing you your posture
- The colour of the avatar (orange or green) denotes the quality of your posture compared to the ideal. We are not asking you to act on this information.

3. How do I find out about my sitting time?



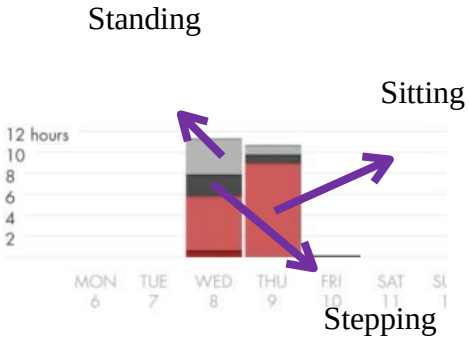
- On the panel across the bottom of the screen, there is a slide titled "Sit Time". This provides you with a count- up of how much time you have been sitting. For example, in the picture on the right, this would mean you have sat for over 5 hours
- By pressing the slide you will be provided with more detailed information. It will look something like this.
- The red box provides the same information as above
- The pie chart shows the proportion time spent in different postures (standing, stepping, and sitting (including driving)) and the percentages are given next to the



posture names. The higher the percentage, the more time you have spent in that posture.

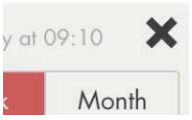
- When you have been wearing the LUMO for at least a few days, you can also start to see how you are getting on a day-to-day basis
- In the top right of the screen, press the 

"week" icon to see the percentages of the postures across multiple days in the form of a bar chart
- The more time spent in a posture each day, the greater amount of colour for that posture. For example, the picture on the right shows Thursday to be the day the wearer sat the most and Wednesday was the day they sat the least and stood the most.



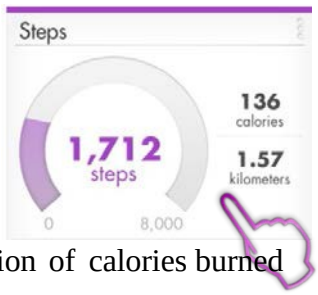
- The pie chart presented here is the overall average time spent in each posture, provided as a percentage.
- You can move between days by touching the left and right arrows
- To go back to today's information, touch the "Today" 

icon
- To close the screen and return to the panel view, touch the cross in the top right corner



4. How do I find out about my standing time?

- On the panel across the bottom of the screen, there is a slide titled "Steps". This provides you with how many steps you have taken for that day. For example, in the picture on the right, this would mean you have taken 1712 steps for that day



- The slide also converts the number of steps into an estimation of calories burned and distance walked (in kilometres)

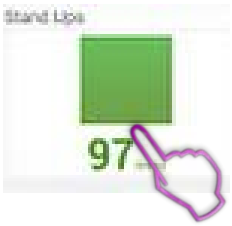
- By pressing the slide you will be provided with more detailed information. It will look something like this

- You can choose whether to see information on a day-to-day basis by touching the "Day" icon at the top of the screen
- On the day view, the bar chart shows the number of steps taken each hour. The higher the bar, the more steps you have taken. The left side of the graph shows the number of steps taken each hour.
- When you have been wearing the LUMO for at least a few days, you can also start to see how you are getting on, on a day-to-day basis
- You can move between days by touching the left and right arrows
- In the top right of the screen, press the "week" icon to see the number of steps taken on multiple days in the form of a bar chart
- The more steps taken each day, the taller the bar.

- The purple bar presented here is the overall number of steps you have taken in the selected week.
- To go back to today's information, touch the "Today" icon
- To close the screen and return to the panel view, touch the cross in the top right corner

5. How do I find out about the number of stand-ups I have done?

- On the panel across the bottom of the screen, there is a slide titled "Stand Ups". This provides you with how many times you have stood up from a seated position. For example, in the picture on the right, this would mean you have stood up 97 times



- By pressing the slide you will be provided with more detailed information. It will look something like this

