Development of a Complex Intervention to Promote Pulmonary Rehabilitation Uptake Post Hospitalisation for an Acute Exacerbation of Chronic Obstructive Pulmonary Disease

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PhD Thesis

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Abstract

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Background: Pulmonary Rehabilitation (PR) uptake rate post-Acute Exacerbation of Chronic Obstructive Pulmonary Disease (AECOPD) is known to be suboptimal. Recent research has advocated for targeting patient care priorities to make PR more appealing to its stakeholders. However, limited data is available about the stakeholders' non-pharmacological patient care priorities and the most bothersome exacerbation impact on the patient.

Objectives: To develop a complex intervention based on the stakeholders' patient care priorities to promote PR uptake post-AECOPD. Explore the key stakeholders' non-pharmacological care priorities and the most bothersome impact of exacerbation on the patient during hospitalisation and post-discharge. Lastly, review the effectiveness of interventions developed to promote conventional PR uptake post-AECOPD.

Methods: The Medical Research Council framework was utilised to develop the intervention. The following research steps were conducted; I) Consider context by identifying the problem and refine the understanding of it (conducted through qualitative study), II) Engage key stakeholders who will use the intervention (conducted through Survey and Delphi studies), III) Review published evidence to identify the effectiveness of the previously developed interventions (conducted through Systematic review), IV) Draw on existing theories, V) Articulate the aspect of the programme theory, and VI) Design the preliminary version of the intervention.

Results: 12 participants were recruited in the qualitative study, 50 hospitalised participants were recruited in the patient survey, 46 Healthcare professionals (HCPs) were recruited in round one of the Delphi survey, 45 in round two and eight studies were included in the systematic review. The data synthesis and mapping resulted in a prototype version of the intervention that is set to be delivered in three phases (introduction, preparation, and action) that included a brief educational package, behavioural therapy, and AECOPD PR pathway.

Conclusion: The findings generated from the exploratory research steps highlighted a need for a phased approach to introduce PR that initially targets barriers and secondly supports the stakeholder's prioritised care needs to facilitate PR engagement.

COVID-19 impact statement

When the Coronavirus disease (COVID-19) pandemic started in March 2020, both of this thesis exploratory studies conducted on hospitalised individuals with AECOPD were still in the early stages of the recruitment process (The qualitative study recruitment started in August 2019, and patient survey studies began in November 2019). As all of the Respiratory Wards of our recruitment facility were impacted, access restrictions were then applied. This prevented me conducting any research activities on the Respiratory Wards for an extended period of time due to the local outbreaks. Consequently, the premature stopping of the recruitment process limited our ability to reach data saturation in the care received aspect of our qualitative exploration and prevented us from achieving the patient survey study target sample size.

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Dedication

I have lived very challenging times throughout this PhD journey. This, First due to me living apart from my children for an extended amount of time, and second because half of this PhD years was conducted during the Covid-19 pandemic. Therefore, this PhD is dedicated to my mother, who was the greatest supporter to my children and me, and without her, I would not be able to continue with this PhD journey.

I also would like to dedicate this PhD to my children, Seba and Lara. You both have been my biggest motivation to finish this PhD so I can reunite with you gain. I love you so much, and I wish we never be apart again.

To my father, you always told me that I could do great things in life. I believed you, and this always made wanting to achieve more.

To my husband, classmate, co-worker and friend Khaled, this PhD is dedicated to you, and I will be waiting for yours.

List of Abstracts arising from this thesis

1. **Acute exacerbation of COPD patients therapy priorities: A survey study**

Bedor Alkhathlan, Neil Greening, Theresa Harvey-Dunstan, Sally Singh
European Respiratory Journal 2021 58: PA2122; DOI**:** 10.1183/13993003.congress-2021.PA2122

2. **Acute exacerbation of COPD- What symptoms bothers patients the most: A survey study**

Bedor Alkhathlan, Neil Greening, Theresa Harvey-Dunstan, Sally Singh
European Respiratory Journal 2021 58: PA1987; DOI**:** 10.1183/13993003.congress-2021.PA1987

3. **Acute exacerbation of COPD: A qualitative exploration of the incident symptomatic experience**

Bedor Alkhathlan, Neil Greening, Theresa Harvey-Dunstan, Sally Singh
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4. **Acute exacerbations of chronic obstructive pulmonary disease (AE-COPD): A qualitative exploratory study of patients' needs following discharge**

Bedor Alkhathlan, Neil Greening, Theresa Harvey-Dunstan, Sally Singh

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5. **Acute Exacerbation of Chronic Obstructive Pulmonary Disease (AECOPD) patients Therapy Priorities: A Survey Study**

This article has been accepted as a poster presentation at the virtual EMTS conference on 23rd September 2021. (Prize winning poster). This abstract included a five-minute live oral presentation of the poster followed by questions.

6. **Building healthcare professionals consensus on non-pharmacological patient care priorities during hospitalisation and post discharge phases following acute exacerbation of chronic obstructive pulmonary disease (AECOPD)**

B. Alkhathlan, S. Ramakrishnan , N. Greening, T. Harvey-Dunstan, S. J. Singh, European Respiratory Society congress 2023.

7. Interventions to Improve Conventional Pulmonary Rehabilitation Uptake Post-Acute Exacerbation of chronic obstructive pulmonary disease: A Systematic Review

B. Alkhathlan, M. Alhotye, N. Greening, T. Harvey-Dunstan, S. J. Singh, European Respiratory Society congress 2023.

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List of Abbreviations

Chronic Obstructive Pulmonary Disease (COPD)

Acute exacerbation of chronic obstructive pulmonary disease (AECOPD)

United Kingdom (UK)

United States of America (USA)

Pulmonary Rehabilitation (PR)

Health Care Professionals (HCP)

Medical Research Council (MRC)

Global Initiatives for Chronic Obstructive Lung Disease (GOLD)

National Institution for Health and Care Excellence (NICE)

Ratio of the Forced Expiratory Volume in the first one second to the Forced Vital Capacity of the lungs (FEV1/FVC ratio)

Predicated Forced Expiratory Volume in one second (FEV1 predicated)

Metric Disability-Adjusted Life Years (DALY)

National Health Services (NHS)

Cough and Sputum Assessment Questionnaire (CASA-Q)

Extended Medical Research Council Dyspnoea Scale (eMRCD)

Short-Acting Beta2 Agonists (SABA)

Short-Acting Muscarinic Antagonists (SAMA)

Long-Acting Beta agonist (LABA)

Long-Acting Muscarinic Antagonist (LAMA)

Inhaled corticosteroids (ICS)

Partial Pressure of Arterial Oxygen (PaO_2)

Kilopascal (kPa)

Kilogram (Kg)

Non-Invasive Ventilation (NIV)

Invasive ventilation (IV)

Absolute Risk Difference (ARD)

Hazard Ratio (HR)

Risk ratio (RR)

Odds ratio (OR)

Confidence Interval (CI)

Probability Value (P-value)

The point estimate (I^2)

Quadriceps Maximum Isometric Voluntary Contraction (QMVC)

Incremental Shuttle Walk (ISW)

Endurance Shuttle Walk (ESW)

Minimal Important Difference (MID)

Six-minute walk test (6MWT)

