UNIVERSITY OF DERBY

PROFILING THE PHYSIOLOGICAL AND PSYCHOLOGICAL EFFECTIVENESS OF SINGLET OXYGEN IN THE MANAGEMENT OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

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"One, surround yourself with people whose eyes light up when they see you.

Two slowly is the fastest way to get to where you want to be.

Three, the top of one mountain is the top of the next so keep climbing."

-André De Shields'

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LIST OF ABBREVIATIONS

AE	*Adverse Event*
AR	*Adverse Reaction*
AOT	*Ambulatory Oxygen Therapy*
CAT	*COPD Assessment Tool*
CASIS	*COPD and Asthma Sleep Impact Scale*
CBT	*Cognitive Behavioural Therapy*
CI	*Chief Investigator*
CIP	*Clinical Investigation Plan*
CIR	*Confidence to try a new intervention ruler*
COPD	*Chronic Obstructive Pulmonary Disease*
CRF	*Case Report Form*
CT	*Clinical Trial*
ESS	*Epworth Sleepiness Scale*
FAS	*Fatigue Assessment Scale*
FEV1	*Forced expiratory volume in one second*
FEV1/ FVC (%)	*Ratio of forced expiratory volume in one second and forced vital capacity*
FVC	*Forced vital capacity*
EQ-5D-5L	*EuroQoL Five dimension quality of life scale*
GCP	*Good Clinical Practise*

GP	*General Practitioner*
IMT	*Inspiratory Muscle Training*
IEC	*Independent Ethics Committee*
IRB	*Independent Review Board*
MHRA	*Medicinal Health Research Authority*
MRC	*Medical Research Council Dyspnoea Scale*
NHS	*National Health Service*
OT	*Oxygen Therapy*
PHQ-4	*Patient Health Questionnaire-4*
PSQI	*Pittsburgh Sleep Quality Index*
PI	*Principal Investigator*
PIS	*Participant Information Sheet*
PV	*PhotoVoice*
PR	*Pulmonary Rehabilitation*
R&I	*Research & Innovation*
REC	*Research Ethics Committee*
RIR	*Readiness to try a new intervention ruler*
QoL	*Quality of Life*
SAE	*Serious Adverse Event*
SOE	*Singlet Oxygen Energy*
SUSAR	*Suspected Unexpected Serious Adverse Reactions*
TA	*Thematic Analysis*

ABSTRACT

COPD is a progressive respiratory disease and is currently the third leading cause of death worldwide. Primary COPD symptoms include breathlessness, cough, and sputum production; these symptoms are linked to a host of secondary physical issues, such as poor sleep quality and fatigue and psychological issues, such as anxiety and depression. These issues have a broad and negative impact on people's quality of life. This thesis aims to understand further the day-to-day effects of COPD symptomology, exploring the experiences of how COPD affects the quality of life and the insight from COPD participants regarding medication(s), in addition to the efficacy of current strategies and interventions and whether there is scope for a non-pharmacological intervention that could potentially fill this void. The overall aim is to increase the knowledge and awareness of the physiological and psychological determinants that affect the quality of life of COPD patients. A variety of different types of data and data collection methods, which includes using Qualtrics online survey, online Microsoft Team interviews, PhotoVoice and receiving photographs using an application called Signal and planning to conduct a double-blinded NHS randomised controlled trial (RCT) in collaboration with external stakeholders.

The main findings are that COPD participants' physiological and psychological symptoms increase in severity as the respiratory condition progresses, which is consistent with previous research literature. However, despite significant differences such as for breathlessness, sleep quality and health-related quality of life, the results that were not expected and were the opposite of the proposed hypotheses were the non-significant results such as for self-compassion, readiness to use a new intervention, as well as confidence to try a new intervention. The results highlight that self-compassion remained moderate across the different COPD severities (medium, high and very high), and the readiness and confidence to try a new intervention were very high across the COPD severities. Also, medication side effects and changing medications. However, despite this, COPD participants have shown readiness and confidence to try new interventions that improve the management of their condition. An abundance of different interventions and strategies that are non-pharmacological based are already being used to help manage COPD symptoms, showing additional support that participants are willing to try anything to improve their quality of life. This thesis highlights the importance of using new qualitative methodologies such as PhotoVoice and the significant insight and vulnerabilities it captures from participants, as well as using patient and public representatives across the research processes.

The thesis also presents a double-blind RCT protocol, co-designed with the patient and public representatives, to collect empirical data on the efficacy and safety of a singlet oxygen energy device (SoeMac) as an adjunct therapy to prescribed medications. This protocol has been developed extensively and is ready to be implemented. To ensure effectiveness, further research should investigate the role of self-compassion and self-conscious emotions such as guilt, self-criticism, shame-based avoidance, and embarrassment for each level of COPD severity (including low COPD severity), COPD participants from ethnic minority backgrounds and younger COPD onset. Concerted attempts driven by physiological and psychological research that underpin clinical interventions are required to ensure that the needs and wants of patients are addressed and that treatments and benefits to patients are accepted and accessible.

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Chapter 1

Introduction and Literature Review

1.0 Introduction

This chapter introduces Chronic Obstructive Pulmonary Disease (COPD), definition, prevalence, symptom profile, severity and progression symptomology, impact of COPD, types of medication, and non-medicinal approaches, in addition to the research aims and objectives.

1.1 Clinical Definition of COPD

Chronic Obstructive Pulmonary Disease (COPD) is a group of lung diseases, including chronic bronchitis and emphysema. It is a chronic respiratory disease that is preventable and treatable but not reversible (Mannino & Braman, 2007). COPD has a complex pathophysiology but limits airflow and gaseous exchange, contributing to a broad and persistent symptom profile (Rossi et al., 2017). COPD is an umbrella term used to explain progressive lung diseases, which are chronic bronchitis and emphysema (Higginson, 2010) primarily caused by airway and alveolar abnormalities, which occur over time and are the result of chronic exposure to noxious gases or particles (GOLD, 2022). Smoking is an example of a noxious gas, as tobacco smoking contains carbon monoxide (Alonso et al., 2003).

1.1.1 Clinical Manifestations of COPD

Chronic bronchitis (CB) is an obstructive ventilatory pattern (see figure 1.1), which includes an obstruction of the airways which is permanent and is less than seventy per cent FEV_1 (forced expiratory volume in 1 second) and FVC (forced vital capacity) ratio (Raherison & Girodet, 2009). CB is a variable occurrence of COPD (Kim & Criner, 2013). CB is caused by the hypersecretion and overproduction of mucus from goblet cells, which triggers the onset of airflow obstruction, which is worsened, remodelling of the epithelial and airway surface tension, which is altered, contributing to the predisposing to collapse (Kim & Criner, 2013). The clinical consequences of CB include increased rates of mortality compared to emphysema only, the number of exacerbations, lower respiratory tract infections, airflow obstruction of worse severity, specifically in smokers, and a decline in lung function, which is accelerated (Kim & Criner, 2013). At the same time, emphysema (see figure 1.1) is where the walls are destructed in the alveolar sacs/ducts, with an abnormal increase in the distal airway size past the terminal bronchiole (Snider, 1985). There are two types of emphysema, which are centrilobular and panlobular. Centrilobular emphysema is when the respiratory bronchioles are dilated or destructed. In contrast, panlobular emphysema is associated with alpha-1 antitrypsin because of the destruction or dilation of the lobules (MacNee, 2005).

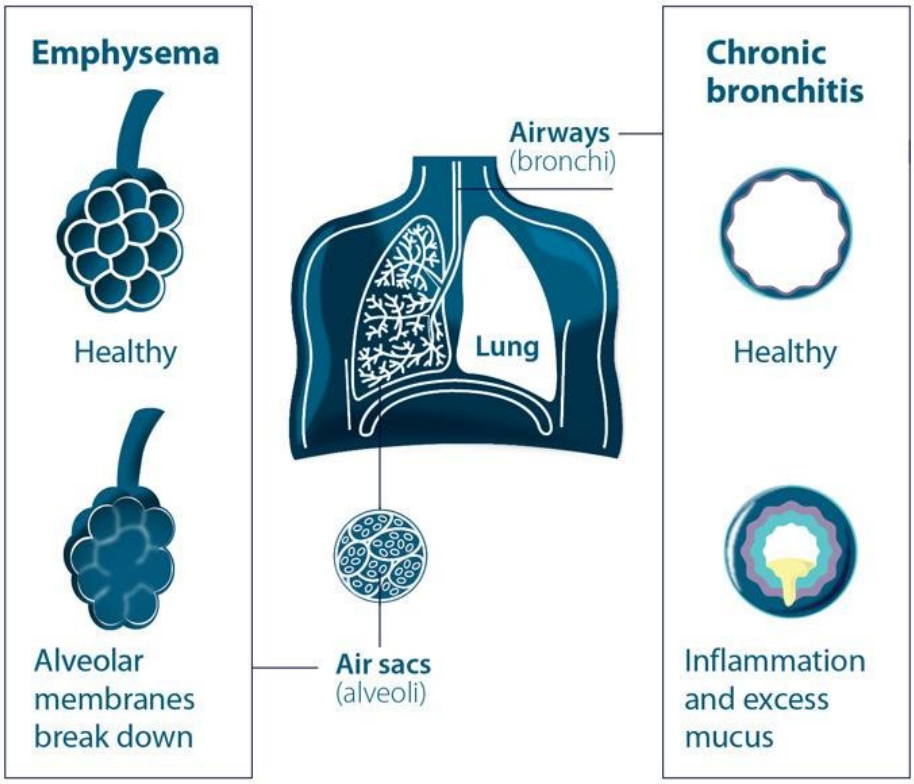


Figure 1.1. Image showing the effect of emphysema within the air sacs and the effect of chronic bronchitis within the airways (diagram from the British Lung Foundation, 2018)

However, research is now showing that many people with COPD are mainly in the middle of emphysema and chronic bronchitis rather than one or the other (Kim & Criner, 2013). Research has now shown that patients that have a severe severity of emphysema can also develop CB, which includes the pathology of small airways, that has been associated with increased mortality rates and a decrease in improvement in lung function following lung volume reduction surgery (Kim & Criner, 2013).

Therefore, COPD is a range of diverse conditions that all are similar in that they are obstructive ventilatory disorders that are not reversible (Raherison & Girodet, 2009), with poor early detection, often underdiagnosed (and if it is diagnosed, it is frequently too late), with many pharmacological treatments that are ineffective for COPD (Raherison & Girodet, 2009).

1.1.2 National Prevalence of COPD

Within the United Kingdom (UK), COPD is the second most common lung condition, affecting approximately 1.2 million people, with prevalence increasing by 27% in the last 10 years (Snell et al., 2016). Furthermore, underdiagnosis is common globally (Gershon et al., 2018), and lung function measurements such as spirometry are being under-utilised (Johnson et al., 2018).

Additionally, COPD patients are often diagnosed when COPD has already progressed, which is often because of having an exacerbation of symptoms and requiring hospitalisation (Balcells et al., 2015). As many as 13.7% (Gershon et al., 2018) to 22% Løkke et al., (2012) of high-risk patients with an airway obstruction within primary care are undiagnosed. This contributes to a significant healthcare burden and decreases the quality of life (Ho et al., 2019). Regarding the prevalence, incidence and mortality rates of COPD, Scotland has the highest, in addition to the North of the UK (Snell et al., 2016). Unfortunately, over 30,000 people present mortality rates each year who have a diagnosis of COPD, making COPD the fifth most significant cause of mortality in the UK and the third worst country in Europe (Snell et al., 2016). As well as this, COPD makes up nearly two per cent of all admissions to hospital and bed days, equating to around 140,000 hospital admissions each year, and 97% of the admissions are for emergency care (Snell et al., 2016).

1.2 Symptom profile

Regarding the primary symptoms of COPD (secondary symptoms to be discussed later in this chapter), breathlessness (dyspnoea) is the most common and characteristic symptom of COPD (GOLD, 2022). Breathlessness is concomitant with the most significant disability, worst prognosis and, over time, the most significant loss of lung function, defined by an increased respiratory effort, with an inspiratory difficulty which is incredibly worse at moderate to advanced stages of COPD, compared to early stages of the respiratory disease (Calverley & Georgopoulos, 2006). During the early stages of breathlessness, patients can modify their behaviour, such as not talking when walking or using the car instead for short journeys. However, as the severity of COPD increases, this no longer helps (Calverley & Georgopoulous, 2006). As well as this cough and mucus (sputum) production, around thirty per cent of patients have, in addition to breathlessness (GOLD, 2022). In most patients with COPD, coughing outweighs breathlessness or appears simultaneously to it (Coughing is a defence mechanism which protects the airways and is the main method for clearing mucus (Ren et al., 2022). Mucus production is a frequent complaint at the early stages of COPD (De Marco et al., 2007). However, sputum production decreases as the airways' limitation worsens (Calverley & Georgopoulos, 2006).

1.3 Causal Factors

Smoking is a significant causative factor in the development and maintenance of the progression of COPD, which makes smoking a continuous factor (March et al., 2006).

Lundbäck et al. (2003) conducted a longitudinal study regarding 1,237 participants with COPD in Sweden; for the participants who were smokers, fifty per cent ended up developing COPD, which was a much higher prevalence than what was previously predicted. On the other hand, the study showed that participants that if COPD patients gave up smoking with smoking cessation, the development of COPD fell by nearly half. However, fifty per cent of the participants were not current smokers and therefore questioned what other risk factors are involved in COPD. Zhang, Wang, Mutlu & Cai., (2021) now predict that the increase in e-cigarette usage, especially within the US, has a high prevalence among adolescents and will be a significant causal factor for e-cigarette smokers in the future to contribute to the onset of COPD in early life (i.e. before 40), as e-cigarette usage is already creating severe adverse effects (Virgili et al., 2022). Therefore, cigarettes and e-cigarettes need to be included in clinical assessments, as well as research.

Yang, Jenkins & Salvi (2022) have stated that over the last ten years, more research and focus have been on patients who develop COPD and have never smoked previously. Other risk factors include air pollution, environmental exposures, including occupational exposures such as dust and fumes not only in developed countries such as the UK but also in developing countries (Blanc et al., 2009), as well as outdoor pollutants and smoke exposure which is passive (Soriano & Rodríguez-Roisin, 2011). Coal dust in the UK, alongside smoking, is a leading cause of COPD (Marine, Gurr & Jacobsen, 1988). Regarding genetics, three per cent of patients with COPD, as well as smoking, is linked to a specific gene called alpha-1-antitrypsin deficiency (AATD) (Stoller & Aboussouan, 2005). As well as this, a consistent associated factor in the development of COPD is asthma; as for those who have asthma and choose to smoke, lung function is rapidly reduced significantly compared to people who have asthma but do not smoke (Lange et al., 1998). Infectious diseases and low economic status are risk factors for the development of COPD, in addition to lung growth that is impaired during childhood (Yang, Jenkins & Salvi, 2022). However, despite the different causes of COPD, which are non-tobacco smoking-related, patients who are not smokers still have as many exacerbations despite having milder chronic respiratory symptoms, airflow limitation and fewer comorbidities (Yang, Jenkins & Salvi, 2022).

1.4 Psychological and Physical Impacts of COPD

The burden of COPD is growing alarmingly (Marshall et al., 2022). However, there is little evidence of effective treatments and interventions that have long-term effectiveness, reducing the physical and psychological impacts of COPD (Lundell et al., 2020), which collectively

negatively impacts the quality of life (Sutrisno, Rondhianto & Susanto, 2023). Therefore, further investigations and explorations are needed to understand the broader needs of COPD (Wong et al., 2014) and find out what can help manage COPD symptomology and reduce physical and psychological impacts. Depression impacts the quality of life. Unfortunately, anxiety and depression are common in patients with COPD. They are more prevalent compared to the general population, as well as other medical conditions such as cancer, diabetes, hypertension and musculoskeletal disorders (March & Guck, 2016; Maurer et al., 2008). The symptoms of anxiety include excessive fear and anxiety, as well as behavioural disturbances such as panic attacks and avoidance. The main features of anxiety disorders, such as excessive fear and anxiety, may be accompanied by behavioural disturbances related to these symptoms, such as panic attacks and avoidance (DSM-5, 2013; Panagioti et al., 2014). Depression, on the other hand, is symptoms such as feelings of irritability, emptiness, and sadness, as well as significant problems with the ability to function in day-to-day life (DSM-5, 2013). Not only do anxiety and depression affect worse clinical outcomes, but they also increase mortality and cost of healthcare (Maurer et al., 2008; Pumar et al., 2014; Dalal et al., 2011). Anxiety and depression are often undertreated and overlooked by patients who have a COPD diagnosis (Kunik et al., 2005). Willgoss & Yohannes, (2013) performed a systematic literature review regarding anxiety and the specific anxiety disorders that COPD patients experience. Four hundred and ten studies were identified, with ten studies that met the specific criteria for review. The sample sizes ranged from twenty to two hundred and four participants, primarily male. For participants whereby the patient was recruited within a hospital setting, up to fifty-five per cent of participants experienced anxiety, compared to up to forty-six per cent of participants in the community. Regarding the specific anxiety disorders, generalised anxiety disorders ranged from six to three per cent, panic disorders (with and without agoraphobia) ranged from zero to forty-one per cent, specific phobias ranged from ten to twenty-seven per cent, and social phobias ranged from five to eleven per cent. As well as this, females were significantly more likely to have anxiety, especially social phobia and specific phobia linked to COPD. Linked to this, Zöckler et al. (2012) conducted a study to analyse the association between COPD-specific anxiety and COPD-specific depression. Ninety-six participants were recruited for the study, and a MANOVA was conducted. Findings showed that patients with COPD-specific depression experienced higher levels of COPD-specific anxiety compared to the patients without depressive symptoms. As well as this, patients with depression showed a fear of social isolation and breathlessness getting more severe as the fear of COPD progressed. Schneider et al., (2010) conducted one of the most extensive studies regarding the risk of developing depression in

association with a previous diagnosis of COPD. The researchers identified and assessed COPD patients using the UK-based General Practice Research database and conducted a nested case-control analysis. Thirty-five thousand seven hundred and twenty-two patients with COPD and thirty-five thousand and seven hundred and twenty-two patients without COPD were compared regarding the diagnosis of depression, and the prevalence of depression was higher in the population with COPD, especially patients with a severe COPD diagnosis. The study highlights that patients with COPD are at high risk of depression from the early stages of the progressive respiratory disease. Understanding COPD and depression is a factor that can prevent emergency department visits and hospitalisations (Albrecht et al., 2017). Albrecht et al., (2017) investigated adherence to COPD medications and antidepressants to examine whether this reduces healthcare utilisation for patients that have multi-morbidities such as depression. The study was a retrospective cohort study, including sixteen thousand and seventy-five participants who met the inclusion criteria—twenty-one per cent of participants achieved adherence to taking the COPD maintenance medication and the ant-depressant medication for depression, for participants that took the COPD maintenance and anti-depressant medication were associated with a decreased risk of emergency department visits and hospitalisations. Therefore, depression should be considered for patients and not just focusing on COPD symptomology. As discussed previously, COPD not only impacts quality of life but can also impact medication adherence, as well as hospital visits and hospitalisations.

1.4.1 Impact on Quality of Life

COPD impacts the quality of life for patients who have a diagnosis of COPD, which significantly decreases as the respiratory disease worsens, affecting patients with a severe severity of COPD the most (Jang et al., 2018). It must be acknowledged that despite HRQoL being severely affected in the later stages of COPD, patients with mild COPD can also experience a substantial decline in HRQoL compared to quality of life before the diagnosis (Ferrer et al., 1995). Fazekas-Pongor et al. (2021) conducted a study investigating the risk factors affecting health-related quality of life. Three hundred and twenty-one participants were recruited in Budapest, and the survey included the St George's Respiratory Questionnaire (SGRQ) and the Short Form Health Survey 36-item (SF-36). A multiple regression analysis was implemented on the three components of the SGRQ and the physical and mental component scales of the SF-36. The findings were that frequent exacerbations, many comorbidities, as well as smoking tobacco are the most significant risk factors that contribute to worse health-related quality of life. However, for health-related quality of life, the

association was stronger for patients who engaged in more regular physical activity and had higher scores for the 6-minute walking distance. Therefore, this study highlights that it is not just lung function that needs to be improved but also a therapy that can capture the complexity of COPD, that can help the participants with the impact of comorbidities, as well as smoking cessation for patients that have chosen to carry on smoking (Fazekas-Pongor et al., 2021). Regarding the role of exacerbations Stöber et al., (2021) conducted a study across 12 months, that included lung function (FEV_1) and found that having one or more severe exacerbations has a significant impact on worsening disease progression and lung function. Therefore Stöber et al., (2021) recommended that if exacerbations could be prevented and a suitable intervention could be implemented, this may slow down COPD disease progression.

In addition to risk factors such as exacerbations, comorbidities and smoking that impact health-related quality of life, other factors contribute to a worse health-related quality of life. Masror-Roudsary et al. (2021) investigated the health-related quality of life in the elderly with COPD, the demographic characteristics, and whether there is a relationship between these factors. Two hundred and seventeen participants were recruited into the study across five different hospitals in Iran. Participants completed the St George's respiratory questionnaire (SGRQ) and the Short Form 36-item questionnaire (SF-36). The data was analysed, and regarding health-related quality of life, the physical component was significantly negatively impacted by COPD compared to the mental component. However, despite this, there was an inverse relationship: the worse the physical component of health-related quality of life, the worse the mental component of health-related quality of life. As well as this, participants that were female, had a low level of education, had had COPD for a longer duration of time and had high levels of hospitalisations. Also, an interesting finding is that Masror-Roudsary et al., (2021) found that patients who were prescribed and therefore used two types of drugs, which are bronchodilators and corticosteroids at the same time reported a worse quality of life, compared to participants that did not take two types of drugs. Medication should improve the quality of life, not decrease it. This is similar to Ozcakir et al.'s (2020) findings that participants who took part in the researcher's study, who were prescribed inhaled corticosteroids, were the secondary cause of osteoporosis in the participants who were elderly. Lee et al., (2017) conducted a study investigating the health-related quality of life and the impact of comorbidities. One thousand two hundred sixty-four participants were recruited and completed the St George's Respiratory Questionnaire (SGRQ). The most significant negative factors that contributed to worse health-related quality of life included lower level of education, cough, breathlessness, comorbidities

with congestive heart failure, hyperlipidaemia and depression. Similar findings from Burgel et al., (2013) also showed that the presence of breathlessness and depression were factors that worsened health-related quality of life, depression being the most significant. Jang et al. (2018) conducted a study that enrolled eighty patients with a severe diagnosis of COPD and asked them to complete the St George's Respiratory Questionnaire (SGRQ) as well as the Short Form 36-item Health Survey (SF-36). Depression, breathlessness, the number of exacerbations and exercise capacity significantly predicted the total health-related quality of life score on the SGRQ. Depression was the most significant determinant of not just COPD-specific but also the general health-related quality of life for patients with COPD. Therefore, the findings highlight the role of depression in health-related quality of life and the impact on treatment and intervention that can decrease depression and, therefore, increase quality of life.

1.4.2 Self-Compassion

Self-compassion is when you can be mindful when negative events happen in life, and you can treat yourself with kindness and humanity, being mindful when considering negative aspects of oneself (Neff, 2011). Patients with COPD have a lower level of self-compassion and a higher level of shame compared to those who do not have a respiratory condition (Harrison et al., 2017). Unfortunately, there is limited research regarding self-compassion and COPD (Benzo et al., 2015). If self-compassion is low, it is often because some people struggle to be kind to themselves and to be mindful when negative life events occur (Neff, 2011). Additional factors contributing to low self-compassion are self-critical oneself and low self-esteem (Neff & Knox, 2016). Therefore, self-compassion can be regarded as an additional psychological secondary symptom in this context. Self-compassion is correlated with health-related quality of life in COPD (Benzo et al., 2015). In addition, COPD has a negative impact on relatives and caregivers because of the limitation that COPD causes, requiring regular care and support (Bouza et al., 2020). Caregivers have discussed in a qualitative study conducted by Cruz, Margques & Figueiredo, (2017) that caring for patients with COPD negatively impacts their physical health, psychologically, socially and financially. An example is that it has put the carer's life on hold, to stand aside and has changed the carer's day-to-day life (Johansson et al., 2023).

1.4.3 Physical Impacts of COPD

COPD can impact activities of daily life. Important factors that contribute to the impact of activities of daily life are respiratory and peripheral muscle weakness in COPD patients, which contribute to the limitation of exercise and breathlessness (Gosselink, Troosters & Decramer,

1996; Hamilton, Killian & Jones, 1995; Gea et al., 2015). COPD patients who experience more breathlessness during exercise have decreased inspiratory muscle strength, which is independent of the severity of airflow obstruction (Killian & Jones, 1988). The impact these have on specific activities of daily life that are affected by COPD and muscle weakness fatigue, Annegarn et al. (2012) recruited 820 COPD patients. It investigated the specific activities that are problematic, using the Canadian occupational performance measure. A total of 2,999 problematic activities in daily life were analysed. The most common were walking, walking up the stairs and cycling. The study highlighted the secondary effects of COPD determinants and the issues that COPD patients are having with mobility despite many medications. Following on from this Kaptain et al., (2021) have shown new insights into the activities of daily living performance in people with COPD. Eighty-four participants took part in the study in Denmark, also investigating the impact of COPD on daily life activities. Similar to Annegarn et al., (2012) participants struggled with mobility inside and outside of the home, in addition to this, bathing, cooking, shopping, washing clothes, cleaning, and lower dressing. Kaptain et al., (2021) have highlighted the importance of exploring activities that require motor and process skills.

1.4.4 Social Impact of COPD

COPD not only impacts the person's lung functioning but also impacts the person socially, depriving COPD patients of a whole and prosperous social life compared to healthy populations (Franssen et al., 2018). COPD patients feel that the chronic lung condition restricts being able to socialise how patients did prior to COPD and also being able to fully engage in family life, which remains rather difficult (Fletcher et al., 2011). In addition, COPD patients often rely highly on family members for support from the early stages of COPD, with tasks that range from leaving home to doing day-to-day activities such as cooking and personal hygiene. As COPD progresses to later stages, family members often become full-time carers with little training and support from healthcare providers (Jarah et al., 2018). Moreover, Franssen et al., (2018), also found that COPD patients are less likely to have a partner and if patients do have a partner, the support that the partner provides is seen by the patient as less than satisfied and are often feeling not fully supported therefore to manage and live with COPD.

1.4.5 Summary of the physical and psychological impacts of COPD

COPD has many different determinants, such as symptoms, the progression of lung disease and how this impacts the patient's everyday life both psychologically and physiologically. Because

of the complexity of COPD, this PhD thesis sets out to further investigate the wide range of symptomology and quality of life impacts, for example. On the other hand, it is also essential to explore the interventions that are currently available for patients, as COPD is a chronic medical condition. It is, therefore, paramount to test a new device, which is the second part of this PhD. If medication and non-medicinal were highly effective in symptom management, patients would not be struggling daily from a biopsychosocial perspective.

1.5 Approaches to managing COPD

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2022 states that the management of COPD must first identify and reduce the exposure to risk factors, such as tobacco smoke, pollution and occupational exposures. To help to reduce symptoms, reduce the severity and risk of exacerbations and to help to improve the quality of health in those with COPD, in addition to tolerance to exercise, is to manage this through pharmacological prescription medications such as inhalers and steroids (GOLD, 2022). Moreover, included in the management of COPD also non-pharmacological treatments, which GOLD advises as smoking cessation, pulmonary rehabilitation, promoting physical activity through education, nutritional support, oxygen therapy, ventilatory support, as well as interventional bronchoscopy and surgery, therefore, should be offered based on the stages and severity of COPD and the progression of the respiratory disease (GOLD, 2022). Ideally, COPD should be prevented (O'Donnell et al., 2008). Prevention is the preferred option. In 2007, China showed for the first time that biomass fuel contributes to the pathogenesis of COPD, which was investigated further, as researchers in Guangzhou, China, found a 12% prevalence of COPD diagnosis since biomass fuel was introduced. In contrast, the prevalence was around 7% (Liu et al., 2007). As a form of preventative strategies, Zhou et al., (2010) created an intervention that integrated different types of strategies that included systematic health education and one-to-one interventions, including treatment and rehabilitation within the community. Of those that took part, many were advised to relocate where risk factors such as sulphur dioxide and dust deposition were significantly lower compared to where participants lived previously, as well as areas with lower concentrations of exhaust fumes. After a 9-year follow-up, participants' lung deterioration had reduced compared to where participants had lived previously in the study, where the risk factors and pollution concentrations were higher. Zhou et al., (2010), therefore have shown that if risk factors can be reduced, community members can be educated about COPD and prevent it. Ideally, those diagnosed could access an intervention as early as possible (Zhou et al., 2020). This highlights that prevention can be effective and is the best

long-term solution nationally and globally in low and middle-income countries. Prevention aims to prevent the onset and diagnosis of COPD. Fortunately, for those diagnosed, several types of management opportunities (in addition to medication) aim to reduce the severity of symptoms, exacerbation and disease progression.

1.5.1 Medical Interventions

Medical interventions for COPD include pharmacological therapy (GOLD, 2022). Pharmacological therapy aims to reduce symptomology, the number of exacerbations, and the severity and help improve exercise and overall health status (GOLD, 2022). In addition, ideally, pharmacological therapy would help to slow and decrease the rate of FEV_1 decline, however, this still has not been shown in individual clinical trials (Aggarwal, Gupta & Jindal, 2006; Pothirat et al., 2015; Llewellin et al., 2002; Jackson & Hubbard, 2003). A study compared patients who have been prescribed inhaled corticosteroids (ICS), especially Triple Therapy (TT), to patients that had withdrawn from ICS TT (Whittaker et al., 2022), measuring both group's forced expiratory volume in 1 second (FEV1). The results from 60 645 COPD patients, patients that withdrew from ICS had a mean rate of FEV1 decline, which was -32.6ml/year and the range (-33.6 to -31.5), compared to -36.4ml/year and the range (-39.4 to -33.4) for patients that remained on TT. Therefore Whittaker et al., (2022) have shown that patients had a similar lung function decline regardless of if the patient withdrew from ICS compared to patients still prescribed and using TT.

1.5.1.1 Types of medication

Bronchodilators are medications that increase FEV1 and are commonly prescribed to prevent or reduce COPD symptomology (Beeh & Beier, 2010). Different types of bronchodilators include beta2-agonists, anticholinergics, combination short-acting beta2 agonist plus anticholinergic in one device, combination long-acting beta2 agonist plus anticholinergic in one device, methylxanthines, combination of long-acting beta2 agonist plus corticosteroid in one device, triple combination in one device, phosphodiesterase-4 inhibitors and mucolytic agents. Within beta2-agonists include short-acting (SABA) such as Salbutamol and terbutaline and long-acting (LABA). Anticholinergics include short-acting (SAMA) and long-acting (LAMA) such as Tiotropium. Combination short-acting beta2 agonist plus anticholinergic in one device (SABA/SAMA), for example, Salbutamol and Ipratropium. Phosphodiesterase-4 inhibitors, which is roflumilast. Mucolytic agents include Carbocysteine (Poole, Sathananthan, Fortescue, 2019).

1.5.1.2 Side Effects of Medication

Side effects of beta2 agonists can include cardiac rhythm disturbances (Hanrahan et al., 2008), and anticholinergic drugs the main side effects can be dryness of mouth, blurred vision, sore throat, constipation and nausea (Oga et al., 2000), methylxanthines can cause headaches, insomnia, nausea, heartburn and can have significant interactions with other medications such as fluvoxamine (GOLD, 2022).

1.5.1.3 Medication Adherence

Many patients with COPD have problems with taking medication, leading to poor medication adherence, which affects clinical outcomes, high healthcare and societal costs, as well as quality of life (Jansem et al., 2021). Regarding non-adherence to medication for patients with COPD, Bhattarai et al. (2020) conducted a systematic review of 38 studies. Behaviour regarding medication-taking was influenced by participants' beliefs about medication, experiences and satisfaction with medication effectiveness and medication side effects, and the relationship with the participant's health provider. In addition to these barriers to adherence, the presence of depression also significantly impacts medication adherence. Similarly, Agh, Inotai, Meszaros, (2011) conducted an observational, cross-sectional study, using the Morisky Medication Adherence Scale, including gender smoking status, COPD severity, lung function and health-related quality of life using the EuroQol 5-dimension questionnaire. 170 participants were recruited into the study, and just over half of the participants were optimally adherent to taking medication. Adherence to the medication was significantly associated with age, smoking status, the number of drugs the participant has currently prescribed, the number of daily doses of each type of medication, as well as quality of life. Similarly, regarding quality of life, Ágh et al., (2015) conducted a systematic literature review, in which 7 studies were included in the final review. The review showed a dual relationship between medication adherence and quality of life. This is in the sense that when participants questioned the effectiveness of the medication and also the side effects, affected adherence, as well as high quality of life, questioning if medication is still required but on the other hand, poor quality of life, can motivate to take medication (Ágh et al., 2015).

Poor medication adherence not only contributes to the likelihood of an exacerbation that requires hospitalisations, which means being absent from work and, therefore, a loss of income (van Boven et al., 2019). The cost of non-adherence to medication in the UK to The National

Health Service (NHS) costs £930 million, which is not specific to COPD but across different medical conditions, which is a substantial cost to the NHS.

1.5.1.4 Poor inhaler technique

In addition to poor medication adherence, poor inhaler technique is also a factor in managing COPD and clinical outcomes (Pothirat et al., 2015), exacerbations and health-economic burden (Usmani et al., 2018). Different inhalers have different specific instructions on how the patient should use them to ensure proper use so the inhaler medication can reach the patient's airways (Laube et al., 2011) and can be overwhelming for patients, especially when using multiple inhalers from different categories (Braido et al., 2016). Therefore, for the inhalers to be effective in assisting patients in managing COPD symptomology, the patient needs to use the correct technique when inhaling the medication (Sulku et al., 2019). Unfortunately, only 25% of patients receive specific training in using the inhaler(s) prescribed by the clinician (Lavorini et al., 2008). Molimard et al., (2017) found that out of 2, 935 patients, 50% mishandled the inhalers, and 6.9% attended hospital because of exacerbations linked to a critical error in inhaler use, which, therefore, could have been prevented if the patients had been taught and shown how to use the inhaler correctly, as part of the management of COPD. Harb et al., (2021) conducted a study investigating the determinants of incorrect inhaler technique. Harb et al., (2021) found that out of 180 patients, incorrect inhaler technique was prevalent for participants who lacked experience, specific inhaler types over other types, older age and a lower Global Initiative for Chronic Obstructive Lung Disease (GOLD) stage (i.e. lower COPD severity). The inhaler technique has not improved over 40 years and has therefore not improved (Sanchis et al., 2016).

1.6 Non-Medicinal Approaches

Whilst medicinal approaches are effective in treating and managing COPD, they rely on face-to-face contact with care providers and regular reviews to ensure they maintain their effectiveness and cause no side effects that impact patient wellbeing (Barrett & Barrett, 2021). Accordingly, there is a drive by the NHS to empower patient self-management and increase the use of adjunct technologies/therapies that can alleviate service demand and increase patient benefit (National Health Service, 2014). The use of adjunct non-medical approaches to help patients, such as pulmonary rehabilitation, is commonplace and demonstrates a level of effectiveness in increasing cardiorespiratory fitness and reducing symptom prevalence (McCarthy et al., 2015). As highlighted within this introduction, despite a variety of medication

types and adjunct therapies, patients still present with a significant symptom profile that is cyclical and prone to exacerbation (Shaw et al., 2014). Increased disease progression includes increased symptom severity and prevalence and includes breathlessness (Jolley et al., 2014), lack of energy (Eckerbald et al., 2014), reduction in physical activities (Vorrink et al., 2011), increase in sedentary behaviour (Lewthwaite et al., 2017), reduced functional status (Mussa et al., 2018), as well as increased prevalence in mental health conditions such as depression (Schneider et al., 2019) and anxiety (Maurer et al., 2008). Issues with medication adherence are commonly reported in the literature, and factors include a low level of higher education, unemployment, and low financial status, as well as a lower socioeconomic status (Gast & Mathes, 2019). In addition to medication adherence, inhaler technique is often very poor (Lavorini et al., 2008), remembering to take the medication (Prajapati & Shrestha, 2016), having to cope and manage the side effects of medications, as well as the interactions of the collective medication (Meek et al., 2019) such as headaches (Izquierdo & Aparicio, 2010), nausea (Calverley et al., 2007), effecting sleep quality (Shackell et al., 2007) as a result. As previously discussed in Chapter 1, not using inhalers correctly collectively impacts the effectiveness of medication and clinical effectiveness (Usmani et al., 2018). A reduction in the clinical efficacy of the medication reduces the quality of life. Therefore, it is imperative to explore the currently available non-medical interventions that could support and assist in improving COPD patients' daily quality of life. Utilising a desire from patients to explore alternative approaches to manage their symptoms and condition, there is a need to provide a critical review of the approaches that might address the patient's need and need to alleviate a historic burden on healthcare services. For a summary of the advantages and disadvantages of each non-medical intervention, please see Table 1.1.

1.6.1 Cognitive Behavioural Therapy (CBT)

An example is psychotherapy, specifically Cognitive Behavioural Therapy (CBT) (Beck, 1995). Cognitive behavioural therapy is based on the notion that mental health is maintained by cognition, emotions and behaviours, perceptions of events, and how an individual construes a situation (Beck, 1964). As an example, it is often considered that individuals with depression, are often extremely negative in the interpretations of events (Beck, 1995). Within CBT, the clinician and client work on core beliefs, dysfunctional assumptions, and negative automatic thoughts, the main three levels of cognition (Beck, 1995). Challenging thoughts that are dysfunctional and then finding the supporting and against evidence of that specific thought, figuring out if the thought is dysfunctional using thought record sheets is jointly worked on

with the client (Hackman, 1997), as well as behavioural activation (scheduling day-to-day activities, attempting to increase physical activity, pleasurable activities) are common (Ekers, Dawson & Bailey, 2013).

CBT is regarded as the preferred psychological therapy within the NHS (Bolsover, 2007). According to a recent systematic literature review, specifically for COPD, CBT is effective for depression and quality of life but not for anxiety (Liang et al., 2021). On the other hand, CBT is effective in a randomised controlled trial involving 279 participants, reducing anxiety after 3 months, compared to leaflets and treatment as usual (Heslop-Marshall et al., 2018). However, the findings cannot be generalised to the UK, as the sample was small. Hynninen et al., (2010) conducted an RCT and found CBT was effective for patients that had a high clinical level of depression and anxiety. However, there was no significant difference between the treatment group and placebo regarding sleep and health status (Hynninen et al., 2010). It is not specific to the COPD clinical population only, but 53% of patients who undertake cognitive behavioural therapy relapse and who have depression (Ali et al., 2017). This means that after having allocated sessions of CBT, just over half that attend those sessions will return to the NHS to receive more CBT, questioning the overall long-term effectiveness of the psychotherapy. In addition, adherence to attending CBT is also poor, with patients dropping out and not returning, therefore not completing the mandatory number of sessions with the psychological professional (Fernandez et al., 2015). Factors that contribute to dropping out of CBT sessions are low self-esteem prior to treatment and the relationship with the psychological professional (Davis, Hooke & Page, 2006). Also, difficulties with CBT itself, negative experiences of the therapist finding the CBT unhelpful and not addressing core underlying issues and feeling worse as a result (Omylinska-Thurston et al., 2019). Specific to COPD patients, Askey-Jones & Hailes, (2021) conducted a qualitative study exploring the benefits of psychoeducation for depression and anxiety. Participants expressed that primary care practitioners and GPs did not take the patient's lung disease and mental health issues seriously and felt that patients were ‘not listened to or heard by GPs when feeling low in mood and alone’. One participant stated that it felt like the GP was saying, ‘Give up smoking and pull yourself together’, ‘blaming you for the problem’ (Askey-Jones & Hailes, 2021). Participants also expressed feeling high levels of shame, embarrassment and shame in self-referring to seek psychological support (Askey-Jones & Hailes, 2021). As well as this long waiting lists, once referred for an appointment and once the sessions started, some looked young, inexperienced and unconfident in the delivery within the sessions (Askey-Jones & Hailes, 2021). Moreover, anxiety and depression are often

undertreated and overlooked in patients who have a COPD diagnosis (Griffith et al., 2021). Therefore, it is imperative to explore further beyond just depression/anxiety, not focusing just on the clinical presentation of symptoms but a holistic approach, formulating all aspects of a patient's life, as COPD has many layers and complexities to it, especially as the condition progresses into later stages (i.e. severity increases). It is essential to understand the full scope of COPD, including internal and external factors, to look at ways to address the daily problems that COPD faces.

Specific to COPD patients, Askey-Jones & Hailes, (2021) conducted a qualitative study exploring the benefits of psychoeducation for depression and anxiety. Patients expressed that primary care practitioners and GPs did not take their lung disease and mental health issues seriously and felt that patients were 'not listened to or heard by GPs when feeling low in mood and alone.' One patient stated that it felt like the GP was saying, 'Give up smoking and pull yourself together,' 'blaming you for the problem' (Askey-Jones & Hailes, 2021). Patients also expressed feeling high levels of shame, embarrassment and shame in self-referring to seek psychological support (Askey-Jones & Hailes, 2021). Additionally, long waiting lists for an appointment and, as with other areas, patients raised questions about session leaders as some 'looked young', were 'inexperienced' and 'lacked' confidence in the delivery within the sessions (Askey-Jones & Hailes, 2021). Whilst CBT may show effectiveness for depression and anxiety in the general population, as well as specifically those with a COPD diagnosis, accessing CBT, waiting lists, poor retention of patients, and relapse are significant barriers for the patient and prolonged psychological distress, which can be managed. Nearly half of patients who access CBT will also relapse, requiring additional support and therefore questioning the long-term and sustainable clinical effectiveness of CBT, as well as whether the financial investment of the NHS is effective or wasted.

Wiles et al., (2016) conducted an RCT to measure the long-term effectiveness and cost-effectiveness of CBT compared to pharmacotherapy for treatment-resistant depression within primary care. The RCT was conducted across 73 primary care practices across the UK for patients with high depression severity who were allocated to usual care with antidepressants or into the CBT group. Patients were asked to complete the Beck Depression Inventory-II questionnaire forty months after the CBT had ended. 136 patients completed the questionnaire within the intervention group and 112 patients within the treatment group. A cost analysis was based on the health and social costs with quality-adjusted life years (QALYs). Changes were observed, with depression scores being distinguishably lower than the treatment-as-usual

group. Furthermore, the average cost of the CBT implemented within the trial was £343 per person, including an incremental cost-effectiveness ratio of £574 per QALY gain. Therefore, the study shows that CBT is effective clinically and cost-effective in the long term, specifically for patients who have not responded well to pharmacotherapy.

1.6.2 Pulmonary Rehabilitation

Pulmonary rehabilitation is a non-pharmacological intervention specifically designed for patients with a chronic respiratory impairment such as COPD, which is multidisciplinary (Reardon et al., 2005). Pulmonary rehabilitation aims to provide an individualised programme to improve and optimise patients' physical and social performance and independence (ATS, 1999). The programmes include exercise training, education regarding COPD, and psychological behavioural interventions (Hill, 2006). Typically, programmes are three sessions a week and a minimum of 6 weeks in total duration (Hill, 2006).

Pulmonary Rehabilitation has been shown to improve breathlessness and fatigue, increase exercise capacity and tolerance, and improve health-related quality of life (McCarthy et al., 2015). Hogg et al. (2012) conducted a prospective observational study regarding pulmonary rehabilitation effectiveness for patients with COPD, explicitly measuring and investigating a pulmonary rehabilitation service across two hospitals and five community buildings. Eight hundred and twelve patients attended the pulmonary rehabilitation, with four hundred and forty-one patients fully completing all sessions across the eight weeks. Significant improvements were found on the shuttle walk test (ISWT), chronic respiratory questionnaire, self-reported dyspnoea scale, and hospital anxiety and depression scale (HADS). This study demonstrates that pulmonary rehabilitation is effective in real-world practice, not just clinical research trials. Furthermore, Souto-Miranda et al., (2022) conducted a systematic literature review to measure which specific measures are being used in pulmonary rehabilitation to measure effectiveness. A total of 267 studies included 43, 153 patients in the final analysis. Despite pulmonary rehabilitation, including education, training, and psychosocial and behavioural interventions, exercise capacity was the most common outcome measured (Souto-Miranda et al., 2022). The least reported outcomes were comorbidities, adverse events and COPD knowledge. Souto-Miranda et al., (2022) concluded that pulmonary rehabilitation should measure similar areas. They should assess each outcome being implemented for patients, for example, psychological, behavioural and COPD knowledge, to test the full spectrum of what aspects of pulmonary rehabilitation are effective in and not just exercise capacity, to evaluate the purpose of the eight-week programme fairly.

Pulmonary rehabilitation is also considered cost-effective compared to pharmacological treatments (Rochester et al., 2015). Pulmonary rehabilitation has, therefore, offered a welcomed adjunct to medicinal approaches to improve COPD outcomes and help manage COPD symptomology. Even if patients are offered pulmonary rehabilitation, some people with COPD do not attend pulmonary rehabilitation sessions that have been offered or start pulmonary rehabilitation but do not return to complete the pulmonary rehabilitation programme. A qualitative study included 19 patients and explored the barriers to pulmonary rehabilitation (Sami et al., 2021). The main themes from the final analysis were a sense of a lack of patient-focused holistic care, poor coordination within the multidisciplinary team during the pulmonary rehabilitation sessions, questioning the training and expertise of staff running the group and concern raised over a lack of support after the programme had ended (Sami et al., 2021). In addition, a study by Hayton et al., (2013) concluded that predictors of non-attendance to pulmonary rehabilitation sessions are current smoking status, social support, as well as the severity of COPD disease markers. A lack of knowledge of what pulmonary rehabilitation is and how to access it is another barrier to accessing pulmonary rehabilitation (Milner et al., 2018); being able and willing to travel to the location where the pulmonary rehabilitation sessions are being conducted can be a contributing factor (Oates et al., 2019), as well as a lack of motivation for COPD patients that have severe COPD and continue to smoke (Sahin & Naz, 2018).

Pulmonary rehabilitation requires commitment, regardless of the mode of delivery, and much of the data so far is sparse, subjective and requires greater attention (Lahham & Holland, 2021). Alongside improving exercise tolerance, there is limited data on other important outcomes, such as anxiety and depression, and the mental well-being of chronic conditions is often overlooked (Souto-Miranda et al., 2022). Despite the GOLD report (2022) stating that pulmonary rehabilitation is suitable for most COPD patients, some NHS trusts have a strict criterion that states someone with COPD needs 3 or more on the MRC scale to be able to access pulmonary rehabilitation (NHS England & NHS Improvement, 2020). This suggests that patients are likely to have a moderate to severe severity of COPD and to have an MRC score of 3 or more. In addition, in some NHS trusts, priority is granted to patients with a forced expiratory volume in the first-second value (FEV_1) less than 50% (NHS England & NHS Improvement, 2020). This is because of challenges with the availability of the required clinical resources and a lack of financial support to meet demand. Current programming requires patients to attend three weekly sessions over six weeks, requiring travelling to NHS

establishments to attend, despite COPD across different severities, including the common issues, which are breathlessness, mobility issues and a lack of energy. Attending three sessions requires motivation and commitment, with the added pressure of costs to the patient, such as petrol and public transport (Hayton et al., 2017). Mathar et al., (2017) conducted a qualitative study involving semi-structured interviews exploring the factors as to why patients declined to attend pulmonary rehabilitation, with nineteen patients who provided consent to take part in the study in Denmark, all with a diagnosis of COPD. Mathar et al., (2017) analysed the interviews with inductive content analysis. The main factor that the majority of patients discussed was that pulmonary rehabilitation was very time-consuming, which contributed to declining the opportunity to take part in pulmonary rehabilitation, in addition to the conflict of existing daily activities in the patient's day-to-day life, i.e., a lack of flexibility, as well as work commitments. On the other hand, online pulmonary rehabilitation can be administered instead of on-site/in-person pulmonary rehabilitation, which patients can do from home using video calling. Lewis et al., (2021) conducted online pulmonary rehabilitation with fourteen patients and measured sit-to-stand, anxiety, health, breathlessness, fatigue, emotion, and mastery. Comparing the mean scores pre-and post-test, the six-week online pulmonary rehabilitation, which was two times a week, was improved across all measures, showing the effectiveness of online pulmonary rehabilitation from the patients' own homes. However, issues included access and competent use of the IT equipment and being motivated to attend pulmonary rehabilitation online. On the other hand, with the support of the research team, the IT issues were overcome, but at the cost of staff resources, something that needs to be considered for future online pulmonary rehabilitation, that it is not necessarily cost-saving being conducted online compared to in person. Lahham et al., (2018) conducted a home-based pulmonary rehabilitation trial, using a physiotherapist discussing exercise goals at the first home visit and then telephoning the patient every week over seven weeks (Lahham et al., 2018). Patients were encouraged to do different exercises for up to thirty minutes a day and complete the educational components of pulmonary rehabilitation. After the trial had ended, Lahham et al., (2018) conducted a qualitative interview with all patients to provide feedback. Unfortunately, despite patients expressing positive effects on physical fitness, breathing and mood, patients report challenges such as the lack of supervision, lack of motivation to initiate the exercise independently, and the lack of community, with some patients expressing the preference for attending in-person sessions, rather than home-based pulmonary rehabilitation. Also, home-based pulmonary rehabilitation requires a physiotherapist to attend to the patient's home, which

costs money, not just petrol or public transport, the time at the patient's home and the time travelling to and from the home.

The cost of pulmonary rehabilitation based on a six-week programme with up to twenty patients costs £12,120 (£660 per person; Chakravorty et al., 2011). However, this figure was back in 2011, and the figure is likely to be much higher now. Within the US pulmonary rehabilitation costs $884 (£732) per session and offering 32 sessions in total, equates to a total of $28, 288 (£23,447) per person (18 in the sessions on average) £1,302 (Mosher et al., 2022). Furthermore, Chakravorty et al. (2011) conducted a cost-of-illness study for patients with advanced COPD, measuring healthcare costs before pulmonary rehabilitation and post-pulmonary rehabilitation with thirty-one patients. The outcome of the cost-illness study was that pulmonary rehabilitation reduced patients' stay in the hospital (a key clinical indicator) by just over two days and observed a reduction in primary care contact. This results in a saving of £791 per patient, to an overall direct cost of £1,313. Chakravorty et al., (2011) therefore argue that pulmonary rehabilitation is a cost-effective strategy for the NHS, as the money saved can be invested in pulmonary rehabilitation and therefore makes it affordable to the NHS to offer across all COPD. Pulmonary rehabilitation, despite cost-effectiveness, is hard to access, which is a significant barrier (Rochester et al., 2015), and increasing accessibility relative to demand would need a mass investment in specialist training and facilities that is relative to the current demand. Access is limited not only because of the low number capacity of the eight-week programmes but also because of long waiting lists and difficulty in service provision in more rural areas (Vogiatzis et al., 2016).

Long-term follow-ups of patient's post-pulmonary rehabilitation highlight poor maintenance, which questions the longevity of pulmonary rehabilitation (Egan et al., 2012). For example, Egan et al., (2012) conducted a pulmonary rehabilitation programme across seven weeks, measuring exercise capacity. Exercise capacity did increase; however, pulmonary rehabilitation did not increase the volume of physical activity (e.g., average daily steps) or change the sedentary time; after 12 months, exercise capacity returned to baseline (Egan et al., 2012). In addition, Yohannes et al., (2021) conducted pulmonary rehabilitation for one hundred and sixty-five patients with COPD, over 8 weeks, within the community, including two-hour sessions, two times a week. The sessions included aerobic exercises and educational components regarding COPD. Breathlessness, quality of life, anxiety, depression and walking which was measured at baseline, eight weeks and after two years. The long-term effects of the pulmonary rehabilitation provided improvement in anxiety and quality of life after two years

of having the pulmonary rehabilitation sessions. However, breathlessness, depression, and walking duration improvements were statistically significant at eight weeks but were not sustained long-term after two years. Yohannes et al., (2021) also found that high scores of anxiety and depression symptoms, actually increased breathlessness and reduced exercise capacity, which may explain why after two years of breathlessness, depression and walking duration improvement were not sustained after eight weeks. Additional factors are the progression of COPD across the two years, the impact of comorbidities, and a reduction in maintaining the specific exercise duration each week, as stated by the researchers. Yohannes et al., (2021) recommend future randomised trials to measure the long-term effects of pulmonary rehabilitation by comparing pulmonary rehabilitation with exercise maintenance components and pulmonary rehabilitation with cognitive behavioural therapy components. From discussing the various studies of pulmonary rehabilitation's short- and long-term effectiveness, is it worth NHS investment? Unfortunately, pulmonary rehabilitation is only accessed by 3% of COPD patients globally (Lahham & Holland, 2021). Therefore, despite the cost-effectiveness of the NHS, with the money saved by reducing primary and secondary care hospitalisations and visits from COPD patients that could pay for pulmonary rehabilitation, the reality is that the programme's long-term effects and access to the PR are questionable. Therefore, the question is whether PR is worth the patient's effort, energy, and time and whether it is money well spent by the NHS. It appears that often when the PR sessions end, the benefits to COPD patients diminish (Burge et al., 2020).

1.6.3 Inspiratory Muscle training (IMT)

Inspiratory muscle training (IMT) is a type of training that aims to improve the strength and endurance of the inspiratory muscles, which has a subsequent benefit on symptom severity (breathlessness) and exercise capacity (Gosselink et al., 2011). IMT requires patients to use devices that create resistance to inspire air, which increases the demand on the breathing muscles and can be non-targeted, targeted, threshold or normocapnic hyperventilation (Geddes et al., 2008). Charususin et al., (2018) conducted a double-blind study to investigate whether IMT was effective within pulmonary rehabilitation. Charususin et al., (2018) recruited two hundred and nineteen patients into the study, measuring inspiratory muscle weakness, six-minute walking distance (6MWD) and the Borg dyspnoea scale, with two groups of patients, one group for the intervention and the second group, as the pulmonary rehabilitation session in the original format. The findings stated that there was no significant difference between each group for the 6MWD measure. However, a difference in muscle function and breathlessness

was observed in the intervention group. On the other hand, Elmorsi et al., (2016), found that inspiratory muscle exercise training also improved muscle function but different to Charususin et al., (2018) found a significant difference in the 6MWD findings. However, there was no change in breathlessness and quality of life.

Zhang et al., (2021) conducted a systematic literature review to evaluate the efficacy of IMT on breathlessness. The specific breathlessness interventions used in the search were the Borg scale and the Medical Research Council (MRC). Fourteen randomised clinical trials and eight hundred and sixty patients were included in the final analysis. The systematic literature review showed that inspiratory muscle training increases respiratory function, as IMT reduces the physiologic load and afferent discharge, contributing to the secondary benefit of IMT, which is improved breathlessness during exercise and daily life for patients with COPD. However, the systematic literature review had limitations, as the patients included in the studies had a moderate to severe severity of COPD determined by the Borg score and Medical Research Council (MRC) scale. This, therefore, excludes the efficacy of muscle training interventions on patients with mild COPD severity and, therefore, cannot be generalised to that specific severity subgroup of COPD patients. In addition, all of the patients in the trials selected by the researchers were male and similar to the mild severity of COPD regarding generalisation; this review's findings cannot be explicitly applied to female COPD patients.

On the other hand, Nikoletou et al., (2016) investigated the effectiveness of IMT at home for patients with COPD. Thirty-nine patients with moderate to severe COPD severity were recruited into the study. Patients were randomised into the intervention group or treatment as usual. Measures that were used included muscle function, incremental shuffle walk test (ISWT), respiratory muscle endurance (RME), chronic respiratory disease questionnaire (CRDQ), hospital anxiety and depression scale (HADS), as well as the short form health survey (SF-36). The study's findings showed no difference between the intervention and control groups for the walk test, muscle endurance, respiratory questionnaire, anxiety and depression scale, and health survey. As well as this there were only thirty-nine patients recruited into the study, the severity was only moderate to severe and similar to Zhang et al., (2021) cannot be generalised to mild COPD severity. Dacha et al., (2017) conducted a study investigating the effect of IMT specifically regarding respiratory muscle function and respiratory pressure swing changes and activation of the diaphragm with twenty patients diagnosed with COPD. This was measured during a breathing task before and after IMT at a constant work rate. The participants were split into two groups, one which had IMT ≥50% maximal inspiratory pressure (PImax)

(10 patients) and the second group, which was the control group that had IMT ≤10%PImax. Dynamic muscle function was measured during the final minute of the baseline breathing test and then at the end. The findings of the IMT group showed an increase in muscle function and were able to achieve deeper breathing, with higher inspiratory flows during the breathing task. However, pressure swings were not significantly different between the IMT and control groups. In addition, breathlessness and inspiratory effort were not statistically significant between both groups.

The research discussed above shows the variation in the different efficacy of using IMT for reducing breathlessness and mobility and helping COPD patients have a better quality of life. None of the studies have a considerable number of patients, and most studies have different outcome measures and, therefore, are difficult to compare. In addition, there is a lack of cost-effectiveness of using IMT within the NHS compared to medicinal products and non-medicinal such as pulmonary rehabilitation. O'Connor et al., (2019) have shown that IMT is cost-effective for patients who have declined to partake in pulmonary rehabilitation sessions, which includes IMT twice a day, five days a week with a physiotherapist visiting once a week by a physiotherapist. However, only 11 patients participated in the study, with no control group. There is likely a lack of high-quality RCT research specifically investigating IMT, as IMT is not recommended for the management of COPD by both the European Respiratory and the American Thoracic Society (O'Donnell et al., 2007; Crowe et al., 2006; Celi et al., 2004). In addition, there is a lack of research showing the long-term effects of IMT clinical groups. The current understanding is derived from the exercise sciences (Romer & McConnell, 2003); therefore, we are just focusing on short-term efficacy. The advantage of IMT is that patients can do this at home. However, similarly to medication and CBT interventions, it requires regular commitment and motivation to reap the rewards and efficacy of IMT fully.

1.6.4 Oxygen Therapy (Ambulatory Oxygen & Long-term Oxygen)

Ambulatory oxygen therapy (AOT) and long-term oxygen will be the specific oxygen therapies discussed, mainly because the NHS prescribed AOT and LTOT in the United Kingdom. Ambulatory oxygen therapy (AOT) is a supplementation of oxygen, which the patient uses during exercise and daily activities and does not have low oxygen in the blood (hypoxemic) when the patient is resting but when exercising develops hypoxemic (McDonald, 2022). On the other hand, long-term oxygen therapy is prescribed when the patient has chronic hypoxemia for a minimum of fifteen hours a day (McDonald, 2022). Therefore, oxygen therapy aims to improve breathlessness, exercise capacity and mobility (Ameer et al., 2014). Ambulatory

oxygen therapy (AOT) is the supplementation of oxygen, which the patient uses during exercise and daily activities and does not have low oxygen in the blood (hypoxemic) when the patient is resting but when exercising develops hypoxemic (McDonald, 2022). Therefore, ambulatory oxygen therapy aims to improve breathlessness, exercise capacity and mobility (Ameer et al., 2014). A systematic literature review to determine the long-term effectiveness of ambulatory oxygen therapy for patients with COPD who do not meet the specific criteria for long-term oxygen therapy. They explicitly focus on exercise capacity improvement, mortality and quality of life. Four studies and three hundred and thirty-one patients met the inclusion criteria. The findings are that ambulatory oxygen therapy is statistically significant for the ambulatory oxygen therapy group for quality of life and breathlessness. Breathlessness post-exercise was reduced within the oxygen intervention group across all four randomised control trials (RCT). However, regarding mortality, exercise capacity and steps taken were non-significant. The findings are surprising, as one of the original aims of ambulatory oxygen is to help with exercise capacity and to help patients with COPD to be more mobile. Similarly, Eaton et al., (2002) conducted a 12-week randomised control study, with one of the objectives of health-related quality of life and if ambulatory oxygen therapy helps with this. The Chronic Respiratory Questionnaire (CRQ), Hospital Anxiety and Depression Scale and short-form Health Scale (SF-36) were used. Across the CRQ, improvements were seen across all domains, as anxiety and depression had significant improvements compared to the non-intervention group of ambulatory oxygen therapy. However, fourteen patients (41% of recruited patients in the study) did not want to continue the ambulatory oxygen, with eleven of the fourteen stating that the reason was poor acceptability or tolerability. This shows that many patients declined ambulatory oxygen despite being hypoxemic during exercise.

Furthermore, regarding patients' declining ambulatory oxygen therapy post the randomised clinical trial, Arnold et al. (2011) conducted a qualitative study regarding why COPD patients are not using ambulatory oxygen therapy at home. Twenty-seven patients were recruited for the semi-structured interviews, asking about their experiences using portable ambulatory oxygen therapy systems. Patients expressed receiving no instructions on how to use AOT, were unsure of the benefits of using AOT, did not have much confidence in using AOT without worrying that the AOT cylinders may run out of oxygen, were embarrassed being seen in public having the AOT on their backs, as well as saying that AOT is heavy and creates an additional challenge to mobility which is challenging for some patients. AOT appears to have clinical effectiveness in improving exercise capacity, reducing psychological distress, and improving

the quality of life for patients prescribed AOT. However, reducing breathlessness demonstrates mixed results with factors such as non-adherence and a lack of user-friendliness, patients' perception, and the perception of others of when patients use ATOT in society.

Long-term oxygen therapy is prescribed when the patient has chronic hypoxemia for at least fifteen hours a day, mainly used at night and during the day if needed (McDonald, 2022). LTOT aims to improve survival for COPD patients with respiratory failure, reduce hospitalisations, and improve health-related quality of life (Rous, 2008). COPD Working Group, (2012) conducted an evidence-based analysis of long-term oxygen therapy effectiveness studies across thirteen years. The quality of available evidence for decreasing mortality in patients with COPD with severe hypoxemia evidence is limited. In addition, limited evidence of poor-quality research suggests that LTOT may benefit $FEV_{1.}$ As well as this, a COPD Working Group (2012) concluded that LTOT also does not increase exercise factors or short or long-term health-related quality of life. Similarly, there is limited research on LTOT and sleep quality, Bradley et al., (1990) showed that LTOT does not increase sleep quality in patients with COPD. Further research is required. Koczulla et al., (2018) also stated that the long-term use of LTOT and the clinical effectiveness on clinical outcomes is still limited. Mesquita et al., (2018) conducted a study following up with patients after extensively using LTOT for 12 months. They found that quality of life had improved compared to the patient group that did not have LTOT. However, the quality of life was still significantly low, and therefore, the effectiveness of LTOT regarding quality of life is questioned. However, LTOT was significantly different compared to the non-LTOT group regarding the reduction of COPD symptoms severity.

Similarly to ambulatory oxygen therapy, there are problems with adherence and compliance with patients with COPD not using long-term oxygen therapy that has been prescribed and advised by health professionals. LTOT adherence ranges from 45% to 70% for COPD patients using LTOT up to fifteen hours a day, impacting COPD management of symptoms and increasing poor mobility and loss of day-to-day function (Cullen, 2006). AlMutairi et al., (2018) conducted a qualitative analysis of three hundred and eleven patients using open-ended questions in a survey regarding patients' perspectives of using long-term therapy devices. From the study findings, the themes generated revealed experiences of decreased day-to-day mobility, which made patients feel lonely and isolated, and quality of life decreased because of poor experience using long-term oxygen, especially with the weight and cumbersome. As well as this, patients expressed anxiety and fear of not being able to have the required breathing support and of the portable oxygen concentrators running out of oxygen while out and about

doing errands. Therefore, the above factors contribute to non-adherence, like ambulatory oxygen therapy, fear of running out of oxygen, and being heavy and therefore not user-friendly, in addition to the machinery noise and an increased cost of electricity (Katsenos et al., 2006).

Furthermore, LTOT costs a considerable amount of money, not only logistically but also in terms of the cost of oxygen and the staff and resource costs linked to this (Ahmadi et al., 2016). Within the UK, 85,000 patients receive oxygen, which costs the NHS over £110 million. However, only 43% are being used correctly or, on the other hand, are not providing the original claim of clinical effectiveness (Duncan & Okosi, 2011), which questions the NHS cost-effectiveness of LTOT and why patients are still being prescribed LTOT. Consequently, long-term oxygens effectiveness is troublesome, and low adherence to using the equipment correctly because of numerous factors such as weight and using LTOT for 15 hours+ every day is challenging. In addition, the cost to the NHS is considerable.

To this point and summarised in Table 1.1, pulmonary rehabilitation, CBT, inspiratory muscle training, and oxygen therapy have been discussed regarding accessibility, clinical effectiveness in both short and long-term, user-friendliness for patients with COPD, and sustainability within the National Health Service. The effectiveness of each intervention is mixed with a wide variation of the specific symptoms of COPD, both primary and secondary. The interventions can help reduce or increase day-to-day functioning and quality of life. A common issue across the interventions is a lack of empirical data from double-blinded randomised clinical trials, a lack of large sample sizes and a lack of strong statistical power. Most studies that have been conducted, therefore, have small sample sizes, lack statistical power, and questionable longevity and clinical impact. COPD patients require effective long-term interventions, require minimal effort and have empirical evidence which is robust and replicable. COPD patients are clinically vulnerable, and it is vitally important to have an effective intervention to help manage COPD symptomology and increase day-to-day quality of life across the progression of the respiratory disease and functioning. Listed in the NHS long-term plan in 2019, it was a priority to explore and increase the use of technological devices to increase opportunities for patients to take control of their care and improve patient outcomes. Whilst a market review of all technologies is outside the project's scope, the role of singlet oxygen energy has been touted as a possible tool that can serve as an adjunct to existing clinical interventions. From here on, the review of available technologies will hone in and critique the available technologies.

Table 1.1. A summary of the pros and cons of the non-medical interventions critiqued until this point

Approach	Pulmonary Rehabilitation	Cognitive Behavioural Therapy	Inspiratory Muscle Training	Oxygen Therapy
Pro's	Improvements in walking and breathlessness Reduction in anxiety and depression	Reduction in anxiety and depression	Improved breathlessness during exercise	
Specific Con's	Strict Criteria need 3 or more on the MRC scale Poor attrition Support finishes on the last session.	Need to have anxiety and depression Facilitators do not understand the role of COPD. Surface level and generic, not specific to COPD	Moderate and Severe COPD Severity criteria	Fear of running out of oxygen when out and about Need to have hypoxemia. Need to charge batteries/refill oxygen tanks. Embarrassed to use it in front of others Heavy
Universal Con's				
• Requires Motivation • Requires implementing behaviour change outside of clinical practice care • Poor adherence/retention/compliance • Limited research for long-term use • Excessive Waiting lists • Mostly applies to moderate and severe COPD severity • Costs NHS money				

1.7 Gap in COPD Research Literature and Clinical Practice

With the prevalence of COPD increasing globally, it is vitally important to minimise any physiological and psychological impact of this progressive disease. Unfortunately, despite the various medicinal and non-medicinal interventions (as discussed in detail above), those with a diagnosis of COPD are still struggling to manage the various symptoms of COPD, as well as impacting day-to-day quality of life.

Even though medicinal interventions such as inhalers and medications, in theory, have 'effectiveness' in reducing breathlessness, there are still side effects, as well as human errors such as poor inhaler technique and poor adherence factors, that decrease the overall effectiveness of the prescription drugs.

Not only does COPD affect the individuals with COPD, but also financially to the NHS here in the UK and other health services globally in trying to help COPD patients manage respiratory illness. With COPD being underdiagnosed and often poorly managed, it contributes to further unneeded and preventative hospitalisations (because of exacerbations), and this will continue and increase in prevalence not only nationally but across the world.

What is lacking is to explore the narratives that underlie the day-to-day experiences of what it is like to live with a chronic respiratory condition such as COPD. As previously discussed in this chapter, there are many quantitative studies which are focused on the statistics, costs and generally the deficits and negative factors that encompass COPD to the individual from the perspective of a hospital service or medication perspective of effectiveness, which is understandable as this is about business and making a profit, as well as a way of saving money. Therefore, with the scope of this PhD, a focus apart from the non-medicinal interventions (as an SME funds this PhD), it is essential to hear the stories and vulnerable narratives of COPD participants using qualitative methodologies. This enables patients to truly express what it is like to live a day in their life, rather than a fixed answer questionnaire that takes away individual stories and often is a fear to put down how they genuinely feel as they do not want to be judged. When asked, questionnaires are often completed from the patient's perspective, without ever knowing the researcher behind the email or research poster. In contrast, with the qualitative methodologies, a face will be given to the name of the researcher, and a relationship will be built in qualitative interviews, where the patients can express their true selves. With questionnaires, patients often feel like they are just a 'number' and are completely forgotten and abandoned without knowing where their data ends up and the study findings. Hopefully,

having the freedom, time and flexibility to learn from patients is a unique opportunity to truly gauge what life is like living with COPD and giving patients the space, as a researcher we can learn from them. The patient has a sense of belonging and will hopefully value being part of the research process, with the endpoint being insightful, innovative, and positive change.

By the end of the PhD, the aim is to have further insight into the physiological and psychological determinants of COPD and the impact these have on daily life, in addition to including a device in a randomised control trial that could be used as an intervention that patients would like to use and implement in day-to-day life, that could help manage COPD symptomology, increase quality of life, reduce hospitalisations and possibly reduce COPD progression.

1.8. Thesis Aims and Objectives

1.8.1 Overall Research Question

- What do patients with COPD need and require to increase quality of life and psychological well-being?

1.8.2 Overall Objectives

- To use a mixed methods approach, using innovative research methodology such as PhotoVoice to find out novel insights into the daily lives and quality of life of patients with COPD

- To understand in greater detail the use of both pharmacological and non-pharmacological interventions and how this contributes to the severity of quality of life in the daily lives of COPD patients

- To propose new intervention(s) from the research conducted in the PhD and to design a clinical trial, with the assistance of a Patient and Public Involvement and Engagement (PPIE) group

1.9. Succinct overview of the thesis

- **Chapter 2 –** *General Methods - Specific methodology and philosophy for each study*

- **Chapter 3 –** *Identifying important determinants of a chronic obstructive pulmonary disease (COPD) symptom profile* – Quantitative study showing the significant and non-significant differences for breathlessness, sleep quality, fatigue, quality of life, self-compassion, readiness and confidence to try a new intervention

- **Chapter 4 –** *A qualitative exploration of the impact of COPD on quality of life: a photovoice methodology* – Showing the value and multi-layered insights of PhotoVoice, with three themes showing 'self-criticism, shame and emotional response to COPD, interactions and relationships with others and strategies and methods to help with wellbeing and managing impact of COPD', with breathlessness filtering across all themes

- **Chapter 5 –** *A qualitative exploration of COPD symptom profile determinants and experiences of medical and non-medical interventions* – Semi-structured interviews, showing three themes which are 'intersectionality of symptom experiences', 'medication issues' and 'self-management and patient involvement'

- **Chapter 6 –** *Critical review of existing non-pharmacological interventions to improve patient-reported outcomes in COPD* – Showcasing and discussing the rationale of non-pharmacological interventions, what singlet oxygen energy (SOE) is and the various SOE machines such as the Valkion and the SoeMac

- **Chapter 7 –** *Development of a clinical trial to determine the feasibility and safety of using the Soemac device with patients with a diagnosis of chronic obstructive pulmonary disease – a focus on implementing feedback from PPIE* – Highlighting the significance of a patient and public involvement and engagement COPD group with the ongoing modification of a clinical trial within the NHS and how this was implemented and showing the final trial design

- **Chapter 8 –** *Discussion* – Concluding the collective points from the PhD, new insights, clinical application, lessons learnt and suggestions for future research

Chapter 2

General Methods

2.0 The overall design of the PhD

As the PhD was sponsored by a small-medium enterprise (SME), the randomised controlled trial formed part of the agreement that superseded the programme of research. Further insight from the literature review and subsequent discussions with the supervisory team and key stakeholders determined that further qualitative research regarding the confidence and readiness for change was required. This would, therefore, increase the chances of success of the intervention (due to increased engagement and compliance), increase the novelty and impact of the intervention, and stimulate research post PhD. Accordingly, to increase the knowledge and understanding to inform the development of a definitive clinical trial, a mixed methods approach was used to obtain a powerful and insightful combination of learning (Almalki, 2016). In isolation, quantitative research can provide the relevant data or statistics about a key question. However, incorporating qualitative research creates space to incorporate the patient's voice and add substance and more profound understanding to the research and subsequent learning (Sale et al., 2002).

2.1 Mixed methods study design

Quantitative research was incorporated as an integral part of this research programme for various reasons. Firstly, testing hypotheses created before the research starts, which are testable and with statistical analysis, determines whether the data supports or does not support the hypotheses (Martin & Bridgmon, 2012). Moreover, quantitative research enables the researcher to collect and analyse data objectively, finding patterns and relationships between variables (Gunter, 2013) to add to the literature on COPD, which reduces bias and subjectivity (Florczak., 2022). Furthermore, quantitative research has larger sample sizes, increases statistical power, and shows true effects or relationships between variables (Fowler & Lapp, 2019). Questionnaires are easy to administer and quick for patients to answer and to analyse the data, compared to qualitative research (Roopa & Rani, 2012). In addition, quantitative research is highly replicable, which means that post PhD other researchers could use the same questionnaires and scales to yield findings which could be compared to the findings of this PhD (as well as previous literature), which therefore increases the scientific rigour and credibility of the research that is conducted in this PhD (Friedhoff et al., 2013). Also, quantitative research aims for the conclusions drawn from the findings to be generalised to broader populations, such as COPD patients. Quantitative research can also provide the evidence needed to inform current clinical practices and provision (Mays, Roberts & Popay, 2004) and technologies, in this context is, psychological therapies, physiology clinical practice and respiratory technologies

such as the SoeMac (as discussed in the thesis). However, despite the many advantages of quantitative as mentioned prior to this section, quantitative research is limited, whereby qualitative research is required to help explore the patient's 'voice' and complex human experiences, which are subjective that quantitative cannot provide in statistics (Chakraborty, 2022).

Therefore, a mixed methods study design which was selected for this programme of research, the Explanatory Sequential Design (ESD; Creswell et al., 2003) model, was favoured as it combines both quantitative and qualitative research approaches and helps to explore whether there are any relationships between specific variables in more depth or for example when there is a result from the quantitative data that was unexpected and needs to be explored further (Creswell et al., 2003). The stages of the Explanatory Sequential Design (ESD) are the quantitative phase, data analysis, qualitative phase, integration of data, and interpretation and conclusion of the findings (Ivankova, Creswell & Stick, 2006). These steps were implemented within this project and are stated in the subsequent chapters. Therefore, once completed, the ESD approach provided deeper and new insights regarding COPD determinants, quality of life and readiness/confidence for change, providing a holistic understanding of a complex research phenomenon.

2.2 Research Philosophy

2.2.1 Ontology and Epistemology

This section will discuss the research philosophy and methodological position adopted by the researcher. Epistemology, on the other hand, relates to the assumptions the researcher holds about knowledge and how this can be created, which informs how they investigate the phenomena (Coyle, 2007); what can be accepted as knowledge? Ontology refers to the assumptions the researcher makes about the nature of the world and the phenomena within it (Chamberlain, 2015). Therefore, reality cannot be known from the researcher's perspective with certainty, and that reality is, in fact, independent of what can and will be observed (Coyle, 2016); essentially, what is the nature of reality? The methodology is a framework that enables the ability to collect, analyse and interpret data linked directly to research questions and hypotheses and, therefore, draw direct conclusions (Al-Ababneh, 2020). Quantitative methodology relies on statistical data to answer research questions, often through surveys. A statistical analysis is then conducted to find patterns, correlations, or causations within the data (Fryer, Larson-Hall & Stewart, 2018). On the other hand, qualitative methodology focuses on further understanding the motivations, experiences and meaning of an individual's or group's

subjective world (Smith & Dunworth, 2003). Interviews are often used, and then transcripts are written to analyse what was expressed. When conducting research, the researcher needs to implement the methodology that best fits the values and biases in individual and group realities of the world (Creswell, 2012). Also, a significant part of the methodology is replicating and receiving results that can be used and published. However, the reality is constructed by an individual or a group when designing and conducting research, considering the outcomes both in interventions and outcomes (Labonté et al., 1999).

Considerations for each study's methodology within this PhD were actively thought of, with the aim of the collective PhD conclusion to be a mixed methods research project (Klassen et al., 2012). The mixed methods approach is deemed to be a research methodology that is considered unique compared to quantitative or qualitative methods (Creswell & Clark, 2011), as it includes assumptions from a philosophical assumption that can provide directions from the data from many different origins within a research project with qualitative and quantitative studies (Dawadi et al., 2021). In complex research phenomena (which is required for this PhD project), mixed methods provide a framework of positivism and interpretivism (Fetters, 2016), combining both quantitative and qualitative methodology. Positivism is the research paradigm of knowledge affirmed by the senses and claimed as knowledge (Bryman, 2012). Meanwhile, interpretivism contrasts with positivism epistemology in that multiple realities exist (Dawadi et al., 2021). Similarly to ontology, the mixed methods approach includes objectivist (whether it is conscious or not, one can gain knowledge) and constructionist (through our interactions, one can gain knowledge) ontology (Klakegg, 2016). This means that from an ontology and epistemological stance, the PhD project does not exclusively sit strictly positivist or constructionist epistemology, in addition to ontology being somewhere between objectivist and constructivist. Collectively, this creates the PhD project to be realist in approach to understanding what reality is and in which way it is created (Allmark & Machaczek, 2018). Furthermore, realism is based on the notion that reality comes independently of the beliefs and understandings of an individual about specific phenomena (O'Reilly & Kiyimba, 2015). Willig (2013) suggests that within a realist approach, the research process generates knowledge that captures and reflects the real world and what is happening in it, positioning the researcher as not being an individual who constructs the findings but someone who can use research skills to uncover evidence from investigating the phenomena.

2.2.2 Quantitative Chapters - Ontology and Epistemology

The survey design (chapter 2) and the clinical trial (chapter 7) (was designed but not conducted) were significantly based on the positivist research paradigm and from an objectivist approach to the study. Hypotheses were formed for the research questions initiated, which means that the study uses quantitative methods; the world is viewed in a measurable and singular conception of reality, regarded as a fact deemed scientific (Creswell & Clark, 2017). The questionnaires used were reliable and valid for measuring various physiological and psychological determinants; using an experimental research design and conducting statistical analysis created good internal validity (McDermott, 2011). Researcher bias and interpretations were reduced, as the measurements were not subjective and were objective measurements that were implemented (Smith & Noble, 2014). Consequently, the study created a solid foundation for the rest of the PhD project, including qualitative studies.

2.2.3 Qualitative Chapters – Ontology and Epistemology

The photovoice qualitative study (chapter 4) and the semi-structured interviews (chapter 5) were both qualitative research methodologies, with the study design from a constructivist philosophy. An interpretivism epistemology was implemented, as there is no single reality and can therefore be understood and interpreted in a variety of ways by both the patients and researcher, which helps to find out the real-world experience of the patient, such as the 'how' and why' to answer the research questions (Holloway, 1997). Furthermore, as previously stated regarding realism, reality does not depend on how we know it in both qualitative studies. It is because it exists independently of the belief of an individual. Clarke, Braun & Hayfield, (2015) state that there is a 'reality out there' and that individuals can provide access to their specific world and version of events, which the researcher can interpret. Therefore, a critical realist approach has been selected (Willig, 2013). Subsequently, as a critical realist researcher, I believe each patient's reality is unique and, therefore, will collectively make up many different versions of reality within the study (Maxwell, 2012). Critical realism, unlike other epistemological positions, encompasses ontology and epistemology rather than separate entities (Yucel, 2018), which means that from a critical realism perspective, the researcher can make assumptions about the world (the reality which is ontology) and how the researcher investigates this (interpreting the said reality which is epistemology; Maxwell, 2012). As a result, the researcher assumes that patients can express their subjective and constructed reality of COPD and QoL through the interviews (chapter 5) that use photographs, which will hopefully help capture the patient's realities and experiences, which is more powerful than

words alone. Photovoice methodology is innovative, adding an element to qualitative methodology of eliciting a perspective and reality of a patient's day-to-day life from an insider's perspective, gaining insight (Sutton-Brown, 2014), which may not have been actively discussed without the photos as a reference point. The follow-up interviews can be interpreted and led by the patient, with the researcher interpreting the realities of the patient and being analysed from a critical realist stance.

2.2.4 Ontology and Epistemology Summary

This research programme of study has mixed methods, including both quantitative and qualitative methodology, using an explanatory sequential design, which has helped design the subsequent studies and help build the PhD narrative. Reality has been discussed, debated, critiqued and interpreted in various ways, which matches the pragmatist research paradigm (Kaushik & Walsh, 2019). Engagement has included internal and external stakeholders and has been a significant part of the PhD integrated into the mixed methods design of the PhD, 'meaningfully engages with difference' (Greene, 2005). Using both qualitative and quantitative methodology has helped solve complex COPD and quality of life phenomena and the proposed research questions, which has helped showcase the reality of what happens and the how and why (Labonté, 1999).

2.3 Survey Methods (Chapter 3)

Briefly here but as described in Chapter 1, this study aimed to investigate the multiple factors within physiology, psychology, and readiness for change and to determine if patients with COPD are willing to try a new intervention to help manage their condition. To address this, a descriptive cohort observational study was conducted using an online survey to explore the physiological and psychological consequences of living with COPD.

2.3.1 Survey Outline

2.3.1.1 Demographics

Participants were asked several questions relating to COVID-19. Participants were required to answer 'yes' or 'no' regarding diagnosis, admission to hospital, experience of symptoms and family members/people in the household with symptoms or a diagnosis of COVID-19. In addition, participants were required to provide details relating to their sex, age, marital status, ethnic origin, occupation, occupation exposure, use of medication, engagement with nonmedical interventions and the presence of comorbidities/multi-morbidities. These options are based on previous surveys distributed by The British Lung Foundation, (2016). Participants

were also asked to indicate which part of the UK they were from to investigate whether the location of where participants lived affected or contributed to their COPD, the severity of the condition and quality of life. For example, the North of the UK is shown to have the highest prevalence of COPD (Snell et al., 2016).

2.3.2 Materials

2.3.2.1 Physiological Measures

COPD Symptomology (CAT)

The COPD Assessment Test (CAT; Jones et al., 2009) measures the impact of COPD on a person's life over time. The CAT is an 8-item scale with a total score of 40. Each question is scored from 1-5 (i.e., 1 = I never cough to 5 = I cough all the time). Higher scores indicate a more severe impact of COPD (8 questions = 1 to 5 = Scores from 0–40 (Low severity 0-10, medium 11-20, high 21-30, very high 31+). The test-retest reliability is shown to be very good to excellent (Cronbach's α=0.80–0.96) (Gupta et al., 2014), and the internal consistency of the scale is excellent: Cronbach's α=0.88 (Jones et al., 2009).

Breathlessness (MRC Dyspnoea Scale)

The Medical Research Council (MRC) Dyspnoea Scale (Bestall et al., 1999) is a measure to grade the effect of breathlessness on a person's daily activities. The scale is 1-item only, and the participant selects one statement between 1 to 5 (1 = Breathless only with strenuous exercise to 5 = Too Breathless to leave the house). The scale allows the participant to state how much their breathlessness affects their mobility. The MRC Dyspnoea scale has been used in previous COPD research and is a valid instrument to implement within this population (Bestall et al., 1999).

Fatigue (FAS)

The Fatigue Assessment Scale (FAS; Michielsen, De Vries & Van Heck, 2003) is a 10-item scale that measures symptoms of chronic fatigue. The scale includes questions that ask about physical and mental symptoms of fatigue. Each item has a 1-5 scale (1= Never to 5=Always). When calculating the total score, some questions are reversed scored. The total score ranges from 10-50. Scores 10-21 = no fatigue/normal severity, and scores 22-50 = substantial fatigue severity. The FAS has an internal consistency (Cronbach's α=0.90) (Michielsen, De Vries & Van Heck, 2003) and validation (De Vries, Michielsen & Van Heck, 2004).

Sleep Quality (PSQI)

Pittsburgh Sleep Quality Index (PSQI; Buysse et al., 1989) is a self-report measure to assess sleep quality. The measure consists of 19 individual items, with a 0-3 (0 = no difficulty to 3 = severe difficulty) interval scale, which creates 7 components (subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication and daytime dysfunction) to produce one global score (range from 0-21). The higher the score, the lower the sleep quality. The PSQI is reliable and valid in the assessment of sleep problems (Grandner et al., 2006), with strong internal consistency and reliability (Cronbach's α=0.83) (Smyth, 1999).

2.3.2.2 Psychological Measures

Quality of life (EQ-5D-5L)

The EQ-5D-5L is routinely used to assess the quality of life in respiratory research (Herdman et al., 2011). The EQ-5D-5L is a responsive and valid scale to measure the quality of life in people with COPD (Nolan et al., 2016). The EQ-5D-5L has two parts, which consist of an EQ-5D index value (see Appendix E for SPSS syntax) used to indicate quality of life on five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. The five dimensions of the EQ-5D have good internal consistency (Cronbach's α=0.85) (Tran et al., 2012). The second part is a separate visual analogue scale called 'EQ-VAS', which assesses overall health status (0 = worst health imaginable and 100 = best health imaginable); this is to help indicate overall health status as part of quality of life, which comes from the EQ-5D index score from the previous questions regarding the five dimensions of quality of life. The EQ VAS is a specific scale to show overall health status, which is important to know; for example, if a participant has an extremely low overall health status score, it is likely to impact quality of life negatively (measured from the EQ-5D index score). The EQ VAS has strong convergent validity with the EQ-5D (r = .73). The index value score from the EQ-5D decreases (worse quality of life) with the decrease of EQ VAS (i.e., lower overall health score) (Nolan et al., 2016).

For the purposes of this study, a third part of the EQ-5D-5L was added. This is similar to the EQ VAS but focuses on overall *mental* health and is known as the EQ-MH-VAS (0 = worst mental health imaginable and 100 = best mental health imaginable). Due to the multi-faceted nature of COPD (i.e., both physiological and psychological impact) and the fact that it is a long-term, chronic medical condition, it was deemed necessary to gauge participants' overall

mental health status in addition to physical health status. To deem reliability using Cronbach analysis was not possible. This was because the EQ-MH-VAS is a scale of 0-100, which is like the EQ VAS overall physical health scale. The 0-100 scales are separate from the five dimensions listed within the EQ-5D-5L (as previously discussed), totalling a specific score ranging from -.161 to 1.000 and is not a 0-100 scale. Based on previous studies (Nolan et al., 2016; Tran, Ohinmaa & Nguyen, 2012), a convergent validity test was conducted to measure the validity of this scale using the total index score from the five dimensions EQ-5D-5L index score and the score from the EQ-VAS 0-100 scale (overall physical health). Based on this, a convergent validity test was conducted on the new EQ-MH-VAS (created for the purposes of this study). This was found to have a positive moderate convergent validity with the EQ-5D overall (r =.47) and a negative strong convergent validity with the anxiety/depression dimension specifically (r = - .621) (see Appendix F for the other four dimensions, which are negative weak spearman coefficients).

Compassion (Self-Compassion Scale – Short Form – (SCS-SF)

The self-compassion-short form (SCS-SF; Raes et al., 2011) is a short version of the self-compassion scale (12 items instead of 26 items) used to measure the level of self-compassion a participant has. The scale has subscales, which include self-kindness, self-judgment, common humanity, isolation, mindfulness, and over-identification. The scale is calculated as a total mean score (some questions are reversed scored). Regarding scoring, a participant scoring 1.0-2.49 is regarded as low, 2.5-3.5 is moderate, and 3.51-5.0 is considered high (Raes et al., 2011). The short version of the self-compassion scale is a reliable alternative to the full version of the Self-Compassion Scale when measuring the total self-compassion scores, with good internal consistency (Cronbach's α=0.86) and a strong correlation with the long version of self-compassion scale r = 0.97 (Raes et al., 2011).

Readiness to try a new intervention ruler (RIR)

The readiness to change ruler was originally a scale that gauged the willingness of a participant to change and help themselves change their behaviour (Miller & Rollnick, 2002). However, for the purpose of this study, it has been adapted to a 'readiness to try a new intervention' ruler to gauge the readiness to change behaviour using a new intervention. Participants were asked to indicate on the ruler, 'If there was an intervention that could help you significantly (hypothetically) for your COPD, how willing would you be to give this a go?' on a scale between 0-10 (1 = Low, 5 = Medium and 10 = High).

Confidence to try a new intervention ruler (CIR)

The confidence for change ruler was created by Miller & Rollnick, (2002) like the readiness for change ruler as discussed above. The CIR is a scale that shows the readiness of the participant to improve their condition and indicates how significant the change is and how much confidence the participant has to implement the change. For the purpose of this study, the ruler has been adapted to gauge how confident the participant is to try the new intervention after the participant has answered the RIR (above). The question states, 'How confident would you feel to give it a go and make this change?' Again, the scale was between 0 and 10 (1 = Low, 5 = Medium, and 10 = High).

2.4 Participant Recruitment

Targeted recruitment of participants was implemented using specific COPD support groups online using social media channels, Facebook and Twitter, as well as Asthma and Lung UK monthly newsletters. All posts, tweets and articles included a direct link to an online questionnaire/survey. To be eligible for inclusion, participants were required to be over the age of 18, live in the UK, be able to understand written information in English and have a confirmed diagnosis of COPD.

2.4.1 Partial responses

One hundred and seventy-seven participants completed a 63-question online survey (147 completed responses; 30 partial responses). Using criteria set out by Bennett (2001) and Dong & Peng (2013) regarding partial responses and data imputation, it is advised that partial responses with more than 10% missing data across each questionnaire in the dataset are omitted to prevent the bias of mean estimates. For partial responses with less than 10% missing data, it is suggested that the missing values are replaced with the mean score. As a result, 22 partial responses in the dataset were omitted, and 8 partial responses were imputated to give a total number of 155 participant responses. However, upon review, one participant reported extreme scores across multiple questionnaires and was omitted from the data set (Osbourne, 2013), giving a total of 154 participants in the final dataset.

2.4.2 Analytic Strategy

The independent variable in this study was COPD severity, measured using the global score from the COPD Assessment Tool (CAT). The global score determines the overall COPD severity: medium, high, and very high. In this case, medium, high, and very high were used as

the three levels of the independent variable. Low COPD severity was not included, as no participants scored within this threshold. The dependent variables were grouped into *physiological factors*: breathlessness (MRC Dyspnoea Scale), fatigue (FAS), sleep quality (PSQI) and *psychological factors*: quality of life (EQ-5D-5L), overall health (EQ-VAS), overall mental health (EQ-MH-VAS), compassion (SCS-SF), readiness to try a new intervention (ruler) and confidence to try a new intervention (ruler). Descriptive statistics were calculated for each variable of interest. Separate ANOVAs were conducted to assess the impact of COPD severity (medium, high, or very high) on both *physiological* (CAT, MRC Dyspnoea Scale, FAS, PSQI) and *psychological* (EQ-5D-5L, EQ-VAS, EQ-MH-VAS, SCS-SF, Readiness to try a new intervention ruler, Confidence to try a new intervention ruler) outcomes. An alpha level of .05 was used for all analyses. A Bonferroni correction to account for multiple comparisons was applied (0.05 divided by 10 dependent variables = 0.005). Post-hoc testing was implemented for significant results using Games-Howell.

2.5 Reflexivity for photovoice (Chapter 4) and semi-structured interviews (Chapter 5)

From the perspective of the researcher's commitments to theory, personal experiences and understanding have been acknowledged, and this has influenced the analysis of the data for this current study (i.e., reflexivity; Coyle, 2007). This personal reflexive account shows how the researcher's own personal experiences and understandings may have influenced the analytical process (Coyle, 2007). To be honest and reflexive, the reflexive account was written in the first person. I have spent considerable time with The British Lung Foundation Breathe Easy group in Nottingham since October 2019, throughout the COVID-19 pandemic via Zoom and recently again in person. Strong relationships have been built over that period, including a deep level of respect between the members of the group and me. Most group members have a diagnosis of COPD. I have seen first-hand the deterioration that COPD has had on the members, not just physically but psychologically. Through open discussions, as well as one-to-one conversations that I held with the group, it is upsetting that COPD has such a significant impact. Since 2019, two members have passed away because of COPD and COVID-19.

Personally, I have had depression for over 15 years, treated with psychotherapy and managed with anti-depressants intermittently. I have tried not to let my own depression 'cloud' my vision to think and expect that all of COPD is negative, despite my own observations of it prior to conducting this study. I have made sure that I used open questions, actively listening to each patient, and probing if required (rather than incorrectly assuming), as every patient is an

individual. I have tried to keep my personal experiences and opinions separate from the research. Suppose the patient has expressed that they have felt depressed or experienced other psychological distress. In that case, I have used my own experience of depression to help shape the questions in a sensitive and non-judgemental manner and provided extra time, understanding and compassion when required. To prevent unconscious bias or influence, I have had regular meetings with my supervisor team, including one-to-one meetings to discuss each patient as I have gone along, and the data collected with my supervisors.

I think the patients that I had got to know well prior to the study commencing helped to build an in-depth discussion online, as the trust and bond between the patient and I had already been formed, enabling more profound and more personal and vulnerable accounts, including mental health perspective, which patients elaborated on further naturally, with the help of the photographs. However, I noticed that patients I did not have a previous bond, the discussion was more fixated on the photographs, and the discussion was not as in-depth and limited expressions of vulnerability. This is not a surprise, as trust and bond take time. Specifically for the qualitative semi-structured interviews (chapter 5), I have been prescribed anti-depressant medication and have tried non-pharmacological interventions. I have managed depression now for just over 15 years. My personal experiences of the NHS have mostly been positive. However, working in the NHS previously has been challenging both physically and psychologically. However, I have tried my utmost not to influence or affect the experiences and insight that patients from this study have informed me about. To prevent unconscious bias or influence, I have had regular meetings with my supervisor team, including one-to-one meetings to discuss each patient as I have gone along and the data collected with my supervisor, Dr Baraniak, who has acted as head supervisor for this qualitative study.

2.6 Photovoice Methods (Chapter 4)

This study utilised a qualitative design, using a photovoice methodology to explore the impact of COPD on quality of life. Ethics approval was obtained by the College of Science & Engineering Research Ethics Committee at The University of Derby (Ethics Approval Reference Number: ETH2021-0357).

2.6.1 Ontology and Epistemology

The researcher's theoretical perspective, both ontologically and epistemologically, has been considered, as it is essential within qualitative research for the method of data collection, method of analysis, and theoretical framework to be aligned so that the research that is

produced can meet the research aims of this study (Braun & Clarke, 2006; Chamberlain, 2015).

2.6.2 Participants

Patients were mainly recruited from the researcher's database of individuals with COPD, who had consented for the researcher to invite them to participate in a related study following the initial survey. Additional patients were recruited via various specific COPD support groups on Facebook, Asthma UK, and The British Lung Foundation. The main criteria for the patients are to be aged 18 or over, live in the UK, understand written information in English and have a diagnosis of COPD. The target number of patients for the sample (N=11) was based on previous Photovoice research studies, which ranged from eight (Genoe & Zimmer, 2017) to eleven patients (Korn et al., 2017). Eight patients were recruited for the study due to data saturation being reached, i.e., when no novel ideas emerged from the data being collected (Fusch & Ness, 2015).

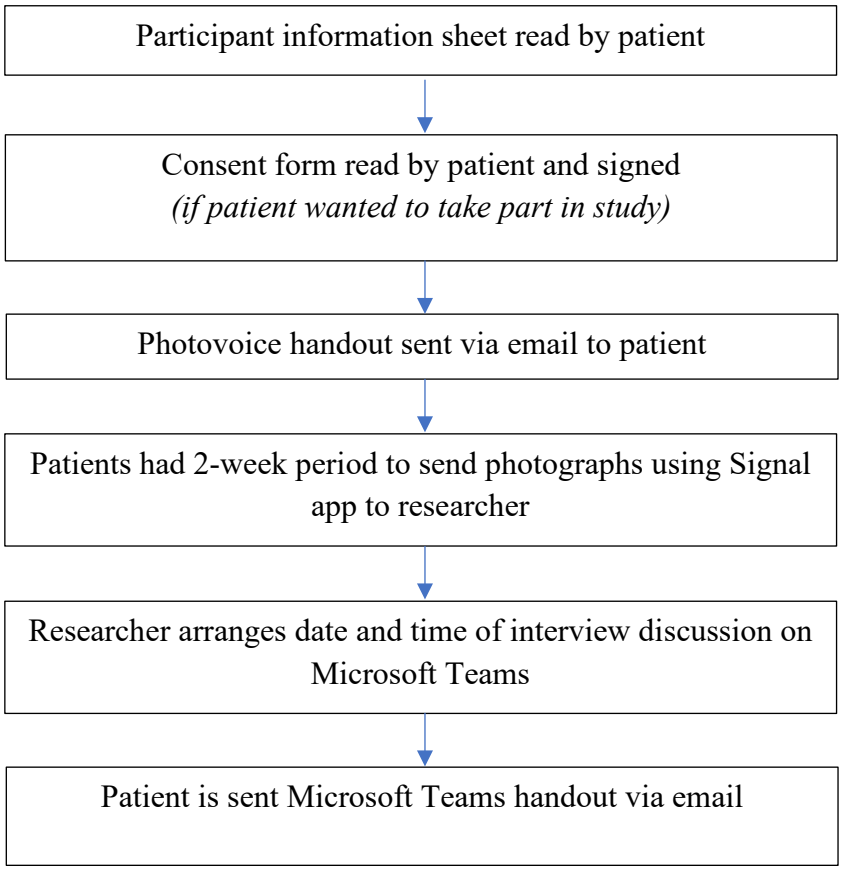
2.6.3 Materials

Patient-facing materials for this study include the patient information sheet (Appendix I) and consent form (Appendix J), which were hosted in Qualtrics and contained detailed information about the study and what would be involved. Within the demographic questions on Qualtrics patients were asked which part of the UK patients are from, sex, age, marital status, ethnic origin, current occupation, type of COPD, duration of COPD, current treatments/medications, nonmedical interventions, comorbidities, smoking status, type of smoking and smoking pack years.

To facilitate engagement with the study, patients received a photovoice handout, which included visual step-by-step instructions for how patients take photographs, how to send them to the researcher (Appendix K), and how to take part in the interviews using Microsoft Teams (see Appendix M). The visual guide regarding the photographs gave some specific details about the research topic to help patients conceptualise what they might take photos of; *"The photographs should provide a visual illustration or expression of your experience of living with COPD and how it impacts or enhances your quality of life. Quality of life refers to your overall health and well-being. Typically, someone with a higher quality of life would be in good health, feel comfortable in their day-to-day life and can take part and enjoy events that arise"* (the definition of health-related quality of life was derived from 'The National Center for Chronic Disease Prevention and Health Promotion, 2021' but was amended to be layman for the purpose

of the study). Quality of life was defined inside the guides and instructions like Topcu et al., (2021). Patients had complete control over the photographs that were sent to the researcher to see if it was linked to their COPD and its impact on quality of life. An exclusion list was included within the guide: 'Do not take photographs of an individual or a person, identifiable landmark, sensitive nature, nudity, within a private organisation without permission.'