- You can choose whether to see information on a day-to-day basis by touching the "Day" icon at the top of the screen
- On the day view, the bar chart shows the number of times you have stood up each hour.
  The higher the bar, the more times you have stood. The left side of the graph shows the number of stand-ups each hour.
- You can move between days by touching the left and right arrows
- When you have been wearing the LUMO for at least a few days, you can also start to see how you are getting on, on a day-to-day basis
- In the top right of the screen, press the "week" icon to see the number of stand-ups on multiple days in the form of a bar chart
- The more times you have stood up each day, the taller the bar. The green bar presented here is the overall number of times you have stood up in the selected week.
- To go back to today's information, touch the "Today" icon
- To close the screen and return to the panel view, touch the cross in the top right corner

Thank you for taking part in the study and please do not hesitate to contact me if you have any questions or concerns

Contact Details

Mark Orme

24-hour Contact Number: 07772810402

m.w.orme@lboro.ac.uk

Appendix U

COPD-SEAT questionnaire

COPD-SEAT Baseline Questionnaire

Participant ID:

This questionnaire is made up of modules that ask you about a specific aspect of your life. Your answers will be treated as strictly confidential and will only be used for research purposes.

Please complete the questionnaire by checking answers or enter a response in the boxes provided next to or below the question. Try to answer every question, except when there is a specific request to skip a section.

Section A – Demographics

D1 - To which of the groups do you consider you belong?

- ☐ White – British
- ☐ White – Irish
- ☐ Any other white background
- ☐ Mixed – White and Black Caribbean
- ☐ Mixed – White and Black African
- ☐ Mixed – White and Asian
- ☐ Asian or Asian British – Indian
- ☐ Asian or Asian British – Pakistani
- ☐ Asian or Asian British – Bangladeshi
- ☐ Any other Asian/Asian British Background
- ☐ Black or Black British – Caribbean
- ☐ Black or Black British – African
- ☐ Any other Black/Black British background
- ☐ Chinese
- ☐ Any other (please specify) ☐

D2 - Do you own or rent the accommodation that you live in?

- ☐ Own outright
- ☐ Own with a mortgage
- ☐ Rent – from local authority, local council, housing association
- ☐ Rent – from private landlord or letting agency
- ☐ Pay part rent and part mortgage
- ☐ Live in accommodation rent free
- ☐ None of the above

D3 - Including yourself, how many people are living together in your household? (Include those who usually live in the house such as students living away from home during term, partners in the armed forces or professions such as pilots)

☐ Do not know

D4 - At what age did you finish your continuous full-time education at school or college?

- ☐ Never went to school
- ☐ 14 or under
- ☐ 15
- ☐ 16
- ☐ 17
- ☐ 18
- ☐ 19 or over

D5 - What is the highest education you have completed?

- ☐ Primary school
- ☐ Some secondary school
- ☐ Completed secondary school
- ☐ Some additional training (e.g. apprenticeship, GNVQ)
- ☐ Undergraduate university
- ☐ Postgraduate university

D6 - Which of the following best describes your current situation? (Please tick only one)

- ☐ In paid employment or self-employed
- ☐ Retired
- ☐ Looking after home and/or family
- ☐ Unable to work because of sickness or disability
- ☐ Unemployed
- ☐ Doing unpaid or voluntary work
- ☐ Full-time or part-time student
- ☐ None of the above

D7 - What is the average total income before tax received by your household?

- ☐ Less than £18,000
- ☐ £18,000 - £30,999
- ☐ £31,000 – £51,999
- ☐ £52,000 - £100,000
- ☐ Greater than £100,000
- ☐ Do not know
- ☐ Prefer not to answer

Section B – General Health

Under each heading, please tick the ONE box that best describes your health TODAY