Consolidated Criteria for Reporting Qualitative Research (COREQ)

Thematic analysis (TA)

Cognitive behavioural therapy (CBT)

Acceptance and Commitment Therapy (ACT)

COPD Assessment Test (CAT)

Multi-Dimensional Dyspnoea profile (MDP)

Patient Activation Measure (PAM-13)

Montreal Cognitive Assessment (MOCA)

Centre for Epidemiological Studies Depression Scale revised version (CESD-R)

Support Needs Approach for Patients (SNAP)

Inter-Quartile Range (IQR)

missing completely at random (MCAR)

Multiple Imputations (MI)

Coronavirus disease (COVID-19)

Forced vital capacity (FVC)

Forced expiratory volume in one second (FEV1)

Randomised Control Trial (RCT)

Cochrane Central Register of Controlled Trials (CENTRAL)

Excerpta Medica Database From Elsevier (EMBASE)

Cumulative Index to Nursing and Allied Health Literature (CINAHL)

Allied and Complementary Medicine (AMED)

Population intervention, comparison, and outcomes (PICO)

Risk-of-Bias tool for Randomised Trials (RoB 2)

Non-Randomised Studies of Intervention (NRSI)

Bristol COPD Knowledge Questionnaire (BCKQ)

Treatment Self-Regulation Questionnaire (TSRQ)

Relative Autonomy Index (RAI)

Post Exacerbation Pulmonary Rehabilitation (PEPR)

Delayed Post Exacerbation Pulmonary Rehabilitation (D-PEPR)

United Kingdom Clinical Care Research Group (UKCCRG)

Patient and Public Involvement (PPI)

Standard deviation (SD)

Inspiratory Muscle Training (IMT)

Meaning and Perspective Transformation (MPT)

Mobility inventory (MI)

Anxiety Sensitivity Index-3 (ASI)

Brief Fatigue Inventory (BFI)

Transformative Learning Theory (TLT)

Relational Frame Theory (RFT)

Chapter 1 . Thesis introduction

1.1 Overview

An acute exacerbation of chronic obstructive pulmonary disease (AECOPD) has been defined as 'an acute worsening of the respiratory symptoms such as worsening in breathlessness, cough, and sputum production or colour that resulted in additional therapy' (NICE, 2019, GOLD, 2019). In a recent European study that investigated the aetiology of AECOPD events, it was found that an AECOPD was mostly attributed to tracheobronchial infections (60%) or air pollution (10%) but, in 30% of cases, was actually due to an unknown cause (Çakmak, 2019). In the literature the reported independent risk factors for frequent exacerbation of COPD events include: worsening lung function and dyspnoea, comorbid depression, prior exacerbation and comorbid cardiovascular diseases (Hurst et al., 2020b). The symptomatic impact of AECOPD, such as increased level of breathlessness due to reduced lung function, can cause a downward spiral of related health consequences like reduced physical activity, mental health and quality of life, as well as increase the chance for further COPD exacerbation which ultimately might increase individual mortality risk (Hurst et al., 2020b). Therefore, to support the pharmacological management given to individuals with AECOPD, other non-pharmacological health care strategies have been implemented to the usual standardised care given to this population to provide better symptom control and enhance the individual's functional capacity and quality of life. Non-pharmacological management strategies include providing action plans that offer symptoms monitoring and exacerbation management, self-management plans that improve individual self-efficacy and individual problem-solving skills and, finally, pulmonary rehabilitation (PR) with its diverse range of programme components that can tackle and improve various aspects of the AECOPD individual's health outcomes such as symptom control, functional capacity, quality of life, improving the individual emotional function, disease knowledge and reducing healthcare utilization (Spruit et al., 2013, Rochester et al., 2015). However, despite the various benefits of PR, individuals post-AECOPD tend to exhibit poor uptake of this non-pharmacological standardised treatment pathway, especially within the

recommended time frame, which is usually four weeks post-hospitalisation following an AECOPD event (NICE, 2019, GOLD, 2019, Jones et al., 2018). In developed countries such as the United Kingdom (UK) and the United States of America (USA), despite the provision of PR programmes being widely spread and established, the reported PR referral, uptake, and adherence rates were consistently poor. For example, in the Jones et al. (2014) UK study, which reported data about referral and uptake post-AECOPD, showed that only 32% of all eligible individuals for PR actually received a referral. Of these, only 21% of the individuals who meet the referral criteria started PR post-hospitalisation of AECOPD(Jones et al., 2014). Similar sub-optimal rates were also found in a USA study (Spitzer et al., 2019). In this study, of the Medicare beneficiaries who were hospitalised for COPD one-month post-discharge PR, uptake rates post exacerbation of COPD were 0.3%. Of this 0.3%, only about 10% completed 35 PR sessions within one year.

Moreover, the Spitzer et al. 2019 study made further attempts to explore the demographical and clinical predictors for PR uptake. Their results showed that younger and healthier individuals, males, white ethnic group, individuals with higher socioeconomic status, number of previous hospitalisations and the severity of an individual's comorbidities were all among the identified predictors for PR participation post-hospitalisation of AECOPD (Spitzer et al., 2019). In recent years, researchers in the field have made more exploration attempts to investigate the reported barriers to engagement in PR post-AECOPD. Results have shown that reasons are multifactorial and could be related to patients, referrers or health services (Jones et al., 2018). Recommended strategies to promote participation in this cornerstone standardised non-pharmacological treatment pathway (PR programme), specifically for the post-exacerbation of the COPD population have been discussed in several publications. For example, in Evans and Steiner (2017), a ‘problem-based approach’ that ensures patient-centred care plans which tackle all problems COPD patients could bring into the consultation room was recommended. Further to this, the authors hypothesised that exacerbating individuals might have different and additional issues that need to be addressed within their recommended treatment plans. They also suggested that PR alone might not be sufficient (Evans and Steiner, 2017). Additionally, interested scholars have highlighted that despite consistent recommendations by national and international guidelines that support the introduction of PR as an effective non-pharmacological management of COPD, the acceptability of such interventions seems to be

very low among the stakeholders. Thus authors have proposed adopting a 'collaborative approach' that accounts for all stakeholder perspectives and therapy priorities when designing further interventions, especially for exacerbated individuals, to maximise their motivation, acceptability and uptake of their health care intervention (Man et al., 2015, Rochester and Singh, 2020).

Among the key findings generated from qualitative research conducted on health care professionals (HCP) to explore their views about how to design a more acceptable PR programme post-AECOPD, HCP suggested allowing patients to 'pick and choose' the therapeutic components to be included in their PR programme in order to promote the acceptability of the PR programme post-AECOPD (Janaudis-Ferreira et al., 2019b). Finally, in a further study by Janaudis-Ferreira et al. (2021), the authors explicitly aimed to gather consensus from researchers in the field through consensus meetings about the top research priorities in the context of PR delivery post-AECOPD. The results of this consensus process identified the following three top research priorities: 1) implementing a phased approach that can give the opportunity for the patients to build trust with their health care providers before engaging in exercise intervention, 2) developing interventions based on a patient-centred approach that takes into account their therapy preferences and 3) improve understanding of the emotional and psychological impact of the AECOPD on the individual (Janaudis-Ferreira et al., 2021).