The photographs were sent to the researcher via the Signal application (app) (and were received by a secure phone to receive the photographs), which is a secured messaging app using a smartphone that can include photographs and videos, which can be sent free of charge). The handout included visual instructions on how to download 'Signal' on Apple or Android devices, take photographs on the devices, send the photographs and the next steps. The guide included the researcher's contact information should the participant need support. Patients sent 5-10 photographs ahead of the interview. Before the interview, patients were sent a Microsoft Teams handout (Appendix L), which provided visual instructions on downloading and using Microsoft Teams. Furthermore, patients were sent a handout with all their own photographs to provide a prompt for them in the interview (Appendix M). At the end of the study, a debrief form was sent to the patient via email (Appendix N).



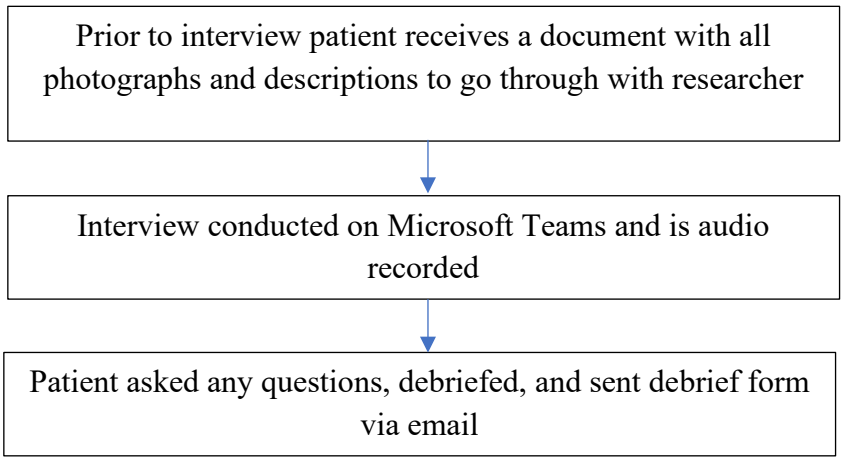


Figure 2.1. Step-by-step process of the specific materials used in the study

An email invitation was sent to patients who had consented to be contacted following the first study. An invitation was also posted to social media. Patients could express an interest in taking part in the study by clicking on the Qualtrics link, where they could access the patient information sheet. If the patient wanted to participate in the study, they completed the consent form, which was recorded through the Qualtrics survey. On receiving consent, the researcher emailed the patient a Photovoice visual instruction guide handout. Patients then had two weeks to return 5-10 photographs and descriptions via the Signal app. Once the researcher had received the photographs and descriptions, they were securely stored on the researcher's university password-protected OneDrive. Patients were contacted using either the Signal app or via email to arrange a suitable date and time to conduct the follow-up interviews, held by video call in Microsoft Teams. These were conducted using the researcher's university-secure Microsoft Teams account. Before the follow-up interview, patients were sent a document containing their photographs and descriptions in the order they had submitted them. The interviews were conducted in a quiet and confidential room. The patient and researcher used the encrypted Microsoft Teams link.

In the interview, following introductions, the patient was reminded about confidentiality, withdrawing at any time, and that the interview would be recorded for the purpose of transcription and analysis. The patient was asked to describe each photograph, its meaning, and how it represents how their COPD impacts their quality of life. Patients used their copies of the photographs, or the researcher could share their screen with the patient through Teams. Patients were free to add details regarding COPD and their quality of life; often, the photographs and discussion reminded patients of additional factors they had previously forgotten when taking the photographs as part of the study. Once all the photographs and

descriptions had been discussed openly by the patient to the researcher, the researcher asked if the patient had anything else to add. When the patient was ready to finish the discussion, the researcher thanked the patient for all the time and effort that they had contributed and forwarded a debrief sheet with final details about their rights and a copy of the researcher's contact details in case of questions or to withdraw from the study. The interviews were audio recorded using Open Broadcast Studio (OBS) software on the researchers' university-managed, password-protected laptop. Each audio recording was transcribed using Express Scribe software using a Phillips foot pedal.

2.6.4 Analytic Strategy

In this photovoice study, the photographs were used as stimuli to promote discussion rather than being used as data per se (Latz & Mulvihill, 2017). This means that the photographs and narratives were used to help patients express the phenomena and meaning of COPD and quality of life during the interviews with the researcher (i.e., patients' voices).

The data used in this study was generated from semi-structured interviews, which were unstructured discussions based on the 5-10 photographs that patients sent to the researcher in advance. Transcripts were analysed using thematic analysis, following the framework from Braun & Clarke, (2006). The themes were identified using an inductive approach, originating from the data rather than a preconceived theory or framework (Braun & Clarke, 2006). Also, the thematic analysis gave the flexibility to analyse the data from the perspective of a phenomenological approach to photovoice follow-up interviews, whereby the meanings from each patient can be identified and see what meanings patients share collectively when they experience a phenomenon and the explanation of its patterns and essence (Van Manen, 2016).

The identification of the meaning of patterns from each transcript was conducted using the specific phases that Braun and Clarke (2006) propose, which include familiarisation with the data, generating initial codes, searching for themes, reviewing themes, and defining and naming themes that followed. The themes for this study will be semantic themes. Braun & Clarke, (2006) stated that semantic themes are themes whereby the meaning of the data is taken from an explicit or surface meaning, and the research is not looking for anything beyond what the patient has expressed in the interview and therefore has been transcribed. The researcher used a critical realist epistemological position (Willig, 2013). In addition, for the consideration

and interpretation of the data, the researcher has acknowledged reflexivity and the role this plays (see reflexivity below).

The initial codes were created using NVIVO, whereby each transcript was inserted into NVIVO, and each code of relevance to the research questions was coded and grouped, summing up the basic meaning of the data (Braun & Clarke, 2006). The codes with similar meanings were initially grouped to form a theme. Several thematic maps were created (Appendix O-W) to help organise, examine, and visually see the relationship between codes, themes, and potential sub-themes. Using NVIVO, each code was manually labelled, as suggested by Braun & Clarke (2006); the main difference is that the transcripts were labelled electronically rather than labelled by hand with paper copies.

2.7 Semi-Structured Interview Study (Chapter 5)

2.7.1 Design

A semi-structured interview qualitative exploration regarding the impact and experiences of COPD and pharmacological/non-pharmacological interventions. Ethics approval was obtained by the College of Science & Engineering Research Ethics Committee at The University of Derby (Ethics Approval Reference Number: ETH2021-0357).

2.7.2 Participants

Patients were identified as eligible for recruitment from an existing database of individuals with COPD who had consented for the researcher to invite them to participate in related studies following the initial survey. Additional patients were recruited via various specific COPD support groups on Facebook, Asthma UK, and The British Lung Foundation. Seven participants recruited within the previous Photovoice study also provided consent to participate in this study (specifically Sue, Jane, Jacqueline, Aimee, Pauline, and Pat [pseudonyms only]). Therefore, a total of fifteen patients were recruited into the study. Most patients were from the East Midlands (N=5) or the Southeast (n=3) of the United Kingdom; over half were female (n=10), and the mean age was 70 years. Half of the patients were married (n=8), all were white British, and nearly all were retired (n=12). The majority had a diagnosis of emphysema (n=10), and over half had lived with COPD for over 7 years (n=10). In relation to medication use, the majority (n=12) had short-acting bronchodilators, half had long-acting bronchodilators and over half (n=9) had an inhaler steroid; most patients (n=11) had pulmonary rehabilitation. Half of the sample had two comorbidities, the most common being hypertension and asthma.

2.7.3 Materials

Patient-facing materials for this study include a participant information sheet (Appendix AG), consent form (Appendix AH), and debrief (Appendix HI). Demographic questions were hosted within Qualtrics (including regional location, sex, age, marital status, ethnic origin, current occupation, type of COPD, duration of COPD, current treatments/medications, nonmedical interventions, comorbidities, smoking status, type of smoking and smoking pack years). A Microsoft Teams handout (Appendix AJ) was sent to patients before the interview. A semi-structured interview schedule (Appendix AL) was used during the interview (five topic areas: COPD symptoms, the impact of COPD, medications, nonmedical interventions, and ideal interventions).

2.7.4 Procedure

An email invitation was sent to patients who had consented to be contacted following the first study. An invitation was also posted to social media. Patients could express an interest in taking part in the study by clicking on the Qualtrics link, where they could access the patient information sheet. If the patient wanted to participate in the study, they completed the consent form, which was recorded through the Qualtrics survey. An overview of the study process can be seen in Figure 3.1.

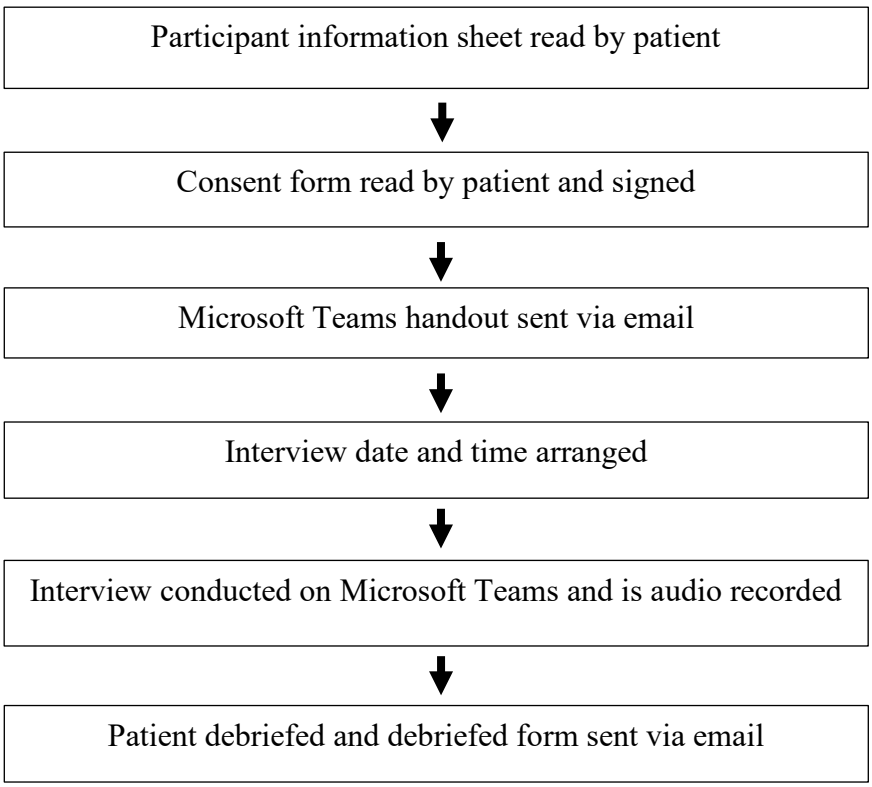


Figure 2.2. Step-by-step process of the procedure of the study

On receiving consent, the researcher emailed the patient to arrange a convenient date and time for the interview, which was conducted on the researcher's university laptop and password-secured Microsoft Teams account. The researcher sent a Microsoft instruction guide handout to support patients in accessing Teams. The interviews were conducted online in a quiet and private space, and meetings were scheduled in advance to produce an encrypted Microsoft Teams link. The interview started with introductions, and the patient was reminded about their rights throughout the research process (especially withdrawal), confidentiality and that the interview would be audio recorded to transcribe and analyse.

The interview schedule was used to direct the interview. Patients did not have to answer any questions that they did not want to, and the researcher moved on to the next question. At the end of the interview, patients had the opportunity to add anything else that they felt had been missed or not covered in sufficient detail. When the patient finished the discussion, the researcher thanked them for their time and effort, reminded them of the following steps and rights regarding withdrawal, and sent a debrief via email. The interviews were audio recorded using Open Broadcast Studio (OBS) software on the researchers' university-managed, password-protected laptop. Each audio recording was transcribed using Express Scribe software using a Phillips foot pedal.

2.7.5 Analytic Strategy

Thematic analysis was conducted for the semi-structured interviews using the framework from Braun & Clarke, (2006). The themes were identified using an inductive approach, originating from the data rather than a preconceived theory or framework (Braun & Clarke, 2006). The identification of the meaning of patterns from each transcript was conducted using the six specific phases that Braun and Clarke (2006) propose: familiarisation with your data, generating initial codes, searching for themes, reviewing themes, and defining and naming themes that followed. The themes for this study will be semantic themes; these are themes whereby the meaning of the data is taken from an explicit or surface meaning, and the research is not looking for anything beyond what the patient has expressed in the interview and, therefore, has been transcribed (Braun & Clarke, 2006). The researcher used a critical realist epistemological position (Willig, 2013). The researcher has acknowledged his position in the research through engagement with reflexivity, and this is detailed below. The initial codes were created using NVIVO; each transcript was inserted into NIVO, and initial codes relevant to the research questions were added and grouped, summarising the data's basic meaning (Braun & Clarke, 2006). The codes with similar meanings were initially grouped to

form a theme. Several thematic maps were created (Appendix AM-AS) to help organise, examine, and visually see the relationship between codes and themes. Using NVIVO, each code was manually labelled, as Braun & Clarke (2006) suggested.

Chapter 3

Identifying important determinants of a Chronic Obstructive Pulmonary Disease (COPD) symptom profile

3.0 Introduction

As outlined in greater detail in Chapter 1, Chronic Obstructive Pulmonary Disease (COPD) is a debilitating chronic disorder with an underlying pathology that impacts lung compliance over time (Cazzola et al., 2007) and is also associated with broader physical and psychosocial impacts that contribute to a reduction in quality of life. COPD can be managed through many different medications, which includes short-acting and long-acting steroid inhalers (and long-acting bronchodilator and steroid inhalers (Grimes et al., 2007) with the aim to improve the quality of life, daily physical activity, and sleep quality, and to reduce breathlessness (Ágh et al., 2015). COPD is not just a lung condition but includes a wide range of comorbidities. The most common and frequent conditions are hypertension, coronary artery disease, diabetes, osteoarthritis, depression, anxiety and asthma, which all impact the quality of life and increase exacerbations and mortality (Dos Santos et al., 2022). Given the current and projected increase in costs to support COPD patients, the current study aims to increase knowledge and understanding of the physiological and psychological consequences of living with COPD and investigate if there are any differences relative to the severity of COPD. In order to do this effectively, there is a need to increase the awareness of COPD patients and assess the viability of innovative/non-medicinal approaches. There is a clear need to have a holistic understanding of COPD patients, including details pertaining to the demographics, ethnicity, educational attainment, and current or previous occupational status, in addition to information about their condition, prognosis, symptoms, current medications with a willingness to change and the broader impact upon the broader determinant of quality of life.

Research in COPD has often focused on identifying specific factors such as depression and COPD (Ng et al., 2009), generally including any participant with the diagnosis of COPD or, on the other hand, specific stages of COPD (Ergün et al., 2011). Limited research considers all stages of COPD (i.e. severities), multiple physiological and psychological factors, readiness to try a new intervention and confidence to try a new intervention. The closest match that incorporates the severity of COPD and health status is a study by Antonelli-Incalzi et al. (2003), who investigated COPD severity based on the GOLD criteria and correlation with differences in the health status of 381 COPD patients. GOLD stages of the severity of COPD differed in SGRQ components but not significantly in cognitive and affective status and quality of sleep. The most significant difference in health status was between stage IIa and stage IIb but not in the other stages. In other words, the progression of COPD severity from stage 0 to IIa does not link to any significant difference in health status. Being female and having comorbidity had a

greater impact on COPD health status (Antonelli-Incalzi et al., 2003). Furthermore, the current study aimed to investigate whether patients with COPD are willing to try a new intervention to help manage COPD using a new intervention, how confident they feel to try the new intervention and if these changes depend on what stage of COPD the patient has (i.e. COPD severity).

To summarise, the current study set out to obtain a holistic understanding of COPD patients and to couple this information specifically with insight relating to a willingness to change/try new interventions that will positively impact their symptoms and quality of life. Specifically, this includes identifying differences in (i) breathlessness, fatigue, sleep quality, quality of life (including overall physical health status and overall mental health status) and self-compassion across differing levels of COPD severity and (ii) determining whether COPD severity affects the readiness to adopt/try new interventions.

3.1 Methods

Following ethics approval obtained by the College of Science & Engineering Research Ethics Committee at The University of Derby (Ethics Approval Reference Number: ETH1920-1638) (Appendix A), a descriptive cohort observational study was conducted using an online survey to explore the physiological and psychological consequences of living with COPD. The survey consisted of 63 questions with the following sub-headings/categories: Participant Information Sheet (Appendix B) and Consent (Appendix C), Demographics, COVID-19, Questionnaires, and Debrief (Appendix D). The online survey platform Qualtrics was utilised.

3.1.1 Participants

Participants were recruited from Facebook, Twitter and Asthma and Lung UK monthly newsletters and could access a Qualtrics online questionnaire survey website link.
Participants had to be over 18 and live in the UK

3.1.2 Demographics

Participants were asked several questions relating to COVID-19. Participants were required to answer ‘yes’ or ‘no’ regarding diagnosis, admission to hospital, experience of symptoms and family members/people in the household with symptoms or a diagnosis of COVID-19. In addition, participants were required to provide details relating to their sex, age, marital status, ethnic origin, occupation, occupation exposure, use of medication, engagement with non-

medical interventions and the presence of comorbidities/multi-morbidities. These options are based on previous surveys that have been distributed by The British Lung Foundation, (2016). Participants were also asked to indicate which part of the UK they were from to investigate whether the location of where participants lived affected or contributed to their COPD, the severity of the condition and quality of life. For example, the North of the UK is shown to have the highest prevalence of COPD (Snell et al., 2016) (please refer to Table 3.1).

3.1.3 Materials

Participants were asked to complete six questionnaires (CAT; MRC Dyspnoea Scale; Fatigue Assessment Scale; Pittsburgh Sleep Quality Index, EQ-5D-5L/EQ-MH-VAS, SCS-SF) and two 'rulers' (readiness to try a new intervention; confidence to try a new intervention). The questionnaires and rulers have been grouped into physiological and psychological measures. For this study, the St George's Respiratory Questionnaire (SGRQ) (Jones et al., 1991) could have been used to provide a global score to measure the impact of COPD on health-related quality of life. However, the severity of COPD was required (without the use of spirometry because of COVID-19 and medical records and was a more reliable measure for participants to disclose which specific COPD stage the participant was, as there was a high possibility of making a mistake) and was acting as the independent variable, with physiological/psychological factors questionnaires and two rulers acting as dependent variables. Moreover, the SGRQ does not provide an in-depth analysis of COPD's impact on quality of life; the areas of focus are breathlessness, daily activities, coughing, and chest. Unfortunately, the SGRQ symptom domains do not have reliable internal consistency (Lo et al., 2015), which is paramount for this study to measure COPD symptoms. This has also been supported by Loubert et al. (2020), who state that SGRW is not an appropriate questionnaire to measure symptom severity or limitation to daily activities in COPD. The CAT is specific to COPD and includes phlegm, chest tightness, ability to walk up a hill, confidence leaving home, sleep and energy. Participants prefer the CAT questionnaire as it is easier to complete and takes less time than the SGRQ (Tsiligianni et al., 2012).

Furthermore, for a PhD and impactful research, relying on and using a global score or a questionnaire that essentially scores a complex area such as sleep on just a simple 0-10 question is not scientific or rigorous enough. Therefore, even though a global score could have been provided for the basis of the PhD as the first study, it is essential to use valid questionnaires that have depth and can reliably capture sleep quality, for example, providing a measurable score (that consists of multiple questions to combine as a global score and prevents the

participant from stating 10 out of 10 which does not truly affect how they are feeling but it is quick and easy), which can then be interpreted alongside the other variables in the study such as self-compassion. To ask participants online to complete six questionnaires and two rulers took time. However, COPD is complex both from a physiological and psychological perspective and, therefore, is needed rather than relying on systemic literature reviews and multiple studies. As the survey was sent out during the early stages of the COVID-19 pandemic, prior to the presentation of each questionnaire, participants were encouraged to provide answers based on their experiences before lockdown. For more details regarding each questionnaire, please see the General Methodology chapter 2. Please see below an outline and justification of why the questionnaires and scales were implemented into this study.

3.1.4 Procedure

Members from both Facebook COPD groups and Asthma and Lung UK could click on the Qualtrics link for this study via the Facebook group or the Asthma and Lung UK newsletter distributed online. The Qualtrics link also included a brief description of what the study would involve, along with the researcher's contact details. If the participant showed an interest in participating, they could read the participant information sheet and the consent form. Once the participant signed the consent form electronically, the participant was permitted to complete the questions within the survey. The participant had the right to withdraw at any time. Once the participant had completed the survey, the participant read the debrief sheet and was thanked for the time they had taken to complete the survey and contact information, should they need it, i.e. Asthma and Lung UK.

3.1.5 Analytic Strategy

The data was screened prior to analysis. 179 survey responses were collected in total. Data from a total of 10 questionnaires were collected, consisting of 63 questions in total (excluding demographic, health status and smoking status questions). Missing data checks revealed that there were 38 partially answered responses (out of 179). Mean imputation was therefore implemented in cases where participants had not fully completed all questions across the data set, as Scheffer, (2002) recommended. This involves replacing missing data with the average score for that question. However, where missing data accounted for more than 10% of the complete data set, that participant was removed in line with Bennett's recommendation (2001). Consequently, 22 partial responses were >10% and were omitted. 8 partial responses were <10%, and the mean was imputated to give a total of 157. When reviewing the data, 3 extreme

scores were identified as likely typos/human error and were removed from the data set. Although a number of outliers were identified, the decision was made to keep all outliers within the data set. All participants have various severities of COPD and a significant number of physiological and psychological issues; therefore, the 40 outliers are rightfully part of the distribution of interest within the data and help decrease the overall error estimation (Leys et al., 2019). In addition, removing 40 outliers would involve losing nearly a quarter of the overall data set, which has ethical and subsequent statistical power implications. Furthermore, outliers are not necessarily problematic – they can represent natural variations of data from an extremely vulnerable population within the UK. Therefore, the final number of participants within the final data set was 154. Data were screened and checked for normality. All skewness and kurtosis z-scores were ≤ 1.96, and Kolmogorov-Smirnov tests were non-significant (see Appendix G). Suggesting that the data was normally distributed. Levene's test were mainly non-significant for the dependent variables, apart from EQ-5D, EQ-MH-VAS, RIR and CIR which were all significant (MRC Dyspnoea Scale = $F(2, 151) = .701$, $p = .498$, FAS = $F(2, 151) = 2.62$, $p = .075$, PSQI = $F(2, 151) = .154$, $p = .857$, EQ-5D = $F(2, 151) = 11.59$, $p = .001$, EQ-VAS = $F(2, 151) = .896$, $p = .410$, EQ-MH-VAS = $F(2, 151) = 5.07$, $p = .007$, SCS-SF = $F(2, 151) = 1.23$, $p = .294$, RIR = $F(2, 151) = 5.80$, $p = .004$, CIR = $F(2, 151) = 3.95$, $p = .021$). As a result, the assumption of homogeneity of variances can only be partially met. Due to the issues with homogeneity, a Welch's ANOVA was conducted to examine differences across the key variables of interest among differing levels of COPD severity. The Welch's ANOVA was chosen in this case as it is equipped to deal with cases where the data is normally distributed but has unequal variances, as well as unequal sample sizes. The independent variable in this study was COPD severity, measured using the global score from CAT (three levels: medium, high and very high). The dependent variables were grouped into physiological and psychological factors. Separate ANOVAs were conducted to assess the impact of COPD severity (medium, high or very high) for both physiological and psychological factors. Bonferroni was implemented, as well as post-hoc testing using Games-Howell.

3.2 Results

3.2.1 Participant Characteristics

The demographic information of participants can be found in Table 3.1. The average age was 62 ± 9 years old (range 29 to 82 years old). Over half (53%) of all participants did not disclose their current or former occupations. However, from the available data, 54% were retired, 17% were unemployed, and 5% worked for local small to medium organisations. Eighty-three

people (54%) reported having emphysema, twenty (13%) had chronic bronchitis, and fifty-one (33%) were not aware of their COPD pathology. Forty-nine people (31%) reported having a confirmed COPD diagnosis for ten years or more, fifty-nine (49%) between 5-10 years and fifty (30%) between 0-5 years. The average number of types of medication for this sample of participants is 3, with one participant reporting the use of 11 types of different medications and 18 participants currently using five different types of medication. The most common medications are short-acting bronchodilator inhalers, used by 81% of participants; long-acting bronchodilator inhalers, taken by 65% of participants; and the next most popular does, 51% of participants take steroid inhalers; these statistics include the same participants i.e. the same participant can be included across all three types of medication. Furthermore, 38% had two comorbidities (physical and/or mental), 33% had hypertension, 32% had asthma, 32% depression, 21% osteoporosis and 18% heart failure/heart disease. For non-medical interventions, unfortunately, only 7 participants had accessed Cognitive Behavioural Therapy, despite 32% of participants experiencing depression.

Table 3.1. Demographics of participants

	N	%
UK Location		
East Midlands	21	14%
South East	22	12%
North West	18	12%
East of England	18	11%
London	17	11%
West Midlands	16	10%
Scotland	12	8%
South West	12	8%
Wales	6	4%
Yorkshire & Humber	6	4%
North East	3	2%
Northern Ireland	2	1%
Isle of Man	1	0.6%
Ethnic origin		
White - British	130	84%
White - Scottish	7	5%
White - Welsh	6	4%
Prefer not to say	4	3%
Other	3	2%
Mixed White and Black	2	1%
White – Irish	2	1%
Occupational Status		
Retired	84	54%
Unemployed	26	17%
Other	44	28%

Type of COPD (n=83)		
Emphysema	83	54%
Chronic bronchitis	20	13%
Did not know	51	33%
Duration of COPD		
10 years+	49	31%
2-5 years	33	21%
5-7 years	30	20%
7-10 years	29	19%
1-2 years	7	5%
6 month – 12 months	6	4%

3.2.2 Descriptive Statistics

The descriptive statistics are presented in Table 3.2 below and include the overall means and deviations based on the scores for each physiological measure. Table 3.3 provides details of the specific means and deviations for each level of the independent variable (medium, high and very high), which excludes CAT (CAT score was used as the independent variable in the study).

Table 3.2. Means and standard deviations for each physiological measure

Physiological Measure	*n*	M	*SD*	Range
CAT	154	24.95	7.22	11-40
MRC Dyspnoea Scale	154	3.11	1.21	1-5
FAS	154	28.08	8.22	14-45
PSQI	154	10.44	4.54	2-21

Table 3.3. Means and standard deviations of the physiological measures at each level of the independent variable

Physiological Measure	*n*	M	*SD*	Range
MRC Dyspnoea Scale **				
Medium	44	2.00	.915	1-4
High	73	3.27	.870	1-5
Very High	37	4.11	1.075	1-5
FAS **				
Medium	44	20.18	4.505	14-30
High	73	28.86	6.577	18-47
Very High	37	35.92	6.029	25-45
PSQI **				
Medium	44	7.59	3.973	2-17
High	73	10.90	4.056	2-21
Very High	37	12.92	4.406	4-21

**No participants were classified as having low COPD severity

3.2.3 COPD Symptomology

As the CAT score was used as the independent variable in this study (with 3 levels: medium, high and very high), there is no Welch's ANOVA result to report.

Table 3.4. Number of participants in each level of the CAT independent variable (COPD Severity)

Level of independent variable	*n*	M	*SD*	Range
**				
Medium	44	15.82	2.617	11-20
High	73	25.81	2.711	21-30
Very High	37	34.11	3.026	31-40

**No participants were classified as having low COPD severity

3.2.3.1 Breathlessness

Analysis of the average MRC Dyspnoea Scale score revealed a significant main effect: *Welch's* $F(2, 79.46) = 48.91$, $p < .001$, indicating that breathlessness score may differ according to the severity of COPD. The estimated omega squared ($\omega^2 = .40$) indicated that approximately 40% of the total variation in the average score on the MRC Dyspnoea Scale is attributable to differences between the three COPD severities (medium, high, very high). Post hoc comparisons were conducted using the Games-Howell post hoc procedure to determine which of the three COPD severities differed significantly in terms of breathlessness as measured by the MRC Dyspnoea Scale. The Games-Howell post hoc procedure was used in this case because the data violated the assumption of homogeneity of variance/equal sample sizes. These results indicate that participants with high severity of COPD (M = 3.27, $SD = .915$, $p < .05$) had a significantly higher average score on the measure of MRC Dyspnoea Scale than participants with a medium severity of COPD (M = 2.00, $SD = .870$, $p < .05$). In addition, participants with a very high COPD severity (M = 4.11, $SD = 1.075$, $p < .05$) had a significantly higher average score on the measure of MRC Dyspnoea Scale (i.e. breathlessness) than participants with medium severity of COPD (M = 2.00, $SD = .870$, $p < .05$), as well as a significantly higher average score on the measure of MRC Dyspnoea Scale than participants with a high severity of COPD (M = 3.27, $SD = .915$, $p < .05$).

3.2.3.2 Fatigue

Analysis of the average Fatigue Assessment Scale (FAS) score revealed a significant main effect: *Welch's* $F(2, 87.46) = 92.43$, $p < .001$, indicating that fatigue scores may differ according to the severity of COPD. The estimated omega squared ($\omega^2 = .48$) indicated that approximately 48% of the total variation in the average score on the Fatigue Assessment Scale is attributable to differences between the three COPD severities (medium, high, very high). Post hoc

comparisons, using the Games-Howell post hoc procedure, were conducted to determine which of the three COPD severities differed significantly for fatigue from the fatigue assessment scale. These results indicate that participants with a high severity of COPD (M = 28.86, *SD* = 6.577) had a significantly higher average score on the measure of fatigue assessment scale than participants with a medium severity of COPD (M = 20.18, *SD* = 4.505, *p* <.05). In addition, participants that have a very high COPD severity (M = 35.92, *SD* = 6.029) had a significantly higher average score on the measure of fatigue assessment scale (i.e. fatigue) than participants with a medium severity of COPD (M = 20.18, *SD* = 4.505, *p* <.05), as well as a significantly higher average score on the measure of fatigue assessment scale than participants with a high severity of COPD (M = 28.86, *SD* = 6.577, *p* <.05).

3.2.3.3 Sleep Quality

Analysis of the average PSQI score revealed a significant main effect: *Welch's F*(2, 82.59) = 17.43, *p* <.001, indicating that sleep quality score may differ according to the severity of COPD. The estimated omega squared (ω^2 = .17) indicated that approximately 17% of the total variation in the average score on PSQI is attributable to differences between the three COPD severities (medium, high, very high). Post hoc comparisons, using the Games-Howell post hoc procedure, were conducted to determine which of the three COPD severities differed significantly for sleep using the PSQI. These results indicate that participants with a high severity of COPD (M = 10.90, *SD* = 4.056) had a significantly higher average score on the measure of PSQI than participants with a medium severity of COPD (M = 7.59, *SD* = 3.973, *p* <.05). In addition, participants with a very high COPD severity (M = 12.92, *SD* = 4.406) had a significantly higher average score on the measure of PSQI (i.e. sleep quality) than participants with a medium severity of COPD (M = 7.59, *SD* = 3.973, *p* <.05), as well as a higher average score on the measure of PSQI than participants with a high severity of COPD (M = 10.90, *SD* = 4.056); however this was not significant.

3.3 Psychological Profile

3.3.1 Descriptive Statistics

Table 3.5 below states the descriptive statistics, which are the overall means and deviations based on the scores for each psychological measure. Table .6 provides details of the specific means and deviations of each level of the independent variable (medium, high and very high), which excludes CAT (CAT score was used as the independent variable in the study).

Table 3.5. Means and standard deviations for each psychological measure

Psychological Measures	*n*	M	*SD*	Range
EQ-5D Index Scores	154	.537	.309	-.161-1.000
EQ-VAS	154	46.93	21.95	4-90
EQ-MH-VAS	154	64.71	24.42	1-100
SCS-SF	154	2.98	.739	.50-4.83
RIR	154	9.05	3.56	3-10
CIR	154	8.25	1.90	2-10

3.3.2 Quality of Life

Analysis of the average EQ-5D index score revealed a significant main effect: *Welch's F*(2, 82.28) = 74.79, $p < .001$, indicating that quality of life score may differ according to the severity of COPD. The estimated omega squared ($\omega^2 = .40$) indicated that approximately 40% of the total variation in average score on EQ-5D index scores is attributable to differences between the three COPD severities (medium, high, very high). Post hoc comparisons, using the Games-Howell post hoc procedure, were conducted to determine which of the three COPD severities differed significantly in quality of life from the EQ-5D. These results indicate that participants with high severity of COPD (M = .52625, *SD* = .266379) had a significantly lower average score on the measure of EQ-5D index scores than participants with a medium severity of COPD (M = .80025, *SD* = .132711, $p < .05$). In addition, participants with a very high COPD severity (M = .24889, *SD* = .274037) had a significantly lower average score on the measure of EQ-5D index score (i.e. quality of life) than participants with a medium severity of COPD (M = .80025, *SD* = .132711, $p < .05$), as well as a significantly lower average score on the measure of EQ-5D index scores than participants with a high severity of COPD (M = .52625, *SD* = .266379, $p < .05$).

Table 3.6. Means and standard deviations of the psychological measures at each level of the independent variable

Psychological Measure	*n*	M	*SD*	Range
EQ-5D Index Scores				
**				
Medium	44	.80025	.132711	.435-1.000
High	73	.52625	.266379	-.153-.872
Very High	37	.24889	.274037	-.161-1.000
EQ-VAS				
**				
Medium	44	63.80	16.984	25-90
High	73	44.35	18.763	9-80
Very High	37	31.76	20.071	4-75
EQ-MH-VAS				
**				
Medium	44	76.43	19.867	17-100
High	73	62.33	22.739	1-100
Very High	37	55.46	27.613	12-100
SCS-SF				
**				
Medium	44	3.06	.79154	1.33-4.83
High	73	2.94	.76540	.50-4.75
Very High	37	2.96	.62376	1.50-4.33
RIR				
**				
Medium	44	9.20	1.002	6-10
High	73	9.25	1.211	4-10
Very High	37	8.59	1.907	3-10
CIR				
**				
Medium	44	8.43	1.500	3-10
High	73	8.21	1.965	2-10
Very High	37	8.11	2.221	3-10

**No participants were classified as having low COPD severity

3.3.3 Overall Physical Health

Analysis of the average EQ-VAS score revealed a significant main effect: *Welch's F*(2, 83.60) = 32.16, p <.001, indicating that overall physical health score may differ according to the severity of COPD. The estimated omega squared (ω^2 = .28) indicated that approximately 28% of the total variation in the average score on EQ-VAS is attributable to differences between the three COPD severities (medium, high, very high). Post hoc comparisons, using the Games-Howell post hoc procedure, were conducted to determine which pairs of the three COPD

severities differed significantly for overall physical health from the EQ-VAS. These results indicate that participants with high severity of COPD (M = 44.35, *SD* = 18.763) had a significantly lower average score on the measure of EQ-VAS than participants with a medium severity of COPD (M = 63.80, *SD* = .16.984, *p* <.05). In addition, participants that have a very high COPD severity (M = 31.76, *SD* = 20.071) had a significantly lower average score on the measure of EQ-VAS (i.e. overall physical health) than participants with a medium severity of COPD (M = 63.80, *SD* = .16.984, *p* <.05), as well as a significantly lower average score on the measure of EQ-VAS scale than participants with high severity of COPD (M = 44.35, *SD* = 18.763, *p* <.05).

3.3.4 Overall Mental Health

Analysis of the average EQ-MH-VAS score revealed a significant main effect: *Welch's F*(2, 81.56) = 9.605, *p* <.001, indicating that overall mental health score may differ according to the severity of COPD. The estimated omega squared (ω^2 = .09) indicated that approximately 9% of the total variation in the average score on the EQ-MH-VAS scale is attributable to differences between the three COPD severities (medium, high, very high). Post hoc comparisons, using the Games-Howell post hoc procedure, were conducted to determine which of the three COPD severities differed significantly for overall mental health from the EQ-MH-VAS. These results indicate that participants with high severity of COPD (M = 62.33, *SD* = 22.739) had a significantly lower average score on the measure of EQ-MH-VAS than participants with a medium severity of COPD (M = 76.43, *SD* = 19.867, *p* <.05). In addition, participants with a very high COPD severity (M = 55.46, *SD* = 27.613) had a significantly lower average score on the measure of EQ-MH-VAS (i.e. overall mental health) than participants with a medium severity of COPD (M = 76.43, *SD* = 19.867, *p* <.05), however a non-significant lower average score on the measure of EQ-MH-VAS than participants with a high severity of COPD (M = 62.33, *SD* = 22.739).

3.3.5 Compassion

Analysis of the average SCS-SF score revealed a non-significant main effect: *Welch's F*(2, 86.36) = .347, indicating that the self-compassion score does not differ significantly according to the severity of COPD. The estimated omega squared (ω^2 = -.00) indicated that approximately 0% of the total variation in the average score on SCS-SF is attributable to differences between the three COPD severities (medium, high, very high). Post hoc comparisons were not conducted because the results were non-significant.

3.3.6 Readiness to try a new intervention

Analysis of the average readiness to try a new intervention score revealed a non-significant main effect; *Welch's F*(2, 78.15) = 1.84, indicating that the readiness for change score does not differ significantly according to the severity of COPD. The estimated omega squared (ω^2 = .00) indicated that approximately 0% of the total variation in the average score on readiness for change ruler is attributable to differences between the three COPD severities (medium, high, very high). Post hoc comparisons were not conducted because the results were non-significant.

3.3.7 Confidence to try a new intervention

Analysis of the average confidence to try a new intervention score revealed a non-significant main effect; *Welch's F*(2, 83.49) = .385, indicating that the confidence to try a new intervention score does not differ significantly according to the severity of COPD. The estimated omega squared (ω^2 = .00) indicated that approximately 0% of the total variation in the average score on the confidence to try a new intervention ruler is attributable to differences between the three COPD severities (medium, high, very high). Post hoc comparisons were not conducted because the results were non-significant.

3.4 Discussion

The present study aimed to investigate if COPD severity significantly impacts physiological symptoms such as breathlessness, fatigue, and sleep quality, as well as psychological symptoms such as quality of life, overall physical health, and overall mental health. A final aim was to examine whether COPD severity affects the levels of readiness to try a new intervention, as well as having the confidence to try a new intervention. The novel key findings are that COPD participants, regardless of COPD severity (medium to very high), have moderate levels of self-compassion. In addition, overall mental health is significantly different across COPD severities, with mental health worsening as the severity of COPD increases. Additional key findings are that readiness to try a new intervention and having the confidence to try a new intervention is high across the COPD severities. The COPD Assessment Test (CAT) was used to determine the severity of COPD in this study (medium, high and very high). This was because, at the time of participant recruitment, conducting spirometry tests to measure lung function was forbidden because of the COVID-19 pandemic; due to minimising the spread of COVID-19 and COPD, participants could not leave home. Upon reflection, if this study were

to be replicated, it should endeavour to use the recommendations set out in the GOLD stages and combine this with spirometry to measure lung function and capacity, then measure for significant differences across the different dependent variables such as SCS-SF, MRC, and PSQI. Using the GOLD stages and spirometry would be more scientific and less reliant on self-administered CAT scores to categorise COPD severity, making sure there are COPD participants with low COPD severity (as this study did not have any).

Existing literature on COPD severity and the specific impact on quality of life and mental health depending on each level of severity was investigated by Antonelli-Incalzi et al., (2003). Antonelli-Incalzi et al., (2003) conducted a study with 381 COPD participants (average age of 73 years old) and used the GOLD classification (lung function test using spirometry) with stage 0, stage I, stage II (spilt in to stage IIa and IIb) and stage III. To compare the GOLD classification with CAT COPD severity, Ghobadi et al., (2012) found that between GOLD and CAT, there are significant correlations, which means that it is valid to compare both studies (as it is the closest match to this current study): CAT (low) = GOLD stage 1, CAT (medium) = GOLD stage IIa/IIb, CAT (high) and CAT (very high) = GOLD stage III. The St Georges Respiratory Questionnaire (SGRQ) was used to measure the health status of the COPD participants, as well as disturbance in physical activity and psycho-social impacts. The study found that both SGRQ symptoms and psycho-social impacts worsened between stage 0 and stage III, with significant differences between stage IIa and III. There were no significant changes between stages 0 to I and from I to IIa for cognitive and affective states and sleep quality. The findings from Antonelli-Incalzi et al., (2003), with the main differences being the impacts of symptoms between stages IIa and III (i.e. the later stages of COPD and poorer lung function and capacity) and no significant differences in cognitive, affective states, in addition to quality of sleep between 0 to I and I to IIa. Across the various variables within this study, there were significant differences between medium, high and very high across breathlessness, fatigue, sleep quality, quality of life, overall physical health and overall mental health, which are vastly different clinical outcomes to Antonelli-Incalzi et al., (2003). Therefore, this study shows that clinical deterioration in COPD participants increases as COPD worsens, i.e. the severity increases.

Despite observing non-significant differences in the self-reporting of compassion across all of the COPD severities, this data (Table 3.5) demonstrates that regardless of medium, high, and very high COPD severity, moderate self-compassion seems applicable, which explains why there is no significant main effect across the specific COPD groups. There is no research

regarding self-compassion across the different COPD severities. The non-significant differences and moderate self-compassion are surprising results and insights. This is because current literature shows that self-compassion, for example, is closely linked to COPD severity (Benzo et al., 2015), which also used the SCS-SF questionnaire. In addition, COPD patients have significantly lower self-compassion than healthy controls; self-compassion was measured using SCS-SF (Harrison et al., 2017). Higher levels of self-compassion are a crucial variable in lowering limiting behaviour patterns and anxiety in patients with COPD (Kenefick, 2016). Potentially, in future research, depression and anxiety should be measured when measuring self-compassion. A possible explanation for this is that self-compassion is complex and shows that those with COPD have a moderate level of kindness to themselves during adverse events and life factors. Is it because, from the point of diagnosis, self-compassion remains at a moderate level because it is required to be able to function and live with a long-term and chronic respiratory condition? Half of the study participants are married, which could be a positive factor in higher self-compassion. Research shows that higher marital satisfaction correlates with higher levels of self-compassion (Maleki et al., 2019) and the duration of the marriage, which is positively correlated with self-compassion (Bibi et al., 2017). Therefore, this may highlight the importance of self-compassion for themselves and others, which has been more actively thought about compared to prior to diagnosis, helping with emotional stability and supporting resilience as COPD progresses. This would warrant further research investigating the level of self-compassion before the COPD diagnosis up to the highest COPD severity and see if there are significant differences. It is advisable to conduct research using the full version of self-compassion (Self-compassion scale, SCS, Neff, 2016) as this would enable specific domains to be analysed separately and interpreted—for example, self-kindness, self-judgement, common humanity, isolation, mindfulness, and over-identity. Unfortunately, the SCS-SF cannot be analysed separately. On the other hand, a new ‘external and internal shame’ scale (EIS; Ferreira, 2022) could also be used, as it is a relatively new questionnaire that focuses on shame only. Both the SCS and EIS could complement one another in investigating further self-compassion and shame in COPD populations across COPD severities. Research is significantly lacking this insight. Despite being non-significant, the findings from this study can add to the significant lack of research on self-compassion in COPD, as it could be a significant variable in supporting effective holistic treatment in managing both physiological and psychological impacts from COPD symptoms.

About the participant demographics, all participants were of white ethnicity and mostly retired. The average age was 62 years old, which is above 50 is the norm for COPD participants (Yin et al., 2017). However, one participant was as young as 29 years of age. Research is now focusing on the 'pre-COPD' stage to try to prevent the stages of COPD from progressing for patients below the age of 50 years of age (Martinez et al., 2022). Out of 1,077 individuals, 65 had the symptoms of pre-COPD (Cosio et al., 2023); therefore, in this study, having a participant aged 29 years old is not unusual. Further research is required for early onset COPD, especially with the high risk of lung damage from electronic vaping cigarettes (Boweler et al., 2017). Could COPD, which has been caused by vaping, have different impacts across both physiological and psychological factors and COPD severity? Over half of the participants were married. Previous literature has stated that COPD patients who are single have worse health outcomes and quality of life (Holm et al., 2014). Therefore, future research should have a study focusing on single COPD patients only, as there could be further factors that may be required, especially from a psychological perspective, which could be increasing levels of depression, for example, and worsening additional health outcomes such as breathlessness, as the patient could be more sedentary for example and lonely. A holistic approach is vital to improving physical and psychological well-being (Wouters & Augustin, 2016). Participants who did disclose occupations were cleaners and trade workers and those working in services (Blanc, 2012), lower socio-economic class (Eisner et al., 2011), with exposures to chemicals and exhaust fumes (Boschetto et al., 2006), and those dust, which collectively matches current literature. The average number of medications within the study sample was 3, the average for COPD patients, including short-acting, long-acting, and steroid inhalers (Ágh et al., 2015). It is shocking to see that despite the various medications, the original aim of medication interventions is to improve quality of life, physical activity, sleep quality, and breathlessness (Ágh et al., 2015). However, this study has shown that the medications are not fulfilling the promises and the original aims—poor clinical outcomes across most areas – breathlessness, fatigue, sleep quality and quality of life. One participant had 11 different types of medications, which adds evidence that medication is not as effective as it should be. Regarding comorbidities again the COPD sample is similar to the norm, with hypertension, heart disease, diabetes, osteoarthritis, psychiatric conditions and asthma (Dos Santos et al, 2022). .On reflection, too many demographics were asked. If replicated, the bare minimum and main demographics, such as age and medications, should be included, with the main focus being the dependent variables. This would have saved the participant time filling in the online survey. With the majority of COPD patients having occupational exposure and smokers of lower socioeconomic class, how

does COPD impact people who are in the higher economic class? Do they have better access to private medical and psychological support, and does COPD severity impact differences across the various physiological and psychological factors? If replicated to have a larger sample and to compare COPD severity and dependent variables, filtered by specific demographics such as socioeconomic class, age and marital status to investigate further, especially under-researched areas such as self-compassion.

Predictions relating to COPD severity can also be accepted, as those with very high COPD severity had a higher level of breathlessness. Patients with a very high COPD severity had a higher level of breathlessness compared to medium and high COPD severity. Therefore, this hypothesis can also be accepted. The hypothesis that the level of fatigue would be significantly different across COPD severities was accepted, as was the prediction regarding post hoc comparisons between medium, high and very high COPD severity, with levels of fatigue being higher among those with very high COPD severity compared to those with medium and high levels. The sleep quality hypothesis can be accepted as the main effect was significant across the COPD severities, showing that sleep quality is low across all three groups. However, despite sleep quality being lower between high and medium severity and very high and medium COPD severity, the prediction for lower sleep quality between very high COPD severity and high severity must be rejected, as it was not significant. Furthermore, for the psychological measures, the hypothesis for quality of life can be accepted, as well as post hoc comparisons demonstrating significantly lower levels of quality of life between very high and high COPD severity, very high and medium and between high and medium COPD severity. The hypothesis for overall physical health can be accepted, as there was a significant difference between medium, high and very high COPD severity, and the prediction that very high compared to high was lower, and high compared to medium had lower average levels of overall physical health status. The overall mental health status hypothesis can also be accepted as there was a significant main effect of lower overall mental health status across all COPD severities. Regarding post-hoc comparisons, the prediction that there would be significantly lower levels of overall mental health for very high COPD severity compared to high and medium COPD severity was accepted. Specifically, the findings showed that levels of overall mental health were significantly lower compared to very high and medium COPD severity and compared to very high and low COPD severity. The self-compassion hypothesis suggested that there would be significant differences in self-compassion levels across each COPD severity and lower levels of self-compassion between very high compared to high and medium severity. Findings

revealed that there were non-significant differences in self-compassion across all COPD severities. Therefore, the hypothesis was rejected, so post hoc comparisons were not conducted. Similarly, for readiness to try a new intervention and confidence to try a new intervention, no significant differences were found, and as such, all hypotheses were rejected. Overall, the findings from this study add support to previous literature, for example, that breathlessness gets worse as COPD progresses in severity (Marciniuk et al., 2011), as does fatigue (Valderramas et al., 2013), sleep quality (Ghoneim et al., 2021), quality of life (Zamzam et al., 2012), overall physical health (Rutten-van Mölken et al., 2006) and overall mental health (Pelgrim et al., 2019). However, as stated above, post-hoc comparisons between very high and high COPD severity were not significantly different for sleep quality. This implies that perhaps after reaching a high severity of COPD, symptom severity plateaus regarding sleep quality remain at this level until mortality. Therefore, interventions should focus on earlier stages to try stabilising sleep quality to prevent the increase in severity. Upon reflection, if the study were conducted in the future, it would be ideal to use a more specific sleep quality/impact scale such as the CASIS (COPD and Asthma Sleep Impact Scale; Pokrzywinski et al., 2009). CASIS has been conducted specifically for the COPD and Asthma clinical population and has shown that prolonged disease duration and severe COPD severity are important indicators for deterioration in the quality of sleep (Koulouris et al., 2022). Using a general sleep quality questionnaire not specific to COPD may, therefore, explain the plateau.

A novel finding of this study was the demonstration of significant differences among different levels of COPD severity in terms of overall mental health (EQ-MH-VAS). The finding of overall mental health being significantly different across medium, high and very high COPD severity adds to current literature showing that as COPD progresses, participants' mental health decreases (Omachi et al., 2009; Schneider et al., 2010). The EQ-MH-VAS was added alongside the EQ-VAS, the visual analogue scale for overall physical health (previously stated as also significantly different with COPD progression), as part of the EQ-5D-5L quotient. Therefore, creating the scale as a pilot to the EQ-5D-5L demonstrates the importance of adding an overall mental health scale within the quotient (alongside the overall physical health scale), as mental health is a significant part of the quality of life. Being able to measure both overall physical health and overall mental health is imperative, especially for long-term chronic medical conditions such as COPD. In the previous section, the EQ-MH-VAS was measured and showed validity. This warrants further research, and the authors of EQ-5D-5L may wish to consider adding this to the future quality-of-life inventories they create at EuroQol group. On the other

hand, despite the scale being easy to administer (with a 0-100 scale), the question is regarding 'overall mental health'. It is not specific, for example, to depression or anxiety. Therefore, in the context of this study, the scale has been used to gauge the impact of COPD on mental health more generally. The specific impact of COPD on depression and anxiety is an area to be explored further in future research.

Regarding the readiness of participants to try a new intervention ruler, despite a non-significant main effect across medium, high and very high COPD severity groups, a high level was observed across all three severity groups, in addition to the confidence to try a new intervention. This could potentially mean that COPD patients are ready to try a new intervention, regardless of whether the patients were at a medium, high or very high severity of COPD. However, the ruler was a scale between 0-10 and therefore could be considered minimalistic and interpreting this insight is with caution. However, it does show some indication of being 'ready', but further investigation is required into what being 'ready' to try a new intervention means. Also, it was not clear what intervention the researcher was referring to. The risk of social desirability bias (Morgado et al., 2017) and patients being vulnerable and knowing the possibility of a trial that was being conducted in the PhD, it is likely the patients scored highly and may not have been a true reflection, for example, if this was replicated elsewhere. The aim of adapting this was to provide a quick and easy method to gauge whether the participant was ready to try something new. On reflection, the 'Readiness to Change Questionnaire' (RCQ) (Heather et al. 1999) could be adapted to COPD patients, as it measures the 'stage of change' and the questionnaire results would be interpretable. Whether readiness and confidence to change are reflected within readiness to change/behaviour change, and therefore, the readiness and confidence to try a new intervention ruler are obsolete? Also, if a patient states they are 10 out of 10 for readiness and 10 out of 10 for confidence, is there evidence and data to suggest that the patient would be motivated and inclined to use an intervention, as data suggests with medications that are simple to use, medication adherence is still an issue that impacts on effectiveness that impacts COPD management of symptomology (Sánchez-Nieto et al., 2022). Further research is required to gauge which type of intervention patients with COPD are ready to try and which they will be confident in implementing to inform those that patients are likely to be more motivated (and able) to engage with.

Overall, the present study has shown, similar to previous literature, that COPD is multi-faceted, and as COPD severity progresses, primary and secondary symptoms collectively worsen (Jenkins et al., 2017). Patients are often affected physiologically with a reduction in lung

function and poor breathlessness, which has a knock-on effect on quality of life and sleep quality (Zohal et al., 2014). As this study is a quantitative study, it would be helpful to conduct a qualitative exploration to explore further the impact of COPD on day-to-day activities and quality of life, as well as experiences and views of medications.

Unfortunately, the study was conducted during the COVID-19 pandemic, and nearly half of the participants had a diagnosis of COVID at the time of taking part. Therefore, this should be considered when interpreting the findings, i.e., the scores could be lower compared to if the same participants answered the same questionnaires now, post-COVID-19 pandemic, when the participants are no longer shielded. Therefore, if the study were replicated, it would be interesting to conduct a follow-up of the same participants and compare the scores during the pandemic to the present day to investigate whether COVID-19 is a confounding variable. Also, the findings from the study cannot be generalised to the whole COPD clinical population, as the study sample was only 154. In addition to this, the study did not have a control group. Therefore, the results could not be compared to healthy controls or another long-term chronic condition such as cancer or multiple sclerosis to be able to conclude whether the specific dependent variable scores such as self-compassion, readiness, and confidence to try a new intervention were unique to COPD participants or similar across different clinical populations or healthy controls. The study's findings are applicable to medium, high, and very high-severity COPD groups but not low COPD severity. Therefore, it is essential to have participants in all COPD severity groups to discuss all the respiratory disease severities to be inclusive. It is important to compare not only all COPD severities but also how patients with COPD feel at the early stages, compared to late stages of COPD, rather than from medium severity to very high, for example. Reflecting on survey length, having ten different questionnaires, in addition to questions on demographics, health status and smoking status, was too long, and many did not fully complete the survey, and therefore, data was omitted. With COPD patients having fatigue and a lack of energy, as well as mental health problems in addition to the COPD physiological symptoms, research surveys must be comprehensible, limited effort and relatively quick and easy in order to capture good quality data without burdening and adding further fatigue on to patients and reducing incompletions and missing data from taking part in the survey.

As well as this, having the survey only online limits accessibility and reduces diversity (due to working from home because of the pandemic and reducing any possible spread of COVID-19 as a safety precaution). Therefore, it is advisable to conduct the study online as well as in paper-

based in the future (with a freepost envelope), advertising within newspapers (for example, the working classes and older adult population group that were in the mines, in manual handling occupations, the workers that were exposed to dust, concrete, fumes) to try and reach the participants that feel that they do not have a voice and hard to reach to participate so that we can improve quality of life for patients with COPD. Areas with the highest prevalence across the UK, Scotland, Wales, and Northern Ireland include Tyne & Wear, Glasgow, Blaenau Gwent, Belfast and Yorkshire. Advertising in newspapers and offering free post envelopes opens up opportunities to reach participants who do not have access to technology and the internet, which is vitally essential for diversity. However, the advantage of using the online survey was that despite the pandemic, participants' demographics came from all over the British Isles, from Scotland to Northern Ireland to The Isle of Man. Also, employing an online survey did not require much paperwork for the participant and additional administration for the researcher. It allowed for gathering substantial data from participants relatively quickly during a COVID-19 pandemic. In addition, another strength of this research is having a wide range of participants of different ages, with the average being 62, the youngest being 29, and the eldest being 82 years old. This shows the variety of data that has been gathered regarding COPD, especially as COPD under the age of 40 years old has a rare prevalence (Price et al., 2011). In addition, despite the concern that older population groups struggle with technology, this study demonstrates that it is possible to successfully use technology in research with participants in their 80s (Mitzner et al., 2010).

Overall, COPD is a complex, chronic, long-term disease. This study shows that despite all of the different medications, participants with COPD are struggling not only with primary physiological symptoms but also secondary psychological symptoms, together impacting the quality of life and worsening as the COPD severity increases, therefore a deterioration of clinical outcomes. The novelty here is that despite the limited current literature regarding self-compassion, which is, on average, low in people with COPD, this study shows that across medium, high, and very high COPD severity, self-compassion is moderate, which is different to the current literature. Further investigation is therefore required. On reflection, as most participants in this study, on average, are on three different types of medication, the management of COPD symptomology and their associated negative impact should be less severe. This suggests that the current system of treatments is not practical and is failing participants in managing COPD symptomology and consequently impacting their quality of life. Additionally, as medication costs the NHS a vast amount of money and hospital

admissions because of poorly managed COPD symptoms are frequent (as discussed in Chapter 1), significant improvements need to be implemented. However, this study contained a small sample of participants, which cannot be generalised but sets a foundation for further exploration and investigation. Despite the non-significance, the study has shown that participants with medium, high and very high COPD severity are ready and confident to try a new intervention but is with caution, as further research needs to be conducted on what it means to be ‘ready’ vs ‘confident’ to try a new intervention and possibly social desirability bias.

Chapter 4

A qualitative exploration of the impact of COPD on quality of life: A PhotoVoice methodology

4.0 Introduction

As previously established COPD significantly negatively impacts quality of life, especially as condition progresses (see discussion in chapters 1 and 2). The World Health Organisation have defined quality of life as "an individual's perception of their position in life in the context of the culture and the value systems in which they live and in relation to their goals, expectations, and standards of concern (WHO, 2024). COPD impacts on a range of patient outcomes such as mobility, self-care, usual activities, feelings of pain and discomfort, psychological distress, including anxiety and depression, ability to self-manage and patient's increasingly depend on care as they experience an increase in exacerbations and hopsitalisations (Borge et al., 2024), all of which in turn impact on a patient's quality of life. Usual activities such as household chores and walking up the stairs become a challenge, with breathlessness and feelings of fatigue becoming worse with poor quality sleep (Vogelmeier et al., 2020). To address this, there is an abundance of pharmacological and non-pharmacological interventions available for patients with COPD, which primarily aim to reduce symptom prevalence and severity and, in turn, improve quality of life (Muralidharan, Hayes, & Mansour, 2015). These include medications such as inhalers and steroids and pulmonary rehabilitation as outlined within the National Institute for Health and Care Excellence (2019). Typically, interventions are prescribed relative to performance status, using biological markers of disease stage and severity such as the MRC breathlessness scale and spirometry outcomes. Based on these markers, COPD patients are prescribed both pharmacological and non-pharmacological support strategies (Brien, Lewith & Thomas, 2016). Whilst multifaceted intervention approaches would influence a range of patient outcomes, services such as pulmonary rehabilitation (which includes education regarding COPD, nutrition, psychological and behavioural interventions) are only available for patients that have severe disease and high scores on the MRC dyspnea scale (a score of three and above out of five) (Gruffydd-Jones & Loveridge, 2011). Additionally, COPD self-management is promoted to improve quality of life through effective coping strategies, influenced by access to adequate social support and promoting greater self-efficacy, which is the belief that the patient has the belief or not in being able to perform a particular behaviour or set of behaviour's (Bandura, 1977). This is needed for patients to implement effective coping strategies as they live with COPD (McCathie, Spence & Tate, 2002). To date, little research has investigated the lived experience of patients with COPD to increase the understanding and awareness of how patients experience and live with the condition and the implications for their quality of life and mental and physical wellbeing.

Innovative methodologies utilising technological advancements and the accessibility of technology have allowed researchers to generate methods to obtain a deeper insight into and understanding of a patient's lived experience. Approaches such as photovoice bring to life and give a 'voice' to patients' experiences as they generate and interpret photographs to explain and illustrate their understanding of their experiences, values and beliefs (Beazley, 2008). The use of graphics creates an opportunity for patients to define not just the situations they see but to be able to represent them to others through photographs (Wang & Burris, 1994) with the meanings that have been elicited for each photograph taken by each patient of great interest (Plunket, Leipert & Ray, 2013). To date, there is one photovoice methodology study in the context of COPD, however this was conducted in Singapore, which is culturally very different to the United Kingdom (UK) (Sumner et al., 2023). The findings showed that breathlessness had a significant impact on participants everyday lives, requiring many changes and support required for daily self-care tasks, with feeling of frustration, anxiety and isolation reported (Sumner et al.). It is important for a photovoice study to be conducted here to explore COPD and its impact on COPD to see what this novel approach to understanding quality of life in COPD might uncover that can support patients and health care in the management of COPD. It is surprising that Sumner is the first photovoice COPD study of its kind as photovoice has been used as a method to understand similar phenomenon in other health conditions. Parker (2021) used PhotoVoice to explore the daily experiences of living with multiple sclerosis (MS), specifically in relation to the invisible symptoms that patient's do not discuss with clinicians and healthcare professionals. The findings provided insight into the daily challenges of MS symptoms and the invisible symptoms that require support from clinicians, but the key finding related to the psychological impact that symptoms had on the patient's quality of life, including their psychological well-being. This insight using photographs and the adjacent semi-structured interviews enabled a perspective that semi-structured interviews and questionnaires would have not been able to provide.

Using PhotoVoice methodology, patients are regarded as experts of their own lives; the research provides patients with the chance to be able to communicate about issues that are important to them, which provides researchers a different perception of the patient's world that they are living in (Ruby, 1991). It is important to incorporate visual methods within qualitative health research, to amplify participant voices, with the potential to find new knowledge, which has not resulted from surveys or qualitative interviews so far. Photovoice therefore enables the researcher to capture the lived experience of the patients regarding the specific phenomenon

the patient is trying to convey (Plunkett et al., 2013), without the influence of the researcher's presuppositions (Brunsden & Goatcher, 2007). This is beneficial for this study as quality of life may mean different things to different patients (Bowling & Windsor, 2001). Using photographs patients can convey deeper meanings of the world that they are living in, as this can encourage patients within the interview discussions to think more reflectively and express not only thoughts but also feelings and other issues that are meaningful to the patient from a phenomenological stance (Glaw et al., 2017; Raggl & Schratz, 2004).

The aim therefore of this study is to explore the impact COPD has on quality of life using photographs that capture patient's experiences as they happen, to help understand the true impact that COPD has on quality of life (physically, psychologically, socially, economically) and the meaning of this on everyday experiences (van Manen, 1997) through a phenomenological lens. Phenomenology will influence data collection and analysis as it is important to understand how individual's make sense of their lived experience of COPD and how these impacts on their quality of life. The findings from the study will add to the depth and breadth of existing literature on the understanding of the impact of COPD on day-to-day quality of life to inform recommendations for holistic self-management strategies to maximise quality of life, which forms part of the aims of the NHS Long Term Plan, (2019) for patients with long-term conditions (as discussed in chapter 1 literature review). A further aim is to make recommendations for health care professionals and providers of strategies they can support patients to adopt in routine care to promote better outcomes for patients.

4.1 Methods

A detailed overview of method and methodology is outlined in Chapter 2. This section presents key details pertaining to the methods used in this study but should be read with reference to chapter 2.

4.1.1 Design

This qualitative study utilised a photovoice methodology to explore the impact of COPD on quality of life. Photovoice involves participants taking several photographs that represent experiences that are important to them and discussing these in a semi structured interview. Whilst the photographs form data in and of themselves, the primary purpose of the photographs is to elicit more detailed responses from participants in the interview.

4.1.2 Ontology and Epistemology

The researcher's theoretical perspective both ontologically and epistemologically has been considered, as it is important within qualitative research for the method of data collection, method of analysis and theoretical framework to be aligned, so that the research that is produced can meet the research aims of this study (Braun & Clarke, 2006; Chamberlain, 2015). In brief the study design is from a constructivist philosophy, with an interpretivism epistemology applied, with interpretation from a critical realist approach. There is a detailed discussion of these in Chapter 2 (general methods regarding study materials).

4.1.3 Participants

Eight patients were recruited from the researcher's database of individuals with COPD, who had consented for the researcher to invite them to participate in related studies following the initial survey conducted as part of this PhD (n=3) or through The British Lung Foundation Breathe Easy group (n=5).

All patients were of White British ethnic origin, with the majority being female (N=7) and aged between 60-77 years (M=70; SD 5.52). Patients had a diagnosis of emphysema (N=5) or chronic bronchitis (N=2), one patient did not know their diagnosis beyond having COPD more broadly. Most of the patients had a diagnosis of at least 5 years, and all but one had physical comorbidities (e.g. hypertension, heart failure, etc.). The majority had a history of smoking (N=5), and half the sample had experience of pulmonary rehabilitation. Please see table 4.1 below for the demographics for the individual patients.

Table 4.1. Demographics of individual patients

Participant (pseudonym)	Age	Type of COPD	Duration of having COPD	Location	Smoking Status	Smoking Years	Comorbidities	Current Medication
Sue	71	Chronic bronchitis	10 years+	East Midlands	Ex-smoker	28.5	Heart Failure/Heart Disease, Asthma, Sleep Apnoea, Anaemia	Inhalers: Salbutamol, Tioropium, Steroid Tablets: Theophyline, Steroid, Antiobotics Other: Nebulised medicine (NM)
Jane	60	Emphysema	10 years+	South East	Never smoked		Hypertension, Asthma	Inhalers: Terbutaline, Steroid
Jacqueline	72	Don't know	5-7 years	East Midlands	Ex-smoker	13	Hypertension, Asthma	Inhalers: Salbutamol, Tiotropium
Aimee	73	Emphysema	10 years+	South West	Ex-Smoker	43	Hypertension, Diabetes, Asthma, Osteoporosis, Anaemia	Inhalers: Salbutamol, Aclidinium, Steroid Tablets: Theophylline, Carbocisteine, Antibiotics Other: Ambulatory

								oxygen therapy (AOT)
Pauline	77	Emphysema	10 years+	London	Ex-smoker	40	Rheumatic disease, Rhinitis	Inhalers: Tiotropium, Steroid Other: AOT
Pat	65	Emphysema	5-7 years	South East	Ex-smoker	11.2		Inhalers: Salbutamol Tablets: Carbocisteine, Steroid, Antibiotics
Teresa	75	Chronic bronchitis	7 – 10 years	North West	Ex-smoker	36.2	Hypertension, Asthma, Osteoporosis, Stroke	Inhalers: Salbuatomol, Tiotropium, Steroid Tablets: Theophylline
Philip	72	Emphysema	2-5 years	North West	Never smoked		Heart Failure/Heart Disease, Diabetes	Tablets: Carbocisteine

4.2 Materials

Patient facing documentation included the patient information sheet (Appendix I) and consent form (Appendix J) (hosted in Qualtrics), a photovoice information and instruction handout (Appendix K) and a study debrief form (Appendix N). Patients used their own mobile telephone device to take photographs; the researcher generated a Microsoft Word handout of each patient's photographs for their reference during the interview process (Appendix M), which were hosted in Microsoft Teams. The Signal mobile phone application was used to facilitate patients sending their photographs to the researcher and a semi-structured interview schedule was used to guide the interviews (Appendix AZ). Software was used to aid recording (Open Broadcast Studio) and transcription (Express Scribe).

4.3 Procedure

Please see the step-by-step procedure in figure 2.1. An email invitation was sent to patients who had consented to take part in further research from the survey study. Patients from the Breathe Easy group were recruited by forwarding an email to the head of the Breathe Easy group Teresa Burgoyne, who sent this to the group. Both patient groups were sent an email which included a link to a Qualtrics survey, including the participant information sheet and consent form. On completion of consent, the PhotoVoice handout was emailed to the patient and a suitable time for the interview arranged. This was scheduled in advance to give patients time to take suitable photographs and send a sample of these to the researcher. This was done prior to the Microsoft Teams interview via Signal mobile application. During the interview a handout with the photographs the patients sent were uploaded onto the computer and formed the basis of the discussion within the interview. The interview was recorded using Open Broadcast Studio, using a password protected laptop and the audio recording was transcribed using Express Scribe prior to analysis.

4.4 Analytic Strategy

The interview transcripts were analysed using Thematic Analysis (Braun & Clarke, 2019), using their six steps including familiarisation of data, generating codes, generating initial themes from the codes, reviewing the themes, and then finalising key themes and reporting the findings. There is a detailed overview of the analytic process in chapter 2 (p.47). Since the original submission of the PhD Braun & Clarke (2019) have revised thematic analysis from

what they described in their original 2006 paper, which is now referred to as reflexive thematic analysis (RTA). Within RTA includes the stages of developing, analysing and interpreting qualitative data. Despite the researcher not utilising this in the analysis of this study, patterns *across w*ere developed, analysed and interpreted by the researcher, and *discussed within supervision to prevent bias and to increase the reliability that the patterns included in the final analysis were accurate to the qualitative* dataset. In addition, as discussed in chapter 2 regarding reflexivity, the role of the researcher's own experiences, knowledge and socioeconomic factors were discussed and acknowledged openly. This included coming from a working-class background, being in a position of power as a PhD researcher, being male and considering what that brought to the interviews (either consciously or subconsciously) and critically interrogating this. The researcher experiences ongoing depression, which enabled him to show empathy and sensitivity as he probed further in the interviews. Having active and reflective supervision with the researcher's female supervisor helped the researcher to construct and accurately analyse, interpret fand finalise the qualitative themes and reflect on how the researcher actively interacted with the data. The data was flooded with information relating to COPD (which the researcher does not have) and patients were much older than the researcher so it was important to consider how this all comes together collectively. As such, despite not using the specific RTA framework from Braun & Clarke, (2019), the thematic analysis closely resembles this with a reflective approach to analysis being taken throughout.

4.5 Ethics

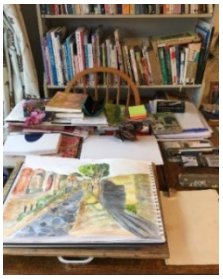
Ethical approval was obtained by the College of Science & Engineering Research Ethics Committee at The University of Derby (Ethics Approval Reference Number: ETH2021-0357).

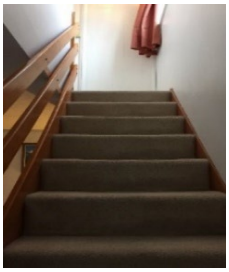
4.6 Findings

A total of 67 photographs (Appendix X-AE) were submitted and discussed across eight semi-structured interviews. The focus of the interviews centred around a discussion of the photographs provided and sought to explore the impact of COPD on quality of life in relation to symptom experience and use this information to contribute new insights into the strategies that patients use to cope with their COPD.

Three themes were generated from the thematic analysis including self-criticism, shame and emotional responses to COPD, interactions and relationships with others and strategies and methods to help with wellbeing and managing the impact of COPD. Embedded throughout these themes is the experience of breathlessness, which underpins the emotional responses that patients feel in relation to loss, change and experience of others. Each of these themes is discussed in turn, evidenced with photographs and quotes from the patients. The themes are represented in figure 4.1.

Thematic Map





Breathlessness – the primary symptom

Theme 1

Self-criticism, shame and emotional response to COPD

Theme 2

Interactions and relationships with others

Theme 3

Strategies and methods to help with wellbeing and managing the impact of COPD

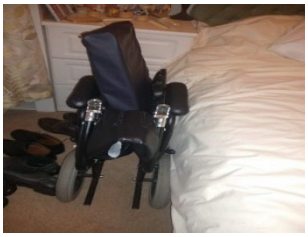


Figure 4.1. Thematic map showing themes and illustrative photographs

4.6.1 Breathlessness – the primary symptom

Breathlessness was the primary symptom reported by all participants which most impacted on their quality of life in a multifaceted way. The experience of breathlessness was linked explicitly to patient's experience of loss, pertaining to loss of physical abilities, loss of opportunity to engage in usual activities and loss of social inclusion. This in turn influenced patient's emotional response to having COPD which is addressed in theme 1. Breathlessness also influenced the way in which participants perceived that they were viewed and treated by others and drove their attempts to self-manage their condition. Breathlessness has been included not as a theme per se, but as something that permeates through all the themes. Whilst the experience of the symptom is discussed briefly first, it is then incorporated as an explanatory factor underpinning all three themes subsequently presented.

Reduced mobility results from the deterioration of lung function as the disease progresses (Sillanpää et al., 2014). Pauline took a photograph on the staircase leading to her third-floor property (figure 4.2) and describes living on the third floor as a "COPD nightmare". The true extent of the impact of this is the push for Pauline to re-house to a more suitable and accessible home, but unfortunately the accommodation being offered is not fit for purpose. It also means that Pauline reduces her activities of daily living to avoid interaction with these stairs, which she must tackle in one go. Breathless also impacts Pauline beyond the home; Pauline describes being faced with stairs whilst out and about as a "heartsink" moment, as the inevitability of a poor and frustrating experience of climbing stairs is recognised. Whilst Pauline says this "bugs" her, she follows this with "that gets to me". "Bugs" implies that this is a minor irritation or frustration but "gets to me" extends this to something that she finds quite frustrating to have to deal with.

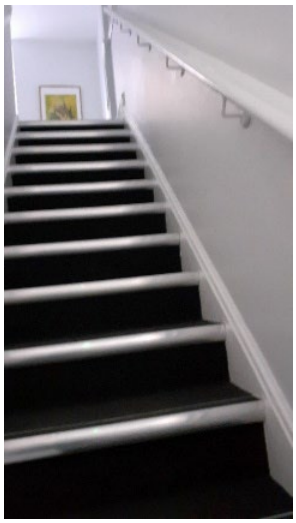


Figure 4.2 Photograph from Pauline

Description underneath 'COPD nightmare living on 3rd floor'.

".....I mean I've pushed to try to rehouse myself and having been in the same premises for a long time and I know where my Wi-Fi plug is and I know where you know the idea of setting everything up and I did see a flat locally that they offered me as a transfer because I'm in housing association property lucky lady really am and the front room was the size of my bathroom I mean it was totally impossible I mean I the

downsizing would do me good" Pauline

"well, you are supposed to take things slow and to manage them but there's no way you know pace yourself this sort of thing you know don't do everything all at once you know…. which is up three floors so it's a lot of stairs rather than I take I take a bit of a time fumbling for my keys at my own front door but it does put me off like oh I'll post that letter tomorrow or I think I've got a delivery downstairs or I'm expecting a you know it's my birthday shall I go down all those stairs to see if I will get any birthday cards fingers crossed Pauline

"…I can just feel my heart sink when I think of stairs and I have tried to avoid them in the past … but if the Tube is out somewhere and I'm faced with stairs it's really yeah it's not a nice feeling at all… it's difficult to describe it other than a heartsink moment it is not fear it's just I'm pretty sure what the result will be and I don't like it and it's the only thing really in COPD that bugs me that gets to me" Pauline

Breathlessness impacted patient's ability to engage in basic tasks such as not be able to walk for very long without having to pause to regain breath, not being able to put socks on or lean over to peel vegetables (figure 4.3) and impacts on activities that they engage in. For Sue to be able to do such a basic task as peel vegetables for her and her husband, it is easier to breathe if she leans forward on to the kitchen worktop, otherwise breathing is difficult, showing the need to adapt to undertake even very basic day-to-day activities. The simplicity of this activity illustrates the permeating impact that breathlessness has on all aspects of patient's lives. Sue states that her husband does come and help afterwards, suggesting that she needs support and that both are a collective team. Pat has had to adapt the type of swimming she does to enable her to continue this activity. Despite feeling "silly" being able to swim is valuable to her and gives her a sense of pride.

Figure 4.3 Photograph from Sue

Figure 4.4 Photograph from Pat

> *"that is right I have to lean when I am doing, I am leaning now I have to lean when I am doing nearly anything right because it seems to open up the lungs...but to me it seems to open the lungs so you can get more air in...I do that when I am washing pots or doing veg sitting talking if I am on my iPad and talking to you and I am leaning...but what I tend to do is I lean with my stomach on the edge of the worktops.....and then I'm like this peeling veg and potatoes and stuff.....sometimes I can't even finish cooking it my husband has to come in and finish cooking the meal"*
> *Sue*

> *"I've had to adapt the swimming to with the breathlessness so I do one alternate lengths of crawl and the other one is old English back stroke I don't know if you know the old English backstroke is the two arms going back together you do frog legs and that looks really silly so I keep my legs together and yeah it's also the time I've got much quicker and you know there's not many of us who could swim like that and I'm so proud to be able to say yes I can this afternoon despite having a bit of a chest at the moment"*
> *Pat*

The experience of breathlessness caused some patients to avoid activity (for example a walk with friends or family) particularly if there was likely to be an incline (see figure 4.5). In other cases, patients reduced or stopped doing activities they enjoy or roles that they held due to the symptoms they experienced or the wider impact of COPD (e.g. not feeling well).

Figure 4.5. Photograph from Sue of a hill she cannot walk up *Description underneath the photograph states "If I only could climb up there. I couldn't do it even through being breathless".*

> *"and we was walking along and I already had walked so far and I had to stop and what I would have liked to do have done would have been to walk up the hills and there was no way that I could do it so I just stopped and they went off (laughter)…I mean when I was younger I used to climb up different hills and so you get to an age or illness and you can't do it and it's sad really…you can't do it…you are missing out on so much and you can't do these things…anything like this that happens my husband says I will take the photos and I will bring them back to you and that is what he does but it is not the same" [Sue]*

As Sue discussed this photograph, she crossed her arms lightly (like an artificial hug) and her tone of voice slowed. Even though at times she chuckled it seemed out of sadness and a strategy to not get upset. Feelings of frustration also came through at not being able to join her husband and family members to the top of the hill. Figure 4.5 provides insight into Sue's perspective; walking behind her husband, the hill she would like to walk ahead but she knows she will be left behind, unable to climb it. Her sense of sadness was mixed with some resentment about the family taking photographs of the views from the top of the hill for her to view when they returned, but she was missing out, waiting at the bottom. As Sue states, "it's not the same".

Aimee expresses that because of the impact of her COPD, she was unable to predict and be certain that she could arrange set specific, regular classes for her yoga clients. This uncertainty resulted in her stopping teaching as she didn't want to let people down, but she expressed disappointment about not being able to continue teaching classes.

"Mean I used to teach yoga at one time but I but I haven't taught for a long time because I can't guarantee how I am going to be feeling and you just can't stop a yoga class one day and for the next two weeks say I'm sorry I'm not well so I don't" Aimee

The experience of breathlessness then underpins decisions that patients make about what they can do moment by moment and day by day. It impacts on their activities of daily living (completing basic tasks like posting a letter), it changes the nature of activities they might engage in with family and friends and impacts on their ability to carry on working activities. The nature of these changes result in emotional distress and impacts patient's relationships with others. These ideas are explored in the next themes.

4.6.2 Theme 1: Self-criticism, shame and emotional response to COPD

Whilst it is widely acknowledged that individuals with long term conditions frequently experience psychological co-morbidities (Harston, 2023), patients in this study report a range of emotions, some that they keep hidden purposefully or inadvertently, in response to their physical symptoms. Of particular interest is the feeling of shame and self-criticism associated with having COPD, resulting from the knowledge about the cause of the condition and the embarrassment associated with the physical symptoms that are highly visible to those around them. As well as taking steps to hide their emotional responses to their condition, patients also adjust their behaviour to hide the impact of their symptoms to avoid feelings of embarrassment. The primary emotion that was described by participants was the feeling of shame; whilst not all participants reported this emotion directly, participants did report behaviours and other similar feelings that denote feelings of shame. For some participants the feelings of self-criticism relating to the cause of their COPD were explicit, with Teresa reporting that her home environment that was filled with tobacco smoke as a small child and her own smoking behaviour had resulted in her COPD. Teresa has clear causal attributions for her condition, understanding her exposure to smoke as being a primary cause and owning the blame for this. This does not allow her to give way for self-pity, but rather she sees this as a means by which she can be proud that her experiences and education of her family mean others are not following in her footsteps.

> *"but I'm easily reduced to a kind of self-criticism which is pretty close and I don't I don't allow I try not to allow myself kind of self-pity because I think why am I like this number one I was born with severe asthma… my grandfather and my grandmother was very heavy smokers… so I think as a little baby lying in my cot I was probably subjected to a very polluted atmosphere and I must have had a genetic tendency… when I was at university very foolishly given the fact I suffered from asthma I started smoking and I smoked for a number of years so therefore I brought this on myself; [partner name] and I always knew it was a silly thing to do but I would think … when I had got over*

this particular crisis of over work then I'll give up and that that took me to 1975 when I was 49 years old before I thought this is ridiculous and I gave up smoking completely… I often have a lowish mood because I think life is so short why did I do it, so it is it is self-blame" Teresa

It was pertinent that patients reported substantial changes in their behaviour to help them hide the impact their COPD had on them. This seemed to be to avoid embarrassment due to feelings of shame towards the impact COPD had on them physically. What was surprising was that this related to hiding the impact from work colleagues, family and even strangers. This hiding was done through a range of behavioural responses, such as taking public transport instead of walking short distances (to avoid turning up at the office in a "dishevelled state"), stopping to look at and admire scenery to facilitate and hide necessary breaks from an activity to reduce breathlessness, and pretending to cross the road to avoid being seen as "weird".

Figure 4.6. Photograph from Jacqueline of a train platform *Quote underneath the photographs "There's a steep hill from the train station to the bus stop I need. It's quite short but hard work and on a cold morning it makes me cough. So, I take more time and wait for the tram to take me up to the flat part of town and the bus stop"*

"I don't want to look dishevelled in the meeting out of breath and coughing all over people, so my default is to get the train and then go get the tram and then I feel okay physically but at the same time I feel bad about it because it's cheating" Jacqueline

|Although evident across the data, Jacqueline provides some explicit examples of how she actively plans strategies to hide her COPD from those around her. The purpose of this seems to be to maintain her "pre-COPD" identity, in addition to her dignity. However, even though she has implemented strategies to protect herself by reducing breathlessness (or the appearance of breathlessness) to manipulate what others think, she feels as though she is 'cheating'. When discussing this photograph Jacqueline explained that prior to the COPD she would have walked to work, without any need for public transport or the avoidance of hills; she was able to walk long distances, without any breathlessness. Therefore, the feeling of cheating was in the sense of avoiding activity by using activity, which minimised the visible appearance to others of her COPD.

Struggling to accept having a diagnosis of COPD, its associated disability and the associated feelings of shame may result from a threat to the patient's identity. Such a change in lifestyle for participants in all areas of their lives had a significant impact, with Teresa describing herself through a photograph as an indoor plant – unable to be where she should and wanted to be (outdoors), and instead, shut in (figure 4.7). She explicitly stated that she would deny having a disability but coming around to the idea that they did have a long-term health condition, demonstrating some ability to identify with the changing status of her health due to COPD.

Figure 4.7. Photograph from Teresa of her indoor plant Description underneath the photograph – *"This is taken by me from my chair in our little back conservatory. This room is where I spend most of my days, because it is bright and the nearest place, I can be to feel almost out in my beloved back garden, but try as I might, I do feel almost shut in, behind the plant, a kind of indoor plant myself these days."*

> *"They said oh do you consider yourself disabled absolutely not but now quite often they say do you have a chronic health condition and I used to say no but I think now I say yes"*
> *Jacqueline*

Stigma associated with conditions such as COPD may play a role in this threat to identity, in that if someone has a long-term condition and/or disability they may be regarded as 'weak' and different to the rest of society (O'Donnell & Habenicht, 2022). This stigmatising adds to the existing shame and guilt associated with having caused the condition in the first place. Below Pat discusses that COPD was the "new me" when diagnosed shortly after the loss of her husband. She was in a position where she felt that she was her condition, but through circumstances she was able to experience a sort of post traumatic growth, not accepting being a 'little old lady and going on holidays' referring to dependent and cared for elderly lady, but regained her identity and her social support, with supportive networks aware of her needs, but not feeling dependent on them.

> *"at first when you're first diagnosed you feel you have this feeling this is me this COPD is me but it's not you know I'm not my condition and yeah and since then I now have a partner……..when my husband died it was like I was a little old lady that had to be taken care of and go on holiday with things like that and I am far too young for that yeah so that the sort of two things are going on here all the time my husband dying and then me not long after being diagnosed yeah they are there if I should need them like my friends are but they are not sort of like worrying or anything which is important I think"*
> *Pat*

A further contribution to feelings of shame comes from an undertone of patients being aware of and accepting their potential (or known) contribution to the onset of their COPD. Patients were able to reflect on and accept the diagnosis and what this means for themselves and for those around them (e.g. people who formed part of their social networks). It was therefore interesting that patients regularly changed their behaviour to hide the direct effects that their COPD had on them, both physically and psychologically, and how others changed their behaviour towards them based on their perceptions of the potential impact of their condition. Patients changed their behaviour to hide the COPD from others, including members of the public (seemingly strangers) or closer networks, such as friends and family. This included changing routes to work and avoiding walking (see figure 4.6) to hide the effect of symptoms such breathlessness and coughing. These issues were particularly important for two patients.

Jacqueline expresses anxiety about what those close to her and those who are strangers may think of her when she is experiencing breathlessness. She describes managing anxiety about

the need to stop by the side of the road to get her breath back by pretending that she is there to cross the road, worried that if she stands there on the pavement breathless, passing strangers will judge her. In the interview Jacqueline did come across as anxious, with closed body language, fast pace and heightened tone of voice. She gave the impression that she may have not discussed this openly before, as her concerns about what others think and the judgements people may have about her have such a significant impact on her psychologically. To pretend and hide your condition feels isolating, exhausting and feeling on edge when out in public, in addition to the breathlessness itself.

> *"… if I'm on my own there's (laughter) there is a particular steep bit in _____ I have to go to fairly regularly that I wait till there is cars coming and then I stop to crossover the road because stopping to crossover the road gives me that breathing space to get my breath back… if I just stopped at the side of the road to get my breath back it would look a bit weird so I wait till there are cars so I can pretend and waiting for the cars" Jacqueline*

Jacqueline also describes clear examples of hiding her symptoms from her family. Jacqueline again describes how she hides her breathlessness from her family to avoid looking "stupid". This is also depicted in one of her photos (figure 4.8).

Figure 4.8. Photograph from Jacqueline of snowdrops

Description underneath photograph states "Snowdrops. On holiday and there's a steep path up to the facilities. Oh, look I say, snowdrops, really I'm just stopping to get my breath back but I feel less stupid if I can pretend to be pointing out something of interest".

It is not just the physiological symptoms that are hidden but also psychological symptoms, whereby patients avoid seeing friends when feeling low because of the impact of their COPD. Avoiding seeing others reduces social interactions and is a loss to patient's sense of belonging and connection. For Sue it appears that only her husband sees the true extent of her COPD symptoms, which serves to preserve her dignity. It also maintains her identity and how others 'see' and think about her, preferring they remember her prior to the COPD diagnosis and manifestation of symptoms. For Pat, taking part in the Photovoice study brought her negative feelings about her COPD to the forefront of her consciousness, which had previously been 'packed away somewhere', hidden from self and others helping her to address these and recognise the impact COPD has on her psychologically.

> *"Oh yeah we have been married 50 odd years now… yes he is he is the only one that sees me really down in the dumps nobody else does because if I don't feel very good and want to see friends I don't go"*
> *Sue*

> *"One of the things that doing this (Pat is referring to Photovoice and taking part in the study) has made me realise I have an awful lot of really negative feelings about having COPD that I don't acknowledge you know I pack them away somewhere and a lot of dealing with it is about not dealing with those feelings so that's been quite an interesting process for me doing this (laughter)"*
> *Pat*

Hiding breathlessness and other COPD symptoms adds support to previous literature from Cooney et al., (2013), which was a qualitative study focusing on the meaning and response to living with COPD. The main themes were participants 'hiding' and 'battling' with the chronic respiratory condition, which 'co-exist', until the condition progresses into the later stages, whereby hiding is not possible anymore and the participant is left with the 'battling'. Cooney et al. also stated that many participants would attempt to hide breathlessness and coughing, making a conscious attempt at being away from other people and hiding the feelings of 'embarrassment', with one specific participant choosing to sit away from others when out of breath and/or coughing.

Hiding COPD symptoms from others appears to be associated with a form of social anxiety, valuing and being overly conscious of what others think of you. Harrison et al. (2017)

conducted a quantitative study exploring self-conscious emotions, reporting that COPD patients do have a significant concern about the view of others which supports the current analysis. However, from the perspective of self-compassion (including self-kindness and self-judgement) it is unlikely that others think any less of people who experience breathless or coughing; it is more likely related to the individual's self-criticism and judgement in the absence of self-kindness. For example, regardless of the cause of COPD (e.g. smoking or occupational exposure), imperfection, mistakes and failure in part is part of life and therefore we should be gentle with ourselves (Smith, Guzman & Erickson, 2018). Lindgren et al.'s (2014) report that individuals with COPD hold feelings of shame and guilt associated with their past actions that may have contributed to the development and onset of their COPD. For these individuals, their diagnosis feels like a 'slap in the face', promoting feelings of 'self-judgement' at being labelled as having COPD. A high level of self-criticism, conscious attention and value of what others (known and unknown) think in relation to the physical and psychological effects of COPD has a significant impact on the wellbeing of individuals with COPD.

Harrison et al. (2017) report that compared to healthy controls, patients with COPD have heightened emotions, including feelings of guilt and shame. Uncertainty for the future and the anticipated deterioration of the condition added a greater significance of being able to accept the COPD diagnosis (Lindgren et al.). Jerpseth et al., (2021) conducted a qualitative study focusing on shame for participants in the later stages of COPD and one of the main themes was a 'mirror of shame' and feeling a sense of being unworthy, with COPD defining their value as a human being, feelings like a burden to themselves and for those that support them. This is linked to the perception that COPD was self-inflicted due to smoking, contributing to feelings of self-blame and anxiety from the stigmatisation from others. This is also reflected in findings by Halding, Heggdal & Wahl (2011). The way an individual responds to their condition and its symptoms influences the way in which they engage with their social networks, which is explored in the next theme.

4.6.3 Theme 2: Interactions and relationships with others

Several patients expressed that their breathlessness and reducing mobility resulted in friends and family treating them somewhat differently, compared to before their COPD diagnosis. Patients all said that friends and family were helpful and supportive, but challenges arose when the support offered caused patients to confront their illness identity as they had to acknowledge and accept their COPD and its associated limitations. Furthermore, patients expressed that

sometimes they do not want assistance, support, or empathy from others as it takes away their sense of independence and personal identity but also appreciate it is difficult for their loved ones to see them struggling and their health deteriorating.

> *"I'm really pleased that she's also a doctor by the way but she doesn't comment I hate people commenting I really hate people oh you ok you know do you want to stop for a bit (growls) (laughter) because that is part of me not acknowledging it I suppose so I really appreciate that she just you know goes to the top with the kids and they just hang around and they wait for me she doesn't draw attention to it at all and that's very positive that's really helpful actually"* *Jacqueline*

> *"……..I have been spending most of my time sitting down in this sofa in the last month then I have probably done in the last six months so you know it is difficult when you are used to being independent and doing stuff yourself and then you can't really so when I'm sitting down I feel quite good but as soon as I start getting up and moving around that is when I realised that I just can't do that and that is quite hard and I think it is hard for the people that are around me even if they understand and know me well I think it can be difficult for them to cope with"* Jane

Given the limitations caused by COPD, equipment such as wheelchairs and walking sticks are often needed to support patients to engage in everyday activities and support integration and inclusion in their social world (see figure 4.9), but in some cases had the opposite effect. The need for aids can be difficult for patients to accept, exacerbated by anxieties about the potential perceptions of friends, family and members of public towards them. For Teresa the use of a wheelchair bought opportunities to increase mobility but resulted in frustration and anger about being excluded from social interactions as the wheelchair acted as a barrier to people communicating directly with her.

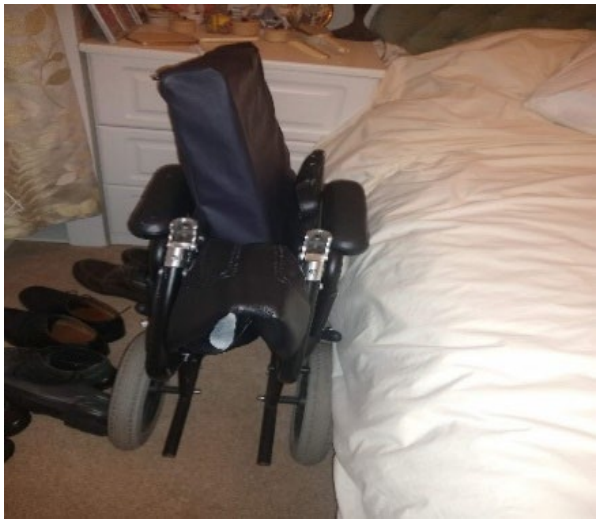


Figure 4.9. Photograph from Teresa of her wheelchair

Description under photograph "This photo is my wheelchair by my bed. I so wish I could be more mobile. Sometimes I decline the offer made by my husband to take me out, because I can't be bothered with the hassle and it can feel very cold and "marginalised" being in a wheelchair, despite a blanket over me!"

> *"I've got used to this [being in a wheelchair] but when you stop to speak to anyone the person that you meet talks to the person who is pushing the wheelchair not just physically in the sense like I'm looking at you now but it's like how is she but I'm in the wheelchair and a sound mind and I can communicate…it just makes me angry and makes me want to laugh really…you've got to look at life as it is haven't you not as one would have it be"*
> *Teresa*

Jane takes has both congruent and incongruent views on how others behave towards her due to her COPD. On the one hand and in accordance with the existing narrative, she sees that people want to protect her through offering support. However, Jane describes this as a response to the fear of breathlessness as something the individual has not experienced themselves, doesn't understand and is afraid to be around. As such Jane sees the support provided in relation to preventing breathlessness as almost a selfish intervention with avoidance of having to witness breathlessness as the primary motive for providing support.

> *"people who have not got any experience of that [breathlessness] before…can then distance people from you if it frightens them they don't want to experience that so they might start to distance themselves from you or they might take the other action which is to they want to stop you from becoming breathless or uncomfortable so they so they molly coddle you a bit… they think that by encouraging me to not do this stuff that makes me breathless they are helping me but unfortunately I am the sort of person that I am a bit of a free spirit and I did not like to be tied down…"*
> *Quote from follow-up interview of photograph below - Jane*

Whilst previous participants reported actively hiding the breathlessness and coughing, Jane states that for her, COPD is an invisible disability and not something that can be seen by others. Despite this she views COPD as highly restrictive, like the outfit worn by her cat due to a skin condition. Whilst the restriction is there for the cat's good and is visible to all, COPD is equally restrictive, and this is seen by some whose purpose becomes to protect you from it. Jane refrains from being "molly coddled", describing herself as a free spirit and the importance of this being retained by those around her is evident. This provides additional support to the notion that COPD brings about changes in relationships for patients with those close to them, regardless of whether the condition is visible through its symptomology or not.

Figure 5.0. Photograph from Jane of her cat *Description underneath photograph states "Picture 3 is about being restricted and different. Living with COPD means that you cannot just go and do things spontaneously or the way you could when young and fit. You feel different although most people don't notice. COPD is also a hidden disability. My cat had a skin problem that had to be covered up. People thought that we were being cruel by dressing him up, but it was done to prevent him causing more harm to himself. COPD is restricting and some don't see it, some see you as different and some want to hold you back to protect you".*

The role of close individuals providing social support for COPD patients is complex. This data reflects support types such as protective buffering and overprotectiveness, which lead to poor outcomes; both support types are associated with distress in patients with COPD as they hide their symptoms and worries about their COPD from their partners, which in turn affect the relationship and the psychological wellbeing of the patient (Meier et al., 2012).

The satisfaction of support appears to be more important than support generally. In the context of previous literature, changing behaviour to avoid social situations that includes stigmatised interactions from others has been shown previously, which includes decreasing social activities, that require the ability to be physically mobile, requires patients to be able to implement adaptations to still be able to take part in social events and activities (Berger, Kapella & Larson, 2011). Feelings of losing independence because of 'over' supportive family

has been reported previously, resulting in a change in dynamics between COPD patients and close family and friends (Gabirel et al., 2014).

Exploring the complexities of the interactions and relationship with others COPD patients face daily, a mixture of wanting to be independent but at the same time wanting to have support, when it is required, without feeling dependent on others and losing a sense of self, dignity and to reduce any form of stigma of feeling less than to others. On the other hand, a third theme explores the role of the various strategies and methods used to help with the wellbeing and the ability to self-manage COPD.

4.6.4 Theme 3: Strategies and methods to help with wellbeing and managing impact of COPD

All patients reported strategies to help them manage the impact of their COPD on their physical, psychological and social wellbeing (quality of life). One of the most prominent discussions through the data related to managing emotional wellbeing, which given the focus of data on the impact of COPD on their emotional health is unsurprising. Implementing problem focused strategies significantly helped patients to function, increasing quality of life and providing a sense of independence. Key strategies included maintaining some physical activity, engaging in meaningful activities (e.g. gardening), utilising practical aids and accessing medical care and support, including pharmacology.

Despite walking being difficult due to breathlessness and mobility issues half of the group expressed that walking (if it is flat and no steep inclines) helps to manage emotional wellbeing. This was especially important for patients whilst shielding during the COVID-19 pandemic (see figure 5.1). Some patients mentioned that walking gave them confidence that their COPD had not disabled every part of their daily life and activities.

Figure 5.1. Photograph from Jacqueline of a hill where she walks.

> *"obviously there were the first few months you were shielding about all the things about being careful where you go and not mixing with people and all the rest of it it's really limited the physical quality of life as well as having impacts emotionally but having said that we are lucky that we live somewhere where we you know it is about four miles away you can drive to and do lots of lovely walks and things so I've been doing that" Jacqueline*

> *"well I think it is just the endorphins really life feels better when I'm moving and you get that chemical effect you know I just feel better and I definitely feel more confident I mean I'm not I've never been a shy person if anything else if anything I am a bit arrogant really and I could do with a bit more humidity but to have confidence when you have a long term condition and to get from day to day is really important particularly you know if you have had a flare up and you think I'm never I'm never gonna get anywhere back to where I was before which is often the case" Jane*

Another activity that several patients found rewarding was gardening. This helped them to escape from the impact that COPD has on their quality of life, providing a form of mindfulness and relaxation (see figure 5.2). This helped them to feel grounded as well as helping to reduce breathlessness, provided a sense of purpose and seeing the flowers grow and blossom gave a sense of satisfaction, independence and achievement for patients (see figure 5.3).