MOBILITY

I have no problems in walking about ..…… ☐

I have slight problems in walking about ……. ☐

I have moderate problems in walking about ……. ☐

I have severe problems in walking about …….. ☐

I am unable to walk about …… ☐

SELF-CARE

I have no problems washing or dressing myself …….. ☐

I have slight problems washing or dressing myself …….. ☐

I have moderate problems washing or dressing myself ……☐

I have severe problems washing or dressing myself …… ☐

I am unable to wash or dress myself …… ☐

PAIN / DISCOMFORT

I have no pain or discomfort …….. ☐

I have slight pain or discomfort ……. ☐

I have moderate pain or discomfort ……. ☐

I have severe pain or discomfort …….. ☐

I have extreme pain or discomfort …… ☐

ANXIETY / DEPRESSION

I am not anxious or depressed …….. ☐

I am slightly anxious or depressed …….. ☐

I am moderately anxious or depressed …… ☐

I am severely anxious or depressed ……. ☐

I am extremely anxious or depressed …….. ☐

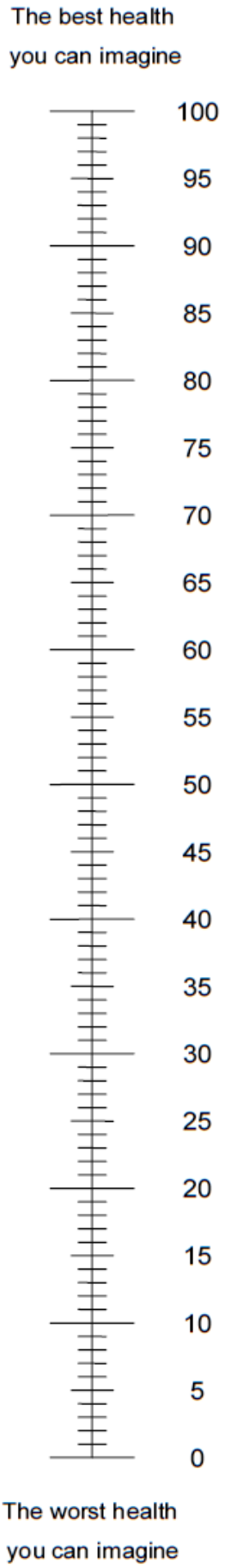
- We would like to know how good or bad your health is TODAY.

- This scale is numbered from 0 to 100

- 100 means the best health you can imagine
- 0 means the worst health you can imagine
- Mark an X on the scale to indicate how your health is TODAY.

- Now, please write the number you marked on the scale in the box below.

YOUR HEALTH TODAY = ☐



Section C – Smoking

S1 - Have you ever smoked cigarettes?

☐ Yes

☐ No

IF "NO" PLEASE GO TO S11

S2 - Do you currently smoke cigarettes?

☐ Yes

☐ No

IF "YES" PLEASE GO TO S5

S3 - How long ago did you stop smoking cigarettes?

☐

S4 - How old were you when you last smoked cigarettes on most days?

☐

☐ Do not know

S5 - How old were you when you started to smoke cigarettes regularly?

☐

S6 - About how many cigarettes a day do/did you usually smoke on weekdays?

☐

S7 - About how many cigarettes a day do/did you usually smoke on weekend days?

☐

S8 - How soon after waking do/did you usually smoke your first cigarette of the day?

- ☐ Less than 5 minutes
- ☐ 5 – 14 minutes
- ☐ 15 – 29 minutes
- ☐ 30 minutes – 1 hour
- ☐ **1 – 2 hours**
- ☐ 2 hours or more

S9 - Has a medical person, for example a doctor or nurse ever advised you to stop smoking altogether because of your health?

- ☐ Yes
- ☐ No

S10 - How long ago was that?

- ☐ Within the last 12 months
- ☐ Over 12 months ago

S11 - Does anyone in your household smoke?

- ☐ Yes, one household member smokes
- ☐ Yes, more than one household member smokes
- ☐ No

S12 - Now, in most weeks, how many hours a week are you exposed to other people's tobacco smoke?

S13 - Did your father ever smoke regularly when you were a child?

- ☐ Yes
- ☐ No

S14 - Did your mother ever smoke regularly when you were a child?

- ☐ Yes
- ☐ No

Section D – Lung Health

LH1 - How old were you when you were first told by a doctor that you had COPD/chronic bronchitis/emphysema?

LH2 - How many times have you been admitted to hospital for any reason in the last 12 months?

LH3 - How many times have you been admitted to hospital for an exacerbation in the last 12 months?

LH4 – Before being admitted to hospital, were you ever too breathless to leave the house?

☐ Yes

☐ No

IF "NO" PLEASE GO TO LH6

LH5 - Was that all or most days, at least once a week, or less often than that?

☐ All or most days

☐ At least once a week

☐ Less often

LH6 – Before being admitted to hospital, please choose the **one** best response which would describe your shortness of breath.