Accordingly, it seems evident from the aforementioned that COPD exacerbation health implications are complex and, as per interested scholars' recommendations, the solution to promote PR uptake post AECOPD to help enable this population to gain the significant and well-documented health benefits associated with engaging in PR programmes post-acute exacerbation of COPD (Puhan et al., 2016), the following multiple approaches should be adopted: A) 'patient-centred care' that tailor the intervention to fit the AECOPD population's specific and complex therapeutic needs, and B) incorporating a 'collaborative approach' by allowing key stakeholders (patient and healthcare professionals) perspectives to be considered within the development process of the intervention. Therefore, we hypothesised that a complex intervention (that includes multiple components which target a range of patient health outcomes, and behaviours delivered by a multidisciplinary team with various skills and expertise (Skivington et al., 2021), and are built based on key

stakeholders (patients and HCP) non-pharmacological patient care priorities) might promote uptake of PR programme post-AECOPD.

However, in order to aid the development process of the above proposed intervention, the following research questions need to be addressed: A) what the patient and HCP non-pharmacological patient care prioritise throughout the COPD exacerbation experience (during hospitalisation and at discharge), B) what the patient perceived as the most bothersome exacerbation impact during the acute and post-acute phases of COPD exacerbation event, and C) review the effectiveness of the previous research attempts of interventions designed to promote conventional PR uptake around the time of COPD exacerbation.

Therefore, this PhD thesis has the following overarching and secondary aims:

1.2 Thesis overarching aim

Develop a complex intervention based on individuals with AECOPD non-pharmacological care priorities to promote PR uptake post-AECOPD.

1.3 Thesis Secondary aims

I. Undertake a series of exploratory qualitative and quantitative research steps to understand the context of the problem and provide insights into the following.

a. Explore patients' experiences related to COPD exacerbation, returning home, Pulmonary Rehabilitation (care received) and provide insight into the patient therapy options

b. Explore the patient's non-pharmacological therapy priorities and the reported most bothersome COPD exacerbation implications throughout the exacerbation phase (at hospitalisation and post-discharge)

II. Seek healthcare professionals (HCPs) consensus on the patients' identified nonpharmacological care interventions priorities throughout the COPD exacerbation phase (at hospitalisation and post-discharge)

III. Review the effectiveness of previously designed interventions to improve PR referral, uptake, and completion post-AECOPD.

1.4 Thesis methods

The updated medical research council (MRC) framework has been adapted to aid the initial development phase (the foundation) of this complex intervention (Skivington et al., 2021). This framework was selected as it offers a dynamic approach that allows developers to use the relevant research actions in the context of the intervention that they are developing, in addition, it also allows developers to revisit research actions or steps as the intervention evolves or when new information appears from the conducted research actions (Skivington et al., 2021). The following initial actions presented in the updated version of the MRC framework cited in the Skivington et al. 2021 publication are used: I) consider the context by identifying the problem to be targeted and refine the understanding of it (qualitative study), II) engage stakeholders who will use the intervention (patient survey and HCP Delphi study), III) review published evidence to identify the effectiveness of previously developed interventions to tackle the problem (systematic review), IV) draw on existing theories by finding single or multiple suitable theories that can be used as the foundation for the new proposed intervention (Synthesis of the evidence from all the research steps), V) Articulate the aspect of the programme theory in a logic model and VI) design the preliminary version of the intervention (prototype). The details of the thesis research steps and methods are presented in table 1.1. Three of the research steps presented in the table happened in sequential order and are labelled as phase one (descriptive qualitative study), phase two (single centre-cross-sectional survey study) and phase three (international Delphi survey study). A visual organisation of the studies in this thesis is presented in figure 1.1 (thesis flow diagram).

Table 1.1Thesis research steps and methods

Design	Setting	Sample	Data Collection method (instrument)	Analysis
Descriptive qualitative study	Respiratory Ward at Glenfield Hospital	AECOPD in-patients	Individual semi-structured interviews	Braun and Clark's method of thematic analysis
Cross-sectional survey (single centre)	Respiratory Ward at Glenfield Hospital	AECOPD in-patients	Survey developed for the study purpose and several validated questionnaires	Descriptive statistical analysis
Delphi survey	Healthcare professionals (HCPs)	International Healthcare Professionals engaged in the care of individuals with acute and post-acute COPD exacerbation	Iterative online survey to gain stakeholders' consensus (HCP)	Descriptive statistical analysis
Systematic review	Existing databases Cochrane Central Register of Controlled Trials, MEDLINE, EMBASE Ovid SP, PsycINFO Ovid, CINAHL EBSCO (Cumulative Index to Nursing and Allied Health Literature), AMED EBSCO (Allied and Complementary Medicine), hand searches of the proceedings of major respiratory Conferences and we searched Google Scholar	Intervetions with a specific aim to improve referral, uptake, completion of pulmonary rehabilitation exercise therapy, physical activity program and/or improve disease knowledge, patient readiness to commence PR, during hospitalisation or post hospitalisation from acute exacerbation of COPD event	Systemic literature search using keywords and Mesh terms in relevant databases and critical appraisal of the retrieved studies	Narrative synthesis