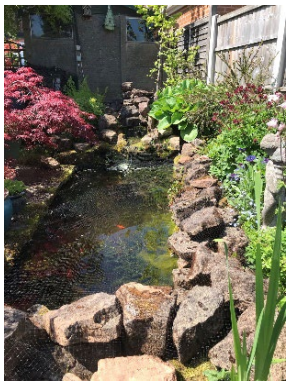


Figure 5.2. Photograph from Sue of her pond full of fish *Description underneath the photograph states "This is my restful place when I feel ill with COPD I just sit there and relax" Associated discussion regarding this photograph from Sue*

Figure 5.3. Photograph from Teresa of her daffodils. Description under photograph states "This photo is a delight for me, because last Autumn I did manage to plant a pot of bulbs, not being a big job, but one I could manage, and here they are flowering. What a joy and satisfaction to me this is! Maybe not a very big achievement by many folk's standards but hey. I did it myself". Teresa

Figure 5.4. Photograph from Pat of her allotment

"yeah, it's excellent yeah it's very rewarding it's also when you're gardening… you're in your own little mindset and time doesn't matter and you've got no idea what the time is or anything and you just get on with it"
Pat

These activities brought a sense of purpose in patient's day-to-day life which used minimal effort but had significant benefits.

> *"I mostly go up get up get dressed and go in to my little conservatory to have a light breakfast because I can see outside in the lightest light and it reminds me that I'm still*

part of the world and I can see every day the garden looks different and the garden as it is how I have made it in the last 12 years so there's always something to see and I find it lifts my mood takes me out of myself and I do have some indoor plants actually the one that I photographed the plant in the foreground was one I had in the garden and I knew it would die over winter so I managed to dig it out well I don't dig as I haven't got the strength but with a small trowel I got it out and put it in that pot and brought it inside and I have nurtured it over winter it didn't die so I again it gives me satisfaction that I'm connected with living things I can see the sky I can see the different weather conditions"

Teresa

Teresa used her love of gardening to illustrate how she was impacted on by COPD. She describes nurturing one of her plans over winter and the satisfaction she had that it didn't die. During the interview there was a sense that the way Teresa treated her plants and garden reflected what she would like to experience in her own life, i.e. to feel connected with the world and still like she is a part of it, to not feel isolated, to have a network of support, a change of environment and to be seen and to feel in the present moment again, despite the COPD symptoms.

Whilst physical activity and being in nature with purpose were important, practical support interventions such as perching stools, shower handles, walking sticks, chair lifts, wheelchairs were reflected in the photographs and portrayed how these things contributed to a sense of independence for patients particularly in relation to mobility within and outside of the home (see figure 5.5). The aids reduced the amount of help patients needed to request and supported them to maintain their dignity particularly relating to hygiene and bathing. These aids also provide a sense of reality for patients; the reminder that they must take time and use these things to enable them to do basic tasks. Existing literature suggests that perching stools help COPD patients to be independent (Scullion & Holmes, 2019), as well as wheelchairs help to improve quality of life (Shore & Juillerat, 2012).

Figure 5.5. Photograph from Teresa of her perching stool *Description from photograph states "This is my perching stool in my bathroom! A reminder for me that the process of getting wash/showered/dressed in the morning is a big effort for me and one I must take my time with, using the help offered by my perching stool, to sit down and rest, put my socks on, etc!! It's also a reminder of the considerable number of pieces of equipment I have to help me, walking sticks, crutches, grabbers to help me pick up thing I can't bend down and reach, back rests in bed etc., grab handles in the shower."*

> *"So yeah my perching stool I couldn't manage without it I'm often reading in the saga magazine about people of my age 75 who have just climbed Everest or some other thing and I think just putting my socks on is a massive effort (laughter)" Teresa*

Finally, patients held great value in treatment approaches uses such as ambulatory oxygen. Two patients within the study must use ambulatory oxygen (see figure 5.6) and both expressed that the ambulatory oxygen works, helping with breathing, being able to walk around without feeling breathless and maintaining some independence. However, both expressed that the ambulatory oxygen tanks are heavy and impractical, which limits their movements and options (e.g. air travel, low oxygen levels). This effects full independence of patients and creates barriers to living a good quality of life without COPD impacting day-to-day life.

Figure 5.6. Photograph from Aimee of her ambulatory oxygen machine

Description under the photograph states "Oxygen concentrator for ambulatory oxygen supplement. Essential when exercising or walking for longer period outside the house".

It is important that patients can draw on multiple strategies beyond standard pharmacological treatment to maximise patients' quality of life. Patients' quality of life is increased if patients can retain their identity and independence. Mindfulness and the ability to relax has shown to be of benefit mentally (Smith, 2021), providing some time away from the negative impact of COPD symptoms such as the breathlessness and coughing. Participating in gardening has been shown to be effective in improving psychological wellbeing and feelings of connectedness, which supports previous research and how it is beneficial for older participants generally (Austin, Johnston & Morgan, 2006). Despite the significance of nature and gardening for COPD participants, research has shown that unfortunately severe COPD participants do considerably less gardening and spending time with nature, compared to COPD participants that have mild to moderate COPD, which suggests that gardening and being in nature may be a temporary strategy but is not effective in the latter stages of COPD (i.e. high severity of symptoms) (Donaire-Gonzalez et al., 2013). In addition, equipment such as perching stools are of benefit to COPD patients and is consistent with previous literature, especially COPD patients that have severe symptoms and are in palliative care (Scullion & Holmes, 2011).

Research regarding nature connection and COPD is limited, so these findings that suggest it may be of value for patients with COPD should be explored further in appropriately designed intervention studies. The latest research has shown significant positive differences in psychological wellbeing for severe COPD patients who have had a nature based virtual reality intervention at home (McAnirlin, 2023). Also, current literature supports the findings here that patients with COPD that engage in multiple self-management strategies report improvement in their quality of life (Brien, Lewith & Thomas, 2016); as COPD progresses non-pharmacological strategies no longer support self-management and quality of life and additional strategies need to be implemented to promote positive patient outcomes. The experience reported about the importance of oxygen therapy, yet it being too heavy and cumbersome is supported by previous findings that this is a common experience which needs to be improved (Crisafulli et al., 2007). Therefore, this highlights the importance of different type of strategies that can help to increase quality of life and psychological wellbeing.

In summary these themes show how breathlessness permeates across all aspects of the daily lives of patients with COPD, impacting patients not only physically, but also psychologically. The photovoice methodology has been able to explore deeper meanings of the impact of COPD on the daily lives of patients, with the added depth of using photographs to capture nuances

and the reality of their lived experiences. This enables the researcher and participants to be able to extend discussions beyond the standard questions and discussion that may take place as part of routine clinical practice. From the psychology of self-criticism, shame and various emotional responses and the systemic factors that includes the interactions in addition to relationships with others in the daily lives of COPD patients, the vast range of strategies both pharmacological and non-pharmacological is very important for patients to feel a sense of independence, dignity, as well as various options of strategies which enable a sense of being able to self-manage. However, participants made it clear that the various strategies only offer so much before additional strategies are required, including psychological interventions such as nature and mindfulness to help maintain and maximise quality of life.

4.7 Discussion

The aims of the study were to explore the impact COPD has on quality of life of daily living regarding symptom experience, using photographs that capture patient's experiences as they happen and to understand the true impact that COPD has on quality of life. In addition to finding new insights into the strategies that patients use to help manage their condition daily. Quality of life is ubiquitous in nature, as the concept of quality of life is different across health-related, political and philosophical sectors (Muldoon et al., 1998), and therefore has been rather a challenge to scientifically conceptualise and operationalise and therefore study (Fallowfield, 2009). For example, what the specific elements are that make up health related quality of life (HRQoL) is unclear and so what the relationships between them is also difficult to ascertain (Ferrans et al., 2005). Regarding this study and PhD thesis, health-related quality of life (HRQoL) has been the focus, which includes physical, social, emotional and social wellbeing of the participants and therefore individuals (Karimi & Brazier, 2016; WHO, 2024). Semi-structured interviews were conducted to discuss patient photographs to be able to capture the complex and unique narratives of individuals living with COPD. Usual methods of exploring quality of life include the use of quantitative measures such as the St George's Respiratory Questionnaire (SGRQ) (Anandan et al., 2023), with patients restricted to fixed and inflexible answers covered within the questionnaire. Whilst the questionnaire can be useful within clinical practice to provide a brief parameter of the patient's level of quality of life and use to compare across time for example, it does not highlight inductively areas of quality of life that are unique to the individual, which is possible using qualitative methods. There is evidence that quality of life instruments does not effectively and reliably capture what is important to patient groups

in relation to their quality of life (Mathias et al., 2024). Ideally a mixture of both quantitative methodologies should be used to enable researchers to answer questions about quality of life that are best answered by the full range of research methods available to them.

Three themes were generated using Thematic Analysis (Braun & Clarke, 2006) namely self-criticism, shame and emotional response to COPD, interactions and relationships with others and strategies and methods to help with wellbeing and managing the impact of COPD. Breathlessness was the primary symptom experienced by participants, which intertwined across all three themes to contribute to understanding patient's experiences of psychological distress, changes to social relationships and strategies for self-management. Each theme is summarised and discussed in turn alongside a discussion of the contribution of these findings to the literature and consideration of the strengths and limitations of this study.

Breathlessness is significantly problematic for individuals with COPD and negatively impacts their quality of life. The photographs and interviews were powerful to show the vulnerability in patient's lives because of their breathlessness, which resulted in poor mobility and in turn limited activities of daily living, social connectedness and decreased psychological and psychosocial wellbeing. Any restoration of mobility gave a sense of control and freedom and the opportunity to engage in valuable activities, which are key to enhancing quality of life (WHO, 2024), such as being able to use a wheelchair. The process of adjustment to COPD is continual with changing demands associated with breathless and associated decreasing mobility. Adjustment processes influenced the emotional wellbeing of patients, with those struggling to accept their condition, its causes and its impact expressing feelings of self-blame, guilt, denial and shame. COPD patients have low self-compassion, high levels of shame with high levels of anxiety and depression, compared to healthy controls (Harrison et al., 2016), and this has been linked with poor adjustment to COPD in relation to everyday living and self-care (Kenefick, 2016). Kenefick found that if self-compassion increases, adjustment to living with COPD is higher and may increase psychological wellbeing as a result and could enhance quality of life. These studies are the only studies to the authors knowledge concerning the role of self-compassion in relation to adjustment and self-care, and so the findings of this study are valuable in highlighting more detail as to how patients respond emotionally to COPD in relation to self-criticism, self-blame and shame.

This study adds to the limited literature regarding the lack of compassion that patients with COPD have on themselves; a significant amount of self-criticism and shame seems to arise

from the belief that they have caused their chronic respiratory condition from their own smoking behaviour. There is some existing literature concerning patient's experience of shame regarding smoking habits and the impact of this on everyday life because of COPD symptomology such as breathlessness (Halding, et al., 2011). This study adds to these findings that patients experience high levels of self-blame and stigmatisation for causing their COPD (Halding et al., 2011), as well as high levels of shame because of the impact COPD has on them and their close family and friends (Jerpseth et al., 2021). Interestingly, Sigurgeirsdottir et al. (2020) found that family members that care for people with COPD also report high levels of shame, especially where the patient seems unable to give up smoking. Future research should explore the role of shame in relation to continued smoking related behaviour and other COPD related self-management behaviours. This study casts a little lighter on these negative emotional responses; it is recommended that interventions might include self-kindness and self-compassion-based components. A relatively recent 'unconditional self-kindness scale' has been published (Smith et al., 2018), which comprises of three subscales, namely 'being critical and rejected by others', 'failing or making a mistake' and 'becoming aware of personal flaws and imperfection'. This scale is yet to be tested with the COPD population but is recommended to be included as a measure to support progression and development in this area of research.

Feelings of self-blame, guilt, denial and shame emerged from the impact of COPD in relation to threat to the patients' identity, and patients being concerned about being perceived as 'weak'. This is congruent with models of adjustment to chronic illness, such as Leventhal's self-regulatory model of illness (Leventhal, 1992) and Moos and Schaeffer's crisis theory of illness (1984). Hiding symptoms seems to be a part of living with COPD, with patients hiding their condition and its impact from anyone they feel might cast judgement (including friends, family and even strangers). This seems to help protect their identity and maintain their dignity. Breathlessness is perceived to be embarrassing and so patients hide it. Hiding breathlessness and avoiding activities that cause breathlessness because they create a sense of shame and associated stigma is consistent with current literature (Cooney et al., 2013; Breaden et al., 2019). Pike, (2018) labelled this within COPD patients as 'shame-based avoidance', alongside guilt and feelings of embarrassment, however the sample of seven participants was small and larger studies need to be conducted. There is a sense of anxiety when around others, which seems to be driven by feelings of self-criticism, self-judgement and shame. Willgoss & Yohannes, (2013) conducted a systematic literature review and one of the main findings is that it is a common for COPD patients to feel embarrassed with being out of breath, especially when

in social environments and being around others, which contributes to feelings of anxiety and worrying about what others think and perceive.

The final theme relating to strategies that help with the self-management of COPD shows that a variety of different strategies ranging from walking, being mindful (e.g. watching fish in the back garden) and using walking frames and handrails helps to maintain some dignity and to manage daily life whilst continuing to experience significant levels of breathlessness and coughing which increases as COPD progresses. This leads to a loss of confidence, with patients needing support from loved ones and carers and experiencing feelings of vulnerability, losing a sense of self and identity. For example, on the one hand wheelchairs help patients to stay mobile but at the same time led them to being treated and perceived differently from others, which is difficult for patients to experience. It is important for patients to be able to maintain their independence (Sharma et al., 2023), yet despite the wide range of strategies utilised by patients, it appears that strategies decline in effectiveness as symptoms progress leading to increased sedentary behaviour, whilst also experiencing a lack of support for their psychological wellbeing during the later stages of COPD (Granados-Santiago et al., 2023). Further research needs to focus on what strategies are useful for each specific stage of COPD, how to support patients to best utilise the right strategies to enable patients to better manage their COPD for the best clinical and personal outcomes.

The photovoice methodology used in this study was the first of its kind to be applied to a COPD population within the UK. Indeed, there is only one further study in this area using this methodology, which was conducted in Singapore with a focus on the impact of COPD on daily living activities. (Sumner et al., 2023). In both studies photovoice has been shown to be an effective and highly beneficial research methodology, which provides patients with a voice that allows them to contribute something different to the standard semi-structured interviewing which even with little structure can be done in a way that imposes the researcher's agenda. This methodology allows the agenda to be driven by the photographs provided by the participant giving a different level of depth to the interviews than can be achieved otherwise. Informed by photographs from patient's daily lives, which include part of their identity and core vulnerabilities and an aid to help patients that struggle to verbalise and communicate (especially in clinical settings such as an interview) can express themselves better.

The findings of this study demonstrate the intersectionality of COPD across biological, psychological and social domains and how this collectively contributes to a diminished quality

of life. The findings support the dyspnoea inactivity vicious circle (figure 5.7; Ramon et al., 2018), which relates to the significant negative impact breathlessness has in the day-to-day functioning of patients with COPD.

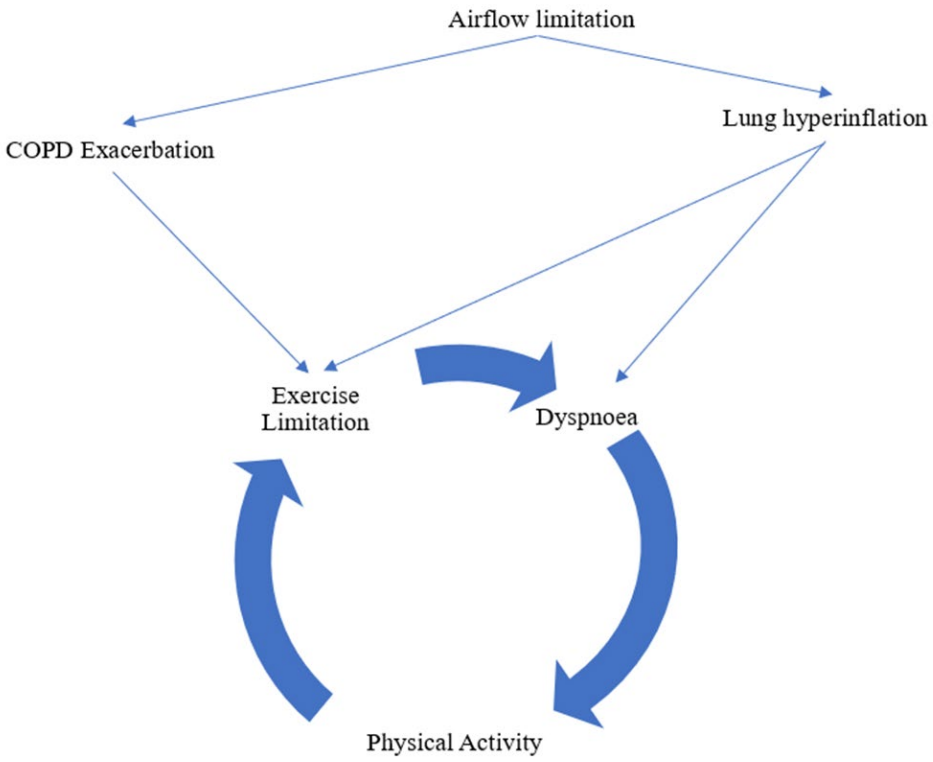


Figure 5.7. Ramon et al., (2018) diagram of the dyspnoea inactivity vicious circle in COPD

This cycle shows how airflow limitation impacts patients physiologically and how their subsequent behavioural response (inactivity) leads to ongoing physical symptoms. This is compounded by physical deconditioning through a lack of activity, causing patients to use more oxygen when they engage in activity which exacerbates feelings of breathlessness. The experience of a COPD exacerbation results in exercise limitation which then re-starts the vicious circle of breathlessness and physical inactivity. Furthermore, another form of airflow limitation such as lung hyperinflation can also cause exercise limitation or breathlessness starting the same vicious circle as the COPD exacerbation which maintains physical inactivity. However, quality of life is not included in this model and so it is proposed based on the findings of this study that quality of life is integrated into the model. For example, the data from this study shows as breathlessness increases, physical activity (which includes mobility, being able to carry out daily activities) are negatively impacted limiting the patients exercise abilities, which in turn increases sedentary behaviour. This lack of mobility and not being able to

complete basic self-care tasks, engage socially with others, reduces quality of life and overall wellbeing. As a result, it shows that quality of life is not only impacted upon by the experience of COPD, but also influences individual's responses to living with COPD physically, psychologically and socially. Therefore, an adapted model is proposed (figure 5.8) to demonstrate how reduced quality of life might be central to this cycle.

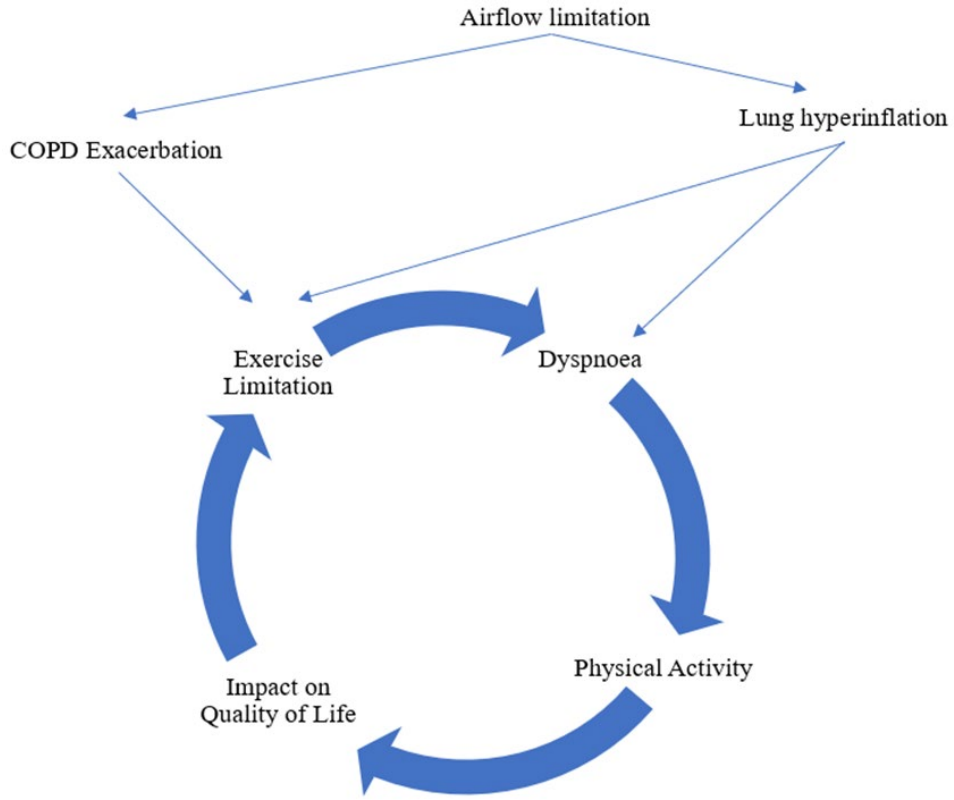


Figure 5.8. An adapted module to illustrate the role of quality of life in impacting and being influenced by disease and behavioural processes (adapted from Ramon et al., 2018).

In this study, photovoice methodology has offered deep insight into the day-to-day experiences of COPD from photographs in 'real time'. The photographs in addition to the patient interviews have allowed for a depth of data which has not been captured before in COPD research, specifically exploring quality of life in its entirety. Time was taken to ensure every patient was supported to take part in this research, given the anticipated barriers of engaging with multiple types of technology. This reduced anxieties and increased patient participation with all who started the study completing it.

Photovoice methodology enabled a shift in usual power dynamics; standard qualitative interviews are usually guided by the researcher's agenda whilst in this study, patients were permitted the flexibility, control and respect to take the photographs that they wanted, and to discuss openly about each photograph, which formed the basis of the interview schedule. This meant that the research was led by the patient. Of course, the researcher probed further regarding pertinent issues raised within the interviews, but the overall agenda and direction of the interview was patient led. The researcher feels that this gave patients a sense of control, respect for the researcher and the opportunity to express true vulnerabilities to living with COPD and the impact it has on quality of life. Also taking photographs across a two-week period, captured issues that in a standard interview study, may have been forgotten or missed. Taking photographs and expressing vulnerabilities to the researcher helped to build a strong rapport that included a mutual trust between the researcher and patient, that bought out the best of the patient to fully be comfortable and transparent, similar to a professional 'partnership'. This is supported from previous literature, whereby confirming that not only do patients have an active role, but this in turn also alters the power dynamic, whereby patients are the experts, which provides empowerment (Cleland & Macleod, 2021; Macdonald et al., 2022). All the interviews felt like a natural, in-depth discussion. Some patients expressed that taking part in the photovoice study was useful on a personal level to them, as a self-exploratory exercise. For example, one patient expressed that their COPD was impacting them more than they realised and needed to access support and others came to realise how valuable their friends and family have been in maximising their quality of life and how short life really is, and that needs to be appreciated. A possible application for photovoice is to be used within clinical practice, especially as COPD progresses, this could help with remembering what to discuss with clinicians with the use of photographs, that could help the clinician (doctors and psychologists) understand in more detail within the short amount of time within the appointment what the patient requires.

Despite its benefits, however, there are limitations of using a photovoice methodology. For example, some aspects of quality of life are hard to take photographs of (e.g. the experience of fatigue). Furthermore, research ethics meant that patients were advised not to take identifying images, which given the personal nature of their condition and the value of support networks makes it difficult to take photos that are meaningful. In future it would be worth considering whether there could be flexibility for patients to take personal and identifiable photos that are not included in the formal reporting but allow them to include personal photographs that

support their own commentary on how COPD impacts them, and the role of others in supporting their quality of life. The benefits for research and for practice could be significant with careful consideration for how these pictures are managed in relation to dissemination and publication. If the patient provides consent and would like to send photographs that are identifiable, this should be respected. A further consideration is the use of video. For example, symptoms relating to mobility are difficult to capture but can easily be explained in the follow up interviews. Short videos could be used alongside photographs, which is a method already tried by Volce (2019) and would offer a novel approach to data collection in the context of understanding the impact of COPD.

Whilst there were no patients in the study who had to withdraw due to barriers with technology, patients without access to the right technology were unable to take part in the study. This suggests some inequality in opportunity to contribute to this study. A funded study in this area would allow researchers to be more inclusive in providing suitable technology to enable wider participation. Furthermore, carers or family members could be included in a similar study alongside patients with COPD to widen the perspective in terms of how COPD impacts on the quality of life not just of the patient but also family units and/or wider social networks. For example, Reuss, Dupis & Whitfield, (2005) conducted a study interviewing family members perspectives on moving loved ones who have chronic physical conditions into long-term care. Exploring a different perspective and narrative (i.e. not the patient only) enabled the experiences and insight which collectively helps to increase the quality of care and support for the patient, as loved ones are often significantly involved in care. Reuss et al.'s (2005) findings included the experiences of carers waiting for the transition from family home to formal care home, who makes the decisions about care, the importance of communication, concerns about the support that will be provided and the perceptions and attitudes of the patient to be supported when moving. Therefore, the primary caregiver could add further insight and detail into their realities through photographs and caring for their loved one. The data from both the patient and primary care caregiver could provide an in-depth bimodal perspective, with great potential for rich and detailed visual data, as well as follow up interview discussions.

In this study the majority of participants were female, retired and married, with a mean age of 70-years old. Whilst this study provided rich detail in relation to these participants, it is important to replicate this work with other patient groups to ensure a clear understanding of these issues for all (e.g. male patients). Perez, et al. (2020) report that females with COPD experience more breathlessness and exacerbations compared to males, suggesting some gender

differences in symptom experience. Increased breathlessness in any sample would give rise to findings of this having an impact on them and needing to implement strategies to manage their symptoms, but there may be differences across patient groups that need to be accounted for and understood through methods such as this which give deeper insight into patient experiences.

Steindal et al., (2017) conducted a qualitative interview study in Norway to understand the experiences of women living with COPD at home. Participants had a mean age of 72 years and were retired. A content analysis resulted in three themes, namely 'having a good life with COPD despite limitations', 'predictability and confidence in getting help', and 'the struggle to achieve balance between insight and compliance with management in COPD'. Similarly, to this study, Steindal, et al. reported that participants found it difficult to use the portable oxygen supplies, as it negatively altered their appearance and they struggled to accept and to use the device when outside of the home. In this study participants did not want to use equipment such as a wheelchair as they felt it led to their exclusion. Participants across both studies utilised equipment such as shower stools to support day-to-day activities which helped them manage their debilitating breathlessness. However, Steindal et al.'s participants reported not having the energy or breath to be able to do basic tasks such as housework or socialising either in or out of the home. They did not actively seek support from their husbands as they felt this impacted their role and identity as a 'female'. This is likely related to the nature of illness as a crisis; Moos and Schaeffer (1984) outline crisis theory, a part of which suggests that illness brings about crisis due to the loss of multiple facets of life (work, social relationships, location etc), which impacts on an individual's sense of self. Working through these crises and sense of loss are vital for supporting adjustment to illness and maximising quality of life. Given participant's life stage and employment status, the contribution of the transition of retirement should not be overlooked. This transition is challenging, is associated with depression (Dang et al., 2022), increase in rumination and loneliness (Tong, Hou & Llang, 2021) and is influenced by family factors, previous occupation, finances and socio-economic status (Wang & Shi, 2014); the impact of also navigating a progressive chronic condition is likely to be significant.

Issues pertaining to employment and caring for younger families were not discussed by participants in this study as patients were retired. Whilst COPD is generally diagnosed in later life (Choi & Rhee, 2020), it can have early onset (Borras-Santos et al., 2019) making it important to understand the impact of COPD on quality of life for those diagnosed early on.

There are generational shifts in perspectives towards smoking behaviour, where smoking used to be accepted in society and was seen to be part of everyday life, to a shift whereby society are aware of the significant effect smoking has on health (Jiménez-Ruiz et al., 2021), which may influence some of the findings here relating to blame in relation to behavioural contributions to the onset of COPD. Knowing the negative effects that smoking has and still choosing to smoke despite the awareness and shift in society, shows that it is a choice of the smoker and the power of nicotine and addiction, including the changeover to electronic cigarettes. With growing awareness of the condition there has been the introduction of protective clothing to minimise exposure in high-risk roles, which also increases emphasis on the capacity, choice and autonomy of individuals in relation to smoking. It is yet to be established in high quality studies whether the use of electronic cigarettes may be associated with younger onset COPD as longitudinal correlational studies have not been conducted (Morjaria et al., 2022).

Participants were recruited via a COPD specific support group (Breathe Easy), which raises some questions about how these groups may impact of quality of life and whether these patients access support due to poor quality of life, or whether they have improved quality of life due to the support they are able to access. Being members of an active and regular community support group with clinician support may explain why participants did not have difficulty talking about the variety of different strategies used to maximise their quality of life. It is important to recruit those who do not access community support groups or other services whether that is because of mental health such as depression (Sohanpal, Seale & Taylor, 2012), mobility and physical capability (for example being sedentary because of poor health and not able to leave the house) (Mathar et al., 2016), avoiding adopting a patient role (Mathar et al.), feeling helpless or lonely (Reijinders et al., 2018), economic hardship (Jeon et al., 2009) and not feeling that their 'voice' is heard nor important (Macdonald, Higgins & Gibson, 2013). Harrison et al., (2015) identified self-conscious cognitions relating to shame and stigma as a further barrier to patient engagement with pulmonary rehabilitation. These barriers to engagement with services (and possibly research) may impact on an individual's quality of life, and limit access to personal and professional support that may facilitate improvements in wellbeing. Engaging those who do not access support in research is vital to understand the true vulnerabilities of this unheard, hidden group. Focusing on the 'able' (both clinically and in relation to research), i.e. those who have access to support, are mobile, are financially stable and who are technology literate does not give the full picture and does not help understand the

extent to which patients are impacted by COPD. Methods to recruit might include primary care registers of individuals with COPD, secondary care clinics or pharmacy.

From the findings of this study, there are several recommendations for clinical practice and COPD patients. Psychological therapy for this group is important to address the feelings of self-criticism, blame and shame, and a compassionate approach within clinical services would support patients with these responses. A place that is psychologically 'safe', a reduction of 'threats' and being able to have self-kindness, warmth and kindness is paramount for COPD participants. It is too simplistic to just focus on anxiety and depression from a clinical mental health model with no consideration of the impact of the physical health condition. If one-to-one psychological support could be provided, a blend of acceptance and commitment therapy (ACT) (Harris, 2006) and compassion focused therapy (CFT) (Gilbert, 2009) would be ideal. CFT focuses on the affect regulation system and recognises that those with high levels of shame and self-criticism have poorer access to the affect regulation system (Gibert, 2009); the aim would be to have warmth, safeness and soothing to increase self-compassion and to access the affect regulation system (Gilbert, 2009). The ACT approach considers the normal brain as destructive, creating psychological suffering and therefore seeks diffusion, acceptance and to work on values of oneself (Harris, 2006). A combination of these approaches may therefore be highly effective; this may be integrated as an approach within pulmonary rehabilitation, or as part of routine care.

Addressing the psychological health of COPD participants to help increase quality of life should also help physiologically. Austin et al., (2021) conducted a mixed methods systematic literature review regarding compassion-based interventions for people with long-term conditions, which focused on people with cancer or persistent pain. Interventions were either up to 12 face-to-face sessions or a brief single compassion exercise. The qualitative synthesis highlighted the significance of a reductions in anxiety and depression, with specific benefits regarding acceptance of the condition, an improvement regarding emotional regulation and lower levels of feelings of isolation. Despite not being specifically to COPD, it shows the benefits of specific compassion focused interventions for chronic long-term physical conditions. Imani, (2019) also conducted a systematic literature review focusing on compassion-based interventions on the effect and benefits on mental health, physical health and coping with long-term chronic conditions. Seventeen studies were identified for review. Positive effects were high for mental health but unclear regarding the benefits on coping with

the physical health condition and if it helps to improve physical health. The quality of the studies was low, and the results therefore need to be interpreted with caution. Differing findings of the efficacy of compassion focused interventions in chronic physical ill health from systematic review suggest a need for more research specific to COPD concerning whether these interventions may be useful in supporting patients' psychological wellbeing, and in turn their physical health and adjustment to living with COPD. Research should seek to understand whether compassion approaches to COPD patients can increase feelings of self-compassion and sense of acceptance whilst reducing anxiety related to breathlessness and concern about what others think of them. This should be offered within specialist services such as pulmonary rehabilitation, but also widely available through integration with psychological services such as Talking Therapies (previously known as Improving Access to Psychological Therapies), which do have some remit for supporting individuals with physical ill health as well as mental ill health (NHS, 2018). Pulmonary rehabilitation programmes within the United Kingdom already involve packed programmes including physical exercise training, patient-directed training, COPD self-management, and behaviour change (Silva et al., 2022); whilst it is recommended that compassion intervention is added alongside behaviour change, programmes may not feasibly add more to these programmes within their capacity. Furthermore, access into pulmonary rehabilitation is often only possible for those with more severe disease, not from the early stages by which point patients may be more severely impacted by their condition. Waiting lists are very long for access to psychological therapies, which limits access to psychological support. Careful consideration needs to be taken concerning how to best integrate appropriate and high-quality psychological support for patients with COPD to address complex psychological needs related to their adjustment and response to their chronic physical ill health.

Patients taking part in this study were those already accessing services and those with the means (technology) to take part. There are other individuals with COPD who do not have the same access to services perhaps due to the debilitating nature of their condition, or because services are not accessible them. Integrating psychological services within the same model of care is not likely to promote access to all patient groups. Careful consideration then needs to be taken as to how access can be widened for all patients. Access to the internet would be useful to enable online delivery by psychologists and/or psychological wellbeing practitioners that are specialist in long term conditions and mental health. If engaging with psychological interventions such as compassion focused therapy (CFT)/Acceptance and commitment therapy

is too burdensome, innovative technologies such as virtual reality could support efforts to promote the psychological wellbeing of COPD patients (McAnirlin, 2023), although additional research is needed into evidence-based interventions of this kind. In addition, men are less likely to attend psychological therapy and the men that do attend, drop out after an average of three sessions (Seidler et al., 2021). Therefore, an intervention such as virtual reality may increase uptake of interventions for male patients.

This study has demonstrated some of the complexity of COPD. Whilst there are common themes generated from the experiences of a range of patients, each is an individual and all have specific needs from a physical, psychological and social perspective. Findings suggest that patients struggle to adjust to living with COPD and manage their physical symptoms, which impacts on their psychological health. Patients report negative psychological outcomes associated with guilt from past health behaviours that may have led to the onset and progression of their lung condition, which results in behaviours which increasingly isolate them from their social networks which has a negative impact on their social wellbeing. Utilising equipment and accepting some support from friends and family is important to alleviate some of the symptoms and help patients manage COPD, but the effect of this is mediated by their psychological state.

In the context of this PhD these findings help to identify factors that impact the quality of life of patients with COPD largely due to of the physical symptoms of COPD and the impact of these on psychological and social wellbeing. The survey study reported in chapter 3 highlighted that a variety of factors impacts quality of life, which decreases as COPD progresses to later stages. This study has added further depth to understanding this, including how patient's emotional responses to COPD such as a lack of self-compassion towards oneself and high levels of self-criticism and shame impact on their quality of life. This study has also utilised a novel methodology (photovoice) and used technology to facilitate engagement from a range of patients to contribute to our understanding of quality of life in patients who are accessing support to help with the management of their condition. Whilst this study has discussed aspects of condition management, medication experiences were not prominent in this data set and so next steps are to explore in detail how patients engage with medication and other non-pharmacological interventions to support them in the management of their condition. Chapter 3 suggests that patients are taking multiple medications to support their symptom management, but this study suggests these may not be fully effective. Given the ongoing impact of COPD

on quality of life, understanding in detail strategies to manage symptoms will help identify alternative methods that might support better quality of life.

Chapter 5

A qualitative exploration of COPD symptom profile determinants and experiences of medical and non-medical interventions

5.0 Introduction

The quantitative study undertaken as part of this PhD and reported in chapter three highlights a range of medications patients take to manage their COPD, but patients continue to report a reduced quality of life and are unable to manage their COPD symptomology effectively. Breathlessness is reported to have a significant impact on patients, and this is echoed in the findings from the photovoice study reported in chapter four. As such it seems that the medical management of COPD through the use of medications and holistic interventions such as pulmonary rehabilitation, which should bring about improvements in the health status of patients through the prevention of deterioration and progression, helping to control symptoms such as breathlessness, reducing exacerbations and improving health status (Montuschi, 2006), do not have the desired effect. As such it is understandable as to why patients with COPD may seek additional interventions to alleviate their experience of symptoms and it is important to explore which pharmacological (i.e. medication) and non-pharmacological (i.e. self-management behaviours) are being used and understand patient's experiences of these including the impact of them on patient outcomes (both positive and negative). Whilst there is some overlap between the aims of this study and the previous photovoice study (both place emphasis on understanding patient's quality of life) they have distinct features. The Photovoice study specifically aimed to explore how COPD impacted on patient's daily experiences of quality of life and the strategies patients used to maximise this. The findings demonstrated the biopsychosocial impacts of COPD, with a richness of data relating to the psychological and emotional impact of COPD. Whilst there was some narrative concerning strategies to effectively manage COPD relating to maximising quality of life, there was not a deliberate focus on what specific interventions and strategies patients use to manage their condition in relation to symptom experience and progression. The focus of this qualitative study was to address this gap. The funding for this PhD came with the intention to conduct a randomised clinical trial to assess the efficacy of a non-medical device to improve symptom experience and quality of life; this study was designed to assess the need for and./or evaluate the effectiveness of such an intervention.

In chapter four one of the primary themes related to the strategies used by patients to maximise their quality of life. These included strategies to manage their emotional wellbeing (e.g. mindfulness), physical and emotional functioning (e.g. through activities such as gardening or walking) and practical strategies such as using chair lifts and wheelchairs to aid mobility. It is telling that medication use was not discussed by patients to a degree that was deemed

substantial enough to inform any of the themes. This gives some indication that it did not come to mind as something that either diminished their quality of life or served to enhance it. This study aims to understand more explicitly the symptom experience of patients with COPD and what interventions and strategies help patients, including medical and non-medical interventions. The research question being addressed through this study is "what is the effect/impact of COPD related symptoms on patients and what are their experiences of medication(s) taking and non-pharmacological interventions?".

5.1 Methods

A detailed overview of method and methodology is outlined in Chapter 2. This section presents key details pertaining to the methods used in this study but should be read with reference to chapter 2.

5.1.1 Design

A qualitative interview study was conducted to explore the symptom experience of patients with COPD and the impact these have, along with the interventions and strategies patients use to address these challenges and patient's perceptions of gaps in what is available to them to help them to live well with COPD.

5.1.2 Ontology and Epistemology

The researcher's theoretical perspective both ontologically and epistemologically has been considered, as it is important within qualitative research for the method of data collection, method of analysis and theoretical framework to be aligned, so that the research that is produced can meet the research aims of this study (Braun & Clarke, 2006; Chamberlain, 2015). There is a detailed discussion of these in Chapter 2 (general methods regarding study materials). In brief the study design is from a realist philosophy and epistemology, which informs the study design and approach to data analysis. For a detailed discussion of the researcher's ontological and epistemological position, please refer to Chapter 2 which concerns the methods used throughout the PhD.

5.1.3 Participants

Fifteen patients were recruited to this study from the researcher's database of individuals with COPD (n=6) (these patients provided consent to be invited to future research through the initial survey study), via COPD support groups on Facebook, Asthma UK and The British Lung

Foundation (n=3_ and through the Photovoice study (n=6) (Sue, Jane, Jacqueline, Aimee, Pauline and Pat [pseudonyms only]). Therefore, a total of fifteen patients were recruited into the study.

All the patients were from the United Kingdom, over half were female (n=10), and the mean age was 70 years. Half of the patients were married (n=8), all were white British, and nearly all were retired (n=12). The majority had a diagnosis of emphysema and had lived with COPD for over seven years (n=10). In relation to medication use, almost all (n=12) had short-acting bronchodilator, half had long-acting bronchodilators and over half (n=9) had an inhaler steroid; most patients (n=11) had pulmonary rehabilitation. Half of the sample had two comorbidities, the most common being hypertension and asthma. A detailed summary of each participant can be found in table 5.1 below.

5.2 Materials

Patient facing materials for this study include a participant information sheet (Appendix AG) and consent form (Appendix AH) and debrief sheet (Appendix HI). A Microsoft Teams handout (Appendix AJ) was sent to patients prior to the interview. A semi structured interview schedule (Appendix AL) was used during the interview. All documentation was shared with participants via email. Interviews were conducted in Microsoft Teams and standard software was utilised for recording (Open Broadcast Studio) and transcribing (Express Scribe) the interviews.

5.3 Procedure

An email invitation was sent to patients who had consented from the first study, which included the participant information sheet and consent form which were Microsoft Word documents that formatted to a pdf and attached to an email, so the forms can be read on multiple devices and programmes, increasing accessibility, therefore. However, patients that were recruited via Facebook, patients expressed an interest in the study by sending an email to the researcher (as the researcher's email was stated on the Facebook post), to which the researcher sent the participant information sheet and consent form. Patients were asked to complete and return their consent form to the researcher via email. After receiving consent, a suitable date and time for interviews was arranged, and these were conducted through Microsoft Teams. A detailed handout was sent to the patient via email before the interview to ensure participants knew how install and use Microsoft Teams. A semi structured interview schedule was used by the researcher to help guide the direction of the interview, although

patient responses were followed up with additional prompts as appropriate. Participants were debriefed verbally and were sent a written copy of the debrief. The interviews were recorded, and the audio recordings were transcribed. Transcripts were analysed using thematic analysis (Braun & Clarke, 2006).

Table 5.1. Qualitative demographics of individual patients

Pseudonym	Age	COPD Type	Duration of disease	Location	Smoking Status	Smoking Years	Comorbidities	Current Medication
Sue	71	Chronic bronchitis	10 years+	East Midlands	Ex Smoker	28.5	Heart Failure/Heart Disease, Asthma, Sleep Apnoea, Anaemia	Inhalers: Salbutamol, Tiotropium, Steroid Tablets: Theophylline, Steroid, Antibiotics Other treatment: Nebulised medicine (NM)
Patrick	70	Emphysema	7 – 10 years	Southeast	Ex Smoker	67.5	Heart Failure/Heart Disease	Inhalers: Salbutamol, Tiotropium
Melissa	66	Emphysema	5-7 years	East Midlands	Ex Smoker	45	Heart Failure/Heart Disease, Cancer	Inhalers: Salbutamol, Tiotropium, Steroid Tablets: Carbocisteine Steroid, Antibiotics Other treatment: NM, Ambulatory oxygen therapy (AOT)
Jane	60	Emphysema	10 years+	Southeast	Never Smoked			Inhalers: Terbutaline, Steroid
Malcolm	79	Emphysema	10 years+	West Midlands	Ex Smoker	30	Asthma	Inhalers: Steroid Other treatment: NM
Jacqueline	72	Don’t know	5-7 years	East Midlands	Ex Smoker	13	Hypertension, Asthma	Inhalers: Salbutamol, Tiotropium

Aimee	73	Emphysema	10 years+	Southwest	Ex Smoker	43	Hypertension, Diabetes, Asthma, Osteoporosis, Anaemia	Inhalers: Salbutamol, Aclidinium, Steroid Tablets: Theophylline, Carbocisteine, Antibiotics Other treatment: AOT
Pauline	77	Emphysema	10 years+	London	Ex Smoker	40	Rheumatic disease, Rhinitis	Inhalers: Tiotropium, Steroid Other treatment: AOT
Pat	65	Emphysema	5-7 years	Southeast	Ex Smoker	11.25		Inhalers: Salbutamol Tablets: Carbocisteine, Steroid, Antibiotics
Yvonne	69	Emphysema	7 – 10 years	Yorkshire & Humber	Ex Smoker	40	Hypertension, Asthma	Inhalers: Tiotropium, Steroid
Teresa	75	Chronic bronchitis	7 – 10 years	Northwest	Ex Smoker	36.25	Hypertension, Asthma, Osteoporosis, Stroke	Inhalers: Salbutamol, Tiotropium, Steroid Tablets: Theophylline
Tracy	76	Emphysema	7 – 10 years	East Midlands	Ex Smoker	50	Hypertension, Cancer	Inhalers: Salbutamol, Tiotropium, Glycopyronium Tablets: Carbocisteine Other treatment: AOT
Suzanne	61	Don’t know	2-5 years	East Midlands	Never Smoked		Rhinitis	Inhalers: Salbutamol, Steroid
Marcus	79	Don’t know	5-7 years	Yorkshire & Humber	Never Smoked		Hypertension	Inhalers: Salbutamol, Glycopyronium
Sophie	67	Emphysema	7 – 10 years	Northwest	Ex Smoker	7.5	Hypertension, Asthma	Inhalers: Salbutamol

5.3 Ethics

Ethical approval was obtained by the College of Science & Engineering Research Ethics Committee at The University of Derby (Ethics Approval Reference Number: ETH2021-0357).

5.4 Analytic Strategy

The interview transcripts were analysed using Braun and Clarke's six steps of thematic analysis (2006). Steps included familiarisation with the data, generation of codes, reviewing the codes and establishing these to generate themes, reviewing the themes and deciding which were most pertinent to the data and reporting these. Analysis was performed by the researcher and discussed in supervision. There was an ongoing process of revision based in reflective practice, interpretation and returning to the data.

5.5 Findings

Fifteen semi-structured interviews were conducted to understand patient's experiences of COPD, specifically their symptom experience and changes to this based on medication use and other medically based interventions (e.g. oxygen therapy), and engagement with non-pharmacological or alternative interventions.

Furthermore, interviews explored strategies and treatment approaches that might better support effective management of COPD and its symptoms. A thematic analysis resulted in the generation of three themes including the intersectionality of symptom experiences (sub-themes – breathlessness and sleep quality), medication issues (sub-themes – side effects and ineffective medications), self-management strategies and patient involvement. Themes are presented below and supported with illustrated quotes (see figure 5.2).

5.6.1 Intersectionality of symptom experiences

All patients expressed that they experience a range of symptoms that impact on their everyday life, which were directly or indirectly related to their COPD, although two evident in the data as the most impactful. These included breathlessness, and poor sleep quality which seemed to be inter-related symptoms as detailed below.

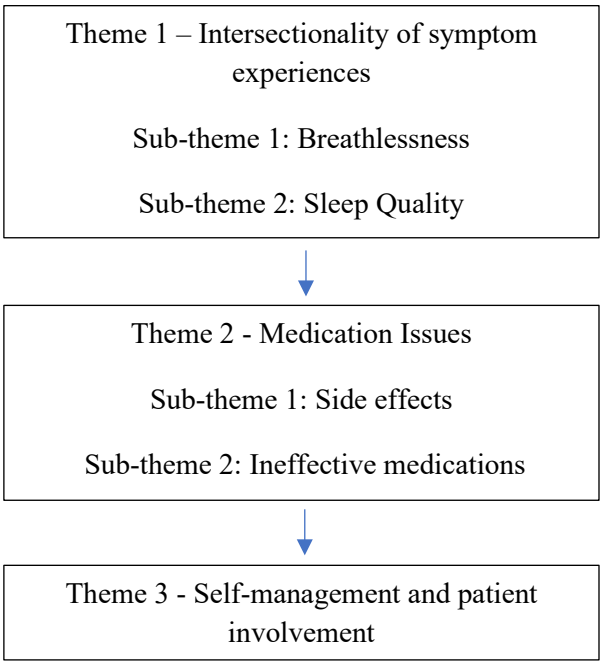


Figure 5.2. Table of themes

5.6.1.1 Breathlessness

The majority of patients reported breathlessness, which impacted on their day-to-day life by affecting their mobility and energy levels. Poor mobility associated with breathlessness meant that patients had to limit leisure activity, such as playing sport and walking long distances, which means that patients were limited in their day-to-day functioning and had limitations in their ability to engage in physical exercise and activity. Several patients in the later stages of COPD expressed that any form of movement resulted in breathlessness, with patients struggling to draw breath and becoming completely sedentary until breathing became possible again. Not only did patients express that it impacted their movement, exercise and ability to breathe, but energy levels as well. Some patients required regular ambulatory oxygen to be able to maintain mobility and an ability to breathe during even most basic tasks such as speaking.

> *"The main one being breathlessness…when I move at all you can see I've got oxygen on which I use when I move about but also for example if I'm taking part in a conversation I need that"*
> *Melissa*

> *"breathing lets you down every time start I start doing a bit of stuff and then the next*

thing is you can't breathe but then it puts you into a frame where you don't think you don't want to do that then why should I put myself in that frame" Marcus.

Breathlessness also severely impacts patient's ability to do basic day-to-day activities, such as washing and drying themselves; some patients mentioned that they require support from spouses, and others suggested that it can take longer, and additional strategies are required to make it more possible as breathing can be a struggle with bending and lifting. Some patients expressed that they had noticed a steady decline as the COPD has progressed.

"The one thing that surprised me is when I have a shower and I come out and dry myself I'm exhausted I'm just out of breath just from drying myself and I find that quite surprising really and I think that's what made me realise that actually I am worse than I was because yeah that would never would have been an issue before" Suzanne

Breathlessness also affected many patients psychologically, reporting a mixture of anxiety and panic, especially at night-time regarding breathlessness and worries about gasping for air. Ambulatory oxygen does help reduce gasping for breath and therefore improves the symptom experience, yet patient still experience intense emotions as they fear the experience of breathlessness. Patients that do not have ambulatory oxygen also struggle with breathlessness at night, which negatively impacts sleep quality and adds to the experience of fatigue and limits daytime activity.

"I am fearful of going to bed at night-time because I know I am going to be gasping but I do use ambulatory oxygen which I know I should only use the oxygen to help me last longer or whatever task I might be doing but if I plug it in and have a really big gasp of oxygen therapy when I have been doing quite a lot so whether I am doing the right thing but it seems to help" Tracy

This shows that breathlessness has a significant impact on day-to-day functioning of COPD patients. Not only does breathlessness impact movement and energy levels but also contributes to the experience of psychological symptoms, i.e., anxiety, especially at night. Both the physical and psychological symptoms impact on sleep quality. Ambulatory oxygen is

beneficial to reduce breathlessness, but not all patients are eligible for this. Poor sleep contributes to have a lack of energy during the day, which was an experience many patients discussed.

5.6.1.2 Sleep Quality

Most patients expressed that sleep quality is a regular problem. Breathlessness directly impacts sleep quality, mainly due to the experience of not being able to breath and the associated fear (either fear in the experience, or fear of the experience). As well as not getting to sleep, patients also report broken sleep because of other COPD symptoms such as phlegm production and associated coughing.

> *"I cough at night in bed and I said I don't think I do and he said well do you wake up at night and I said yes and he said well that might be because you are coughing but I'm not coughing the rest of the night I don't think it is actually I don't think it is but yeah my sleep is poor I'm either awake I sleep till four and then I'm awake or I wake up one after going to bed at 10:30 and then I'm awake until four or five yeah" Yvonne*

The impact of sleep quality on patients was explored further, with two main impacts; the first was falling asleep during the day and the second was insomnia-induced fatigue, in addition to existing fatigue due to breathlessness. Daytime sleeping was not a choice, but something done naturally because of feeling so tired and depleted of energy. When patients did not sleep properly, everyday tasks became difficult to do both mentally and physically, resulting in a lack of motivation to do basic tasks around the house and becoming sedentary. Leaving poor sleep quality unmanaged results in poor wellbeing in the long-term.

> *"I do fall asleep I I've been known to do it through probably started in my 30s if I was not actually taking part in something I was just being a watching or something like being in a church or something and suddenly falling asleep but I do that a lot more now especially in the evening so I guess that's me catching up on sleep or something but I will suddenly and I won't know I'm falling asleep it is only when I wake up that I realise that I've been asleep" Pat*

> *"I get very tired yeah I just have no energy so I'll go out and do about 40 minutes or so then I have to come back in I can do longer than that but then I'm really awful later*

on so and again it is thinking about other things that I want to do later shall I go for a walk cook tea you know and all of those things need energy to do them so and some days I am fighting and doing them regardless but other days I'm not" Suzanne

"so socially it's quite difficult I can't do a whole day now either can't do a day in an evening I can only really do half a day of any decent exercise tolerance I mean exertional tolerance and struggling to breathe is quite frustrating so most of my life is online which is fine yeah I think socially it makes a difference" Teresa

The lack of energy that patients described was a feeling of tiredness on a regular basis. Several patients carry on day-to-day life accepting the tiredness, but other patients discussed having no energy so that they had to manage their activities and tasks each day to prevent depleting energy levels, and to give themselves an opportunity to recharge and not burn out. This lack of energy led to several patients avoiding going out socialising because this requires not just physical energy but also mental energy; for patients it is easier to avoid and cancel than to attend social gatherings. This symptom experience then impacts on both abilities to engage in routine activities of daily life and also patients' ability to engage socially. Breathlessness is not just about feeling out of breath. As detailed in the dyspnoea-inactivity cycle (Roman, et al., 2018), it impacts energy levels (Rigby, 2021), reduces physical activity (Bowden et al., 2011) and has psychological effects, including feels if fear and fright (Al-Gamal & Yorke, 2014). This is outlined in the dyspnoea-anxiety-dyspnoea cycle (Bailey, 2004) which highlights the notion that breathlessness causes anxiety, which leads the patient to engage in shallow/rapid breathing, which results in increased feelings of anxiety and causes the patient to reduce activity; this leads to physical deconditioning and patients feeling weaker and more breathless. Medications used by patients with COPD are designed to reduce inflammation and obstruction within the airway to alleviate feelings of breathlessness (NICE, 2019) the extent to which patients report feelings of breathlessness suggest these medications may not be effective in reducing the symptoms of breathlessness sufficiently.

Reduced mobility has been linked with being breathless, which impacts patient's ability to walk, and engage with day-to-day tasks, including self-care such as getting dressed and bathing. Not being able to walk, especially up inclines, or undertake basic self-care

significantly reduces quality of life. Previous research has shown that patients with moderate to very severe COPD performed worse on the 6-minute walk test (an assessment of exercise tolerance for people with COPD), and this performance was impacted upon by severe symptoms of breathlessness and depressive symptoms, so not just the primary issue which is lung function (Spruit et al., 2010). Despite patients within the study mentioning that the mobility is linked to breathlessness, an alternative account is that it could also be because of a deficit in muscle strength, mass and quality, which needs to be taken in to account (Roig et al., 2011).

A lack of energy/fatigue intersects with breathlessness and mobility, which were expressed by patients in this study and in previous research (Jennings et al., 2022; Ocon, 2013; Roman et al., 2018). Fatigue has been shown to decrease patients with COPD's quality of life (Kouijzer et al., 2018). early support and management of fatigue is recommended (Kouijzer et al.), although there is yet to be developed an effective intervention for fatigue in COPD, which is regarded as the 'forgotten' symptom (Spruit et al., 2017). Furthermore, the extent of daytime sleepiness related to sleep disturbance has been reported in previous studies with patients with COPD reported higher levels of sleepiness than those in an asthma or healthy control group (e.g., Vukoja et al., 2018).

Despite not being a theme, it would it important to highlight how each symptom is not unified in its own right. As mentioned within this theme, breathlessness impacts not only mobility but also energy levels. This then impacts sleep quality and then effects energy levels the day after a poor quality of sleep. This shows the intersectionality of COPD symptoms (figure 3.3). Showing support of this study from the findings of this study is by Lim et., (2017), showed that symptoms in COPD are clustered. The higher the cluster of symptoms, the poorer the quality of life for the person with COPD. Lim et al., (2017) recommend and advise that symptoms should be managed regarding treatment by clusters, rather than individually.

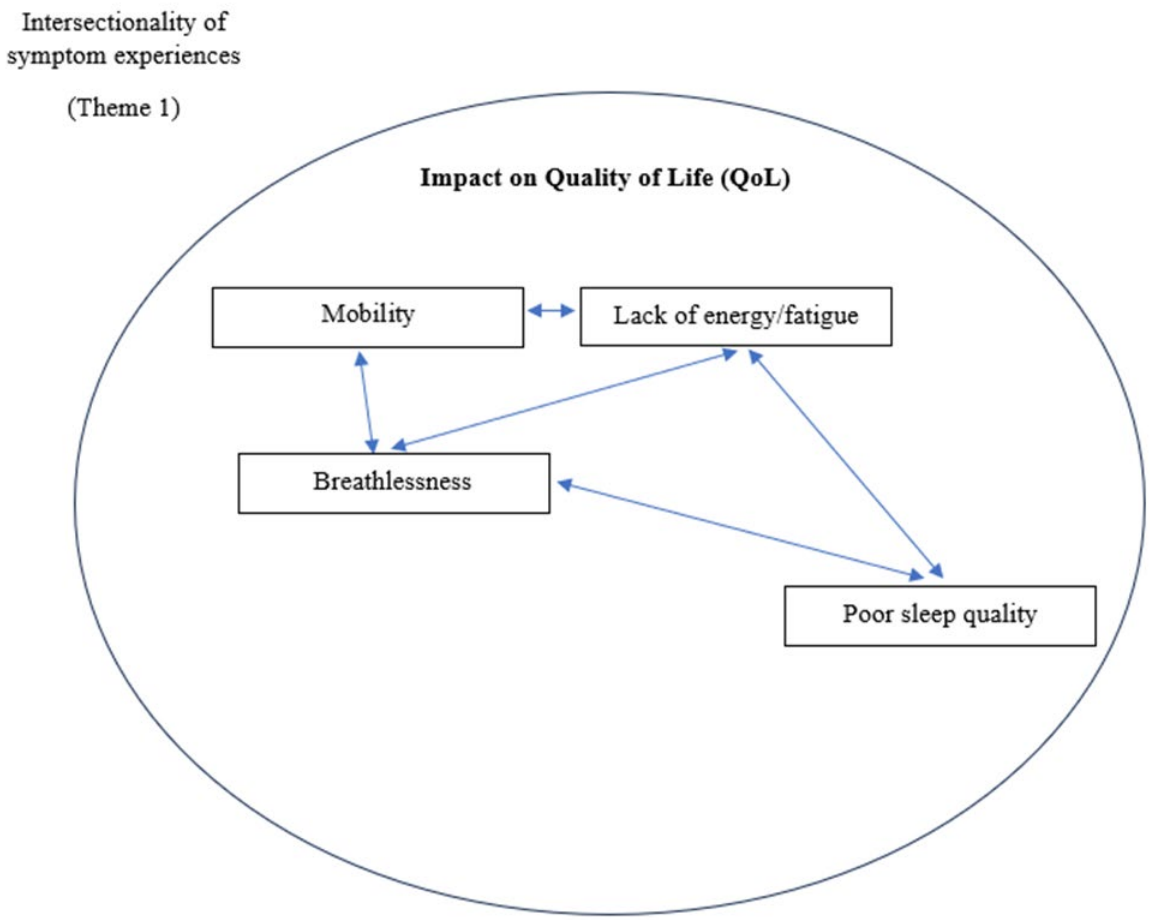


Figure 5.3. Intersectional effect of symptoms on quality of life

In summary, the main symptom impacting patients with COPD is breathlessness, resulting in poor sleep quality and significantly reduced energy levels and excessive fatigue. The experience of breathlessness and its impact on behaviour due to fatigue has a 'knock on effect', and impacts patients physiologically, psychologically and socially. These symptoms require effective management to reduce their impact on quality of life, for example from pharmacological treatment.

5.6.3 Medication Issues

Issues with medication were evident for all patients within the study. This included patients experiencing medication side effects and ineffective medication leading to patients having to change their medications.

5.6.3.1 Side effects

A significant number of patients reported direct medication side effects, some of which have also been reported in previous literature such as physical shaking and/or weakened bones and

fractures (Nizet et al., 2004; Sarkar et al., 2015), oral thrush from steroid inhalers (Dekhuijzen et al., 2016), increased heart rate and palpitations and damaged vocal cords (Leong et al., 2020). There were also side effects related to taking medications at the wrong time, for example steroids taken too late in the day left patients being unable to sleep, which impacted on sleep quality and mood. Despite the side effects, patients still take their medications. Without them their symptoms are unmanageable; patients are aware that there are no alternatives without side effects. Some patients alter the dose of their medication in an attempt to reduce the side effects of the medications, acknowledging that they need the drug to enable them to function, but altering the dose from what was recommended or advised with the aim to reduce the side effects. Some patients are unable to sleep because of medication may possible be a form of 'secondry' insomnia, however further investigation and exploration is required (Stepanski & Rybarczyk, 2006).

> *"it is the same as the roflumilast that potentially the side effects of that potentially are not very nice currently but then I'm gonna do a cost benefit analysis haven't I well you know judging by the disease progression in the last four years and I can see what that is then what I want potentially the next four years if I've got four years but I want to be like yeah because it's not it's not quantity of life for me its quality of life really that matters and it's difficult weighing it all up I put off going on statins for a long time…… if I want to reduce my risk of stroke or heart disease then it makes sense to take them and it has done the trick and it has lowered my cholesterol so that's a huge help really so it is weighing that up all the time I think" Aimee*

> *"Terbutaline and it has worked well the trouble is more recently over the last few years it's side effect of increasing your heart rate has been quite detrimental so I've ended up with a tachycardia palpitations of which that may not be the absolute cause but it certainly affecting it so I've pulled away from using it quite a lot I used to be very dependent on it and I would have I don't know probably about 12 doses a day on average and that would be on good days let alone bad days these days I'm probably only having one or two doses every few days of the Terbutaline I'm starting now to use it a bit more frequently because I need it more so I then also more or less around" Jane*

5.6.3.2 Ineffective medication

As well as experiencing significant side effects from their prescribed medications, patients also expressed doubt as to the efficacy of the medications, with some patients not noticing any difference with breathlessness and continuing to get breathless even doing basic day to day tasks (e.g. moving around the house). Medication changes may be needed due to side effects, but as well as managing ongoing symptom experience, as COPD progresses and symptom severity increases, medication changes are to be expected either in changes to the dose or the drug required as they become ineffective in the management of progressive disease. Many patients strongly expressed the negative experiences of changing medications not just from new and additional side effects as drugs interact with one another, but also due to changes in dosing instructions and getting used to new medications more broadly. Not getting medication right to manage disease progression is a risk as greater disease severity of COPD can be a risk factor for mortality (Jenson et al., 2013).

> *"salbutamol I can take anytime and they always tell me to take it before any exercise how do I do that probably not know I take it every morning and the other inhaler is meant to open up my lungs but I don't feel any difference and I take the medication (laughter) I go and do something and I still think what is the point in that and I still take it because you know it might be worse if I don't take it and I am on heart medication as well blood thinning tablets I have enough tablets do I like taking them no but I do I do as I am told it's meant to assist me but I don't… yeah absolutely and as I say if I stop taking the inhalers I don't think I would feel any different that is how they affect me I can't turn around after taking them and think oh crikey I can go for 10 minutes and run up the stairs and pick up some washing and bring it down again I still have to go up the stairs and get my breath back and then walk down the stairs" Patrick*

> *"I have just been having one issue and they are all so interrelated I seem to have been losing excessive protein from my kidneys so they changed my medication which included a diuretic to stop my ankles from swelling because my circulation is not very good there and we changed over to another medicine which should have been more helpful in there controlling the output of the kidneys but now we have now been able to stabilise that so we are changing back to the diuretic and when I was off the diuretic*

the ankles on my legs swelled really badly"
Tracy

Some patients question the effectiveness of their medication as they believe 'it is no longer working'. It is common for patients to be taking multiple medications for their COPD (see Chapter 3) with patients usually taking up to three different drugs. COPD progresses as the airways become increasingly obstructed and inflamed, and the tissue where oxygen is exchanged becomes damaged and is destroyed (Hogg, 2004). Effectiveness of medication is vital to help patients manage their COPD symptomology, function day-to-day and maintain a healthy level of quality of life. The development of new more effective medications is costly, with the costs to develop a new drug estimated up to US$1134 million (Adams & Brantner, 2006). There is also a need for long drug trials, with around 1,000 patients required for follow up for up to 3 years to assess efficacy and so timely studies are unrealistic and not practical (Anthonisen, 1991). Alternative nonpharmacological treatments could be developed that can support patients with symptom experience and quality of life. There is still very much a need for an intervention that can halt the progression of COPD and to help prolong life and improve quality of life. Currently the only method which can slow progression is smoking cessation, as lung function has shown to increase by 17% if patients quit smoking (Doo et al., 2023). Unfortunately, many COPD patients try to implement smoking cessation but are unable to quit on a long-term basis, as the addiction to nicotine is prevalent (Madawala et al., 2023).

Patients with COPD need medications to be able to live and function with a progressive and debilitating respiratory disease but experience negative outcomes associated with medication use due to side effects and medications not being effective enough to mask their symptoms or prevent disease progression. It is not surprising that when patients experience negative adverse effects from medications, creates anxiety and does contribute to patients struggling to alter medication dosages and to try new medication treatments, when anxiety is prevalent (Volpato et al., 2021). According to the Horne et al., (2013) According to the beliefs that patients have about their medications (which includes effectiveness and side effects), has a significant impact on the adherence to whether patients take the medication whether patients take the medication or not. Horne et al., (2013) found that across 3,777 studies, the higher the adherence is significantly associated with the necessity of treatment and medications that have less adverse side effects and therefore the patient have less concerns about the treatment that has been prescribed to them from their clinician. From this, Horne et al., (2013) created the 'Necessity-

Concerns Framework', which is a model that help clinicians to understand the experiences of patients and their beliefs about treatments that are advised, especially from the perspective of increasing adherence and engaging the patients if the patient feels heard about their worries and anxieties of side effects from treatment.

5.6.4 Self-management and patient involvement

Whilst patients engage with services and seek professional support with the medical management of their condition, the reality is that patients spend very little time accessing this compared to the time spent managing their condition and its effects. Half of the patients discussed how they take responsibility for and seek to control their COPD. This involves taking prescribed medication as already discussed, but also strategies based on patient's own research and trial and error. Being actively involved in the management and care of their condition is important to patients, not going along passively with the recommendations of healthcare professionals, but actively engaging with them in an informed manner enables them to collaboratively manage their condition.

Practical strategies to manage COPD included the use of practical aids (e.g. stairlifts, scooters, walking sticks) and non-medical devices to aid physical symptoms, such respiratory flutters (device to help clear excess mucus). These helped patients to maintain some sense of normality, being able to access the upstairs of their homes for example. This helped patients to maintain a sense of independence and to be able to have some normality without being fully impacted from COPD symptoms, such as still being able to be mobile by using a stair lift to go up the stairs or a scooter when leaving the house to reach a destination.

> *"you know what's the best treatment you know because I don't think you know it's medicine in the West is so reductionist I don't think I'm not happy just to go along and then say well you take X Y Z I like to do my own research I like to be involved in my care as you can imagine I like to be involved in my care I like to have somebody who I can work with to do that the Dr we have a superb in house pharmacist here he is absolutely brilliant so yeah so medication is not only for the COPD but for the comorbidities as well"*
> *Yvonne*

> *"yes I do and I have every device known to man to help me I have a stairlift I have a car with a hoist in the back so I can put a portable scooter and I have two scooters and*

I live on a bit of a slight hill and I am not far from _____ in _____ I could happily walk to _____ but I couldn't walk back because of the hill up to my house so those are the main restrictions but yes I do have to plan my route very carefully if I have to visit anywhere if I am booking a hotel I have to make sure you know there are accessible rooms and stuff like that" Teresa

These aids and accessories help patients to live well with COPD and to adjust to living with lung disease; however, do not remain effective in the long term, as the disease progresses. During the later stages of severe disease, obstruction means that patients may rely on ambulatory oxygen as mobility even with aids becomes increasingly difficult. Pharmacological interventions therefore are necessary alongside other strategies to help patients live as well as possible with the effects of their COPD and both strategies support patients.

"when I move at all you can see I've got oxygen on which I use when I move about but also for example if I'm taking part in a conversation I need that.... that extra shot of blast so with it does affect me moving about so basically I'm more or less apart from the odd trip out I'm limited and confined to home" Pauline

Many patients expressed self-managing COPD as much as possible; this gave a sense of control, whilst also acknowledging having the condition, enabling them to exert independence and not depending on medical interventions alone, as long as possible before it gets to the stage of COPD whereby daily medication and support is required. A focus on promoting self-management in long term conditions is part of the NHS-long term plan, (2019), as well as the supported self-management (SSM) initiative (National Health Service, 2020). What this means is that within the NHS, healthcare services are to empower, support and encourage patients with long term chronic conditions such as COPD to help patients to manage their condition independently, to try to give patients control and to reduce the dependence on NHS clinical services (NHS, 2020). The importance of finding new means of managing COPD was evident for all patients, the majority of whom were willing to try out new intervention and medication options despite have a rough experience with medication. This included taking part in trials testing new interventions; patients felt it was important to be part of research that would help to either find a cure or to make daily life easier and more bearable for COPD patients to manage

and live with, although patients felt unsure as to how to get involved in these opportunities. Several patients reported feeling forgotten about as these kinds of opportunities were not offered as part of their routine care but felt that being included in COPD treatment advances would give a sense of purpose and belonging. Jane expressed being involved with the scientific committee of the British Lung Foundation and felt this gave real her purpose and a sense of usefulness to be able to draw on her own experiences of COPD to inform research and guidelines. Being willing to make a difference and try a new intervention therefore from the patient perspective is not to just be offered a new intervention to implement but to be included in each process of this.

> *"you know what I mean but the more I can put into the COPD environment that something that might come out of it that I have said to you that might come up with better cures in the future and it might help me unless you are open and honest with people you are not going to get any feedback will come back and benefit you" Patrick*

> *"I've never I've never been put in that position no one has ever said to me do you want to try this do you want to try that I will try anything if I felt it was going to help and the doctor felt it was going to help I would straight away try it anything is better than this but I have never been asked to participate in anything" Yvonne*

> "*yeah definitely yeah if something like that came up and interestingly in working on the scientific committee with the British lung foundation and asthma UK the fatigue part of it is very it's recognised but it's not nobody's really thought of anything that would address that part of it so no there's no research specifically about looking at novel therapy for fatigue and helping to give people energy etc so that that could be quite a panacea I think for people living with COPD yeah" Jane*

The desire of patients with COPD in this sample, despite their ongoing struggles to manage their COPD, was to be involved in moving knowledge and treatments on to better support their own management of their condition as well as make the experiences of patients with COPD in the future better, particularly in relation to their own specific symptom experiences that they struggle to manage (e.g. fatigue).

Self-management of a long-term chronic condition can help to main a good level of quality of life (Taylor & Pinnock, 2017). Self-management requires the patient to work with health professionals and engage in behaviour change to support their adjustment to living with their condition and enable them to live well with COPD, despite a complex range of social, emotional and/or medical factors, including anxiety and depression (Kelly et al., 2022). Patients in this study were motivated to engage in self-management, including taking responsibility for and control of their condition, despite its challenges, and actively engaging in efforts to improve treatments and approaches for managing COPD. The importance of a range of self-management aids was evident in the findings of the PhotoVoice study (chapter 4) and is reflected in this study too. Patients discussed the usefulness of practical aids to support mobility and independence (e.g. a scooter, stair lift, wheelchair, walking frame, etc.). Electric scooters have been shown to reduce energy expenditure and increase quality of life by allowing the person with COPD to be more mobile (Cully et al., 2006) stair lifts are similar to previous patients' experiences through qualitative research study (Barnett, 2005), as well as a walking frame (rollator) that helps to increase physical activity in patients with COPD (Probst et al., 2004). Regarding the Fitbit shows the patient cares about the status of health and trying to change behaviour to be more physically active and supports previous research showing the benefits of patients using Fitbit devices (Wilde et al., 2022).

Moreover, half of patients made it clear of the strong desire and willingness to try out new interventions, despite a rough experience with medication, patients are keen to try new medications and other intervention strategies. This includes interventions that are within new research trials or interventions that are currently on the market that can be purchased or new interventions that are offered by the NHS. Patients expressed the importance of taking part in research, with the aim to either find a cure or to make daily life easier and more bearable for COPD patients to manage and live with. Research regarding COPD and having no clear benefits to the patients themselves, would be likely that they would not take part in this.

> *"you know what I mean but the more I can put into the COPD environment that something that might come out of it that I have said to you that might come up with better cures in the future and it might help me unless you are open and honest with people you are not going to get any feedback will come back and benefit you" Patrick*

Being informed of new interventions to COPD patients is important not just research but also a clinical perspective. Therefore, patients medical professionals at medication reviews could offer opportunities to take part within research trials to test a new intervention or be offered to try a new intervention that has been shown to be effective and safe to use. Unfortunately, several patients when asked probed further about any opportunities that have been offered and this was not the case, some patients felt forgotten about and being included in COPD treatment advances would give a sense of purpose and belonging.

> *"I've never I've never been put in that position no one has ever said to me do you want to try this do you want to try that I will try anything if I felt it was going to help and the doctor felt it was going to help I would straight away try it anything is better than this but I have never been asked to participate in anything" Yvonne*

Moreover, specifically Jane expressed being involved with the scientific committee and being part of the British Lung Foundation, having a purpose and being of use by expressing her daily experiences of COPD, to help inform research and guidelines. This in turn adds to the other patients within the study and the data, that a willingness to try a new intervention, as she has highlighted the need for an intervention that can help increase energy levels, to reduce fatigue. Being willing to make a difference and try a new intervention therefore from the patient perspective is not to just be offered a new intervention to implement but to be included in each process of this.

> "*yeah definitely yeah if something like that came up and interestingly in working on the scientific committee with the British lung foundation and asthma UK the fatigue part of it is very it's recognised but it's not nobody's really thought of anything that would address that part of it so no there's no research specifically about looking at novel therapy for fatigue and helping to give people energy etc so that that could be quite a panacea I think for people living with COPD yeah" Jane*

It is useful to know that even though COPD patients are struggling daily with COPD symptoms and medication issues, that they continue to want to be actively engaged in the management of their condition and support efforts to develop new ways to effectively manage and maximise their quality of life. The desire and willingness of most patients to take part in research trials

and interventions is positive; this was not something the researcher anticipated discussing within the interviews but is something that patients volunteered as a way they could bring about improvements to their experience of living with COPD, and that of others. Despite their willingness to try new products and take part in research, patients are not actively recruited to trials despite the need for high numbers of patients to be involved in research to explore fully the impact of interventions on appropriate patient related outcomes. Robbs, (2019) highlighted the importance of research for informing not only academic research but also clinical practice, and partnership between the two. The NHS constitution clearly states that conducting research is a core function of the NHS (Department of Health & Social Care, 2021). The National Institute of Health Research (NIHR) Clinical Research Network (CRN) can and does work closely with primary care to help establish and deliver research with institutions and charities (National Institute for Health and Care, 2022); it is important that clinical settings are engaged as research partners to effectively recruit patients from across settings into studies that are appropriate for them to engage with.

5.7 Discussion

This thematic analysis generated three themes, namely the intersectionality of symptom experiences, medication issues and self-management and patient voice. The main findings from the developed themes and associated data are that all patients expressed the various different symptoms that were impacting the day-to-day quality of life. One of the main sub themes being breathlessness, which impacted on mobility, in addition to sleep quality and energy levels/fatigue, which worsens as the respiratory disease progresses. Regarding poor sleep quality and impacting on energy levels and fatigue the following day, post poor sleep, is consistent with previous research and this study adds to current literature (Hirata et al., 2020). Hirata et al., (2020) found that sleep quality was better in females compared to males. Participants that had a higher quality of sleep, was more physically active and less sedentary. Regarding females having better sleep quality compared to males, this needs to explore and researched further, as this has clinical implications. Therefore, rather than a focus on just breathlessness with medications such as inhalers and tablets, clinicians and researchers need to also focus on an intervention that can improve sleep quality, as this is showing to be a key factor in the overall quality of life of patients with COPD and is vitally important to investigate and explore further. For example, sleep hygiene could be more of a focus in pulmonary rehabilitation, in addition to as soon as the patient has been diagnosed with COPD as a main intervention.

It is surprising that despite the array of medications, patients within this study are still finding it difficult to catch a breath. The main aim of medications is to help reduce breathlessness, by improving lung function, so patients can be mobile and be able to do basic daily activities (Sharma et al., 2023). However, this study adds to recent literature that clinically there need to be changes to be made, in an attempt for COPD patients to be able to have less chronic breathlessness. Doe et al., (2023) conducted a qualitative study with thirty-four patients regarding the current care pathway and their experiences. One of the main themes that came from this study how complex breathlessness is and from these how clinical decisions are made by clinicians. The recommendations from Doe's study, is that rather than for clinicians to focus on 'disease' management i.e. COPD, it rather should focus on 'symptom' management of COPD. This is applicable and matches with the findings of this study, that breathlessness is significantly impacting quality of life and appears that current medications are not clinical effective, and patients are suffering chronically on a daily basis.

The effect of the symptoms was not just physical but also psychological such as anxiety because of fear of not being able to breathe at nighttime. Regarding the psychological factors such as patients being fearful of not being able to breathe, should not be overlooked by clinicians and with the focus on physical symptoms, it is not surprising that the fear of not being able to breathe whether it is preventing a patient to sleep or during the day is probably not asked early on in COPD. This fear is consistent with current literature, mainly from other qualitative studies that have been able to capture this insight into the fear of stopping breathing and waking up the next morning after falling asleep (Barnett, 2005; Shackell et al., 2007). Within questionnaires that are used in research and clinical settings, a new COPD questionnaire to measure sleep quality called 'CASIS', measures the subjective experience of breathing when sleeping (Pokrzywinski et al., 2009). However, the question is fixed with 'never' to 'very often'. Therefore, it is recommended to perhaps add a specific question in future research using the CASIS questionnaire that asks the patient regarding if they 'fear' losing their breath during sleep and not waking up. This is important to investigate further, as it can then be incorporated with further evidence, within medication reviews, new interventions and psychological therapies such as cognitive behavioural therapy 'sleep hygiene'.

Regarding medication issues, patients highlighted that side effects can add to further health problems and impacting daily quality of life such as heart palpitations, shaking and weakened bones. In addition, side effects have come from changing medications, which has contributed

to patients feeling anxious and further negatively impacted on a daily basis. The side effects and impacting COPD patients' quality of life and anxiety of changing medications adds to existing literature (Restrepo et al., 2008). It is understandable that patients are anxious changing medications if they experience adverse side effects. In addition to this, whether the patient had anxiety and/or depression prior to COPD needs to be addressed as well, as this may decrease medication adherence, as the anxiety around medication changes and side effects, could be an added anxiety, which could overwhelm. High anxiety, poor medication adherence, an exacerbation of COPD symptoms such as breathlessness, side effects, is a spiral of negative factors which will impact the patient's quality of life and should be prevented and avoided. Previous research highlights patients with high levels of anxiety/depression are significant reasons of poor medication adherence and not taking medication as prescribed and instructed (Restrepo et al., 2008). The implications of the findings of the patients struggling with the daily use of medications, the role of anxiety and the physical impact of the effects of taking medications, it is advised that clinicians should continually update themselves on the research such as this study and add this into clinical settings i.e. the alliance between the patient and clinician. A possible suggestion is similar to a study that explored nurses in the advanced stages of COPD in Norway (Kvangarsnes et al., 2013). Nurses implemented a compassionate approach to the care of COPD patients, with a focus on a validating and trustworthy relationship, as well as a seeing and treating each patient with unique needs, rather than treating each patient as a 'COPD', therefore with standard treatment (Kvangarsnes et al., 2013). This approach could be implemented within the NHS here in the UK with COPD patients.

Furthermore, a couple of possible suggestions would be advised. For example, in therapy with a psychologist, it could be worthwhile to explore the patients experience in medications and the role of anxiety, as this is likely to be causing not only psychological distress but poor medication adherence too. If it is not in therapy because of a lack of psychologists or long waiting lists, this should be automatically offered through pulmonary rehabilitation from the day of COPD diagnosis and not when anxiety is a severe severity. To work through strategies on managing anxieties and to decrease psychological distress therefore but rather than a standard strategy, formulation and therapy should be personalised and individual to that specific COPD patient (Tselebis et al., 2016).

On the other hand, despite COPD patients struggling with their health and psychological wellbeing, patients have expressed a great desire and willingness to be more involved in

treatment planning and to try new interventions. This shows the true extent that COPD patients do want to help themselves to manage COPD symptomology and to be able to maximise quality of life from a self-management perspective, which supports the NHS long-term plan initiative, therefore. The implications of these findings are consistent with current literature (Wodskou et al., 2014) and shows that it is imperative for COPD patients to be actively involved and heard, both in clinical and research settings. One way that previous researchers have done is create 'Working Together for Change', which was a new approach across two workshops. Patients with COPD were able to express their experiences of COPD and medications for example, with professionals such as clinicians were present, could listen to the patients and counteract this by being able to have active and open discussions collectively to learn from COPD daily insights and experiences. This is similar to the 'Integrated Care Model' design, with the same aims of listening to COPD patients, and also including those that actively support the daily care such as carers (Sunde et al., 2014). Implementing the 'Integrated Care Model' has shown to be effective in reducing the frequency of exacerbations as symptoms are managed better and as a result less admissions to hospital, reducing the long-term cost to the health service therefore (Cosio et al., 2021). The Integrated Care Model should be conducted within the NHS to inform clinical practice, on the other hand should be implemented within research studies as well to inform research study design and operationalisation.

This thematic analysis utilised an inductive approach to coding and the generation of themes that to add new knowledge and understanding of issues facing patients with COPD in comparison to a deductive approach which would involve the generation of themes from pre-existing codes or templates based on existing knowledge and theory (Clarke & Braun, 2013). Although deductive approaches have the room for the generation of new knowledge, there is a risk that the theory driven approach may have resulted in the loss of ideas that were not coded as part of pre-existing templates. Given the knowledge that already exists about quality of life and its relationship to living with chronic ill health, a hybrid approach of both inductive and deductive coding and theme development may be beneficial (Fereday & Muir-Cochrane, 2006). This would then mean that the approach would be an integration between data driven codes, in addition to codes that have derived from theory, meaning a mixture of both, rather than solely creating codes blind from the data or just from current literature and theory. Therefore, it would be interesting to implement theory, previous published research within the deductive approach as outlined by Braun & Clarke, (2006., 2012), rather than depending on just scanning the text and creating a template. This would make the code creation and theme

development more rigor but on the other hand flexible enough to capture inductive codes and theme development, which would be missed if it were purely deductive thematic analysis, as well as making the data set more manageable. The way this hybrid would be conducted is to have existing published research and theory to be used as a predetermined template, so the researcher is aware of possible areas of the topic that may arise and factors that are nuanced, individual and novel to be highlighted and probed. This means that in theory, the researcher to deliberate more purposefully on the data not fitting the pre-determined codes, to enable maximising the significant potential for the generation of new knowledge. Swain, (2018) used the hybrid approach to thematic analysis and stated in detail how the researcher applied this, in three phases and seven stages. The main difference between the hybrid approach and a standard thematic analysis, is the use of tables and what Swain called 'Priori' and 'Posteriori' Coding, with multiple different tables that are modified as the researcher becomes more familiar with the transcripts but on the other hand, had an insight in to possible codes using the 'priori' codes which are linked to the research area, existing literature and the studies research aims and objectives. However, the process of using a hybrid approach is with caution, as it would be advised to have regular supervision as a research team, to help prevent bias and emphasis on specific areas of the interviews, because some pre-determined codes (i.e. priori), may be of interest to the researcher conducting the interviews, that are not specifically aligned with the specific aims and objectives of the said study.

Some patients were already known to the researcher who volunteered for Breath Easy where patients were recruited from. When recruiting participants for the study, the researcher was very careful to ensure patients did not feel any coercion to take part, and it was clear that patients' access to Breathe Easy would not be impacted if they chose not to take part. With some participants knowing the researcher already, in addition to some participants had already taken part in the photovoice study, there was established rapport between the researcher and some of the patients taking part in these interviews. It seemed that this led to more in depth and detailed discussions with those patients compared to the patients that only took part in the semi structured interviews. Particularly towards the end of the interviews, rapport was strongest with more open, honest conversation, and patients willing to express their vulnerability in relation to their condition. It might be that utilising two opportunities to collect data in fast succession supported the collection of high-quality data and might be considered in studies in the future.

The original design was for the study to be conducted in person, however because of COVID-19 some patients had been instructed to shield due to risks to their health and so the study was re-designed to be conducted online. The advantage of being on Teams was that patients were able to stay at home and so were at ease and comfortable, with reduced risk of exacerbating symptoms associated with travel. The nature of the interview topic was sensitive, and this also meant they were in an environment where they could access personal support following the interview if required. Whilst rapport was built with all participants throughout the interview, an in-person setting might have facilitated this more efficiently. However, according to De Villiers, Farooq & Molinari, (2022) found that the rapport during online interviews within qualitative research between a researcher and participant can be facilitated and built upon using video call technology. In addition, Wakelin, McAra-Couper & Fleming, (2024) conducted a study during COVID-19 using Microsoft Teams and despite some participants having connectivity problems, the researchers stated that using Teams can build rapport and the essence of a person and state that using online interview platforms should not be seen as less than or inferior to face to face interviewing. As the researcher of this study, with older patients, online interviewing is great for increasing accessibility. However, from the perspective of a researcher with some patients, sitting at a table with a coffee and biscuit, would have been better interviews compared to online and would have felt more comfortable. This is supported by Johnson, Scheitle & Ecklund, (2019) that investigated the quality of qualitative interviews and found that face to face interviews conducted had more word density and conversation turns compared to telephone and online interviews. On the other hand, regarding the duration of interviews, interviewer subjective ratings and coding, there were not significant differences between face-to-face, telephone and online interviews. Johnson et al., (2019) therefore concluded that despite online and telephone interviews are necessary and have advantages over in person interviews, it is not the same in regard to the high quality of richness of data when in conducting interviews face to face.

Whilst there were benefits to conducting interviews online, this also generated barriers and made participation inaccessible for some patients. Patients could only take part if they had access to and were able to use technology effectively, including access to a smartphone or tablet, and the ability to download new software and then use them as part of the study process. Future research should have the flexibility of face-to-face interviews to support engagement from those who were excluded due to these factors. Wider recruitment from outside of Breath Easy patient groups would widen the participation pool to include patients who do not access

support services such as those provided through Breathe Easy. It is also important to identify methods to recruit patients who do not access other health services, including primary and secondary care.

Whilst the specific type of COPD was reported for each patient (i.e. chronic bronchitis, emphysema), patients were not asked to report their disease severity. COPD can be classified as mild through to severe disease (GOLD, 2022) and whilst any experience of disease may impact on patients, it could be anticipated that patients will be increasingly affected by their condition as it progresses. It may be helpful in future research to account for disease severity in qualitative and quantitative work to identify any issues specifically impacting patients throughout the disease process, which may help to best target interventions and support for patients. Measures such as the COPD Assessment Test (chapter 3) could be used to capture disease severity and analyse data in light of severity scores to identify any unique patterns. Similarly, there is evidence that some people living with long term conditions adjust very well (Carroll et al., 2022). Utilising a similar process to establish quality of life scores would enable researchers to capture data specific to those patients who are impacted to differing levels by their condition, again enabling the findings of research to offer specific recommendations to support specific patient groups.

The demographic characteristics of patients in this study were homogenous (as appropriate in qualitative research) and this study offers detailed information about the impact of COPD in terms of symptom experience, medication use and self-management strategies for female, British white patients aged around 70 years who already access some form of support, had access to the internet and were competent in the use of technology. As this is the first study of its kind in the UK, extending this to a wider demographic of patients would be useful to explore detailed experiences of patients from the wider patient group. Groups to consider include those who are ambivalent to taking part in research, those struggling with mental health such as anxiety and depression which is highly prevalent in patients with COPD (Jarab et al., 2024) those that have comorbidity and multi morbidity and those with more severe and uncontrolled disease who may be experiencing regular exacerbations and frequent hospital admissions (Almagro et al., 2024). In addition, research is lacking in younger patients with COPD who are in employment and those who may meet diagnostic criteria but are not yet diagnosed (currently 70-80% of patients with COPD are undiagnosed; Lin et al., 2023). Future research could include participants that are undiagnosed using the undiagnosed COPD and asthma population questionnaire' (UCAP-Q case-finding questionnaire) (Huynh et al., 2022), with a

sensitivity percentage of 97% for accurately diagnosing COPD. Consideration would need to be made of the potential ethical implications for such a tool in a research context.

This study highlights the chronic and progressive impact of COPD symptomology on daily life. COPD negatively effects patients physically, psychologically and socially because of the intersectionality of the various symptoms. The side effects from medication add further long-term health problems impacting mobility, which impairs patients functioning further, resulting in a reduction in social activity. Despite the wide array of problems and the impact on quality of life, patients want to self-manage their condition. Part of this is through engaging with medical treatments, although this is variable depending on the side effects experienced. Patients engage in a range of strategies to self-manage and are keen to be involved in supporting efforts to develop new interventions that may help alleviate their symptoms. Given the ongoing impact of COPD despite current strategies for managing the disease medically and psychosocially, there is scope for the development of further interventions to alleviate symptoms and improve psychosocial health. This insight informs the next chapters of this PhD.

Chapter 6

Critical Review of Existing Non-Pharmacological Interventions to Improve Patient Reported Outcomes in COPD

6.0 Introduction

As highlighted in Chapter 1, many different approaches can be used by healthcare professionals and patients to manage COPD and prevent disease progression. Furthermore, Chapter 3 highlights that the average medication taken by patients to manage their condition was three, with one patient reporting regular use of eleven different medications. Whilst medicinal approaches are effective in treating and managing COPD, as outlined in Chapter 1, these approaches rely on face-to-face contact with care providers and regular reviews to ensure they maintain their effectiveness and cause no side effects that impact patient wellbeing (Barrett & Barrett, 2021). Accordingly, there is a drive by the NHS to empower patient self-management and increase the use of adjunct technologies/therapies that can alleviate service demand and increase patient benefit (National Health Service, 2023). The use of adjunct non-medical approaches to help patients, such as pulmonary rehabilitation, is commonplace and demonstrates a level of effectiveness in increasing cardiorespiratory fitness and reducing symptom prevalence (McCarthy et al., 2015). As highlighted throughout this project, despite a variety of medication types and adjunct therapies, patients still present with a significant symptom profile that is cyclical and prone to exacerbation and progression (Shaw et al., 2014). Increased disease progression includes increased symptom severity and prevalence and includes breathlessness (Jolley et al., 2014), lack of energy (Eckerbald et al., 2014), reduction in physical activities (Vorrink et al., 2011), increase in sedentary behaviour (Lewthwaite et al., 2017), reduced functional status (Mussa et al., 2018), as well as increased prevalence in mental health conditions such as depression (Schneider et al., 2019) and anxiety (Maurer et al., 2008).

Chapters 4 and 5 highlight that patients recognise the importance and role of non-medical approaches and that these can be useful in supporting day-to-day symptom management and functional status. Self-management was also highlighted as a key area by patients who expressed that these approaches gave them a ‘sense of control’ and ‘independence’ rather than depending solely on medications and support from healthcare providers. This was explicitly highlighted in Chapter 3, where a photovoice methodology highlighted different strategies, patients use to manage their condition. It included perching stools, rollators, and chair stair lifts, increasing mobility and confidence. COPD patients demonstrated these approaches to support increased breathlessness, lack of energy and fatigue. Combining the findings here with those from Chapter 2, COPD patients demonstrated a readiness to try new interventions and the confidence to try innovative approaches. Accordingly, Chapter 3 demonstrates that patients are willing to try new interventions to manage COPD independently through self-management

if offered to patients by the clinicians. However, patients expressed some uncertainty about side effects and a lack of user-friendliness that would dictate their likelihood of using these over sustained periods. Moreover, it highlighted historic issues with accessing non-medical interventions from the NHS, such as pulmonary rehabilitation and CBT. However, even with access to pulmonary rehabilitation and cognitive therapy, there was scepticism as to whether these approaches would reduce the impact that COPD has on day-to-day functioning and quality of life as initially thought.

Issues with medication adherence are commonly reported in the literature as well. Factors include a low level of higher education, unemployment, a low financial status, and a lower socioeconomic status (Gast & Mathes, 2019). In addition to medication adherence, inhaler technique is often inferior (Lavorini et al., 2008), remembering to take the medication (Prajapati & Shrestha, 2016), having to cope and manage the side effects of medications, as well as the interactions of the collective medication (Meek et al., 2019) such as headaches (Izquierdo & Aparicio, 2010), nausea (Calverley et al., 2007), effecting sleep quality (Shackell et al., 2007) as a result. As previously discussed in Chapter 1, not using inhalers correctly collectively impacts the effectiveness of medication and clinical effectiveness (Usmani et al., 2018). A reduction in the clinical efficacy of the medication reduces the quality of life. Therefore, it is imperative to explore the currently available non-medical interventions that could support and assist in improving COPD patients' daily quality of life.

Utilising a desire from patients to explore alternative approaches to manage their symptoms and respiratory condition, there is a need to provide a critical review of the approaches that might address the patient's need and need to alleviate a historic burden on healthcare services. Furthermore, as briefly discussed in the previous Chapter 5 regarding the hard-to-access participants, it is vitally essential for the 'hidden, silenced and unheard' participants to be somehow part of the collective voice that is within the majority of the COPD population, which includes a significant number of participants that are going undiagnosed, not medicated and therefore living with unmanaged COPD symptomology. Within this PhD to date, COPD participants who have both medical and non-medical interventions are still struggling; it is difficult to comprehend what the quality of life is for those patients. Often, the participants who participate in research, clinical trials and feedback to primary and secondary care services are more 'able,' have access to resources and are more likely to have stable and managed conditions with interventions. Also, a sense of self-confidence to speak up and share the views of the patient's daily life, without a fear of judgement or clinical care being altered, and to have

the belief that the patient's voice is being heard and not just a ‘tick box’, as well as being educated and able to articulate how the patient is feeling and experiencing.

Participants who are struggling with managing COPD symptoms, higher severity and multi-comorbidities, who are struggling with day-to-day life, including mobility, self-care and depression, are essentially going unnoticed, and many are going undiagnosed (McMillan Boyles et al., 2011), suffering from poor overall physical and mental health as evidenced in chapter 2. With regular medication reviews and specific instructions for each type of medication (and some need to be renewed; otherwise, the medication is ineffective), new medications that need to be picked up from pharmacies require mobility, resources (as shown in Chapter 4) and the motivation for behaviour change (Cavalheri et al., 2016), being significantly harder for those with depression (Tomczyk et al., 2020). For patients who have poor mobility and a high severity of depression, motivation is likely to be minimal, and, for many (Rosenberg et al., 2013), it is limited. COPD patients who have a long-term partner and a family that the patient can depend on, these COPD patients can have the ability to function (Castelino et al., 2017). However, patients who are barely ‘surviving’ and not ‘thriving’ are the patients who are secretly struggling and are only being noticed when experiencing an exacerbation and an ambulance is required (Sneath et al., 2022). When a patient is experiencing an exacerbation of symptoms, it is often unbearable and frightening (Ceyhan, 2023). It makes the patient feel helpless, unhopeful, not in control, unsupported, and a burden to the NHS (Hurst et al., 2020). Furthermore, from the perspective of the NHS, each exacerbation is significantly costly, with only short-term benefits to the patient (i.e., it is not cost-effective) (Wright et al., 2022). An NHS service that is dependent on funding from the government, which is declining annually, means that waiting lists and access to interventions, both medical and non-medical interventions, are taking significantly longer to receive, contributing to further decline of health and mental health status.

Suggestions of how to perhaps get the voice of the hard-to-reach participants are to: follow up from hospital exacerbations, maintain letters, in addition to emails and phone calls, a mail merge to COPD patients within primary care from the patient's local GP surgery to be invited to research studies, new interventions and feedback of services and phone calls that do not have a fixed abode, home visits to the most severe and immobile COPD patients, extra support for COPD patients that are living by themselves, allow loved ones and family members be an advocate by helping COPD patients take part in research, clinical trials, accessing new intervention and sharing feedback, enabling the patient's voice, with the assistance of the loved

one acting as a career, for example, a letter or email that is also accessed by them, such as the offer to use the SoeMac device (will be discussed in the next section below), that can be communicated to the COPD patient. Health visitors include occupational therapists and nurses who visit COPD patients in the patients' homes to invite and offer patients to participate in research or provide feedback. An initiative from the British Lung Foundation National Institute of Health Research or local council should be able to help to provide internet access and access to smart devices, whereby patients who are struggling to access services and are essentially 'off the radar' could enable the patients to start to feel connected and to be part of the community and know the patients are not alone and should not feel ashamed or a burden to others and the NHS of the chronic condition respiratory condition. Also, there is a sense of flexibility for COPD patients. For example, suppose the patient's COPD symptoms have flared on the day of the medication review and can no longer attend. In that case, there should be flexibility and not an adverse responsive reaction from the NHS, and this should also be applied to research. For example, if patients do not pick up the phone or turn up to a research clinical trial appointment, the data should be rearranged to reflect this when the data is analysed.

From a horizon scan, various candidate non-medical approaches have been discussed and critically evaluated throughout this thesis. These include pulmonary rehabilitation, CBT, inspiratory muscle training, and oxygen therapy, which have been discussed in the merit of the available academic evidence and data from this thesis; for a summary, please see Table 1 in Chapter 1. Therefore, the below focuses specifically on oxygen therapy interventions only. It is, therefore, vitally important for an intervention that is effective and positive to arise for COPD patients who are struggling from a biopsychosocial perspective. An intervention that is not medical, with limited to non-existent side effects, that has minimal effort (that does not require a high level of motivation or behaviour change), does not require regular medication reviews and GP routine visits and limited maintenance, and can be delivered to the home of the COPD patient, so leaving the house is not required, is what COPD patients desperately require, that enables an increase in quality of life and COPD symptomology that is managed more effectively compared to current medical interventions such as the inhalers.

6.1 Singlet Oxygen Energy (SOE) Device

Considering the practicalities of candidate approaches, there is potential for singlet oxygen energy devices to be an effective intervention for patients with COPD. However, there is limited empirical data from formal trials on these products. However, 35 years of anecdotal

evidence and many small studies, plus thousands of products being used worldwide, suggest that the manufacturers of these products express that the devices offer benefits for various health issues. Furthermore, there are no known reported safety concerns, but similarly to the clinical effectiveness, no robust clinical trials with appropriate authorisations have been conducted. So, in conclusion, the below section explains what SOE is, the history of SOE, as well as the current SOE devices that are on the market, discussing the strengths and weaknesses of each one (Valkion, Airnergy Professional Plus, Vital Air 5 Plus and SoeMac). Therefore, despite many years of positive anecdotal and subjective evidence, this is not scientific or robust enough to deem the clinical effectiveness, clinical benefits and safety of SOE and its possible potential for patients with COPD. As a result, the aim is to use the most appropriate for COPD patients and to use it as part of a formalised NHS double-blinded clinical trial, not just for clinical effectiveness that SOE makes a difference but also for safety.