0 "I only get breathless with strenuous exercise"

1 "I get short of breath when hurrying on the level or walking up a slight hill"

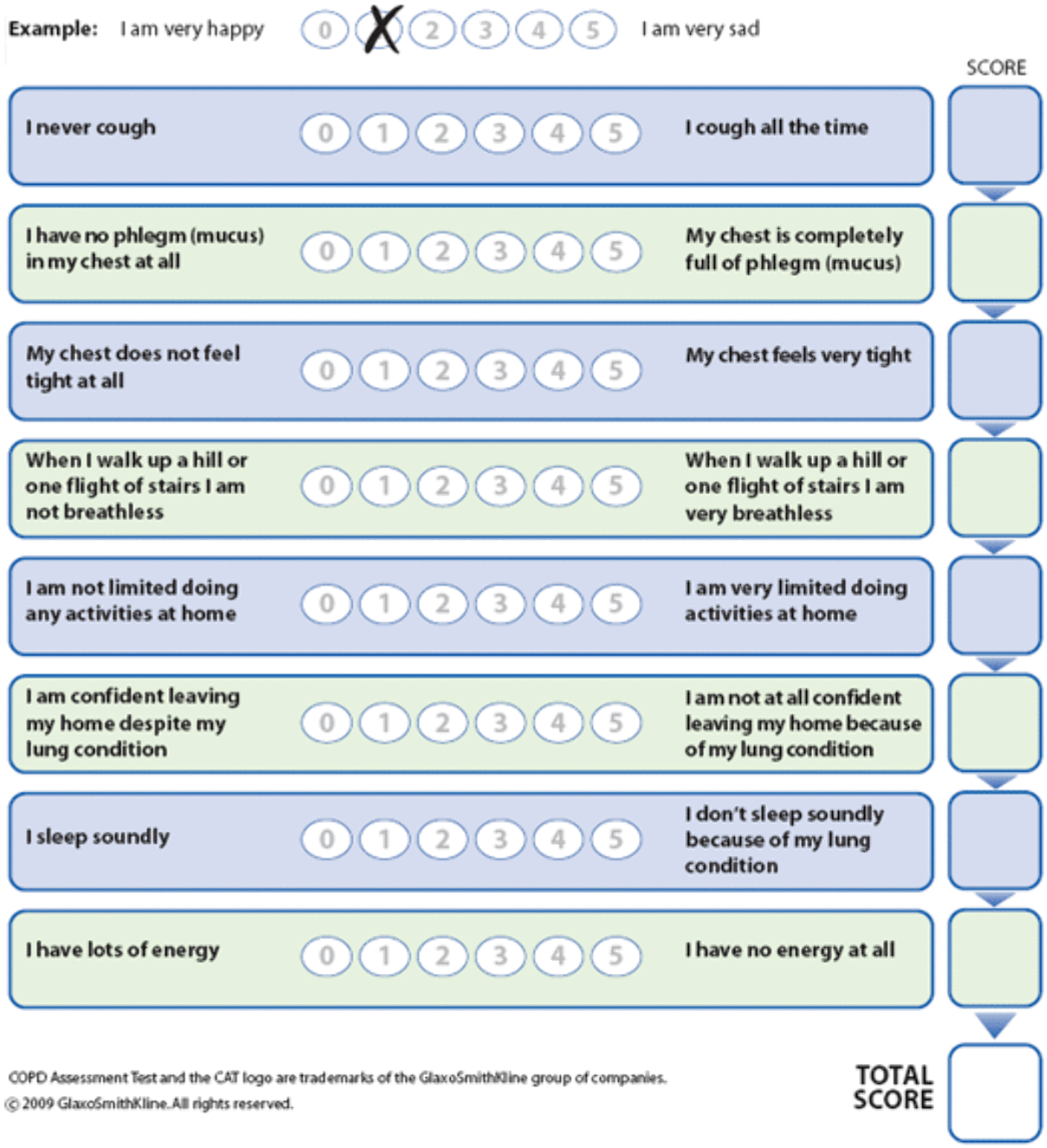
2 "I walk slower than people of the same age on the level because of breathlessness or have to stop for breath when walking at my own pace on the level"

3 "I stop for breath after walking about 100 yards or after a few minutes on the level"