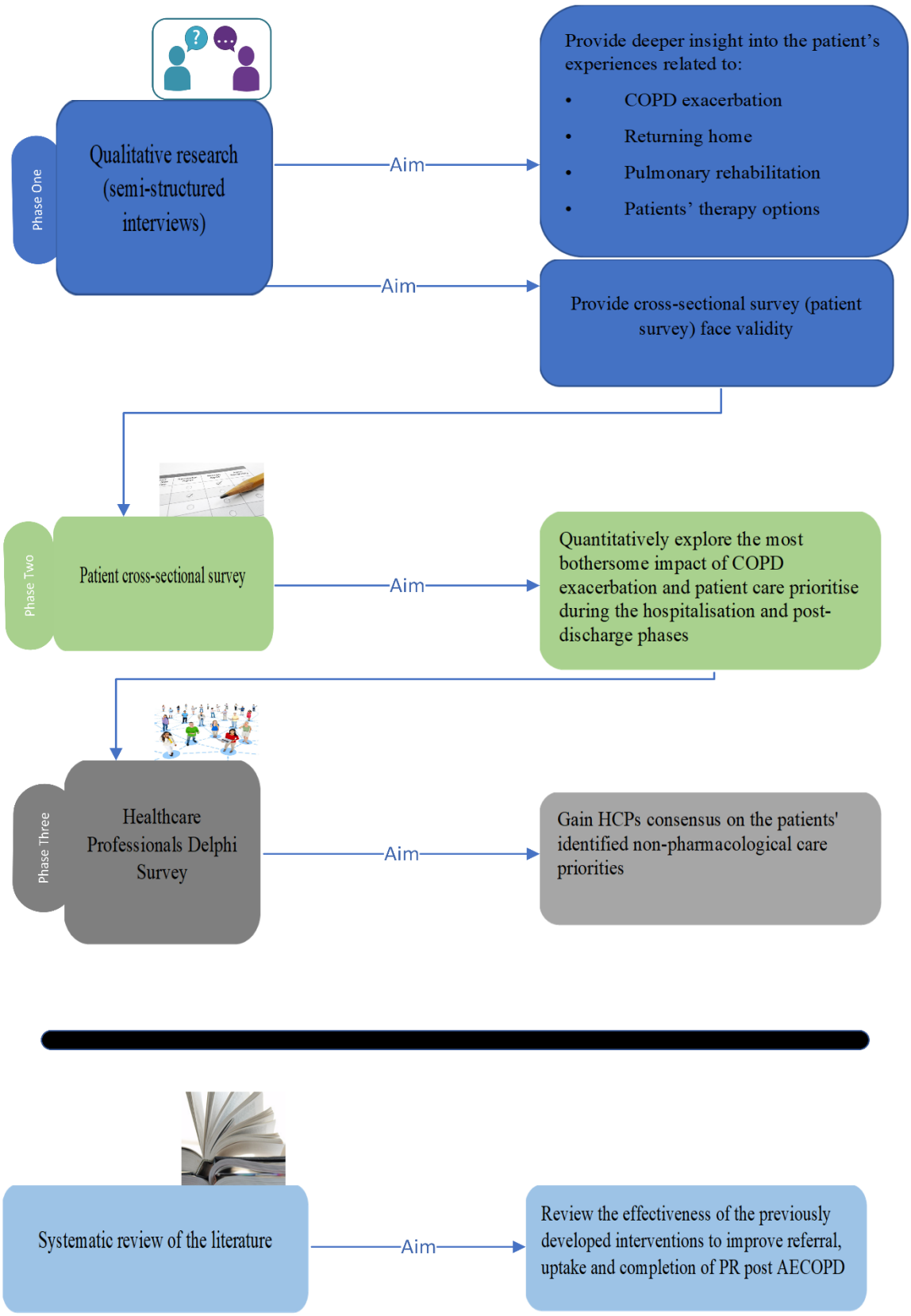

Figure 1.1Thesis flow diagram

Chapter 2 . Background

2.1 Definition of chronic obstructive pulmonary disease

Chronic obstructive pulmonary disease (COPD) is a complex respiratory syndrome that is common, preventable, and manageable (GOLD, 2019). It is characterised by airflow limitation due to obstruction of the small airways and lung parenchymal abnormalities as well as other clinical, functional and radiological findings that are variable in its clinical presentations in each individual patient (Agusti et al., 2010).

Diagnosis of COPD is suspected based on its clinical manifestations (signs and symptoms) and is routinely supported by spirometry findings. Breathlessness, chronic cough, regular sputum production, wheezes and frequent bronchitis are all among the clinical manifestations of COPD and the spirometric results of post-bronchodilator of a FEV_1/FVC ratio of 0.7 confirms the diagnosis of COPD (NICE, 2019). Since breathlessness is considered as the primary symptom of COPD, the National Institution for Health and Care Excellence (NICE) for COPD disease updated guidance published in 2019 and recommended using the MRC dyspnoea scale to grade the breathlessness according to the level of exertion. This scale starts from grade one where it states that individual are not troubled by breathlessness unless he or she is engaged in strenuous exercise, up to grade 5 where an individual is too breathless to leave the house, or whenever he or she dresses or undresses (Williams, 2017). The NICE 2019 COPD guidelines additionally suggest performing further investigation at the time of initial diagnosis to help exclude other pathologies, such as performing a chest radiograph and a full blood count to rule out anaemia and polycythaemia (NICE, 2019).

According to recent COPD international guidelines (NICE, 2019, GOLD, 2019), the classification of the degree of airflow obstruction is measured by the FEV_1/FVC ratio and

FEV_1% predicted values post-bronchodilator spirometry test, and are classified as the following:

- Post-bronchodilator FEV_1/FVC <0.7, FEV_1% predicated ≥80% = Stage 1 (Mild)
- Post-bronchodilator FEV_1/FVC <0.7, FEV_1 % predicated 50-79% = Stage 2 (Moderate)
- Post-bronchodilator FEV_1/FVC <0.7, FEV_1 % predicated 30-49% = Stage 3 (Severe)
- Post-bronchodilator FEV_1/FVC <0.7, FEV_1 % predicated <30 % = Stage 4 (Very severe)

2.2 Definition of acute exacerbation of chronic obstructive pulmonary disease (AE-COPD)

An acute exacerbation of chronic obstructive pulmonary disease (AE-COPD) is defined as significant worsening or 'flare-ups' of the disease symptoms, e.g. breathlessness, cough, change in sputum colour and production from baseline measures to the peak, suddenly or in short gradual onset, which requires an adjustment in the usual patient treatment (Aaron et al., 2012, Kim and Aaron, 2018). To better understand acute COPD exacerbation, it is essential to understand the predisposing causes of such an incident. AE-COPD results from respiratory tract infections (bacterial or viral) or due to environmental amplifying factors such as smoke or air pollution that attack the respiratory system, and therefore impose some debilitating respiratory and physiological symptoms, especially to vulnerable COPD patients such as the elderly or those with the susceptible immune system (Aaron et al., 2012, Kim and Aaron, 2018).

According to the updated GOLD 2018 guidelines, COPD exacerbations are classified as the following:

- Mild exacerbations that are treated only with bronchodilators

- Moderate exacerbations that are treated with bronchodilator and antibiotic or antiviral agents
- Severe exacerbations that require emergency department admissions and/or hospitalisation

2.3 Pathology of acute exacerbation of COPD

During an exacerbation, there is a greater increase in airway inflammation in response to microorganism attacks by bacteria, viruses or exposure to pollutants found in the environment, e.g., inhalation of noxious particles or gases. The accompanying mechanisms of airway inflammation can cause airway wall edema, an increase in mucus production and changes in the airway tone. These structural changes and inflammatory responses provoke the primary symptoms that are clinically manifested during an exacerbation, such as worsening dyspnoea, an increase in the amount and consistency of sputum and constant cough. Additionally, the structural changes caused by the inflammation response can create air trapping, which leads to an increase in the work of breathing and ultimately imposes an exerted strain on respiratory muscle function (Wedzicha, 2012).

Because an exacerbation is a heterogeneous event, the clinical presentation might vary widely among patients. Therefore, considering the severity of the underlying disease and the severity of the exacerbation, combined might guide the initial stages of a proper diagnosis. In the event of an exacerbation that does not respond to bronchodilator therapy, clinicians tend to perform sputum sampling to detect the isolated microorganism that has caused the exacerbation event. However, it is important to remember that patients with a very severe underlying disease might have a host of bacteria in a stable state (bacterial colonization), which makes it difficult to predict the exact causative bacteria in an exacerbation event and therefore hinder the effect of the antibacterial agent (Wedzicha, 2012).

A recent study investigated 75 isolated causative microorganism samples from sputum and blood cultures taken from patients who did not receive antibiotic agents one month prior to their admission following an exacerbation event. Results found that mainly *Haemophilus influenzae (n=12), Streptococcus pneumonia (n=9)* and *Moraxella*

catarrhalis were the cause of most of the bacterial infections during an exacerbation event (Çakmak, 2019).