6.2 Science of Singlet Oxygen Energy (SOE)

Singlet oxygen technology is based upon irradiation of a photosensitiser molecule, e.g., phthalocyanines, with a specific wavelength of red light to convert oxygen (in its stable or triplet state) to singlet oxygen (^{1}O, SO), an unstable type of reactive oxygen species. In a Type I reaction, electrons are transferred between the substrate and oxygen to generate singlet oxygen, which has a half-life of seconds to microseconds. In comparison, singlet oxygen is generated via an energy transfer process in a Type II reaction during a collision of the excited sensitiser with triplet oxygen in the air (De Rosa & Crutchley, 2002; Grossweiner). SOE-based products use the type II mechanism to generate singlet oxygen energy (SOE). The energised singlet oxygen is formed by the action of an LED light array on an appropriate photosensitiser on the internal catalyst, and the energy is released (as photons at 634 nm) as the singlet oxygen relaxes to ground-state oxygen. This Type II process is extremely rapid, and the singlet oxygen reverts to its stable triplet state in nanoseconds (DeRosa & Crutchley, 2002; Hulten et al, 1999). The effects of SOE are based on an energy transfer process that occurs in the air or gaseous phase and should not be confused with the cytotoxic effect of singlet oxygen that is used, for example, in photodynamic therapy (PDT) for cancer treatments (Hopper, 2000; Cieplik et al., 2017). In PDT, the same chemical reaction, i.e., the action of light on a photosensitised chemical, takes place within the body to generate singlet oxygen, which is cytotoxic and can be used for the local destruction of tumour cells. PDT is a well-used and described interventional procedure recommended by NICE to treat a variety of cancers (Hopper, 2000; Cieplik et al., 2017).

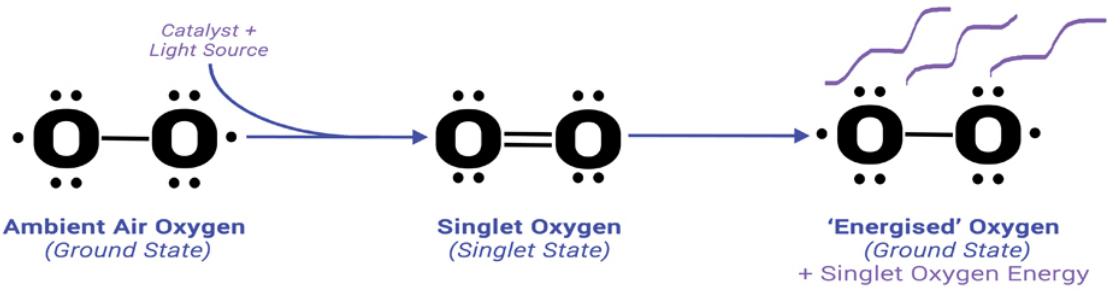


Figure 6.1. Diagram showing the process of energised oxygen from ambient air to singlet oxygen energy (SOE)

6.3 History of SOE Inhalation Technology

The heart of singlet oxygen energy products is based upon technology conceived initially by Tony van der Valk and Jörg Klemm, who began developing this technology in 1987. They worked with several partners in different countries to manufacture and market products, mainly concentrating on inhalation therapy. Over the years, several studies have been performed with products using activation chambers (catalysts) based on the original concepts designed by Tony and Jörg (please see Figure 6.2 of the timeline of the history and varieties of different SOE devices.

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Figure 6.2. Timeline of the origin of singlet oxygen energy devices and the development of different types of devices from 1987 to 2017

6.4 Critical Review of SOE Devices

The four devices that will be discussed are Valkion, Vital Air 5 Plus, AirNergy Professional Plus and SoeMac, reviewing the strengths and weaknesses of each device. A 12 Volt adaptor powers these products and utilises technology from Tony and Jorg's ground-breaking work.

6.4.1 Valkion

Valkion is the original SOE device, invented and built by Tony Van Der Valk in Sweden. The name derives from Valk and Ion. The company still exists today but is exceedingly tiny and inactive.

In a pre-clinical laboratory study measuring isolated human blood monocytes treated with SOE energy, Hulten, in 1999, produced data to show a significant decrease in reactive oxygen species (ROS) from treated cells, without any loss of cell viability, compared to non-treated cells. In addition, the data shows that air diffusion of SOE can attenuate the oxidative stress response in human blood cells. Therefore, the data shows performance support of singlet oxygen energy from the Valkion device. As well as this Lindgard et al., (2003) added further support to the Valkion device, showing support that the mode of action in air diffusion of SOE can increase the energy status of muscle cells in rats, in addition to the energy state of skeletal muscle during ischemia-reperfusion injury.

The strengths of the Valkion are that it is the original product of SOE. In addition, there is a wide variety of anecdotal evidence in users and different health conditions. The nasal cannula uses a fibre optic cable that is for focused application. However, there is little evidence to suggest this offers any benefit. Regarding weaknesses of the Valkion, the instructions are relatively complex and require a water container to be filled and managed. Using a nasal cannula restricts users' mobility, as they must remain connected to the device. The long-term effect of using the Valkion is unknown, as the treatment lasts relatively short, between 10-30 minutes. The device costs £2,500, which is not feasible for patients with COPD or the NHS.

6.4.2 Airnergy Professional Plus (Airnergy International AG)

The Airnergy company was founded by Jorg and Guido Bierta to continue Tony's work after his death. They based the company in Hennef, near Koln, and traded successfully for several years. They evolved the product offering to several similar but different-looking machines. However, they encountered financial problems, and the company liquidated, then reformed as

NES Airnergy, but just run by Guido. Jorg continued to assist for a while but also collaborated with other companies.

The strengths of the Airnergy Professional Plus are a wide variety of assorted products, some offering variable delivery levels of SOE. In addition to this, there is a vast range of anecdotal evidence in users and different health conditions. The instructions are complex, as water needs to be added to the container and requires being filled and managed by the patient. Using a nasal cannula restricts users' mobility, as they must remain connected to the device. On the other hand, servicing the machines is complex and relatively expensive and requires returning to the facility in Germany. Like the Valkion, the Airnergy Professional Plus is a short treatment of 10-30 minutes, and the long-term efficacy is questionable. Furthermore, the cost of some Airnergy machines is high, making it nearly impossible for most who are struggling with their health to afford one. The cost of the Airnergy ranges between £3,500 and £10,000.

6.4.3 Vital Air 5 Plus

A Vital Air 5 plus is an evolution from the Valkion and the Airnergy machines, and again, Jorg was involved and worked with them to develop and replicate the Airnergy machines with a more modern look and a lower cost than the Airnergy products. The strengths of the Vital Air 5 Plus are that it has a lower cost compared to the Airnergy device, and the delivery is also through a nasal cannula for breathing. However, Airnergy requires the patient to fill up the water container regularly and understanding how to use the device is difficult because the instruction manual is complex. The use of the nasal cannula restricts the patient’s mobility during the day or at night-time (depending on when the patient uses the machine), as the patient must remain connected to the device. Again, like the Valkion and Airnergy SOE devices, the treatment is relatively short, between 10-30 minutes, and no data shows the long-term efficacy of using the Vital Air 5 plus. The Vital Air 5 Plus costs between £3 450 and £4 195.

6.4.4 SoeMac

The SoeMac is an evolution of technology from the above machines and Tony and Jorg’s early research (Valkion, 1988). Jorg worked for this company for two years whilst the product was developed and managed by a British entrepreneur, Neil Stentiford. Their objective was to offer the benefits of SOE technology to a broad range of people at a fraction of the cost and ultimately help improve a million people's lives. So far, they have sold 10,000+ machines and are waiting to commence a formal Clinical Trial with a significant UK Hospital and University. Upon successful completion, SoeMac will be an approved medical device available to the Health

Service. Initial connections have been made with NICE (National Institute for Health and Care Excellence) to have them recommend the SoeMac to the NHS.

Evidence of the efficacy of the SoeMac device (Figure 6.3) has been determined from small, observational studies producing anecdotal evidence. Erpenbach, Brailey, Quade & Stentiford (Unpublished Data, 2010) evaluated whether a SoeTie device (a precursor to the SoeMac device where the SOE is delivered via nasal cannula) led to an improved lung function and, therefore, improved physical endurance in COPD patients. Eight COPD patients used the device for a 30-minute session five days/week for four weeks. FEV_1 and distance covered during a 6-minute walk test improved at weeks 2, 4 and 8 compared to baseline, but only the 6MWT data reached statistical significance. Erpenbach et al., (Unpublished Data, 2011) followed this up by completing a second study conducted with the current SoeMac device at home for 8 hours a day for four weeks with a washout period measured at 4 and 8 weeks. The main findings were an increase in the 6MWT at four weeks sustained across the washout period at both 4- and 8-week time points. Two patients received dummy devices, and no improvement in the 6MWT was seen. Therefore, it demonstrates the potential of increasing walking distance and, as a result, mobility. Previous research has shown that an increase in 6MWT can improve patients' quality of life with COPD (Zeng et al., 2019). Anecdotal evidence Furthermore, regarding the SoeMac device, anecdotal evidence gathered by SoeHealth Ltd over time through testimonials highlight that there are potential benefits such as a decrease in breathlessness, coughing less, longer duration of sleep which collectively contributes to feeling more restful, energised and feeling better in themselves (SoeHealth Ltd, 2022).

Figure 6.3 Image of the SoeMac Device

The strengths and weaknesses of patients using the SoeMac device are that it is lightweight, portable, and affordable to the patient and NHS for £419. Compared to the other three SOE devices, a cannula is not required, meaning the device is non-invasive and non-intrusive. The instructions on how to use the device are simple and not complex, mainly because there is no water container that needs regular filling by the patient. There is no specific time for using the device (i.e., only 10-30 minutes). This means the patient can use the SoeMac device for as long as required. In addition, the patient can use the SoeMac device during the day or in the evening when they are awake or asleep. The SoeMac device must be switched on and off within 30 cm from the patient (for example, a bedside cabinet). Therefore, it requires minimal effort, energy and motivation to use daily. Also, the SoeMac device is not sensitive to specific COPD severities and accommodates mild to severe cases. However, a weakness of the SoeMac device is that it only has a single strength of singlet oxygen energy, meaning there are no different options for different pressures of oxygen the patient receives.

However, the SoeMac fits COPD patients' requirements better than the devices above. As described at the beginning of this chapter, patients have expressed within studies from this PhD that they are ready and confident to try a new intervention. Within the British Lung Foundation Breathe Easy groups (the researcher attends regularly), the SoeMac device was put forward to the group in an informal setting (the formal PPIE group findings are discussed within the next chapter regarding the clinical trial). The researcher described the SoeMac device and showed the group members how to use it. Many members expressed that not having a face mask and that it can be switched on at night, being able to move in bed when asleep without worrying about nasal cannula and additional tubes and does not involve any other task other than switching it on when going to sleep and switching it off in the morning, the majority of the group were ecstatic and eager and asked about how to acquire and implement. In addition, the SoeMac has the requirements the NHS is pushing for regarding innovative technologies to help self-manage long-term conditions. Please see Figure 6.4 for a visual mind map of why the SoeMac device is preferable and applicable to COPD patients, compared to the other Singlet Oxygen Energy (SOE) devices and non-device non-medical interventions.

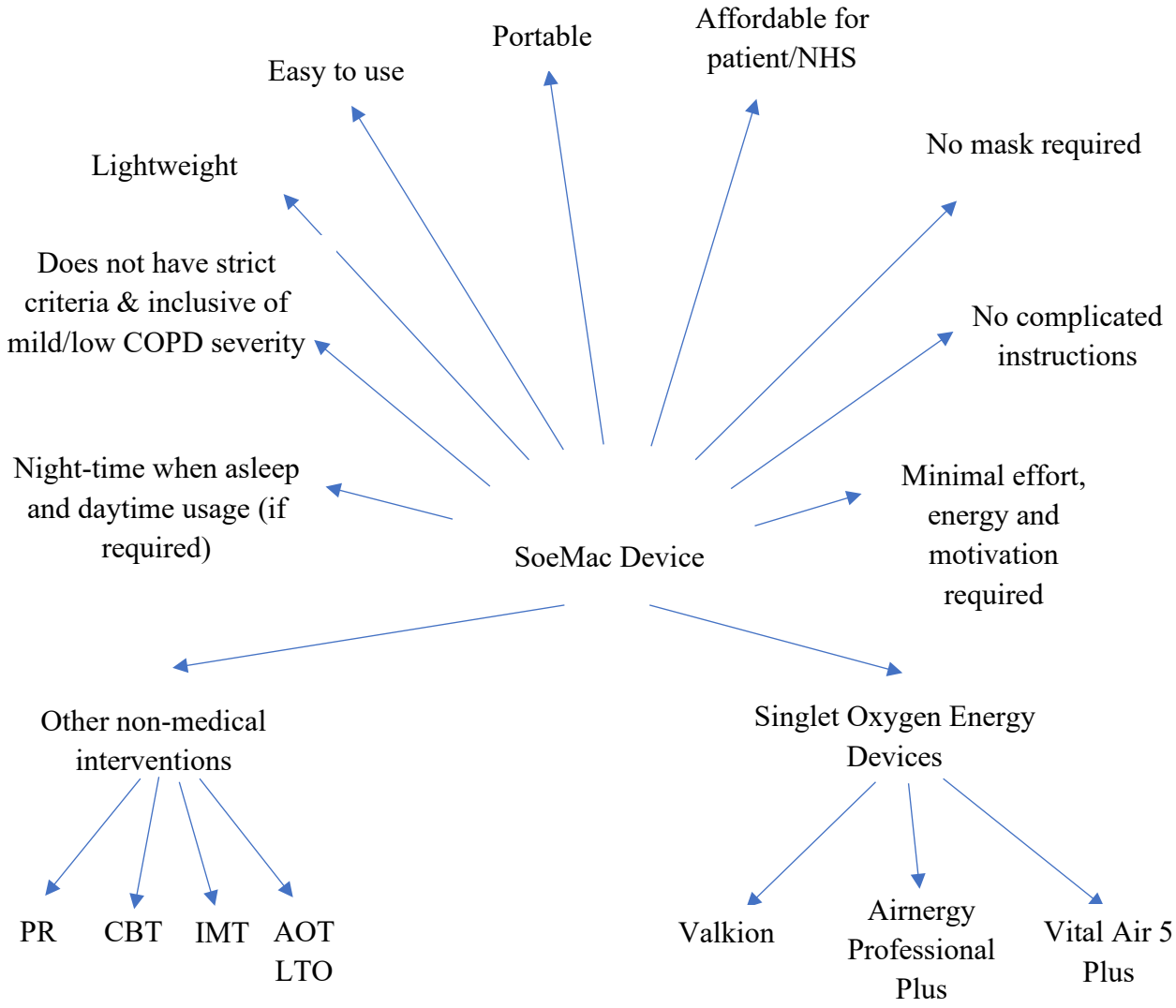

Figure 6.4. Justification summary as to why the SoeMac device is preferable to the other SOE devices and non-medical interventions

6.5 Conclusion

The challenge, therefore, with COPD patients' clinical management of COPD symptomology and quality of life is that despite clinical effectiveness and proven benefits not just from the medical interventions such as inhalers and tablets, in addition to the non-medical interventions such as PR and CBT, adherence is a common theme for each one. With an ageing population that is living longer, and smoking rates being maintained, the scalability of this is vast. Poor adherence contributes to poor efficacy of the intervention. Not just adherence but other factors such as motivation, inability to access interventions and the cost to the NHS for poor adherence, non-attendance and poor inhaler techniques are a costly, long-term burden for the NHS. As the efficacy of the interventions is reduced, the symptom management of COPD is impacted and,

as a result, contributes to GP appointments and hospitalisations (because of exacerbations) that could have been prevented, adding to further financial implications for the health system. Therefore, it is vitally important to find a possible solution as part of an intervention that uses innovative technology, which could significantly reduce the burden on the NHS, thereby reducing contact with the NHS primary and secondary care and, as a result, saving the health system a vast amount of money. The SoeMac device has been selected from the critical review of this chapter against the other SOE devices and non-medical device interventions. Therefore, the opportunity warrants the use of the SoeMac device in a robust and highly scientific NHS double-blinded trial to test that it is safe for COPD patients to use and the clinical effectiveness to measure if it can help COPD patients manage COPD symptomology.

Chapter 7

Development of a clinical trial to determine the feasibility and safety of using the SoeMac device with patients with a diagnosis of Chronic Obstructive Pulmonary Disease – a focus on implementing feedback from PPIE

7.0 Introduction

COPD is a debilitating and progressive lung disease that is poorly managed (Cataldo, 2023) (as discussed throughout the PhD chapters). Within the quantitative study (see chapter 3), patients expressed the readiness and confidence to try a new intervention. In addition, within the photovoice qualitative study (see chapter 4), patients emphasised the importance of additional interventions that were not medical, such as rollators, wheelchairs and stair lifts that helped to provide a feeling of independence and self-management of COPD, away from clinician-prescribed medication. Moreover, this was explored within the semi-structured qualitative interviews (chapter 5), in which participants indicated that if an intervention was easy to use and was offered by clinicians with no side effects, participants would accept the invitation to try a new intervention. Taken together, the findings from the three studies show that despite COPD, participants significantly struggle both physically and psychologically, which negatively impacts their daily quality of life. Despite this, patients are still showing a desire to try out new interventions.

Moreover, as discussed in Chapter 6, many people with COPD are hard to access both within clinical practice and research for a variety of reasons. These include patients who have poor mobility or low finances and are unable to attend GP medication reviews and collect medication from pharmacies. Missing medication reviews and being unable to collect medication from pharmacies contribute to patients being unable to manage COPD symptomology and negatively impacting their quality of life as a result of this.

Often, medications have specific instructions (i.e. what time to take the medications, some with and without food), and some have expiratory dates and therefore need replacing. Having so many medications and tasks to remember daily can get overwhelming, meaning that an intervention that is easier to use, user-friendly and fits into daily life is paramount to adequate intervention adherence (Poletti et al., 2023).

Taking medications and being disciplined requires motivation, and this can be difficult for many COPD patients struggling psychologically with depression, making the easiest of tasks rather a challenge (Poletti et al., 2023). The findings from Study 1 show that many symptoms, such as breathlessness and a decrease in quality of life, which includes mobility, increase in severity as COPD progresses. This means that for participants with mild severity of COPD compared to severe COPD, it is easier to participate in research or regularly attend reviews, as physical activity is still achievable at the early stages and decreases as COPD severity worsens

(Vestbo et al., 2013). Also, patients receive regular support from caregivers because symptoms in the later stages of the condition are so debilitating, and those who live independently do not receive regular support (Trivedi et al., 2012). This means that patients who have severe COPD symptomology, unsupported and unable to leave the house, are often 'silent' and 'off the radar' until the participant has an exacerbation and requires secondary care support, which is not unusual for COPD patients to downplay the true impact of the condition often, the support that is required and feel a burden to receive regular treatment (Barnes et al., 2013).

Also, from a research perspective, it is equally as difficult to access and invite these patients who are not attending GP reviews, participating in research or local community groups. Similarly, participants who do attend interventions such as pulmonary rehabilitation can often 'drop out' because of an exacerbation or hospitalisation (Fischer et al., 2009). Therefore, as part of the clinical trial process, it is essential to explore how to implement feedback from the PPIE group to help design the trial to make it as accessible as possible to hard-to-access patients and to decrease the number of participants that disengage and withdraw from the research.

As previously highlighted in Chapter 6, preliminary data using singlet oxygen energy (SOE) delivered by the SoeMac device has the potential to influence COPD patient outcomes positively and is also aligned with the needs and wants of patients. Additionally, medicinal technologies are part of a broad initiative from the NHS to increase patient outcomes whilst reducing the growing financial and physical burden on clinical resources (National Health Service, 2014). Compared to pulmonary rehabilitation, relaxation muscle techniques and CBT, which have been critically appraised in Chapter 1, and singlet oxygen devices such as the Valkion and Airnergy, SoeMac is the non-medical intervention that has the potential to be clinically effective for patients with COPD. However, whilst these devices provide an opportunity, there is currently a lack of empirical and robust clinical data that demonstrates acceptance and effectiveness in clinical populations and, more specifically, within the context of this PhD, a COPD population.

From this, the critical review (chapter 1) of existing and current non-pharmacological interventions that are currently available, the SoeMac device was discussed (chapter 7) and justified why this was selected to take forward to be used in a formal and highly scientific double-blinded randomised controlled trial. The SoeMac device was the best match for COPD patients compared to the other interventions listed (explained in detail in Chapter 1), such as

the device requiring minimal effort. Accordingly, this chapter/study aimed to develop a clinical protocol to test the safety, feasibility, and effectiveness of the SoeMac device in COPD patients.

Unfortunately, the clinical trial did not start because of the COVID-19 pandemic. Therefore, in this chapter, the trial's development will be explained based on the significant contribution from a Patient, Public, Involvement, and Engagement (PPIE) group. A protocol summary will be presented. The full version of the trial protocol can be found in Appendix AX.

7.0.1. Trial Partners

Before discussing the PPIE involvement, it is essential to state the various project partners involved in the study, including the head of the British Lung Foundation Support Group Nottingham West, Mrs Teresa Burgoyne. Please see below and figure 7.1.

The University of Derby (UoD):
Samuel Grimwood is a researcher involved in leading protocol development, study documentation, study design, NHS Health Research Authority (HRA), Medicines and Healthcare Products Regulatory Agency (MHRA) approval, statistical design, recruitment strategy, and operationalisation. Supervised by Director of Studies Professor Mark Faghy (respiratory physiologist) and Co-Investigator for the trial (Working closely with the Chief Investigator study documentation, study initiation, management, monitoring and financing of the study), Dr Emma Sharpe (academic psychologist and statistician) and Dr Amy Baraniak (health psychologist).

Nottingham University Hospitals NHS Trust (NUH):
Dr Milind Sovani – acting as Chief Investigator and taking overall responsibility for the trial, patient safety and all study aspects. Elaine Blackshaw will also act as trial manager to coordinate study activity and support recruitment and operationalisation of the study.

The Centre for Healthcare Equipment & Technology Adoption (CHEATA)
Dr Sarah Bolton – Supporting with the MHRA forms specifically for the SoeMac device, as well as creating documentation such as the clinical evaluation report, collating all of the evidence to date regarding the creation of the SoeMac device and the technology behind it.

SoeHealth Ltd – Manufacturer of the SoeMac product:

Mr Neil Stentiford – Managing Director – Director and majority company owner. Provide SoeMac devices for the study and be informed monthly of the status and progression of the study.

Patient, Public Involvement and Engagement:

Coordinated by Mrs Teresa Burgoyne, British Lung Foundation (BLF) Support Group Nottingham West and a Patient Representative on the Greater Nottingham CCG Patient and Public Engagement and Primary Care Quality Committees.

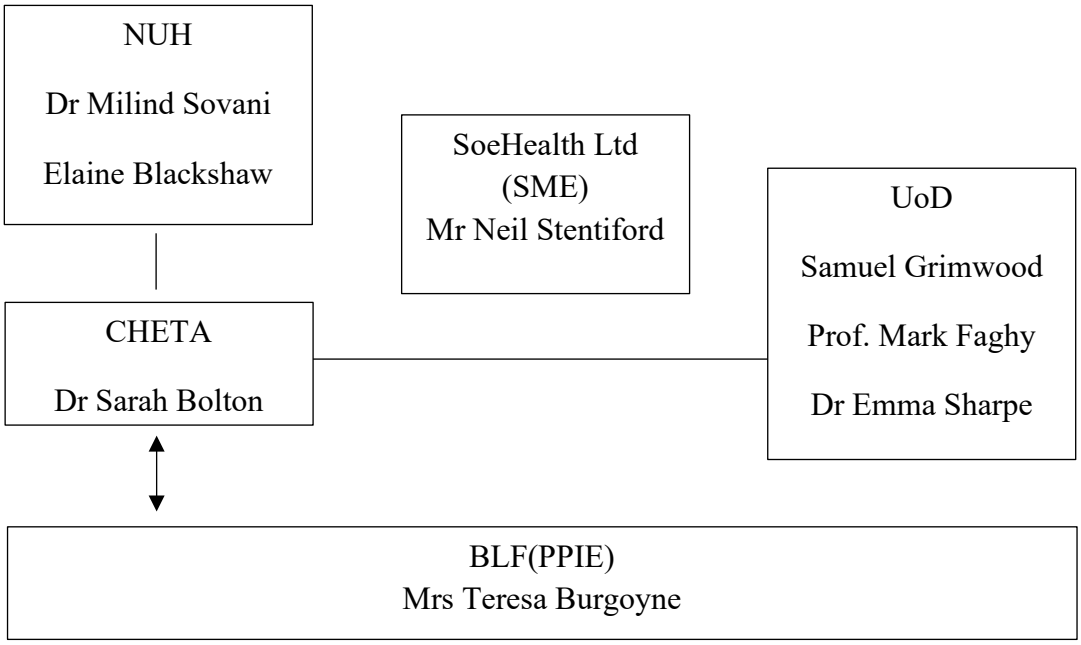

Figure 7.1. Schematic of the project partners involved in the trial.

7.1. PPIE Involvement

Patient, Public Involvement and Engagement (PPIE) has been significant within medical services within hospitals but has lacked within research settings (Sacristán et al., 2016). It is an initiative for lived experience from participants in research or clinical practice settings to help improve the research project or clinical setting. It enables those with lived experience of a medical or mental health condition to provide insight and input (i.e. giving space to be heard and protected space for the participant's voice to be heard) in this context to help shape the design of a clinical trial within COPD using the SoeMac device and to make it as user friendly as possible.

Actively listening to participants with lived experience of the condition you are researching can significantly benefit your research project in many ways. For example, it can help with your participant recruitment forms (for the participant-facing documentation such as the participant information sheet, debrief form, and consent form) and the study design, including the questionnaires and the specific tasks the participants must complete. This enables the participants' voices to actively change the study to make it more participant friendly. For example, PPIE can help with participant retention (reduction in dropout) and maintain good data quality (reducing error because of poor energy levels and making mistakes, having to delete the data/reducing quality of data and data analysis/interpretation).

7.1.1. British Lung Foundation Nottingham West community support group – PPIE

A patient, public involvement, and engagement (PPIE) group was formed and coordinated with Mrs Teresa Burgoyne at the British Lung Foundation Nottingham West support group. Seven participants consented to sit on a PPIE steering group to discuss input directly with each trial development stage. During initial discussions, participants expressed a genuine interest in being involved in research and having their voices heard and incorporated into future research design. Informed by Chapters 3-5 data, PPIE representatives were questioned on the motivators of clinical research and what would make a future clinical trial appear interesting and worth the participant's involvement. The role of technologies was discussed, and they expressed a desire to use devices that are the primary motivator. A SoeMac device was demonstrated in subsequent discussions, the potential benefits were discussed, and the safety and efficacy were highlighted as critical considerations.

7.1.2. The stages of the PPIE group

Samuel attended The British Lung Foundation Nottingham West support group with Ms Blackshaw (Trial Manager).

As the researcher of the trial, Samuel had already built a good, robust, professional relationship with Ms Burgoyne at the PPIE group (which, on reflection, helped build trust with the members of the group, as the members of the group all have an extremely trustworthy and close bond with Ms Burgoyne).

As the PPIE panel was within the same building as the monthly meetings of the British Lung Foundation group, many members were arriving to attend the monthly meeting. However, they were informed about the PPIE panel by Ms Burgoyne at the start of the meeting. Samuel answered a variety of questions about what it means, why as researchers are asking for views and insight (as it was clear many had never been asked before to provide opinions), and after 30 minutes, seven members of the group gave verbal consent to join the PPIE panel and were informed the members can leave at any time, should the participant wish to do so.

A large table was organised, with large A3 posters, which had 'What do you like about this study 😊' and 'What do you not like about this study ☹'. Each questionnaire of the original design of the trial was printed out and laid on the table. Also, some light refreshments were provided, including cups of water.

The seven members (average age of 75 years old, five females and two males, all participants diagnosed with COPD) sat at the table; Samuel and Elaine went through the study design, the questionnaires, the duration, and the SoeMac device, for example. Initially, the plan was for each member to express their views and opinions, but many felt uncomfortable. So, individual pieces of paper and pens were provided if the group member wanted to write down any thoughts. One group member did not want to write anything down but instead asked Samuel to assist in writing down what the group member was saying and wanted to discuss, as it felt too formal and reminded the participant of being in an exam.

Linking back to the hard-to-access participants, which was discussed in the introduction of this chapter and the previous chapter (chapter 6), it is essential to try to make research studies as accessible as possible to all COPD participants. Also, it is imperative to make the study participant-friendly from the perspective of being able to complete the study from start to finish and also to fill in all questionnaires, making the data high quality and not compromised because

of missing data, for example. Furthermore, participants can also drop out of studies for various reasons, so it is vitally important to gauge the insight of hard-to-access participants and from the perspective of lived experience to make the study achievable for the wide range of diversity in COPD populations.

One participant, in particular, seemed to be passive-aggressive in how the participant communicated with Samuel and Elaine. ‘All of the study is rubbish’, ‘waste of time’, ‘what is the point of me giving you my opinion, I have never been listened to before, I do not get the support I need, why at the age of 72 should I even take part in the study once you have got in up and running’, ‘I am essentially getting out of breath, I am struggling and I am desperate for help’. Both Samuel and Elaine calmly validated the group member and how the participant was feeling and explained the significant need for a new intervention that could be effective in managing COPD. After 15 minutes, the member of the group calmed down, sat down and provided valuable insight into what the member of the group thought and provided both good and constructive feedback (one of which was that the study duration was too long, and that the member of the group would drop out as a result of this). On reflection, this specific group member later informed Samuel and Elaine that the only reason for attending the community group was that someone within the British Lung Foundation could pick up the group members and bring them to the community support group. Otherwise, the group member would not have attended the meeting and said the participant is sedentary, with no one to talk to and a support worker twice a week.

The PPIE panel lasted for around 60 minutes in total. Samuel and Elaine sat together and reviewed notes that had been handed in for the members of the group who felt uncomfortable talking to Samuel and Elaine, in addition to the opposite for the group members who did not want to write but wanted to discuss instead verbally. All group members were thanked for their time and informed that no identifiable information was collected. The next stage was implementing the feedback into the protocol and study design.

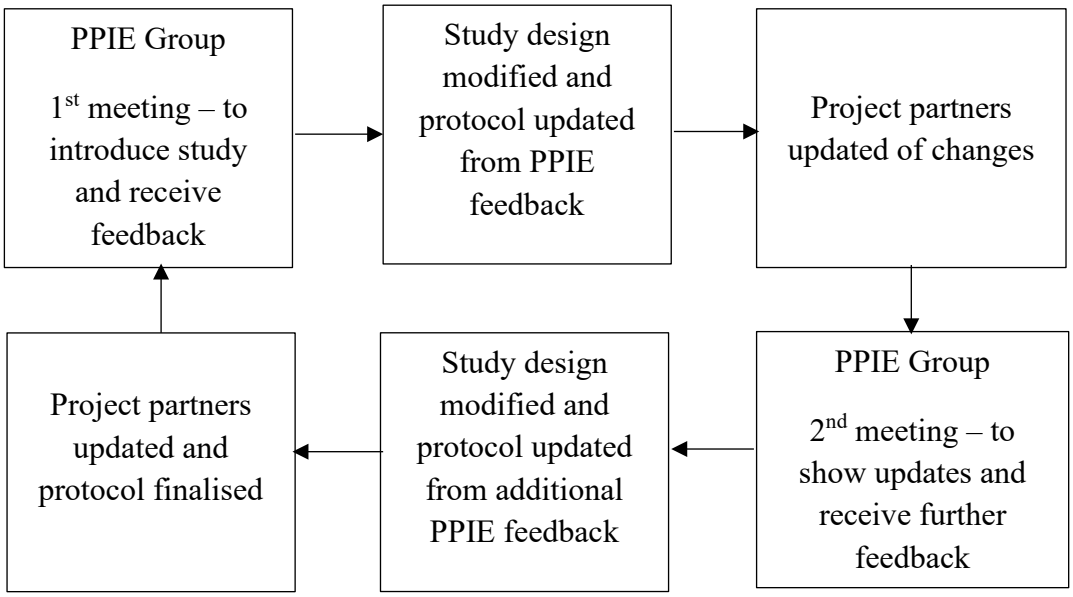

Figure 7.2. Process of PPIE feedback implementation

7.1.3. The specific changes that were implemented from the PPIE group.

The points below are central points of feedback the members of the PPIE group provided:

- Participants expressed delight that the device was not medically based and would not interfere with existing medications (see appendix AY) email correspondence to the head of PPIE, Ms Burgoyne, after receiving feedback from the group).
- The ease of using a SoeMac device was appealing to participants. The simplicity of switching the device on before going to sleep and turning it off when getting out of bed in the morning required minimal effort.
- One participant expressed previous issues with using devices that incorporated the use of masks, which often gave nasty rashes and blisters on their face, which was unpleasant and painful. The SoeMac device does not require a mask and is positioned next to the bed at night; the participant was pleased and very eager to use the device.
- Another participant was worried that it required a medication review with the GP and having to travel to collect it, as the participant's mobility was extremely poor.
- Furthermore, participants were concerned about the SoeMac device causing side effects and interacting with the participants existing medication.

- A participant also expressed frustration with the number of interventions out there that are not effective.
- Participants expressed that they would be interested in taking part in the study.
- Calling every two weeks for the adverse events was well received, as participants expressed that it reassured participants the research team had not forgotten about the participant's participation.

Collectively, the potential offered by the SoeMac device was welcomed. The feedback from the PPIE group was then used to inform the support of conducting a formal trial with critical partners and stakeholders.

A revised protocol was returned to the PPIE group, with Ms Burygoyne and the seven members present to see if the changes could be finalised. Upon the second meeting, the following points from the review highlighted several considerations that are detailed here:

- Reduce the study duration from 12 weeks to 8 weeks as participants felt that 12 weeks was too long and felt that they would likely drop out and withdraw from the study. Eight weeks, participants felt it was more manageable
- CAT and MRC Breathlessness Scale to keep as initially planned, as the PPI participants were familiar with these from clinical practice with GP and respiratory specialists.
- Reduce the number of questionnaires, as it takes too long and may get tired when completing them on the telephone. As COPD patients suffer from fatigue and lack of energy (Lewko et al., 2012), this is a priority to change within the study design.
- Accordingly, the Fatigue Assessment Scale (FAS) was removed. Removing the FAS would, therefore, remove nine questions the participant does not have to answer each time (x3 baseline; mid; end = 27 questions). Instead, the CAT questionnaire was incorporated as it effectively shows fatigue (Stridsman et al., 2018). The CAT is already being asked and, therefore, does not require any further questionnaires for the participant to answer.
- The PSQI (9 questions; x3 baseline; mid; end = 27 questions) and daily sleep diary (x84 stating sleep quality, time the SoeMac is switched on and off; 84 days from Day 0 to Day 84) will be removed. The PSQI participants felt the questionnaires were not specific to COPD. Also, the sleep diary was tedious to do every morning for the full 84 days and anxiety regarding whether the participant would forget. This would then create

extra work for the study team to collect the missing data, potentially affecting the final statistical plan or having to conduct a mean imputation. The 'COPD and Asthma Sleep Impact Scale' (CASIS) (Pokrzywinski et al., 2009) was deemed more appropriate, in addition to the existing ESS questionnaire already included. CASIS Sleep Diary – (Self-reported at Baseline, Day 42 ± 7 Days & 56 ± 7 Days) The COPD and Asthma Sleep Impact Scale is a 7-item questionnaire to measure the impact of sleep associated with COPD and breathing problems. Each question can be answered on a scale between 1-5 (1= Never, 2=Rarely, 3=Sometimes, 4=Often and 5=Very often). The higher the score, the poorer the sleep quality. CASIS has good internal consistency, test-retest reliability and construct validity (Pokrzywinski et al., 2009). As well as this, it is deemed helpful in helping to understand the impact of COPD on sleep outcomes. Participants liked the questions and felt that as they were specific to COPD, they felt more inclined to fill them out three times across the new study duration of 8 weeks.

- Regarding the sleep diary removal, the content of the sleep diary was not lost (when the SoeMac was switched on, switched off, if the participant used the device and the participant's sleep quality on a scale). For the biweekly call/video call from day 14 (week 2) to day 48 (week 8), participants will be asked, 'Have you used the device each night?' yes/no and also ', Approximately how many evenings did you not use the device' states several evenings missed. This then reduces the sleep diary to a total of 2 questions (x4 week 2, 4, 6, 8 = 8 questions rather than 84 questions), saving the participant time and energy.
- EQ-5D-5L to be removed - repetition with CAT. However, the main thing missing is the anxiety/depression question. Therefore, the PHQ-4 is to be added. PHQ-4 – (Self-reported at Baseline, Day 42± 7 Days & 56 ± 7 Days) The Patient Health Questionnaire-4 (Kroenke et al., 2009) has been developed to allow for an ultra-brief and accurate measurement of the core symptoms and signs of depression and anxiety. It is a 4-item scale. The total PHQ–4 score complements the subscale scores as an overall measure of symptom burden, functional impairment and disability. The PHQ-4 is not a diagnostic tool but an indicator. In addition to this, the PHQ-4 has good construct validity and internal reliability (Kroenke et al., 2009).
- As well as this, in addition to side effect questions to be asked biweekly on the telephone/video call, questions regarding psychological changes were added to the clinical research network (CRN), again to go with the PHQ-4 and to gauge further detail

and if the participant did not experience any psychological changes, i.e. for example low mood had lifted in severity, the participant would say 'no' and move on to the next question, as it was a questionnaire. To receive paper copies of questionnaires, rather than just electronic PPIE group advised and changed from verbal answers only to paper copies of questionnaires to be sent in the study packs. Therefore, this is to maintain adherence and high-quality data with no missing data. From this constructive feedback, the study design and all study documentation were amended and communicated back to the team for discussion and review. Taking on board the daily feedback from expert patients living with COPD was extremely valuable. The aim and hope are for the changes to increase patient adherence, successful recruitment and a complete trial, with high-quality data, showing whether the SoeMac device is safe and effective in this clinical population.

The protocol and study documentation were updated and sent for review with NUH research governance from the above changes to the study design. The hypothesis and research aim, outcomes and objectives were also updated:

7.1.4. Lessons learnt from using a PPIE group

Despite taking a long time to change the trial to fully remote, a common factor is accessing medication reviews or pulmonary rehabilitation or community groups. This means that it should decrease dropouts and participants who disengage. Firstly, the participant will not need to leave the house because of debilitating COPD symptoms, causing the restriction of mobility. Also, reducing the trial duration and the questionnaires should help participants maintain focus and motivation to complete the trial from start to finish and complete all questionnaires fully. For participants with depression, for example, the easy-to-use SoeMac device, which does not require anything other than switching the device on, should also enable participants with COPD and depression to take part and to have the desire not to stop participating. Taking into account that COPD participants drop out of pulmonary rehabilitation because of hospitalisations, exacerbations, and depression (Fischer et al., 2009), flexibility is paramount within the clinical trial and acknowledging this insight from the planned date of participant contact will be up to 7 days after the proposed date for example on week 2, so the research team can get in contact with the participant and will not be withdrawn from not being able to attend the designated appointment on the original time because of a decline in COPD symptomology. Reducing the study duration, making the questionnaires more specific to COPD and reducing the number of

questionnaires to maintain participant retention would not have been implemented if it was not for the PPIE group, showing the research application across many factors in the research process.

Going to a remote local group within Nottinghamshire enabled the voices of COPD participants who all came forward to take part, who all stated that they had never been involved or had their 'voices' heard before. It provided a platform where participants could share insight, which would not have been possible internally with the project partners or from conducting literature reviews. One of the significant highlights was that the group members found it challenging to see the purpose at the start, a lack of trust, and expressed the poor quality of care received for many years. The experience of PPIE restored faith in being able to express thoughts and that everyone in the PPIE group was listened to, was highly valued and made a significantly positive difference to the study.

On reflection, additional British Lung Foundation community groups within the UK should have been attended, offering PPIE involvement for the protocol development and study design. It would be interesting to explore if feedback would have been different at a British Lung Foundation group, as Samuel would not have had an existing professional relationship with the head of the community group, essentially going in blind if visiting a new and different British Lung Foundation community group. However, without the trust and bond between Samuel and the head of another group for PPIE, would the members not engage in the PPIE? Would participants be more honest within PPIE if a research assistant who was not part of the project reduce any possible bias and participant desirability bias effect?

If replicated to try and reach the hard-to-access participants the primary and secondary care NHS services, letters within the county of Derbyshire could have been sent and offered a video call on an individual basis or an offer for a home visit (if it was not during a COVID pandemic) or to travel to a local meeting location near to the participants home that could be financially reimbursed. Also, if letters were sent to give a brief overview of the study and questionnaires, participants could have time to reflect and go through them before contacting Samuel by letter, email, telephone call, in person, or video call, for example.

In addition, a pre-existing framework to support, evaluate and report patient and public involvement in research should be implemented. Greenhalgh et al. (2019) conducted a systematic review of frameworks for over 65, which were all vastly different. There is a need for an evidence-based framework to apply and use in a PPIE group. For example, rather than

just having posters regarding what is good and what needs to be improved about the study, perhaps have a section on how to prevent disengagement and factors that the participants feel could contribute to this. Greenhalgh et al., (2019) highlighted that in PPIE, participants are expected to be asked for feedback about being in a PPIE group, which can help make future PPIE more effective for protocol and study development.

For such a significant role in the trial protocol development and study design, next time, a financial incentive should be offered, as the National Health Service (NHS) pays for the members of the PPIE group for the time given for the meetings, which may increase the number of participants that would like to take part in the PPIE group.

7.2. Summary of the finalised trial

A summary of the finalised trial post-PPIE group is in Table 7.1 below. The additional details of each section have been discussed in their entirety within Appendix AX. Also, a schematic showing each stage of what participants need to complete at each time interval from start to finish of the study (figure 7.3). Furthermore, a flow chart showcases the specific independent and dependent variables, which are the same for the active and control groups (figure 7.4).

Table 7.1. Summary of the trial

Clinical Investigation Title	A pilot study testing the safety and efficacy of singlet oxygen energy delivered via the SoeMac device in people living with Chronic Obstructive Pulmonary Disease (COPD)
Introduction & Rationale	
COPD is associated with airflow limitation because of increased airway resistance and reduced lung compliance. This dysfunction may exacerbate the sensations of breathlessness, reduced physical capacity/activity levels and disrupted sleep, commonly reported COPD symptoms. Breathlessness results in exercise limitation, difficulty performing activities of daily living (ADL), and a gradual reduction in quality of life (QoL) until death. Chapter 3 (Study 1) highlighted that sleep quality decreases as COPD progresses. Following on from this, in patients with COPD, compared to wakefulness, sleep is associated with a reduction in minute ventilation, resulting in a drop in the partial pressure of oxygen (PaO2) falls and a rise in the pressure of carbon dioxide (PaCO2) increases (Hulten & Hendricks, 1988; Lopes et al., 1983). This, in turn, leads to oxygen desaturation. Patients with COPD experience interrupted sleep, spend less time in rapid eye movement (REM) sleep, and wake up feeling tired. This sleep disturbance is related to the degree of airflow obstruction and COPD-related symptoms such as cough and breathlessness. In a cross-sectional European survey from five European countries, Price et al. (2013) collected data from primary care physicians and respiratory specialists on nearly 2,800 patients with COPD. In this cohort, nearly 80% of patients experienced night-time symptoms. This included trouble falling asleep, staying asleep, waking during the night and waking up feeling tired. Patients with night-time symptoms were more breathless and had frequent exacerbations in the previous 12 months and received more maintenance therapy than those without. Patients with night-time symptoms were also more likely to find getting up in the morning challenging and had poorer sleep quality.	

Evidence of the efficacy of the SoeMac device to date has been determined from small, observational studies producing a body of anecdotal evidence. Erpenbach, Brailey, Quade & Stentiford (Unpublished Data, 2010) evaluated whether a SoeTie device (a precursor to the SoeMac device where the SOE is delivered via nasal cannula) led to an improved lung function and, therefore, improved physical endurance in COPD patients. Eight COPD participants used the device for a 30-minute session 5 days/week for 4 weeks. Lung function (FEV1) and distance covered during a 6-minute walk test improved at weeks 2, 4 and 8 compared to baseline, but only the 6MWT data reached statistical significance. Erpenbach et al., (Unpublished Data, 2011) followed this up by completing a second study conducted with the current SoeMac device at home for 8 hours a day for 4 weeks with a washout period measured at 4 and 8 weeks. The main findings were an increase in the 6MWT at 4 weeks sustained across the washout period at both 4- and 8-week time points. Two patients received dummy devices, and no improvement in the 6MWT was seen. Furthermore, Stentiford, Burgoyne & Reeve (Unpublished Data) at The British Lung Foundation Breathe Easy Nottingham West also conducted a small cohort observational study (n=17) to study the effect on sleep and quality of life (QoL). The study duration was 12 weeks, with QoL questionnaires completed monthly. Participants stated to the research team that they were having a better night's sleep, which was more prolonged and more profound (i.e., instead of restless sleep). Also, participants reported that breathing seemed to be more accessible, coughing less frequently and, as a result, not waking up because of this during the night. Collectively, these benefits contributed to many participants stating in the questionnaires that when they woke up, they felt that they had more energy, felt relaxed and refreshed. Participants feeling refreshed, relaxed and energised, further research needs to be conducted to investigate if the positive impact contributed to an improvement from a physical health perspective (i.e. COPD symptomology, sleep quality) but also psychologically (i.e. depression/anxiety). Unfortunately, around 40% of patients with COPD experience depressive symptoms, such as a loss of interest in pleasurable activities, and 36% exhibit anxiety symptoms, such as feeling nervous and fearful (Yohannes, Baldwin & Connolly, 2000).	
Clinical investigation Design	A double-blind prospective observational cohort study
Clinical investigation Participants	Adults (≥40 years) with COPD (≥10 CAT score)
Planned Sample Size	A minimum of 48 participants (including a 15% drop-out rate, 24 in each group) and a maximum of 100
Number of Participants	48 participants (24 in the active group; 24 in the placebo group)
Recruitment of Participants	The assistance of the Clinical Research Network (CRN), several GP surgeries, and research nurses will be asked during COPD clinic check-ups. To offer study and to go through participant information sheets for participants interested in taking part and will go through eligibility criteria (i.e. CAT score >10). If the participant is eligible and provides consent using a consent form, the CI and PI, Dr Sovani Milind, will go through the criteria and consent form and authorise accordingly. If the participant is medically unsafe to participate (i.e., with additional comorbidities), a letter will be sent to the participant in the post, thanking the participant for the interest in participating in the study. The trial manager, Ms Blackshaw, will contact the participant and inform the participant of the following steps. A study pack will be

	sent in the post, including an anonymised identification number and the questionnaires CAT, CASIS, ESS, and PHQ-4. The participant will also be able to ask any questions about the study. This will be the start of the participant's enrolment into the trial.
Randomisation	Double-blind randomisation. Participants will receive an active SoeMac device or a dummy SoeMac device using an independent source at The University of Derby. Each device will have a number (i.e. 001, 002, 003). In the case of AE/SAE, individual code break envelopes will be produced and accessible by the trial manager and CI. When the trial has formally ended, all participants will be fully unblinded, and the SoeMac device and sleep diary will have been returned to NUH (as the CAT, CASIS, ESS, and PHQ-4 are completed over the phone between the trial manager and participant). Participants will be able to have a SoeMac device for personal use. Participants will contact the manufacturer SoeHealth Ltd. They will be provided with a unique discount code, where they will obtain the SoeMac free of charge as goodwill for taking part and completing participation in the trial.
Follow-up Duration	None
Planned Clinical Investigation Period	Start date: TBC End date: TBC
Aim	Evaluate the safety of using a SoeMac device at night and its effects on self-reported Chronic Obstructive Pulmonary Disease (COPD) symptomology, sleep quality and psychological well-being in people with COPD.
Primary Outcome	Determine:0 a) The frequency and severity of reported severe adverse events (SAE) and adverse events (AE) following exposure to the SoeMac device b) Self-reported changes in the CAT score
Secondary Outcome	Quantify changes in participant-reported outcomes regarding sleep quality (CASIS, ESS) and psychological well-being (PHQ-4) following 56 days (8 weeks) of exposure to a SoeMac device.
Primary Endpoints	a) Self-reported safety and efficacy following exposure to using the SoeMac device (measured at baseline, week 4 and week 8) b) CAT score changes (measured at baseline, week 4 and week 8)
Secondary Endpoints	Improved self-reported symptom profile relating to sleep quality and psychological well-being (measured at baseline, week 4 and week 8)
Data Analysis	
See Figure 7.4 for the independent and dependent variables. The frequency of contact with the NHS and reported AEs/SAEs will be measured from baseline, then every two weeks, until the end of the study (Part A of the primary objective and outcome). Part B of the primary objective and outcome is to measure from baseline, mid and at the end of the study to	

measure if there are any changes in each group (active and control group) (independent variable) in the scores for the CAT questionnaire.

The secondary objectives and outcomes are the independent variables of the two groups (active vs control). The dependent variables are the CASIS and PHQ-4 questionnaires. Participants in both groups will complete at baseline, mid and end of the study.

Descriptive statistics will be calculated for all outcomes of interest. The primary outcomes regarding the frequency of contact with the NHS and reported AEs/SAEs (please see Section 6) and the CAT scores. The secondary outcomes are sleep behaviour (CASIS) and psychological well-being (PHQ-4).

All outcomes of interest (i.e. Contact with the NHS and reported AE's/SAE's and the questionnaires CAT, CASIS, PHQ-4, ESS) will be presented as proportions and means with standard deviations or medians with interquartile ranges, depending on the distribution of data. This includes – Height, Weight, Age, Sex, Ethnicity, Medical & Psychological Morbidities (GP Diagnosed Co & Multi), COPD Medication/Treatments, Smoking Pack Years, and Smoking Status. As well as device-related questions such as device usage (average amount of evenings used across 56 days), side effects (what the side effect is, how many, duration, mean and range for each specific side effect), health changes (positive and negative, what the health change is, how many, duration; mean and range for each health change for both groups), wellbeing changes (positive and/or negative, what the wellbeing change is, how many, duration; mean and range for each wellbeing change).

Data will be collected from the Baseline every 2 weeks. At the end of Day 56, contact with the NHS and reported AE's/Saes for Part A of the primary objective and outcome. In contrast, the CAT scores will be collected at baseline, mid (halfway through the study, Day 28) and at the end of the study (Day 56) (Part B of primary objectives and outcomes).
Regarding the secondary objectives/outcomes, the questionnaires, CASIS, ESS and PHQ-4 will be collected at baseline, mid (halfway through the study, Day 28) and at the end of the study (Day 56).

The contact with the NHS and reported AE's/SAEs will be calculated by how often the NHS has been contacted; therefore, ANOVAs will be conducted.

For AE's (dependent variable) in the active group, a one-way ANOVA will be conducted 5 (time point: baseline, day 14, day 28, day 42 & 56) x 1 (Active Group). Similarly, AE's (dependent variable) in the placebo group will also be measured using a one-way ANOVA 5 (time point: baseline, day 14, day 28, day 42 & 56) x 1 (Placebo Group). If statistical significance is observed, post-hoc testing such as Tukey's Honestly Significant Different (HSD) test or Discriminant Analysis will be implemented for both ANOVAs.

Regarding the SAEs (dependent variable) in the active group, a one-way ANOVA will be conducted 5 (time point: baseline, day 14, day 28, day 42 & 56) x 1 (Active Group). Similarly, SAEs (dependent variable) in the placebo group will also be measured using a one-way ANOVA 5 (time point: baseline, day 14, day 28, day 42 & 56) x 1 (Placebo Group). If statistical significance is observed, post-hoc testing such as Tukey's Honestly Significant Different (HSD) test or Discriminant Analysis will be implemented for both ANOVAs.

Furthermore, regarding the CAT questionnaire scores, two separate one-way ANOVAs will be conducted using a 3 (time point; baseline, mid & end of study) x 1 (Active group) ANOVA. The same ANOVA will be conducted for the control group 3 (time point; baseline, mid & end of study) x 1 (Control group). This is to examine to see if there is an overall significance in each ANOVA. If there is an overall significance in CAT score for either ANOVA's Tukey's Honestly Significant Different (HSD) test or discriminant analysis will be implemented for post-hoc testing to specify the specific time point, if there was a significant difference, etc.

In addition to the two ANOVAs for the CAT score (using the global score), a paired samples t-test will be conducted. All 8 domains (i.e. cough, mucus, chest tightness, breathlessness, activities, confidence, sleep and energy levels) of the CAT questionnaire will be analysed using t-tests for each

group (active; placebo) and for each domain (8) and across data point 1 vs data point 2, data point 2 vs data point 3, and as data point 1 vs data point 3 will be conducted. Conducting the t-tests will show if there is a difference between the data points for each separate domain and for both groups separately.

Similarly, two separate one-way ANOVAs will be conducted for the CASIS questionnaire using a 3 (time point; baseline, mid & end of study) x 1 (Active group) ANOVA. The same ANOVA will be conducted for the control group 3 (time point; baseline, mid & end of study) x 1 (Control group). This is to examine to see if there is an overall significance in each ANOVA. Suppose there is an overall significance in CASIS score for either ANOVA's Tukey's Honestly Significant Different (HSD) test or discriminant analysis. In that case, it will be implemented for post-hoc testing to specify the specific time point, if there was a significant difference, etc.

On the other hand, for the PHQ-4 questionnaire scores, two separate one-way ANOVAs will be conducted using a 3 (time point; baseline, mid & end of study) x 1 (Active group) ANOVA. The same ANOVA will be conducted for the control group 3 (time point; baseline, mid & end of study) x 1 (Control group). This is to examine to see if there is an overall significance in each ANOVA. If there is an overall significance in PHQ-4 score for either ANOVA's Tukey's Honestly Significant Different (HSD) test or discriminant analysis will be implemented for post-hoc testing to specify the specific time point, if there was a significant difference, etc.

As well as the two ANOVAs, paired samples t-tests for the PHQ-4 will also be conducted. The global score (x4 items and each score totalled) of the PHQ-4 will be used in the ANOVAs for depression and anxiety. On the other hand, the PHQ-4 can also be split, as for 2 of the questions, the total score is for depression, and for the other 2 questions, the total score is for anxiety. Therefore, t-tests will be used for the anxiety score and separately for the depression score for each group (active; placebo) across data point 1 vs data point 2, data point 2 vs data point 3, and data point 1 vs data point 3 will be conducted. Conducting the t-tests will show if there is a difference between the data points for depression and anxiety individually.

All of the statistical tests planned above are based on the assumption that the tests needed will be parametric (i.e. ANOVA and paired samples t-test). However, after data analysis has been conducted and the data is skewed or does not meet assumptions, non-parametric tests will be implemented instead (i.e. Kruskal Wallis and Wilcoxon Signed-Rank test).

Device Name	SoeMac
Manufacturer Name	Soe Health Ltd
Principle Intended Use	The device works by the participant drawing in the air that the device produces in the air, which is a bio-usable form of energised oxygen that the participant breathes in overnight when they go to sleep until they wake up.
Length of Time the Device Has Been Used	The SoeMac device has been on the market for approximately 10 years as a wellbeing device

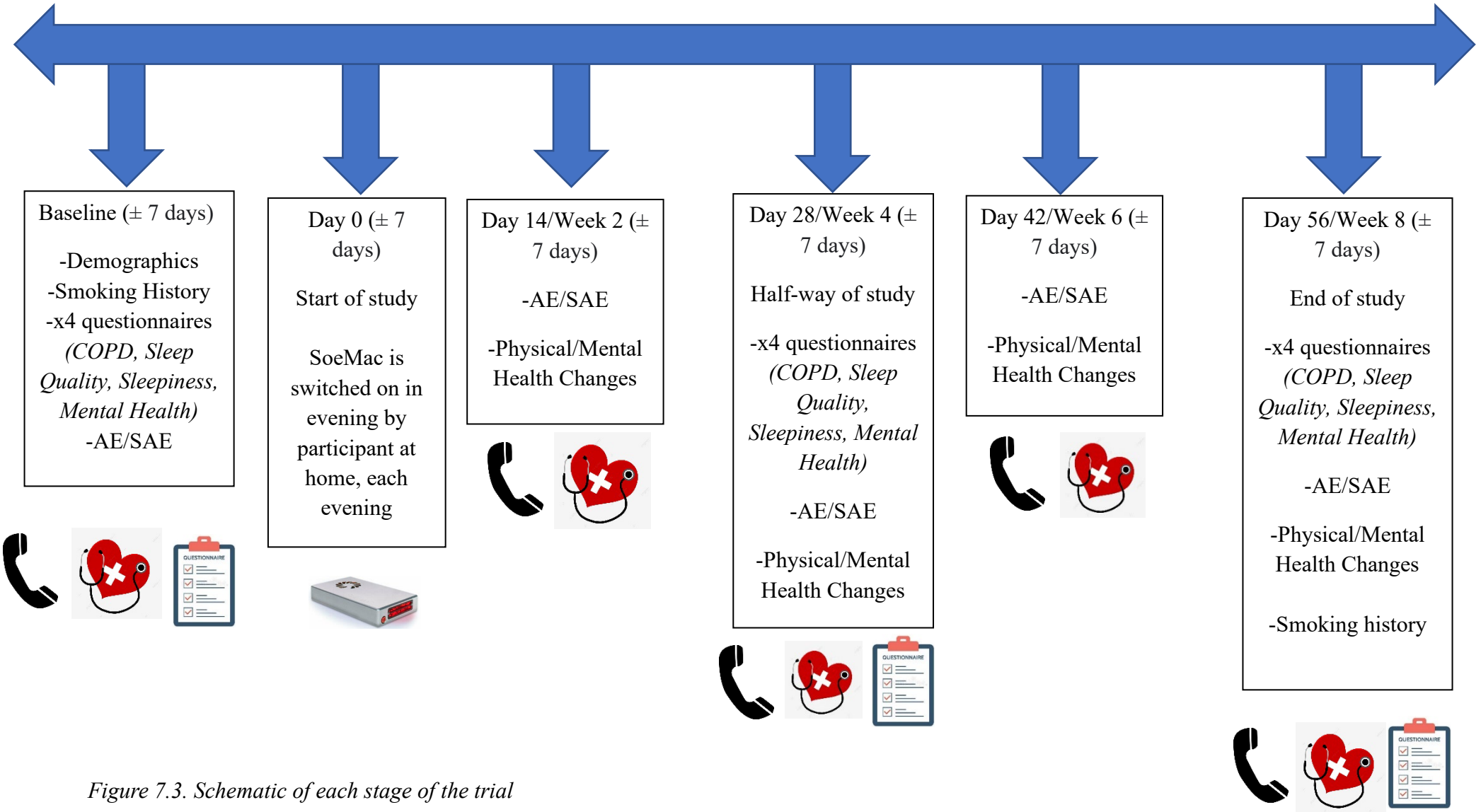

Figure 7.3. Schematic of each stage of the trial

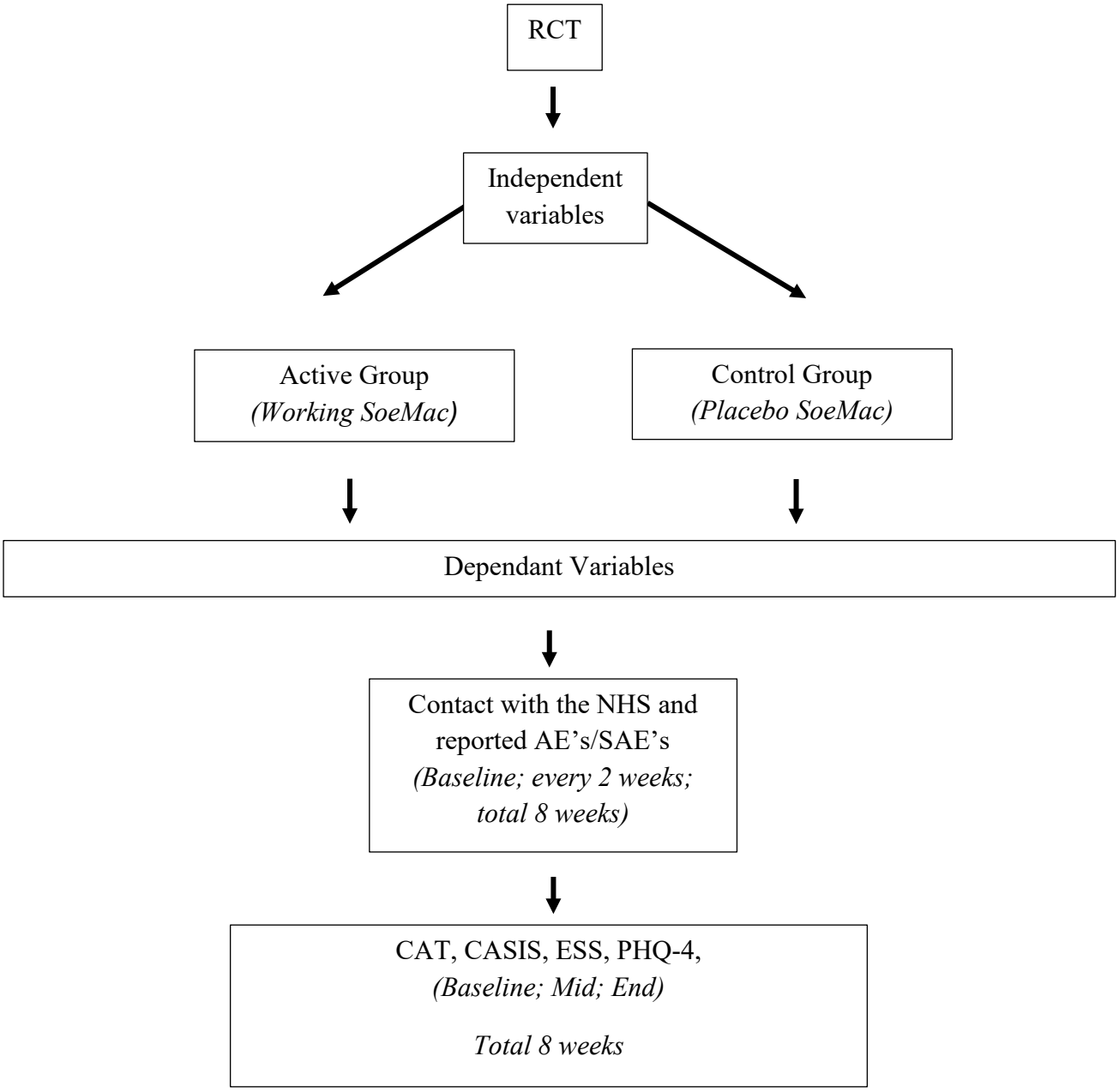

Figure 7.4. Independent Variables (IV) & Dependent Variables (DV) Flow Chart

7.3. Summary

Initially, the trial was postponed in 2020 because of the COVID-19 pandemic, and this time enabled the space and time to conduct the PPIE group. The PPIE group provided an understanding of COPD patients' behaviours and needs to participate in the trial and how this insight can be implemented into the trial's design. This made the trial more robust and participant-friendly, significantly modifying and factoring this PPIE feedback into the study design and operationalisation, making the trial ready to be sent to ethics and upon approval to be conducted.

Unfortunately, post-COVID-19, significant delays occurred, with multiple factors concurring, which took considerable time to liaise between stakeholders and regulatory organisations. This meant that the trial was not approved and finalised before the end of the PhD. Therefore, the trial did not commence.

Despite the various challenges originating from COVID-19 and COPD participants (who were deemed clinically vulnerable if participants caught the COVID-19 virus), there is still a strong motivation and aspiration to start the trial and to operationalise and complete it to its entirety. The trial will likely be a success and somewhat unique, with the possibility that the SoeMac device is effective and could create a paradigm shift within applied physiology and psychology research.

Chapter 8

Discussion

8.0 Introduction

From the onset, this programme of research was initially devised to test the safety and efficacy of singlet oxygen energy and the impact this has on the symptom profile and psychological well-being of people living with COPD. The main part of this programme of research was to design, implement and evaluate via a randomised clinical trial to gather empirical data that could inform a series of subsequent investigations to offer additional insights into the broader benefits of non-pharmacological interventions. Within the first six months of beginning the PhD, the onset of the global COVID-19 pandemic resulted in a seismic shift in the research focus, predominantly influenced by imposed restrictions on research activity and redistribution of clinical services to address the global health emergency. Whilst at the start of the pandemic, it was unknown how long these restrictions would be in place, and work continued to develop a protocol that could be implemented when suitable, but as it transpired, the restrictions on clinical research activities were only removed with around 12 months of the PhD programme left. During this period, concurrent research projects were established to increase the knowledge of psychological well-being. This included investigating and exploring the daily lives of COPD participants, how COPD impacts from a physiological and psychological perspective, and how this collectively negatively impacts the quality of life. The narrative under this is regarding what existing strategies COPD participants use daily and the advantages and disadvantages of these strategies to understand better what works and what does not. What do COPD participants require that is currently not being offered and implemented to help increase the quality of life, which are non-medicinal, require minimal effort, and can be used independently?

8.1 Summary of Main Thesis Findings

Chapter 3 supported existing research that COPD participants' physiological and psychological symptoms living with COPD increase in severity as the respiratory condition progresses. However, despite significant differences such as for breathlessness, sleep quality and health-related quality of life, the results that were not expected and were the opposite of the proposed hypotheses were the non-significant results such as for self-compassion, readiness to use a new intervention, as well as confidence to try a new intervention. The non-significant results were essential not to be ignored, as the results showed self-compassion remained moderate across the different COPD severities, and the readiness and confidence to try a new intervention were very high across the COPD severities.

8.1.1 Self-Compassion

What is novel about this PhD thesis is that it shows moderate levels of self-compassion across medium, high, and very high COPD severity. For example, the study does not support existing research such as Harrison et al., (2017) showing that COPD participants have lower self-compassion than healthy controls. Therefore, from the previous literature it could be assumed that COPD patients might exude low levels of self-compassion and therefore possessing a moderate level of self-compassion was surprising. This is because it was expected that as disease progression increases the psychological consequences of COPD, self-compassion would also decrease. With possible factors such as for many COPD participants (from previous literature), the onset of COPD comes from tobacco smoking, meaning that self-criticism and shame should have been higher, for example (which collectively sits within self-compassion). Also, it was expected that self-compassion would be significantly lower in very high COPD severity compared to, for example, a low or medium severity of COPD, which was one of the original hypotheses of the study.

Harrison et al., (2017) states that COPD participants have significantly lower levels of self-compassion to healthy controls (Harrison et al., 2017) and did not have moderate levels of self-compassion therefore comparing to PhD findings. Harrison et al., (2017) similarly used the SCS-SF (Self-compassion Scale Short Form) (Neff, 2016) to measure self-compassion. However, the authors of the SCS-SF (Neff, 2003) state that compared to the full version, which is the Self-compassion scale (SCS) (Neff, 2016), it is not recommended to analyse the separate domains of the SCS-SF (i.e. shame, self-kindness) because it is less reliable. As a result, the findings of Harrison et al., (2017) should be interpreted with caution (i.e. lower self-compassion is reliable, but regarding the specific claims that COPD participants have lower shame compared to healthy controls, needs more in-depth research using the SCS (Neff, 2016), which is reliable and valid to analyse the specific domains of self-compassion. This is why in this PhD, the total score was analysed only from the SCS-SF and then used within the statistical analysis to compare each COPD severity group. Unfortunately, COPD severity was not part of Harrison et al., (2017) study and therefore cannot be directly compared to PhD findings. It is important to understand further why COPD participants in this PhD have moderate levels of self-compassion (medium, high and very high COPD severity). The novelty within this finding warrants further investigation as a higher number of participants, including those with low severity of COPD/recently diagnosed with COPD, participants outside of the UK, participants that are BAME ethnicity, participants that are below 62 years of age, using the complete self-

compassion questionnaire (SCS) (Neff, 2016) questionnaire which captures feelings of guilt, shame, self-kindness, in addition to the self-conscious emotion's questionnaire (Pike, 2013) which highlights feeling of 'embarrassment' and 'shame-based avoidance'. Similar to Harrison et al., (2017) the study should include healthy controls, to compare COPD severities with health controls, regarding self-compassion and self-conscious emotions of similar demographics and ages. Further exploration of this finding would benefit the design and implementation of future interventions as current educational and behavioural approaches are engrained in causal factors, which could perturb people with a high sense of shame from engaging and completing such interventions if this exacerbates feelings of blame and shame.

8.1.2 Readiness/Confidence to Engage with New Interventions

Regarding readiness to try a new intervention and the confidence to try a new intervention, it was expected that confidence and readiness, like self-compassion, would decrease as COPD severity increases. This is because of the variety of medications, side effects and the significant decrease in mobility. For example, there would be a sense of giving up, low motivation and understanding the outcome of COPD (being unable to have mobility without an oxygen tank, unable to do self-care, having a full-time career and a shorter life expectancy) as the respiratory condition decreases. On the other hand, as the results showed a high level of readiness and confidence to try a new intervention, the findings were warranted to conduct the trial. However, the rulers were not sufficient, and the other findings from chapter three were not enough as a standalone study as it was essential to explore further the behaviours and needs that COPD participants use daily to help maintain quality of life and what aspects of COPD help and what aspects hinder quality of life, with a focus on strategies which are both medicinal and non-medicinal.

Despite not being in-depth or a valid measure of 'readiness' and 'confidence' to try a new intervention, it is the first study that has tried to attempt to create a 0-10 scale, which is easy for the participant to administer and also helps as a researcher gauge where the participant is at, regarding both readiness and confidence to try a new intervention. The ruler was inspired from 'readiness to change ruler' by Hesse, (2006), and the findings showed that the readiness to change ruler is related to actual behaviour change. However, the study was focused on 'ready to change' for participants with substance abuse disorders and, therefore, cannot be compared to this PhD and COPD participants.

On reflection, gauging the motivation, discipline and self-reported levels of 'readiness' and 'confidence' compared to actual behavioural change is complex, and the real reason for creating the rulers is to understand are the participants going to use new non-medicinal treatments, alongside current medications genuinely and if the participants do, would the participants have the confidence to follow through, in addition to using a non-medicinal treatment (i.e. a device) that the participant has not heard of before (i.e. a questionnaire desired response vs reality).

Therefore, creating a non-medicinal adherence questionnaire (or scale) for use within clinical practice and research settings is essential. For example, instead of creating a questionnaire, it may be possible to adapt current medication adherence questionnaires such as the 'MARS-5' (Chan et al., 2020). The MARS-5 includes questions regarding adherence, as well as issues of nonadherence, for example, forgetting to take medication. If the MARS-5 could be adapted for non-medicinal treatments such as devices, questions regarding motivation and depression could be added to gauge the likelihood of implementing the non-medicinal treatment into everyday life and if it is possible to do so and results, therefore, in behaviour change. It does not have to be for COPD participants only, but perhaps collectively for respiratory participants.

8.1.3 The Value of Qualitative Methodologies/Approaches

Chapter Four implemented the first photovoice study with a COPD population within the United Kingdom. To date, and following the viva for this PhD, another photovoice study was published by Summer et al., (2023), which the research was conducted in Singapore. Of interest the study by Summer et al., (2023) demonstrates increased anxiety, feelings of isolation and similar findings regarding breathlessness and the negative impact on activities of daily living. The findings agree with those within Chapters 3, 4 and 5. This shows that despite the photovoice study being conducted in the Western world in the United Kingdom, the findings are similar cross-culturally to the participants of the Eastern world in a multicultural Asian country, showing that there are similar negative impacts of COPD that are consistent.

On the other hand, the novelty of the photovoice study within this PhD compared to Summer et al., (2023) is that the focus was on how COPD impacts quality of life more broadly. In contrast, Summer et al., (2023) focused on the impact of COPD on the activities of daily living. Therefore, the added findings of the photovoice study from this PhD had an extra layer of findings, which included external psychological factors to do with others, such as the role and impact of friends, loved ones, and strangers—for example, not wanting to be treated differently

because of COPD and the symptoms that participants try to hide intentionally (similar findings from Cooney et al, 2013 as discussed in chapter 4) and overall anxiety about what others think as well, not being seen as 'weak' when coughing or out of breath or while using a wheelchair or oxygen tank for example. This impacts participant using ambulatory oxygen, wheelchairs, and coughing. Some try to avoid the flare-up of COPD symptoms by changing plans that would induce breathlessness or avoiding using a wheelchair in public. This worry, concern and anxiety of others need to be explored further, as it appears not to be generalised anxiety but more a social anxiety of having COPD and how society views this. A sense of maintaining independence is consistent, but, on the other hand, one needs support from others to function. It feels that comparing to Summer et al., (2023) the photographs seem to not have a 'deep meaning' for example a vacuum or a flight of stairs. In this PhD photovoice study, photographs such as the flowers (showing the distraction of hiding the breathlessness from others) (figure 4.5), the fish in the pond (to help with mindfulness) (figure 4.9), the cat (showing the hidden struggles of a condition and not wanting to tell people or for loved ones to find out) (figure 4.7), the daffodils inside the conservatory (showing the increasing amount of being stuck inside the house and trying to carry on and flourish) (figure 5.2) and therefore feel the photographs have a 'deeper' meaning to participants core feelings, emotions and this shows vulnerability which does not come from Summer et al., (2023) study and is the significant advantage of a photovoice methodology.

Speaking more broadly to the qualitative findings, in both the photovoice (chapter 4) and the semi-structured interviews (chapter 5), participants expressed internal psychological factors and living with COPD. However, the focus on quality of life, medications and strategies, similar to Chapter 3 (survey), was not expected regarding the moderate self-compassion across all COPD severities. However, even though the self-compassion was moderate within Chapter 3, the internal psychological factors included negative feelings and emotions such as self-blame, guilt and denial of having COPD, which shows that the participants that took part in the qualitative studies have a low level of self-compassion and a high level of self-criticism for causing the onset of COPD because of tobacco smoking and also the impact that breathlessness has, which impacts mobility and being able to do daily tasks such as self-care and walking.

Also, the differences between the PhD photovoice study and Summer et al., (2023) are that all eight participants were male participants the majority being Chinese ethnicity, compared to the PhD which seven out of eight were female and white British. In addition, the study was conducted by two female researchers, compared to the PhD researcher, who is male. Regarding

the process of the study, Summer et al., (2023) conducted interviews in person (which included an interview to discuss the study before taking photographs and having just a follow-up interview after the photographs had been received), whereas the PhD was conducted online using video calling using the Signal app and no prior interviews were conducted, only to follow up after the photographs had been sent to the researcher. On reflection, the researchers (Summer et al., 2023) conducted the initial interviews to build rapport and to answer any questions, which may have helped COPD participants to articulate further after sending the photographs because of the rapport built, and this would be of benefit to do for both the researcher and the participant, in addition to conducting the interviews in person. However, the study in the PhD as discussed in Chapter 4, was because of the COVID pandemic and participants were shielding. Therefore, despite similarities between both studies regarding photovoice methodology and findings, there are as many differences as possible, showcasing the novelty of the PhD photovoice study and being the first of its kind outside of Asia.

8.1.4 Medication Strategies and Patient Experiences

In parallel with the psychological factors, having problems with medication, such as side effects and anxiety when changing, ambulatory oxygen, which can be heavy to use, was to be expected. Strategies such as mindfulness, yoga, and gardening help provide purpose and instant satisfaction, which requires a small amount of energy and mobility and supports existing research. It was apparent that participants also raised the need to try new strategies and be involved in research. However, this warrants further research and more participants to generalise these findings to all COPD populations. It became clear linking with the survey (chapter 3), COPD participants have many different medications, strategies and interventions and, despite this, have a low quality of life, which warrants a novel device such as the SoeMac, as the current medication and non-medicinal is not effective long-term and fit for purpose from low to very high COPD severity. Furthermore, the qualitative studies showed that breathlessness affects sleep, coughing during the night, and then affecting energy levels and mobility – collectively, which appears not to be managed effectively in current medication and strategies/interventions. Therefore, this is why the trial reflected this to measure the pre-, mid and end outcomes across COPD symptoms, which include sleep quality, breathlessness, fatigue, mobility, and psychological well-being (anxiety and depression)

8.2 Research Limitations

As in the case in other clinical research areas, the demographic of participants in this thesis was predominantly white females. As highlighted throughout other areas of the thesis, this does not represent the known demographic of COPD participants. Indeed, in Chapter 2, the data highlights that over half of the participants were male. Further research is needed to find out why there were not more men taking part, as it is vitally important to understand whether there are similarities and differences between female COPD participants, how COPD impacts the quality of life, and what strategies are beneficial in helping to manage COPD symptomology. The need to ensure increased representation must also consider the spread across the life course, acknowledging an increase in the prevalence and diagnosis of younger adults with COPD. There should also be a concerted effort to increase the representation of ethnic minority groups in all areas of clinical research; within this thesis, all participants are white and from western areas. People from ethnic minority groups make up a disproportionate amount of COPD diagnoses and, more broadly, chronic disease conditions in the UK and worldwide, but this is commonly not represented within clinical research. Alongside ensuring that research is conducted with representation, there is an additional need to increase the strategies and pathways to learn from the hard-to-reach communities. Again, this is a systematic issue across the clinical research domain. However, dedicated approaches should be implemented within research design and delivery plans to ensure that research is genuinely inclusive and widely represents the patients affected by chronic disease. Whilst it is acknowledged that these are hard to reach, it is not to say that they are inaccessible. Increasing the knowledge and understanding from working closely with these populations would significantly impact the understanding of behavioural indicators and the design, implementation and outcomes of subsequently designed interventions. A further consideration of research must address the issue of attrition with participation in descriptive and intervention studies. Historically, COPD interventions possess one of the highest levels of attrition and drop. However, the reasons and implications of this on patient well-being have yet to be determined in detail by explorative approaches.

8.3 Future Research

Due to the nature of the PhD, as discussed in previous chapters, it has naturally produced two parts of the PhD, which are psychological and then the research regarding the SoeMac device and the trial, with significant input from PPIE.

Conducting the trial is imperative for future research to test the suitability, feasibility and acceptance of novel technologies. The protocol has been finalised, and the next stage is for the MHRA to provide approval, and the trial can be commenced. Whether it is within the first or second feasibility trial, the use of detailed lung function assessments should be added back in, these were removed due to COVID-19 restrictions. This is important to enable an objective measure in the trial to measure the effectiveness of the SoeMac. In addition, the GENEActiv accelerometers, which could measure if daily physical activity had increased or decreased, compared the SoeMac active group to the placebo group. The operationalisation of the trial should be offered as a hybrid approach, providing an option whether participants would like a home visit or to have the appointments via video call, for the documentation to be posted, etc. The PPIE group should be updated, and various meetings to gain feedback regarding participant retention and to reduce drop-out rates, if this occurs during the trial, in addition to suggestions from the PPIE group to try and access the hard-to-reach participants that are 'off the radar', that do not attend medication reviews or local COPD events or that do not have an active online presence/social media for example. Active flexibility should be granted for participants who are unwell and may need the study appointments to be rescheduled rather than to remove the participant from the study (i.e. if the participant does not attend more than 1 study appointment). Moreover, try to access participants who are hard to access, 'off the radar' and do not currently have a voice in research and within clinical settings. The SoeMac device has the significance of a paradigm shift in physiology and psychology.

Regarding self-compassion, it is recommended to have a study which had COPD participants that are below the average age (i.e. below 62 years old), including COPD participants that have low severity and have a balance of men and women. These participants represent a multicultural United Kingdom and from different socioeconomic backgrounds. Also, to have as many COPD participants as possible and a healthy control group, not only to compare COPD severity but to collectively measure if there are significant differences between COPD participants and healthy controls to gauge where the most significant differences are. Based on the PhD findings of moderate self-compassion using the SCS-SF, which used an overall score for self-compassion, it would be interesting to analyse the level of specific components of self-compassion (i.e. low, moderate, high) and measure this for each COPD severity (i.e. low, medium, high and very high), in addition to healthy controls. This should be done using the SCS (Neff, 2016) which measures self-kindness, self-judgement, common humanity, isolation, mindfulness, over identified. The possible hypotheses would be that COPD participants with a

high COPD severity would have higher levels of self-judgement compared to healthy controls, as well as COPD participants with a low COPD severity. On the other hand, another hypothesis would be that common humanity would be moderate to high across all COPD severities with no significant differences compared to healthy controls. In addition, isolation could be significantly higher in high COPD severity because of the nature of COPD at the later stages with mobility and higher psychological distress, compared to low COPD severity and healthy controls. In addition to the various findings from the two qualitative chapters, Pike (2013) questionnaire should be used to measure self-conscious emotions, which the qualitative chapters highlighted, such as guilt and embarrassment, and shame-based avoidance, again for each COPD severity and healthy controls to measure for significant differences and also to analyse where the specific significant differences are. The hypotheses would be that both guilt and embarrassment and shame-based avoidance would be significantly higher in COPD participants with high severity of COPD compared to low COPD severity and healthy controls. The study's results could help inform psychological therapy or psychological input within pulmonary rehabilitation programmes to reduce psychological distress, increase self-compassion, and help COPD participants understand further self-conscious emotions. An audit within the clinical service could measure psychological distress using the PHQ-9 and the GAD-7, as well as the SCS (Neff, 2016) and Pike, (2013) prior to the added psychological input, mid and post to deem effectiveness and comparing this to treatment as usual group (without pulmonary rehabilitation) and comparing this to treatment as usual with the standard pulmonary rehabilitation sessions. Depending on the findings from a research perspective, qualitative follow-up interviews (which could include a photovoice methodology) could be conducted to explore further the high-level domains and vice versa, the lower level of specific domains of self-compassion, as COPD is complex and affects participants from a biopsychosocial perspective. It is essential to conduct further research from the perspective of the younger and older COPD participants and to view COPD from the specific stages/severity of COPD to provide effective treatments and, therefore, effective clinical services.

8.4 Conclusion

Current pharmacology and psychological therapies, pulmonary rehabilitation and non-medicinal strategies are not fit for purpose, i.e. they are not practical, especially as COPD progresses in severity, impacting managing COPD symptomology, affecting sleep quality, energy levels, psychological well-being (guilt, shame, anxiety with COPD symptoms) and activities in daily living, getting worse as the chronic respiratory condition progresses.

Accessing pulmonary rehabilitation and effective strategies should not be a barrier in the 21st century. There is a great need for a non-medicinal intervention that can be used with existing medicinal strategies to help manage COPD symptomology, quality of life and psychological well-being. There is still no intervention that can restore damaged lung tissue and improve lung function. COPD participants have made mistakes of smoking throughout their lives, but with effective interventions, they deserve to live a prosperous life with the same life expectancy as everyone else. Change is needed and fast – from the participants' perspective and the health system's cost.

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CHAPTER 10
APPENDICES

APPENDIX A

ETHICS APPROVAL

Ethics ETH1920-1638: Samuel Grimwood : Decision

Sent on **08 Apr 2020** by **Charlotte Dakin** Download as PDF...

Dear Samuel

ETH1920-1638

Thank you for submitting your application to the College of Life and Natural Sciences Research Ethics Committee, which has now been reviewed and considered.

The outcome of your application is:

approved.

One note from the Committee is that participant-facing documents must be fully scrutinised and any punctuation and grammatical errors are corrected (e.g. line re. purpose of the study and the line re. near future.)

If any changes to the study described in the application are necessary, you must notify the Committee and may be required to make a resubmission of the application.

On behalf of the Committee, we wish you the best of luck with your study.

Yours sincerely

Charlotte Dakin

Appendix B
Participant information sheet

Participant Information Sheet

Study title

Identifying important determinants of a Chronic Obstructive Pulmonary Disorder (COPD) symptom profile in patients.

Invitation

You have been invited to participate in this 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.

Purpose of the study

The purpose of the research is to identify from patients the most important determinants and areas of consideration for future research in COPD patients and those that support them.

COPD can increase levels of breathlessness, fatigue and limits airflow which can significantly impact taking part in day-to-day activities. This can negatively affect quality of life and can cause sleep problems and depression.

Despite having a wide range of medical treatments available, COPD is still decreasing lung function and directly impacts the quality of life of those that are living with the respiratory condition.

Therefore, it is important to understand further the interlink between the physiological and psychological factors of COPD.

The aim to try and provide new insight by conducting this research and to attempt to design an intervention that could reduce the impact of COPD on quality of life of the person living with the condition and by improving lung function. As well as this to be able to increase self-compassion and to decrease levels of depression.

It is therefore important to investigate this further to set the foundation for future research from the findings of this study.

Why have I been selected? Am I eligible to take part?

You are eligible to take part if:

- You have COPD
- 18 years old & above
- Live in the UK
- Able to understand written information in English

Do I have to take part?

Taking part is voluntary. You have the right to refuse to participate and you may withdraw your consent at any time without jeopardy. If you complete the survey and you change your mind, you can withdraw by contacting the research team on the number below The LSREC recommends that you can withdraw up to 2 weeks after participation in the study, unless there is a significant reason, which will be considered.

What will taking part in the study involve?

You will see a screen, with the details of this study, and you will be able to consent to taking part by selecting 'yes or no' to taking part. This will act as an online signature.

After consenting to take part in this research, you will then be asked straight away to fill in some information about yourself (i.e., your age, occupation, medication for your COPD).

If you would still like to continue you will be asked specific questions about your day-to-day life experiences of living with COPD: Comorbid health conditions, breathlessness, and specific questions about COPD.

As well as the impact it has on your wellbeing: quality of life, sleep quality, anxiety and depression, emotions about how you feel about living with COPD and self-compassion.

The whole study will take place on the internet and the answers that you submit, will be saved. The lead researcher will receive the anonymised data via a secure database.

Completing the survey will take approximately 25-35 minutes. You can pause if you would like to do so and resume at a later date.

At the end of the study you will have the option to provide your email address, to be contacted by the research team about participating in future research regarding supporting someone with COPD. If you decided this is what you would like to do, your email address

would be stored on our secure research database (For GDPR and data protection information, please refer to the section ‘Further guidance on the use of your data and your rights’).This is completely optional.

What if I can’t get online?

This is an online study and so you will need to be able to access the internet to take part (i.e., a laptop/computer, smartphone, tablet/iPad). If you do not have any device that connects to the internet, please contact the primary researcher and we will find alternative paper-based arrangements.

What are the possible risks of taking part?

There will be no risk participating in this study, beyond that experienced in day-to-day life. There are no special precautions that you need to take before or after taking part in the study. Whilst the risk of participation I considered negligible agreement to participate in this research does not compromise your legal rights and should something go wrong.

What are the possible benefits of taking part?

We are trying to find out more information about the factors that impact the quality of life with people who have COPD. We cannot promise that this study will help you directly, but the information that you kindly provide, could add to existing knowledge in this specific area of COPD and make a significant difference and impact.

Also, as a thank you for taking part in this study you will have the chance to be enrolled into a prize draw in a chance to win one of five gift cards. Winning participants will be drawn at random by an impartial member of the University of Derby’s, University Research Knowledge Exchange Office (URKEO). If you win, you will be contacted via email to claim your prize. 1st prize will be a £50 Amazon gift card, 2nd prize will be a £25 gift card and then 3 separate prizes of £10. To be enrolled into this draw please state your email address at the end of the survey, so the URKEO can email you if you have won. Again this is optional and your email address will only be used for the prize draw. Once the price draw has been conducted, your email address will only be used for the prize draw. Once the prize draw has been conducted, your email address will be deleted from The University of Derby’s server (For GDPR and data protection information, please refer to the section ‘Further guidance on the use of your data and your rights.)/

What will happen to the results of the study?

The information will be stored securely at The University of Derby for a minimum of 7 years and only the lead researcher will have access it. Your decision to participate is completely voluntary. Should you wish to withdraw from the research you may do so at any point, up to two weeks after participation (this is because your data will be formally screened, cleaned and prepared for data analysis which will be conducted and therefore the research team will not be able to remove your anonymised data). You will not need to give any reason or explanation for doing so. To withdraw your data simply contact the researcher or research team on the details below with your unique participant code (i.e., the 5-digit memorable code).

Can I get advice from the research team about my COPD?

Unfortunately the research team is unable to offer you any advice on COPD. If you do need any advice or help, we would recommend your contact your doctor or relevant health professional.

What if I become distressed during the study?

It is not anticipated that there will be any reason for you to become distressed during this study but if you do please contact your GP, The Samaritans (Available 24 hours a day to provide confidential emotional support for people who are experiencing feelings of distress, despair or suicidal thoughts, www.samaritans.org, 116 123 (free to call from within the UK and Ireland), 24 hours a day, email: jo@samaritans.org), Lifeline 0808 808 8000 (is also available seven days a week to contact if you need help), or The British Lung Foundation https://www.blf.org.uk/support-for-you/copd; 03000 030 555; Mon-Fri; 9am – 5pm.

Who is conducting and funding the research?

The research is being conducted by Mr. Samuel Grimwood, as part of his PhD at The University of Derby and the supervisory team is Dr Mark Faghy (Director of Studies), Dr Emma Sharpe and Professor Gyan Tripathi. The research is funded through The University of Derby, The European Regional Development Fund (ERDF) and SoeHealth Ltd.

What if I have any questions?

If you would like more information about this research, ask any questions, withdraw consent or to make a complaint, please contact one of the research team on the details below.

Contact details

Mr Samuel Grimwood
s.grimwood@derby.ac.uk

Dr Mark Faghy
m.faghy@derby.ac.uk
+44 (0) 1332 592109

Dr Emma Sharpe
e.sharpe@derby.ac.uk
+44 (0) 1332 593737

Professor Gyan Tripathi
G.Tripathi@derby.ac.uk
+44 (0) 1332 622773

Further guidance on the use of your data and your rights.

The lead researcher will be collecting data from your participation in this study. This data is for us to understand the quality of life for people who are living with COPD. It is also in the public interest of enhancing academic research is this area.

- Not seek more information from you than what is essential and necessary for the study.
- Make sure that you are not identified by the data by anonymising it using ID codes.
- Use your anonymised data only for the purposes of this study and for any relevant publications that arise from it.
- Store data safely in password-protected databases to which only the named researchers have access.
- Not keep your information for longer than is necessary (usually for seven years).
- Safely destroy your data by shredding or permanently deleting them.

Data will be stored securely on Qualtrics and on The University of Derby's server. The server and database are protected by several measures including anti-virus and anti-spyware applications, firewalls, encryption technology and permissions.

Data will be stored securely until the study end date and will be securely stored according to the ICH-GCP standards and GDPR Act (2018) data protection principles. If you would like to ask any questions specifically related to data storage and GDPR guidelines, please get in contact with our Data Protection Officer (DPO) James Eaglesfield on (01332) 591762 or our Deputy DPO Helen Rishworth on (01332) 591954. Alternatively, you can email gdpr@derby.ac.uk.

During the study, the researcher will share documents with the supervisory team, that are authorised personnel working within the College of Life and Natural Sciences at The University of Derby. The researcher and supervisory team will comply with the requirements of the Data Protection Act 1998.

Researchers on the project with access to the data are supervised by highly qualified and experienced staff and have been very careful to ensure the security of your data. The study was approved for its ethical standards by The University of Derby Human Sciences Research Ethics Committee. Further information about the project can be obtained from Mr Samuel Grimwood (s.grimwood@derby.ac.uk), Dr Mark Faghy (m.faghy@derby.ac.uk, +44 (0) 1332 592109), Dr Emma Sharpe (e.sharpe@derby.ac.uk, +44 (0) 1332 593737), Professor Gyan Tripathi (G.Tripathi@derby.ac.uk, +44 (0) 1332 622773) at the University of Derby, Kedleston Road, Derby DE22 1GB.

Appendix C

Consent Form

Participant Statement of Consent to Participate in the Investigation Entitled:

***** Identifying important determinants of a Chronic Obstructive Pulmonary Disorder (COPD) symptom profile in patients*****

1) I understand that I have agreed to participate in a research study exploring the impact of COPD on my quality of life.

2) I have read a copy of the participant information sheet.

3) I have also read and understood the risks and side effects that may result from participating in the study.

4) I confirm that I have had the opportunity to ask questions about the study and, where I have asked questions, these have been answered to my satisfaction.

5) I undertake to abide by University regulations and the advice of researchers regarding safety.

6) I am aware that I can withdraw my consent to participate in the procedure at any time up to two weeks after participation and for any reason, without having to explain my withdrawal and that my personal data will be destroyed and that my medical care or legal rights will not be affected.

7) I understand that any personal information that I provide till be treated as confidential and my identity will be kept strictly anonymous.

8) I confirm that I have had the University's policy relating to the storage and subsequent destruction of sensitive information explained to me.
Available online:
https://www.derby.ac.uk/services/its/data-governance/privacy-notices/research/

9) I understand that sensitive information I have provided through my participation in this study, in the form of contact details, will be handled in accordance with this policy.

10) I understand that my data will be held for a maximum duration of 7 years from the commencement of the study and will be destroyed by the beginning of 2027.

11) I confirm that I have completed the online survey and know of no reason, medical or otherwise that would prevent me from partaking in this research.

12) I understand that the information collected about me will be used to support other research in the future and may be shared anonymously with other researchers.

13) I understand that any information that will be kept strictly confidential and that no personal information will be included in the study report or other publication.

14) I understand that I will have the option at the end of the survey, to provide my email address, to be contacted by the research team, for additional research that we will be in addition to this survey in regard to having COPD. Should you wish to agree your email

address will be stored on a Microsoft Excel 2016 spreadsheet, which will be password protected and only accessed by the research team on The University of Derby's server. The database will be protected by several measures including anti-virus and anti-spyware applications, firewalls, encryption technology and permissions. Data will be stored securely for a period of up to 7 years from the study end date and will be securely stored according to the ICH-GCP standards and GDPR data protection principles. You can request to have your email address to be omitted from the database by contacting the researcher.

15) I understand that I will have the option at the end of the survey, to provide my email address, to be enrolled into a prize draw in a chance to win a gift card. Your email address will only be used for URKEO to contact you if you win a gift card. Therefore, once the prize draw has been conducted your email address will be deleted. The database will be protected by several measures including anti-virus and anti-spyware applications, firewalls, encryption technology and permissions. Data will be stored securely for a period of up to 7 years from the study end date and will be securely stored according to the ICH-GCP standards and GDPR data protection principles. You can request to have your email address to be omitted from the database by contacting the researcher.

I have read and understood all the information above and agree to take part in this study

Yes/No

I agree to provide my email address to be contacted for future research in regards to COPD

Yes/No

I agree to provide my email address to be contacted to be enrolled for the prize draw

Yes/No

Participant ID: _____ (please use the last two letters of your postcode and the last two digits of your phone number and if you have COPD add the letter (P) i.e. BN22P. Your data will be stored under this ID to ensure confidentiality. You will be asked to recall this ID if you wish to withdraw your data)

Appendix D

Debrief Form

Debrief Information

Debrief Form

Thank you for your participation in this study. Your participation is greatly appreciated.

Purpose of the Study:
The purpose of this study is to explore the physiological and psychological factors of COPD and how it impacts your day-to-day life.

The aim to try and create an intervention(s) that could be of benefit in reducing the impact of COPD on quality of life by improving lung function and creating a psychological intervention that could be effective in increasing self-compassion and decreasing levels of depression and fatigue.

Thankyou for taking the time to participate in this study which will help us to understand further the physiological and psychological factors of COPD and to set the foundation for future research from the findings that we will get once the study has finished.

Withdrawal Procedure:
Your identity will remain confidential if the results of the study are published. Potential places for publication could be scientific journals (i.e., Elsevier - Social Science & Medicine). The contact details are listed below. May you be assured that your data will be deleted immediately, and you will not appear in any part of the report. Your decision to participate is completely voluntary. Should you wish to withdraw from the research you may do so at any point, up to two weeks after participation (this is because your data will be formally screened, cleaned and prepared for data analysis which will be conducted and therefore the research team will not be able to remove your anonymised data). You will not need to give any reason or explanation for doing so. To withdraw your data simply contact the researcher or research team on the details below with your unique participant code (i.e., the 5-digit memorable code).

Final Report:
If you would like to receive a one-page summary of the findings when it is completed, please feel free to contact the researcher. The contact details are listed below.

Useful Contact Information:
For any further information regarding the topic of COPD and mental health, please see below, for further details of several organisations that may be useful. They will be able to offer professional advice and guidance that cannot be obtained from the researcher or their supervisory team.

British Lung Foundation: https://www.blf.org.uk/support-for-you/copd; 03000 030 555;

9am-5pm

MIND: www.mind.org.uk

Samaritans: www.samaritans.org,**116 123**, 24 hours a day, email: jo@samaritans.org

If you have any questions or concerns regarding this study, its purpose, or procedures, or if you have a research-related problem, please feel free to contact via email, the researcher or their supervisors:

Mr Samuel Grimwoood – s.grimwood@derby.ac.uk; Dr Mark Faghy - m.faghy@derby.ac.uk
Dr Emma Sharpe – e.sharpe@derby.ac.uk; Professor Gyan Tripathi - G.Tripathi@derby.ac.uk

Once again, thank you for your participation in this study.

Appendix E

EQ-5D SPSS Syntax Index Scores

Scores: 11111 = .0 - 1 = -1, 2222 = 0.299 - 1 = -.0701, 55555 = 1.277 - 1 = 0.277. High quality of life = -1

Computing EQ-5D-5L index values with SPSS using the English (ENG) Devlin value set

Version 1.1 (Updated 16/11/2020)

The variables for the 5 dimensions of the EQ-5D-5L descriptive system should be named

'mobility', 'selfcare', 'activity', 'pain', and 'anxiety'.

If they are given different names the syntax code below will not work properly.

The 5 variables should contain the values for the different dimensions in the

EQ-5D health profile (i.e. 1, 2, 3, 4 or 5). The variable 'EQindex' contains the values of the

EQ-5D-5L index values on the basis of the ENG set of weights.

You can copy and paste the syntax below directly into a SPSS syntax window.

****

SPSS syntax code for the computation of index

values with ENG TTO value set

**********;

IF (mobility=1) disut_mo=0.

IF (mobility=2) disut_mo=0.058.

IF (mobility=3) disut_mo=0.076.

IF (mobility=4) disut_mo=0.207.

IF (mobility=5) disut_mo=0.274.

IF (selfcare=1) disut_sc=0.

IF (selfcare=2) disut_sc=0.050.

IF (selfcare=3) disut_sc=0.080.

IF (selfcare=4) disut_sc=0.164.

IF (selfcare=5) disut_sc=0.203.

IF (activity=1) disut_ua=0.

IF (activity=2) disut_ua=0.050.

IF (activity=3) disut_ua=0.063.

IF (activity=4) disut_ua=0.162.

IF (activity=5) disut_ua=0.184.

IF (pain=1) disut_pd=0.

IF (pain=2) disut_pd=0.063.

IF (pain=3) disut_pd=0.084.

IF (pain=4) disut_pd=0.276.

IF (pain=5) disut_pd=0.335.