4 "I am too breathless to leave the house" or "I am breathless when dressing"

Grade

Section E – COPD Health – Part 1



Section E – COPD Health – Part 2

Below is a list of statements that other people with your illness have said are important**. Please circle or mark one number per line to indicate your response as it applies to the <u>past 7 days</u>.**

	PHYSICAL WELL-BEING	Not	A little	Some-	Quite	Very
GP1	I have a lack of energy	0	1	2	3	4
GP2	I have nausea	0	1	2	3	4
GP3	Because of my physical condition, I have trouble meeting the needs of my family	0	1	2	3	4
GP4	I have pain	0	1	2	3	4
GP5	I am bothered by side effects of treatment	0	1	2	3	4
GP6	I feel ill	0	1	2	3	4
GP7	I am forced to spend time in bed	0	1	2	3	4

.....

	SOCIAL/FAMILY WELL-BEING	Not at all	A little bit	Some-what	Quite a bit	Very much
GS1	I feel close to my friends	0	1	2	3	4
GS2	I get emotional support from my family	0	1	2	3	4
GS3	I get support from my friends.....	0	1	2	3	4
GS4	My family has accepted my illness	0	1	2	3	4
GS5	I am satisfied with family communication about my illness.....	0	1	2	3	4
GS6	I feel close to my partner (or the person who is my main support)	0	1	2	3	4
Q1	*Regardless of your current level of sexual activity, please answer the following question. If you prefer not to answer please mark this box and go to the next section.*					
GS7	I am satisfied with my sex life	0	1	2	3	4

EMOTIONAL WELL-BEING

		Not at all	A little bit	Some-what	Quite a bit	Very much
GE1	I feel sad	0	1	2	3	4
GE2	I am satisfied with how I am coping with my illness.....	0	1	2	3	4
GE3	I am losing hope in the fight against my illness.....	0	1	2	3	4
GE4	I feel nervous.....	0	1	2	3	4
GE5	I worry about dying.....	0	1	2	3	4
GE6	I worry that my condition will get worse	0	1	2	3	4

FUNCTIONAL WELL-BEING

		Not at all	A little bit	Some-what	Quite a bit	Very much
GF1	I am able to work (include work at home)	0	1	2	3	4
GF2	My work (include work at home) is fulfilling.....	0	1	2	3	4
GF3	I am able to enjoy life.....	0	1	2	3	4
GF4	I have accepted my illness.....	0	1	2	3	4
GF5	I am sleeping well	0	1	2	3	4
GF6	I am enjoying the things I usually do for fun	0	1	2	3	4
GF7	I am content with the quality of my life right now.....	0	1	2	3	4

ADDITIONAL CONCERNS

		Not at all	A little bit	Some-what	Quite a bit	Very much
HI7	I feel fatigued	0	1	2	3	4
HI12	I feel weak all over	0	1	2	3	4
An1	I feel listless ("washed out")	0	1	2	3	4
An2	I feel tired	0	1	2	3	4
An3	I have trouble starting things because I am tired.....	0	1	2	3	4
An4	I have trouble finishing things because I am tired	0	1	2	3	4
An5	I have energy	0	1	2	3	4
An7	I am able to do my usual activities.....	0	1	2	3	4
An8	I need to sleep during the day	0	1	2	3	4
An12	I am too tired to eat	0	1	2	3	4
An14	I need help doing my usual activities	0	1	2	3	4
An15	I am frustrated by being too tired to do the things I want to do.....	0	1	2	3	4
An16	I have to limit my social activity because I am tired.....	0	1	2	3	4

Section F – Physical Activity and Sitting

PA1 - In the last 4 weeks, which form of transport have you used most often to get about? (Not including any journeys to and from work; please only select the most frequent mode of transport used)

- ☐ Car/motor vehicle
- ☐ Walk
- ☐ Public transport
- ☐ Cycle
- ☐ None of the above

PA2 - How many times in the last 4 weeks did you do swimming?

- ☐ None
- ☐ Once in the last 4 weeks
- ☐ 2 – 3 times in the last 4 weeks
- ☐ Once a week
- ☐ 2 – 3 times a week
- ☐ 4 – 5 times a week
- ☐ Every day
- ☐ Do not know

PA3 - How many times in the last 4 weeks did you do cycling?