As stated above, exacerbations can also be caused as a result of viral infection. In Asia, the influenza virus has been one of the most common causes of virally infected exacerbation events, while picornavirus has been more common in Europe, Australia and North America (Ko et al., 2016). Other relatively common causative viral infections are respiratory scynctial virus, coronavirus, and parainfluenza. In general, several studies have found that viral infections are more common during the winter and spring seasons (Wark et al., 2013, Ko et al., 2007). Moreover, patients with viral infections can have more extended hospitalization periods and more deterioration in hypoxaemia and lung function (Mohan et al., 2010).

Co-infection with bacteria and viruses can also occur in an exacerbation event and is linked with more severe disease implications such as more severe functional impairment and a longer hospitalisation period (Aaron, 2019).

Additionally, non-infective aetiologies such as indoor and outdoor air pollution caused by cigarette smoking and inhalation of bio-mass fuels can play a role in triggering a respiratory deterioration in COPDers and therefore cause an exacerbation event.

2.4 Chronic obstructive pulmonary disease prevalence

In 2013, COPD in the United Kingdom was considered to be the most common respiratory disease or syndrome, with a prevalence of 33 cases per 1000 persons in 2013 (Merinopoulou et al., 2016). Globally, COPD is projected to be the third leading cause of death by the year 2030 (Mathers and Loncar, 2006). Moreover, by using the metric disability-adjusted life years (DALY) measure, it is projected that in the year 2030, COPD will be the seventh leading cause of disease burden globally (Mathers and Loncar, 2006).

2.5 COPD exacerbation frequency and financial burden

In a large UK-based cohort study that included a total of 151,203 patients, the exacerbation rate was found to increase annually among all COPD severities classified by the GOLD (2013) guidelines (figure 2) (Merinopoulou et al., 2016). Merinopoulou and colleagues (2016) suggested that an upward trend within all disease categories was due to the disease's natural progression, which increases the likelihood of the occurrence of multiple episodes or attacks of exacerbation following the first attack when risk factors are not controlled (Merinopoulou et al., 2016).

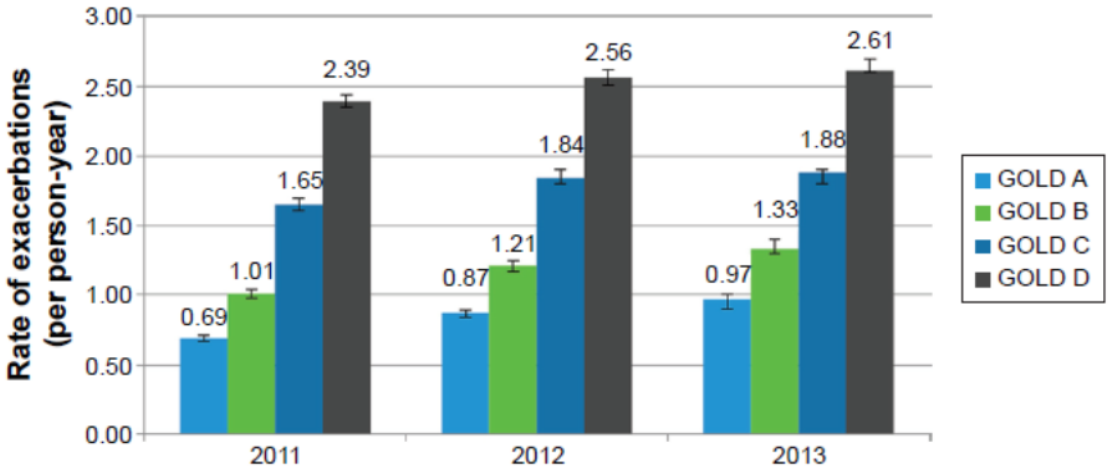

Figure 2.1 Annual rates of exacerbations at follow-up (per person-year), (Original figure source Merinopoulou et al., 2016)

Another UK multi-centre retrospective observational study estimated the mean frequency of COPD exacerbation > three a year occurred in 9% (27 out of the 314 patients) of mild and moderate COPD patients, 19% (27 out of the 145 patients) with severe COPD, and 29% (15 out of the 52 patients) with very severe COPD (Thomas et al., 2014).

Thus, it is widely believed that the increase in the number of exacerbations within these patient populations will lead to an increase in the utilisation of health services which will cost the National Health Service (NHS) an estimated £982 million annually to manage COPD disease alone. This substantial financial burden will continue to rise if gaps in management strategies and models of care remain unfilled (Thomas et al., 2014).

2.6 Acute COPD exacerbation experience and symptoms burden

In order to help design a programme that could bridge and facilitate the PR uptake within the post-acute COPD exacerbation population, it is essential to gain a better understanding of the acute COPD exacerbation experience and symptoms burden. This will help with finding potential supportive and non-pharmacological evidence-based therapies that can help with providing individualised therapy experiences for patients by improving the patient's interest in taking post-AE_COPD PR as lack of interest was identified in a US based study as the most frequent reason for patients not attending rehabilitation (Benzo et al., 2015).

COPD exacerbation symptom burden, reported in an interview-based observational study by Kessler et al. (2006), showed that patients reported suffering from various symptoms such as breathlessness (38%), fatigue and tiredness (10%), upper respiratory tract infection (10%), cough (9%) and pain (8%) during an exacerbation attack (Kessler et al., 2006). Furthermore, their analysis identified that the majority of the patients (n=81 of the 125) reported exacerbation attacks impacted their mood and caused them to experience a variety of negative feelings such as 81% felt a lack of energy, 64% had depression, 62% were anxious, 58% had panic attacks, 47% experienced anger and 30% felt guilt (Kessler et al., 2006). A much older cohort study by Seemungal et al. (1998) described that patients who had suffered COPD exacerbation in the previous year most often had daily symptoms of cough and sputum (58%), sputum production (62%), cough (45%), dyspnoea (49%) (Seemungal et al., 1998). Additionally, one of this study's interesting findings showed that COPD exacerbation rate was found to be more frequent among patients who had daily cough symptoms (Seemungal et al., 1998). Suffering from cough in patients with COPD was found

to be significantly related to cause an impairment in the health-related quality of life compared to the dyspnoea symptom (Deslee et al., 2016).

This finding highlights the need to maintain the addition of cough management component within the chronic care services, and especially within PR service.

2.7 Pharmacological therapy for acute exacerbation of COPD

As an increase in breathlessness is a dominant feature of acute exacerbation of COPD, an increase in the doses of short-acting bronchodilators (Short-Acting Beta2 Agonists (SABA) and Short-Acting Muscarinic Antagonists (SAMA)) are indicated with or without short-acting anticholinergics (GOLD, 2019). Inhaled therapy delivery systems can be given through both nebulisers and hand-held inhalers (GOLD, 2019, NICE, 2019). The chosen delivery system should be based on the dose of the drug needed, the patient's ability to use the device and the resources available to supervise the therapy administration and, finally, an air-driven nebuliser should be considered if the COPD individual is hypercapnic or acidotic (NICE, 2019). In the absence of contraindications, hospitalised or community-based COPD exacerbation individuals with significant levels of increased breathlessness could be prescribed a course of oral corticosteroids such as 30 mg oral prednisolone for 5 days, with the consideration of adding of osteoporosis prophylaxis treatment for individuals with frequent use of oral corticosteroids. Moreover, in COPD exacerbation pharmacological management other medication, such as intravenous theophylline can be added to the treatment regimen whenever there is inadequate response to nebulised bronchodilation therapy (NICE, 2019).