IF (anxiety=1) disut_ad=0.

```
IF (anxiety=2) disut_ad=0.078.

IF (anxiety=3) disut_ad=0.104.

IF (anxiety=4) disut_ad=0.285.

IF (anxiety=5) disut_ad=0.289.

Compute disut_total= disut_mo +disut_sc +disut_ua +disut_pd +disut_ad.

Compute EQindex = 1-disut_total.

Formats EQindex(F8.3).

execute
```

Appendix F

The convergent validity results correlation of EQ-5D-5L with EQ-MH-VAS (Spearman coefficients results)

Dimension	EQ-MH-VAS
Mobility	**-.289****
Self-Care	**-.299****
Usual Activities	**-.319****
Pain/Discomfort	**-.378****
Anxiety/Depression	**-.621****
EQ-5D Index Score	**.472****

**. Correlation is significant at the 0.01 level (2-tailed).

Correlations

			Mobility	Self_care	Usual_activity	Pain_discomfort	Anxiety_dep	EQMHVAS	EQ-5D - Index Scores
Spearman's rho	Mobility	Correlation Coefficient	1.000	.754**	.790**	.623**	.483**	-.289**	-.854**
		Sig. (2-tailed)	.	.000	.000	.000	.000	.000	.000
		N	154	154	154	154	154	154	154
	Self_care	Correlation Coefficient	.754**	1.000	.801**	.630**	.469**	-.299**	-.822**
		Sig. (2-tailed)	.000	.	.000	.000	.000	.000	.000
		N	154	154	154	154	154	154	154
	Usual_activity	Correlation Coefficient	.790**	.801**	1.000	.597**	.418**	-.319**	-.824**
		Sig. (2-tailed)	.000	.000	.	.000	.000	.000	.000
		N	154	154	154	154	154	154	154
	Pain_discomfort	Correlation Coefficient	.623**	.630**	.597**	1.000	.424**	-.378**	-.763**
		Sig. (2-tailed)	.000	.000	.000	.	.000	.000	.000
		N	154	154	154	154	154	154	154
	Anxiety_dep	Correlation Coefficient	.483**	.469**	.418**	.424**	1.000	-.621**	-.656**
		Sig. (2-tailed)	.000	.000	.000	.000	.	.000	.000
		N	154	154	154	154	154	154	154
	EQMHVAS	Correlation Coefficient	-.289**	-.299**	-.319**	-.378**	-.621**	1.000	.472**
		Sig. (2-tailed)	.000	.000	.000	.000	.000	.	.000
		N	154	154	154	154	154	154	154
	EQ-5D - Index Scores	Correlation Coefficient	-.854**	-.822**	-.824**	-.763**	-.656**	.472**	1.000
		Sig. (2-tailed)	.000	.000	.000	.000	.000	.000	.
		N	154	154	154	154	154	154	154

**. Correlation is significant at the 0.01 level (2-tailed).

Appendix G
Skewness, kurtosis and Kolmogorov-Smirnov

Descriptive Statistics

	N	Minimum	Maximum	Mean	Std. Deviation	Skewness		Kurtosis	
	Statistic	Statistic	Statistic	Statistic	Statistic	Statistic	Std. Error	Statistic	Std. Error
"Breathlessness	154	1	5	3.11	1.213	-.192	.195	-1.008	.389
EQ-5D - Index Scores	154	-.161	1.000	.53790	.309950	-.654	.195	-.659	.389
Physical Health Scale_EQVAS1	154	4	90	46.93	21.953	-.047	.195	-1.063	.389
Mental Health Scale_EQVAS2	154	1	100	64.71	24.425	-.573	.195	-.559	.389
FAS TOTAL SCORE	154	14	47	28.08	8.228	.358	.195	-.646	.389
GLOBAL PSQI SCORE TOTAL	154	2	21	10.44	4.546	.008	.195	-.815	.389
Compassion	154	.50	3.42	1.4180	.58513	1.435	.195	1.608	.389

One-Sample Kolmogorov-Smirnov Test

			"Breathlessness	EQ-5D - Index Scores	Physical Health Scale_EQVAS1	Mental Health Scale_EQVAS2	FAS TOTAL SCORE	GLOBAL PSQI SCORE TOTAL	Compassion	"Readiness for Change Ruler	Confidence in making channge
N			154	154	154	154	154	154	154	154	154
Normal Parameters[a,b]	Mean		3.11	.53790	46.93	64.71	28.08	10.44	1.4180	4.05	8.25
	Std. Deviation		1.213	.309950	21.953	24.425	8.228	4.546	.58513	3.560	1.904
Most Extreme Differences	Absolute		.216	.145	.094	.131	.092	.095	.203	.363	.198
	Positive		.164	.076	.078	.074	.092	.089	.203	.363	.179
	Negative		-.216	-.145	-.094	-.131	-.063	-.095	-.125	-.196	-.198
Test Statistic			.216	.145	.094	.131	.092	.095	.203	.363	.198
Asymp. Sig. (2-tailed)[c]			<.001	<.001	.002	<.001	.003	.002	<.001	<.001	<.001
Monte Carlo Sig. (2-tailed)[d]	Sig.		.000	.000	.002	.000	.003	.002	.000	.000	.000
	99% Confidence Interval	Lower Bound	.000	.000	.001	.000	.001	.001	.000	.000	.000
		Upper Bound	.000	.000	.003	.000	.004	.003	.000	.000	.000

a. Test distribution is Normal.

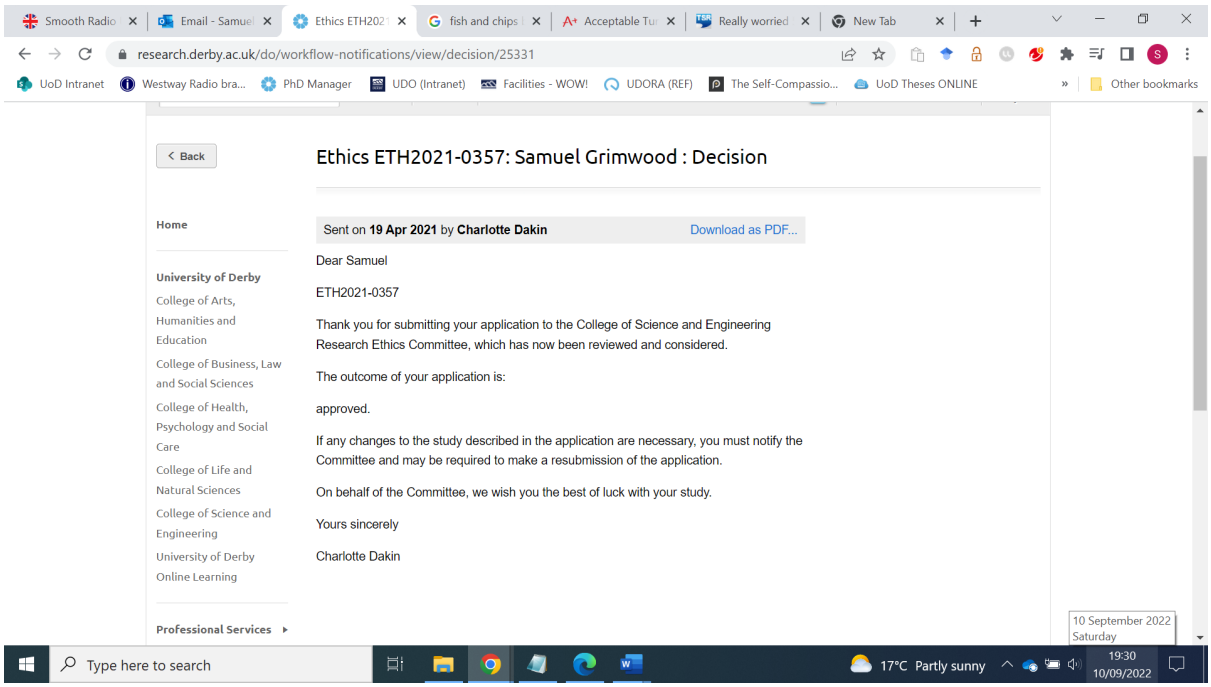
b. Calculated from data.

c. Lilliefors Significance Correction.

d. Lilliefors' method based on 10000 Monte Carlo samples with starting seed 2000000.

Appendix H

Ethics Approval



Appendix I

Participant information sheet

Participant Information Sheet
(Option 1)

Study title

A qualitative exploration of the experiences of having COPD, symptom profile determinants and its impact on quality of life, using a Photovoice methodology.

Invitation

You have been invited to participate in this 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 the time to read the following information carefully.

Purpose of the study

The purpose of the research is to increase our understanding of your experiences of living with COPD and its impact on your quality of life. We are also hoping to explore some of the strategies that you find most effective in helping to managing this disease.

Our previous study provided an insight into the physiological and psychological factors which underpin COPD. However, this study was questionnaire based, which meant that the unique and personal experiences of living with COPD had not been captured. As a result, you will be asked to take a number of photographs to provide a visual illustration of what living with COPD means to you, and to take part in an online interview to discuss each photograph with the researcher and the meaning behind each photograph that has been taken. As well as this a second online interview to explore in depth your first-hand experience of living with COPD, how it impacts your quality of life and the medication/strategies that you use.

Collectively the aim of this ongoing project is to provide new insight and to attempt to design an intervention that could improve the quality of life of people living with COPD.

Why have I been selected? Am I eligible to take part?

You are eligible to take part if:

- You have COPD

- 18 years old & above
- Live in the UK
- Able to understand written information in English
- <u>Own a device that can:</u>

  Take photographs

  Send photographs via 'Signal'
  (a free app similar to WhatsApp)
  Be used to take part in an interview, using video call software 'Microsoft Teams' (free to use)

Do I have to take part?

Taking part is completely voluntary. You have the right to refuse to participate and you may withdraw your consent at any time without jeopardy. If you decide to take part in the interview and send the photographs but change your mind, you can withdraw from the study by contacting the research team on the number below It is advised that you can withdraw up to 2 weeks after participation in the study, unless there is a significant reason, which will be considered. To withdraw your data simply contact the researcher or research team on the details below with your unique participant code (i.e., the 5-digit memorable code). This code will be unique to you (consisting of the last two letters of your postcode and last three digits of your phone number).

What will taking part in the study involve?

After reading this participant information within this page on Qualtrics (online portal that you are accessed, via the link you clicked on that was sent to you), after you have finished reading this information about the study, please click on the arrow below and you will be directed to the consent section, which will state also the researchers contact details, for the opportunity to ask any further questions Should you wish to take part in the study, you will be able to consent by selecting 'yes' or 'no' which the researcher will receive online. This will act as an online signature.

After consenting to take part in this research, you will then be asked straight away to fill in some information about yourself (i.e. your age, occupation) and that relating to your experience of COPD (i.e. Additional health conditions, Medication, Stage of COPD, FEV Score, Breathlessness Scale & Quality of life).

If you are eligible for the study and you have provided consent, you will be able to state your email address, as well as stating your unique participant code (i.e., 5-digit memorable code). This code will be unique to you (consisting of the last two letters of your postcode and last three digits of your phone number). Stating your email address is strictly for contacting the researcher and for the researcher to contact you regarding this study. Your email address will also be used to send study documentation during the study. Your email address will be stored securely on the University of Derby's server and email addresses will be sent securely using the University of Derby's Microsoft Outlook. Your data will remain completely anonymous throughout the study and will not be linked to any other personal information or data that you provide in the study.

If you consent to take part in this study, you will be emailed by the researcher regarding the next steps in due course, which will include a PhotoVoice visual instruction guide (outlining what photographs you can take and how to send them across). Once this information has been sent to you, you will have up to 14 days to take 5-10 photographs which should aim to provide an expression and insight in what it is like living with COPD and how it impacts or enhances your quality of life. These photos will be taking by using your smartphone or digital camera, and you will be asked to provide a description of each photograph (e.g. why have you decided to take it and/or how were you feeling at the time), to be sent to the researcher via 'Signal' (an app similar to WhatsApp but is more secure, which means our messages and your photographs are confidential between us). Please see below 'What should I take photographs of'?

The photographs will be sent using a secure University email address and the photographs will only be received by the lead researcher, who will anonymizer the photographs and will save on a secure database (a separate visual booklet will be available to guide you through the process).

After 14 days the photographs and descriptions will have been sent to the researcher and an online interview (one of two interviews for the study) will be conducted which will take between 45 minutes to 1 hour in total duration, to discuss the 5-10 photographs that you have taken, what they mean to you and why you have taken them, in relation to living with COPD and your quality of life.

Soon after this, a second online interview will be conducted (which is separate to the discussion of photographs in the previous online interview). The second interview is to discuss in more detail to explore the effect of COPD on your quality of life and about your

current COPD medical treatment i.e., your inhaler(s). This will also take between 45 minutes - 1 hour in total duration.

Both interviews will be conducted using Microsoft Teams and is free of charge to access (easily downloadable from the android or app store free of charge, if using a smartphone or ipad/tablet and similarly on a computer/laptop) and you will be sent a unique and specific link/details by the researcher, close to the time of the arranged online interview. The interview will be recorded for research purposes and will be saved on a secure database.

At the end of the study you will have the option to provide your email address, to be contacted by the research team about participating in future research regarding your COPD. If you decided this is what you would like to do, your email address would be stored on our secure research database (For GDPR and data protection information, please refer to the section 'Further guidance on the use of your data and your rights'). This is completely optional.

Step-by-Step Procedure

Stage 1 – Read the participant information sheet, consent to take part (should you wish) and answer demographic questions online.

Stage 2 – Researcher emails you and sends you a step-by-step guide on how to take photos (and provide descriptions) and how to send these to the researcher.

Stage 3 – Photographs are sent to researcher and are collated in preparation for the online interview.

Stage 4 – Online interview to be conducted to discuss the photographs that you have taken, with the aid of your photographs and descriptions on one document (shared on the computer and/or sent to you on email to go through online with the researcher).

Stage 5 – A second online interview to discuss about the effect of COPD on your quality of life and questions about your current COPD medical treatment (this is optional).

Stage 6 – Debrief Form sent to your email address.

What photographs do I need to take?

The content of the photographs that you take is completely up to you – however the aim is that they reflect or illustrate your experience of living with COPD and/or how the disease is impacting on your quality of life. There is not a photograph that is correct or incorrect, as it is

personal to you. You will be sent a visual guide as a pdf to your email address, in how to take photographs, the descriptions of each photograph and how to send securely to the researcher (using 'Signal,' which is an app similar to WhatsApp).

Although we will encourage you to express creativity when taking photographs, we ask that you please do not take photographs relating to:

- An individual or a person
- An identifiable landmark
- A sensitive nature
- Nudity
- Within a private organisation without permission (i.e., Supermarket)

What if I am unable to take photographs?

A core component of this study is to take photographs capturing your day-to-day life with COPD, including a description of each photograph that has been taken. If you are unable to take photographs in this way, we kindly ask that you do not take part in the study.

What if I cannot get online?

This is an online study and so you will need to be able to access the internet to take part (i.e., a laptop/computer, smartphone, tablet/iPad). Unfortunately, because of the current COVID-19 pandemic, an in person one-to-one interview cannot be arranged as an alternative at this moment in time.

What are the possible risks of taking part?

Taking Photographs –

You should not take any photographs that put you at risk or in danger (e.g., taking a photo in a dangerous place that may cause you harm or risk of falling)

Interview -

Talking about your experiences of having COPD can be difficult. If you feel uncomfortable, you can pause during both interviews, refuse to answer or if you do not wish to continue in the study, you are free to withdraw at any time.

During the interview if the researcher feels that you have said something that is affecting your personal safety and you are in danger, confidentiality will be breached, and the researcher will be obliged to contact the relevant authorities.

When being interviewed, it is natural sometimes to mention personal names, and other facts when discussing your COPD and medication. Therefore, as the interview is being recorded and analysed for the purposes of this research project, any identifiable names will be omitted and changed.

There will be no risk participating in this study, beyond that experienced in day-to-day life. There are no special precautions that you need to take before or after taking part in the study. Whilst the risk of participation I considered negligible agreement to participate in this research does not compromise your legal rights and should something go wrong.

What are the possible benefits of taking part?

We are trying to find out more information about the factors that impact the quality of life among people who have COPD and the strategies that appear to be most effective in managing the respiratory condition. We cannot promise that this study will help you directly, but the information that you kindly provide could add to existing knowledge in this specific area of COPD and make a significant difference and impact.

Also, as a thank you for taking part in this study you will have the chance to be enrolled into a prize draw in a chance to win one of five gift cards. Winning participants will be drawn at random by an impartial member of the University of Derby's, University Research Knowledge Exchange Office (URKEO). If you win, you will be contacted via email to claim your prize. 1st prize will be a £50 Amazon gift card, 2nd prize will be a £25 gift card and then 3 separate prizes of £10. To be enrolled into this draw please state your email address at the end of the survey, so the URKEO can email you if you have won. Again, this is optional and your email address will only be used for the prize draw and once the prize draw has been conducted, your email address will be deleted from The University of Derby's server (For GDPR and data protection information, please refer to the section 'Further guidance on the use of your data and your rights.)/

What will happen to the results of the study?

The information from the study, including the interview will be recorded, transcribed and both the photographs and descriptions will be stored securely at the University of Derby for a minimum of 7 years. Your decision to participate is completely voluntary.

All information collected will be anonymised using your unique 5-digit code. Quotes from the interviews, photographs and your photograph descriptions may be selected and therefore included in a PhD thesis, publications, and conferences. You will have full copyright of your photographs. Again, this will be fully anonymised and no identifiable information will be used.

Should you wish to withdraw from the research you may do so at any point, up to two weeks after participation. You will not need to give any reason or explanation for doing so. To withdraw your data simply contact the researcher or research team on the details below with your unique participant code (i.e., the 5-digit memorable code).

Can I get advice from the research team about my COPD?
Unfortunately the research team is unable to offer you any advice on COPD. If you do need any advice or help, we would recommend your contact your doctor or relevant health professional.

What if I become distressed during the study?
It is not anticipated that there will be any reason for you to become distressed during this study but if you do please contact your GP, The Samaritans (available 24 hours a day to provide confidential emotional support for people who are experiencing feelings of distress, despair or suicidal thoughts, www.samaritans.org, 116 123 (free to call from within the UK and Ireland), 24 hours a day, email: jo@samaritans.org), Lifeline 0808 808 8000 (is also available seven days a week to contact if you need help), or The British Lung Foundation https://www.blf.org.uk/support-for-you/copd; 03000 030 555; Mon-Fri; 9am – 5pm.

Who is conducting and funding the research?

The research is being conducted by Mr. Samuel Grimwood, as part of his PhD at The University of Derby and the supervisory team is Dr Mark Faghy (Director of Studies), Dr Amy Baraniak, Dr Emma Sharpe, and Professor Gyan Tripathi. The research is funded through The University of Derby, The European Regional Development Fund (ERDF) and SoeHealth Ltd.

What if I have any questions?

If you would like more information about this research, ask any questions, withdraw consent or to make a complaint, please contact one of the research team on the details below.

Contact details

Mr Samuel Grimwood
s.grimwood@derby.ac.uk
+44(0) 7557800951

Dr Amy Baraniak
a.baraniak@derby.ac.uk
+44(0) 1332 59304

Dr Mark Faghy
m.faghy@derby.ac.uk
+44 (0) 1332 592109

Further guidance on the use of your data and your rights.

The lead researcher will be collecting data from your participation in this study. This data is for us to understand further the effect of COPD on quality of life and effective strategies in managing the respiratory condition. It is also in the public interest of enhancing academic research is this area.

- Not seek more information from you than what is essential and necessary for the study.
- Make sure that you are not identified by the data by anonymising it using ID codes.
- Use your anonymised data only for the purposes of this study and for any relevant publications that arise from it.
- Store data safely in password-protected databases to which only the named researchers have access.
- Not keep your information for longer than is necessary (usually for seven years).
- Safely destroy your data by shredding or permanently deleting them.

Data will be stored securely on Qualtrics and on The University of Derby's server. The server and database are protected by several measures including anti-virus and anti-spyware applications, firewalls, encryption technology and permissions.

Data will be stored securely until the study end date and will be securely stored according to the ICH-GCP standards and GDPR Act (2018) data protection principles. If you would like to ask any questions specifically related to data storage and GDPR guidelines, please get in contact with our Data Protection Officer (DPO) Helen Selby on (01332) 591762 or our Deputy DPO Helen Rishworth on (01332) 591954. Alternatively, you can email gdpr@derby.ac.uk.

During the study, the researcher will share documents with the supervisory team, that are authorised personnel working within the College of Science & Engineering at The University of Derby. The researcher and supervisory team will comply with the requirements of the Data Protection Act 1998.

Researchers on the project with access to the data are supervised by highly qualified and experienced staff and have been very careful to ensure the security of your data. The study was approved for its ethical standards by The University of Derby Human Sciences Research Ethics Committee. Further information about the project can be obtained from Mr Samuel Grimwood (s.grimwood@derby.ac.uk, +44(0) 7557800951), Dr Amy Baraniak (a.baraniak@derby.ac.uk, +44(0) 1332 59304) and Dr Mark Faghy (m.faghy@derby.ac.uk, +44 (0) 1332 592109) at the University of Derby, Kedleston Road, Derby DE22 1GB.

Appendix J

Consent Form

Participant Statement of Consent to Participate in the Investigation Entitled:

**

A qualitative exploration of the experiences of having COPD, symptom profile determinants and its impact on quality of life, using a PhotoVoice methodology.

**

Option 1

2) The information that you supply in this study will be held and processed in line with the UK GDPR/ Data Protection Act 2008/ EU GDPR. Information will be used by the University of Derby (as data controller) to anonymise, analyse and interpret for a PhD research project.

3) I understand that I have agreed to participate in a research study exploring the impact of COPD on my quality of life for both part 1 *(Taking and sending photographs regarding COPD and the impact on your quality of life & Online Interview to discuss the meaning behind your photographs)* and part 2 *(Second Online Interview, regarding your experiences of COPD and your medication/strategies)* of the study.

   (The photographs/descriptions will be sent using Signal, which is an app similar to WhatsApp, which is free to download) and Microsoft Teams for the interviews (free to download and instructions will be provided).

3) I have read a copy of the participant information sheet.

4) I have also read and understood the risks and side effects that may result from participating in the study.

5) I confirm that I have had the opportunity to ask questions about the study and, where I have asked questions, these have been answered to my satisfaction.

6) I am aware that I can withdraw my consent to participate in the procedure at any time up to two weeks after participation and for any reason, without having to explain my withdrawal and that my personal data will be destroyed and that my medical care or legal rights will not be affected.

7) I understand that any personal information that I provide till be treated as confidential and my identity will be kept strictly anonymous.

8) I confirm that I have had the University's policy relating to the storage and subsequent destruction of sensitive information explained to me.
   Available online:
   https://www.derby.ac.uk/services/its/data-governance/privacy-notices/research/

9) I understand that sensitive information I have provided through my participation in this study, in the form of contact details, will be handled in accordance with this policy.

10) I understand that my data will be held for a maximum duration of 7 years from the commencement of the study and will be securely destroyed by the beginning of 2027.

11) I confirm that I know of no reason, medical or otherwise that would prevent me from partaking in this research.

12) I understand that the information collected about me will be used to support other research in the future and may be shared anonymously with other researchers.

13) I understand that any information that will be kept strictly confidential and that no personal information will be included in the study report or other publication.

14) I understand that providing my email address at the start of the survey will be used to be contacted by the researcher for enrolment on to this study

15) I understand that I will have the option at the end of the survey, to provide my email address, to be contacted by the research team, for additional research that we will be in addition to this study in regard to having COPD. Should you wish to agree your email address will be stored on a Microsoft Excel 2016 spreadsheet, which will be password protected and only accessed by the research team on The University of Derby's server. The database will be protected by several measures including anti-virus and anti-spyware applications, firewalls, encryption technology and permissions. Data will be stored securely for a period of up to 7 years from the study end date and will be securely stored according to the ICH-GCP standards and GDPR data protection principles. You can request to have your email address to be omitted from the database by contacting the researcher.

16) I understand that I will have the option at the end of the survey, to provide my email address, to be enrolled into a prize draw in a chance to win a gift card. Your email address will only be used for URKEO to contact you if you win a gift card. Therefore, once the prize draw has been conducted your email address will be deleted. The database will be protected by several measures including anti-virus and anti-spyware applications, firewalls, encryption technology and permissions. Data will be stored securely for a period of up to 7 years from the study end date and will be securely stored according to the ICH-GCP standards and GDPR data protection principles. You can request to have your email address to be omitted from the database by contacting the researcher.

Our lawful basis for processing this data is consent.

I have read and understood all the information above and agree to take part in this study, giving my consent for my data to be collected and stored as per this consent form

Yes/No

I agree to provide my email address to be contacted to enrol on to the above study, to partake in the taking photographs regarding COPD + online video call interview to discuss the photographs I have taken, as well as an additional online video call interview regarding my COPD and the medication/strategies I use. Photographs will be sent using Signal app and the interviews will be conducted using Microsoft Teams.

Yes/No

I understand that the online interviews will be audio recorded within the Microsoft Teams programme, for the researcher to transcribe and anonymise to conduct a collective analysis at the end of the study.

Yes/No

I agree to provide my email address to be contacted for future research in regards to COPD

Yes/No

I agree to provide my email address to be contacted to be enrolled for the prize draw

Yes/No

Participant ID: _____ (please use the last two letters of your postcode and the last three digits of your phone number i.e. BN223. Your data will be stored under this ID to ensure confidentiality. You will be asked to recall this ID if you wish to withdraw your data)

Appendix K

Photovoice Instruction Guide

PhotoVoice Guide

Option 1

This guide outlines for you the aims/purpose of the study, how and what to take photographs of and provides a step-by-step on how to send them to me.

If you have any questions, please contact:

Samuel Grimwood

s.grimwood@derby.ac.uk

+44(0) 7557800951

Researchers Contact Details	8

Study Aims and Purpose for PhotoVoice

**Please take 5-10 photographs and send these to the researcher by using Signal *(to be sent within 14 days of receiving this guide).*

The photographs should provide a visual illustration or expression of *your experience* of living with COPD and how it impacts or enhances your quality of life. Quality of life refers to your overall health and wellbeing. Typically, someone with a higher quality of life would be in good health, feel comfortable in their day-to-day life and is able to take part and enjoy events that arise.

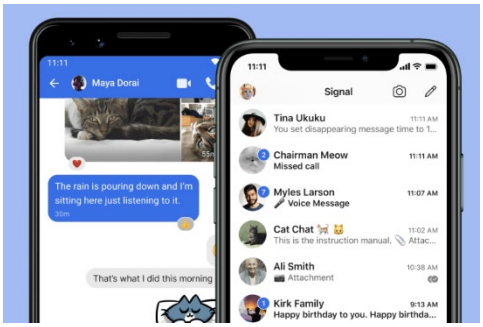
There is not a correct or incorrect photograph and description, as it is personal to you.

However, please do not take photographs:

- Of an individual or a person
- An identifiable landmark
- Sensitive nature
- Nudity

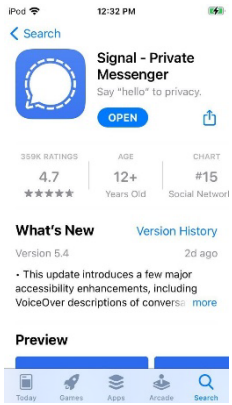
- Within a private organisation without permission (i.e. Supermarket)

How to send photographs/descriptions you have taken using Signal

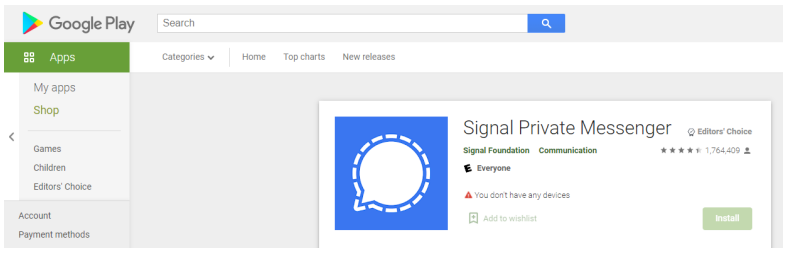


To do this on Mobile/Tablet/iPhone:

On an iPhone - Click on the App Store



On an Android – Click on the Play Store



Type in 'Signal' and it will come up 'Signal – Private Messenger'

For specific support – please see the instructions on the Signal website - https://support.signal.org/hc/en-us

How to attach photographs on devices (android and iPhone)

1. In Signal, tap compose to view your Signal contact list.

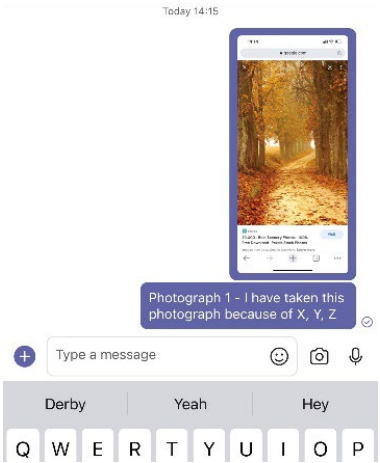
2. Select a contact (if you have saved researcher's mobile number on your phone) or alternatively enter the researchers number and create a conversation/message.

3. Click the camera icon and then select the photographs that you would like to send to the researcher (in photos for Apple or gallery for Android)
(If they are not showing, make sure you have allowed permissions for the Signal app to access your photographs – go to settings, down to Signal and allow Signal permissions to access your photographs. If not switch off your phone and turn on again).

4. Tap to send

5. The researcher will then receive the 5-10 photographs and for each photograph – please provide a description of each photograph. This can be done with the photograph individually or you can list each description and label 'Photograph 1, 2, 3'.

e.g.

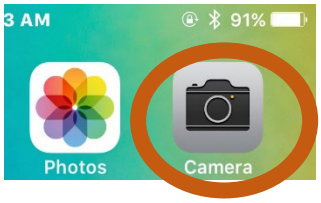


Any issues - please follow these troubleshooting steps - https://support.signal.org/hc/en-us/articles/360009303072 or contact researcher.

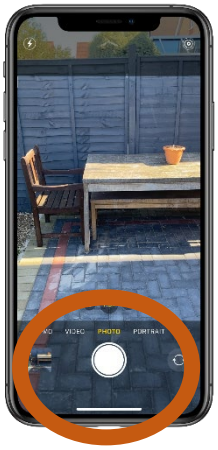
Taking photographs using your mobile or tablet device

iPhone/iPad Instructions ***(Android please see page 3) -***

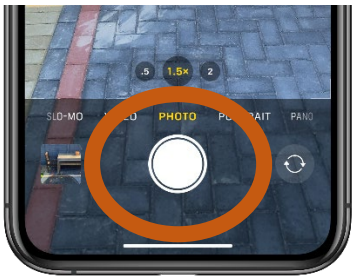
1) On the Home screen, tap the Camera app icon. Or from the Lock screen, double-tap Home and then flick the Camera icon on the bottom-right corner of the screen in an upward motion.

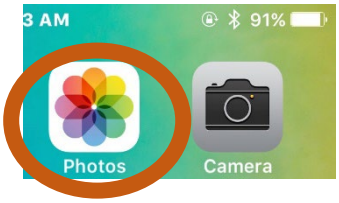


2) Keep your eyes fixed on the iPhone display.
3) To take the photograph use the camera icon white button



4) To view the photo, you took click on the photograph in the bottom corner of the screen or the photo's icon on the home screen

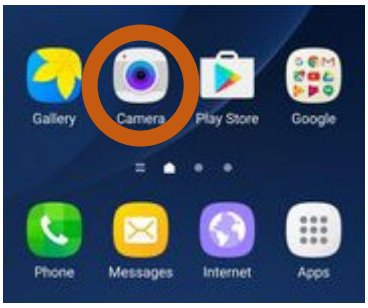




Android Instructions (i.e. Samsung, LG, Sony etc)

Step 1 – Taking photographs using your mobile or tablet device

1. Start the Camera app.

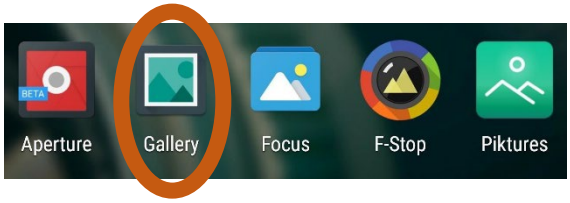


2. Point the camera at the subject.

3. Touch the Shutter icon.

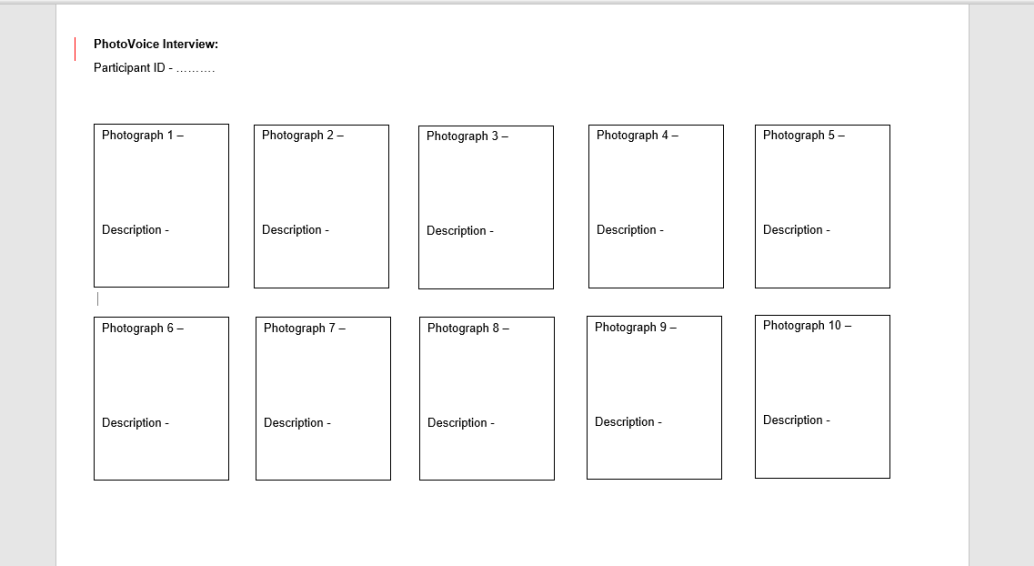
   The phone makes a noise when the picture is snapped.

4. To view the photograph you can click on gallery on the home page



Next Steps:

First online interview (1 out of 2) will be arranged with you and the photographs and descriptions that you send the researcher will be collated on to one document (see below).

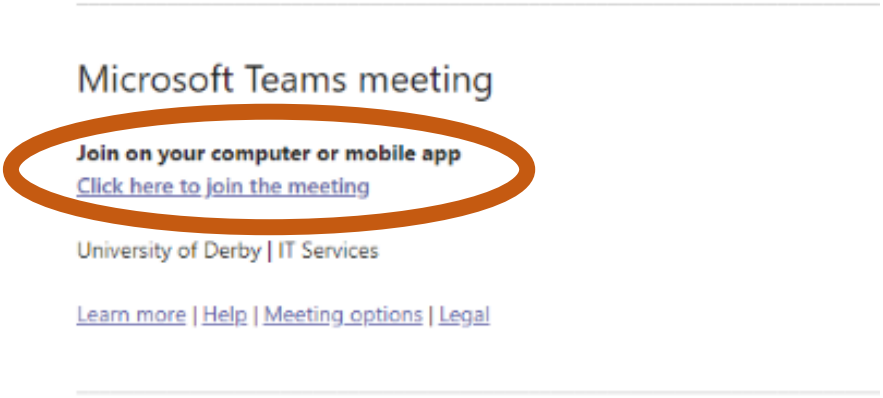


PhotoVoice Interview:

Participant ID - .....

Photograph 1 – Description -	Photograph 2 – Description -	Photograph 3 – Description -	Photograph 4 – Description -	Photograph 5 – Description -
Photograph 6 – Description -	Photograph 7 – Description -	Photograph 8 – Description -	Photograph 9 – Description -	Photograph 10 – Description -

This will be shared online/sent to you by email to discuss and go through each photograph during the semi-structured interview using Microsoft Teams again. An invitation on email will be sent to you, which will include a link to Teams.



Microsoft Teams meeting

Join on your computer or mobile app

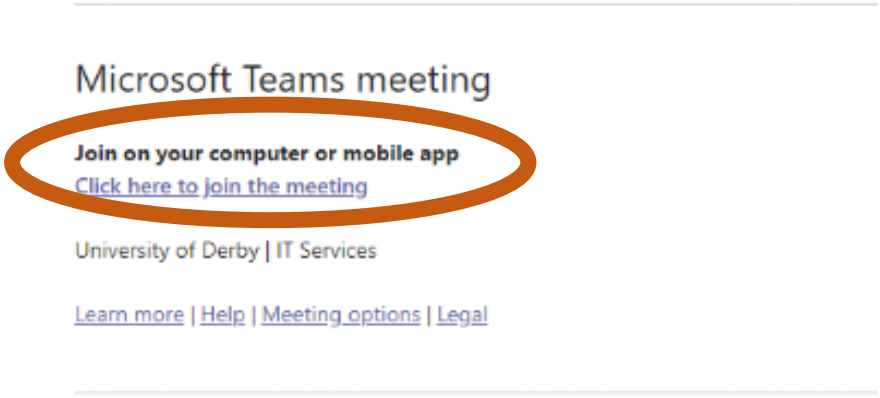
Click here to join the meeting

University of Derby | IT Services

Learn more | Help | Meeting options | Legal

After your first interview –

Second interview (2 of 2) will be arranged with you at a date and time that is convenient for you, using Microsoft Teams. This interview is regarding some questions regarding your COPD and medication/strategies.



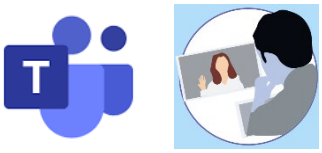
Any problems - Please contact the researcher below:

Samuel Grimwood
Email Address - s.grimwood@derby.ac.uk
Mobile Number – +44(0) 7557800951
University of Derby, Kedleston Road, Derby DE22 1GB.

Appendix L

Microsoft Teams Instruction Guide

How to use Microsoft Teams for interviewing



Option 1-3

All interviews will be conducted via Microsoft Teams.

You may already have a Teams account; if this is the case you can use your existing account.

If you do not have a Teams account, you can access Teams via your internet browser (without having to download or create an account) or you can download to your device (you will have to create a log in and follow steps).

Please use the contents to navigate to the most appropriate section for you.

If you have any questions, please contact:
Samuel Grimwood
s.grimwood@derby.ac.uk

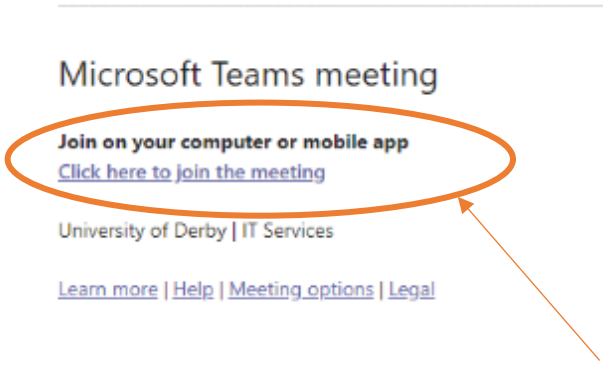
+44(0) 7557800951

Contents	Pages
How to use Microsoft Teams using:	
- **Smartphone, Tablet/iPad**	**2-5**
- **Computer *(to download the app)***	**7-11**
- **Computer *(to use the internet browser)***	**12-13**
- **Computer *(if you already have Microsoft Teams downloaded on your PC)***	**13-14**

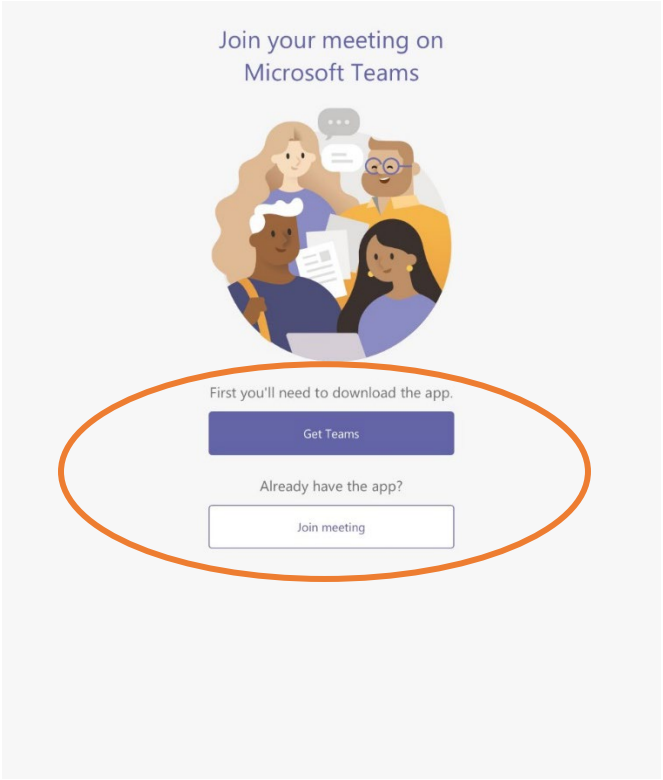
Researchers Contact Details	**15**

Using your Smartphone/Tablets/iPad:

If you to your emails and you will see an invitation to the interview from the researcher and open up the email.



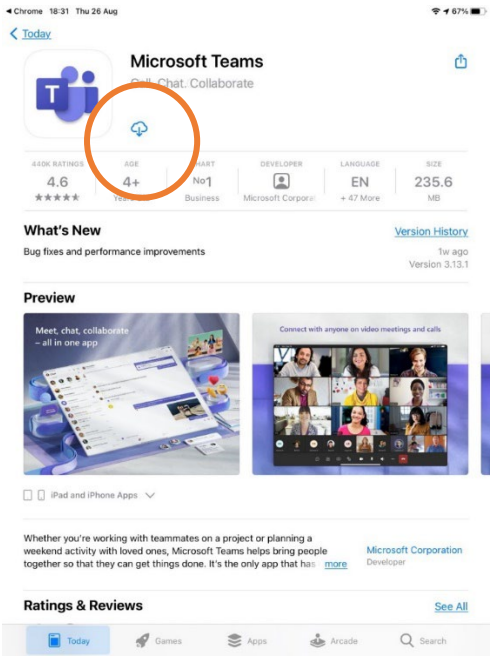
- Tap on the link ‘click here to join the meeting’



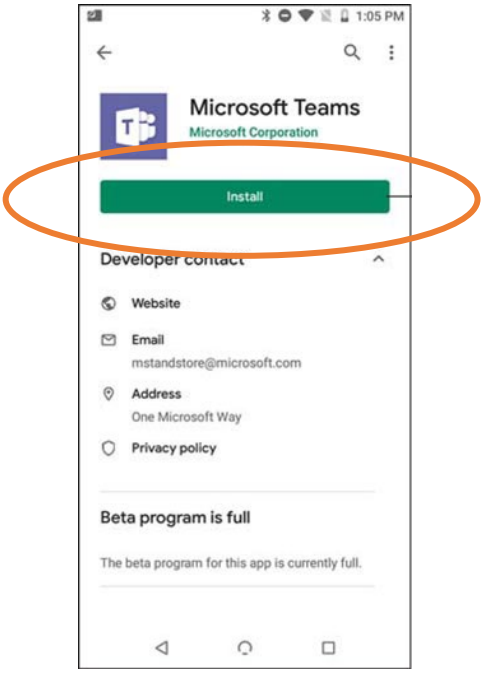
- A screen similar to this will pop up. If you already have Teams click on ‘Join meeting’ and enter your Microsoft Account details. If not click on ‘Get Teams’.

- You will then have one of the below screens come up on your device depending on whether it is an Apple or Android device.

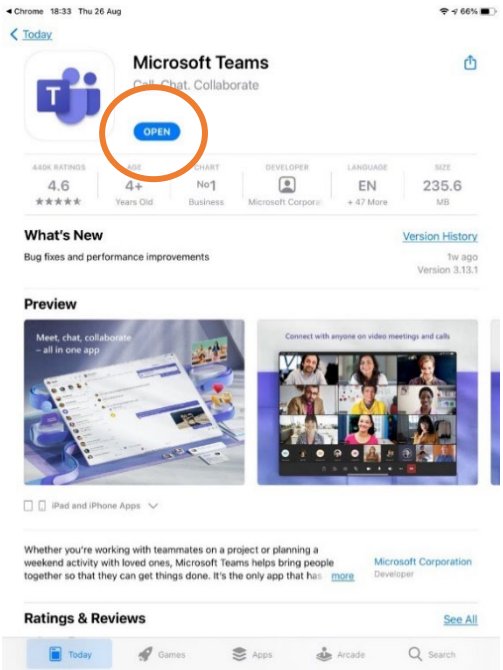
Apple



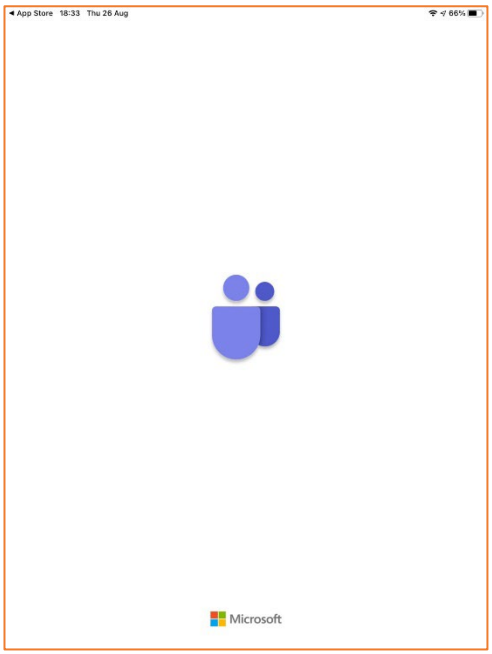
Android



- Click on open (Android devices will be similar, as examples the Apple instructions are below)



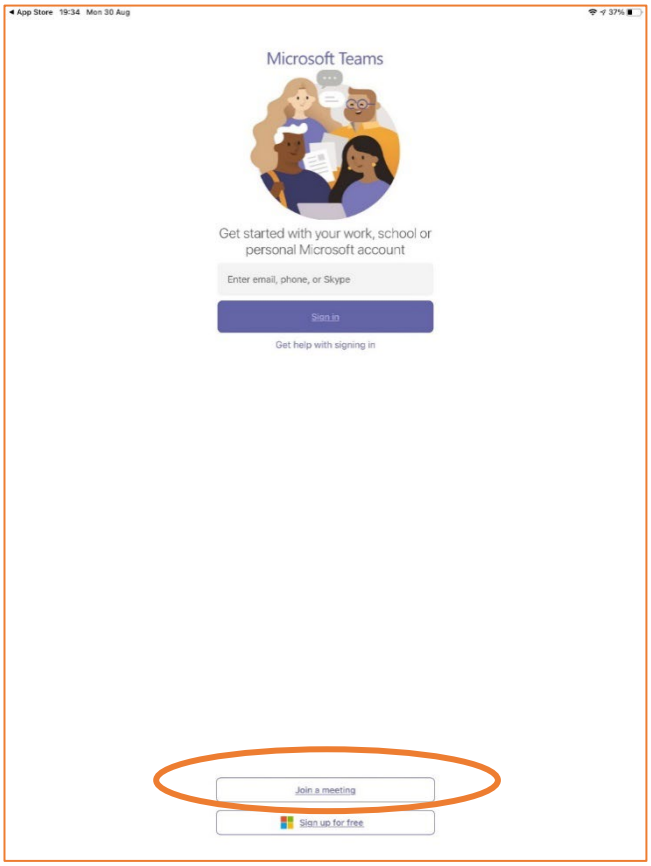
- The below screen will appear



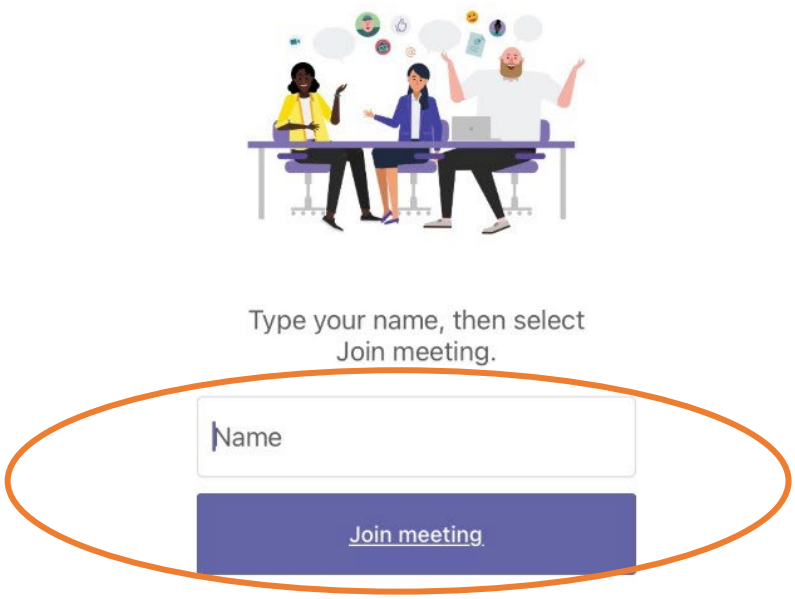
- If you do not want a Microsoft Account – click on ‘sign in and join’ and then click on ‘Join as a guest’.

- If you have an account, please enter your details and sign in

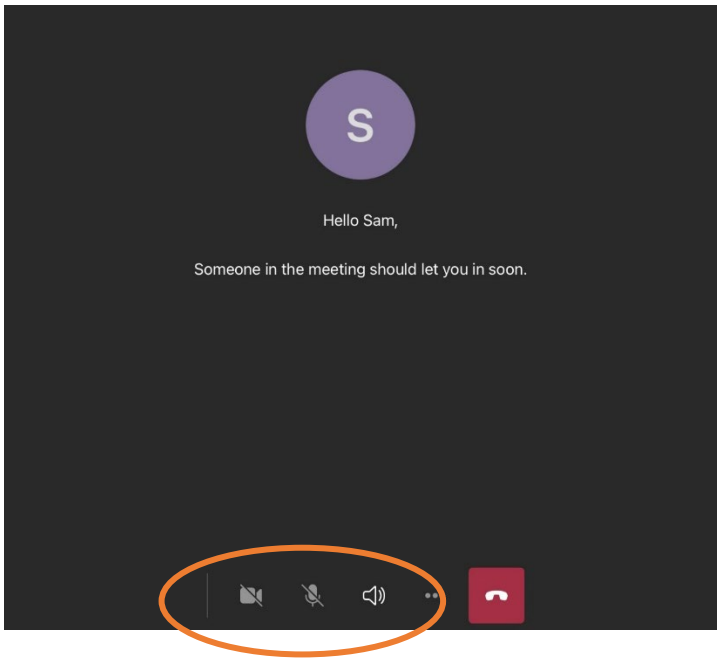
- If you would like to create an account, click on ‘sign up for free’ and follow the instructions



- If you clicked on ‘join as a guest’ the below screen will appear. Type your participant ID (5-digit memorable code) into the box and click ‘join meeting’



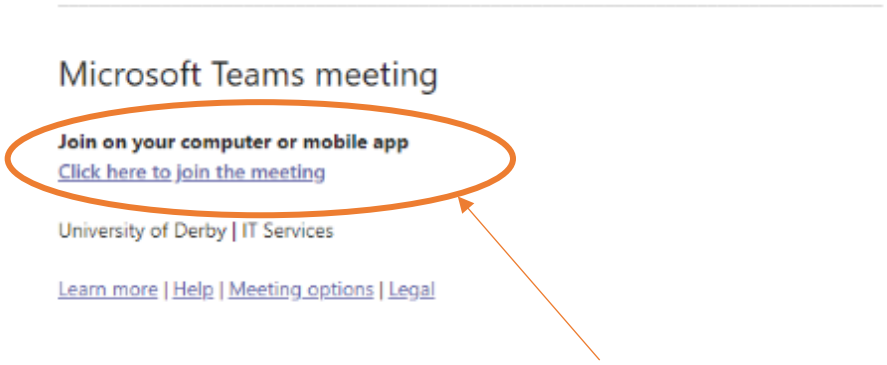
- You will then see the below screen appear



- Make sure you tap on the camera and microphone. The researcher will then let you in to the meeting.

If using a COMPUTER

Go to your emails and you will see an invitation to the interview from the researcher and open up the email.

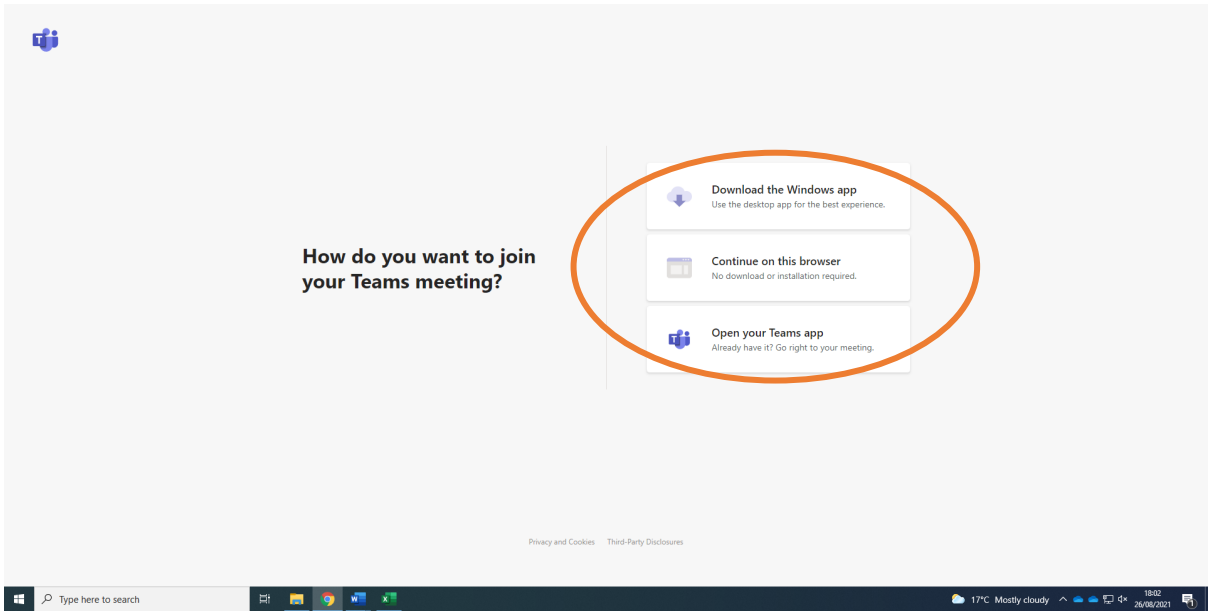


- Click on the link ‘click here to join the meeting’

- You will see the below options on a PC, using Google Chrome web browser

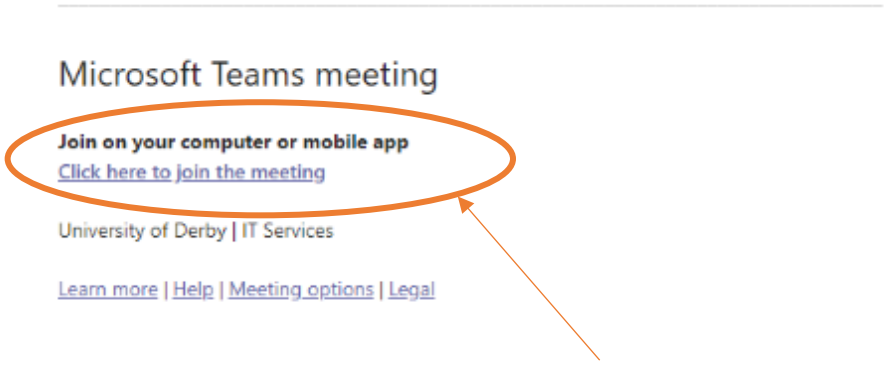
  You can either:

  1) To download the app on your PC
  2) To use your internet browser (no download needed)
  3) If you already have Teams app downloaded

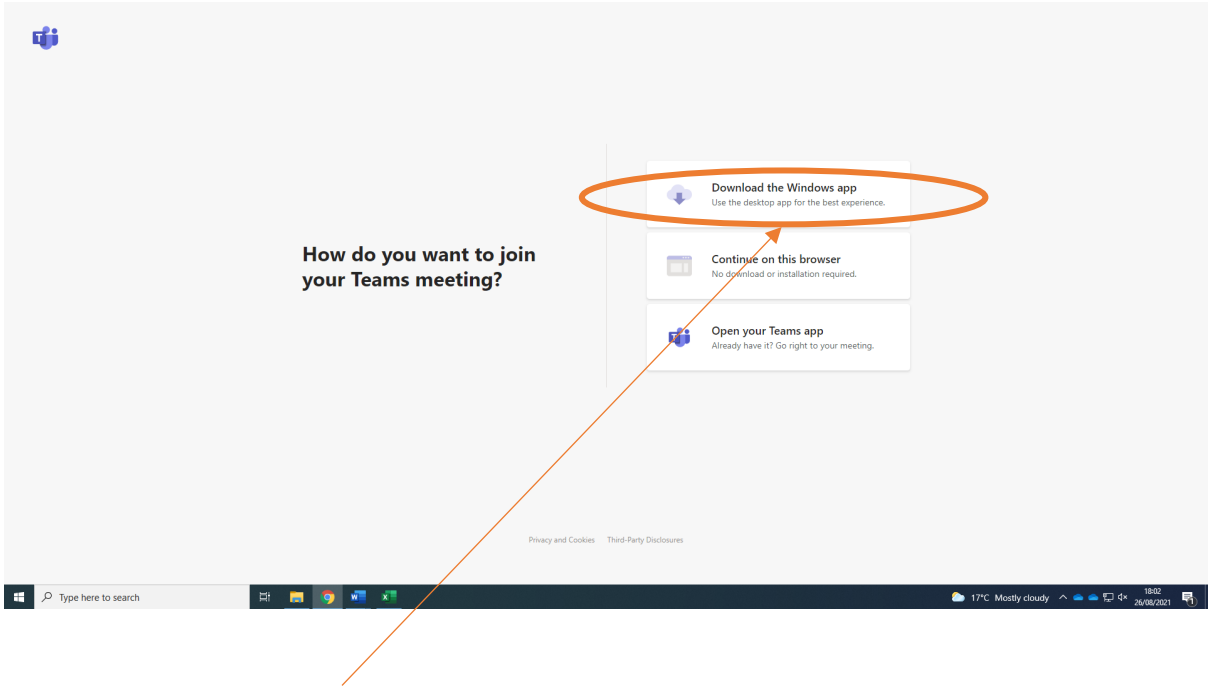


1: Download app on PC

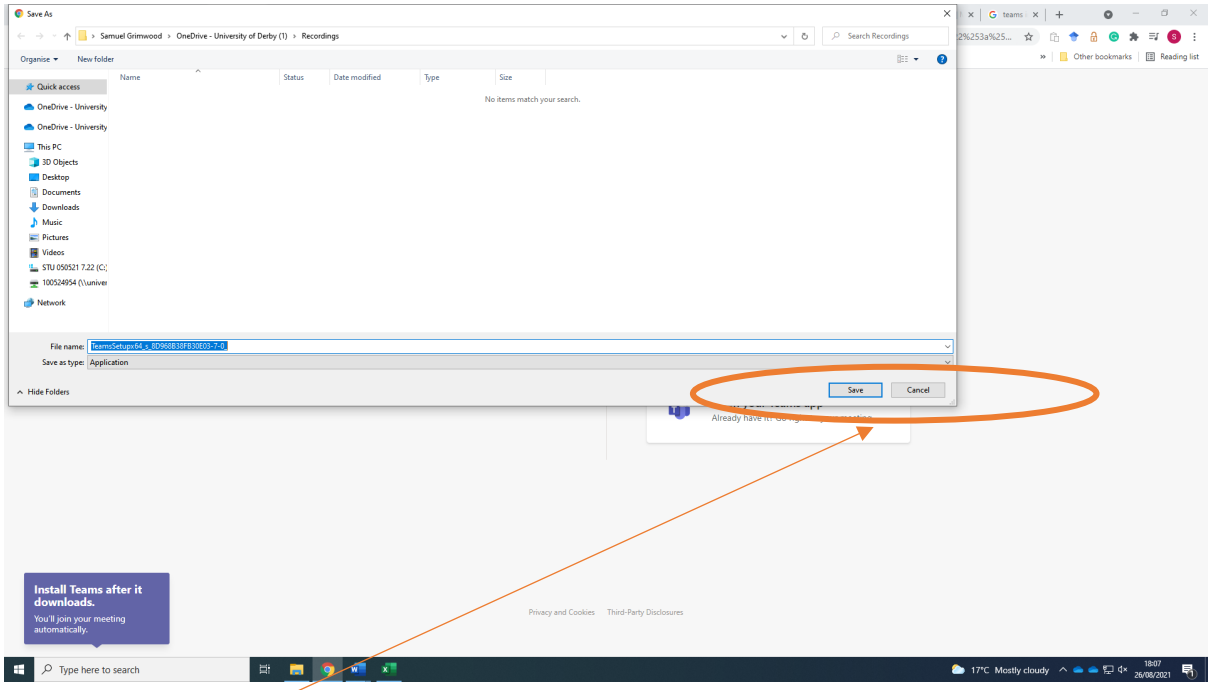
Go to your emails and you will see an invitation to the interview from the researcher and open up the email.



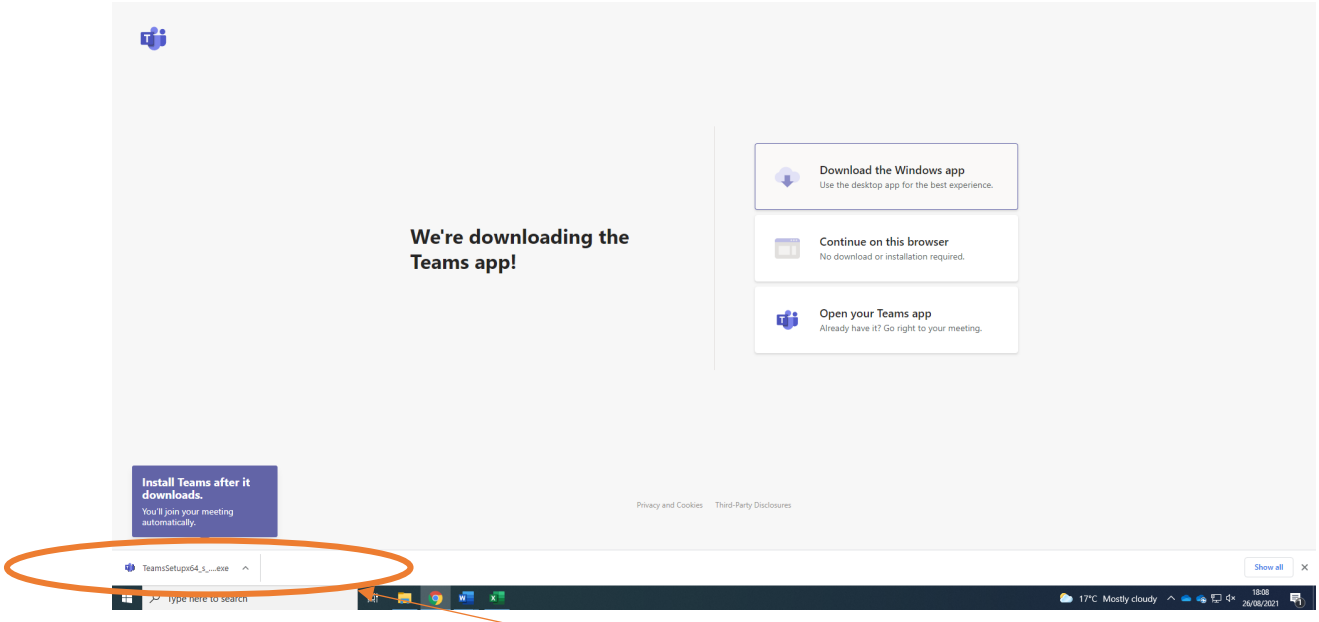
- Tap on the link ‘click here to join the meeting’



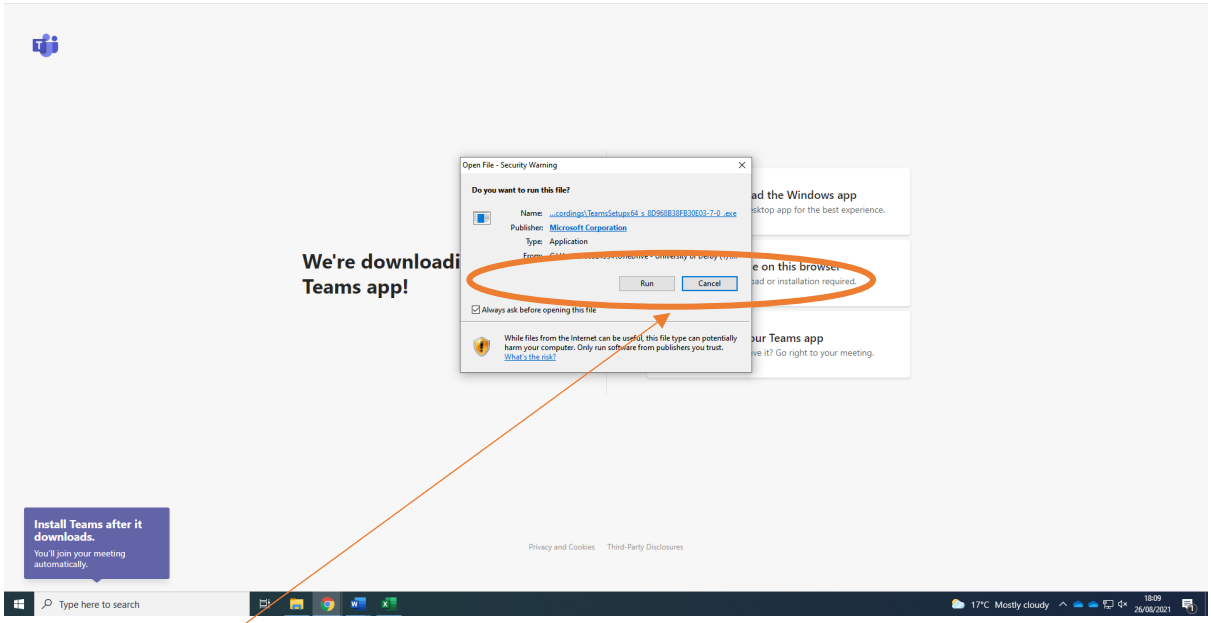
Click on ‘download the windows app’



Click on ‘save’

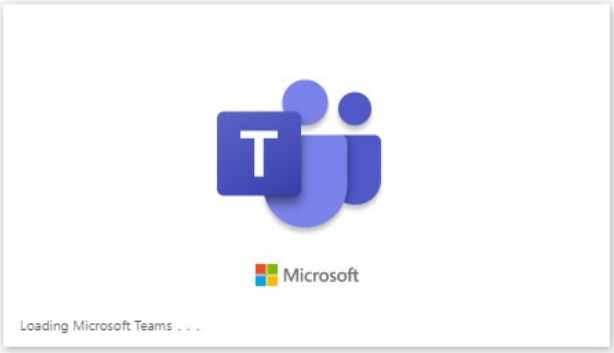


Click on the downloaded file in the bottom left-hand corner

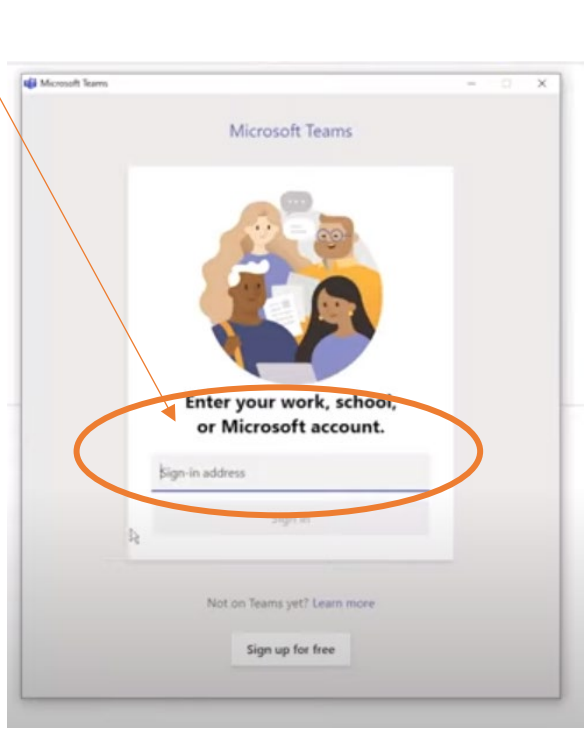


Click on ‘run’

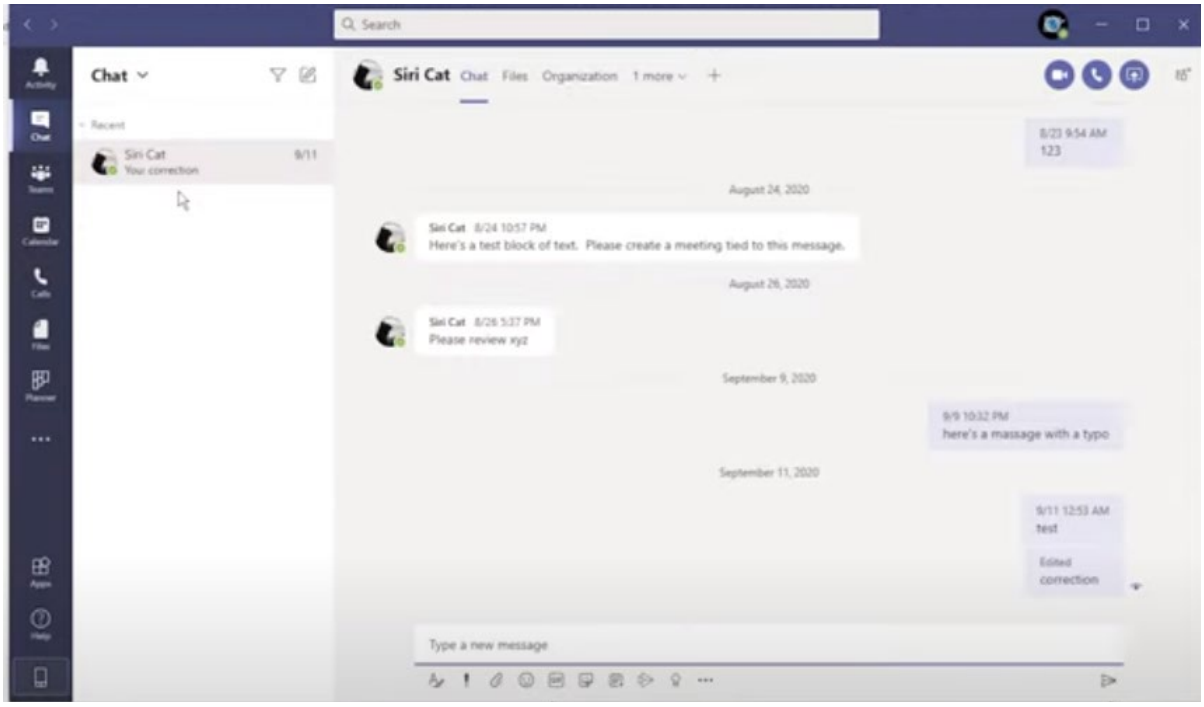
You will see the Microsoft Teams logo pop up on your screen



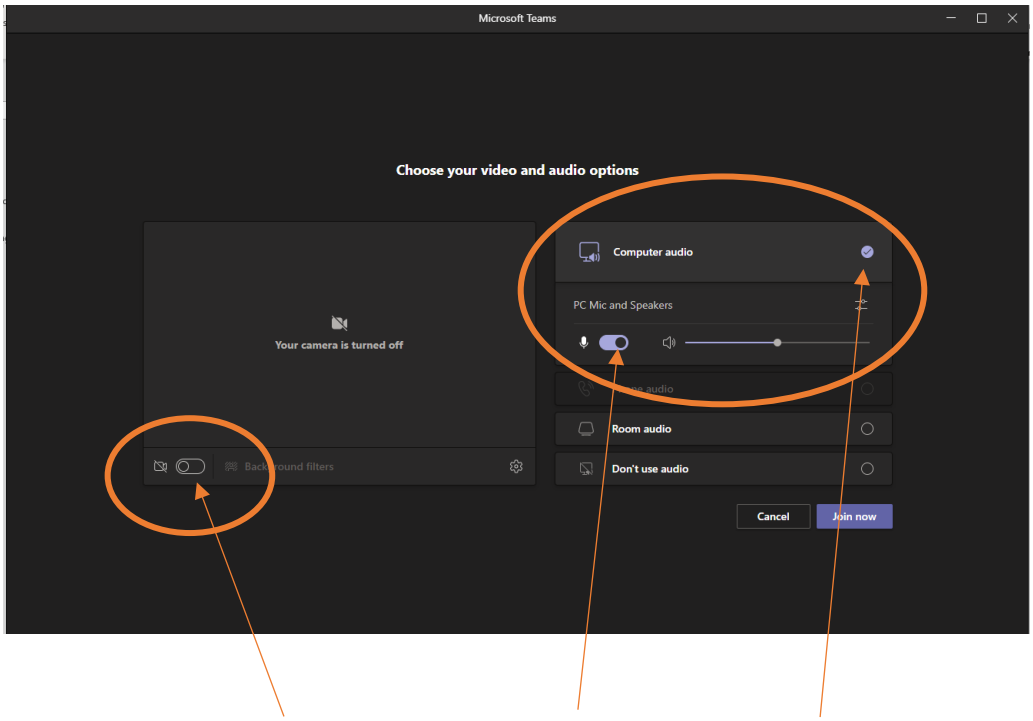
When the screen pops up you have to enter your Microsoft Account. If you haven't got a Microsoft Account, click on 'Sign up for free' and follow the instructions. Once you have the log in credentials you can enter them to access Microsoft Teams.



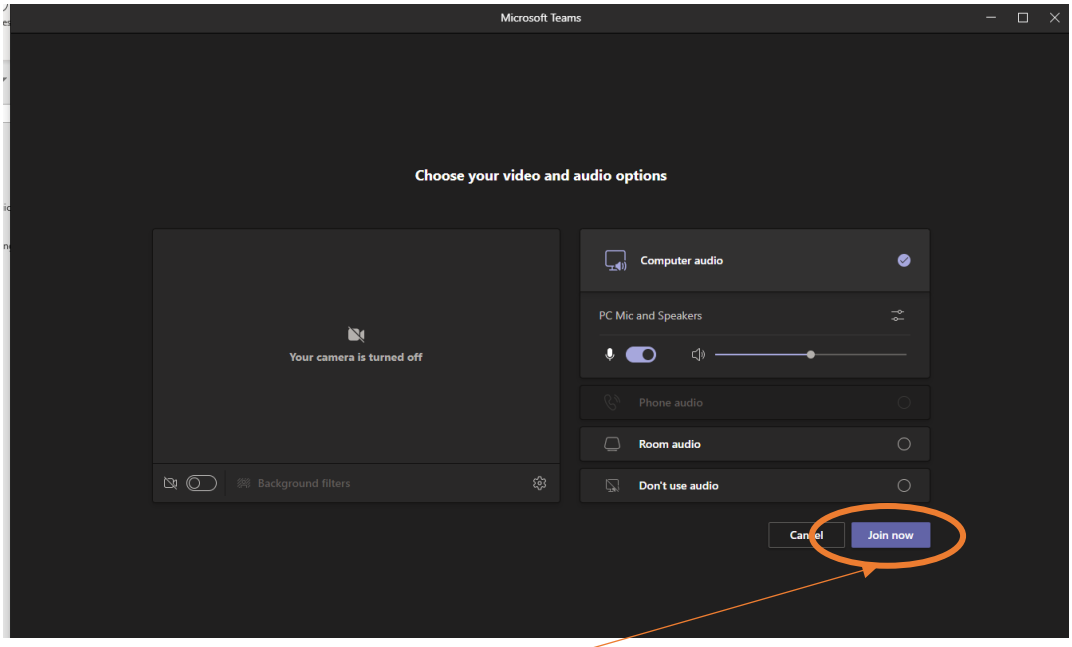
- Once you enter your Microsoft Account details it will look like the below box



- This screen should pop up and the black screen below



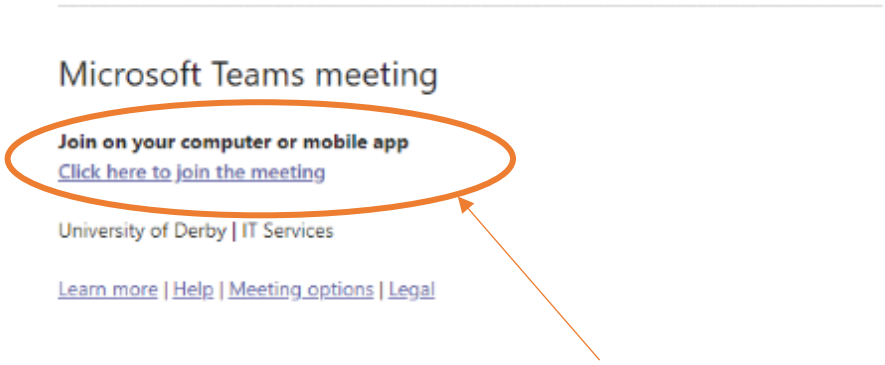
- Switch on the camera and click on PC mic and computer audio and PC mic



- Then click on join now and you will see the researcher

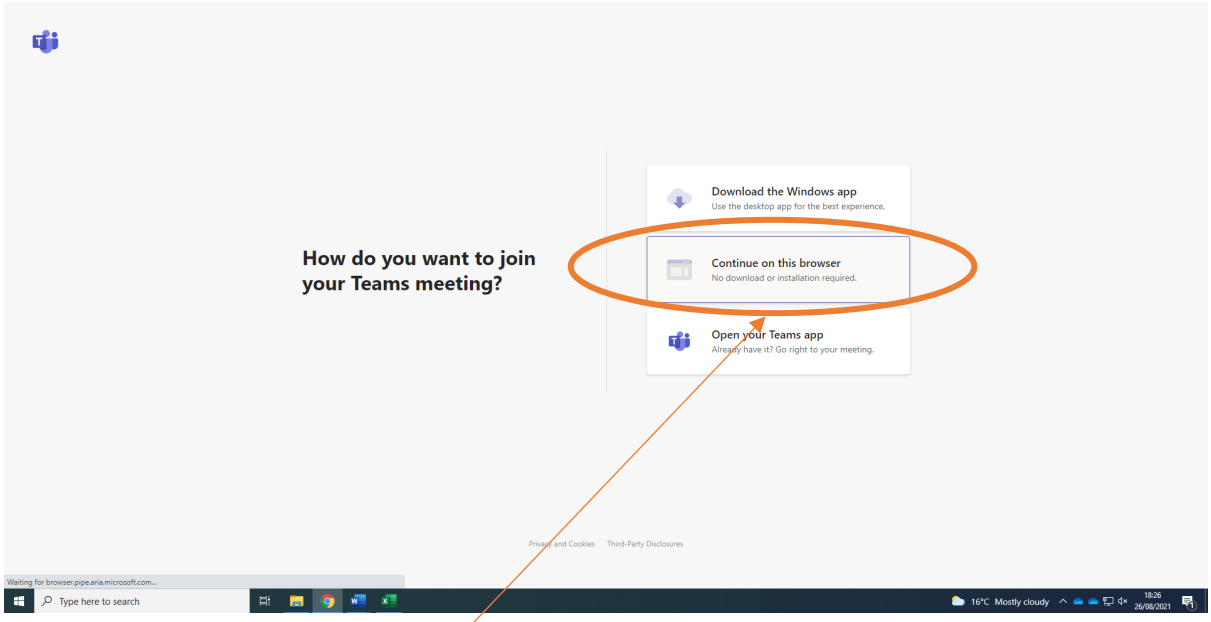
2 – ‘Continue on this browser’

Go to your emails and you will see an invitation to the interview from the researcher and open up the email.

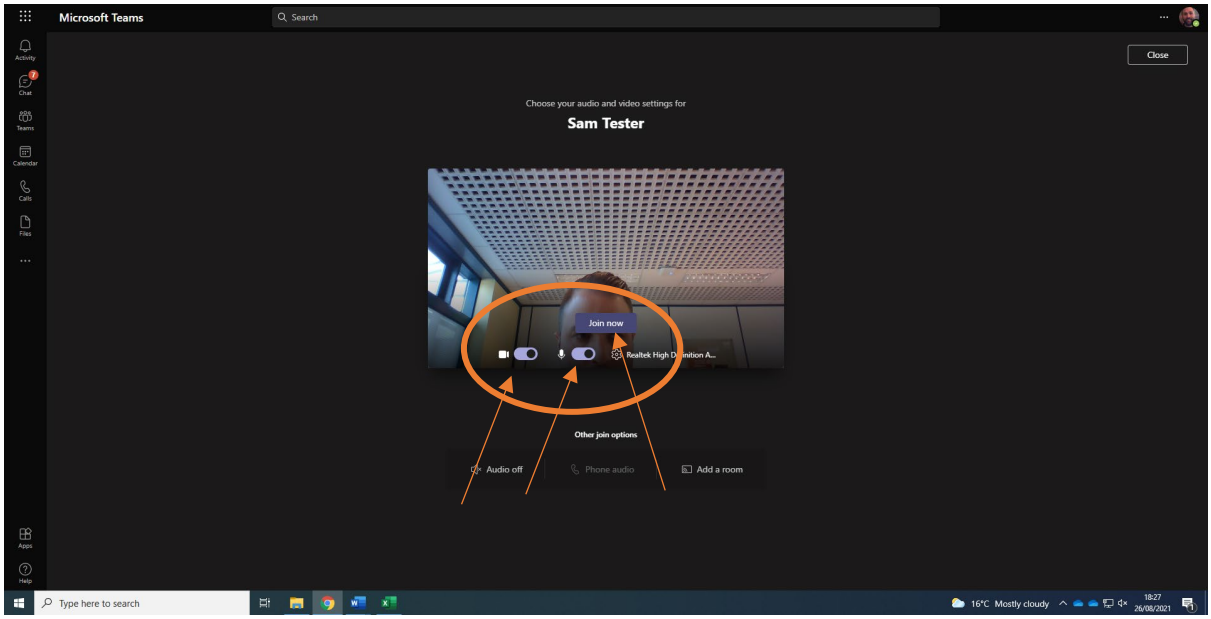


- Tap on the link ‘click here to join the meeting’

No download needed



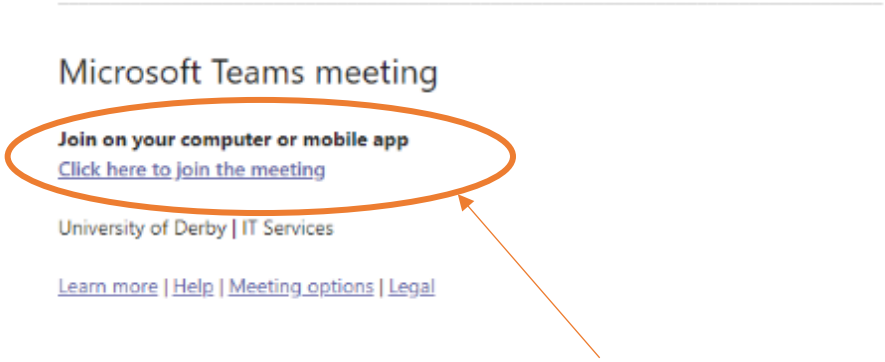
- Click on ‘continue on this browser’



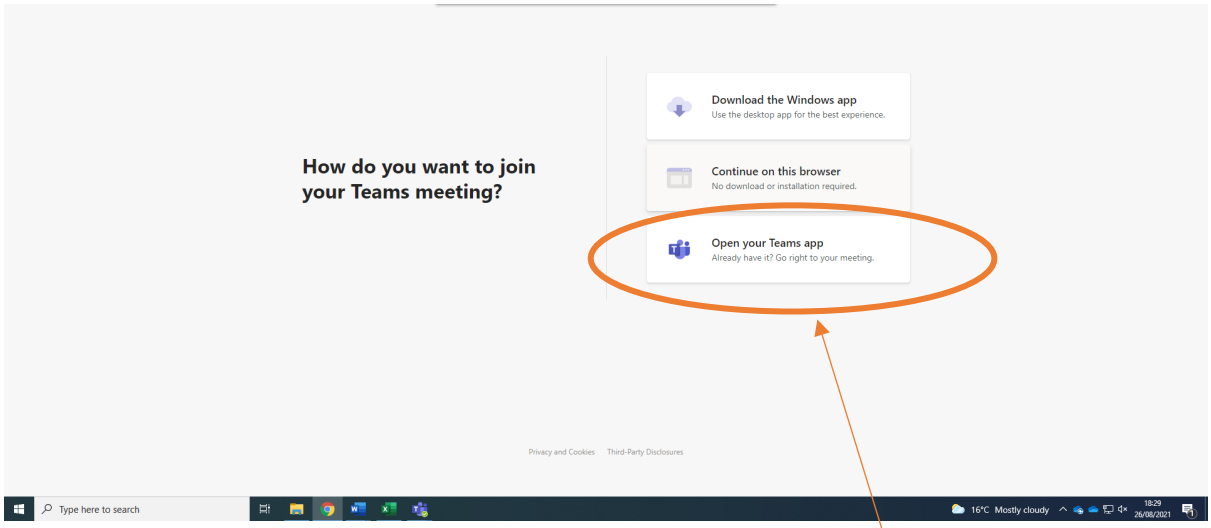
- Your screen will look like the above and you should be able to see yourself. (Make sure your camera is on and microphone and then click ‘join now’ and you will see the researcher)

3 – ‘Open your Teams app’

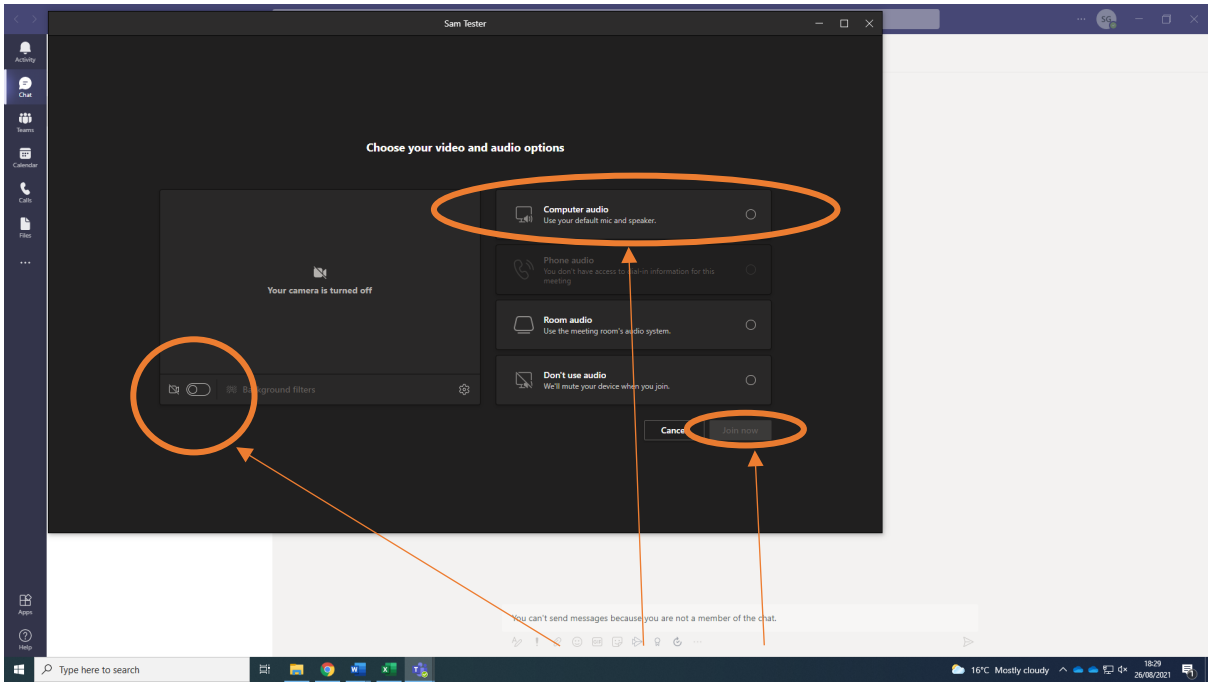
Go to your emails and you will see an invitation to the interview from the researcher and open the email.



- Tap on the link ‘click here to join the meeting’



- If you already have Teams download, click on ‘Open your Teams app’



- Above screen will appear – make sure your camera is on and microphone and then click ‘join now’ and you will see the researcher

Any problems - Please contact the researcher below:

Samuel Grimwood

Email Address - s.grimwood@derby.ac.uk

Mobile Number – +44(0) 7557800951

University of Derby, Kedleston Road, Derby DE22 1GB.

Appendix M

Photovoice Worksheet

PhotoVoice Interview:

Participant ID - ……..

Photograph 1 – Description -	Photograph 2 – Description -	Photograph 3 – Description -	Photograph 4 – Description -	Photograph 5 – Description -
Photograph 6 – Description -	Photograph 7 – Description -	Photograph 8 – Description -	Photograph 9 – Description -	Photograph 10 – Description -

Appendix N

Debrief Form

Debrief Information

Option 1

Debrief Form
Thank you for your participation in this study. Your participation is greatly appreciated.

Purpose of the Study:
The purpose of the research is to increase our understanding of your experiences of living with COPD and to explore the strategies that are most effective in managing this disorder.

COPD can increase levels of breathlessness, fatigue and limits airflow which can significantly impact taking part in day-to-day activities. This can negatively affect quality of life and can cause sleep problems and depression.

Despite having a wide range of medical treatments available, COPD is still decreasing lung function and directly impacts the quality of life of those that are living with the respiratory condition.

The aim of this study is to help to inform intervention(s) that could be of benefit in reducing the impact of COPD on quality of life. Findings from this study may also help to improve lung function in those with COPD, increasing both mobility and reducing low mood.

Thank you for taking the time to participate in this study. You sending through your photographs and discussing your experiences of living with COPD and the medication you take and the strategies you use, is extremely insightful and very much appreciated. This will help us to understand further the physiological and psychological factors implicated in COPD and assist in setting the foundation for future research.

Withdrawal Procedure:
Your identity will remain confidential if the results of the study are published. Potential places for publication could be scientific journals (i.e. Elsevier - Social Science & Medicine). The contact details are listed below. May you be assured that your data will be deleted immediately, and you will not appear in any part of the report. Your decision to participate is completely voluntary. Should you wish to withdraw from the research you may do so at any point, up to two weeks after participation (this is because your data will be formally screened, cleaned and prepared for data analysis which will be conducted and therefore the research team will not be able to remove your anonymised data). You will not need to give any reason or explanation for doing so. To withdraw your data simply contact the researcher or research team on the details below with your unique participant code (i.e. the 5-digit memorable code).

Final Report:
If you would like to receive a one-page summary of the findings when it is completed, please feel free to contact the researcher. The contact details are listed below.

Useful Contact Information:
For any further information regarding the topic of COPD and mental health, please see below, for further details of several organisations that may be useful. They will be able to offer professional advice and guidance that cannot be obtained from the researcher or their supervisory team.

British Lung Foundation: https://www.blf.org.uk/support-for-you/copd; 03000 030 555; 9am-5pm

MIND: www.mind.org.uk

Samaritans: www.samaritans.org,**116 123**, 24 hours a day, jo@samaritans.org

If you have any questions or concerns regarding this study, its purpose or procedures, or if you have a research-related problem, please feel free to contact via email, the researcher or their supervisors:

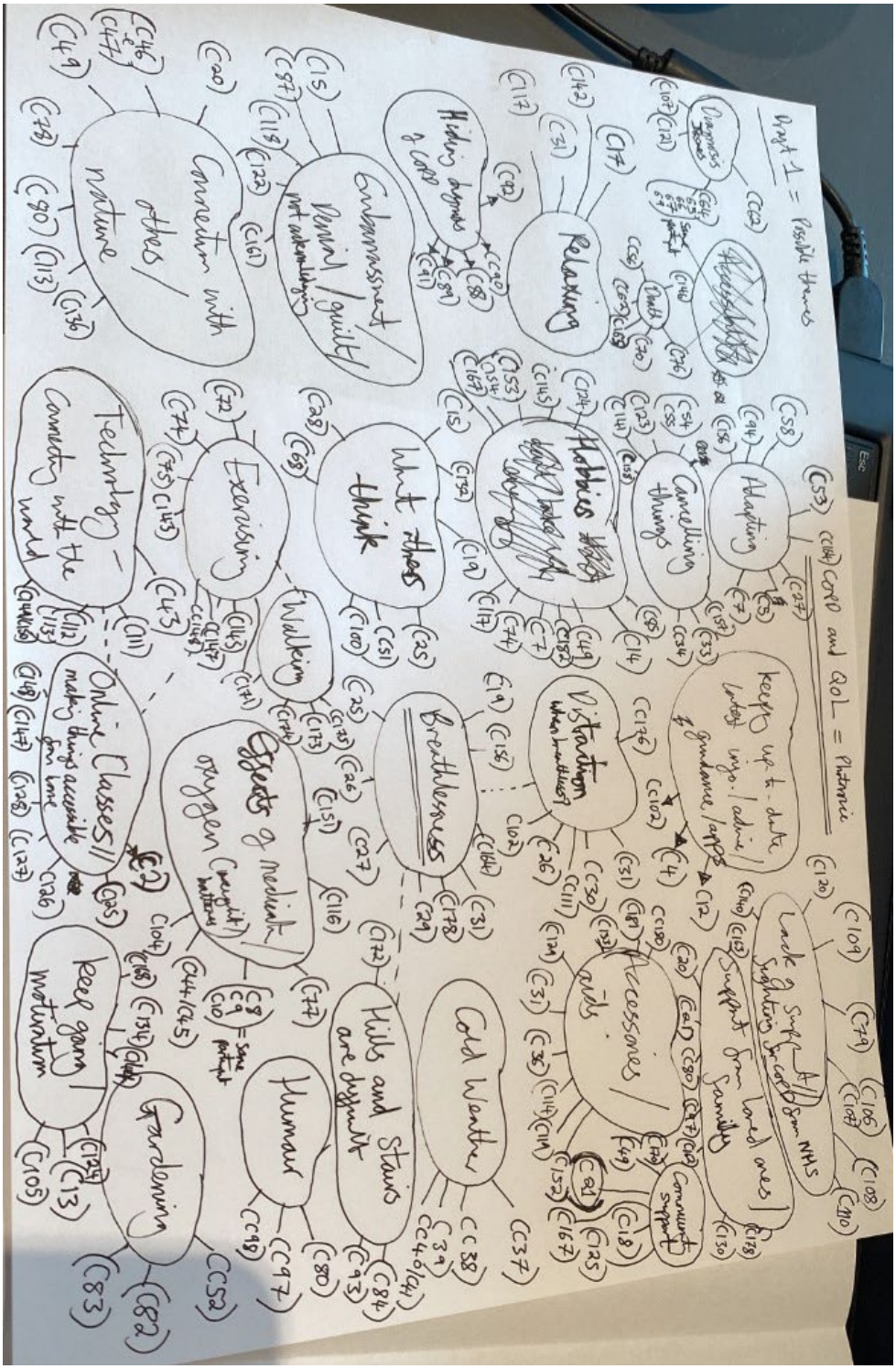
Mr Samuel Grimwoood – s.grimwood@derby.ac.uk

Dr Mark Faghy - m.faghy@derby.ac.uk
Dr Amy Baraniak a.baraniak@derby.ac.uk

Once again, thank you for your participation in this study.