- ☐ None
- ☐ Once in the last 4 weeks
- ☐ 2 – 3 times in the last 4 weeks
- ☐ Once a week
- ☐ 2 – 3 times a week
- ☐ 4 – 5 times a week
- ☐ Every day
- ☐ Do not know

PA4 - Which of the following do you attend once a week or more often? (you can select more than one)

- ☐ Sports club or gym
- ☐ Pub or social club
- ☐ Religious group
- ☐ Adult education class
- ☐ Other group activity
- ☐ None of the above

PA5 - Which of the following best describes your usual walking pace?

- ☐ A slow pace
- ☐ An average pace
- ☐ A fairly brisk pace
- ☐ A fast pace

PA6 - We are interested in finding out about the kinds of physical activities that people do as part of their everyday lives. The questions will ask you about the time you spent being physically active in the **last 7 days**. Please answer each question even if you do not consider yourself to be an active person. Please think about the activities you do at work, as part of your house and gardening, to get from place to place, and in your spare time for recreation, exercise or sport.

Think about all the **vigorous** activities that you did in the **last 7 days**. **Vigorous** physical activities refer to activities that take hard physical effort and make you breathe much harder than normal. Think *only* about those physical activities that you did for at least 10 minutes at a time.

7. During the **last 7 days**, on how many days did you do **vigorous** physical activities like heavy lifting, digging, aerobics, or fast bicycling?

_____days per week

☐ No vigorous physical activities → ***Skip to question 3***

8. How much time did you usually spend doing **vigorous** physical activities on one of those days?

_____hours per day

_____minutes per day

Think about all the **moderate** activities that you did in the **last 7 days**. **Moderate** activities refer to activities that take moderate physical effort and make you breathe somewhat harder than normal. Think only about those physical activities that you did for at least 10 minutes at a time.

9. During the **last 7 days**, on how many days did you do **moderate** physical activities like carrying light loads, bicycling at a regular pace, or doubles tennis? Do not include walking.

_____days per week

☐ No moderate physical activities → ***Skip to question 5***

10. How much time did you usually spend doing **moderate** physical activities on one of those days?

_____hours per day

_____minutes per day

Think about the time you spent **walking** in the **last 7 days**. This includes at work and at home, walking to travel from place to place, and any other walking that you might do solely for recreation, sport, exercise, or leisure.

11. During the **last 7 days**, on how many days did you **walk** for at least 10 minutes at a time?

days per week

☐ No walking → ***Go to next section***

12. How much time did you usually spend **walking** on one of those days?

hours per day

_____minutes per day

PA7 - Please think about how much time you spend sitting on a **typical** week day and weekend day.

When filling in the table below, if you take part in more than one of the activities at the same time, e.g. watching television whilst using a laptop computer, please record time spent taking part in the activity you mainly focus on e.g. it may be you watch television and only use the laptop when you get an email. In this case you would record time spent watching television.

Please estimate how many hours you spend SITTING EACH DAY in the following situations: ***(please write your answer)***

	On a WEEK Day		**On a WEEKEND Day**	
	Hours	**Minutes**	**Hours**	**Minutes**
While travelling to and from places				
While at work				
While watching television				
While using a computer at home				
In your leisure time, NOT including television (e.g. visiting friends, movies, dining out, etc)				

Section G – Anxiety and Depression

Please **circle one response** from the four given for each question. Answer how it **currently** describes your feelings.

Your answer should be your **immediate response**.

A	**I feel tense or 'wound up':**	
	Most of the time	3
	A lot of the time	2
	From time to time, occasionally	1
	Not at all	0

D	**I still enjoy the things I used to enjoy:**	
	Definitely as much	0
	Not quite so much	1
	Only a little	2
	Hardly at all	3

A	**I get a sort of frightened feeling as if something awful is about to happen:**	
	Very definitely and quite badly	3
	Yes, but not too badly	2
	A little, but it doesn't worry me	1
	Not at all	0

D	**I can laugh and see the funny side of things:**	
	As much as I always could	0
	Not quite so much now	1
	Definitely not so much now	2
	Not at all	3

A	**Worrying thoughts go through my mind:**	
	A great deal of the time	3
	A lot of the time	2
	From time to time, but not too often	1
	Only occasionally	0