In conjunction with corticosteroids medication, supplementary oxygen should be offered if patients suffer from hypoxaemia (Partial Pressure of Arterial Oxygen (PaO_2) < 7 kPa or less than 8 kPa with pulmonary hypertension cor pulmonale or polycythaemia sufferers), an administration of antibiotics should also be considered for individuals with exacerbations who suffer from a change in their sputum volume of colour (NICE, 2019). Finally, non-invasive ventilation (NIV) and invasive ventilation (IV) can be considered in

hospitalised exacerbated individuals when persistent respiratory failure presents despite optimal medial intervention (NICE, 2019, GOLD, 2019).

2.8 Non-pharmacological therapy options for acute exacerbation of COPD

Several COPD guidelines suggest that the solution to improving and maximising the overall treatment outcomes is by incorporating evidence-based supportive approaches such as pulmonary rehabilitation (PR), which is defined as "a comprehensive intervention based on thorough patient assessment followed by patient-tailored therapies that include, but are not limited to, exercise training, education and behaviour change, designed to improve the physical and psychological condition of people with chronic respiratory disease and to promote the long-term adherence to health-enhancing behaviours."(Spruit et al., 2013).

Additionally, smoking cessation programmes have been recommended to help patients who are active smokers quit smoking, along with preventative vaccinations and palliative care which "encompass approaches of symptoms control as well as management of terminal patients close to death" (GOLD, 2019, NICE, 2019). All these multidisciplinary approaches were found very effective to manage complex diseases such as COPD.

2.9 Pulmonary rehabilitation benefits post-acute exacerbation of COPD

In the event of AECOPD, individuals can experience loss in physical and lung function and deterioration in their daily COPD symptoms such as dyspnoea, sputum production and coughing and, finally, an increase in the risk of hospitalization and mortality (Torres-Sanchez et al., 2017, Lindenauer et al., 2020). These complex implications of the AECOPD require complex treatment plans to address the affected individual various needs. One of the recommended standardised non-pharmacological pathways is delivering PR post suffering from an AECOPD event (NICE, 2019). The integration of PR into the post-AECOPD individuals' management plans has several well-documented positive health-related outcomes, such as improving the individual level of dyspnoea, exercise capacity and health-related quality of life measures (Puhan et al., 2016). However, there is conflicting

evidence regarding other health-related outcomes, such as the risk of mortality. This conflicting evidence has been largely attributed to the heterogeneity that exists in the PR interventional studies in terms of timing of the intervention delivery, content, risk of bias in the studies, and intervention fidelity measures (Puhan et al., 2016, Greening et al., 2014, Lindenauer et al., 2020). For example, in one study (Greening et al., 2014), which introduced PR early at the time of hospitalisation post suffering from chronic respiratory disease, the study reported an increase in mortality at the 12-month follow-up period (Odds Ratio (OR), 1.74, 95% confidence interval 1.05 to 2.88, P=0.03) in the intervention group that was exposed to a partial period of early supervised PR at hospitalisation and a period of unsupervised PR sessions post-discharge (Greening et al., 2014). However, the cumulative evidence generated from the mortality outcome sub-analysis published by Puhan et al. (2016) of studies that included only fully supervised early PR programmes (where the Greening et al. 2014 RCT study was excluded) resulted in a positive effect of PR in reducing mortality (it is important to mention that the included studies in the sub-analysis had small participant numbers and, in addition, unclear or high risk of bias) (Puhan et al., 2016).

Another systematic review published in 2018 looked at the mortality outcome with a relatively small pooled sample size (n=319) and included only supervised early PR interventions that were delivered during hospitalisation or within 4 weeks of hospital discharge. The results of this meta-analysis showed a statistically significant reduction in mortality at the end of the treatment favouring the PR group with a risk ratio (RR) of (RR = 0.58; 95% CI: [0.35 to 0.98]) with moderate quality of evidence (Ryrsø et al., 2018). Furthermore, one of the largest studies that reported improving one-year survival post PR to date, was a recent American retrospective cohort study that used a large dataset of health records of 197,376 Medicare beneficiaries to investigate the association between the initiation of pulmonary rehabilitation after hospitalisation for COPD and one-year survival (Lindenauer et al., 2020). Results showed that despite participant records reporting that only 2,721 (1.5%) patients received PR within 90 days of hospitalisation, among those who did, mortality risk was reported to be lower across starting dates ranging from 30 days or less (Absolute Risk Difference (ARD), –4.6% [95% CI, –5.9% to –3.2%]; Hazard ratio (HR), 0.74 [95% Confidence Interval (CI), 0.67 to 0.82]; Probability Value (P-value) P < .001), or within 90 days of hospital discharge (ARD, –11.1% [95% CI, –13.2% to –8.4%]; HR, 0.40 [95% CI, 0.30 to 0.54]; P < .001) (Lindenauer et al., 2020).

Reduction in health care utilisation post COPD exacerbation is an extension of the well-documented PR benefits following AECOPD. Hospital re-admission outcomes were reported within two meta-analyses that looked at the benefits of PR on COPD-related hospital admission (Ryrsø et al., 2018, Moore et al., 2016). The results of the first meta-analysis that reviewed the benefits of early PR (within 4 weeks of AECOPD) showed, with moderate quality of evidence, that PR reduced hospital readmissions risks (risk ratio (RR) = 0.47 (95% CI: [0.29 to 0.75]), and no significant difference were found between programmes delivered during hospitalisation or after discharge ($P = 0.93$) (Ryrsø et al., 2018). The second meta-analysis by Moore et al. (2016) showed that there was a significantly higher rate of hospitalizations/patient-year among patients in the year before PR (1.24 hospitalizations/patient-year; 95% CI, 0.66-2.34) compared with after PR (0.47 hospitalizations/patient-year; 95% CI, 0.28-0.79) (Moore et al., 2016).

PR for the COPD exacerbation population can also produce health benefits related to the individual physical capacity. For example, in the Seymour et al. (2010) study, where 60 individuals with AECOPD partake in outpatient pulmonary rehabilitation, the results showed that there was a change in Quadriceps strength measured by maximum Isometric Voluntary Contraction force (QMVC) in patients in the intervention group demonstrated by a significant increase in QMVC (5.1 kg,95% CI 2.5 to 7.6, p<0.01) compared with the usual care group. Additionally, walking capacity measured by the Incremental Shuttle Walk Test (ISW) and Endurance Shuttle Walk Test (ESW) was also increased in the intervention group compared to the usual care group (ISW (51 meters, 95% CI 22 to 79, p<0.01) and ESW [189 meters, 95% CI 28 to 350, p0.02]) (Seymour et al., 2010). An additional positive effect of PR on improving the individual's exercise capacity post-AECOPD was reported in the meta-analysis of thirteen studies with a total of 819 participants, where the Six-Minute Walk Distance (6MWD) was improved by 62 meters (95% CI, 38 to 86), and shuttle Walk Test Distance (SWT) by 48 meters (95% CI -1 to 97) (Puhan et al., 2016).