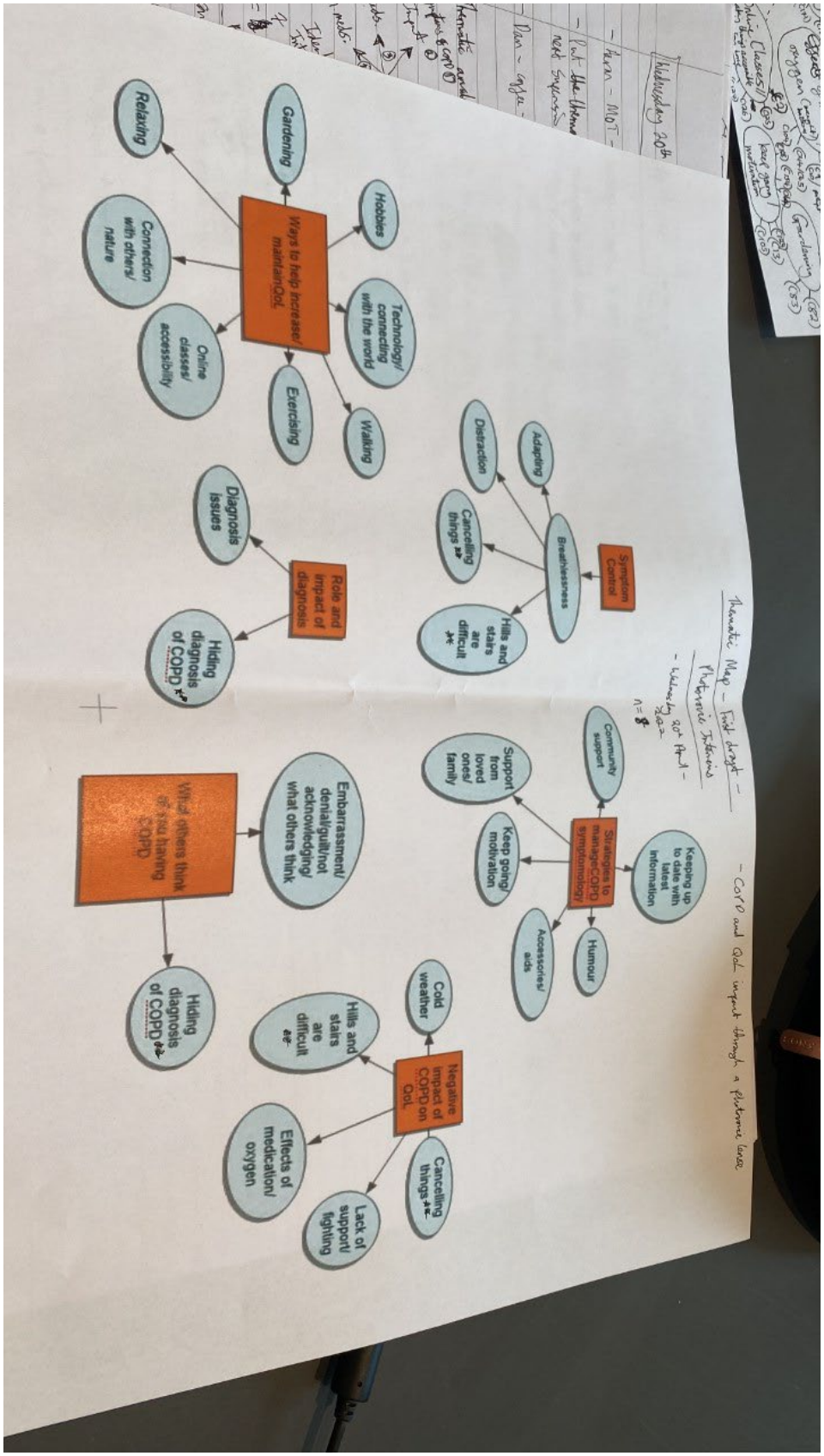
Appendix O

Early theme map creation 1



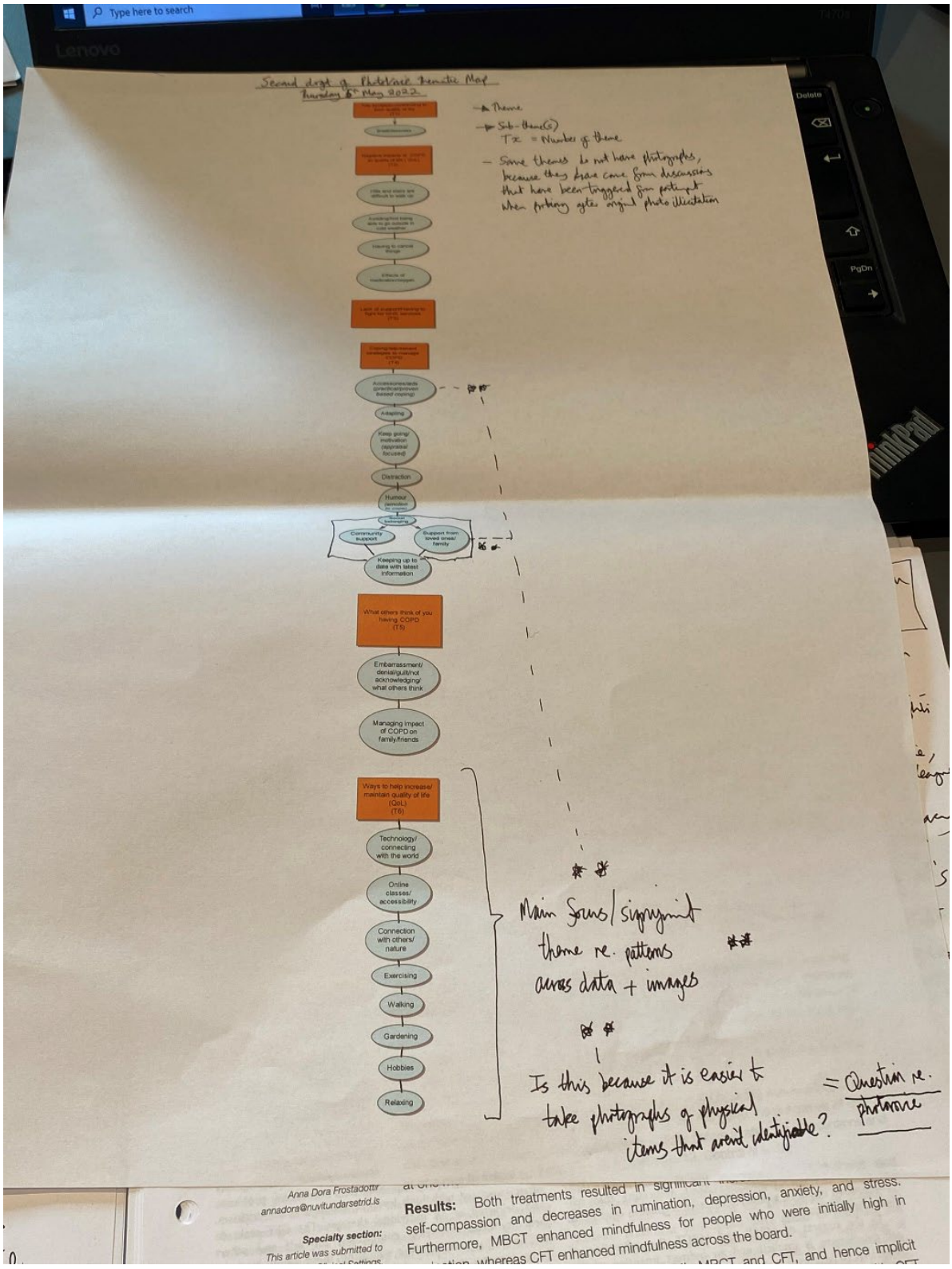
Appendix P

Early theme creation 2



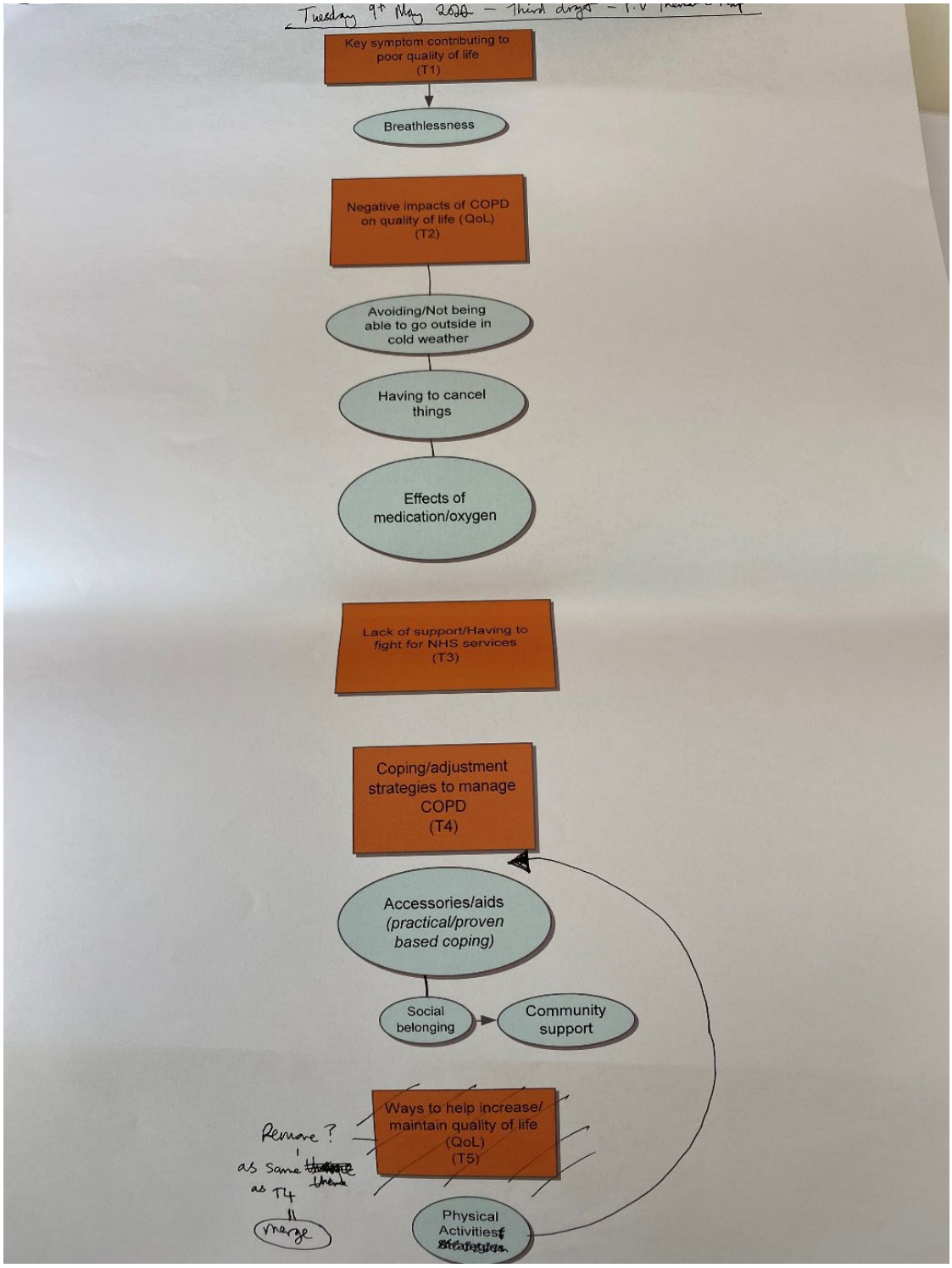
Appendix Q

Early theme creation 3



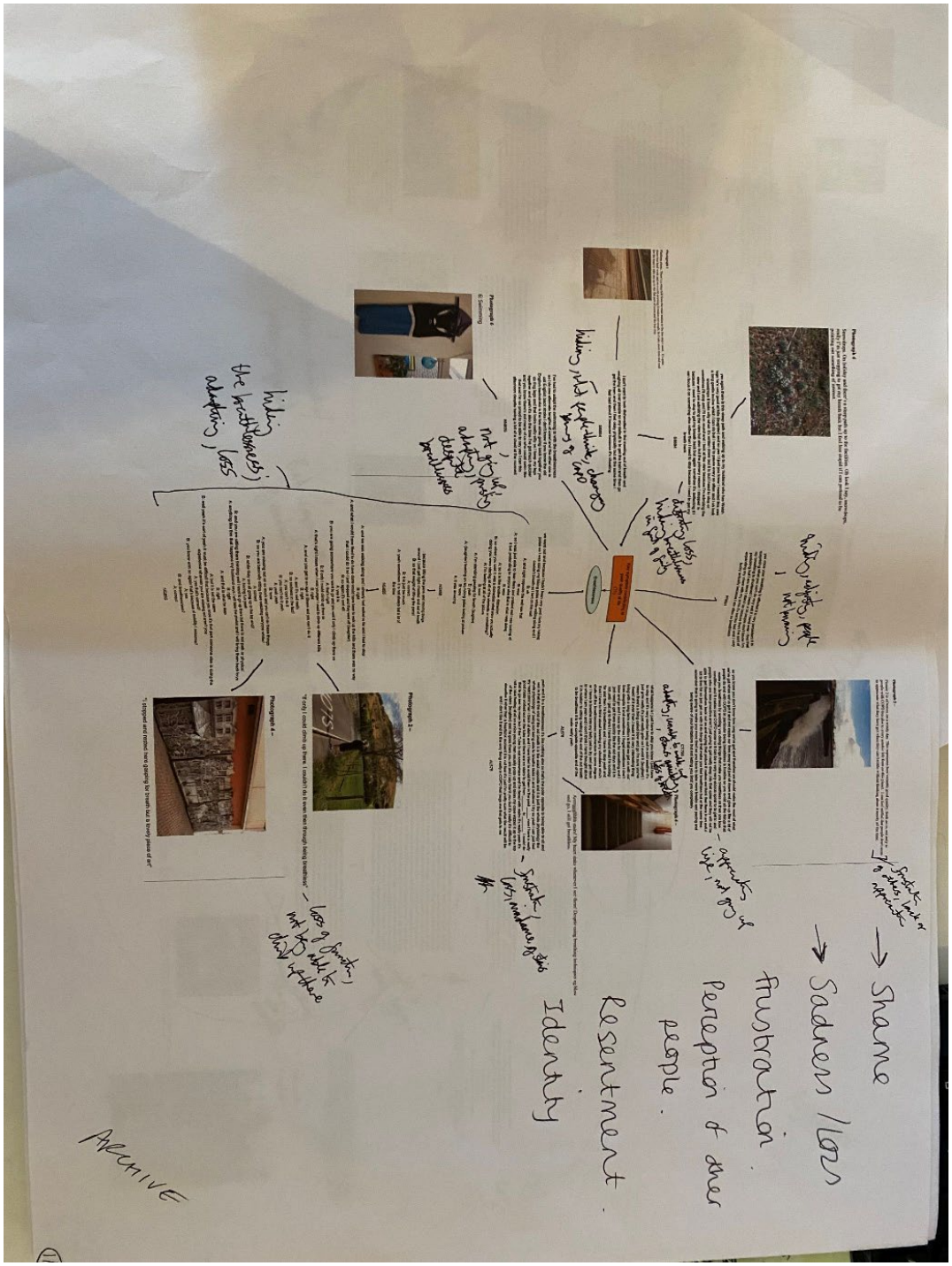
Appendix R

Early theme creation 4



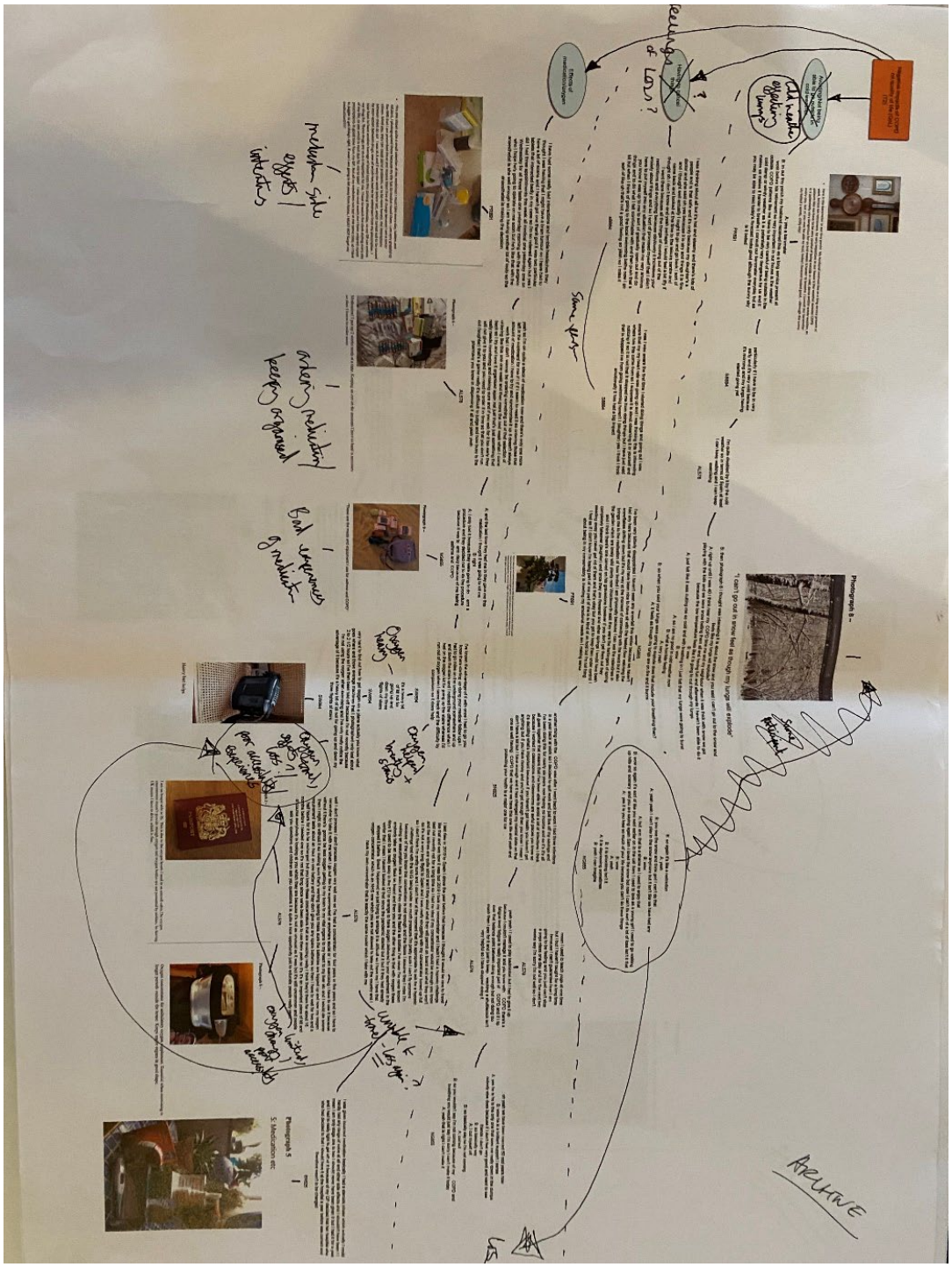
Appendix S

Early theme creation 5



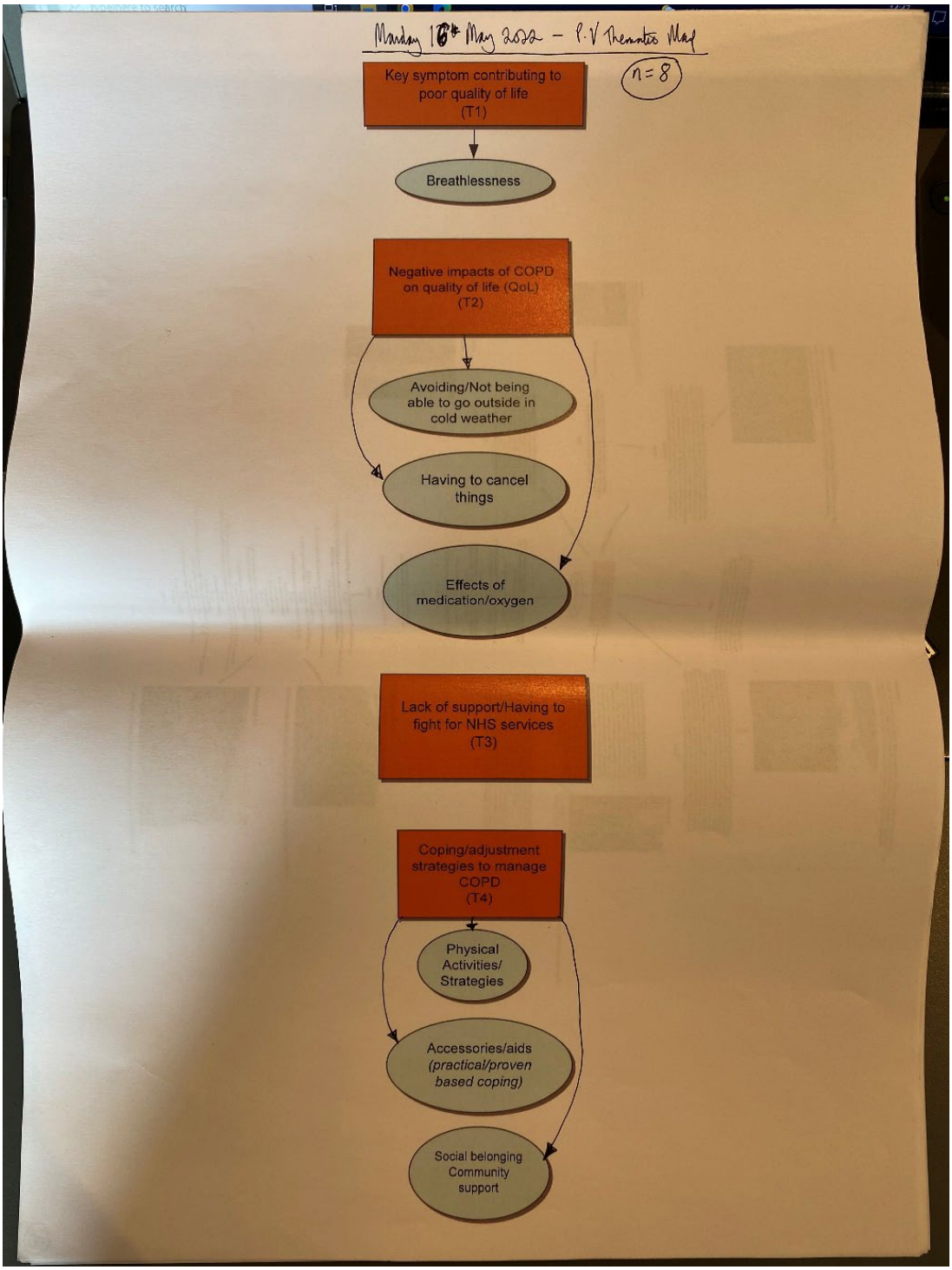
Appendix T

Early theme creation 6



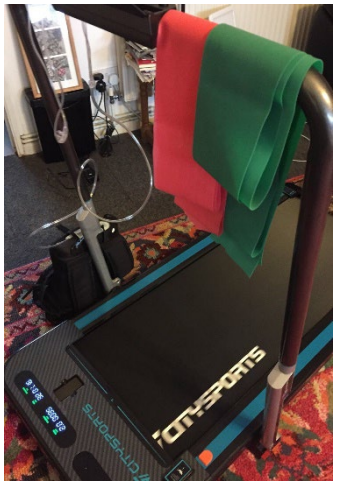
Appendix W

Early theme creation 7



Appendix X

Photographs from patient Aimee



Treadmill, resistance bands and 02 concentrator. It is very important to me to keep fit, especially through

winter in UK. (I am usually abroad, somewhere warmer, during the UK winters.

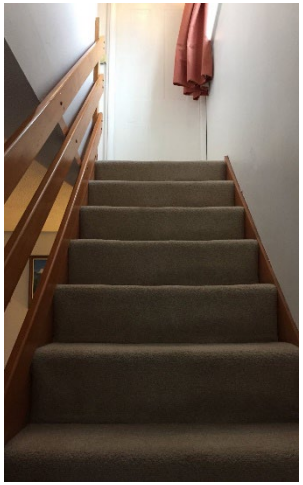
I am no longer able to fly. This is due to the oxygen levels I need in an aircraft cabin.The oxygen

concentrator doesn't provide enough oxygen and oxygen bottles are not permitted by airlines. So leaving

UK means I have to drive, which is fine

Yoga and meditation are a huge help and support to me. I have been a meditator for 30 years. Being able

to manage my thinking is enormously helpful.



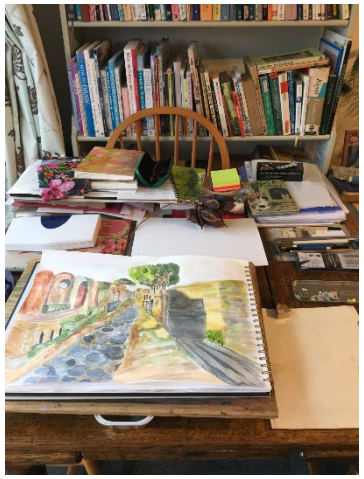
Arrrrggghhhh stairs! My heart sinks whenever I see them! Despite using breathing techniques eg blow and go, I still get breathless

Oxygen concentrator for ambulatory oxygen supplement. Essential when exercising or walking for

longer periods outside the house. Keeps major organs in good shape.

Medication! I put up 2 weeks meds at a time. Keeping an eye on the amounts I have to hand is necessary so then I know to order more.

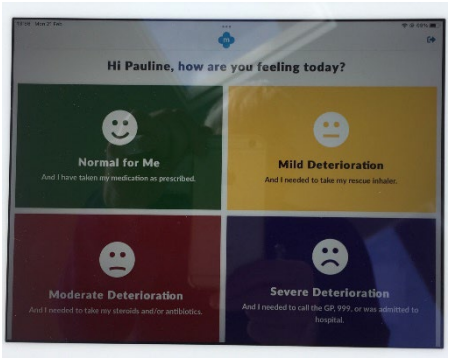
Housework- it is a bit of a struggle for me these days. I need to pace myself, so doing a bit each day.



Art has been a huge help during recent years. I needed to have a new interest when I was unable to

continue to walk distances or play badminton anymore

Grab handle on the side of the bath to help me be safe and stable during exacerbations!

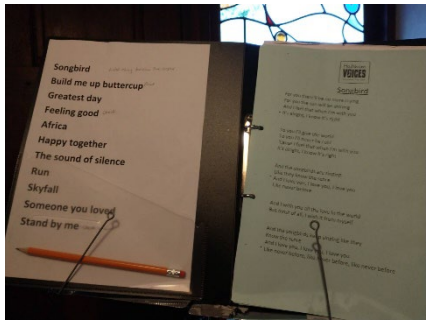


Self management app to help me stay on track with good self care ! Provided by the NHS and was a

struggle to get hold of last year, but managed to do so after 3 months

Appendix Y

Photographs from patient Pat



1. Choir

2. Flute

3. Jack-in-a-box representing my children

4. My bike

5. Medication etc

6. Swimming

7. My partner

8. Growing my food in my field

9. Walking

10. Volunteering

Appendix Z

Photographs from patient Sue

"My jungle. Too late to get there through COPD problems"

"If only I could climb up there. I couldn't do it even then through being breathless"

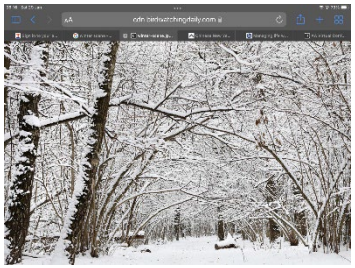
"This is my rest full place when I feel ill with COPD I just sit there and relax"

"I stopped and rested here grasping for breath but a lovely piece of art"

"Probably my last holiday aboard but a good one would need to take my wheel chair to help me get around"

"Having to lean to peel veg as it's better for me to breathe"

"Had to have chair lift as I struggle with the stairs"



"I can't go out in the snow feel as though my lungs will explode"

"These are the meds and equipment I use for asthma and COPD"

Appendix AA

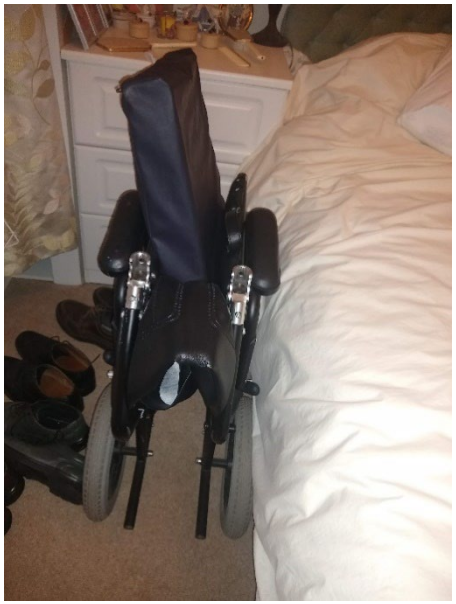
Photographs from patient Teresa

This is taken by me from my chair in our little back conservatory. This room is where I spend most of my days, because it is bright and the nearest place I can be to feel almost out in my beloved back garden, but try as I might, I do feel almost shut in, behind the plant,- a kind of indoor plant myself these days.

This photo shows my back garden from one angle. When we came to live here in this little semi-detached bungalow, (leaving behind a large Victorian semi with four bedrooms), it was very much downsizing, owing to my slowly deteriorating health. The garden was poor. I worked on it round the year, every time I could. It was an effort and it was the scene of a very difficult event for me, when in 2016, I had a simple fall from standing height just outside the garage you can see, while I was attempting to do some gardening. I broke my hip, badly, and had to have an emergency hip replacement. My bones are weak because I have ingested so many, many courses of prednisolone over the years, owing to my respiratory condition! I yearn to go out and do some Spring clearing in the garden, but it is really difficult these days and though I love to look at the garden, I feel somewhat frustrated to see what needs doing, ready for summer!

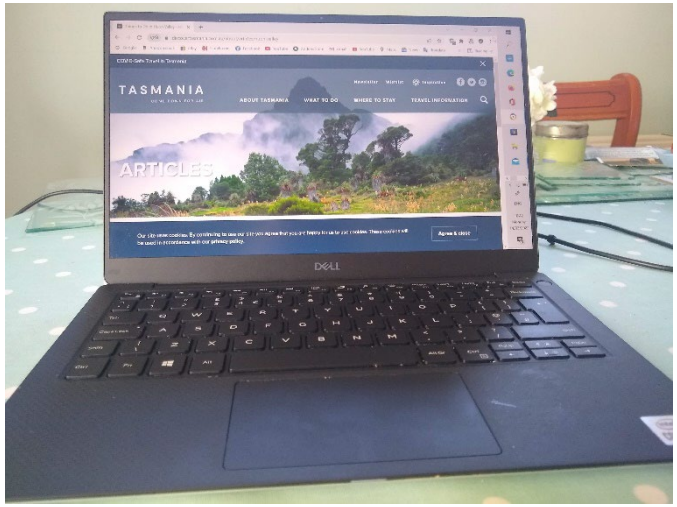
This photo is a delight for me, because last Autumn I did manage to plant a pot of bulbs, not being a big job, but one I could manage, and here they are flowering. What a joy and satisfaction to me this is! Maybe not a very big achievement by many folk's standards but hey, I did it myself! Bought the bulbs, got someone to carry the compost and then I assembled it all myself!

This one shows quite a small selection of the medicines I must take every day, tablets and inhalers. I photographed these because my life has to revolve round them. I am very grateful to the NHS that I am prescribed these and receive them free of charge because I am a senior citizen. Mind you, they can cause some problems, or to be more honest, the interactions between them do so! I was at A and E only the week before last, which turned out to be caused by inter-action between drugs, one of which has had to be withdrawn from my prescription. I now have to have another barrage of blood tests this coming Wednesday, so my GP can rethink my drug list. These drugs are so-o-o important for me. I have to watch the clock during every day of my life, to see which is next due for me to take! I also must watch out I have ordered repeat prescriptions in good time from my GP. Not all my medicines run out at the same time, so I have to juggle to get things right. If ever I am going to be away from home, I MUST NOT forget my medication!!!!!!

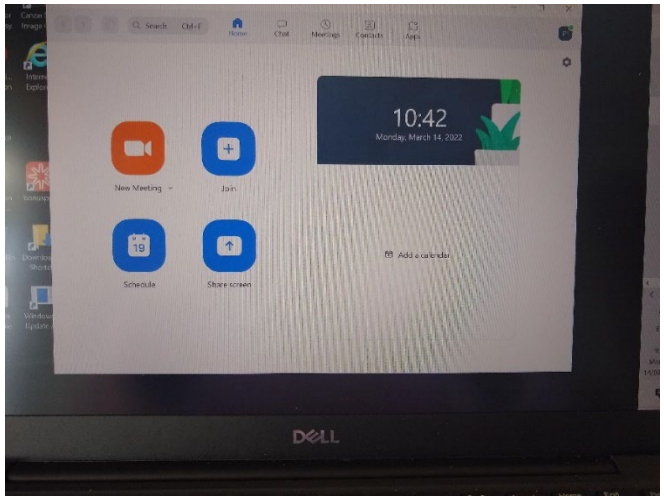


This photo is my wheelchair by my bed. I so wish I could be more mobile. Sometimes I decline the offer made by my husband to take me out, because I can't be bothered with the hassle and also it can feel very cold and "marginalised" being in a wheelchair, despite a blanket over me! This is a love/hate relationship I have with the wheel chair. I am HOPING I may be well enough to have a knee replacement operation one day, - maybe then I can walk out again on my sticks, but all will depend on the state of my lungs, whether or not I am well enough for surgery.

This is my perching stool in my bathroom! A reminder for me that the process of getting washed/showered/dressed in the morning is a big effort for me and one I must take my time with, using the help offered by my perching stool, to sit down and rest, put my socks on, etc.!! It's also a reminder of the considerable number of pieces of equipment I have to help me, walking sticks, crutches, grabbers to help me pick up things I can't bend down and reach, back rests in bed etc., grab handles in the shower.



You can see a photo of my laptop screen, showing Tasmania. My very dear middle daughter, Vanessa, emigrated to Tasmania in 2004 and lives in the Huon Valley, well south of Hobart, with her partner and their two children. We used to travel there every year and stay for two months, also visiting my sole surviving sibling, Bill and his family, who live in Sydney on the mainland, and my cousins who live in the state of Victoria. Wonderful memories! Covid has prevented us travelling since our return in February 2020, - but my health may prevent me from ever returning, plus, I can only travel now with the comfort of Business Class, which may be unaffordable. I console myself keeping up with the lovely scenery, Australian newspapers and so on, all of them available readily on my little laptop here in XX!



Here is Zoom on my laptop, - wherein I access almost ALL my social life these days! Family zooms, British Lung Foundation group zooms, Breathe Easy zooms, etc.etc. Vital communication link for me and I make sure I have at least one per day to attend, as otherwise I start to feel a bit low, to be honest.

Here is the barometer in our tiny porch! My husband received this as a long service present at work, before his retirement. So very important in our house is the weather outside! COPD patients like me have to be very careful of being outside in cold, damp and/or windy weather, as it is potentially very dangerous for us and makes it harder to breathe. I consult our barometer every day, but as you may be able to read, today's forecast looked good, - although the sunny sky belied a windy, chilly day!

Finally, a view from our front drive, looking out onto the main road where we live! I often love to look out of the window at the world going by and the buses stopping over the road at the bus-stop, on their way into Southport, or the folk waiting patiently at the bus-stop, wondering where they are going and speculating about their lives! (Actually, you can't see the bus-stop from my photo, unfortunately, but I can take another one if you wish, Samuel.) Looking outside like this makes me a little wistful, but also hopeful and determined to be out and about more in the months ahead, when the better weather comes. I can't sit out in the front garden in summer, owing to pollution from the road vehicles, - in that case, I sit in the back and listen to the birds!

Appendix AB

Photographs from patient Jacqueline

Photograph 1

Platform photo. There's a steep hill from the train station to the bus stop I need. It's quite shore but hard work and on a cold morning it makes me cough. So I take more time and wait for the tram to take me up to the flat part of town and the bus stop.

Photograph 2

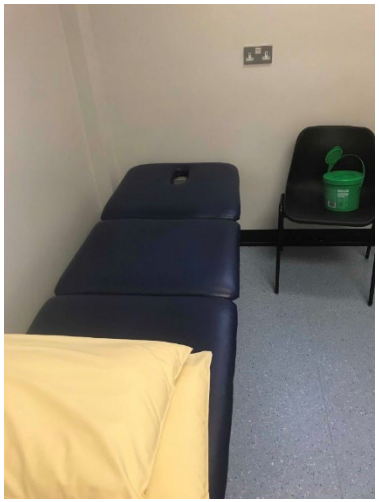
Yoga mat - 2 photos- I do weekly yoga and really enjoy it, I don't feel disenfranchised by it. I was given a very posh yoga mat for Christmas and have matching blocks and strap. It helps to look the part.

Photograph 3

Post lunch and off to the swimming pool. There's a particularly steep section of path and while the children dance up it and my daughter in law pushes the buggy up with ease I fall further and further behind. She's very kind and doesn't comment, just waits at the top for me to catch up.

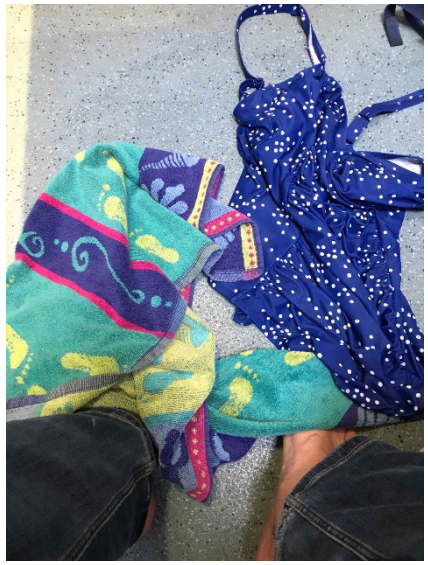
Photograph 4

Snowdrops. On holiday and there's a steep path up to the facilities. Oh look I say, snowdrops, really I'm just stopping to get my breath back but I feel less stupid if I can pretend to be pointing out something of interest.



Photograph 5

Physio table.I've been referred to the physio for pelvic floor exercises. Coughing has a major impact on the pelvic floor but this is never mentioned in relation to COPD. In fact there's no help at all with physical impacts or exercise suggestions, a huge gap. (I had to do a lot of explaining to the physio about why I wanted to take the photo!)

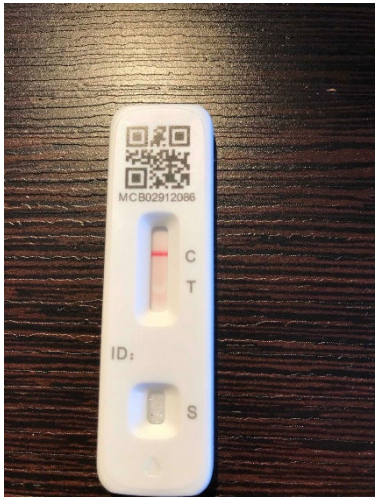


Photograph 6

Swimming things. Swimming with the grandchildren on holiday makes me realise I haven't swum for 2 years since COVID. Initially obviously pools weren't open but even when they were I had so much anxiety about safety I never went back. I'm not a fast or confident swimmer but I used to enjoy a weekly swim. Something else the pandemic's taken away.

Photograph 7

5 year old doesn't want to ride her bike to the hire place on the last day. I offer to carry it, OK on the flat but I have to stop every few yards on the hill. Daughter in law picks it up and carries it in one hand while pushing buggy, toddler, rucksack etc with the other.



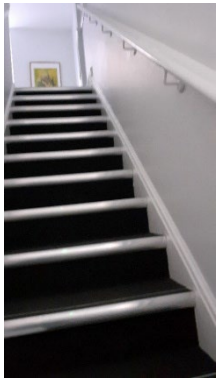
Photograph 8

LFT The bastard's got me at last (although this doesn't look like a positive test it was) despite all the shielding, following the rules, mask wearing etc. Initially I was seized with real panic but just had to trust in being fully vaccinated and boostered and it's been like flu but copable with. It was a reminder of the terror I felt at the start of the pandemic and the lack of information for people with lung conditions.

Appendix AC

Photographs from patient Pauline

Heavy but helps

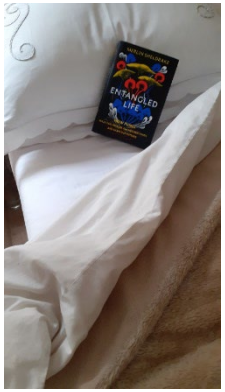


COPD nightmare, living on 3rd floor BUT

Too much time sitting down and online meetings

Glory days, fresh air

Family love



Bed and good book

Feeding friends and family

OUCH

TOO much TV

Appendix AD

Photographs from patient Jane

Photograph 1 –

Picture 1 is an altered image of me that is over-exposed and I have no nose. This represents the difficulty breathing with COPD and feeling suffocated a lot of the time.

Photograph 2 –

Picture 2 is of waves on a windy day. This represents how valuable good quality, fresh air is, not only to people with COPD but also to every aerobic life form on this planet. I can feel miffed that people don't seem to appreciate what they have got when they can breathe without thinking about it nearly all the time.

Photograph 3 –

Picture 3 is about being restricted and different. Living with COPD means that you cannot just go and do things spontaneously or the way you could when young and fit. You feel different although most people don't notice. COPD is also a hidden disability. My cat had a skin problem that had to be covered up. People thought that we were being cruel by dressing him up, but it was done to prevent him causing more harm to himself. COPD is restricting and some don't see it, some see you as different and some want to hold you back to protect you.

Photograph 4 –

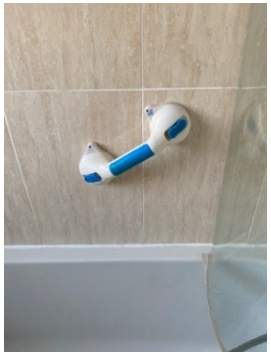
Picture 4 is skeletons in the window and represents being more aware of my mortality. It's a difficult thing to consider one's own mortality and yet there is humour within this. It can help to realise that your life may be shorter than expected but this means living life to the full and not passing up opportunities. Being honest with friends and family is cathartic and can lead to open conversations and even shared humour.

Photograph 5 –

Picture 5 is sunrays in clouds representing self-realisation in that there is no need to feel sorry for oneself when times are rough, because beauty and life are all around us. The sense of power in this photo is both humbling and inspiring.

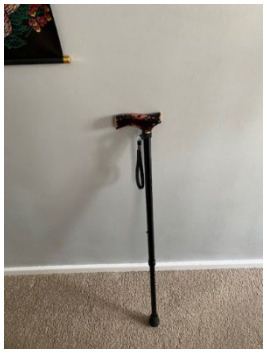
Appendix AE

Photographs from patient Philip



Photograph 1

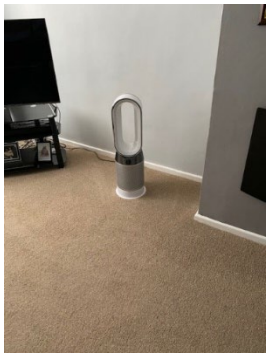
Handle to help in and out of shower



Photograph 2

My stick

This is to help me out and about and in the home



Photograph 3

Dyson

This is expensive to run but it will clean the air

Photograph 4

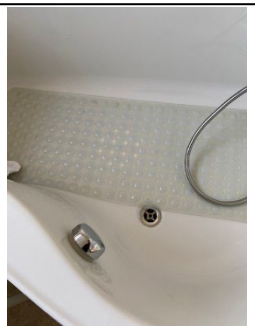
Door handle

Why you may ask well i will grip a hold of then if my stick is not around like at night holding on helps keep me stay

Photograph 5

Keeping safe

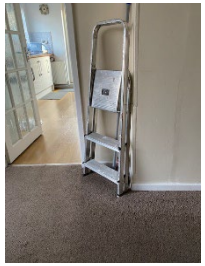
The stool in bathroom is great as standing washing I am able to hold my breath



Photograph 6

Bath

The mat in the bath use to shower stops slipping



Photograph 7

Oh dear

Yes the small ladder i only use that for the top of the shelf in kitchen this all way causes problem with the family

Appendix AF

Ethics

Ethics ETH2021-0357: Samuel Grimwood : Decision

Sent on **19 Apr 2021** by **Charlotte Dakin** Download as PDF...

Dear Samuel

ETH2021-0357

Thank you for submitting your application to the College of Science and Engineering Research Ethics Committee, which has now been reviewed and considered.

The outcome of your application is:

approved.

If any changes to the study described in the application are necessary, you must notify the Committee and may be required to make a resubmission of the application.

On behalf of the Committee, we wish you the best of luck with your study.

Yours sincerely

Charlotte Dakin

Appendix AG

Participant information sheet

Participant Information Sheet
(Option 3)

Study title

A qualitative exploration of the experiences of having COPD, symptom profile determinants and its impact on quality of life, using a Photovoice methodology.

Invitation

You have been invited to participate in this 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 the time to read the following information carefully.

Purpose of the study

The purpose of the research is to increase our understanding of your experiences of living with COPD and its impact on your quality of life.

Our previous study provided an insight into the physiological and psychological factors which underpin COPD. However, this study was questionnaire based, which meant that the unique and personal experiences of living with COPD had not been captured. As a result, the purpose of this study is to explore your first-hand experience of living with COPD within a semi-structured one to one interview and how it is impacting on your day-to-day quality of life and your views and experiences of the medication and strategies that you currently undertake.

Collectively the aim of this ongoing project is to provide new insight and to attempt to design an intervention that could improve the quality of life of people living with COPD.

Why have I been selected? Am I eligible to take part?

You are eligible to take part if:

- You have COPD
- 18 years old & above
- Live in the UK

- Able to understand written information in English

- Own a device that can:

  Be used to take part in an interview using video call software Microsoft Teams

Do I have to take part?

Taking part is completely voluntary. You have the right to refuse to participate and you may withdraw your consent at any time without jeopardy. You can withdraw up to 2 weeks after participation in the study, unless there is a significant reason, which will be considered. To withdraw your data simply contact the researcher or research team on the details below with your unique participant code (i.e. the 5-digit memorable code). This code will be unique to you (consisting of the last two letters of your postcode and last three digits of your phone number).

What will taking part in the study involve?

After reading this participant information within this page on Qualtrics (online portal that you are accessed, via the link you clicked on that was sent to you), after you have finished reading this information about the study, please click on the arrow below and you will be directed to the consent section, which will state also the researchers contact details, for the opportunity to ask any further questions Should you wish to take part in the study, you will be able to consent by selecting 'yes' or 'no' which the researcher will receive online. This will act as an online signature.

After consenting to take part in this research, you will then be asked straight away to fill in some information about yourself (i.e. your age, occupation) and that relating to your experience of COPD (i.e. Additional health conditions, Medication, Stage of COPD, FEV Score, Breathlessness Scale & Quality of life).

If you are eligible for the study and you have provided consent, you will be able to state your email address, as well as stating your unique participant code (i.e. 5-digit memorable code). This code will be unique to you (consisting of the last two letters of your postcode and last three digits of your phone number). Stating your email address is strictly for contacting the researcher and for the researcher to contact you regarding this study. Your email address will also be used to send study documentation during the study. Your email address will be stored securely on the University of Derby's server and email addresses will be sent securely using the University of Derby's Microsoft Outlook. Your data will remain completely

anonymous throughout the study and will not be linked to any other personal information or data that you provide in the study.

If you consent to take part in this study, you will be emailed by the researcher regarding the next steps in due course, which will be an online interview that will be conducted is to discuss in detail exploring the effect of COPD on your quality of life and about your current COPD medical treatment i.e. your inhaler(s) and strategies. This will also take between 45 minutes - 1 hour in total duration. The interview will be conducted using Microsoft Teams and is free of charge to access (easily downloadable from the android or app store free of charge, if using a smartphone or ipad/tablet and similarly on a computer/laptop) and you will be sent a unique and specific link/details by the researcher, close to the time of the arranged online interview. The interview will be recorded for research purposes and will be saved on a secure database.

At the end of the study, you will have the option to provide your email address, to be contacted by the research team about participating in future research regarding your COPD. If you decided this is what you would like to do, your email address would be stored on our secure research database (For GDPR and data protection information, please refer to the section 'Further guidance on the use of your data and your rights'). This is completely optional.

Step-by-Step Procedure

Stage 1 – Read the participant information sheet, consent to take part (should you wish) and answer demographic questions online.

Stage 2 – Researcher emails you to arrange when to conduct the

online interview to discuss about the effect of COPD on your quality of life and questions about your current COPD medical treatment and strategies that you use.

Stage 3– Debrief Form sent to your email address.

What if I cannot get online?

This is an online study and so you will need to be able to access the internet to take part (i.e. a laptop/computer, smartphone, tablet/iPad). Unfortunately, because of the current COVID-19 pandemic, an in person one-to-one interview cannot be arranged as an alternative at this moment in time.

What are the possible risks of taking part?

Interview -

Talking about your experiences of having COPD can be difficult. If you feel uncomfortable, you can pause during both interviews, refuse to answer or if you do not wish to continue in the study, you are free to withdraw at any time.

During the interview if the researcher feels that you have said something that is affecting your personal safety and you are in danger, confidentiality will be breached, and the researcher will be obliged to contact the relevant authorities.

When being interviewed, it is natural sometimes to mention personal names, and other facts when discussing your COPD and medication. Therefore, as the interview is being recorded and analysed for the purposes of this research project, any identifiable names will be omitted and changed.

There will be no risk participating in this study, beyond that experienced in day-to-day life. There are no special precautions that you need to take before or after taking part in the study. Whilst the risk of participation I considered negligible agreement to participate in this research does not compromise your legal rights and should something go wrong.

What are the possible benefits of taking part?

We are trying to find out more information about the factors that impact the quality of life among people who have COPD and the strategies that appear to be most effective in managing the respiratory condition. We cannot promise that this study will help you directly, but the information that you kindly provide could add to existing knowledge in this specific area of COPD and make a significant difference and impact.

Also, as a thank you for taking part in this study you will have the chance to be enrolled into a prize draw in a chance to win one of five gift cards. Winning participants will be drawn at random by an impartial member of the University of Derby's, University Research Knowledge Exchange Office (URKEO). If you win, you will be contacted via email to claim your prize. 1st prize will be a £50 Amazon gift card, 2nd prize will be a £25 gift card and then 3 separate prizes of £10. To be enrolled into this draw please state your email address at the end of the survey, so the URKEO can email you if you have won. Again this is optional and your email address will only be used for the prize draw and once the prize draw has been conducted, your email address will be deleted from The University of Derby's server (For GDPR and data protection information, please refer to the section 'Further guidance on the use of your data and your rights.)/

What will happen to the results of the study?

The information from the study from the interview will be recorded and transcribed and will be stored securely at the University of Derby for a minimum of 7 years. Your decision to participate is completely voluntary.

All information collected will be anonymised using your unique 5-digit code. Quotes from the interviews may be selected and therefore included in a PhD thesis, publications, and conferences. Again, this will be fully anonymised and no identifiable information will be used.

Should you wish to withdraw from the research you may do so at any point, up to two weeks after participation. You will not need to give any reason or explanation for doing so. To withdraw your data simply contact the researcher or research team on the details below with your unique participant code (i.e. the 5-digit memorable code).

Can I get advice from the research team about my COPD?
Unfortunately the research team is unable to offer you any advice on COPD. If you do need any advice or help, we would recommend your contact your doctor or relevant health professional.

What if I become distressed during the study?
It is not anticipated that there will be any reason for you to become distressed during this study but if you do please contact your GP, The Samaritans (available 24 hours a day to provide confidential emotional support for people who are experiencing feelings of distress, despair or suicidal thoughts, www.samaritans.org, 116 123 (free to call from within the UK and Ireland), 24 hours a day, email: jo@samaritans.org), Lifeline 0808 808 8000 (is also available seven days a week to contact if you need help), or The British Lung Foundation https://www.blf.org.uk/support-for-you/copd; 03000 030 555; Mon-Fri; 9am – 5pm.

Who is conducting and funding the research?

The research is being conducted by Mr. Samuel Grimwood, as part of his PhD at The University of Derby and the supervisory team is Dr Mark Faghy (Director of Studies), Dr Amy Baraniak, Dr Emma Sharpe, and Professor Gyan Tripathi. The research is funded through The University of Derby, The European Regional Development Fund (ERDF) and SoeHealth Ltd.

What if I have any questions?

If you would like more information about this research, ask any questions, withdraw consent or to make a complaint, please contact one of the research team on the details below.

Contact details

Mr Samuel Grimwood	Dr Amy Baraniak	Dr Mark Faghy
s.grimwood@derby.ac.u	a.baraniak@derby.ac.u	m.faghy@derby.ac.uk
+44(0) 7557800951	+44(0) 1332 59304	+44 (0) 1332 592109

Further guidance on the use of your data and your rights.

The lead researcher will be collecting data from your participation in this study. This data is for us to understand further the effect of COPD on quality of life and effective strategies in managing the respiratory condition. It is also in the public interest of enhancing academic research is this area.

- Not seek more information from you than what is essential and necessary for the study.
- Make sure that you are not identified by the data by anonymising it using ID codes.
- Use your anonymised data only for the purposes of this study and for any relevant publications that arise from it.
- Store data safely in password-protected databases to which only the named researchers have access.
- Not keep your information for longer than is necessary (usually for seven years).
- Safely destroy your data by shredding or permanently deleting them.

Data will be stored securely on Qualtrics and on The University of Derby's server. The server and database are protected by several measures including anti-virus and anti-spyware applications, firewalls, encryption technology and permissions.

Data will be stored securely until the study end date and will be securely stored according to the ICH-GCP standards and GDPR Act (2018) data protection principles. If you would like to ask any questions specifically related to data storage and GDPR guidelines, please get in contact with our Data Protection Officer (DPO) Helen Rishworth on (01332) 591954. Alternatively, you can email gdpr@derby.ac.uk.

During the study, the researcher will share documents with the supervisory team, that are authorised personnel working within the College of Science & Engineering at The University of Derby. The researcher and supervisory team will comply with the requirements of the Data Protection Act 1998.

Researchers on the project with access to the data are supervised by highly qualified and experienced staff and have been very careful to ensure the security of your data. The study was approved for its ethical standards by The University of Derby Human Sciences Research Ethics Committee. Further information about the project can be obtained from Mr Samuel Grimwood (s.grimwood@derby.ac.uk, +44(0) 7557800951), Dr Amy Baraniak (a.baraniak@derby.ac.uk, +44(0) 1332 59304) and Dr Mark Faghy (m.faghy@derby.ac.uk, +44 (0) 1332 592109) at The University of Derby, Kedleston Road, Derby, DE22 1GB.

Appendix AH

Consent Form

Participant Statement of Consent to Participate in the Investigation Entitled:

**

A qualitative exploration of the experiences of having COPD, symptom profile determinants and its impact on quality of life, using a PhotoVoice methodology.

**

Option 3

4) The information that you supply in this study will be held and processed in line with the UK GDPR/ Data Protection Act 2008/ EU GDPR. Information will be used by the University of Derby (as data controller) to anonymise, analyse and interpret for a PhD research project.

5) I understand that I have agreed to participate in a research study exploring the impact of COPD on my quality of life, for part 2 *(Online Interview, regarding your experiences of COPD and your medication/strategies)* of the study.

   (The online interview will be conducted using Microsoft Teams and is free of charge to download and instructions will be provided)

3) I have read a copy of the participant information sheet.

4) I have also read and understood the risks and side effects that may result from participating in the study.

5) I confirm that I have had the opportunity to ask questions about the study and, where I have asked questions, these have been answered to my satisfaction.

6) I am aware that I can withdraw my consent to participate in the procedure at any time up to two weeks after participation and for any reason, without having to explain my withdrawal and that my personal data will be destroyed and that my medical care or legal rights will not be affected.

7) I understand that any personal information that I provide till be treated as confidential and my identity will be kept strictly anonymous.

8) I confirm that I have had the University's policy relating to the storage and subsequent destruction of sensitive information explained to me.
   Available online:
   https://www.derby.ac.uk/services/its/data-governance/privacy-notices/research/

9) I understand that sensitive information I have provided through my participation in this study, in the form of contact details, will be handled in accordance with this policy.

10) I understand that my data will be held for a maximum duration of 7 years from the commencement of the study and will be securely destroyed by the beginning of 2027.

11) I confirm that I know of no reason, medical or otherwise that would prevent me from partaking in this research.

12) I understand that the information collected about me will be used to support other research in the future and may be shared anonymously with other researchers.

13) I understand that any information that will be kept strictly confidential and that no personal information will be included in the study report or other publication.

14) I understand that providing my email address at the start of the survey will be used to be contacted by the researcher for enrolment on to this study

15) I understand that I will have the option at the end of the survey, to provide my email address, to be contacted by the research team, for additional research that we will be in addition to this study in regard to having COPD. Should you wish to agree your email address will be stored on a Microsoft Excel 2016 spreadsheet, which will be password protected and only accessed by the research team on The University of Derby's server. The database will be protected by several measures including anti-virus and anti-spyware applications, firewalls, encryption technology and permissions. Data will be stored securely for a period of up to 7 years from the study end date and will be securely stored according to the ICH-GCP standards and GDPR data protection principles. You can request to have your email address to be omitted from the database by contacting the researcher.

16) I understand that I will have the option at the end of the survey, to provide my email address, to be enrolled into a prize draw in a chance to win a gift card. Your email address will only be used for URKEO to contact you if you win a gift card. Therefore, once the prize draw has been conducted your email address will be deleted. The database will be protected by several measures including anti-virus and anti-spyware applications, firewalls, encryption technology and permissions. Data will be stored securely for a period of up to 7 years from the study end date and will be securely stored according to the ICH-GCP standards and GDPR data protection principles. You can request to have your email address to be omitted from the database by contacting the researcher.

Our lawful basis for processing this data is consent.

I have read and understood all the information above and agree to take part in this study, giving my consent for my data to be collected and stored as per this consent form

Yes/No

I agree to provide my email address to be contacted to enrol on to the above study, to partake in an Online Video Call interview regarding my COPD experiences and medication/strategies. The interview will be conducted using Microsoft Teams.

Yes/No

I understand that the online interview will be audio recorded within the Microsoft Teams programme, for the researcher to transcribe and anonymise to conduct a collective analysis at the end of the study.

Yes/No

I agree to provide my email address to be contacted for future research in regards to COPD

Yes/No

I agree to provide my email address to be contacted to be enrolled for the prize draw

Yes/No

Participant ID: _____ (please use the last two letters of your postcode and the last three digits of your phone number i.e. BN223. Your data will be stored under this ID to ensure confidentiality. You will be asked to recall this ID if you wish to withdraw your data)

Appendix AI

Debrief Information

Option 3

Debrief Form
Thank you for your participation in this study. Your participation is greatly appreciated.

Purpose of the Study:
The purpose of the research is to increase our understanding of your experiences of living with COPD and to explore the strategies that are most effective in managing this disorder.

COPD can increase levels of breathlessness, fatigue and limits airflow which can significantly impact taking part in day-to-day activities. This can negatively affect quality of life and can cause sleep problems and depression.

Despite having a wide range of medical treatments available, COPD is still decreasing lung function and directly impacts the quality of life of those that are living with the respiratory condition.

The aim of this study is to help to inform intervention(s) that could be of benefit in reducing the impact of COPD on quality of life. Findings from this study may also help to improve lung function in those with COPD, increasing both mobility and reducing low mood.

Thank you for taking the time to participate in this study. Discussing your experiences of living with COPD and the medication you take and the strategies you use, is extremely insightful and very much appreciated. This will help us to understand further the physiological and psychological factors implicated in COPD and assist in setting the foundation for future research.

Withdrawal Procedure:
Your identity will remain confidential if the results of the study are published. Potential places for publication could be scientific journals (i.e. Elsevier - Social Science & Medicine). The contact details are listed below. May you be assured that your data will be deleted immediately, and you will not appear in any part of the report. Your decision to participate is completely voluntary. Should you wish to withdraw from the research you may do so at any point, up to two weeks after participation (this is because your data will be formally screened, cleaned and prepared for data analysis which will be conducted and therefore the research team will not be able to remove your anonymised data). You will not need to give any reason or explanation for doing so. To withdraw your data simply contact the researcher or research team on the details below with your unique participant code (i.e. the 5-digit memorable code).

Final Report:

If you would like to receive a one-page summary of the findings when it is completed, please feel free to contact the researcher. The contact details are listed below.

Useful Contact Information:
For any further information regarding the topic of COPD and mental health, please see below, for further details of several organisations that may be useful. They will be able to offer professional advice and guidance that cannot be obtained from the researcher or their supervisory team.

British Lung Foundation: https://www.blf.org.uk/support-for-you/copd; 03000 030 555; 9am-5pm

MIND: www.mind.org.uk

Samaritans: www.samaritans.org,**116 123**, 24 hours a day, jo@samaritans.org

If you have any questions or concerns regarding this study, its purpose or procedures, or if you have a research-related problem, please feel free to contact via email, the researcher or their supervisors:

Mr Samuel Grimwoood – s.grimwood@derby.ac.uk

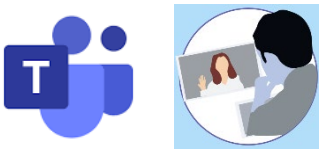
Dr Mark Faghy - m.faghy@derby.ac.uk
Dr Amy Baraniak a.baraniak@derby.ac.uk

Once again, thank you for your participation in this study.

Appendix AJ

Microsoft Teams handout

How to use Microsoft Teams for interviewing



Option 1-3

All interviews will be conducted via Microsoft Teams.

You may already have a Teams account; if this is the case you can use your existing account.

If you do not have a Teams account, you can access Teams via your internet browser (without having to download or create an account) or you can download to your device (you will have to create a log in and follow steps).

Please use the contents to navigate to the most appropriate section for you.

If you have any questions, please contact:
Samuel Grimwood
s.grimwood@derby.ac.uk

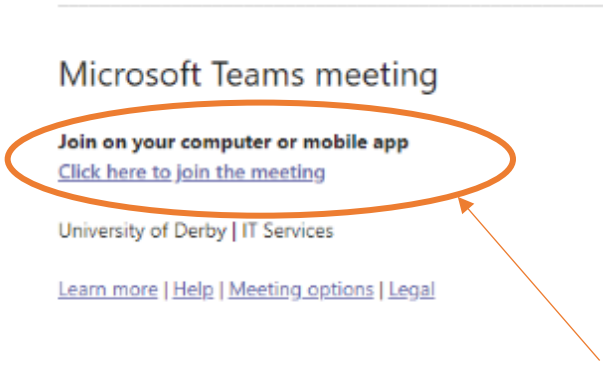
+44(0) 7557800951

Contents	Pages
How to use Microsoft Teams using:	
- **Smartphone, Tablet/iPad**	**2-5**
- **Computer *(to download the app)***	**7-11**
- **Computer *(to use the internet browser)***	**12-13**
- **Computer *(if you already have Microsoft Teams downloaded on your PC)***	**13-14**

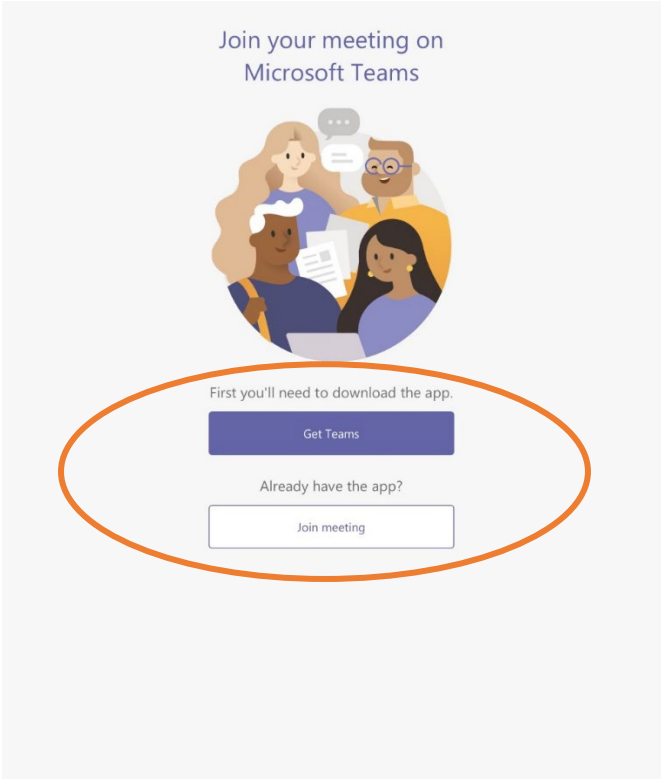
Researchers Contact Details	**15**

Using your Smartphone/Tablets/iPad:

If you to your emails and you will see an invitation to the interview from the researcher and open up the email.



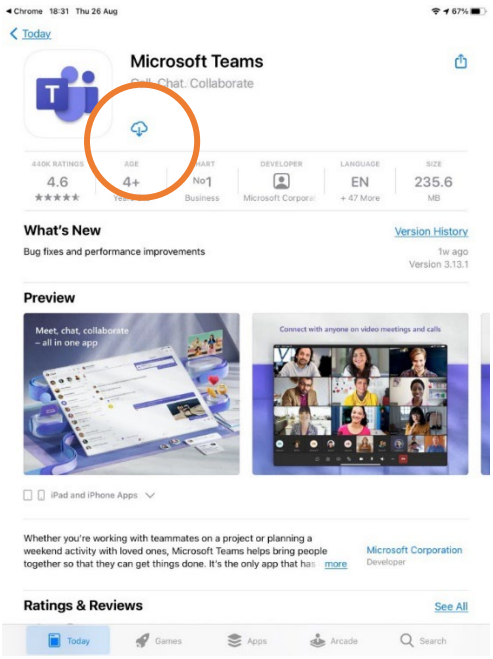
- Tap on the link ‘click here to join the meeting’



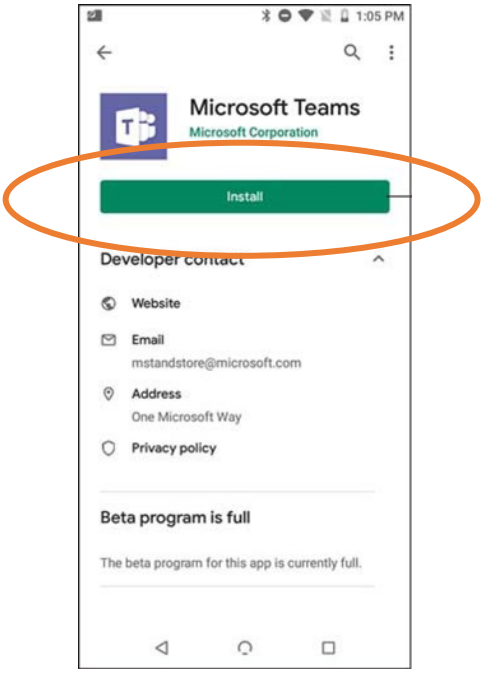
- A screen similar to this will pop up. If you already have Teams click on ‘Join meeting’ and enter your Microsoft Account details. If not click on ‘Get Teams’.

- You will then have one of the below screens come up on your device depending on whether it is an Apple or Android device.

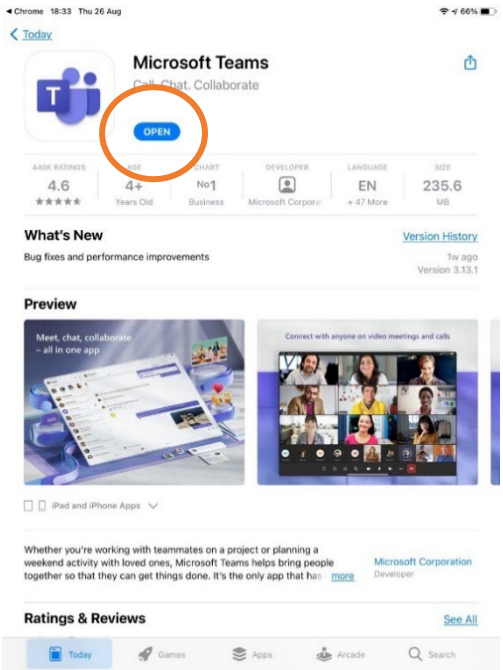
Apple



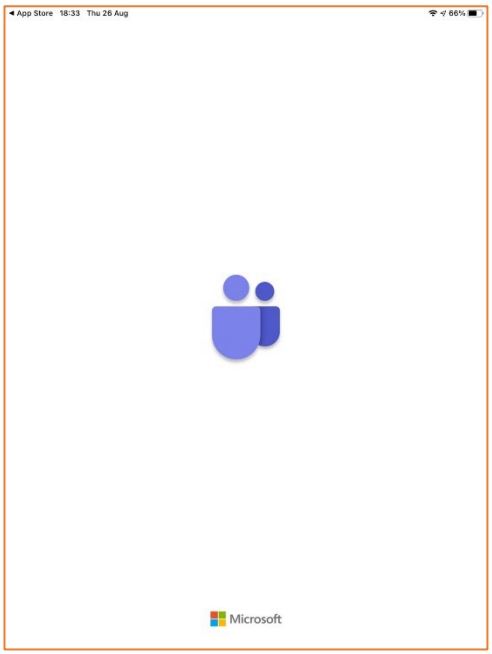
Android



- Click on open (Android devices will be similar, as examples the Apple instructions are below)



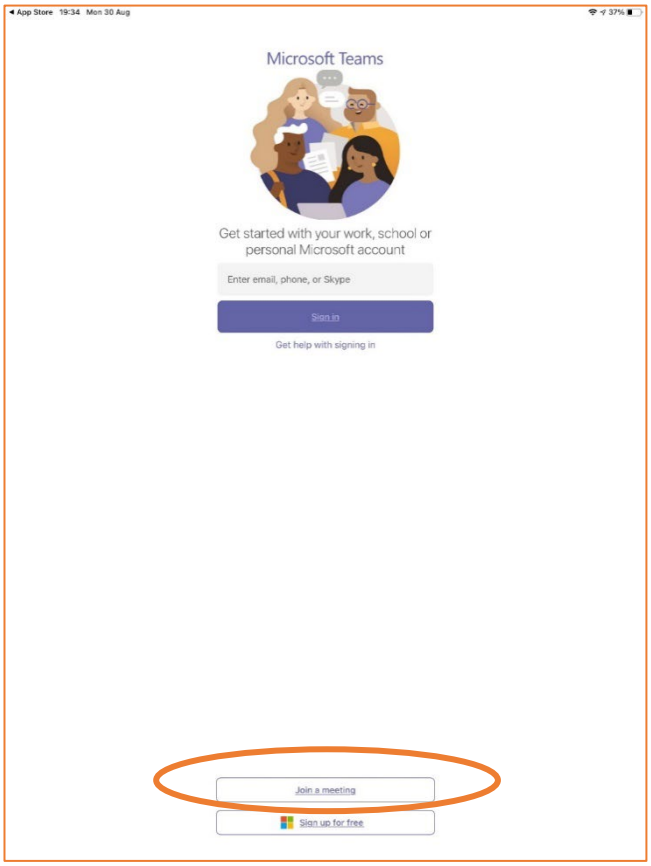
- The below screen will appear



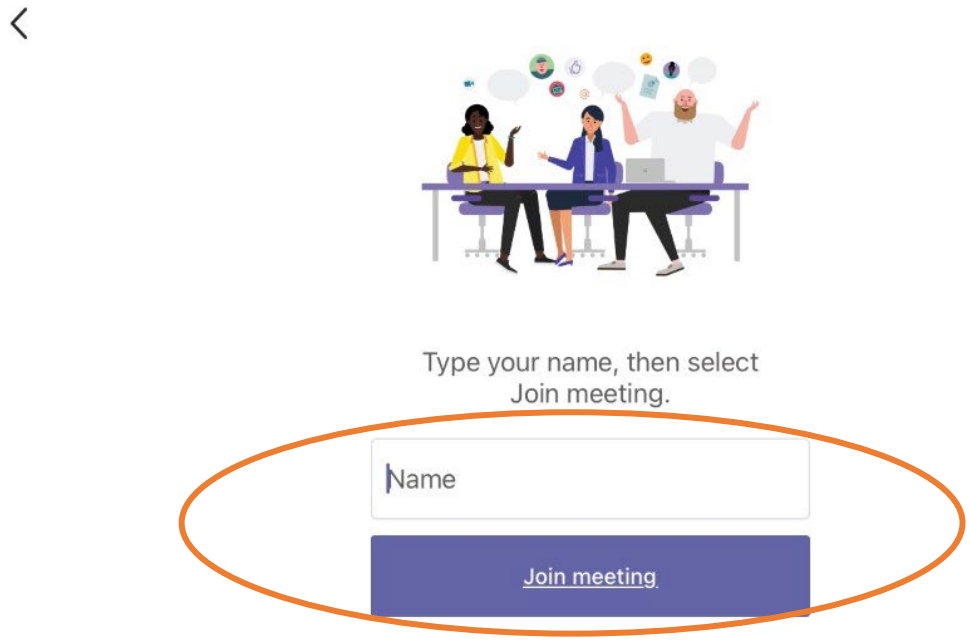
- If you do not want a Microsoft Account – click on ‘sign in and join’ and then click on ‘Join as a guest’.

- If you have an account, please enter your details and sign in

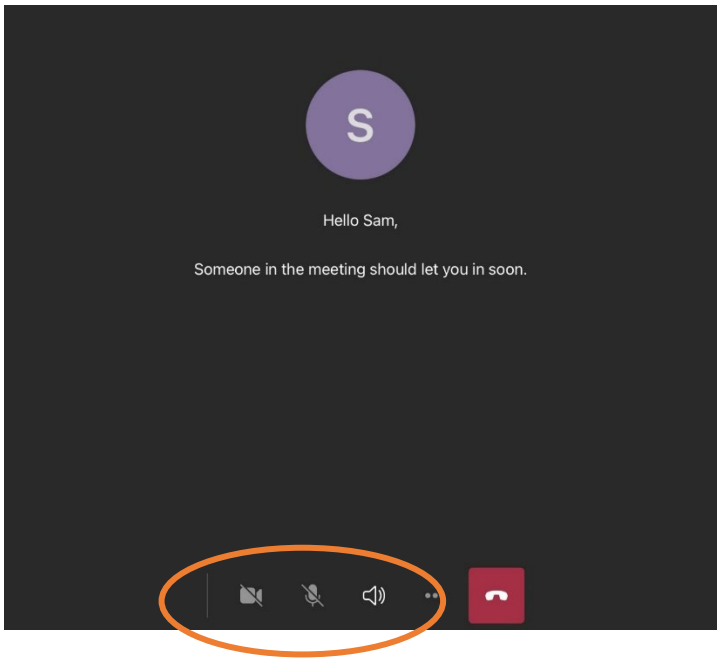
- If you would like to create an account, click on ‘sign up for free’ and follow the instructions



- If you clicked on ‘join as a guest’ the below screen will appear. Type your participant ID (5-digit memorable code) into the box and click ‘join meeting’



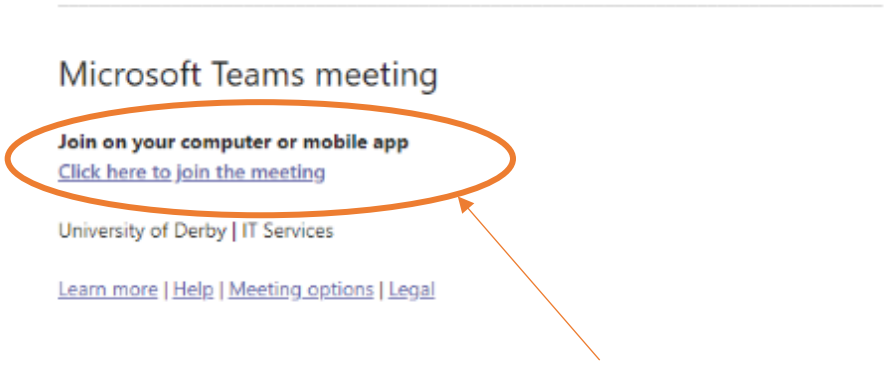
- You will then see the below screen appear



- Make sure you tap on the camera and microphone. The researcher will then let you in to the meeting.

If using a COMPUTER

Go to your emails and you will see an invitation to the interview from the researcher and open up the email.

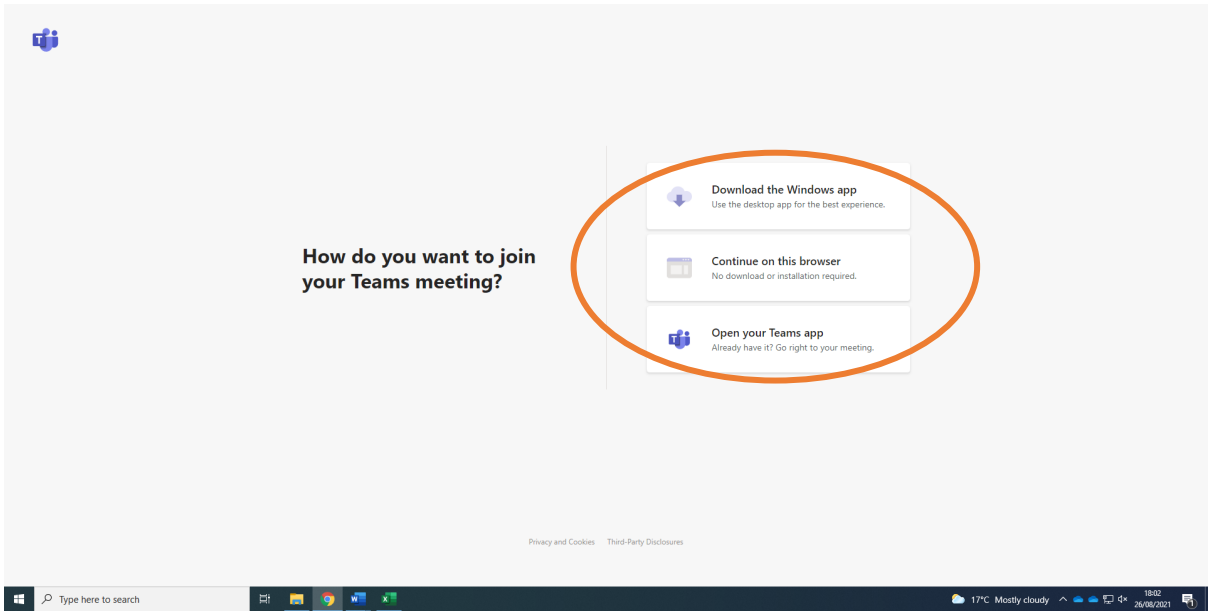


- Click on the link ‘click here to join the meeting’

- You will see the below options on a PC, using Google Chrome web browser

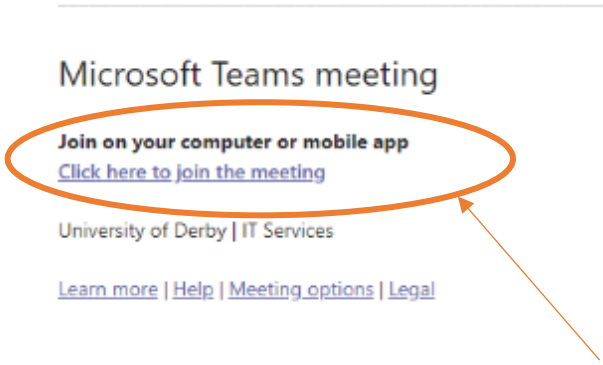
  You can either:

  1) To download the app on your PC
  2) To use your internet browser (no download needed)
  3) If you already have Teams app downloaded

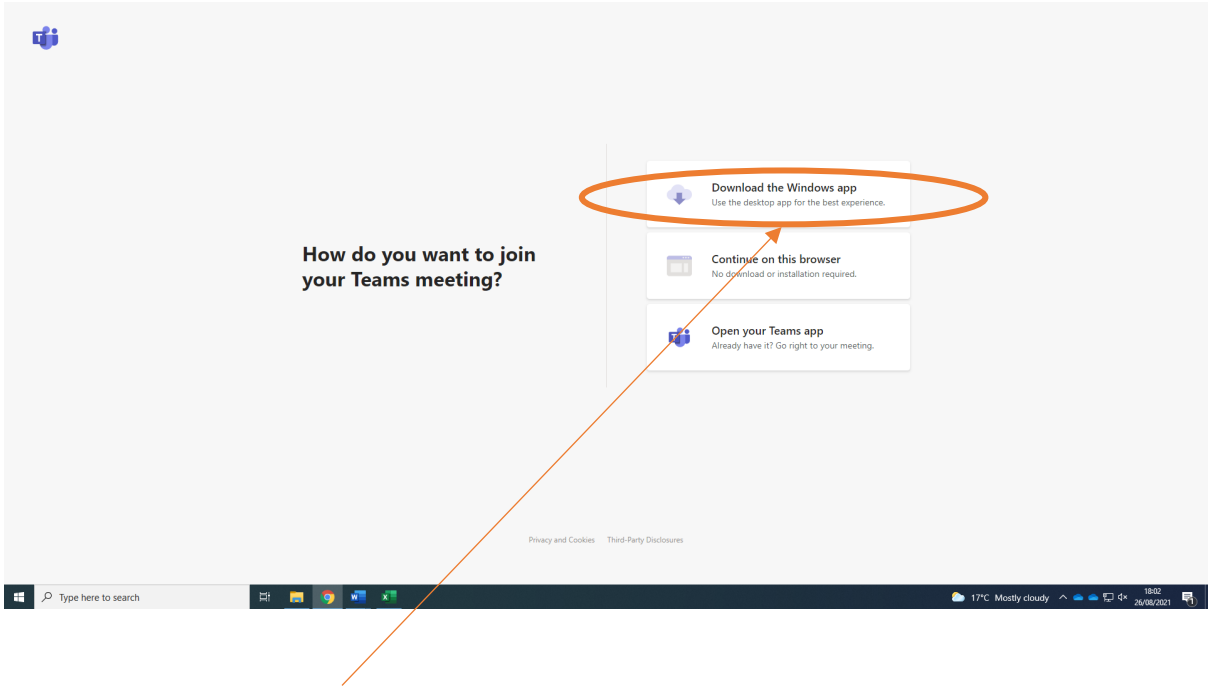


1: Download app on PC

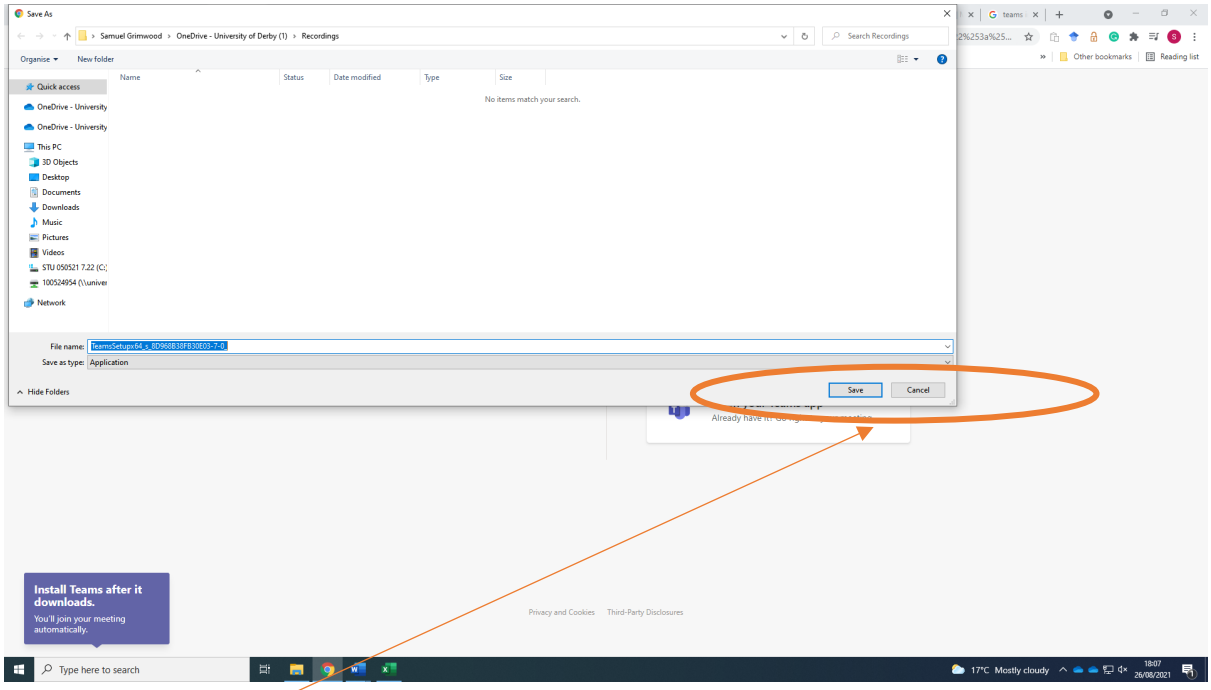
Go to your emails and you will see an invitation to the interview from the researcher and open up the email.



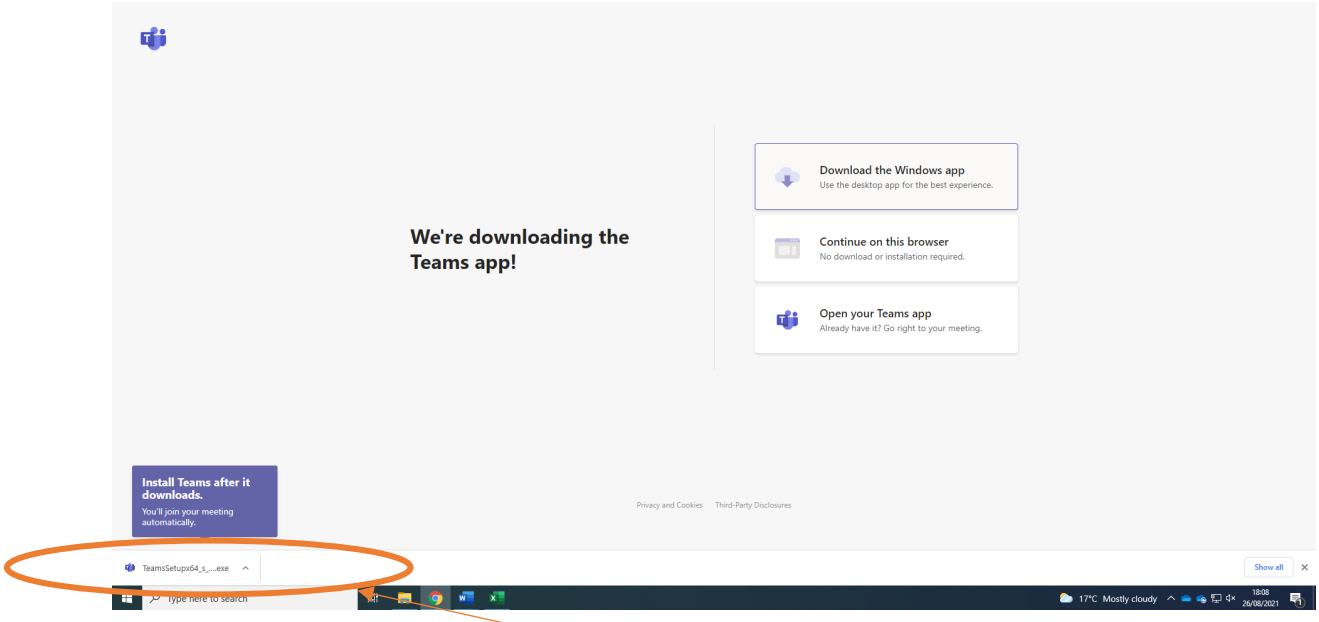
- Tap on the link ‘click here to join the meeting’



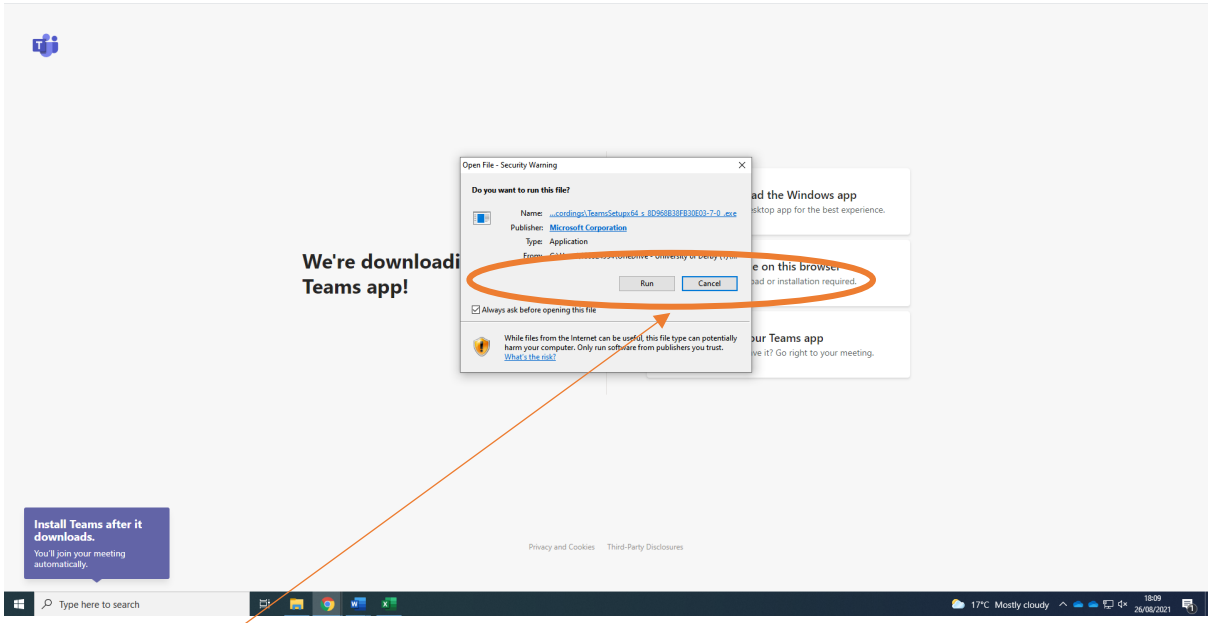
Click on ‘download the windows app’



Click on ‘save’

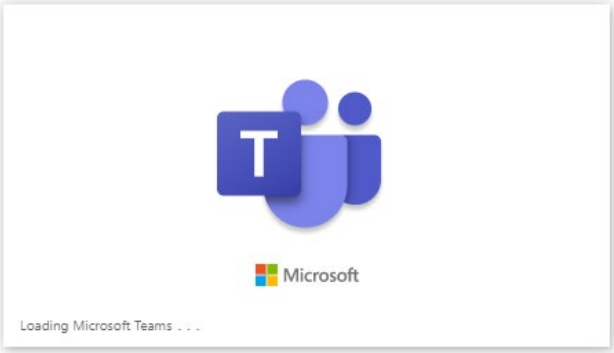


Click on the downloaded file in the bottom left-hand corner

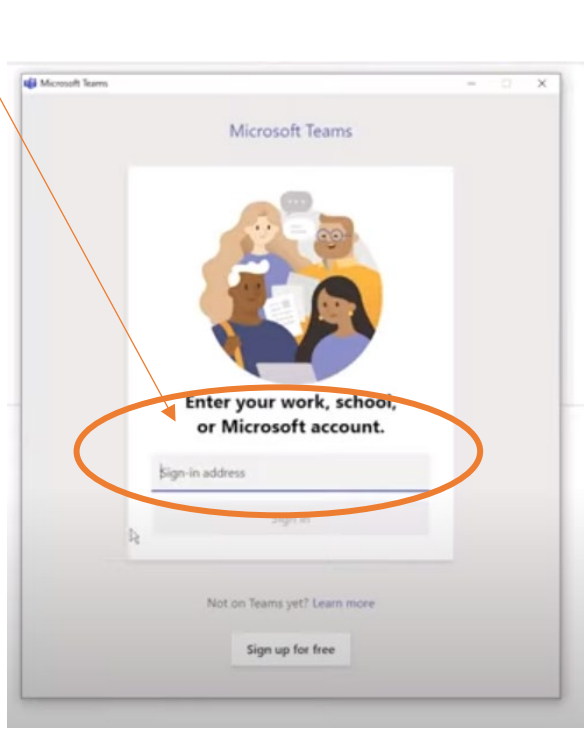


Click on ‘run’

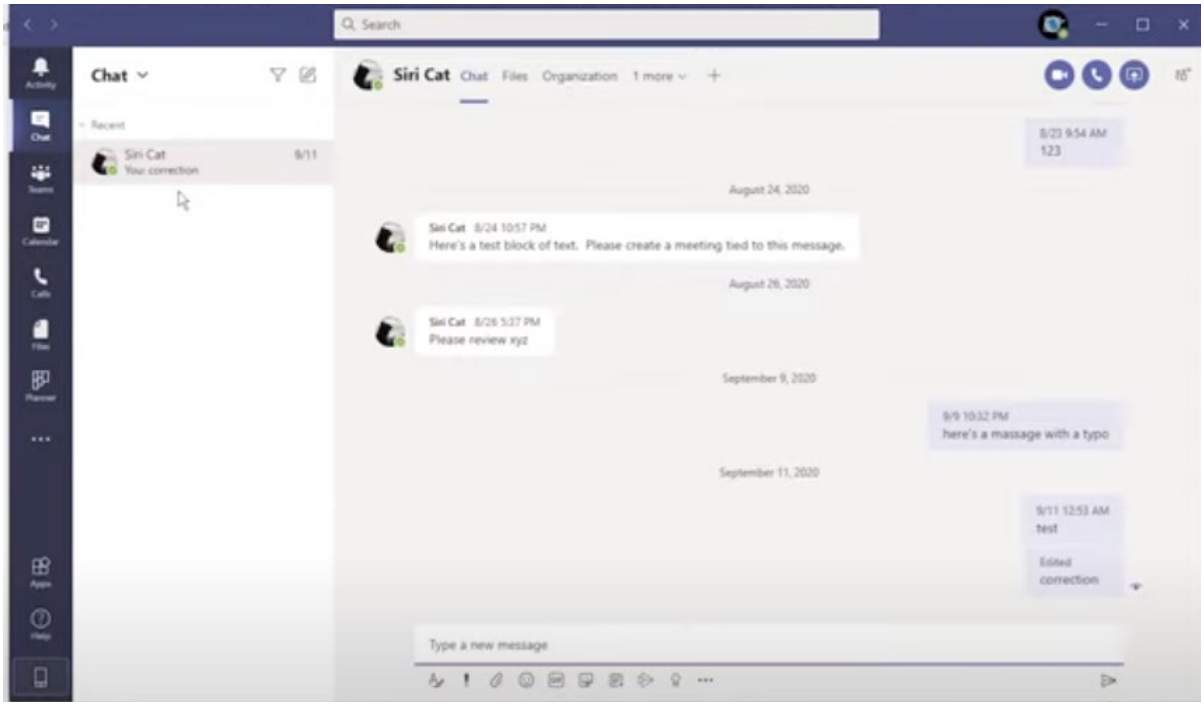
You will see the Microsoft Teams logo pop up on your screen



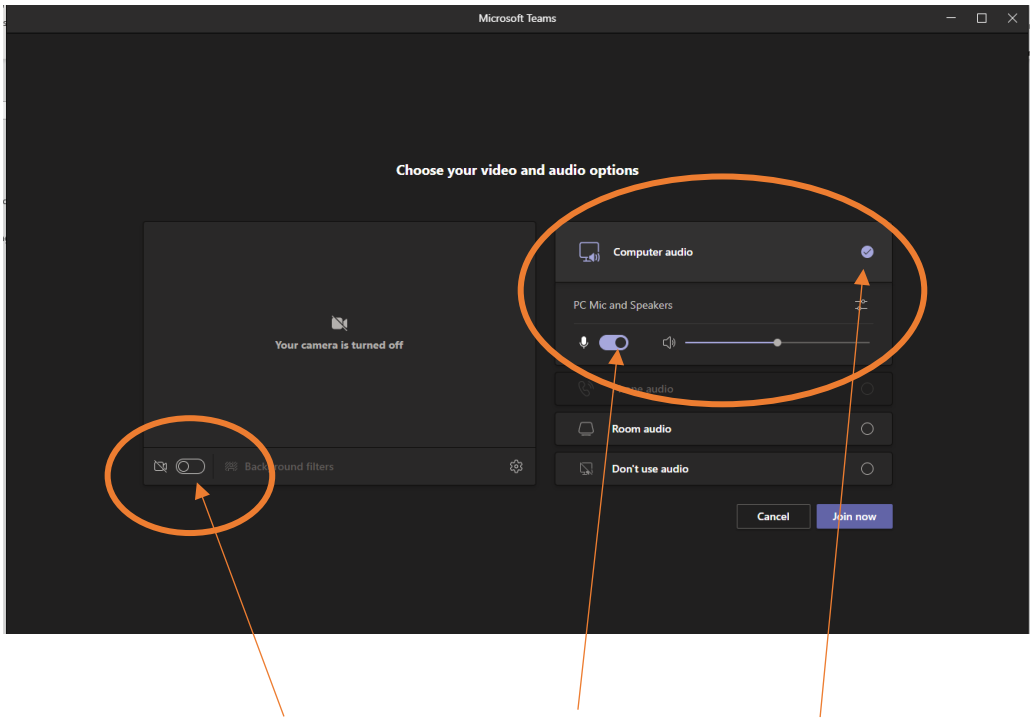
When the screen pops up you have to enter your Microsoft Account. If you haven't got a Microsoft Account, click on 'Sign up for free' and follow the instructions. Once you have the log in credentials you can enter them to access Microsoft Teams.



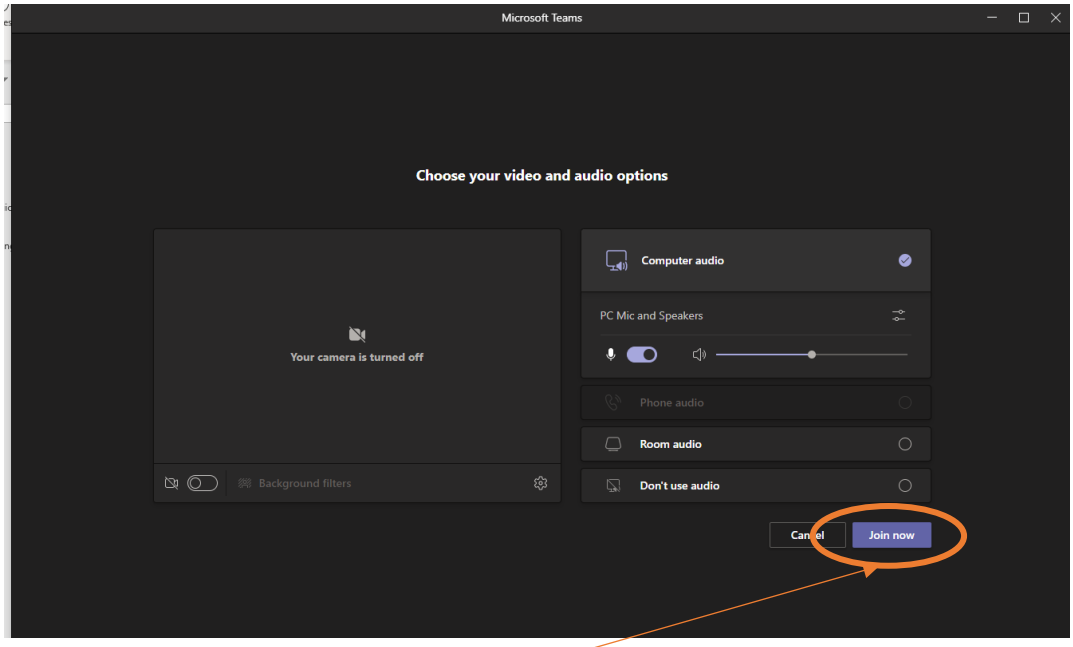
- Once you enter your Microsoft Account details it will look like the below box



- This screen should pop up and the black screen below



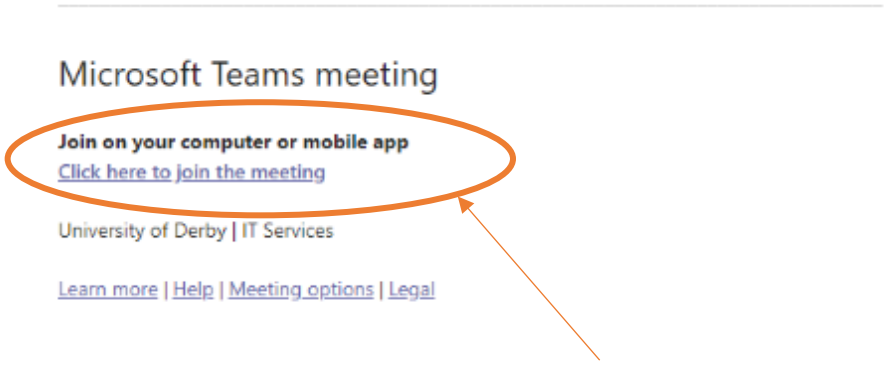
- Switch on the camera and click on PC mic and computer audio and PC mic



- Then click on join now and you will see the researcher

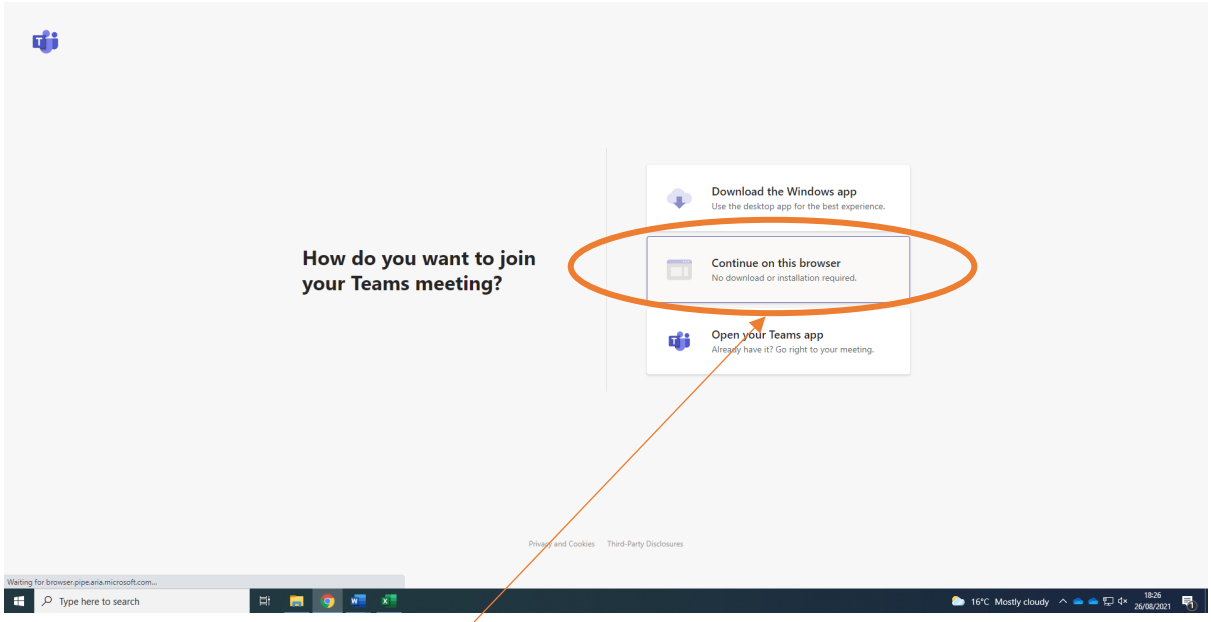
2 – 'Continue on this browser'

Go to your emails and you will see an invitation to the interview from the researcher and open up the email.