D	I feel cheerful:	
	Not at all	3
	Not often	2
	Sometimes	1
	Most of the time	0

A	I can sit at ease and feel relaxed:	
	Definitely	0
	Usually	1
	Not Often	2
	Not at all	3

D	I feel as if I am slowed down:	
	Nearly all the time	3
	Very often	2
	Sometimes	1
	Not at all	0

A	I get a sort of frightened feeling like 'butterflies' in the stomach:	
	Not at all	0
	Occasionally	1
	Quite Often	2
	Very Often	3

D	I have lost interest in my appearance:	
	Definitely	3
	I don't take as much care as I should	2
	I may not take quite as much care	1
	I take just as much care as ever	0

A	I feel restless as I have to be on the move:	
	Very much indeed	3
	Quite a lot	2
	Not very much	1
	Not at all	0

D	**I look forward with enjoyment to things:**	
	As much as I ever did	0
	Rather less than I used to	1
	Definitely less than I used to	2
	Hardly at all	3

A	**I get sudden feelings of panic:**	
	Very often indeed	3
	Quite often	2
	Not very often	1
	Not at all	0

D	**I can enjoy a good book or radio or TV program:**	
	Often	0
	Sometimes	1
	Not often	2
	Very seldom	3

Section H – Falling

Now we would like to ask some questions about how concerned you are about the possibility of falling.

For each of the following activities, please circle the opinion closest to your own to show how concerned you are that you might fall if you did this activity.

Please reply thinking about how you usually do the activity. If you currently don't do the activity (e.g. if someone does your shopping for you), please answer to show whether you think you would be concerned about falling IF you did the activity.

		Not at all concerned *1*	*Somewhat concerned* *2*	*Fairly concerned* *3*	*Very concerned* *4*
1	Cleaning the house (e.g. sweep, vacuum or dust)	*1*	*2*	*3*	*4*
2	Getting dressed or undressed	*1*	*2*	*3*	*4*
3	Preparing simple meals	*1*	*2*	*3*	*4*
4	Taking a bath or shower	*1*	*2*	*3*	*4*
5	Going to the shop	*1*	*2*	*3*	*4*
6	Getting in or out of a chair	*1*	*2*	*3*	*4*
7	Going up or down stairs	*1*	*2*	*3*	*4*
8	Walking around in the neighbourhood	*1*	*2*	*3*	*4*
9	Reaching for something above your head or on the ground	*1*	*2*	*3*	*4*
10	Going to answer the telephone before it stops ringing	*1*	*2*	*3*	*4*
11	Walking on a slippery surface (e.g. wet or icy)	*1*	*2*	*3*	*4*
12	Visiting a friend or relative	*1*	*2*	*3*	*4*
13	Walking in a place with crowds	*1*	*2*	*3*	*4*
14	Walking on an uneven surface (e.g. rocky ground, poorly maintained pavement)	*1*	*2*	*3*	*4*
15	Walking up or down a slope	*1*	*2*	*3*	*4*
16	Going out to a social event (e.g. religious service, family gathering or club meeting)	*1*	*2*	*3*	*4*

Section I – Technology

T1 - Do you own a smartphone (a phone which has similar capability to a computer e.g. internet access)?

- ☐ Yes
- ☐ No

IF "NO" PLEASE GO TO T4

T2 – What type of smartphone do you own? (Please tick all that apply)

- ☐ Apple/iPhone
- ☐ Android
- ☐ Blackberry
- ☐ Any other (please specify) ____

T3 – What do you use your smartphone for? (Please tick all that apply)

- ☐ To go on the internet
- ☐ Entertainment (e.g. games, videos)
- ☐ Business/work
- ☐ Emails
- ☐ Communication (calls, texts)
- ☐ Social networking (e.g. Facebook, Twitter)
- ☐ Reading books/articles
- ☐ Online banking
- ☐ Shopping/book holidays
- ☐ Downloading and using applications (e.g. weather, news)
- ☐ Any other (please specify) ____

T4 – Do you own a personal computer (e.g. desktop, laptop, tablet)?

- ☐ Yes
- ☐ No

IF "NO" YOU HAVE COMPLETED THE QUESTIONNAIRE

T5 – What type of computer do you own?