Moreover, the Puhan et al. (2016) meta-analysis results showed further PR benefits related to the individual's health-related quality of life measures, as data with high-quality evidence suggested that pulmonary rehabilitation for post-AECOPD improves the individual health-related quality of life measures captured by the St George's Respiratory Questionnaire (SGRQ) (The SGRQ total scores were statistically significant and was

regarded above the minimal important difference (MID) of four points, the mean difference was (MD) -7.80, 95% CI -12.12 to -3.47; I^2 = 64%). Results of this meta-analysis also showed a statistical significance for the impact and activities domain of the SGRQ and for fatigue, emotional function and dyspnoea domains of the Chronic Respiratory Questionnaire (CRQ) (Puhan et al., 2016).

Finally, in a recent meta-analysis by Lu et al., (2023) that included a large number of RCTs studies (twenty studies with a total of n=1274 participants) and reviewed the effectiveness of the initiation of early PR programmes either during hospitalisation because of AECOPD or shortly following the discharge phase. The results of this meta-analysis confirmed the significant overall benefits of PR in relation to improved outcomes of 6 MWD, quality of life measures and dyspnoea score. However, the subgroup analysis conducted in this review revealed trends of less PR benefits within the mortality and re-admission outcomes (although statistically non-significant) when PR was introduced at the admission phase (Lu et al., 2023).

2.10 Pulmonary rehabilitation up-take post-acute COPD exacerbations

Despite the wide provision of PR in the UK, the uptake of PR remains suboptimal within the AECOPD population. According to one year UK audit data (2011-2012), that investigated the percentage of uptake of PR following hospital admission of AECOPD, results showed that only 90 referrals were made from the 286 PR-eligible patients, and out of those 90 referrals 60 individuals started the PR programme post hospitalisation, which is only constitute 21% of all PR eligible individuals (Jones et al., 2014). Moreover, another UK study by Harrison et al. (2014) showed that only 70 individuals with AECOPD (55%) in their study accepted PR referrals and out of those who accepted a referral a small number of the participants 39 (30%) attended the first session of the PR programme (Harrison et al., 2014a).

International studies have reported even lower PR uptake numbers. For example, results from a large US cohort study that reviewed a total of 223,832 Medicare beneficiaries hospitalised for COPD exacerbation in 2012 showed about 2.7% (n=6,111) eligible PR individuals received PR with 12 months of hospital discharge, and only 1.9% (n=4,225) received PR within 6 months of post-AECOPD discharge (Spitzer et al., 2019). Despite the

COPD clinical guidelines (NICE, 2019, GOLD, 2019) recommendations for the implementation of PR as a standardised adjunct therapy for the management of COPD exacerbation, findings in the Spitzer et al. (2019) study reported that the number of prior admissions reduced the individual probability of receiving PR intervention (Spitzer et al., 2019).

A study by Steele et al. (2010) that investigated the impact of COPD exacerbation on PR participation revealed that 10 (33%) out of the 30 patients who had exacerbations during their outpatient PR did not complete the programme. However, Steele et al. (2010) did report that exacerbators who completed the outpatient PR programme performed as well as non-exacerbator participants in the Six-Minute Walk Test (6MWT), which is regarded as a significant predictor of a patient's physical function (Steele et al., 2010). Therefore, it would be reasonable to conclude that it is essential that, following an AECOPD, efforts should always be made to ensure that patients are encouraged to attend a PR post-acute exacerbation event to allow them to gain the well-documented PR benefits related to improved functional capacity and health-related quality of live measures (Steele et al., 2010, Puhan et al., 2016).

2.11 Barriers to pulmonary rehabilitation uptake following acute exacerbation of COPD

Proposing ways to help improve PR uptake following an AECOPD requires an in-depth understanding of the reported participation barriers. To date, several studies have attempted to provide insight into this aspect, and reasons were found to be multifactorial and can be related to referrers, patients and healthcare systems (detailed reasons are found in Figure 2.2) (Jones et al., 2018).

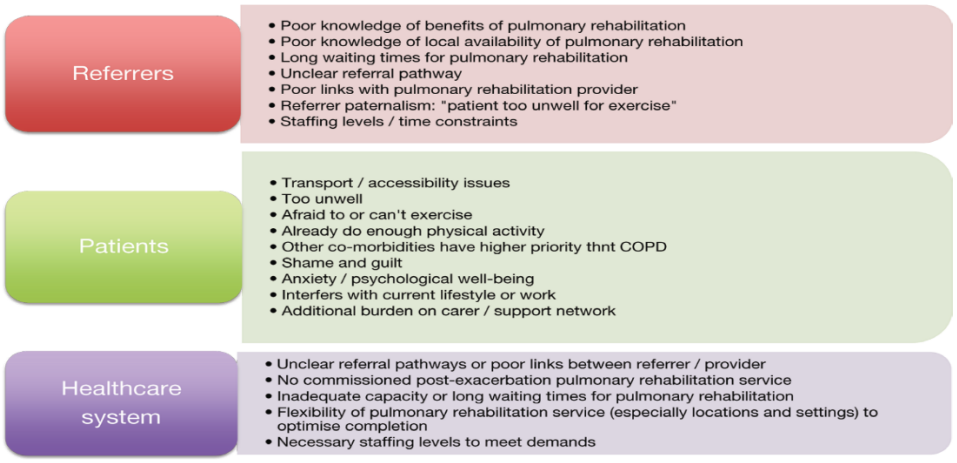

Figure 2.2 Reasons for poor referral, uptake, and completion of PR post-AECOPD, (Original figure source Jones et al., 2018)

Similar patient barriers reported in Jones et al. (2018) were also cited in the Benzo et al. (2015) study, where barriers to implementing a structured physical activity programme post-hospitalisation of AECOPD were investigated. In this study, the findings showed that 39% of the 531 participants reported a lack of interest in participation in physical intervention, 24% declined as a result of being ill or frail, 11% were due to having a busy lifestyle, 11% because of transportation issues, 6% to comorbidities, 7% to commitment issues and 2% as a result of lack of social support (Benzo et al., 2015).

An in-depth insight regarding the reasons why individuals with COPD exacerbation decline participation in PR post-hospitalisation was reported by Harrison et al. (2015) qualitative study, where participants reported various psychological emotions as the reason behind their decision to decline participation, such as; reduced self-worth, feelings of guilt due to the self-inflicted nature of the disease, reluctancy and feeling threatened by external support that patients usually perceived will change nothing regarding their deteriorating health condition and, finally, as a result of desperation to avoid returning back to the hospital following their recent health crisis (Harrison et al., 2015b).

2.12 Different approaches to increase pulmonary rehabilitation uptake following acute exacerbation of COPD

Low uptake of PR uptake post-AECOPD hospitalisation has been identified and reported as early as 2012 (Hopkinson et al., 2012, Jones et al., 2014). However, since then research attempts to develop intervention to promote PR uptake has been very limited with only a slight noticeable increase in recent years. Exploring these research attempts has shown variations in how researchers have tried to augment this PR uptake gap. In some instances, this has been via designing supplementary or bridge interventions such as COPD discharge bundles, educational manuals and PR taster sessions, as well as via incorporating educational videos to improve the uptake of conventional PR (Barker et al., 2021, Barker et al., 2020, Houchen-Wolloff et al., 2021, Revitt et al., 2018, Milner et al., 2019, Janaudis-Ferreira et al., 2018, Sewell et al., 2017, Hopkinson et al., 2012). Details and narrative synthesis of these research attempts are found in chapter five of this thesis.