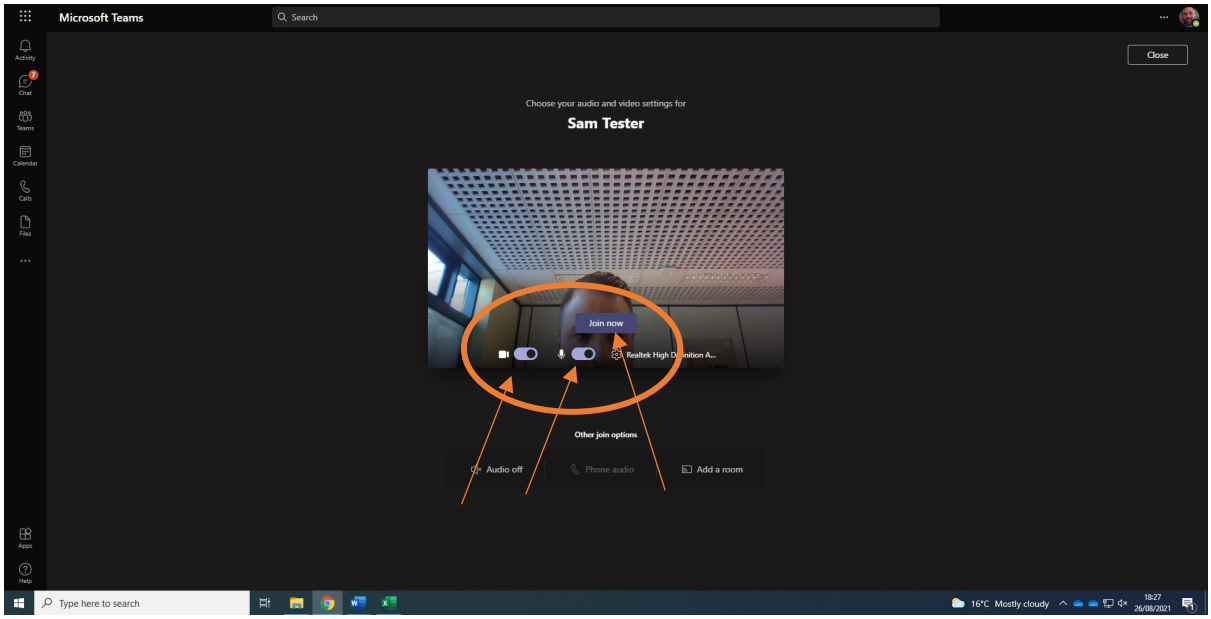


- Tap on the link ‘click here to join the meeting’

No download needed



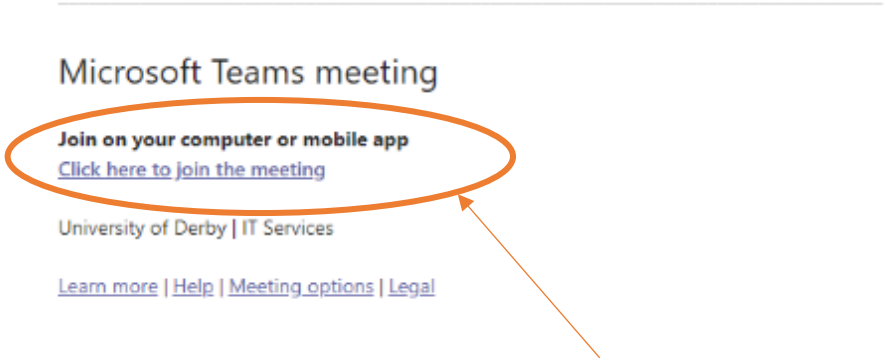
- Click on ‘continue on this browser’



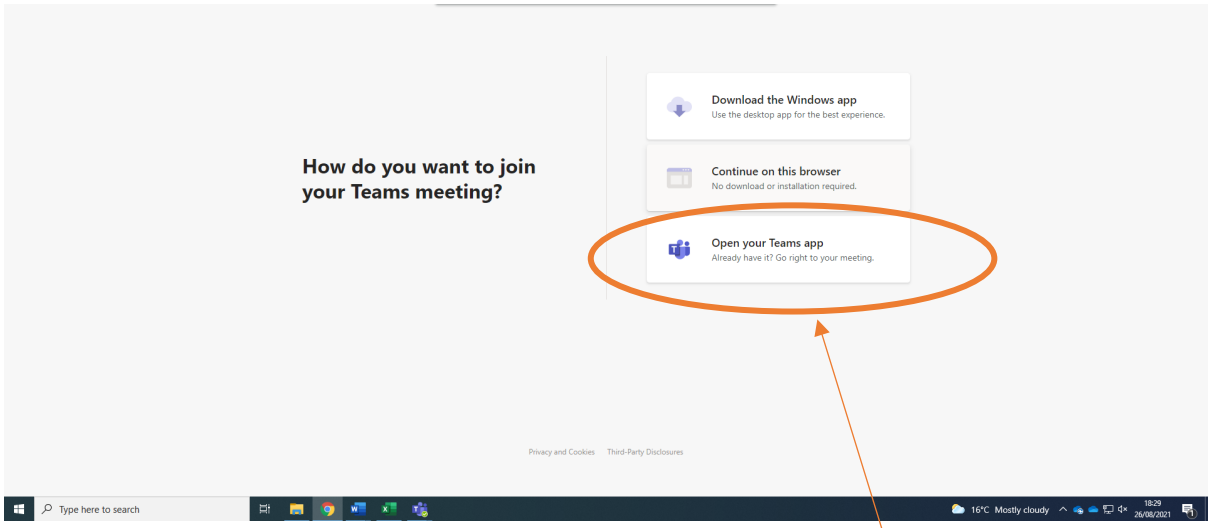
- Your screen will look like the above and you should be able to see yourself. (Make sure your camera is on and microphone and then click 'join now' and you will see the researcher)

4 – 'Open your Teams app'

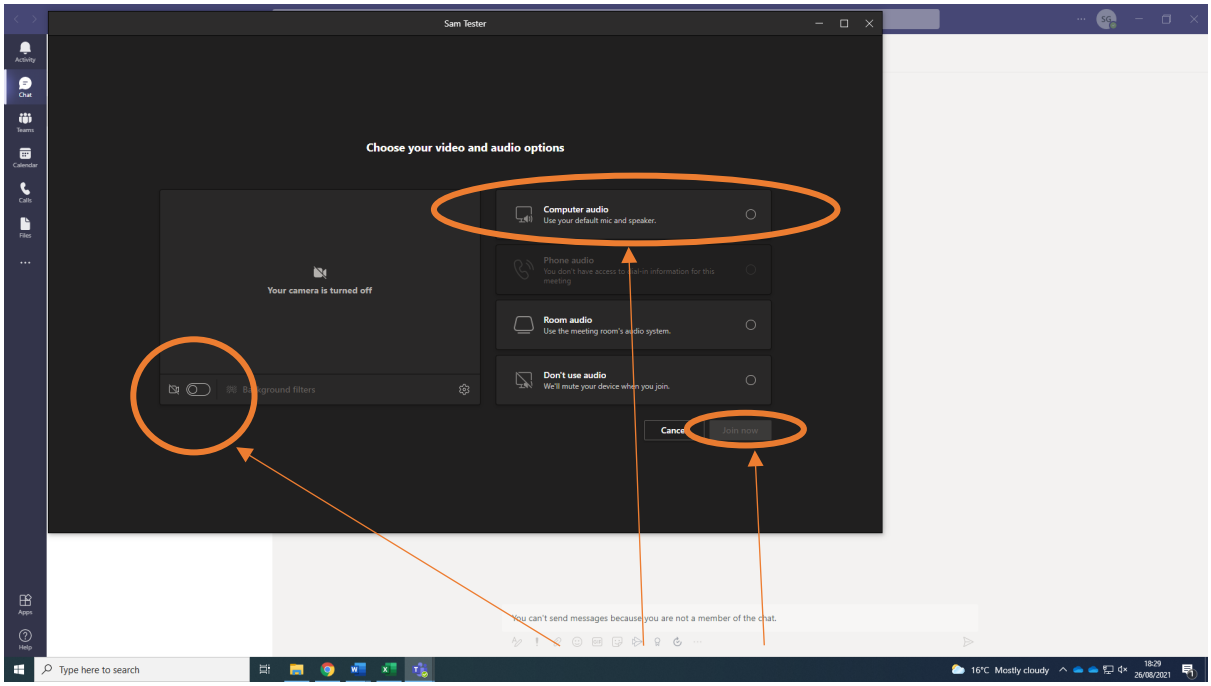
Go to your emails and you will see an invitation to the interview from the researcher and open the email.



- Tap on the link 'click here to join the meeting'



- If you already have Teams download, click on ‘Open your Teams app’



- Above screen will appear – make sure your camera is on and microphone and then click ‘join now’ and you will see the researcher

Any problems - Please contact the researcher below:

Samuel Grimwood

Email Address - s.grimwood@derby.ac.uk

Mobile Number – +44(0) 7557800951

University of Derby, Kedleston Road, Derby DE22 1GB.

Appendix AL
Interview Schedule

COPD/Medication Interview – Schedule – Participant ID - …….

1) COPD symptoms

a) What are the main symptoms that you experience on a day-to-day basis regarding your COPD?

2) Effect on day-to-day life

a) What is it like living with these symptoms/COPD?
b) Effect(s)/impact(s) this having on you and your quality of life?

3) Medication, experiences, improvements

a) What medication/inhalers are you currently using?

b) How long have you been prescribed these?

c) Which ones do you prefer?

Why is this? What do you like or not like about (X, X, X)?

4) Alternative non-medical interventions, experiences, thoughts

a) What are your views and/or experiences of alternative non-medical treatments?
(i.e. Pulmonary rehabilitation, giving up smoking, air purifiers)
- *Likes & Dislikes?*
- *Why?*

5) Ideal intervention/what would it help on

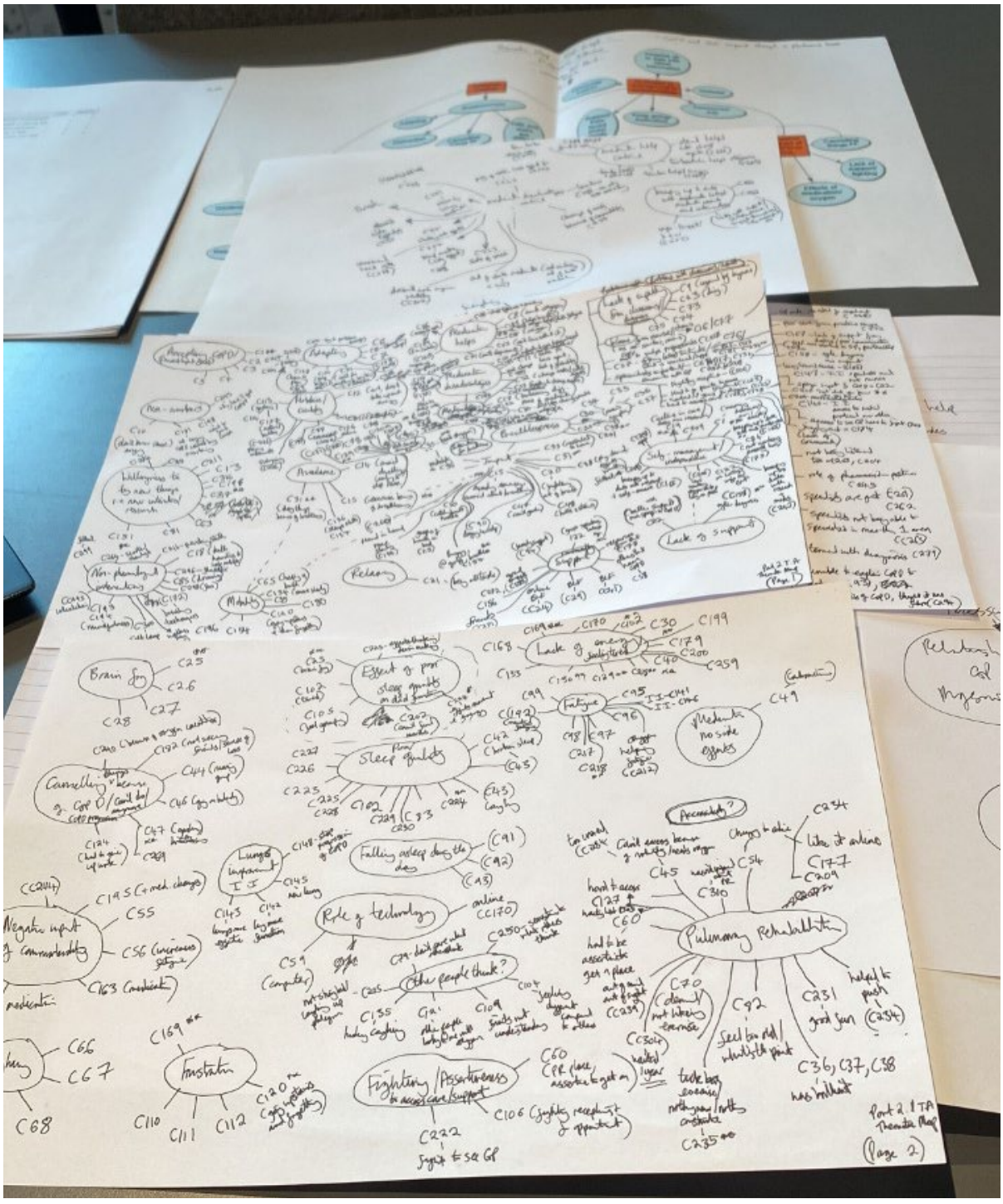
a) If you had a magic wand, what would the perfect type treatment be for your COPD?

b) How would you want it to be?
Looks/function/how much effort, time, training would you need or be required?
Medical or Non-Medical?

c) What parts of your COPD would you like the treatment to help on, that your current medications aren't?

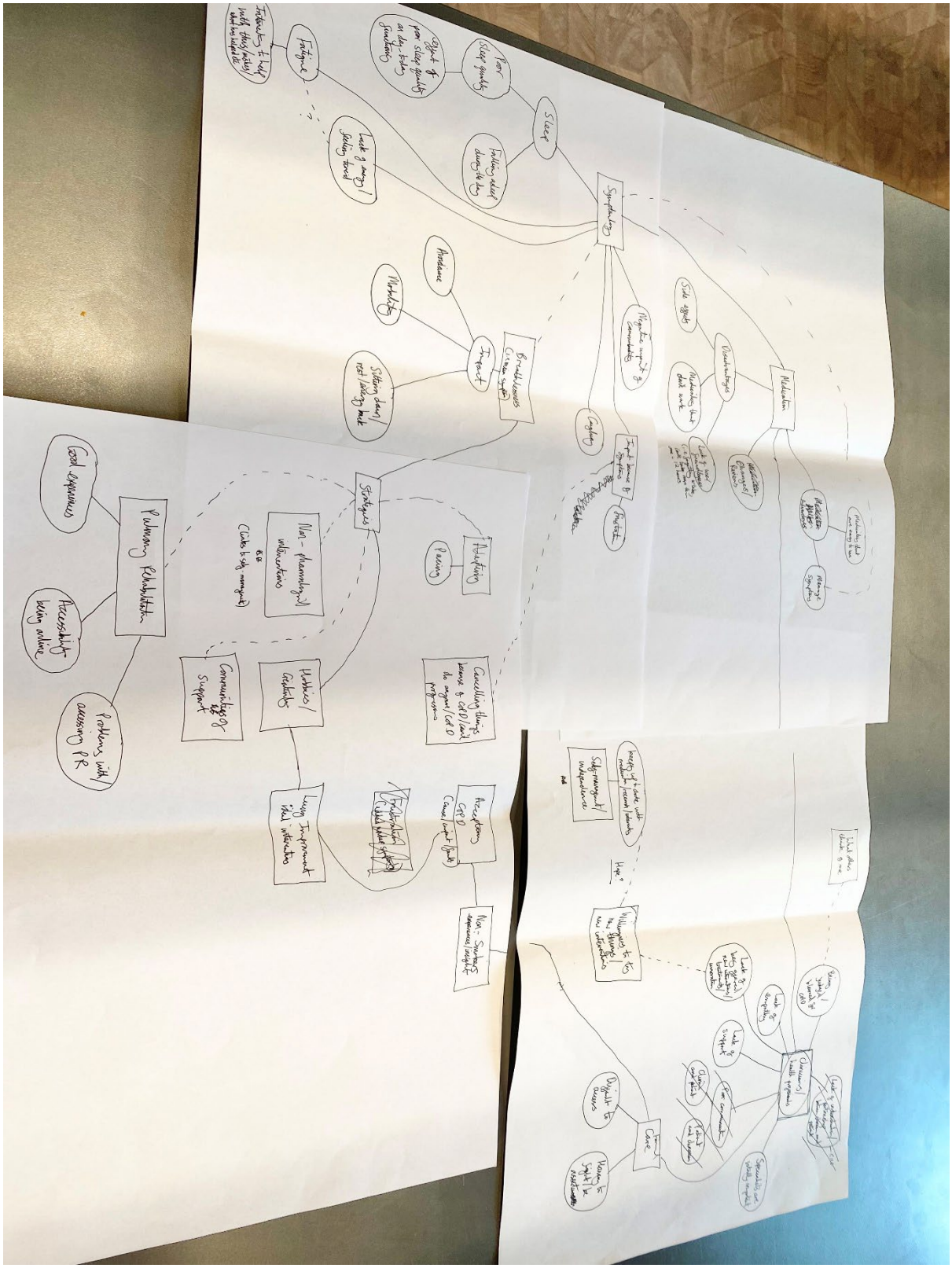
Appendix AM

First version of thematic map



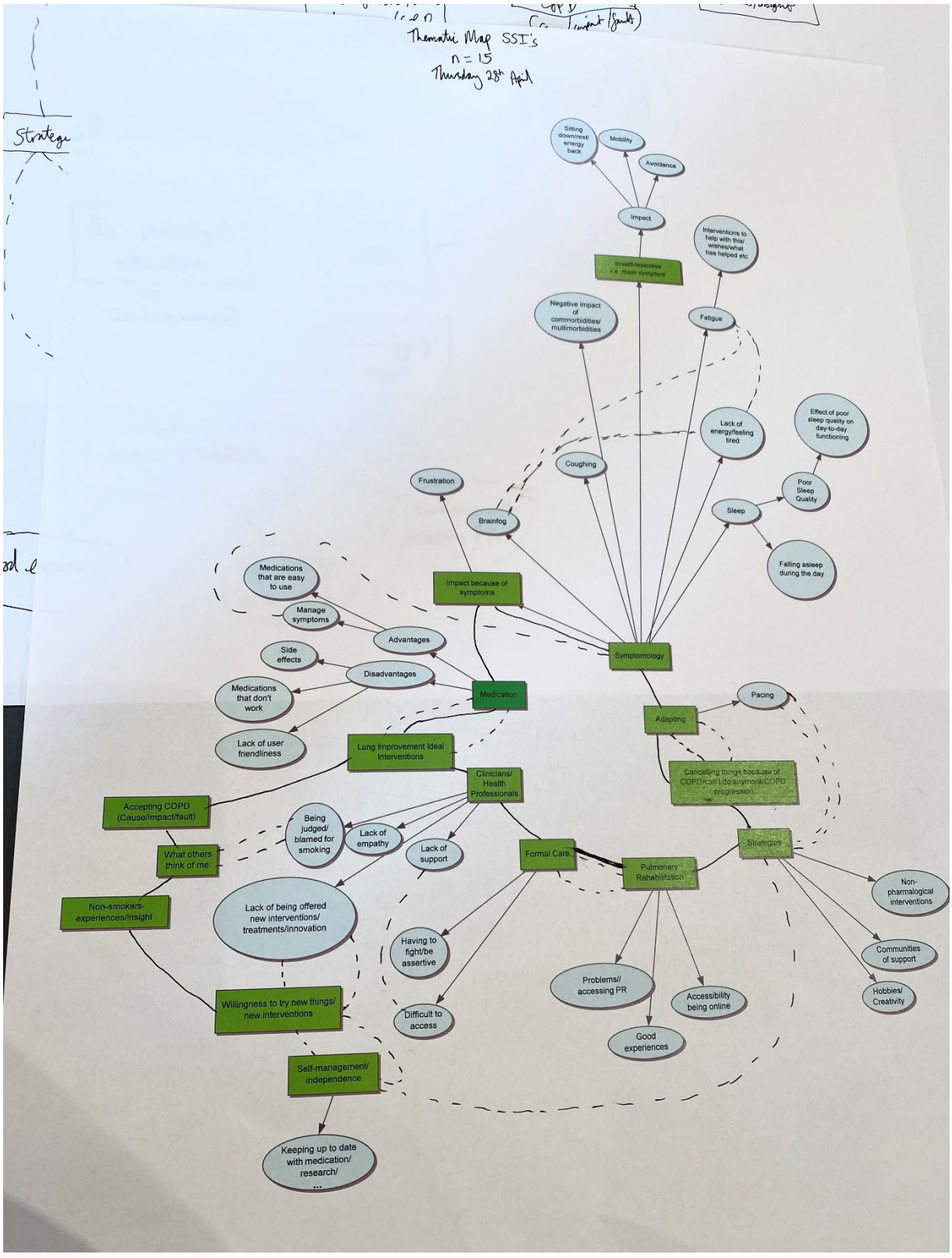
Appendix AN

Second version of the thematic map



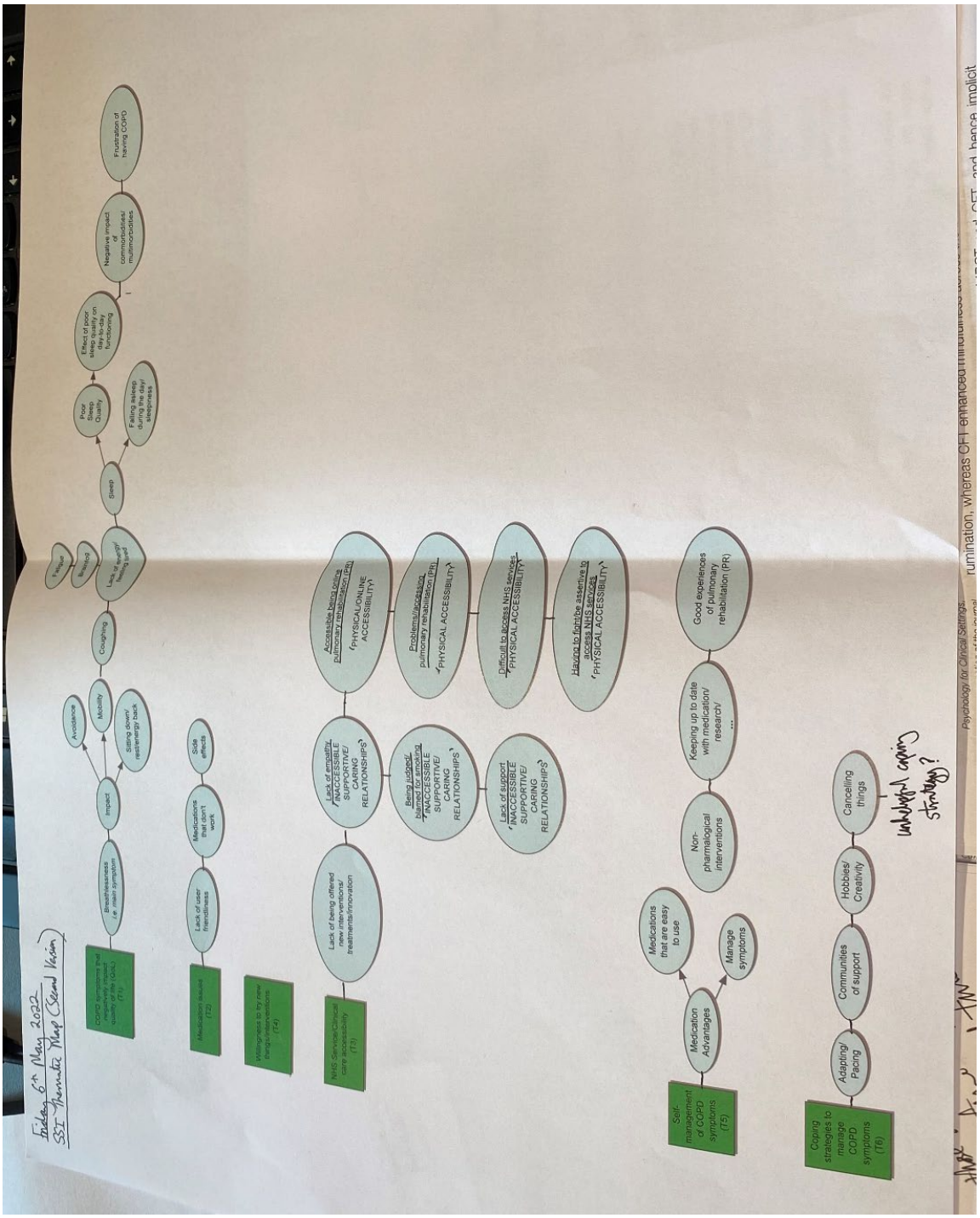
Appendix AO

Third version of the thematic map



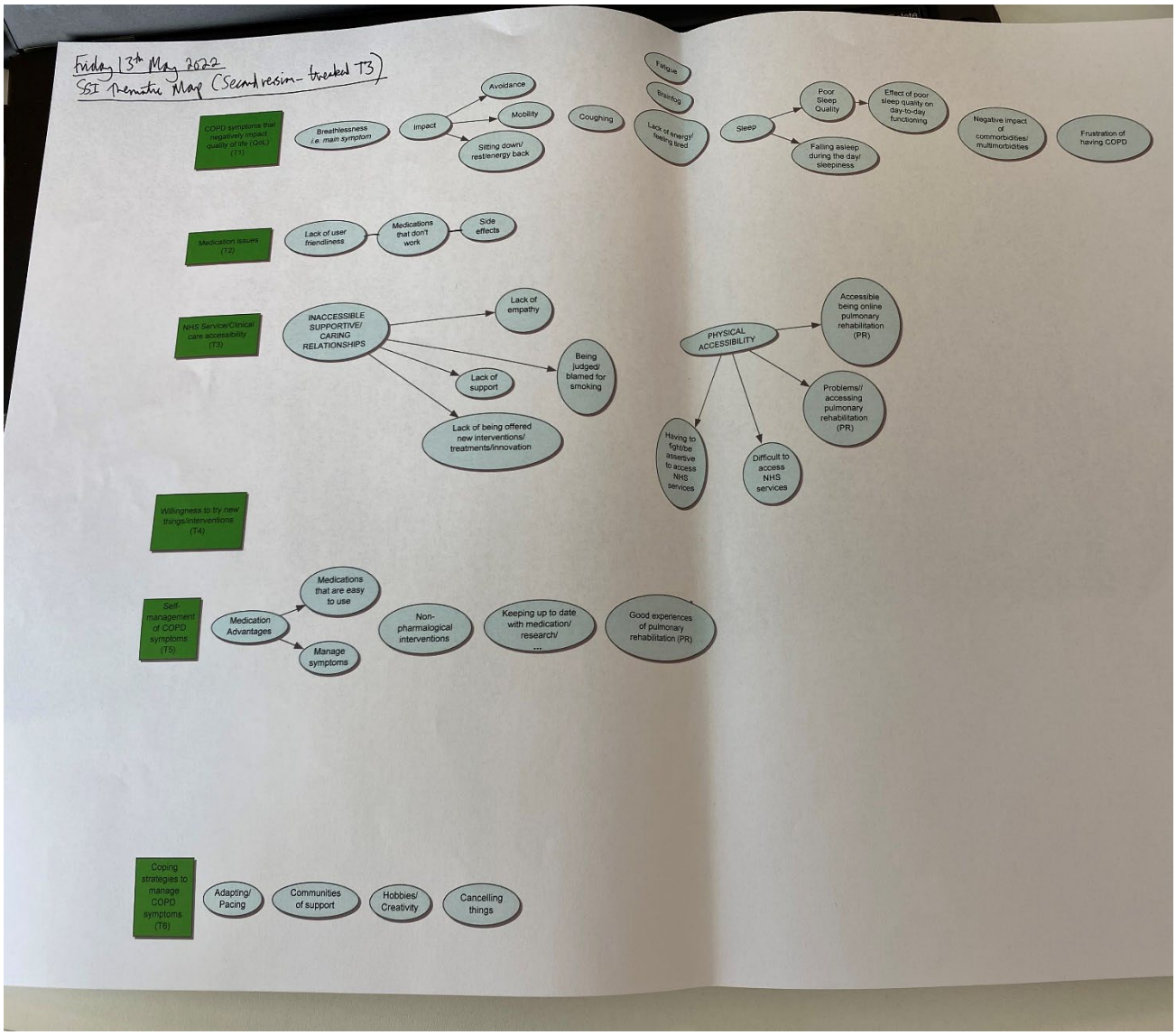
Appendix AP

Forth version of the thematic map



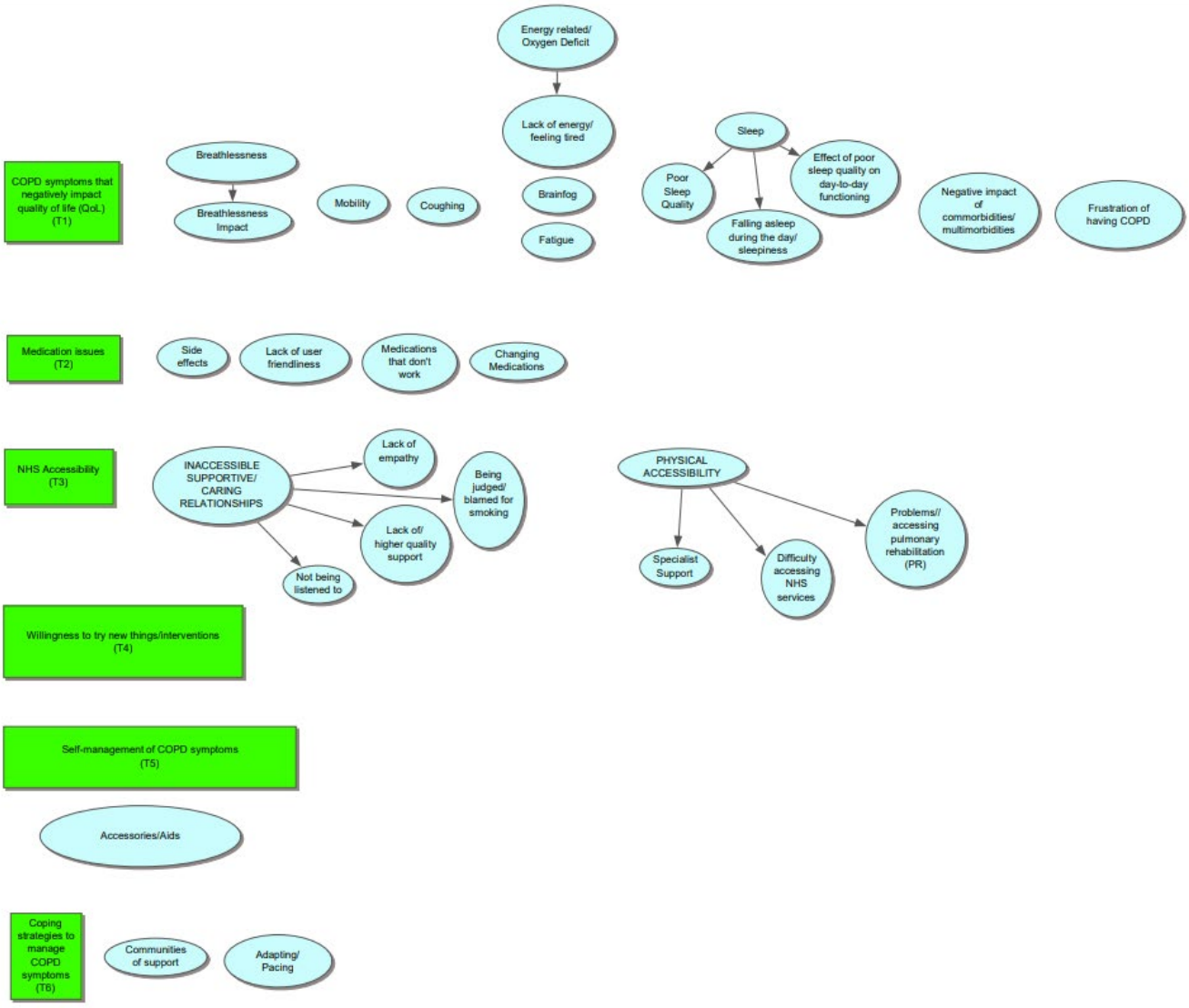
Appendix AQ

Fifth version of thematic map



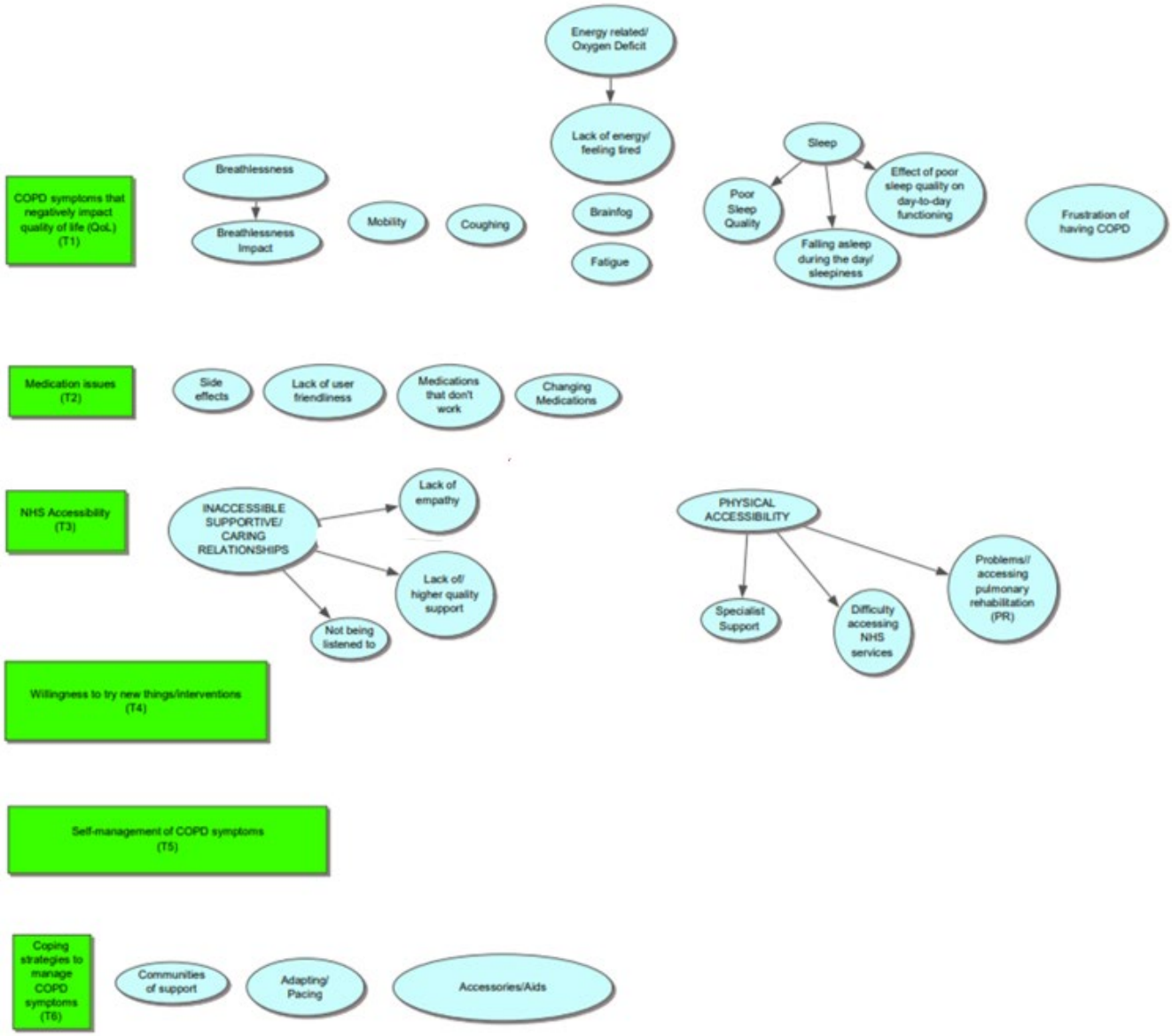
Appendix AR

Sixth version of the thematic map



Appendix AS

Seventh version of the thematic map



Appendix AT

Sleep Diary

Sleep Diary

Study Title:

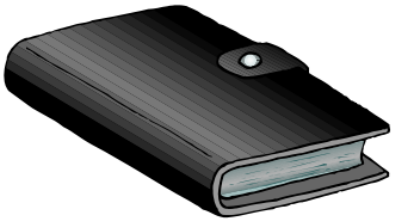
A pilot study testing the safety and efficacy of singlet oxygen energy delivered via the SoeMac device in people living with Chronic Obstructive Pulmonary Disease (COPD)

Contact Details:

Please contact the Trial Manager, on,

cheata@nuh.nhs.uk

07305597462



Participant ID:……

Nottingham University Hospital NHS Trust

UNIVERSITY of DERBY

Introduction

This diary log has been developed for you to record your progress through this research project on a daily basis.

Snapshot of what you need to do:

1) Complete Questionnaires (Start, Halfway & End)

2) You will start using the SoeMac device that we have given you. Then you should switch this on each night when you go to bed.

3) Each morning we need you to record the time that you went to bed and the time that you got up in the morning. We would like you to think about how well you slept

4) We will phone you every two weeks to see how you are getting on with the device.

At the halfway stage we will ask you some specific questions about your symptoms (we will provide you with the questionnaires to complete.)

Study Contacts

If you have any questions relating to the study, need support on how to use the device or you think your device may be faulty then please do not hesitate to contact members of the research team using the details provided:

Trial Manager — 07305597462

(Monday to Friday: 9 am to 5 pm)

If you call outside of these hours please leave a voicemail and we will call you as soon as possible

Using the SoeMac Device

The SoeMac is a wellness product (Pre-CE registered device with the Medicines and Healthcare Regulatory Agency, MHRA) that uses a patent protected technology to produce and deliver singlet oxygen energy (SOE) to the body.

1) Within 7 Days after you have received the SoeMac device, you will be telephoned with instructions and this will be the first evening of you using the device. We would like you to position the SoeMac device next to your bed and switch it on each night when you go to bed until the end of the trial. You will do this for 84 days in total, from the evening you switch the device on.

2) The device is does have a red light on the front which you can use to make sure it is switched on and a very small fan which makes a small noise.

3) We ask that you place the device on your bedside table and in a position that will not interrupt your sleep.

4) When you wake up each morning make sure you fill in the table in this diary so that we know how much sleep you had and how well you slept.

Study Timeline

	1) You have seen the advert regarding the study or heard about it **Telephone Call 1:** 2) You call the trial manager and express an interest in the study and you are sent the participant information sheet. You can ask any questions you may have about the trial If you are interested in taking part in the trial, you provide contact information for the trial manager to get in touch regarding screening for eligibility. **Session Duration – 10-15 Minutes** **Telephone Call 2:** 3) Screening is conducted upon you providing consent to do so. Screening will include questions regarding your COPD and health. If you are eligible, a verbal consent script will be read out to you over the telephone, for you to provide full consent to take part in the study should you wish. A consent form will be sent to if you wish via post or email. **Session Duration – 10-15 Minutes**
	Your GP will be asked to confirm the eligibility details you provided during screening and after receiving these details, all information you have provided regarding your COPD and health will be reviewed by the Chief Investigator.

	If authorized by Dr Milind Sovani and you are eligible You will be sent a letter or email confirming that you have been enrolled on to the study and will be sent a SoeMac device, questionnaires and details of the next steps. On the other hand, if you are ineligible you will be sent a letter or email and unfortunately you will not be enrolled on to the study at this time. You will be posted Study Pack 1= x6 Questionnaires & Partial Sleep Diary
Baseline	**Telephone Call 3** (Within 7 days after Posting Study Pack 1) **To go through x6 Questionnaires** **Session duration: 60 minutes – 90 minutes**
Start	**SoeMac Device** Randomly allocated to either active or placebo SoeMac device You will be posted: **Study Pack 2=** Full Sleep Diary + SoeMac + Freepost Envelope

Day 0/ Week 1	**Telephone Call** (Within 7 days from posting SoeMac device to you) Instruct you how to use the device and complete the sleep diary **Session Duration: 15 minutes** Start using the SoeMac device every night (This counts as Day 0 and you will use the device until Day 84)
Week 2 (Day 14)	We will phone you to see how you are getting on with the device **Session Duration: 15 minutes**
Week 3	Use the Device as normal
Week 4 (Day 28)	We will phone you to see how you are getting on with the device **Session Duration: 15 minutes**
Week 5	Use the Device as normal
Week 6 (Day 42) ***Half-Way****	We will phone you to see how you are getting on and ask for some information about your symptoms **Session Duration: 15 minutes** Questionnaires (x6) to complete **Session Duration: 15 – 30 minutes**
Week 7	Use the Device as normal

Week 8 (Day 56)	We will phone you to see how you are getting on with the device **Session Duration: 15 minutes**
Week 9	Use the Device as normal
Week 10 (Day 70)	We will phone you to see how you are getting on with the device **Session Duration: 15 minutes**
Week 11	Use the Device as normal
Week 12 (Day 84) *End of Study*	**Finish using the device** (Day 84) From Day 0 when you first switched on your SoeMac to Day 84 We will telephone you Questionnaires (x6) We will ask you about your health and how you have got on with the device You post the sleep diary back to the trial manager, when you have finished the trial. When the trial has formally finished, all devices will be unblinded. You will be able to keep the SoeMac device for personal use, by using a special discount code direct to the manufacturer of the SoeMac device (free of charge).

Week 1: Daily Diary

Please record the following data on a daily basis:

Week Beginning: Date: _ _ / _ _ / 202 _

	Time to you went to bed (e.g. 22:00)	Time you got up (e.g. 08:30)	Sleep Quality (see rating below)	Did you use the device last night? (Y=Yes/N=No)
Day 0				
Day 1				
Day 2				
Day 3				
Day 4				
Day 5				
Day 6				

Rating your sleep quality (1-5):
1- Poor, 2 - Fair, 3 - Average, 4 - Good, 5 - Excellent

Remember to switch on your SoeMac Device each evening when you go to bed.

Date: …/…/…..
Time: …:...

Date from: …/…/….. Date to: …/…/…..

Week 14: Daily Diary *(TO BE USED IF NEEDED)*

Please record the following data on a daily basis:

Week Beginning: Date: _ _ / _ _ / 20 _ _

	Time to you went to bed (e.g. 22:00)	Time you got up (e.g. 08:30)	Sleep Quality (see rating below)	Did you use the device last night? (Y=Yes/N=No)
Day 92				
Day 93				
Day 94				
Day 95				
Day 96				
Day 97				
Day 98				

Rating your sleep quality (1-5):
1- Poor, 2 - Fair, 3 - Average, 4 - Good, 5 - Excellent

Notes:

Please use this space to record any notes that you may have

e,g. perhaps the ease of using the device, perceived benefits you have experience or improvements that you feel could be made to the trial or the device.

This is entirely voluntary & optional.

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Appendix AS

Participant information sheet

Nottingham University Hospitals NHS
NHS Trust

A multi-centre pilot study to test the safety and efficacy of singlet oxygen energy delivered via the SoeMac device in people living with Chronic Obstructive Pulmonary Disorder (COPD)

IRAS Reference: 280361

Participant Information Sheet: Version 2.0, Dated 18-Jan-2022

Chief & Principal Investigator: Dr Milind Sovani

Contact details

Chief/Principal Investigator

Name: Dr Milind Sovani

Contact: Milind.Sovani@nuh.nhs.uk or 0115 924 9924

Trial Manager/Study Nurse

Name: Elaine Blackshaw

Contact: XXXXXXXXXXXXX@nuh.nhs.uk or 07305 597 462

1. What is the purpose of the pilot study?

The SoeMac is a (pre-CE marked) wellness product i.e. it is not a medical device and is not registered as such with the MHRA (Medicines and Healthcare Regulatory Agency) at this moment in time. It uses a patent-protected technology to produce and deliver an energised form of oxygen, called singlet oxygen energy (SOE) that is breathed in while you sleep. This higher energy oxygen vibrates a little more than usual but is temporary i.e. lasts only a very short time (nanoseconds). This temporary energised oxygen is easier for the body to use. The device is positioned next to the bed whilst you sleep, you do not need to use face masks etc such as you would when using CPAP / nebulisers etc.

The SoeMac has not been formally tested within a clinical trial setting. Therefore, we would like to investigate the effectiveness of this device by carrying out a clinical trial in COPD patients to see if this will help improve the quality of life and to see if there are any side effects. Previous small-scale research has been conducted. However, the research so far has been community based, and not scientifically designed or validated.

This study will be a multi-centre double-blind randomised controlled trial to test the safety and effectiveness of the SoeMac device.

A randomised trial is when we make comparisons between different treatments, so in this instance, we will have a SoeMac device which is active (i.e. full working capacity) and a SoeMac device which is a placebo (i.e. a dummy / doesn't make energised oxygen).

You will be assigned randomly to either an active or placebo group. The results of both groups will then be compared to see if the active SoeMac device is more effective than the placebo device.

The study is double-blind, which means that you and the researchers will not know whether you will have received an active or a placebo device. This ensures that results are not influenced by knowing which device is being used.

The randomisation schedule and blinding will be carried out by an independent source at The University of Derby, Sport Outdoor and Exercise Science Technical Team. Each SoeMac device will be numbered, and the serial number of each device will be registered with us so at the end of the study we can see what device each you had and analyse the results.

If you are willing to participate in this research, you will speak with the practice nurse and sign a consent form allowing them to access your medical records for research purposes. Your practice nurse will then access your medical records and provide details of your medical history to us on a form we provide. They will also complete a questionnaire (CAT) with you which assesses your degree of COPD.

If you are eligible to take part, then your practice nurse will pass your contact details to the trial manager of the study to contact you by phone.

The trial manager will then phone you and ask you more questions regarding your health and hospital admissions and then you will be sent a parcel containing three questionnaire packs and a SoeMac device. You will position the SoeMac device next to your bed and switch this on when you go to bed each night until we tell you to send it back to us, approx. 8 weeks.

Completed questionnaires give us information about your COPD symptoms, sleep quality and mental health and allow us to assess whether your symptoms are improving or not and so it is important to complete them fully and not leave questions unanswered.

When you have received the SoeMac device you will need to complete the questionnaires in pack 1 and post these back to the trial manager in the stamped addressed envelope that we provide. Please take your time completing these, and make sure you have answered all of the questions clearly using a bold pen so that there is no confusion regarding your answers. If you are unsure about any questions you can ring the trial manager for clarity.

Once the questionnaires have been sent back to the trial manager you can switch on the SoeMac device and you must use it every evening until the end of the study (approx. 8 weeks).

You will repeat the questionnaires you did at the start of the study after 4 weeks (pack 2) and again after 8 weeks (pack 3) of using the device. At each time point we will contact you to ask how you have

been getting on and remind you to do this. Additionally, we will telephone you every two weeks to ask how you are getting on with the device and carry out a health check. At the end of the study, you will have option to have a SoeMac device delivered for personal use free of charge.

2. Who has reviewed this study?

All research in the NHS is looked at by an independent group of people called a Research Ethics Committee, to protect your safety, rights, well-being, and dignity. This study has been reviewed and given a favourable opinion by the NHS by the Research Ethics Committee (Ethics approval number 280361). The study has also been reviewed and approved by the Research & Innovation department of Nottingham University Hospitals NHS Trust. The trial will be monitored by a research trial monitor (NUH NHS Trust, R&I Department) who will continue to review the progress of the study and check study documents for accuracy.

The research has been joint funded by MediLink - Med Tech Trials Innovation Support Grant (MTT-ISG) and the University of Derby Human Science Research Centre – Research Excellence Funding and is being carried out by Nottingham University Hospitals NHS Trust who will act as the sponsor for the research. SoeHealth Ltd (manufacturer of SoeMac) has not funded the study. However, SoeHealth Ltd have provided the SoeMac devices free to the researchers, who are conducting the study.

3. Why have I been sent this Participant Information Sheet?

This participant information sheet has been posted to you from your GP practice, taking part in this research, and because you are due to have a health review with your practice nurse. If you are interested in taking part then please tell your practice nurse at this review and she will check if you are eligible. However there is no obligation to take part and you can decline this without it having any effect on the healthcare your GP practice provides. To take part in the study the main criteria is the following:

- You must be at least 40 years old.
- You must have been a current or previous smoker – your nurse will discuss this with you.
- You must have a diagnosis of COPD from your GP/Doctor, your nurse will check this is documented in your medical records.
- You must be able to understand English sufficiently to read the documents, complete the questionnaires and speak to the trial manager on the telephone.

There are other criteria which the nurse will assess from your medical records once you have given consent to do this for the purposes of this research.

When you have signed the consent form the nurse will review your medical history with you and access your medical notes to ensure accuracy. We will need to know your most recent lung function measurements (FEV1/FEC). You will also be asked questions regarding your smoking history and past healthcare appointments. Your nurse will also complete a Questionnaire (CAT) with you with questions about your COPD. This questionnaire has been devised and approved for use in assessing COPD and you may have completed it in the past.

You do not have to take part in the study, your participation is completely voluntary and it is up to you to decide whether or not to take part.

If you are eligible and willing to take part your data will be anonymised and stored securely, you have the right to withdraw at any time and you will be giving permission for the medical history your nurse has documented, the CAT questionnaire and your contact details to be sent to the trial manager who will contact you by telephone to ask a few further questions, and send you the SoeMac device and questionnaire packs. You will be able to have a copy of the consent form for personal use and the practice nurse will also keep copies of the consent form. If you decide to take part, you are free to leave the study at any time and without giving a reason.

4. What do I have to do?

If you decide to take part after you have given consent, and if you meet the criteria to take part in the study, you will be given a study anonymised ID number. Your contact details will then be forwarded to the trial manager who will get in contact with you and explain the next stages. You will receive a study parcel that contains the SOEMAC device and three questionnaire packs labelled 1 -3 and stamped addressed envelopes. The questionnaire packs contain four questionnaires to be completed at the start i.e. before you use the machine, and 4 and eight weeks after the start. You will complete these when instructed by the trial manager at each telephone consultation, Telephone appointments are flexible and we aim to fit in with your daily schedules. There are additional telephone calls to ask how you are, these are at 2 and 6 weeks after you start using the device. If we receive questionnaires that are unclear or not fully completed, we may ring you to check your answer.

Study duration:

You will take part in the study for 8 weeks approx. We will be calling you every two weeks to ask you about your health, and also to give instructions on when to fill out the questionnaires you will have received in the parcel we posted to you. There is some flexibility on the timing of the telephone calls so there is no need to worry if you are not immediately available and you do not have to worry about remembering when the questionnaires need to be completed.

The Study Involves:

1. Completion of the consent form by your practice nurse and an assessment of your health/ smoking history etc to check you are the type of patient we need for this research study.

2. A telephone consultation with the trial manager where we will ask you a few further questions for our study records. We will then send out the SoeMac device and questionnaire packs with stamped addressed envelopes.

3. Completion of questionnaires in pack 1 and post back to us

4. Place the device by your bed and switch on every night until the end of the study at 8 weeks – but not until you have completed the questionnaires in pack 1.

5. Phone call two weeks after using the device to ask about your health and how you have been

6. Phone call four weeks after using the device to ask about your health, how you have been and to ask you to complete the questionnaires in pack 2 and post back to us in the stamped addressed envelope.

7. Phone call 6 weeks after using the device to ask about your health and how you have been.

8. Phone call eight weeks after using the device to ask about your health, how you have been and to ask you to complete the questionnaires in pack 3 and post back to us in the stamped addressed envelope. This is the end of the study and we will ask you to post the SoeMac device back to us – the postage will be paid by us.

You have the option to request a free SoeMac for your own use after the study has finished. We will give you a special discount code that can be used with the manufacturer (by phone or internet order), and a device will be posted to you free of charge.

5. What is the device that is being tested?

The device being tested as part of this study is called a SoeMac, which is currently marketed as a complementary wellness therapy. The SoeMac device does not yet have a CE mark, and this cannot be obtained until clinical studies have provided the necessary proof of effectiveness and safety.

An ethics committee and the MHRA have given us approval to carry out this study.

You will be provided with either an active (i.e. full working capacity) or placebo device (i.e. a dummy) and you and the research team will not know which device you have received.

The SoeMac is plugged into a power socket and will need to be positioned by your bed on a bedside table. It needs to be switched on throughout the night until you wake up in the morning. As you can see from the pictures below, the device contains a small red light - LED which is visible when the device is turned on so you will need to position the device near your bed and in a position where this light will not disrupt your sleep. There are currently no alternative treatments on the market which patients can buy using this technology.

The SoeMac device has been purchased over the counter i.e. without medical prescription / authorization as a well-being device by over 6000 purchasers. There have been no reports of any serious side effects or health problems using this device. The safety and effectiveness data of the SoeMac device at this moment in time has been collected from small scale studies, which have not been carried out as rigorously as the randomized controlled trial we are conducting.

The laboratory data demonstrates that the device produces singlet oxygen energy, and that there are no toxic or additional molecules produced by the device. This data supports the safety requirements of the device. Additionally, the electrical components used in the construction of the device are not new and are routinely used in device manufacture. The device has passed the current British standards for electrical safety.

6. What are the possible benefits?

You may find that there are benefits from taking part in the study, although we cannot promise that, and it is possible you may not benefit from using it at all. The manufacturer has conducted a post-market analysis where 249 voluntary testimonials have been received and summarized. These testimonials suggest that using the SoeMac device might have various health benefits such as improved sleep quality, energy and activity levels, as well as decreasing breathlessness. However, the SoeMac device has to date, not been tested using a high quality, manufacturer independent, scientific study and this is what we are doing. Your participation in this study is completely voluntary and once your

participation has ended you will be given the opportunity to own a SoeMac device for personal use, free of charge, and as a thank you for completing the trial.

7. What are the disadvantages?

a) What are the side effects of any treatment received while taking part?

If you decide to take part in the study, you must report any new, or changes to existing problems you have, to the research team. We have provided you with a contact number at the top of this information sheet for you to phone if at any time you become worried, and we will be ringing you every two weeks.

Should you experience any problems or have any questions relating to the research then we encourage you to contact the research team on the details provided above. If you have issues relating to your COPD, then please seek advice from your GP or practice nurse.

The use of the SoeMac device has not been tested in a clinical trial previously except for some small-scale studies conducted by the company who produce the device.

There have been no reports of patients having serious side effects from using the device.

However, some minor side effects have been reported and these are:

- Mild headaches during first few days of use
- Clearance of excess mucus from the lungs
- Aching in the joints
- Excess and smelly wind
- A few people have returned the device as the red light and whirring noise has interfered with their sleep.

Please note that these symptoms may or may not be caused by the device, and you may not experience them. The symptoms are entirely normal and should not cause you to worry. When we telephone you every 2 weeks to carry out a health check, we will ask you if you have noticed anything different when using this device.

b) What are possible disadvantages/risks of taking part?

There are no known identified risks of taking part in this research. However, as the device is powered by electricity, we ask that you provide ample space around the device whilst this is

working. Try to avoid placing liquid items such as drinks next to the device to prevent spillage on the device.

Should you experience any problems or have any questions relating to the research then we encourage you to contact the research team on the details provided at the start of the document. If you experience any COPD or health concerns, you should contact your doctor for advice. Please also report these health concerns to the trial team.

We appreciate that there are multiple phone calls and questionnaires as part of this study, so there is a time burden if you do decide to take part, however we aim to fit in with your free time and convenience.

8. Informing your General Practitioner (GP)

Your GP practice is part of this research study and will be aware you are taking part in this research study because they have been involved in recruiting you into it

9. What will happen to my data?

a) Will taking part in this study be kept confidential?

If you consent to take part in this study, the records obtained while you are in this study as well as related health records will always remain strictly confidential. The information will be held securely on paper and electronically at the Nottingham University Hospitals NHS Trust under the provisions of the Data Protection Act 2018. Your name will not be passed to anyone else outside of the research team or the sponsor, who is not involved in the trial.

Your full name will only appear on your consent form. However, all other trial documents will not identify you by name, only by a unique anonymised ID, we will not be using hospital numbers. As required when carrying out trials we have a participant enrolment log that will contain your personal details and will link to the participant ID and is how we know how to contact you. This document will be kept securely.

Your study records will be available to people authorised to work on the trial but may also need to be made available to people authorised by the Research Sponsor, which is the organisation responsible for ensuring that the study is carried out correctly. A copy of your consent form may be sent to the Research Sponsor during the study. By signing the consent form, you agree to this access for the current study and any further research that may be conducted, even if you withdraw from the current study.

The information collected about you may also be shown to authorised people from the UK Regulatory Authority (e.g., MHRA) and Independent Ethics Committee; this is to ensure that the

study is carried out to the highest possible scientific standards. All will have a duty of confidentiality to you as a research participant.

If you withdraw consent from further study treatment, unless you object, your data will remain on file and will be included in the final study analysis.

In line with Good Clinical Practice guidelines, at the end of the study, your data will be securely archived for a minimum of 25 years. Arrangements for confidential destruction will then be made.

b) Use of your personal data in research

The sponsor for this study is Nottingham University Hospitals NHS Trust, based in the United Kingdom. All information that you provide, will be kept confidential and will be kept safe and secure, under the provisions of the General Data Protection Regulation (GDPR) and Data Protection Act 2018. Nottingham University Hospitals NHS Trust will act as a data controller, which means that they are responsible for looking after your information and using it properly. They will keep identifiable information for 25 years after the study has finished.

Following the consent procedure we will need to use information from you for this research project. This information will include your initials, name, address, telephone number and/or email address, and you will have consented for this. Study personnel will use this information to carry out the research and ensure the research is being done properly, for example, to contact you and for us to send you a SoeMac device. People who do not need to know who you are, will not be able to see your name or contact details. Your data will have a code number instead.

Once the study has been completed all anonymised data will be used for analysis by researchers at the University of Derby. Upon completion of the analysis, all raw data will be disposed of according to appropriate governing bodies. The anonymised results of the evaluation will be shared with the project funders and the company who developed the device.

If deemed appropriate, the findings may also be published in peer-reviewed academic or scientific journals. In this instance, all your data will be completely anonymous and will not contain any identifiable information. We need to manage the information you provide in specific ways for the research to be reliable. This means that we will not be able to let you see or change the data we hold about you. Your rights to access, change or move your information are limited, as we need to manage your information in specific ways for the research to be reliable and accurate. To safeguard your rights, we will use the minimum personally identifiable information possible. You can find out more about how we use your information at the following link (https://www.nuh.nhs.uk/gdpr) or by contacting the Information Commissioners Office 0303 123 1113.

You can stop being part of the study by opting out at any time, without giving a reason. If you withdraw consent from the study, your data will be omitted from the analysis if this withdrawal occurs within 1 month after your participation in the study has finished. If you withdraw more than 1

month after your participation has finished, your data will still be used in the analysis. This is because the data will be analysed immediately after the study ends, and it will be impossible to remove your data from this.

The information collected about you may also be shown to authorised people from the Health Research Authority (HRA) and the Medicines and Healthcare products Regulatory Agency (MHRA) and the independent Ethics Committee to ensure that the study is carried out to the highest possible scientific standards. All will have a duty of confidentiality to you as a research participant.

You can find out more about how we use your information:

- at www.hra.nhs.uk/information-about-patients/
- our GDPR leaflet available on request from researchsponsor@nuh.nhs.uk; or by the following link www.nuh.nhs.uk/gdpr
- by asking one of the research team
- by emailing the Data Protection Officer for NUH at dpo@nuh.nhs.uk,
- by ringing the Data Protection Officer for NUH on 0115 924 9924 (extension 63975) by visiting www.nuh.nhs.uk/gdpr

10. What happens if new information becomes available?

Sometimes during a clinical research trial, new information becomes available on the devices that are being studied. If this happens, we will tell you about it and discuss with you whether you want to or should continue in the study. If you decide to continue in the study, you will be asked to sign an updated verbal consent form. On receiving new information, we might consider it to be in your best interests to withdraw you from the study, and the researchers will discuss this with you and inform you what happens next.

11. What will happen if I do not want to carry on with the study?

To withdraw from the study please just contact any of the research team. You can withdraw at any time, for any reason without having to explain your reasons for withdrawing. You can withdraw from participation up to 1 month after your participation in the study has finished. Once this time has passed, it will not be possible to withdraw your data from the research.

12. What happens when the study is finished?

At the end of the study, you will send the SoeMac device back to the study team, using the freepost envelope provided. You will be provided a special discount code by the study team, to receive a SoeMac device for personal use free of charge. You can order this directly from the manufacturer using the internet or by phone. This is a token of thanks and appreciation for taking the time to participate in this study.

When the study has formally finished, the data from the trial will remain and be fully anonymised and will be analysed. The data will be part of a (university student) PhD thesis and may be published in journal articles. The journal articles will likely be open access i.e. researchers do not have to pay to read about the study.

13. What if there is a problem?

If you have a concern about any aspect of this study, you should ask to speak with the researchers who will do their best to answer your question. If you remain unhappy and wish to complain formally, you and wish to complain formally, you can do this through the sponsor team.

Email: researchsponsor@nuh.nhs.uk, or by phoning 0115 970 9049.

If something does go wrong and you are harmed during the research study, there are no special compensation arrangements. If you are harmed and this is due to someone's negligence, then you may have grounds for legal action for compensation, but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available to you.

14. Further Information

You are encouraged to ask any questions you wish before, during or after the study. If you have any questions about the study please speak to the practice nurse on the day of your COPD clinic appointment who will be able to provide you with up-to-date information about the study and the study procedures. You can also contact the trial manager for further information before, and / or after speaking to the practice nurse and the contact details are at the top of this document.

If you would like to take part in the study, please inform the practice nurse, who after assessing you are eligible will pass your contact details along with the completed eligibility form and CAT questionnaire to the trial manager. You will keep a signed copy of the consent form to keep for personal use and the practice nurse will keep a copy for your medical records and for the trial records.

Thank you for taking the time to read this information sheet and to consider taking part in this study.

Appendix AT

Consent form

Nottingham University Hospitals NHS
NHS Trust

Participant Consent Form

Version: 2.0 Date: 18th January 2021

A multi centre pilot study to test the safety and efficacy of singlet oxygen energy delivered via the SoeMac device in people living with Chronic Obstructive Pulmonary Disorder (COPD)

Chief Investigator: Dr Milind Sovani

Participant Study ID: ..... Initials: .....

Participant to initial each box

1. I _____ (insert name) confirm that I have read and understood the participant information sheet for the above study. ☐
2. I confirm that I have had the opportunity to consider the information, ask questions and I have received satisfactory answers. ☐
3. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason. I understand I can withdraw my data up until 1 month after participation. ☐
4. I consent to the storage including electronic, of personal information for the purposes of this study. I understand that any information that could identify me will be kept strictly confidential and that no personal information will be included in the study report or other publication. I agree to take part in the above evaluation. ☐
5. I give consent for my practice manager to send my contact details, signed consent and eligibility data to the trial manager to get in touch with me to discuss next stages of taking part in the study. Information will be sent securely using NHS electronic methods. ☐
6. I agree to take part in the above study. ☐

_____	_____	_____
Name of the participant *(Print)*	Date	Participant signature
_____	_____	_____
Name of person taking consent *(Print)*	Date	Signature

Appendix 8_Consent Form_18th January 2022_v2.0
IRAS 280361

Appendix AW

AE/SAE Section 14 of NHS Protocol

14.1 DEFINITIONS

14.1.1 Adverse Event (AE)

Any untoward medical occurrence in a clinical study where participants are administered a medicinal product, which does not necessarily have to have a causal relationship with this treatment (i.e., the SoeMac Device). An AE can, therefore, be any unfavourable and unintended sign, symptom or disease temporally linked with the use of the study medical device (SoeMac Device), whether or not considered related to the study device (SoeMac Device).

An AE includes:

- Exacerbation of pre-existing illness
- Increase in frequency or intensity of a pre-existing episodic event or condition
- Condition detected or diagnosed after study intervention (SoeMac Device) even though it may have been present before the start of the study
- Continuous persistent disease or symptoms present at baseline that worsens following the start of the study

An AE does not include:

- Medical or surgical procedure (e.g., surgery, tooth extraction) but the condition that leads to the procedure is an AE
- Pre-existing disease or conditions present or detected at the start of the study that did not worsen
- Situations where an untoward medical occurrence has occurred (e.g. hospitalisations for cosmetic elective surgery)
- Disease or disorder being studied, or sign or symptom associated with the disease or disorder unless more severe than expected for the participant's condition
- Overdose of concurrent medication without any signs or symptoms

14.1.2 Adverse Device Effect (ADE)

All untoward and unintended responses to the medical device.

The phrase "responses to a medical device" means that a causal relationship between the device under investigation and an AE is at least a reasonable possibility, i.e., the relationship cannot be ruled out.

All cases judged by either the reporting medically qualified professional or the sponsor as having a reasonable suspected causal relationship to the device qualifies as a device effect.

This also includes any event resulting from insufficiencies or inadequacies in the instruction for use or deployment of the device and includes any event that is a result of a user error.

14.1.3 Serious Adverse Event (SAE)

SAE is an adverse event that:

- Led to death.
- Led to foetal distress, foetal death or congenital abnormality or birth defect.
- Led to a serious deterioration in the health of the subject that:
    - Resulted in a life-threatening illness or injury.

    - NOTE: The term "life-threatening" in the definition of "serious" refers to an event in which the participant was at risk of death at the time of the event; it does not refer to an event that hypothetically might have caused death if it were more severe.
- Resulted in a permanent impairment of a body structure or a body function.
- Required in-patient hospitalisation or prolongation of existing hospitalisation.
- This resulted in medical or surgical intervention to prevent permanent impairment to a body structure or a body function.
- Other important medical events
    - Other events that may not result in death, are not life-threatening or do not require hospitalisation, may be considered a serious adverse event when, based upon appropriate medical judgement, the event may jeopardise the patient and may require medical or surgical intervention to prevent one of the outcomes listed above.

To ensure no confusion or misunderstanding of the difference between the terms "serious" and "severe", which are not synonymous, the following note of clarification is provided:

The term "severe" is often used to describe the intensity (severity) of a specific event (as in mild, moderate, or severe myocardial infarction); the event itself, however, may be of relatively minor medical significance (such as severe headache). This is not the same as "serious," which is based on patient/event outcome or action criteria usually associated with events that pose a threat to a participant's life or functioning. Seriousness (not severity) serves as a guide for defining regulatory reporting obligations.

14.1.4 Serious Adverse Device Effects (SADE)

A serious adverse device effect (SADE) is any untoward medical occurrence seen in a patient that can be attributed wholly or partly to the device which resulted in any of the characteristics or led to characteristics of a serious adverse event.

SADE is also any event that may have led to these consequences if suitable action had not been taken or intervention had not been made or if circumstances have been less opportune.

All cases judged by either the reporting medically qualified professional or the sponsor.

14.1.5 Unanticipated Serious Adverse Device Effect (USADE)

Any serious adverse device effect on health or safety or any life-threatening problem or death caused by, or associated with a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that related to the rights, safety or welfare of the subject.

14.2 REPORTING OF AEs

All AEs occurring during the clinical investigation observed by the investigator or reported by the participant, whether or not attributed to the device under investigation will be recorded on the CRF as specified in the clinical investigation plan. All ADEs will be recorded in the CRF.

The following information will be recorded: description, date of onset and end date, severity, assessment of relatedness to the device, other suspect drug or device and action is taken. Follow-up information should be provided as necessary.

The relationship of AEs to the device will be assessed by a medically qualified investigator or the sponsor/manufacturer and will be followed up until resolution or the event is considered stable.

All ADE that results in a participant's withdrawal from the clinical investigation or is present at the end of the clinical investigation, should be followed up until a satisfactory resolution occurs.

Where relevant, any pregnancy occurring during the clinical investigation and the outcome of the pregnancy should be recorded and followed up for congenital abnormality or birth defect.

14.3 REPORTING PROCEDURES FOR ALL SAEs/ SADEs/ USADEs

For Non-CE marked device clinical investigation: All SAE/SADE/USADEs need to be reported to the sponsor/legal representative, manufacturer and NUH R&I **immediately**; regardless of relationship to the device.

All SAEs, must be reported to R&I within one working day of discovery or notification of the event. As Sponsor, R&I at NUH will report all SUSARs /USADEs to the Competent Authorities (MHRA and the Research Ethics Committee) concerned. Fatal or life-threatening SUSARs/USADEs must be reported within 7 days and all other SUSARs/USADEs within 15 days. The CI will inform all investigators concerned with relevant information about SUSARs that could adversely affect the safety of participants.

Reporting to the MHRA will be done in liaison with the Chief Investigator and the Manufacturer.

The Manufacturer has a legal obligation to report all events that need to be reported to the Nominated Competent Authority immediately (without any unjustifiable delay) after a link is established between the event and the device, but no more than:

- 2 days following the awareness of the event for Serious Public Health Threat.
- 10 days following awareness of the event for Death or unanticipated serious deterioration in health.
- 30 days following the awareness of the event for all other event meeting the SAE criteria.

Reporting Procedures for All Adverse Events

Adverse event (AE) and Serious Adverse Event (SAE) will use NUH NHS Trust reporting procedures.

All adverse events should be recorded on the CRF. Reporting of AE/SAEs/ADs/ADEs/USADEs to the Sponsor should be done on the appropriate Sponsor template. Any questions concerning adverse event reporting should be directed to the Chief Investigator in the first instance. Local Investigators will be contacting all participants in both the experimental and control group every 2 weeks from Day 0 (after baseline) (i.e. Day 14, Day 28, Day 42, Day 56) and the adverse events will verbally be asked on the last week of the trial on Day 56. This is to check if any participant has experienced an AE or SAE. All participants will be provided with contact details for a trial phone, where they can communicate AE/SAE throughout the study and will be operated during working hours (Monday to Friday 9-5). Outside of these working hours, participants are encouraged to leave a voicemail and the study team will contact them back as soon as possible during working hours.

The following information will be recorded: description, date of onset and end date, severity, assessment of relatedness to using the SoeMac Device and action is taken. Follow-up information should be provided as necessary. AEs considered related to the study device (SoeMac Device) as judged by a medically qualified investigator or the sponsor will be followed until resolution or the event is considered stable. All related AEs that result in a participant's withdrawal from the study or are present at the end of the study, should be followed up until a satisfactory resolution occurs. It will be the responsibility of the Chief Investigator's clinical judgement whether an AE is of sufficient severity to require the participant's to refrain from using the SoeMac Device and the participant's involvement in the study will be terminated. The relationship of AEs to the study device (SoeMac Device) will be assessed by a medically qualified investigator. All such events, whether expected or not will be recorded

An SAE form should be completed and forwarded to the sponsor or delegated representative within 24 hours. The chief investigator Dr Sovani Milind will review and sign all SAE reports. However, relapse and death due to COPD and hospitalisations for elective treatment of a pre-existing condition do not need reporting as SAEs. All SAEs should be reported to the study sponsor and the Research Ethics Committee where in the opinion of the Chief Investigator, the event was:

- 'Related', i.e., resulted from the administration of any of the research procedures; and
- 'Unexpected', i.e. an event that is not listed in the protocol as an expected occurrence

SAE reports must be sent to R&I using one of the following methods:

i. Email: RDSAE@nuh.nhs.uk

ii. Hand Delivered (Not Mailed): R&I, NHSP, C Floor, South Block, QMC

iii. Telephone: Landline: 0115 9709049 (If written report not immediately possible) or for mobile because of remote working – Ms Elaine Blackshaw Trial Manager - 07305 597 462 (who can then escalate to R&I)

The governance and quality team will facilitate an independent assessment of the event within 1 working day of receiving the SAE report.

The intensity of the AE will initially be assessed according to the following definitions:

Mild: An event easily tolerated by the participant, causing minimal discomfort and not interfering with everyday activities

Moderate: An event sufficiently discomforting to interfere with everyday activities

Severe: An event that prevents everyday activities

All AE and SAE Reporting documentation (i.e. NHS National Patient Safety Agency, National Research Ethics Service, Report of Adverse Event (AE) and Serious Adverse Event) physical copies of these will be kept in the Trial Master File.

14.4 ANNUAL REPORTS

The CI shall submit yearly throughout the clinical investigation or on request a Safety Report to R&I, the Competent Authority MHRA and Ethics Committee.

Appendix AX
SoeMac Full Trial

Clinical Investigation Title:

A pilot study to test the safety and efficacy of singlet oxygen energy delivered via the SoeMac device in people living with Chronic Obstructive Pulmonary Disease (COPD).

Clinical Investigation Acronym: SAESOE

Trial Design: Double Blind Randomised Control Trial (RCT) of a medical device.

Short aim:
Evaluating the safety of using a SoeMac device at night, and its effects on self-reported Chronic Obstructive Pulmonary Disease (COPD) symptomology, sleep quality and psychological well-being in people living with COPD.

Version: 2.0 (11-Jan-2022)

Research Reference Numbers

Sponsor	Nottingham University Hospitals NHS Trust
Funder	MediLink: Med Tech Trials Innovation Support Grant (MTT-ISG). Funding (50%) Financial Support Given - £33,197.76 University of Derby: Human Science Research Centre – Research Excellence Investment Funding (50%). Financial Support Given - £28,366.45
Funding Reference Number	MediLink: MTT-ISG-INS-126 University of Derby: DER1100052647
Chief Investigator	Dr Milind Sovani
CT.gov reference	Insert ISRCTN number.
REC Reference Number	Insert REC reference number.
Sponsor Reference Number	19RM035
IRAS Number	280361
Version Number and Date	Version 2.0 11th January 2022

Confidentiality Statement
This document contains confidential information that must not be disclosed to anyone other than the Sponsor, the Investigator Team, host NHS Trust (s), regulatory authorities, and members of the Research Ethics Committee.

CLINICAL INVESTIGATION PLAN AUTHORISATION

Chief & Principal Investigator

Name: Dr Milind Sovani

Title: Assistant Professor (Hon) Consultant Respiratory Physician and Sleep Medicine Specialist

Signature:

Date:

Sponsor

Name: Maria Koufali

Title: Managing Director of Research and Innovation

Signature:

Date:

TABLE OF CONTENTS

CLINICAL INVESTIGATION MANAGEMENT GROUP

Chief Investigator (CI) Name: Dr Milind Sovani Address: Nottingham University Hospitals NHS Trust (NUH) Queen Medical Centre (QMC) Derby Road Nottingham NG7 2UH Telephone: 01159 249924 (ext. 62185) Email: Milind.Sovani@nuh.nhs.uk	Co-Investigator Name: Professor Mark Faghy Address: Human Science Research Centre (HSRC) University of Derby (UoD) Kedleston Road Derby DE22 1GB Telephone: 01332 592109 Email: M.Faghy@derby.ac.uk
Trial Manager & Trial Coordinator Name: Ms Elaine Blackshaw Address: Medical Physics, NUH, QMC, Derby Road, Nottingham, NG7 2UH Telephone: 07305597462 & 01159 709283 (ext. 82934) NUH Email: Elaine.blackshaw@nuh.nhs.uk University of Nottingham (UoN) Email: Elaine.Blackshaw@nottingham .ac.uk N.B. Ms Blackshaw has a paid contract with NUH, as well as an honorary contract with UoN.	Academic Supervisor Name: Dr Amy Baraniak Address: College of Health, Psychology and Social Care (CHPSC), UoD, Kedleston Road Derby, DE22 1GB Telephone: TBC Email: a.baraniak@derby.ac.uk
Trial Researcher Name: Mr Samuel Grimwood Address: HSRC, UoD, Kedleston Road, Derby, DE22 1GB Telephone: 07557800951 Email: S.Grimwood@Derby.ac.uk	Statistician Name: Dr Emma Sharpe Address: CHPSC, UoD, Kedleston Road, Derby, DE22 1GB Telephone: TBC Email: E.Sharpe@Derby.ac.uk

Independent Trial Management Committee (TMC) TO BE APPOINTED Name: TBC Address: TBC Telephone: TBC Email: TBC	

Peer Reviewers	
Name: Patient Public Involvement Representatives Address: Nottingham University Hospitals NHS Trust (NUH) Queen Medical Centre (QMC), Derby Road, Nottingham NG7 2UH Telephone: 0115 849 3318 Ext: 65318 Email: NUHvoluntary.services@nuh.nhs.uk	Name: Mrs Teresa Burgoyne Job Title: Retired Respiratory Nurse, Secretary for the British Lung Foundation Support Group Nottingham West and a Patient Representative on the Greater Nottingham CCG Patient and Public Engagement and Primary Care Quality Committees Telephone: 07809 430616 Email: Tburg69@sky.com
Key Protocol Contributors	
Name: Dr Sarah Bolton Address: Centre for Healthcare Equipment and Technology Adoption NUH, QMC, Derby Road, Nottingham, NG7 2UH Telephone: 01159 709107 Email: Sarah.Bolton@nuh.nhs.uk	Name: Mr Neil Stentiford Address: SOE Health Ltd 42D Derby Road Nottingham NG9 2TG Telephone: 07957 828891 Email: neils@soemac.com

ROLE OF STUDY SPONSOR AND FUNDER

Study Sponsor:

Nottingham University Hospitals NHS Trust is the designated sponsor and takes responsibility for fulfilling the sponsor requirements as outlined in the Research Governance Framework for Health and Social Care. The study sponsor will ensure that clear arrangements are reached, documented, and carried out, providing for proper initiation, management, monitoring, and financing of the research.

Study Funder:

The funding bodies are MediLink - Med Tech Trials Innovation Support Grant (MTT-ISG) and the University of Derby Human Science Research Centre – Research Excellence Funding. The research team will maintain full control over the design, conduct, analysis, and publication of the study.

Protocol Contributors:

The protocol was conceived, designed, and produced by the research team and will be conducted, analysed, and interpreted independently by the Research Funder and Sponsor.

ROLES AND RESPONSIBILITIES OF STUDY MANAGEMENT COMMITTEES/GROUPS & INDIVIDUALS

Protocol Contributors:

Dr Mark Faghy and Mr Samuel Grimwood (University of Derby) have written the protocol with a positive contribution from Dr Milind Sovani (Nottingham University Hospitals NHS Trust), Dr Sarah Bolton (Centre for Healthcare Equipment Technology Assessment, CHEATA and Nottingham University Hospitals NHS Trust) and Ms Elaine Blackshaw (Nottingham University Hospitals NHS Trust). These authors will be responsible for study design, delivery conduct, and dissemination of results. Dr Emma Sharpe and Mr Samuel Grimwood (University of Derby) have advised on the statistical analysis plan and will be responsible for data analysis and interpretation.

Patient and Participant Involvement (PPI):

The protocol and supporting documentation have kindly been reviewed voluntarily by members of the Nottingham University Hospitals NHS Trust respiratory Patient and Public Involvement group and Mrs Teresa Burgoyne. Mrs Burgoyne is a retired respiratory nurse and secretary for the British Lung Foundation Support Group Notts West and a patient representative on the Greater Nottingham CCG Patient and Public Engagement and Primary Care Quality Committees. Mrs Burgoyne will act as part of the trial management committee to ensure that the project maintains a patient and translatable approach and also as a point of contact for sustained engagement with patient groups in the East Midlands area.

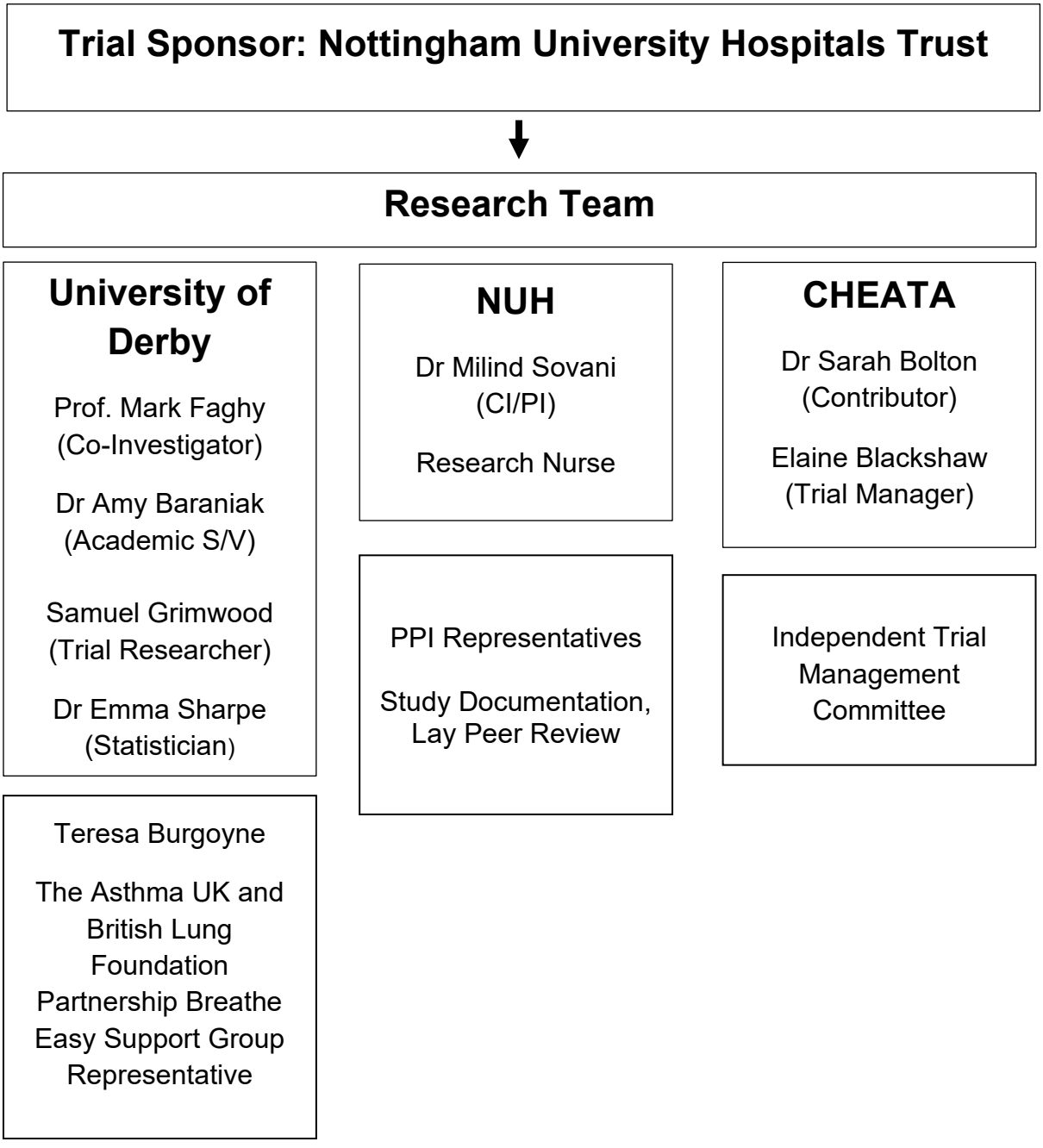


FIGURE 1 – Overview of the research study team.

Clinical investigation Coordination Centre

For general queries, supply of clinical investigation documentation, and collection of data, please contact:

Clinical investigation Coordinator: Ms Elaine Blackshaw
Address: Medical Physics, NUH, QMC, Derby Road, Nottingham, NG7 2UH

Telephone: 07305597462 01159 709283 (ext. 82934)
NUH Email: Elaine.Blackshaw@nuh.nhs.uk
UoN Email: Elaine.Blackshaw@nottingham.ac.uk

Clinical Queries

Clinical queries should be directed to Dr Milind Sovani who will direct the query to the appropriate person.

Sponsor

Nottingham University Hospitals NHS Trust is the main research sponsor for this clinical investigation. For further information regarding the sponsorship conditions, please contact the Head of Regulatory Compliance at:

Nottingham University Hospitals NHS Trust
Research & Innovation, Nottingham Health Science Partners
C Floor, South Block
Queens Medical Centre
Derby Road
Nottingham
NG7 2UH
Email: ResearchSponsor@nuh.nhs.uk

Funders

MediLink: Med Tech Trials Innovation Support Grant (MTT-ISG). Funders ref: MTT-ISG-INS-126 (50%).

University of Derby: Human Science Research Centre – Research Excellence Investment Funding (50%).

Research Funders	Financial Support Given
MediLink - Med Tech Trials Innovation Support Grant (MTT-ISG). Biocity Nottingham Pennyfoot St Nottingham NG1 1GF 0115 822 3154 info@medilinkem.com	£33,197.76
University of Derby Human Science Research Centre – Research Excellence Funding. University of Derby Human Science Research Centre - Research Excellence Funding Kedleston Road Derby DE22 1GB Professor Gyan Tripathi G.Tripathi@derby.ac.uk 01332592109	£28,366.45

This CIP describes the SAESOE clinical investigation and provides information about procedures for entering participants. Every care was taken in its drafting, but corrections or amendments may be necessary. These will be circulated to investigators in the clinical investigation. Problems relating to this clinical investigation should be referred, in the first instance, to the Chief Investigator.

This clinical investigation will adhere to the principles outlined in the NHS Research Governance Framework for Health and Social Care (2nd edition). It will be conducted in compliance with the CIP, the Data Protection Act and other regulatory requirements as appropriate.

KEYWORDS:

- COPD
- Singlet Oxygen Energy
- Symptom Profile
- Quality of Life
- Health and Medical Technologies
- Sleep Quality
- Daytime Activity
- Safety
- Activities of Daily Life
- Breathlessness

1. AMENDMENT HISTORY

Amendment No.	CIP Version No.	Date Issued	Author(s) of Changes	Details of Changes

2. CLINICAL INVESTIGATION PLAN APPROVAL

A pilot study to test the safety and efficacy of singlet oxygen energy delivered via the SoeMac device in people living with Chronic Obstructive Pulmonary Disease (COPD)

_____	_____	_____
Chief Investigator	Signature	Date
_____	_____	_____
Clinical investigation Statistician	Signature	Date
_____	_____	_____
Sponsor Representative	Signature	Date

3. ABBREVIATIONS

AE	Adverse Event
AR	Adverse Reaction
CAT	COPD Assessment Tool
CASIS	COPD and Asthma Sleep Impact Scale
CI	Chief Investigator
CIP	Clinical Investigation Plan
COPD	Chronic Obstructive Pulmonary Disease
CRA	Clinical Research Associate
CRF	Case Report Form
CRO	Clinical Research Organisation
CT	Clinical Trial
CTA	Clinical Trial Authorisation
EC	Ethics Committee (see REC)
ESS	Epworth Sleepiness Scale
GCP	Good Clinical Practise
GP	General Practitioner
IB	Investigator Brochure
ICF	Informed Consent Form
IEC	Independent Ethics Committee
IMP	Investigational Medicinal Products
IRB	Independent Review Board
ISF	Investigator Site File
MHRA	Medicinal Health Research Authority
NHS	National Health Service
NRES	National Research Ethics Service
PHQ-4	Patient Health Questionnaire-4
PI	Principle Investigator
PIS	Participant Information Sheet
R&I	Research & Innovation
REC	Research Ethics Committee
QoL	Quality of Life
SAE	Serious Adverse Event
SAESOE	Safety and Efficacy of the SoeMac in COPD
SAR	Serious Adverse Reaction
SmPC/SPC	Summary of Products Characteristics
SOP	Standard Operating Procedure
SUSAR	Suspected Unexpected Serious Adverse Reactions
TMF	Trial Master File

4. CLINICAL INVESTIGATION SUMMARY

Clinical Investigation Title	A pilot study testing the safety and efficacy of singlet oxygen energy delivered via the SoeMac device in people living with Chronic Obstructive Pulmonary Disease (COPD)
Sponsor Reference Number	19RM035
Clinical Phase	N/A
Clinical investigation Design	A double-blind prospective observational cohort study
Clinical investigation Participants	Adults (≥40 years) with COPD (≥10 CAT score)
Planned Sample Size	A minimum of 48 participants (including a 15% drop-out rate; 24 in each group) and a maximum of 100
Number of Participants	48 participants (24 in active group; 24 in placebo group)
Follow-up Duration	None
Planned Clinical investigation Period	Start date: TBC End date: TBC
Aim	Evaluate the safety of using a SoeMac device at night, and its effects on self-reported Chronic Obstructive Pulmonary Disease (COPD) symptomology, sleep quality and psychological well-being in people living with COPD.
Primary Outcome	Determine: a) The frequency and severity of reported serious adverse events and adverse events following exposure to the SoeMac device b) Self-reported changes in the CAT score
Secondary Outcome	Quantify changes in participant-reported outcomes regarding sleep quality and psychological well-being, following 56 days (8 weeks) of exposure to a SoeMac device
Primary End points	a) Self-reported safety and efficacy following exposure to using the SoeMac device b) CAT score changes
Secondary End points	Improved self-reported symptom profile relating to sleep quality and psychological well-being.
Device Name	SoeMac
Manufacturer Name	Soe Health Ltd
Principle Intended Use	The device works by the participant drawing in the air that the device produces in the air, which is a bio-usable form of

	energised oxygen that the participant simply breathes in overnight when they go to sleep until they wake up.
Length of Time the Device has been Used	The SoeMac device has been on the market for approximately 10 years as a wellbeing device

5. INTRODUCTION

Currently, Chronic Obstructive Pulmonary Disease (COPD) is the third biggest cause of death in the UK (Burney et al., 2015) and costs the NHS approximately £1.9bn each year (Hertel et al., 2012; Punekar, Shukla, & Müllerova, 2014). Currently, it affects approximately 1.2 million people, though the figure is likely to be higher due to a large number of estimated cases that are as yet undiagnosed (Quint et al., 2016). Additionally, COPD sufferers are associated with reduced exercise capacity that over time is linked to a series of important secondary outcomes that include continued and increased contact with primary care, reduced health and wellbeing and important social parameters (e.g. increased isolation). COPD exacerbations leading to hospital admission costs the NHS an average of £3,726 per episode (Hertel et al., 2012), therefore, interventions that result in increased disease management or increased capacity for exercise and improved sleep outcomes are highly desirable.

COPD is a progressive and debilitating obstructive lung disease associated with airflow limitation because of increased airway resistance and reduced lung compliance. This dysfunction may exacerbate the sensations of breathlessness (dyspnoea), reduced physical capacity/activity levels and disrupted sleep; which are all commonly reported COPD symptoms. Breathlessness results in exercise limitation, difficulty in performing activities of daily living (ADL), and a gradual reduction in quality of life (QoL) until death. In patients with COPD, compared to wakefulness, sleep is associated with a reduction in minute ventilation, resulting in a drop in the partial pressure of oxygen (PaO2) falls and a rise in pressure of carbon dioxide (PaCO2) increases (Hudgel & Hendricks, 1988; Lopes et al., 1983). This, in turn, leads to oxygen desaturation. Patients with COPD experience interrupted sleep spend less time in rapid eye movement (REM) sleep and wake up feeling tired. This sleep disturbance is related to the degree of airflow obstruction as well as COPD related symptoms such as cough and breathlessness. In a cross-sectional European survey from five European countries Price et al., (2013) collected data from primary care physicians and respiratory specialists on nearly 2,800 patients with COPD. In this cohort, nearly 80% of patients experienced night-time symptoms. This included trouble falling asleep, staying asleep, waking during the night and waking up feeling tired. Patients with night-time symptoms were more breathless and had frequent exacerbations in the previous 12 months and received more maintenance therapy than those without. Patients with night-time symptoms were also more likely to find it difficult getting up in the morning and had poorer QoL.

Evidence of the efficacy of the SoeMac device to date has been determined from small, observational studies producing a body of anecdotal evidence. Erpenbach, Brailey, Quade & Stentiford, (Unpublished Data, 2010) evaluated whether a SoeTie device (a precursor to the SoeMac device where the SOE is delivered via nasal cannula) led to an improved lung function and therefore improved physical endurance in COPD patients. Eight COPD participants used the device for a single 30-minute session 5 days/week for 4 weeks. Lung function (FEV1) and distance covered during a 6-minute walk test were both improved at weeks 2, 4 and 8

compared to baseline but only the 6MWT data reached statistical significance. Erpenbach et al., (Unpublished Data, 2011) followed this up by completing a second study that was conducted with the current SoeMac device at home for 8 hours a day for 4 weeks with a washout period measured at 4 and 8 weeks. The main findings were an increase in the 6MWT at 4 weeks that was sustained across the washout period at both 4 and 8 week time points. Two patients received dummy devices and no improvement in the 6MWT was seen. Furthermore, Stentiford, Burgoyne & Reeve (Unpublished Data) at The British Lung Foundation Breathe Easy Nottingham West also conducted a small cohort observational study (n=17) to study the effect on sleep and quality of life (QoL). The duration of the study was 12 weeks, with QoL questionnaires completed monthly. Participants stated to the research team, that they were having a better night sleep, which was longer in duration and it was a deep sleep (i.e. instead of restless sleep). Also, participants reported that breathing seemed to be easier, coughing less frequently and as a result not waking up because of this during the night. Collectively these benefits contributed to many participants stating in the questionnaires, that when they woke up, they felt that they had more energy, felt relaxed and refreshed. Participants feeling refreshed, relaxed and energised, further research needs to be conducted to investigate if the positive impact, contributed to an improvement from a physical health perspective (i.e. COPD symptomology, sleep quality) but also psychologically (i.e. depression/anxiety). Unfortunately around 40% of patients with COPD, experience depressive symptoms such as loss of interest in pleasurable activities, and 36% exhibit anxiety symptoms, such as feeling nervous and fearful (Yohannes, Baldwin & Connolly, 2000).

Combining the previous work of the device, the company has conducted a post-market analysis where 249 voluntary testimonials have been received. Collectively, these testimonials provide similar anecdotal observations to previous observational studies and suggest that using the SoeMac can improve important patient outcomes associated with their COPD symptomology (e.g. sleep quality, breathlessness, energy and activity levels, psychological well-being). However, the SoeMac has yet to be tested with a larger-scale study, with scientifically empirical and robust methodologies.

To date, the effectiveness of Singlet Oxygen Energy has only been conducted in small, uncontrolled observational studies providing anecdotal evidence that regular use of the SoeMac device improves symptom profile (including reductions in fatigue and improved sleep quality) when used overnight. We hypothesise that overnight bedside use could provide better sleep quality and improvement in daytime symptoms. Accordingly, we wish to conduct a randomised control trial to determine the safety and efficacy of using the SoeMac device.

Rationale:
The use of devices that aim to improve patient outcomes in clinical groups has increased dramatically in recent years and has obtained increased support from the established Task Force for Lung Health and NHS 5 Year Forward View. The SoeMac device is currently sold as a wellness product but there is limited evidence that supports the safety and efficacy of the device, data that needs to be collected to support the transition to a Class I medical device that is registered with the Medicines and Healthcare products Regulatory Agency (MHRA).

There is growing evidence that demonstrates the biological relevance of Singlet Oxygen ($^1O_2$) and SOE. For example, other SOE-generating devices have been used in pre-clinical laboratory

research including the Valkion and the Oxylight, generating evidence to support the mode of action of the SoeMac device. These studies examined the effect of the SOE on either isolated human blood cells or animal tissue in vivo (Hulten et al, 1999; Lindgård et al, 2003; Lindgård et al, 2007; Lukes et al, 2005; Lundberg et al, 2002). The results demonstrated a decrease in reactive oxygen species, an increase in nitric oxide and an increase in the energy levels of cells in vivo and support the mode of action of the SoeMac device. However, the potential benefits could be extensive and apply to other clinical groups. Accordingly, there is a need to conduct more rigorous research that seeks to determine the safety and efficacy of this device for patients with COPD.

6. CLINICAL INVESTIGATION OBJECTIVES

6.1 OBJECTIVES

1) Evaluate the safety of using a SoeMac device at night, and its effects on self-reported Chronic Obstructive Pulmonary Disease (COPD) symptomology, sleep quality and psychological well-being in people living with COPD.

6.1.1 Primary objectives

2) Determine efficacy and the frequency and severity of reported serious adverse events and adverse events following exposure to the SoeMac device.
3) Quantify a change in the participant-reported outcome from the COPD Assessent Test (CAT) scores.

6.1.2 Secondary objective

4) Quantify changes in participant-reported outcomessleep quality and psychological well-being) following 56 days (8 weeks) of exposure to a SoeMac device.