- ☐ Laptop
- ☐ Desktop computer
- ☐ Tablet
- ☐ Any other (please specify) [ ]

T6 - What do you use your computer for? (Please tick all that apply)

- ☐ To go on the internet
- ☐ Entertainment (e.g. games, videos)
- ☐ Business/work
- ☐ Emails
- ☐ Communication (calls, texts)
- ☐ Social networking (e.g. Facebook, Twitter)
- ☐ Reading books/articles
- ☐ Online banking
- ☐ Shopping/book holidays
- ☐ Downloading and using applications (e.g. weather, news)
- ☐ Any other (please specify) [ ]

Thank you for completing the questionnaire

Appendix V

Full list of publications and conference presentations

Published journal articles

Orme, M., Wijndaele, K., Sharp, S.J., Westgate, K., Ekelund, U., Brage, S. Combined influence of epoch length, cut-point and bout duration on accelerometry-derived physical activity. *International Journal of Behaviour, Nutrition and Physical Activity*. 2014; 11: 34.

Orme, M.W., Weedon, A.E., Esliger, D.W., Saukko, P., Morgan, M.D., Steiner, M.C., Downey, J., Singh, S.J., Sherar, L.S. Study protocol for chronic obstructive pulmonary disease-Sitting and ExacerbAtions Trial (COPD-SEAT): a randomised controlled feasibility trial of a home-based self-monitoring sedentary behaviour intervention. *BMJ Open*. 2016; 6:e013014.

Orme, M.W., Esliger, D.W., Kingsnorth, A., Morgan, M.D., Steiner, M.C., Singh, S.J., Malcolm, D., Sherar, L.S. Physical Activity and Respiratory Health (PhARaoH): data from a cross-sectional study. *Journal of Open Health Data*. 4(1):e4.

Journal articles submitted/under review

Orme, M.W., Weedon, A.E., Saukko, P., Esliger, D.W., Morgan, M.D., Steiner, M.C., Downey, J., Singh, S.J., Sherar, L.S. A feasibility study of a home-based self-monitoring sedentary behaviour randomised controlled trial in COPD patients suffering from an acute exacerbation: Trial results. (Submitted).

Trethewey, R., Esliger, D., Petherick, E., Evans, R., Greening, N., James, B., Kingsnorth, A., Morgan, M., Orme, M., Sherar, L., Singh, S., Toms, N., Steiner, M. The influence of muscle mass in the assessment of lower limb strength in COPD. (Submitted).

Whelan, M.E., Morgan, P.S., Sherar, L.B., Orme, M.W., Esliger, D.W. Can functional magnetic resonance imaging studies help with the optimisation of health messaging for lifestyle behaviour change? A systematic review. (Under review).

Conference Oral presentations

Physical Activity and Respiratory Health (PhARaoH) Study: Preliminary findings. 24-28th June 2014. Exercise is Medicine Conference, Puijo, Finland.

Physical activity and respiratory health (PhARaoH) study: objective profiling of physical activity and time sedentary in COPD patients grouped by lung function and self-reported disability. 23rd February 2015. Health and Wellbeing Student Conference, Loughborough University, UK.

Conference poster presentations

Physical activity and respiratory health (PhARaoH) study. 17th February 2014. Health and Wellbeing Student Conference, Loughborough University, UK.

Physical Activity and Respiratory Health (PhARaoH) Study: Preliminary findings. 1st September 2014. Members of the Society for the Study of Human Biology Conference, Loughborough University, UK.

Objective physical activity, physical function and perceived health among COPD patients with differing symptom severities. 26-30th September 2015. European Respiratory Society, Amsterdam, The Netherlands.

Feasibility of a home-based sedentary behaviour intervention for COPD patients post exacerbation: Sitting and ExacerbAtions Trial (COPD-SEAT). 24-25th February 2016. UCL 2nd Behaviour Change Conference, London, UK.

Feasibility of a home-based sedentary behaviour intervention for COPD patients post exacerbation: Sitting and ExacerbAtions Trial (COPD-SEAT). 14th June 2016. School of Sport, Exercise and Health Sciences Postgraduate Research Conference, Loughborough, UK.