6.1.3 Primary Outcomes:

Frequency of contact with NHS Primary/Secondary Care & Adverse/Serious Adverse Events (Assessed at Baseline, Day 14 ± 7 Days, 28 ± 7 Days, 42 ± 7 Days & 56 ± 7 Days (Every 2 weeks from Baseline) (Appendix 1):

5) Participants will be asked to self-report details of any contact with the NHS primary/secondary care (i.e. GP or Specialist at a hospital) every two weeks from Baseline until the end of the study (Day 56/8 weeks); as well as any adverse (AE) or serious adverse events (SAE) from the SoeMac device during the trial. Details regarding what primary care source was accessed and whether it led to hospital admission shall be collected. No further details will be requested/recorded.

Impact of COPD:

6) CAT – (Self-reported at Baseline, Day 42 ± 7 Days & 56 ± 7 Days)

The COPD Assessment Tool (CAT, Appendix 2) is designed to measure the impact of COPD on a person's life, and how changes occur over time. The CAT is a short (8 item scale) and has been validated in 50 languages for use within academic research simple to administer. The questions relate to a participant's symptom prevalence and are scored out of 40. Each of the 8 questions are specifically linked with specific COPD symptomology (i.e. cough, mucus, chest tightness, breathlessness, activities, confidence, sleep and energy). Question 8 which asks about energy, can be used to screen fatigue (Stridsman et al., 2018).

6.1.4 Secondary Outcomes:

Sleep Behaviour:

CASIS– (Self-reported at Baseline, Day 42 ± 7 Days & 56 ± 7 Days) The COPD and Asthma Sleep Impact Scale (CASIS, Appendix 3) is a 7-item questionnaire to measure the impact of sleep that is associated with COPD and breathing problems. Each question can be answered on a scale between 1-5 (1= Never, 2=Rarely, 3=Sometimes, 4=Often and 5=Very often). Higher the score, the poorer the sleep quality. CASIS has good internal consistency, test-retest reliability and construct validity. As well as this, it is deemed to be useful in helping to understand the impact that COPD specifically has on sleep outcomes.

- ESS – (Self-reported at Baseline, Day 42 ± 7 Days & 84 ± 7 Days)

  The Epworth Sleepiness Scale (ESS, Appendix 4), is used to measure daytime sleepiness. The questionnaire rates how likely the participant is to doze off during the day, in different situations. Participants have to rate from 0=would never doze to 3=high chance of dozing, for eight statements e.g. 'In a car, while stopped for a few minutes in traffic'.

Psychological Well-being:

7) PHQ-4 – (Self-reported at Baseline, Day 42± 7 Days & 56 ± 7 Days)

   The Patient Health Questionnaire-4 (PHQ-4, Appendix 5) has been developed to allow for an ultra-brief and accurate measurement of the core symptoms and signs of depression and anxiety. It is a 4-item scale. The total PHQ–4 score complements the subscale scores as an overall measure of symptom burden, as well as functional impairment and disability. The PHQ-4 is not a diagnostic tool but an indicator. As well as this the PHQ-4 has good construct validity and internal reliability.

7. CLINICAL INVESTIGATION DESIGN

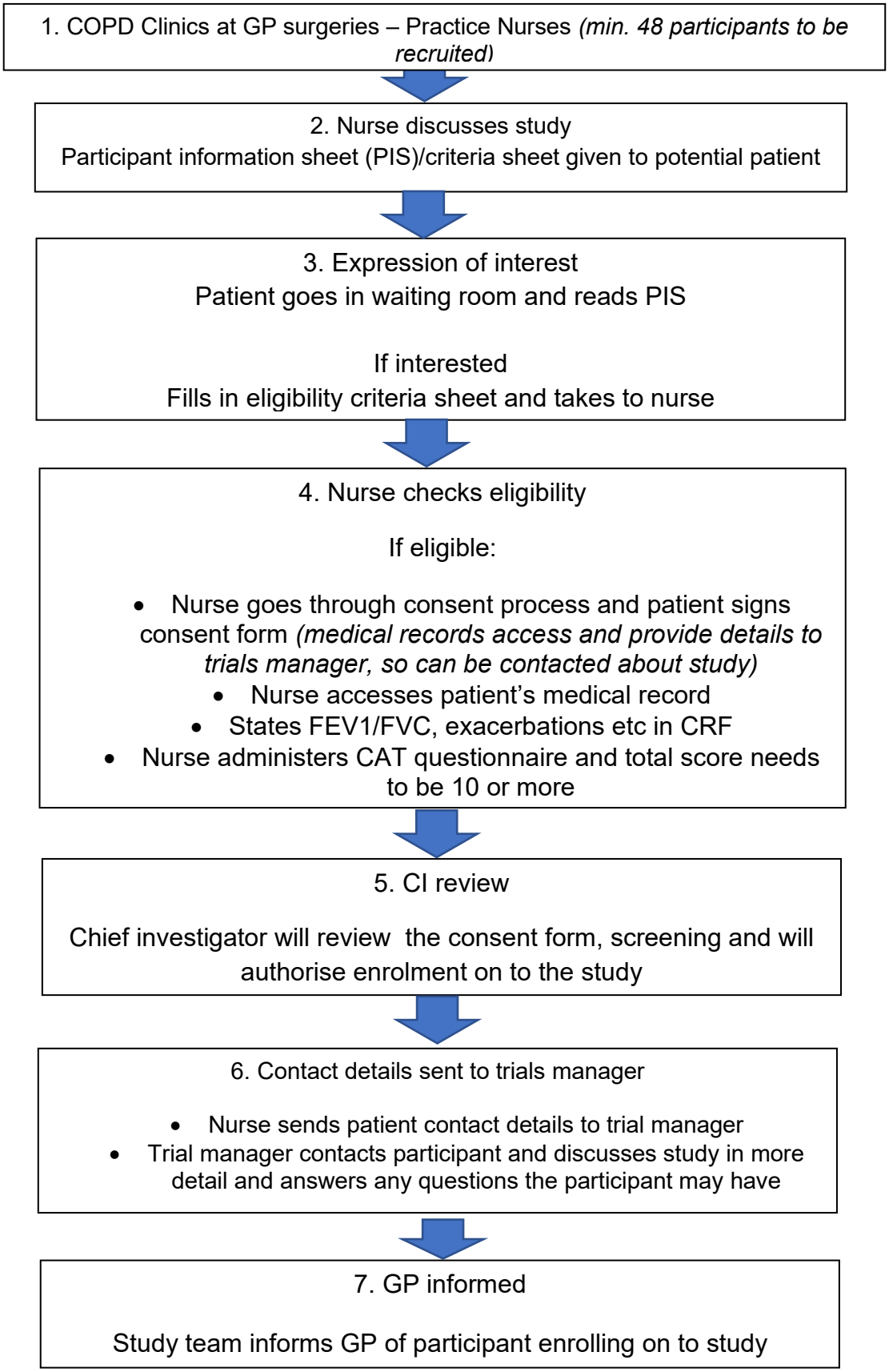
A pilot double-blind, randomised control trial (RCT) will be conducted using a cohort of participants identified from Clinical Research Network (CRN) East Midlands GP surgeries . The study protocol has been designed to enable remote delivery and to ensure compliance with current COVID-19 restrictions. Eligible participants will be randomly allocated to either an experimental or control group. All participants will be provided (via post) with a SoeMac device (Figure 2) that is powered electronically and is positioned by the participants' bed on a bedside table for example and operates throughout the night, to the early morning, when the participant awakens and gets out of bed to start the day.

Figure 2 – SoeMac Device

Participants in the control group will receive an identical device, however, the active components of the device will be removed by the manufacturer. Devices in both groups will look identical ensuring effective blinding can occur. Blinding will be achieved by using an independent source (The University of Derby, Sport Outdoor and Exercise Science Technical Team). The technical team (which includes Mr Kyle Farley) will receive the devices from the company (half of the devices will be placebo control devices) and they will number these (i.e. 001, 002, 003) taking note of the serial number of the device which is located on the base of the device. Numbered devices will be distributed to participants once data collection has begun. The details of the device number and serial numbers will be stored in a sealed envelope (sealed by the technicians) and kept within the site file until after data collection is complete and un-blinding occurs. Individual code break envelopes will be produced in the case of SAE. All devices will be clearly labelled ‘For clinical investigation use only’.

Instructions on how to use the SoeMac device are provided within the SoeMac box that will be provided at the start of the study and will be explained in detail by the research team. Participants will be able to have a SoeMac device for personal use, after the trial has finished, as an expression of thanks and appreciation. All devices will be sent back to the study team. Participants who wish to be sent a SoeMac device for personal use will need to contact SOE Health Ltd, using a special discount code and participants will be sent the device free of charge.

Figure 3a - Study Schematic



Conducted on the telephone by study team

8. Bas
d

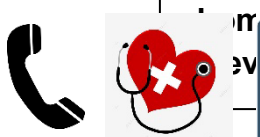
-Demo
-Sn
Hi

quest
(COP

9. Day 0 (± 7 days)

Start of study

SoeMac is switched on in evening by participant at



10. Week 2 (± 7 days)

-AE/SAE

-
Physical/Menta



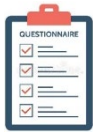
11. Week 4 (± 7 days)

Half-way of study

-x4 questionnaires *(COPD, Sleep Quality, Sleepiness, Mental Health)*

-AE/SAE





12. Week 6 (± 7 days)

-AE/SAE

-
Physical/Menta


13. Week 8 (± 7 days)

End of study

-x4 questionnaires *(COPD, Sleep Quality, Sleepiness, Mental Health)*

-AE/SAE

-Physical/Mental Health Changes



8. CLINICAL INVESTIGATION POPULATION

8.1 NUMBER OF PARTICIPANTS

We will aim to recruit a minimum of 48 participants through to final follow-up visit at day 56 (a minimum of 24 in placebo; 24 in the active group). Any additional participants that are recruited in the study will be beneficial for clinically relevant significance, a maximum of 100 participants (50 in active; 50 in placebo group). The total duration of the study from participant recruitment, screening and enrolment will be up to 12 months.

Potential participants will be sourced from the Clinical Research Network (CRN) East Midlands GP surgeries. In the first instance, up to 5 GP surgeries will be assisting with recruiting and consent and will be operating as a multi-site study. The process of recruitment is outlined in figure 3. The aim is to recruit a minimum of 24 in placebo and 24 in the active group. 24 in each group, as an absolute minimum of 48 participants and a maximum of 100 (50 in active; 50 in placebo). There is not a set number of participants to be recruited with each GP site, as recruitment is opportunistic at standard routine COPD clinics.

8.2 INCLUSION CRITERIA

Adult participants (≥40 years of age) will be screened for eligibility using the below:

- Participants of any gender
- ≥ 40 years of age (40 years old & above)
- CAT Score ≥ 10
- Current or previous smoker (number of packs per day) x (years) ≥ 20 pack-years
- Previous diagnosis of COPD from GP/Doctor
- No exacerbation in 6 weeks before study participation
- Able to understand verbal and written information in English
- Able to communicate via the telephone/virtual meetings
- No hearing impairment that prevents use of telephone
- Non-pregnant women
- No current positive COVID-19 infection within last 6 months

8.3 EXCLUSION CRITERIA

- <40 years old (less than 40 years old)
- CAT Score <10
- No previous history of smoking
- Previous smoker with pack-years (number of packs per day) x (years) <20
- Previous use of SoeMac Device
- Use of oxygen at night
- Lung cancer
- Unstable cardiovascular status (e.g., ongoing angina)
- Recent myocardial infarction (heart attack; within last 6 months)
- Exacerbation of COPD within the last 6 weeks
- No diagnosis of COPD
- A disclosed hearing impairment that prevents use of telephone
- Sleep Apnoea
- Pregnant Women

- Any other device that is used *all* night to assist with their breathing

Within the last 6 months:

- A current or positive COVID-19 infection and within the last <6 months

9. PARTICIPANT SELECTION AND ENROLMENT

9.1 IDENTIFYING PARTICIPANTS

Ms Elaine Blackshaw from Nottingham University Hospitals NHS Trust (NUHT) will be the Trial Manager and Coordinator for the study.

Mr Samuel Grimwood (PhD student, under the supervision of Dr Amy Baraniak) from the HSRC at The University of Derby, as well as assisting with the participant recruitment process (Please see Figure 3).

With the assistance of the practice nurses of each GP surgery that is assigned to assist with recruitment will ask during routine COPD clinic check-ups, whether the participant is interested in taking part in the study. If the participant expresses interest, the practice nurse will discuss the study (i.e. the aims, what it is involved, duration) and gives the participant a participant information sheet (Appendix 6), as well as an eligibility criteria sheet (Appendix 7). The participant reads the participant information sheet and if they would like to take part in the study, they complete the eligibility criteria sheet. Once complete, the participant takes the eligibility criteria sheet to the practice nurse. The final part of the eligibility criteria sheet is for the nurse to go through the COPD Assessment Test (CAT; Appendix 2), which has to a total score of 10 or more to be deemed as eligible. If the participant is eligible, the practice nurse will go through the consent form (Appendix 8) with the participant and will answer any questions the participant may have. The practice nurse and participant will sign two copies, one to keep as a study team and the second to be kept by the participant for personal use. Within the consent form will state accessing the participants medical records at the GP surgery, as well as sending contact details to be trial manager etc. The nurse will then access the participants medical records and will state whether the information that the participant has provided is correct, as well as state lung function and recent exacerbations within the criteria sheet. Prior to the participant leaving, the practice nurse will talk about the next steps of the study, which is for the participants contact details to be sent securely using NHS email address, for the trial manager to get in contact.

The chief and principal investigator Dr Sovani Milind will go through the criteria sheet and consent form (Appendix 7, 8) and will then see whether the participant is safe to take part in the trial and will authorise accordingly, which will be documented within the screening CRF (Appendix 7). If Dr Sovani Milind does not authorise the participant to be enrolled on the trial, the participant will be informed of this. This will be either telephone, email or via post (Appendix 9) whichever they opted for at the start of the trial within the consent form (Appendix 8).

If the participant has been authorised to be enrolled on the trial, the participants GP will be informed (Appendix 10). The trial manager will get in contact with the participant, to

introduce themselves to the participant and to mention that the next steps will be for a study pack to be sent and if they have any further questions that they may have and they have the right to withdraw at any stage. The participant will then be assigned a unique participant study identification number which will be used to complete each participants CRF. Each participant will then be sent study pack (see Figure 3) which are the questionnaires (CAT, CASIS, ESS, PHQ-4,) in the post. This will be the start of the enrolment into the trial for the participant.

9.2 CONSENTING PARTICIPANTS

If after reading the participant information sheet (Appendix 6) and the participant is eligible, the practice nurse with the participant will go through the consent form and answer any questions the participant may have. If the participant would like to take part in the study, consent will be provided, by signing a copy of the consent form for themselves as a personal copy, as well as the practice nurse, for the study team.

Within the consent form, consent to take part in the trial, for contact details to be sent to the trial manager, as well as informing the participants GP should they be authorised by the CI Dr Sovani and is enrolled on to the study. It states clearly that the participant is free to withdraw from the clinical investigation at any time for any reason without prejudice to future care, and with no obligation to give the reason for withdrawal.

9.3 SCREENING FOR ELIGIBLE PARTICIPANTS

Participants complete the eligibility criteria sheet and is completed with the practice nurse. To add the lung function information, medical records will be accessed by the practice manager, and will only be accessed, after the participant has given consent to take part in the study. Participants will be allocated a screening number.

Demographics: Height, weight, age, sex and smoking status (previously/current).

COPD Information: Information about the participants COPD will be recorded. The diagnosis of COPD, when this was conducted and how. Also, the score from the COPD Assessment Tool (CAT; Appendix 2) will be asked and the practice nurse will go through the CAT with the participant.. The CAT questionnaire has 8 short questions, with a scale between 0 and 5. The max score is 40. As well as this, exacerbation history and current status, FEV1/FVC will be accessed on the participants medical records by the practice nurse.

Specific Medical History: Specific medical questions will be asked for example cancer, cardiovascular, infarction. Also pregnancy, as well as sleep apnoea.

Oxygen Usage: Participants will be asked if they are being administered oxygen at night time.

SoeMac Device Usage: If the participant has used a SoeMac device or is currently using a SoeMac device.

Multiple Study Participation: Information whether the participant is taking part in other research studies or clinical trials, especially if they are medical device or pharmacologically related.

English Comprehension: Participants who are unable to understand verbal English will not be eligible for this study. This is due to the necessity of telephone contact which is a key aspect of this study. Translating the telephone interviews into different languages and conducting telephone interviews in different languages via translators will have considerable cost and resources implications which are considered inappropriate for the nature of this study and the expected small numbers that this would apply to.

Verbal consent must be obtained before the participant undertakes any activities that are specifically for the study. All study documentation (i.e. participant information sheet, participant consent form) will be kept in the Trial Master File.

Communication: According to the Accessible Information Standards (NHS Publications Gateway, 2016), participants should be asked to self-define their communication support needs (and not their disability). For example, the participant may inform the trial manager or practice nurse voluntarily or the trial manager or practice nurse could ask the participant directly (e.g. if the participant finds it difficult to read small printed text).

Furthermore, if the participant struggles to read and would appreciate the participant information sheet to be read aloud by the trial manager or practice nurse, again this could be implemented if the participant asks for this requirement.

Also, if the participant can read and understand verbal English but feels highly anxious or finds it difficult to answer questions and feels comfortable to have their partner present when going through the Participant Information Sheet as well as the telephone screening and/or the questionnaires throughout the study, permission from the participant, will be required but operationally would be permitted.

Therefore, adaptions will be implemented in this study to entail study participation enrolment as accessible as possible.

Hearing Impairment: Unfortunately, if the participant does have a hearing impairment that impairs them significantly from talking on the telephone, they will not be able to partake in the study, with the main mode of communication is via a telephone call. This will be clearly stated in the participant information sheet.

COVID-19 Infection : Questions will be asked whether the participant has been exposed to COVID-19 and if they have a positive COVID-19 infection.

9.4 RANDOMISATION

As stated in the clinical investigation design section, randomisation will be conducted within the clinical trial and will be double-blind. Participants will receive either an active or a 'dummy' device, and the device in the control group will look identical however the active components of the device will be removed by the manufacturer. Blinding will be achieved by using an independent source (The University of Derby, Sport Outdoor and Exercise Science Technical Team). The technical team will receive the devices from the manufacturer (half of the devices will be placebo control devices) and they will number these (i.e. 001, 002, 003) taking note of the serial number of the device which is located on the base of the device. The devices will then be sent to the trial managers office at NUH. From here, the trial manager will distribute each numbered device, and these will only be distributed to participants once data collection has begun. The details of the device number and serial numbers will be stored in a sealed envelope (sealed by the technicians) and kept within the site file until after data collection is complete and un-blinding occurs. All devices will be clearly labelled 'For clinical investigation use only'.

If the device becomes faulty, the device will be sent back to the trial managers office at NUH and will be exchanged by the manufacturer. The replacement device will be sent to the participant via the trial manager at NUH. The trial manager will not know if the device is active or placebo, as the manufacturer will only know because of fixing the device, it will become apparent if the device is active or placebo. The information regarding the device will be in the strictest confidence and will remain double-blind, therefore. Please see section 10.3 'Device Accountability' for further information.

In the case of AE/SAE/ADE/SADE/USADE individual code break envelopes will be produced. The study team will have access to these codes. Details of the specific participant, the date and time, the specific member of the team will be documented, and the participant ID will be stated across all documentation. When the individual codes have been accessed, the delegate conducting the unbinding will see whether the participant has been using an active or non-active device (dummy). When unbinding is implemented the clinical investigator Dr Milind Sovani will be formally informed via email and telephone. Dr Milind Sovani will then recommend the next steps of whether the participant can remain in the trial or if they need to be removed from continuing the trial. The unblinded participant and all documentation that has been created will be used and linked to the data analysis at the end of the trial (overseen by Dr Emma Sharpe and conducted by Samuel Grimwood), as the specific participant that had to be unblinded and if they have been removed from participating within the trial, will be omitted from the final data set (if within 1 month from the completion of the trial/the final data analysis has not been conducted and disseminated i.e. within a journal). The participant will be informed of whether they were assigned an active or non-active device. The participant will be able to ask any questions or concerns they may have during the debrief. Any points that were raised by the participant will be stated formally in the documentation. Further information on AE/SAE/SADE/USADE reporting can be found in section 14.

When the trial has formally ended, all participants will be fully unblinded and the SoeMac device and sleep diary will have been returned to NUH. Participants will be able to have a SoeMac device for personal use. Participants will contact the manufacturer SoeHealth Ltd. They will be provided with a special discount code, where they will obtain the SoeMac free of charge, as goodwill for taking part and completing participation in the trial.

INTERIM DATA ANALYSIS

An interim data analysis may be conducted prior to the end of the study. A code break will be conducted, therefore meaning the subset of collected data will be unblinded. Conducting an interim analysis ensures patient safety, progress of the study, and if conduct is appropriate.

As well as this, the interim analysis may be included Samuel Grimwood's PhD thesis if enough participants are recruited in time prior to September 2022. Because of significant delays because of changes to study design due to the COVID-19 pandemic, has meant that the study will not have completed prior to Samuel completing his PhD. Ideally, a subset of 60% of the sample size in each group, will be when the code break will planned and the data extracted and analysed. 60% of 48 is 28, divided by 2 groups, is 14 in active group and 14 in placebo group. 60% is recommended by previous research to conduct an interim analysis according to Edwards et al., (2020). However, for the purposes of the PhD thesis, bare minimum is 3 in total, to be able to conduct the one-way ANOVA's and paired sample t-tests (see Section 13) for the interim data analysis.

Within the interim data analysis, the same statistical methods and analysis will be conducted by Samuel and overseen by Dr Emma Sharpe. The results of the interim analysis will remain confidential to the CI Dr Milind Sovani only, Samuel and Dr Emma Sharpe. This is to prevent and omit any chance of bias for the rest of the study to be conducted and finished with data collection with the trial manager and the practice nurses.

9.5 WITHDRAWAL OF PARTICIPANTS

Each participant has the right to withdraw from the study at any time. Participants may be withdrawn from the study either at their request or at the discretion of the Chief Investigator. Participants will be made aware (via The Participant Information Sheet and Verbal Form) that if they withdraw from the study more than 1 month after the trial has finished the data which has been collected, it is likely the data will have been analysed and disseminated, making it impossible to erase from the data set (i.e. published journal). The Chief Investigator may withdraw a participant from the study at any time if they consider that the participant's health is compromised by remaining in the study or the participant is not sufficiently cooperative. The reasons for any participant withdrawal will be recorded on the study completion form of the CRF. The data collected from withdrawn participants will be included in the study report.

The Chief Investigator may discontinue a participant from the study at any time if they consider it necessary for any reason including but not limited to:

- Ineligibility (arising during study or retrospective having been overlooked at screening)

- Significant protocol deviation
- Significant non-compliance with study requirements
- An AE/ADE which requires discontinuation of the SoeMac device or results in the inability to continue to comply with study procedures
- COPD progression requires discontinuation of using the SoeMac device and therefore an inability to continue to comply with study procedures.
- Consent is withdrawn
- Lost to follow up
- Reports a positive COVID-19 infection during study involvement
- • The reason for withdrawal will be clearly stated and recorded in the CRF. If the participant is withdrawn due to an AE, the Chief Investigator will arrange for a follow-up telephone call until the AE has resolved or stabilised.

If the participant who has given informed consent, loses the capacity to consent during the study, the participant and all identifiable data will be withdrawn from the study. However, if the participant loses the capacity to consent during the study after 1 month from the end of the study, it will not be possible to omit the data from the final data set, that would have been formally analysed and possibly disseminated.

10. MEDICAL DEVICE

10.1 DEVICE DETAILS

- SoeMac
- It is not CE marked.
- There are no other devices other than the SoeMac device in this clinical trial (Active and Placebo SoeMac devices)

10.2 DEVICE MANUFACTURER

Mr Neil Stentiford
SOE Health Ltd
42d Derby Road
Beeston
Nottingham
NG9 2TG

10.3 DEVICE ACCOUNTABILITY

Regarding device accountability, an Excel Spreadsheet will be used, to document the journey of each SoeMac device:

- From the manufacturer
- The technical team at The University of Derby (Mr Kyle Farley)
- Received by Trial manager at NUH
- When the Trial manager dispatched to the participant
- If the device has been received by the participant (will be asked on the telephone call within 7 days of sending study pack 1 (or 3)
- If the device becomes faulty, exchanged and details of replacement device being sent to the participant and how many days extra days they will be in the trial (i.e. if the participant had to wait 3 days for a replacement, they will have 3 extra days on to end of the trial, to accommodate for the 3 evenings without a SoeMac device)
- When the participant has completed the trial and has sent it securely back to the trial manager at NUH
- Confirmation when the trial manager has received the device
- When the manufacturer collects the device
- Within the spreadsheet, state if the participant expresses an interest to acquire a SoeMac device for personal use, will be provided with a special discount code by the study team and they will contact the manufacturer directly, once the trial has ended.

The manufacturer of the SoeMac device has stated that regarding faults of the device, statistically may be around 1% in total. This means that within the trial, there may be 1 or 2 devices that may be faulty and will need to be replaced as soon as possible. Should a device become faulty, the participant must inform the trial manager as soon as possible. Using the Freepost envelope provided in the study pack to the participant, the participant will send the device back to the trial managers office at NUH. The manufacturer will be informed and the

device will be collected. The manufacturer will know if the device is active or placebo (as the device will be opened, to fix the device and will become clear if it is active or placebo, therefore) and will exchange the device to replace and separate records will be updated. Whether the device is active or placebo will not be stated or informed to the trial manager or any of the study team, remaining in strict confidence. The manufacturer will not know the participant ID or address of the participant. The manufacturer will drop the device off to the trial manager at NUH. If the participant lives within 20 miles of NUH, the device will be dropped off to the participant's address as a priority as soon as possible. If the participant lives more than 20 miles from NUH, the device will be sent recorded delivery. This will be documented within the device accountability log (Appendix 11), along with the specific details from the start to the end of the trial detailing the handling of the SoeMac device. If for example, the participant has not been able to use the SoeMac device for 1-3 days because of the device being exchanged because of faults, the days that the participant has not been using the device, will be extended on to the duration of the participation in the trial (e.g. 1-3 days + 56 days).

10.4 STORAGE CONDITIONS

Store the device indoors and in a dry environment. Clean with wet wipe once a month and filter change every 4 weeks (e.g. for this trial, therefore the participant will change the filter three times). Instructions will be provided.

There are no foreseen maintenance issues with the SoeMac device. If however there is a maintenance issue with the device, the participant will be able to contact one of the study team who will send out a replacement to the participant as soon as possible. The faulty device should be returned to the study team.

The study aims to recruit 48 participants (24 in each group), with no stated maximum. The manufacturer of the SoeMac devices will provide the amount of 48 devices as a minimum and will supply the required devices, for participants that have been screened, consented and recruited into the study. The devices will be sent to The University of Derby Sport Outdoor and Exercise Science Technical Team who blind each device, 50% will be active and 50% will be placebo devices. The team will number each device from 001; 002; 003 for example and will take note of the serial number of the device which is located on the base of the device. The details of the device number and serial numbers will be stored in a sealed envelope (sealed by the technicians) and kept within the site file until after data collection is complete and un-blinding occurs. Individual code break envelopes will be produced in the case of SAE.

Once the devices have been randomised, all devices will be securely sent to the Trial Manager’s office at NUH QMC and will be securely stored in a locked cabinet and locked office. Numbered devices will be distributed to participants once data collection has begun. Once the study has finished and participants are unblinded, participants who were in the control group will have their SoeMac device exchanged for an active device.

In line with the studies, ambition to recruit 48 participants, the first forty-eight devices that will be randomised will contain 24 active and 24 placebo devices. Thereafter if any additional participants are recruited, randomisation will occur in batches of 10.

Cleaning and Distribution of the SoeMac device:

The manufacturer SoeHealth will pack the SoeMac device in a sealed plastic bag, using gloves and a mask, ready to send to the University of Derby's technical team. The packaging will be wiped clean using infection control approved antibacterial wipes 'Clinell Universal'. Clinell Universal wipes are effective against COVID-19 virus within 30 seconds (GAMA Healthcare Ltd, 2020). There will be at least 1 week between manufacturing and distribution of the SoeMac device, where the device will have no contact with people, significantly reducing the transmission of COVID-19.

The SoeMac devices will be randomised double-blind (which means that the devices will not be known, which are active and non-active) by The University of Derby, Sport Outdoor and Exercise Science Technical Team. The devices will be handled with care, with gloves and antibacterial wipes. The technical team will objectively randomise each SoeMac device (see section 9.4). The specific codes will be clearly stated on each SoeMac device. These will be collected in bulk by the study team and will be dropped off to the trial managers office at NUH QMC.

From NUH QMC, with the study documentation (study pack 2 or 4) within the package, the trial manager will send securely to each participant, (documenting the specific SoeMac that has been sent to the participant, using the CRF), using recorded special delivery, using the specific order that each SoeMac device has been allocated from The University of Derby's technical team. The same process will be implemented for both the active and non-active groups (see figure 4).

At the end of the trial, each participant from both the active and non-active groups will send their SoeMac device back to NUH in a prepaid recorded delivery Freepost envelope. This will be discussed with the participant on the last telephone consultation. Participants will be advised to wipe the SoeMac device using anti-bacterial wipes on the SoeMac device, before placing it in the sealed bag, within the envelope and returning. Devices returned will be quarantined for 7 days upon arrival at NUH, to reduce transmission of any possible COVID-19 between participant, trial manager and manufacturer. Participants will be asked if they would like to have their SoeMac device returned to them for personal use (i.e. for them to keep) at no cost.

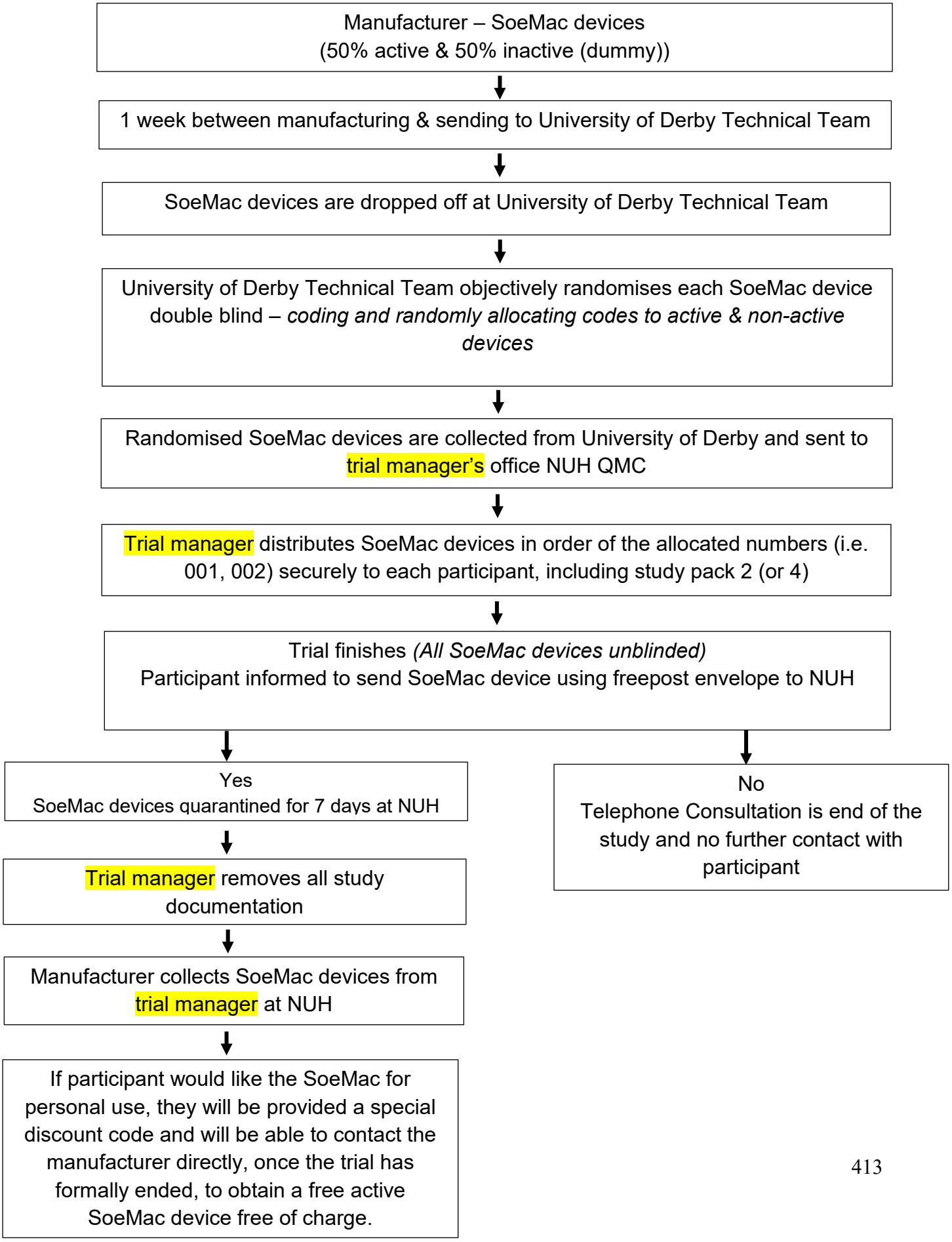
The manufacturer will collect all SoeMac devices from NUH, which will be arranged between the manufacturer and the trial manager. The envelopes and SoeMac devices will be handled with care, including gloves and anti-bacterial wipes.

The codes of each device will be unblinded and the codes of each device will be provided by The University of Derby's technical team.

For participants that have said yes to acquiring a SoeMac device for personal use, the specific SoeMac they have been using for the trial will be sent back to them. Active devices will be serviced, and placebo devices will be converted to active. Once the manufacturer has serviced/converted all SoeMac devices, they will be sent back to the trial manager at NUH. The trial manager will have the information for each participant, their specific SoeMac device

number and will securely send the SoeMac device back to the participant. The SoeMac device will be placed within a sealed bag, in a box, inside a padded envelope. Each envelope and SoeMac device will be handled with care, including gloves and anti-bacterial wipes.

Figure 4: SOEMAC DISTRIBUTION FLOWCHART:



10.5 OTHER MEDICATIONS

Treatment as usual

The participant from study enrolment to the end of the study (post-study follow up) will continue to take their usual prescribed medication (i.e. LABA Inhaler or tablet) that the participant's clinician has advised. The SoeMac device is an addition to the participants COPD symptom management and not a replacement to prescribed medication and/or treatment. GPs will be informed that the participant has enrolled in the study. For clinically related issues please see Section 6.6 'Adverse/Serious Adverse Events'.

11. CLINICAL INVESTIGATION ASSESSMENTS

11.1 SAFETY ASSESSMENTS:

No specific safety assessments are required for the investigation. The study is to be conducted remotely with all interactions via telephone or video consultation. The device does not contact the patient directly and is judged to be low/minimal risk.

The Medical Devices Management Committee at NUH have reviewed the use of the SoeMac and granted a concession to use the device in the proposed study providing Ethical approval and a Letter of No Objection is received from the MHRA.

The SoeMac does not directly contact the patient but the expelled air from the SoeMac is inhaled by the user. To comply with the biocompatibility standards, the device has been tested at Nottingham Trent University according to standard BS EN 18562-1-2017 and BS EN 18562-3-2017 Biocompatibility evaluation of breathing gas pathways in healthcare. The GC-MS testing demonstrated that no VOC is expelled from the device and that the exhaust air is no different in composition from the ambient air. The results are documented in the Technical Dossier and Clinical Evaluation Report.

11.2 CLINICAL INVESTIGATION ASSESSMENTS

Refer to a schedule of events table in the appendices. Refer to Figure 5 for study assessments.

12. DATA COLLECTION

Source documents are original documents, data, and records from which participants' CRF data are obtained. These include, but are not limited to, the telephone screening, consent forms, AE/SAE reporting documents, participants questionnaires for example (please see below).

All documents will be stored safely in confidential conditions. On all clinical investigation-specific documents, other than the signed consent, the participant will be referred to by the clinical investigation participant number/code, not by name.

The data below will be collected within the clinical trial:

Demographics:

- Height
- Weight
- Age
- Sex
- Ethnicity
- Medical & Psychological Morbidities (GP Diagnosed Co & Multi)
- COPD Medication/Treatments
- Smoking Pack Years
- Smoking Status
-

Device Related:

- Device usage
- Side effects
- Health changes
- Wellbeing changes

Inferential:
Frequency of contact with NHS Primary/Secondary Care & Adverse/Serious Adverse Events:

- Assessed at Baseline, Day 14 ± 7 Days, 28 ± 7 Days, 42 ± 7 Days & 56 ± 7 Days (Every 2 weeks from Baseline)

  Participants will be asked to self-report details of any contact with the NHS primary/secondary care (i.e. GP or Specialist at a hospital) every two weeks from Baseline until the end of the study (Day 56/8 weeks). As well as any adverse (AE) or serious adverse events (SAE) from the SoeMac device during the trial and any medication changes. No further details will be requested/recorded.

Impact of COPD:

- CAT – (Self-reported at Baseline, Day 42 ± 7 Days & 56 ± 7 Days)

The COPD Assessment Tool (CAT, Appendix 2) is designed to measure the impact of COPD on a person's life, and how changes occur over time. The CAT is a short (8 item scale) and has been validated in 50 languages for use within academic research simple to administer. The questions relate to a participant's symptom prevalence and are scored out of 40. Each of the 8 questions are specifically linked with specific COPD symptomology (i.e. cough, mucus, chest tightness, breathlessness, activities, confidence, sleep and energy). Question 8 which asks about energy, can be used to screen fatigue (Stridsman et al., 2018).

Sleep Behaviour:

- CASIS – (Self-reported at Baseline, Day 42 ± 7 Days & 56 ± 7 Days)

  The COPD and Asthma Sleep Impact Scale (CASIS, Appendix 3) is a 7-item questionnaire to measure the impact of sleep that is associated with COPD and breathing problems. Each question can be answered on a scale between 1-5 (1= Never, 2=Rarely, 3=Sometimes, 4=Often and 5=Very often). Higher the score, the poorer the sleep quality. CASIS has good internal consistency, test-retest reliability and construct validity. As well as this, it is deemed to be useful in helping to understand the impact that COPD specifically has on sleep outcomes.

  ESS – (Self-reported at Baseline, Day 42 ± 7 Days & 84 ± 7 Days The Epworth Sleepiness Scale (ESS, Appendix 4), is used to measure daytime sleepiness. The questionnaire rates how likely the participant is to doze off during the day, in different situations. Participants have to rate from 0=would never doze to 3=high chance of dozing, for eight statements e.g. 'In a car, while stopped for a few minutes in traffic'.

Psychological Well-being:

8) PHQ-4 – (Self-reported at Baseline, Day 42± 7 Days & 56 ± 7 Days)

   The Patient Health Questionnaire-4 (PHQ-4, Appendix 5) has been developed to allow for an ultra-brief and accurate measurement of the core symptoms and signs of depression and anxiety. It is a 4-item scale. The total PHQ–4 score complements the subscale scores as an overall measure of symptom burden, as well as functional impairment and disability. The PHQ-4 is not a diagnostic tool but an indicator. As well as this the PHQ-4 has good construct validity and internal reliability.

13. STATISTICS

13.1 DESCRIPTION OF STATISTICAL METHODS

A double-blind, randomised control trial will be conducted, utilising a prospective, observational cohort design. This will be used to determine the efficacy of the SoeMac device, in improving self-reported outcomes among those living with COPD, over 8 weeks.

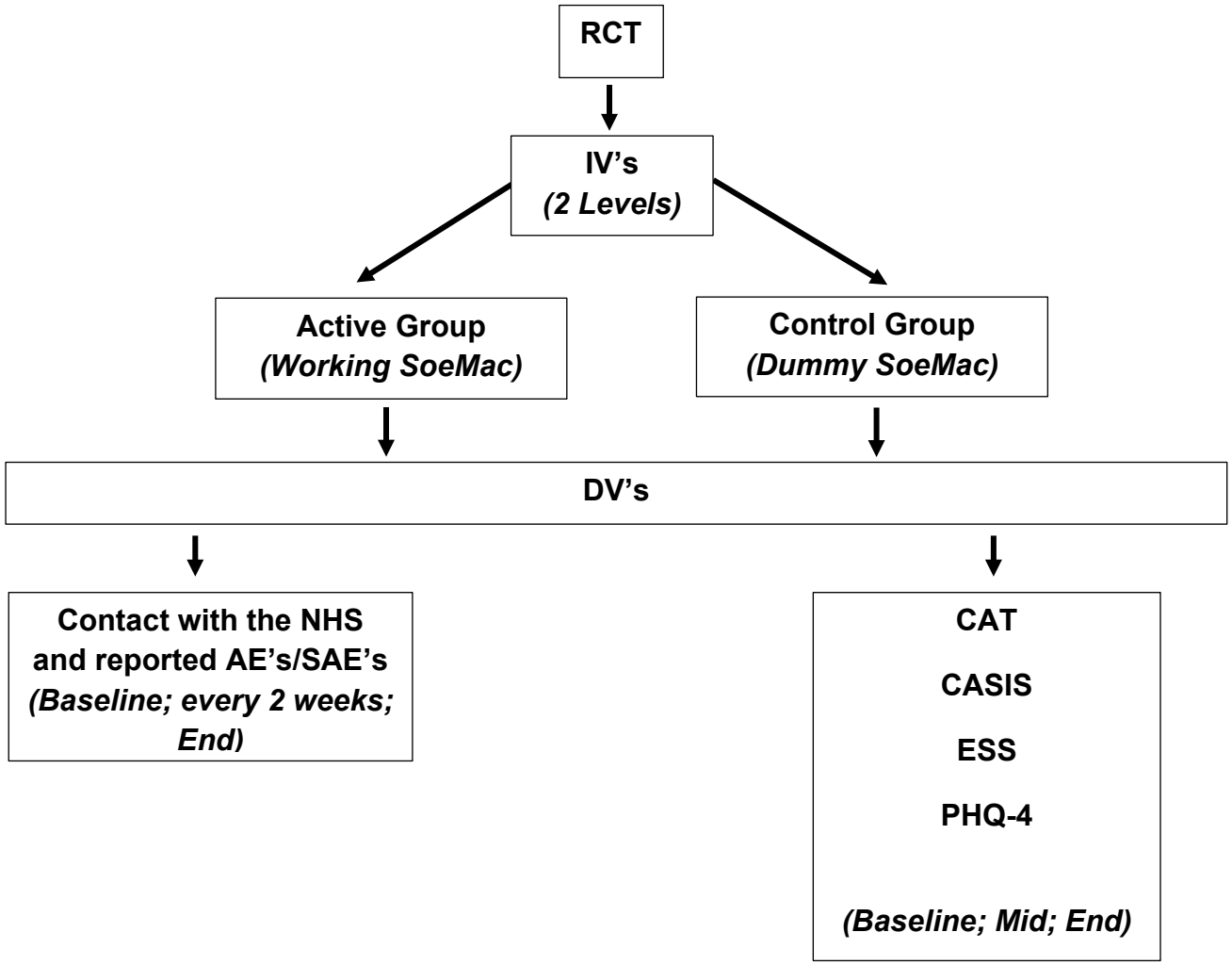
Frequency of contact with the NHS and reported AE's/SAE's will be measured from baseline, then every 2 weeks, until the end of the study (Part A of the primary objective and outcome). Part B of the primary objective and outcome is to measure from baseline, mid and at the end of the study to measure if there are any changes in each group (active and control group) (independent variable) in the scores for CAT questionnaire.

The secondary objectives and outcomes, are the independent variables which are the two groups (active vs control). The dependent variables are the CASIS and PHQ-4 questionnaires. Participants in both groups will complete at baseline, mid and end of the study.

As this is a pilot study and a trial that has used a device similar to the SoeMac, has not been conducted previously, the minimum number of participants which would be beneficial would be 24 participants in both groups (active; placebo). However, if recruitment of participants is successful (i.e. more than 48 have been enrolled on to the trial, with relative ease and within the planned time frame), further participants would add significant value and rigour to the trial. For example, according to the prospective power analysis (please see Section 13.2 Number of Participants), ideally, a sample size of 48, would provide the correct amount of power statistically to the trial. Therefore, this means that the bare minimum to be recruited into this trial would be 48 will be recruited. The statistical analysis will be conducted by the University of Derby (Samuel Grimwood, overseen by Dr Emma Sharpe) using SPSS version 28.

Descriptive statistics will be calculated for all outcomes of interest. The primary outcomes regarding frequency of the contact with the NHS and reported AE's/SAE's (please see Section 6) and the CAT scores. The secondary outcomes are sleep behaviour (CASIS) and psychological well-being (PHQ-4).

FIGURE 5 - Independent Variables (IV) & Dependent Variables (DV) Flow Chart:



All outcomes of interest (i.e. Contact with the NHS and reported AE's/SAE's and the questionnaires CAT, CASIS, PHQ-4, ESS) will be presented as proportions and means with standard deviations or medians with interquartile ranges, depending on the distribution of data. This includes – Height, Weight, Age, Sex, Ethnicity, Medical & Psychological Morbidities (GP Diagnosed Co & Multi), COPD Medication/Treatments, Smoking Pack Years, Smoking Status. As well as device related questions such as device usage (average amount of evenings used across 56 days), side effects (what the side effect is, how many, duration; mean and range for each specific side effect), health changes (positive and/or negative, what the health change is, how many, duration; mean and range for each health change for both groups), wellbeing changes (positive and/or negative, what the wellbeing change is, how many, duration; mean and range for each wellbeing change).

Data will be collected from Baseline, every 2 weeks and at the end at Day 56 for contact with the NHS and reported AE's/SAE's for the Part A of the primary objective and outcome, whereas the CAT scores will be collected at baseline , mid (halfway through the study Day 28) and at the end of the study (Day 56) (Part B of primary objectives and outcomes).

In regards to the secondary objectives/outcomes the questionnaires, CASIS, ESS and PHQ-4 will be collected at baseline , mid (halfway through the study Day 28) and at the end of the study (Day 56).

The contact with the NHS and reported AE's/SAE's will be calculated how many times the NHS has been contacted and therefore ANOVA's will be conducted.

For AE's (dependent variable) in the active group, a one-way ANOVA will be conducted 5 (time point: baseline, day 14, day 28, day 42 & 56) x 1 (Active Group). Similarly AE's (dependent variable) in the placebo group, will be measured also using a one-way ANOVA 5 (time point: baseline, day 14, day 28, day 42 & 56) x 1 (Placebo Group). Post-hoc testing such as Tukey's Honestly Significant Different (HSD) test or Discriminant Analysis will be implemented for both ANOVA's if statistical significance is observed.

Regarding the SAE's (dependent variable) in the active group, a one-way ANOVA will be conducted 5 (time point: baseline, day 14, day 28, day 42 & 56) x 1 (Active Group). Similarly SAE's (dependent variable) in the placebo group, will be measured also using a one-way ANOVA 5 (time point: baseline, day 14, day 28, day 42 & 56) x 1 (Placebo Group). Post-hoc testing such as Tukey's Honestly Significant Different (HSD) test or Discriminant Analysis will be implemented for both ANOVA's if statistical significance is observed.

Furthermore in regards to the CAT questionnaires scores, two separate one-way ANOVA's will be conducted using a 3 (time point; baseline, mid & end of study) x 1 (Active group) ANOVA. The same ANOVA will be conducted for the control group 3 (time point; baseline, mid & end of study) x 1 (Control group). This is to examine to see if there is an overall significance in each ANOVA. If there is an overall significance in CAT score for either ANOVA's Tukey's Honestly Significant Different (HSD) test or discriminant analysis will be implemented for post-hoc testing, to specify the specific time point, if there was a significant difference etc.

In addition to the two ANOVA's for the CAT score (using the global score), a paired samples t-test will be conducted. All 8 domains (i.e. cough, mucus, chest tightness, breathlessness, activities, confidence, sleep and energy levels) of the CAT questionnaire will be analysed using t-test's. For each group (active; placebo) and for each domain (8) and across data point 1 vs data point 2, data point 2 vs data point 3, as well as data point 1 vs data point 3 will be conducted. Conducting the t-tests will show if there is a difference between the data points for each separate domain and for both groups separately.

Similarly for the CASIS questionnaire, two separate one-way ANOVA's will be conducted using a 3 (time point; baseline, mid & end of study) x 1 (Active group) ANOVA. The same ANOVA will be conducted for the control group 3 (time point; baseline, mid & end of study) x 1 (Control group). This is to examine to see if there is an overall significance in each ANOVA. If there is an overall significance in CASIS score for either ANOVA's Tukey's Honestly Significant Different (HSD) test or discriminant analysis will be implemented for post-hoc testing, to specify the specific time point, if there was a significant difference etc.

On the other hand for the PHQ-4 questionnaires scores, two separate one-way ANOVA's will be conducted using a 3 (time point; baseline, mid & end of study) x 1 (Active group) ANOVA. The same ANOVA will be conducted for the control group 3 (time point; baseline, mid & end of study) x 1 (Control group). This is to examine to see if there is an overall significance in each ANOVA. If there is an overall significance in PHQ-4 score for either ANOVA's Tukey's Honestly Significant Different (HSD) test or discriminant analysis will be implemented for post-hoc testing, to specify the specific time point, if there was a significant difference etc.

In addition to the two ANOVA's, paired samples t-tests for the PHQ-4 will also be conducted. The global score (x4 item and each score is totalled) of the PHQ-4 will be used in the ANOVA's which is depression and anxiety. On the other hand, the PHQ-4 can also be spilt, as 2 of the questions the total score is for depression and the other 2 questions the total score is for anxiety. Therefore, t-tests will be used for the anxiety score and separately for the depression score, for each group (active; placebo), across data point 1 vs data point 2, data point 2 vs data point 3, as well as data point 1 vs data point 3 will be conducted. Conducting the t-tests will show if there is a difference between the data points for depression and/or anxiety individually.

For all of the statistical tests that are planned above, is based on the assumption that the tests needed will be parametric (i.e. ANOVA and paired samples t-test). However if after data analysis has been conducted and the data is skewed or does not meet assumptions, non-parametric tests will be implemented instead (i.e. Kruskal Wallis and Wilcoxon Signed-Rank test).

Pass/Fail criteria to be applied to the results of the clinical investigation:
Participants in both the experimental and placebo group will have exposure to the SoeMac. The experimental group will be exposed to singlet oxygen energy (SOE), compared to the placebo group, which will not be exposed to SOE. The pass/fail criteria will be applied to the results of this clinical trial, based on whether the SoeMac device is safe to use and any reported AE's and SAE's, changes in CAT score (i.e. primary objectives/outcomes) and improvements to sleep quality and psychological well-being(i.e. secondary objective/outcomes) etc.

13.2 THE NUMBER OF PARTICIPANTS

Sample Size Analysis

As this RCT is to evaluate the safety and efficacy of using the SoeMac device, which has yet to be scientifically tested as a pilot study, the preliminary findings are to provide a foundation to further evaluate the SoeMac device for additional larger-scale studies and therefore a significantly higher number of participants will be recruited.

As such as this is a foundation pilot study, it is advised and important to recruit a minimum of 48 participants (24 in the active group; 24 in the placebo group) which has been derived by other non-pharmacological randomised clinical trials in respiratory (Chan et al., 2006; Freitas et al., 2021) to collect data to be able to analysis and show the evaluation of the safety and efficacy of the SoeMac device for a minimum worthwhile effect. As this is a minimum number of participants, it is not the max. This means that within the study duration of participant recruitment more participants can be recruited (i.e., if eligible) to take part in the study, with a max number of 100 participants (50 participants in active; 50 in placebo group).

Power Calculation Analysis – (G*Power 3.1.9.4)

G* Power 3.1.9.4 a prospective power analysis was conducted to achieve a medium effect size with an alpha level of 0.05, with an effect size of 0.20, creates a minimum sample size total of 42, 21 in the active group and 21 participants in the placebo group to meet the power of 0.8 (3 condition in total which are the data points, the experimental group – pre, mid, end; placebo group – pre; mid; end = 42, 42 divided by 3 = 14 x 3 = 42), with 1 measurement (CAT). This means to avoid a type I or a type II error and to have clinically relevant significance, a minimum of 42 participants would be needed to avoid a type I (rejecting the null hypothesis but the null hypothesis is true in reality) or a type II error (failing to reject the null hypothesis but the null hypothesis is false in reality). As this study is a double-blind randomised clinical trial, the statistical power is based on the primary objective and primary endpoint (Valojerdi, Tanha & Janani, 2017). Therefore, the statistical power is based on the global CAT score.

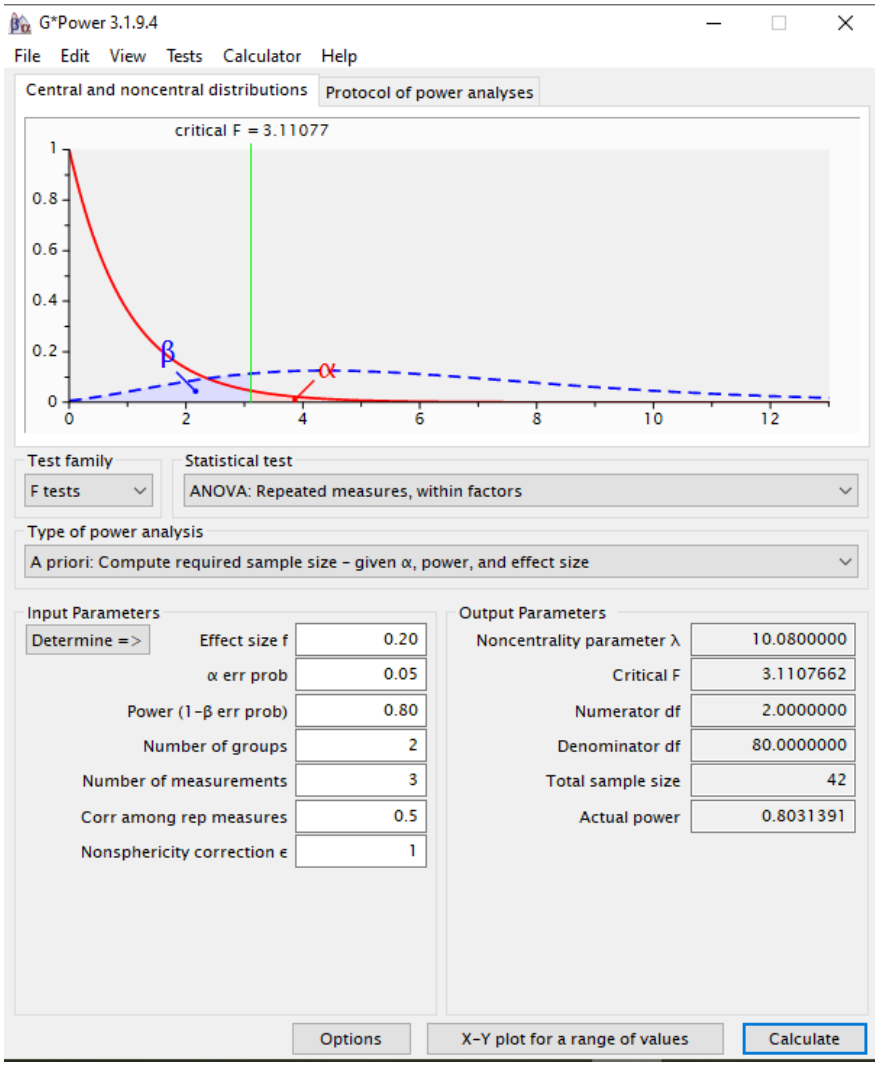


Figure 6 – G Power 3.1.9.4 Screenshot of Power Calculation Analysis

Expected Dropout rate:

Dropout rates are to be expected and is a common occurrence in randomised clinical trials (Bell et al., 2013). A review was conducted in 2004, reviewing from top medical journals, 71 randomised controlled trials and showed that on average the dropout rates are around 20% or more in 18% of the trials (Wood, White & Thompson, 2004). Similarly, a review was conducted from 328 treatment groups, consisting of 18, 585 randomised subjects from 163 drug trials, with a dropout rate of 33% (Wahlbeck et al., 2001).

However as the majority of randomised clinical trials are conducted in hospital clinics, away from home cannot be applied to this study. As this study because of COVID-19, has been adapted for the study to take place within the community i.e. with the participants home meaning they do not have to travel to and from the hospital clinic, questionnaires are kept to a minimum of 3, across 3 data points, as well as being in contact with the participants every 2 weeks, across 8 weeks, therefore building up rapport between the research team and each participant. As well as this treatment as usual and medication is not being stopped

or altered. All of these factors will therefore have a positive impact in reducing dropout rates and increasing participant adherence. A randomised clinical trial was conducted within the community with COPD patients and the dropout rate was 15% (Hernández et al., 2015).Therefore, within this clinical trial, it will be advised based on the above research from Hernández et al., (2015) to expect a dropout rate of around 15% . This means depending on the rate of the recruitment and intake of participants, additional participants will need to be recruited, to take into account dropout rates and to reduce the potential source of bias (Bell et al., 2013). Calculations have been therefore been conducted for the recruitment figures of n=42 from the power analysis workings.

Total of n=48; n=24 (groups; experimental & control):

- n=48 + 15% = 48 (n=24 per group)

Based on the above calculations it would be advised to recruit a minimum of 24 participants per group (experimental & control) (48 in total), to account for potential dropouts. This will increase the chances of having a data set of 24 participants per group or 48 in total.

13.3 THE LEVEL OF STATISTICAL SIGNIFICANCE

The level of significance will be 0.05 and 80% (0.8) statistical power. This is recommended by Cohen (1988, 1992), as a 0.2 probability of not being able to retrieve an effect that is genuine, the level of power ideally should be 0.8, which means that there is an 80% chance of seeing a genuine effect and if one exists.

13.4 CRITERIA FOR THE TERMINATION OF THE CLINICAL INVESTIGATION

The clinical trial will be terminated on the statistical grounds from either an insufficient sample size of participants, a lack of power, a high dropout rate and if the trial reaches the end of its time frame.

Insufficient Sample Size/Lack of Power:

Many clinical trials do end before the trial has even started (Morgan, 2017). According to William et al., (2015) 12% of clinical trials that have been listed, have been terminated, with the main reason being that the trials had an insufficient number of participants recruited to the clinical trial. At the start of the trial, depending on the ease of participant recruitment, the aim will be to recruit a minimum of 48 participants (24 in each group; experimental/control). However, if less than 48 are recruited for example 47 and below (<47) (23 and less per group; experimental <23/control <23), it is advised for the trial to be terminated. This is because the trial will not have the minimum number of participants for adequate sample size and will be a loss of study power. Therefore, the minimum of participants is needed, so power of 80% (0.8) is achieved, to mitigate the problem, as often sufficient power in clinical trials is still problematic (Lamberink et al., 2018). A significant factor that can contribute to poor recruitment and early termination of a clinical trial can be because of strict inclusion/exclusion criteria (William et al., 2015). Therefore, the inclusion/exclusion criteria for this proposed clinical trial has been modified and reviewed, to accommodate and to decrease the likelihood of the criteria being too strict, significantly impacting study recruitment numbers and terminating the trial prematurely. As well as this, after 4 weeks

from the onset of the study commencing, the recruitment enrolment figures will be reviewed, collectively as a study team. If for example, the recruitment target (i.e. a minimum of 24 participants in each group; active and placebo, factors will be explored as to why this is and if the criteria are still too conservative, this may be altered and decided by the chief investigator. If the criteria are altered, this will be reviewed in another 4 weeks, to review whether recruitment enrolment figures have increased, to match with the desired recruitment targets.

High Dropout Rate:

Similarly, if participants have been recruited, screened, and enrolled on to the clinical trial but before the completion of the trial decision to withdraw, and the number of participants dropping out is significantly high, this is another reason for the trial to be terminated. This is because there is a set period for the trial to start and to finish, which includes a set time for participant recruitment and enrolment (i.e., 8 weeks from start to finish +-7 days) with the required minimum of participants, as stated above. As mentioned in section 13.2, it is likely there will be participants that withdraw and therefore drop out, which is to be expected. Therefore, based on a dropout rate of 15%, as the aim is to recruit a minimum of 48 participants in total (i.e. 24 participants in each group; experimental/control), includes a likelihood of a 15% drop out which is 6 additional participants (42 + 6 = 48), therefore accommodating the minimum data set according to the power calculations. It is of paramount importance for the minimum at least which is a dataset that consists of 48 participants within the final data set and has enrolled fully within the trial from start to finish, as this is needed to be able to conduct the statistical analysis to analyse the primary outcome as a priority and then the secondary outcomes. If the figure falls below 48 (i.e., <47) in total (<23 per group) without the time to recruit further participants and not having the time or resources because it is too late in the trial timeframe, the trial will be terminated.

The calculations of <48 i.e., 47 participants or less in total for the clinical trial to be terminated as an example at >15% i.e. 16% and above:

- n=48 – 8 = 40 (16%)

Therefore, based on the above estimate calculations including dropout rates, if the dropout rates are a minimum of 15% and above >15%-16% based on the absolute minimum number of participant numbers, this will be a significant drop out rate and the trial will be terminated.

Missing/Incomplete Data:

Data that is missing, can seriously compromise inferences from a clinical trial that has been conducted, reducing the ability to draw definitive conclusions (Little et al., 2012), causal links (Dziura et al., 2013), the reliability of the results and degrading the efficiency of the data (Kwak & Kim, 2017).

Recent statistical guidance has stated that if there is more than 40% of data missing in important variables (i.e., CAT, CASIS, ESS, PHQ-4) then results, can only be used for generating the hypothesis (Don & Peng, 2013; Jakobsen et al., 2017). Also, missing data which equates to over 40% is considered as very large on important variables (Clark & Altman, 2003). Therefore, if more than >40% of the data set is missing or there is less than 60% in total has been completed for the majority of the bare minimum of n=24 per group (n=48) participants,

the trial will be terminated, as imputing the missing a final data set, that the majority includes missing data values of >40% (<60% completed data set) and above of the important variables would create bias and inferences would not be able to be drawn. Consequently, this omits the objectives of the trial i.e., if the SoeMac device is safe to use and if it reduces COPD symptomology and increases, sleep quality and psychological wellbeing, compared to the control group.

13.5 PROCEDURE FOR ACCOUNTING FOR MISSING, UNUSED AND SPURIOUS DATA
Missing Data:

For data analysis to be conducted, the statistical procedures that are planned require a complete data set, without having missing values.

If the minimum number of participants have been recruited >n=48 in total, with the majority having complete data sets (i.e., 100%), some participants data will be below 60% completion and is to be expected and will be excluded (see Section 13.7 Inclusion in Analysis).

On the other hand, some participant's data will be between 60% to 99%. Therefore, instead of excluding and omitting from the final dataset to be analysed, the missing data will be reviewed, and the specific procedure will be adhered to – Multiple Imputation (MI) or list-wise deletion. It is likely as the final data set will be comparing means of several different dependent variables (see Section 13.1) and therefore questionnaires that are required to complete across three data points, it is likely data will be missing, before inputting into SPSS and analysed using an ANOVA, as well as paired samples t-test. For example, if the data is 'missing at random (MAR), a multiple imputation analysis will be conducted. MI is a valid method for handling missing data in randomised clinical trials and can be used with most types of different data (Sterne et al., 2009). When conducting the MI, the practical guide by Jakobsen, Gluud & Winkel, (2017) will be adhered to. Finch, (2016) used both list-wise deletion and multiple imputation and when using multiple imputation analysis, with data that was missing at random, the data maintained the Type I error and had power comparable to the complete data condition. As well as this, when 40% of the data were missing at random, the type I error rates were inflated but not for lower percents (Finch, 2016). As well as this Logan et al., (2014) used MI, for the researchers' randomised controlled study to replace missing values for all outcome measures. MI has been applied to public health research including COPD, compared to simple imputation methods, when conducting an MI, stated better standard deviation estimates compared to single mean imputation (Zhou, Eckert & Tierney, 2001). On the other hand, alternative approaches for handling missing data such as mean substitution, regression imputation and hot-deck imputation is inadequate and unable to reproduce accurately, population parameters and standard errors (Schafer & Graham, 2002). Therefore, MI will be implemented for missing values for MAR.

As standard practice, to make sure that the data is MAR, Little's test, will be implemented and if the test for 'missing completely at random (MCAR) data is significant, it can be assumed that the data is MAR and a MI can be conducted (Schafer & Graham, 2002). If the Little's test is non-significant, the data is, therefore, MCAR, with no systemic cause and therefore list-wise deletion will be used. This means that the missing data will not be calculated and imputed but will be omitted from the final dataset (Allison, 2001).

Unused Data: All data will be used, as only data that will be used to demonstrate the safety and effectiveness of the SoeMac device and whether the device reduces COPD symptomology and increases sleep quality and psychological wellbeing will be collected. Anonymised data will be used in future publications. Consequently, there will not be any data that will be unused.

Spurious Data: No data will be considered spurious in the final data analysis, as the data will be checked and cleaned before any analysis is to be conducted, as data cleaning is essential. This includes winsorising, which will reduce any possible spurious and extreme outliers, with a specified percentile of the data (Salkind, 2010). Winsorising was used within a randomised control study by Logan et al., (2014) whereby replacing data values below the 5^{th} percentile, with the 5^{th} percentile value and the same procedure for values above the 95^{th} percentile with the 95^{th} percentile value, which reduced extreme outliers. A similar approach will be adopted for the winsorising of this clinical trial final data set. Checking and cleaning the final data set before the final data analysis, ensures that conclusions can be drawn from the data received, making the claims are as generalisable as possible (Osbourne, 2010). Therefore, if there is a causal link between variables, it is certain that it will be and not a spurious correlation (Osbourne, 2010).

13.6 PROCEDURES FOR REPORTING ANY DEVIATIONS(S) FROM THE ORIGINAL STATISTICAL PLAN

The data analysis will be conducted according to Section 13.1 'Description of statistical methods. There are no known reasons for which it is planned to deviate from these analysis methods, as stated within the original statistical plan. If, however, a change is made, the change will be documented in the final study report, along with a justification for the change.

13.7 INCLUSION IN ANALYSIS

All double-blind randomised participants that are eligible (i.e., ≥ 40 years of age, CAT Score ≥ 10, Previous smoker (number of packs per day) x (years) must be ≥ 20 pack-years, Previous diagnosis of COPD from GP/Doctor) (see Study Schematic), who has COPD, consented and they have completed the clinical trial, will be included in the final data analysis. The received data from 48 participants and above, with more than >60% completion/less than 40% missing data of the primary and secondary outcomes, shall be included in the final data analysis i.e., participants from both the experimental and the control group. (see section 13.1).

Therefore, there are no exclusion criteria per se for specific participants within the final data set, not to be included in the data analysis. However, the data that would be excluded would-be participants that have completed the trial but they have completed less than 60% of the questionnaires, who will be excluded/omitted using list-wise deletion. This is because the imputation analysis will be impossible to use, and potentially bias the final data set (Jackobsen et al., 2017). The data will be analysed as stated in Section 13.1 'Description of statistical methods, using an ANOVA , with post hoc testing, as well as paired samples t-test.

14. SAFETY REPORTING

14.1 DEFINITIONS

14.1.1 Adverse Event (AE)

Any untoward medical occurrence in a clinical study where participants are administered a medicinal product, which does not necessarily have to have a causal relationship with this treatment (i.e., the SoeMac Device). An AE can, therefore, be any unfavourable and unintended sign, symptom or disease temporally linked with the use of the study medical device (SoeMac Device), whether or not considered related to the study device (SoeMac Device).

An AE includes:

- Exacerbation of pre-existing illness
- Increase in frequency or intensity of a pre-existing episodic event or condition
- Condition detected or diagnosed after study intervention (SoeMac Device) even though it may have been present before the start of the study
- Continuous persistent disease or symptoms present at baseline that worsens following the start of the study

An AE does not include:

- Medical or surgical procedure (e.g., surgery, tooth extraction) but the condition that leads to the procedure is an AE
- Pre-existing disease or conditions present or detected at the start of the study that did not worsen
- Situations where an untoward medical occurrence has occurred (e.g. hospitalisations for cosmetic elective surgery)
- Disease or disorder being studied, or sign or symptom associated with the disease or disorder unless more severe than expected for the participant's condition
- Overdose of concurrent medication without any signs or symptoms

14.1.2 Adverse Device Effect (ADE)

All untoward and unintended responses to the medical device.

The phrase "responses to a medical device" means that a causal relationship between the device under investigation and an AE is at least a reasonable possibility, i.e., the relationship cannot be ruled out.

All cases judged by either the reporting medically qualified professional or the sponsor as having a reasonable suspected causal relationship to the device qualifies as a device effect.

This also includes any event resulting from insufficiencies or inadequacies in the instruction for use or deployment of the device and includes any event that is a result of a user error.

14.1.3 Serious Adverse Event (SAE)

SAE is an adverse event that:

- Led to death.
- Led to foetal distress, foetal death or congenital abnormality or birth defect.
- Led to a serious deterioration in the health of the subject that:
    - Resulted in a life-threatening illness or injury.

  - NOTE: The term "life-threatening" in the definition of "serious" refers to an event in which the participant was at risk of death at the time of the event; it does not refer to an event that hypothetically might have caused death if it were more severe.
- Resulted in a permanent impairment of a body structure or a body function.
- Required in-patient hospitalisation or prolongation of existing hospitalisation.
- This resulted in medical or surgical intervention to prevent permanent impairment to a body structure or a body function.
- Other important medical events
  - Other events that may not result in death, are not life-threatening or do not require hospitalisation, may be considered a serious adverse event when, based upon appropriate medical judgement, the event may jeopardise the patient and may require medical or surgical intervention to prevent one of the outcomes listed above.

To ensure no confusion or misunderstanding of the difference between the terms "serious" and "severe", which are not synonymous, the following note of clarification is provided:

The term "severe" is often used to describe the intensity (severity) of a specific event (as in mild, moderate, or severe myocardial infarction); the event itself, however, may be of relatively minor medical significance (such as severe headache). This is not the same as "serious," which is based on patient/event outcome or action criteria usually associated with events that pose a threat to a participant's life or functioning. Seriousness (not severity) serves as a guide for defining regulatory reporting obligations.

14.1.4 Serious Adverse Device Effects (SADE)

A serious adverse device effect (SADE) is any untoward medical occurrence seen in a patient that can be attributed wholly or partly to the device which resulted in any of the characteristics or led to characteristics of a serious adverse event.

SADE is also any event that may have led to these consequences if suitable action had not been taken or intervention had not been made or if circumstances have been less opportune.

All cases judged by either the reporting medically qualified professional or the sponsor.

14.1.5 Unanticipated Serious Adverse Device Effect (USADE)

Any serious adverse device effect on health or safety or any life-threatening problem or death caused by, or associated with a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that related to the rights, safety or welfare of the subject.

14.2 REPORTING OF AEs

All AEs occurring during the clinical investigation observed by the investigator or reported by the participant, whether or not attributed to the device under investigation will be recorded on the CRF as specified in the clinical investigation plan. All ADEs will be recorded in the CRF.

The following information will be recorded: description, date of onset and end date, severity, assessment of relatedness to the device, other suspect drug or device and action is taken. Follow-up information should be provided as necessary.

The relationship of AEs to the device will be assessed by a medically qualified investigator or the sponsor/manufacturer and will be followed up until resolution or the event is considered stable.

All ADE that results in a participant's withdrawal from the clinical investigation or is present at the end of the clinical investigation, should be followed up until a satisfactory resolution occurs.

Where relevant, any pregnancy occurring during the clinical investigation and the outcome of the pregnancy should be recorded and followed up for congenital abnormality or birth defect.

14.3 REPORTING PROCEDURES FOR ALL SAEs/ SADEs/ USADEs

For Non-CE marked device clinical investigation: All SAE/SADE/USADEs need to be reported to the sponsor/legal representative and manufacture and NUH R&I **immediately**; regardless of relationship to the device.

All SAEs, must be reported to R&I within one working day of discovery or notification of the event. As Sponsor, R&I at NUH will report all SUSARs /USADEs to the Competent Authorities (MHRA and the Research Ethics Committee) concerned. Fatal or life-threatening SUSARs/USADEs must be reported within 7 days and all other SUSARs/USADEs within 15 days. The CI will inform all investigators concerned with relevant information about SUSARs that could adversely affect the safety of participants.

Reporting to the MHRA will be done in liaison with the Chief Investigator and the Manufacturer.

The Manufacturer has a legal obligation to report all events that need to be reported to the Nominated Competent Authority immediately (without any unjustifiable delay) after a link is established between the event and the device, but no more than:

- 2 days following the awareness of the event for Serious Public Health Threat.
- 10 days following awareness of the event for Death or unanticipated serious deterioration in health.
- 30 days following the awareness of the event for all other event meeting the SAE criteria.

Reporting Procedures for All Adverse Events

Adverse event (AE) and Serious Adverse Event (SAE) will use NUH NHS Trust reporting procedures.

All adverse events should be recorded on the CRF. Reporting of AE/SAEs/ADs/ADEs/USADEs to the Sponsor should be done on the appropriate Sponsor template. Any questions concerning adverse event reporting should be directed to the Chief Investigator in the first instance. Local Investigators will be contacting all participants in both the experimental and control group every 2 weeks from Day 0 (after baseline) (i.e. Day 14, Day 28, Day 42, Day 56, Day 70) and the adverse events will verbally be asked on the last week of the trial on Day 84. This is to check if any participant has experienced an AE or SAE. All participants will be provided with contact details for a trial phone, where they can communicate AE/SAE throughout the study and will be operated during working hours (Monday to Friday 9-5). Outside of these working hours, participants are encouraged to leave a voicemail and the study team will contact them back as soon as possible during working hours.

The following information will be recorded: description, date of onset and end date, severity, assessment of relatedness to using the SoeMac Device and action is taken. Follow-up information should be provided as necessary. AEs considered related to the study device (SoeMac Device) as judged by a medically qualified investigator or the sponsor will be followed until resolution or the event is considered stable. All related AEs that result in a participant's withdrawal from the study or are present at the end of the study, should be followed up until a satisfactory resolution occurs. It will be the responsibility of the Chief Investigator's clinical judgement whether an AE is of sufficient severity to require the participant's removal from using the SoeMac Device and the participant's involvement in the study will be terminated. The relationship of AEs to the study device (SoeMac Device) will be assessed by a medically qualified investigator. All such events, whether expected or not will be recorded

An SAE form should be completed and forwarded to the sponsor or delegated representative within 24 hours. The chief investigator Dr Sovani Milind will review and sign all SAE reports. However, relapse and death due to COPD and hospitalisations for elective treatment of a pre-existing condition do not need reporting as SAEs. All SAEs should be reported to the study sponsor and the Research Ethics Committee where in the opinion of the Chief Investigator, the event was:

- 'Related', i.e., resulted from the administration of any of the research procedures; and
- 'Unexpected', i.e. an event that is not listed in the protocol as an expected occurrence

SAE reports must be sent to R&I using one of the following methods:

i. Email: RDSAE@nuh.nhs.uk

ii. Hand Delivered (Not Mailed): R&I, NHSP, C Floor, South Block, QMC

iii. Telephone: Landline: 0115 9709049 (If written report not immediately possible) or for mobile because of remote working – Ms Elaine Blackshaw Trial Manager - 07305 597 462 (who can then escalate to R&I)

The governance and quality team will facilitate an independent assessment of the event within 1 working day of receiving the SAE report.

The intensity of the AE will initially be assessed according to the following definitions:

Mild: An event easily tolerated by the participant, causing minimal discomfort and not interfering with everyday activities

Moderate: An event sufficiently discomforting to interfere with everyday activities

Severe: An event that prevents everyday activities

All AE and SAE Reporting documentation (i.e. NHS National Patient Safety Agency, National Research Ethics Service, Report of Adverse Event (AE) and Serious Adverse Event) physical copies of these will be kept in the Trial Master File.

14.4 ANNUAL REPORTS

In addition to the expedited reporting above, the CI shall submit once a year throughout the clinical investigation or on request a Safety Report to R&I, the Competent Authority MHRA and Ethics Committee.

15. CLINICAL INVESTIGATION MANAGEMENT

15.1 CLINICAL INVESTIGATION MANAGEMENT GROUP

Detail who will form part of the clinical investigation management group what their role will be and what they will be responsible for.

Trial Management Committee:

An independent trial management committee (TMC) will be established to oversee and review adverse events (AEs) and serious adverse events (SAEs), and they will be responsible for reviewing documentation including AE and SAE forms. The TMC will consist of an experienced respiratory clinician, the trial monitor, and the named statistician (Dr Emma Sharpe) and will meet on an 8-weekly basis throughout the process of data collection and where necessary if a post data collection AE/SAE is reported.

15.2 CLINICAL INVESTIGATION STEERING COMMITTEE

As with the TMC, we will establish a clinical investigation steering committee that will meet throughout the delivery of the trial, on an 8-weekly basis. The committee will consist of the core research group and independent clinical, patient, regulatory, and representation from the sponsor.

15.3 DATA MONITORING COMMITTEE

The data monitoring committee will consist of representation from the core research group (including the PI and named statistician) alongside representation from clinical staff, an independent data analysis consultant and the research sponsor.

15.4 INSPECTION OF RECORDS

Investigators and institutions involved in the clinical investigation will permit clinical investigation related monitoring and audits on behalf of the sponsor and regulatory inspection(s). In the event of an audit or monitoring, the Investigator agrees to allow the representatives of the sponsor direct access to all clinical investigation records and source documentation. In the event of regulatory inspection, the Investigator agrees to allow inspectors direct access to all clinical investigation records and source documentation.

15.5 RISK ASSESSMENT

A risk assessment will be performed by the Sponsor to determine if monitoring is required and if so, at what level.

15.6 CLINICAL INVESTIGATION MONITORING

A Sponsor representative will visit the Investigator site before the start of the clinical investigation and during the clinical investigation if required, following the monitoring plan. Monitoring will be performed according to ICH GCP. Data will be evaluated for compliance with the clinical investigation plan and accuracy of source documents. Following written standard operating procedures, the monitors will verify that the clinical investigation is conducted, and data are generated, documented, and reported in compliance with the clinical investigation plan, GCP and the applicable regulatory requirements.

16. GOOD CLINICAL PRACTICE

Describe ethical considerations relating to the clinical investigation. Include general and clinical investigation specific ethical considerations.

Participants will be approached in line with Good Clinical Practice (GCP) guidelines. An open and honest discussion regarding study aims, methods, risks, and benefits will occur, including a discussion of data collection and confidentiality. Baseline data will be collected by a member of the research team following information governance principles and according to Data Protection Act regulations. This information will be obtained, with the consent of each participant, through direct questioning of the participant.

16.1 DECLARATION OF HELSINKI

The Investigator will ensure that this clinical investigation is conducted in full conformity with the current revision of the Declaration of Helsinki (last amended October 2000, with additional footnotes, added 2002 and 2004).

16.2 ICH GUIDELINES FOR GCP

The Investigator will ensure that this clinical investigation is conducted in full conformity with relevant regulations and with the ICH Guidelines for Good Clinical Practice (CPMP/ICH/135/95) July 1996.

16.3 APPROVALS

Consider the following text:

The clinical investigation plan, informed consent form, participant information sheet and any proposed advertising material will be submitted to an appropriate Research Ethics Committee (REC), regulatory authorities (MHRA in the UK), and host institution(s) for written approval.

The Investigator will submit and, where necessary, obtain approval from the above parties for all substantial amendments to the original approved documents.

16.4 PARTICIPANT CONFIDENTIALITY

The clinical investigation staff will ensure that the participants' anonymity is maintained. The participants will be identified only by initials and a participant's ID number on the CRF and any electronic database. All documents will be stored securely and only accessible by clinical investigation staff and authorised personnel. The clinical investigation will comply with the Data Protection Act which requires data to be anonymised as soon as it is practical to do so.

16.5 OTHER ETHICAL CONSIDERATIONS

Assessment and management of risk

All research and related activities will be conducted according to the good clinical practice (GCP) guidelines and established guidelines/protocols derived from the relevant bodies/organisations. All members of the research team will be competent in all forms of assessment before being involved in the data collection process.

Lone Working Policy

The study is designed to be delivered remotely therefore the Lone Working Policy is not applicable in this instance.

Research Ethics Committee (REC) Review & Reports

The study protocol along with supplementary documents (consent form, participant information sheets) will be submitted via IRAS to HRA REC for ethical review and approval. All correspondence with REC will be retained in the Trial Master File.

The study will not commence before the protocol, and associated documents have received approval and review from the Medicines and Healthcare products Regulatory Agency (MHRA), Research Ethics Committee (REC) and the respective National Health Service (NHS) Research & Innovation (R&I) department.

Any deviations to the Clinical Investigation Plan will be reported to MHRA including a justification and an evaluation of the impact of those deviations on the veracity of the data generated and the conclusions that can be drawn from the investigation about the performance and safety of the device.

Any deviations from the literature search protocol should be noted in the literature search report.

Protocol Compliance

All study staff must remain compliant with the study protocol in its current form (Effective date 21-07-2021). Deviations, non-compliance, or breaches from the approved protocol

should be reported at the earliest opportunity to the Chief Investigator and study Sponsor. Frequent and recurrent deviations are not acceptable and require immediate remedial action to be taken.

16.6 DATA PROTECTION AND PARTICIPANT CONFIDENTIALITY

All investigators and study site staff will comply with the requirements of the Data Protection Act 2018 with regards to the collection, storage, processing, and disclosure of personal information and will uphold the Act's core principles. This includes a trial independent monitor which will carry out the monitoring of the study data as an ongoing activity.

Staff involved in the study will ensure that all participants' confidentiality is maintained. The participants will be identified only by full name (for telephone and postal correspondence), and a unique participant study identification number on the CRF and central electronic database. All documents will be stored securely and only accessible by staff involved in the study and authorised personnel. The study will comply with the Data Protection Act (in the UK) and with local legal requirements alongside the principles of ICH-GCP (worldwide); in line with this, all data will be anonymised as soon as it is practical to do so. The fully anonymised study data will be stored for at least 25 years (as per SOP-RES-028) following the closure of the study and thereafter disposed of in line with regulatory requirements. No participant will be individually identified in any subsequent publications relating to this study.

The study database will be kept on Microsoft Excel© and hosted on the Nottingham University Hospitals NHS Trust server. The server and database are protected by several measures including anti-virus and anti-spyware applications, firewalls, encryption technology and permissions. Data will be entered onto the paper CRF and retained and stored securely until the study end date. The data will be securely stored in line with ICH-GCP standards and data protection principles. The data stored will be checked for missing or unusual values and for consistency within participants over time. If any problems are identified, the appropriate CRFs will be reviewed in discussion with relevant local site personnel and queried for confirmation or correction as required until resolution.

The Chief and Principal Investigators, sponsor, and authorised staff will have access to participants' data. The Chief Investigator and/or Principal Investigators will facilitate access to study records for monitoring, audits, and regulatory inspections.

16.7 ACCESS TO THE FINAL STUDY DATASET

The study database will be kept on Microsoft Excel© and hosted on the Nottingham University Hospitals NHS Trust server. The server and database are protected by many measures including anti-virus and anti-spyware applications, firewalls, encryption technology and permissions. Data will be entered onto the paper CRF and retained and stored securely until the study end date.

The data will be securely stored in line with ICH-GCP standards and data protection principles. The data stored will be checked for missing or unusual values and for consistency within participants over time. If any problems are identified, the appropriate CRFs will be reviewed in discussion with relevant local site personnel and queried for confirmation or correction as required until resolution.

The Chief and Principal Investigators and authorised staff will have access to participants' data. The Chief Investigator and/or Principal Investigators will facilitate access to study records for monitoring, audits, and regulatory inspections.

17. CLINICAL INVESTIGATION CONDUCT RESPONSIBILITIES

17.1 CLINICAL INVESTIGATION PLAN AMENDMENTS

Amendments to the clinical investigation plan must be submitted to the Sponsor for review before submitting to the appropriate REC, Regulatory Authority, and local R&D for approval.

Amendments to the study protocol will be handled according to the Health Research Authority's guidelines for Non-CTIMP studies. Decisions to amend the protocol will be the responsibility of the Sponsor in consultation with the Chief Investigator and Principal Investigator. The Sponsor will have responsibility for determining the category of each amendment (Substantial versus Non-Substantial). All substantial and non-substantial amendments will be reported directly to the Nottingham University Hospitals Trust Research Ethics Committee. It will be authorised by the Sponsor and Chief Investigator before submission. The appropriate documentation, clearly detailing changes, will be emailed to the responsible REC for review. Should a protocol amendment be made that requires REC approval, the changes in the protocol will not be instituted until the amendment and revised participant consent forms and participant information sheets (if appropriate) have been reviewed and received approval from the REC and R&I departments. A protocol amendment intended to eliminate an apparent immediate hazard to participants may be implemented immediately providing that the MHRA, R&I and REC are notified as soon as possible, and approval is requested. Minor protocol amendments only for logistical or administrative changes may be implemented immediately and therefore the REC will be informed.

17.2 CLINICAL INVESTIGATION PLAN VIOLATIONS, DEVIATIONS AND SERIOUS BREACHES

The CI will not implement any deviation from the clinical investigation plan without agreement from the Sponsor, except where necessary to eliminate an immediate hazard to clinical investigation participants.

If the CI needs to deviate from the clinical investigation plan, the nature of and reasons for the deviation will be recorded in the CRF and notified to the Sponsor. If this necessitates a subsequent clinical investigation plan amendment, this will be submitted to the Sponsor for approval and then to the appropriate REC, Regulatory Authority and local NHS R&I for review and approvals as appropriate. It is Sponsor policy that waivers to the clinical investigation plan will not be approved.

If a serious breach of GCP is suspected, this will be reported to the Sponsor immediately. Refer to SOP-RES-017 "Non-Compliance and Serious Breach Reporting".

17.3 CLINICAL INVESTIGATION RECORD RETENTION

All clinical investigation documentation will be kept for 25 years from the clinical investigation plan defined end of clinical investigation point. When the minimum retention period has elapsed, clinical investigation documentation will not be destroyed without permission from the sponsor.

In compliance with the ICH/GCP guidelines, regulations and following the University Hospitals NHS Trust Code of Research Conduct and Research Ethics the Chief Investigator will maintain all records and documents regarding the conduct of the study.

These will be retained for at least 25 years (or for longer if required). If the Chief Investigator is no longer able to maintain the data records, an alternative person will be nominated to take over this responsibility.

The Trial Master File and Trial documents held by the Chief Investigator on behalf of the Sponsor shall be finally archived by the sponsor Nottingham Hospitals NHS Trust. This archive shall include all study databases and associated meta-data encryption codes.

17.4 END OF CLINICAL INVESTIGATION

The end of clinical investigation is defined as the last telephone consultation with the participant, and they have been provided with instructions on how to send the SoeMac device back to the study team, they have asked any questions they may have and that will be the end of the study.

The Investigators and/or the clinical investigation steering committee and/or the co-sponsor(s) have the right at any time to terminate the clinical investigation for clinical or administrative reasons.

The end of the clinical investigation will be reported to the REC and Regulatory Authority within 90 days, or 15 days if the clinical investigation is terminated prematurely. The Investigators will inform participants of the premature clinical investigation closure and ensure that the appropriate follow up is arranged for all participants involved.

A summary report of the clinical investigation will be provided to the REC and Regulatory Authority within 1 year of the end of the clinical investigation.

The end of the study is the date of the last remote telephone consultation (post-study follow up) of the last participant enrolled.

17.5 INSURANCE AND INDEMNITY

NHS bodies are legally liable for the negligent acts and omissions of their employees. If you are harmed whilst taking part in a clinical investigation as a result of negligence on the part of a member of the clinical investigation team this liability coverage would apply.

Non-negligent harm is not covered by the NHS indemnity scheme. The Nottingham University Hospitals NHS Trust, therefore, cannot agree in advance to pay compensation in these circumstances. In exceptional circumstances, an ex-gratia payment may be offered.

This study is funded by Medilink (Ref. MTT-ISG-INS-126) 50% and the University of Derby – Research Excellence Funding 50%. Indemnity will be provided by the University of Derby who is acting as co-funder for this study.

Insurance and indemnity for Dr Mark Faghy and Samuel Grimwood who are contracted at the University of Derby, as an institution is a member of U.M. Association Limited and Excess Cover providers led by QBE UK Limited and therefore are the acting insurance and indemnity providers in this instance. NUH indemnity/insurance does not apply to Dr Mark Faghy, Dr Amy

Baraniak, Dr Emma Sharpe and Samuel Grimwood, as they do not have a contractual link with NUH (Appendix 12, 13).

However, insurance and indemnity are provided by NHS NUH as the sponsor of the trial for the Trial Manager Elaine Blackshaw, and research nurse who will have an NHS Employment Contract.

Mr Neil Stentiford from the manufacturer SoeHealth Ltd has indemnity and public liability led by QBE UK Limited for the SoeMac device (Appendix 14), which includes the use of the SoeMac device within this study (Appendix 15).

17.6 PARTICIPANT INCENTIVES

Participants will be able to acquire a SoeMac device for personal use once the participant has fully enrolled on the study, the study has formally ended. The participant will be provided with a special discount code by the study team, should they wish to obtain a SoeMac device and they will be able to order this directly from the manufacturer free of charge. This is a token of thanks. Participants will not receive payment nor will they be able to exchange the SoeMac device for financial payment.

17.7 FUNDING

- MediLink: Med Tech Trials Innovation Support Grant (MTT-ISG). Funders ref: MTT-ISG-INS-126 (£33,197.76).
- University of Derby: Human Science Research Centre – Research Excellence Investment Funding (£28,366.45).

18. REPORTING, PUBLICATIONS AND NOTIFICATIONS OF RESULTS

18.1 AUTHORSHIP POLICY

Ownership of the data arising from this clinical investigation resides with the clinical investigation team. On completion of the clinical investigation, the clinical investigation data will be analysed and tabulated, and a clinical investigation report will be prepared following ICH guidelines.

Authorship will be determined by the research team on the final study report and subsequent publications, following the International Committee of Medical Journal Editors guidance for authorship of manuscripts submitted for publication. Professional writers will not be employed.

18.2 PUBLICATION

The publication policy should cover authorship, acknowledgements, and review procedures for scientific publications. If there is a department or institution policy, or agreement, the clinical investigation plan can refer to it.

18.3 PEER REVIEW

Detail procedures for peer review – these may be funder specific or involve an internal department.

All data arising from this study will be owned by the Sponsor and shared with named academics from the University of Derby. On completion of the study, the data will be analysed and tabulated, and a Final Study Report prepared by Dr Mark Faghy and Mr Samuel Grimwood. The full study report will be accessible via the R&I team at the Nottingham University Hospitals NHS Trust and the principal investigator.

There shall be no publication or dissemination of the conclusions of the study, including all or any part of the results of the study, without the prior written consent of the Chief Investigator and the Sponsor, such consent not to be unreasonably withheld or delayed.

There shall be no publication or other dissemination of the conclusions of the study until the Sponsor has published the conclusions of the study. Each publication shall acknowledge MediLink and the University of Derby Human Science Research Centre as the funders of the study and the Nottingham University Hospitals NHS Trust as the study sponsor.

There are no plans to notify the participants of the outcome of the study. Participants may specifically request results from the PI; this information would be provided after study results have been published. The study protocol, full study report, anonymised participant-level dataset, and statistical code for generating the results will not be made publicly available.

Manuscripts resulting from the research will be conceived, written, and published at the discretion of the Chief Investigator, in conjunction with the Principal investigator and other members of the research team as appropriate. This activity will be independent of the Research Funder, who will not have any control over the content or results of any publications. It is anticipated that the research will lead to publications in subject-specific international peer-reviewed journals and presentations at international conferences.

19. REFERENCES

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Appendix AX

PhotoVoice Interview Schedule

+

Collated Photos Worksheet *(shared or sent to participant)*

5-10 Photographs

45 minutes to 1 hour

Purpose of interview: To go through each photograph

The photographs should be providing a visual illustration or expression of *your experience* of living with COPD and how it impacts or enhances your quality of life.

The photographs should be an expression and insight in what it is like living with COPD and how it impacts or enhances your quality of life.

Quality of life refers to your overall health and wellbeing. Typically, someone with a higher quality of life would be in good health, feel comfortable in their day-to-day life and is able to take part and enjoy events that arise.

Questions –

1) Please could we go through each photograph that you have taken along with the description you have stated for each one?

   How is each photo linked to you living with COPD? How does this reflect its impact on your quality of life?

   - It would be helpful to explain to me the meaning of each photo
   - What does this mean to you?
   - Why did you decide to take this particular photo?

*** As a reminder to you, there is not a correct or incorrect photo, description and insight, as it is your reflection of your personal day-to-day life*

Appendix AY

Feedback from PPIE to Tersea

Re: BLF Patient Panel - Feedback - 13th October

Samuel Grimwood <S.Grimwood@derby.ac.uk>

Thu 14/10/2021 14:02

To: tburg69@sky.com <tburg69@sky.com>

Cc: Elaine Blackshaw <Elaine.Blackshaw@nottingham.ac.uk>; Neils <Neils@soemac.com>

Hi Teresa

Thankyou for your below feedback in regards to the SAESOE trial.

The patient panel yesterday was a success and appreciate you giving us permission for this to happen.

As promised I wanted to provide you with a summary of what was raised by your members:

- 7 in attendance
- Overwhelming and too many questionnaires and things to do, including sleep diary as well as the 21 questionnaires across the 12 weeks + sleep diary everyday across 84 days
- Lack of motivation
- Lack of trust in the trial, feeling that it will be just like every other trial whereby they take part and left to it, without being informed of the outcomes and results of the study/publications
- Many questionnaires are unfamiliar and not COPD specific, which confused them and not prepared or willing to complete. Happier with questionnaires they are familiar with for example CAT and MRC scale
- They liked the sleep diary, as it was simple but many said they would not be willing to complete and likely to forget to fill it in and then back fill at the end of the week etc and said everyday it is too much to do. Said that fatigue, low mood and lack of energy is already present and therefore this trial adding on to their daily burden is a problem
- Said many of the questionnaires are too long and repetitive – i.e. the x2 sleep questionnaires and then the sleep diary
- They said the AE/SAE phone call every 2 weeks they liked – because they felt that they are then not forgotten about and if something does happen with the SoeMac or their health deteriorates they can talk to us
- Phone calls many said that 60-90 minutes is too long and not happy
- When asked – what would you prefer – they said max 15 minutes and if not less. Some said 30 minutes but that really is max.
- A couple of members said 12 weeks is far too long and said they would lose motivation – happy if it was less, around 6- 8 weeks and have start and end questionnaires (removing data-point half-way) and then every 2 weeks with AE/SAE's
- Sleep diary most said they would happy to complete on its own OR to have a couple of questionnaires across x3 data points but not both the sleep diary and 7 questionnaires three times
- Too many sleep related questionnaires – Epworth, PSQI and then sleep diary
- Most did not like PSQI and too complicated
- EQ-5D-5L not specific to COPD and concerned that their pain or arthritis could influence their QoL and how do we know if it is the SoeMac that has decreased or increased their QoL based on the genera EQ-5D-5L? Happy to complete a more specific COPD QoL however, as several said it was interesting to be asked about their mental health i.e. depression/anxiety which is often overlooked
- Epworth – majority disliked this scale as well

I have noted Teresa that you also have said there are too many sleep questionnaires and the trial needs to be as simple as possible.

The next stages:
If you could please reply to this email to acknowledge that you have read the above, would be greatly appreciated.

I will need to propose a new plan of the changes needed with the team. Then before finalising ask for your feedback again with the revised study design.

We cannot make changes until we have had the formal REC ethics meeting but there is no harm in having a think of what we should and can-do post REC meeting and go from there.

Of course, COPD patients' feedback is paramount, as well as yours as patient representation and I will do my utmost to make sure that changes are made based on the above feedback. Participant adherence is key as well and to have a complete dataset at the end of the trial.

The way the current study has been designed, from the feedback above there are concerns of significant problems with participant recruitment, adherence, missing data, high participant drop out/study being ended prematurely according to NHS Nottingham's R&I policies.

I will be in touch

Kind regards

Samuel Grimwood MSc MBPsS
PhD Student & Postgraduate Research Assistant

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Top 20 Psychology Department - Guardian University Rankings 2022
- *https://www.theguardian.com/education/ng-interactive/2021/sep/11/the-best-uk-universities-2022-rankings*

From: tburg69@sky.com <tburg69@sky.com>
Sent: 08 October 2021 16:42
To: Samuel Grimwood <S.Grimwood@derby.ac.uk>
Subject: Re: BLF Patient Panel

Good afternoon Sam,
Yes happy to have you both at the Breathe Easy meeting on Wednesday.

I feel we are at the stage where it is important to get some patient feedback on the expectations of the patient.
Looking at all the questionaires I would like to see if the patients feel that it is realistic and achievable.
In the protacol you mention drop out rate of 30% I'm sure you appreciate it could easily be higher if we ask too much of the patients.
The sleep diary is fine and to be expected I think patients would expect that. 6 Questionaires at the start , after 6 weeks and 12 week may be seen as a bit onerous. There seems an abundance of sleep questionaires (3) Are they all essential?
Lets see what the patient response is and if they feel that 6 questionaires and the time it may take are acceptable.
Can I just bring to your attention a couple of typos and areas I need clarifying please
1.On the main protacol pg 15 Principle intended use might need re writing
The device works
by the participant
drawing in the air
that the device
produces in the air,
which is a bio-
usable form of
energised oxygen
that the participant simply breathes in overnight when they go to sleep until they wake up.

2. Pg 34 10.4 Storage instructions
Clean with wet wipe once a month and filter change every 4 weeks (e.g. for this trial, therefore the participant will change the filter three times). Instructions will be provided. No where on the patient information or the sleep diary is filter changes mentioned and how to do it
3. Please review all timings for patients In protacol it says Baseline questionaire 60-90 mins in sleep diary it says 30-45 mins In protacol week 6 says 60 mins in sleep diary it says 15-30 mins None of the timings given to the patient match up to the protacol.
Kindest regards,
Teresa Burgoyne

On Thursday, 7 October 2021, 19:08:19 BST, Samuel Grimwood <s.grimwood@derby.ac.uk> wrote:

Hi Teresa

Following on from our discussion I was wondering if it is still ok to attend your BLF meeting next Wednesday 13th October regarding a patient panel, whereby receiving important and insightful feedback for the SAESOE trial?

I will finalise with you and Dr Baraniak, the questions that I will ask and a visual study timeline of what is happening/involved across the 12-week study period etc.

Any feedback that is presented to me - I will state within this email chain and inform you of this and will present this to the SAESOE research team, as retrospective feedback that we will have to take on board and action, therefore.

As well as your BLF member's feedback, it is important also to receive your input and feedback on what you think of the study design, questionnaires and what is being asked for participants to do as the study's patient representative. Please send this to me in reply to this email when you get chance