Additionally, researchers in the field have made several other attempts to replace conventional PR with other forms of PR post-hospitalisation from AECOPD such as, for example, remotely via Telehealth, delivering early in-patient PR or early outpatient PR (Bhatt et al., 2019, Greening et al., 2014, Cox et al., 2021, Seymour et al., 2010). Although such interventions have not been specifically designed to target PR uptake, none of the studies listed in their protocols primary or secondary measured endpoints that included PR programme uptake outcomes and were predominantly focused on collecting measures related to patient health-related clinical outcomes and health care utilisation such as hospital readmission. However, data about conventional PR uptake can still be found reported somewhere within the studies' manuscripts. For example in the Bhatt et al. (2019) study where telerehabilitation intervention was delivered to post-hospitalisation COPD individuals over 12 weeks duration (consisted of 36 exercise sessions with an educational component), resulted in promising telerehabilitation PR uptake in the intervention group (n=66 (82.5%) participants out of the full study cohort n=80 participants) versus only ten participants (6% out of the n=160 unexposed group) attended conventional PR within three months post hospitalisation (Bhatt et al., 2019). Further to this, Greening et al. (2014) also reported PR uptake data within their trial manuscript, with results showing that the recorded uptake of PR after three months of the study's recruitment was significantly reduced

(14% v 22%, P=0.04) in the intervention group that received early supervised PR within 48 hours of admission compared to the usual care group who received PR in three months after discharge. (Greening et al., 2014).

Notwithstanding, all of the aforementioned valuable research attempts are still currently considered as not sufficient to guide clinical practice regarding the best approach that could help promote the uptake of PR post-AECOPD. Thus, there is still a great need to continue developing and evaluating PR-targeted interventions specifically designed for the post-AECOPD population where it can augment the uptake of PR and address this population's specific needs.

Chapter 3 . Acute Exacerbation of COPD: A Multifaceted Qualitative Exploration of the Exacerbation Event

3.1 Background

Chronic Obstructive Pulmonary disease (COPD) is a complex respiratory disease that has many clinical and economic consequences such as a decline in lung function, quality of life and exercise capacity, and it leads to an increase in mortality risk and in health resources utilisation (Kim and Aaron, 2018). The number of people in the United Kingdom (UK) who are affected with this disease is projected to rise and, currently, it is estimated that 80,000 people are diagnosed with COPD each year and considered the fifth most common cause of death in the UK (NICE, 2019, Putting, updated 2022). COPD individuals who are exposed to COPD exacerbation risk factors such as respiratory infections, seasonal variations in outdoor temperature and air pollution can experience flare-ups of their COPD symptoms (AECOPD), clinically manifested as an increase in shortness of breath, coughing, and sputum production which require a change in a patient's prescribed medicine (Kim and Aaron, 2018, Hurst et al., 2020b). In a retrospective interview-based study conducted in multiple countries in Europe, physicians reported COPD patients mostly suffered from a mean of 4.6 exacerbations in a year and those exacerbations resulted in 2.7 unplanned visits to hospital (Kessler et al., 2006). Additionally, among the reported independent risk factors for COPD individuals who experience more than or equal to 2 exacerbations per year are female gender, reduced lung function, poor quality of life, suffering from prior exacerbations, suffering from comorbidities, elevated white blood cell count and blood eosinophil count (Hurst et al., 2020b). In the UK alone, caring for individuals with COPD costs the National Health System (NHS) an estimated 800 million pounds (Directorate, 2012).

In line with the above financial burden, interested researchers in the field have sought to provide deeper insight into how COPD individuals experience COPD exacerbation to help clinicians understand the broader impact of the exacerbation on the affected individual. For example, one of the early attempts was conducted by Kessler et al. (2006) study which was an international interview-based study that included 125 outpatient participants. In this study, participants reported various symptoms and emotions related to COPD exacerbation, namely increased breathlessness, cough, fatigue, pain, substantial anxiety, fear of dying, suffocation, isolation and becoming increasingly dependent on others to perform daily activities (Kessler et al., 2006). Additionally, a further qualitative investigation into this patient population was conducted in order to identify patient illness perceptions clusters in post-AECOPD patients. This investigation resulted in grouping patients win three distinct clusters that labelled patients as: 1) in control, 2) disengaged and 3) distressed. The results of this study also reported that patients in cluster three (distressed) experienced more severe symptoms, signs of anxiety and depression, worse health status and self-efficacy than the participants in cluster one (in control) (Harrison et al., 2014a).

However, it is important to mention that the above studies recruited mostly elderly participants in the post-discharge setting and depended largely on the patients' recall ability of their COPD exacerbation experience, which could be an underestimated representation of the true impact of AECOPD during the actual time of the AECOPD event (Kessler et al., 2006, Harrison et al., 2014d). Additionally, interested scholars in the field have suggested that frequent exacerbators might require additional therapy or prevention strategies other than standardised pharmacological (inhalers and anti-inflammatory agents) and non-pharmacological therapies (pulmonary rehabilitation) that is currently provided to them, and encouraged exploring those needs (Evans and Steiner, 2017).

Therefore, in this study, the aim is to offer a first-time opportunity to give an in-depth comprehensive insight into the patient's COPD exacerbations, returning home and pulmonary rehabilitation experience and finally explore the patient's therapy options or needs post-discharge. This investigation was conducted during the acute phase of the attack (in hospitalisation) to capture the patient's authentic experience when its current and fresh

in the patient's mind, in an effort to establish an in-depth and comprehensive understanding of this phenomenon and help minimize the possible recall bias presented in retrospective studies.

3.2 Methods

3.2.1 Ethical approval

Participants were enrolled as part of this nested qualitative study, which was developed on the back of a main study that investigated hospital-associated disability following an acute exacerbation of COPD. Participants were approached within up to 36 hours following admission after suffering from an AECOPD and invited to take part in the study. Upon gaining patient approval , a consent form was completed at the bedside. The protocol was approved by the East Midlands Research Ethics Committee-Leicester Research Ethics Committee with the following Ethics Ref: IRAS 239167.

3.2.2 Designing the study interview guide

The study interview questions were developed with the help of the study lead author (BSA), and by a group of experts in the field of pulmonary rehabilitation (SS & THD), a health psychologist (CB) and a consultant in Respiratory Medicine (NG). The process began with brainstorming a list of questions related to the areas of investigation. Four concepts of investigation were identified: Experiences at; 1) COPD exacerbation, 2) returning home, 3) care received and 4) exploring the participants' therapy options. Open-ended questions were used and the questions were organized in logical order by using the funnel technique, namely moving from the general questions to more specific questions (Clarke and Braun, 2013). Prompts and probes were added to the questions to enable participants to expand on

their answers and provide more detail, and a clean-up-question was added at the end of the interview to enable participants to raise uncovered aspects important to them. Afterwards, the questions were drafted in an interview-guide which was then tested with a small cohort of the targeted patient group (hospitalisation acute exacerbators of COPD).

3.2.3 Interview questions piloting process

Four patients admitted to Respiratory wards were given a copy of the interview guide and were asked to answer the questions, in order to determine the ability of the questions to capture the desired information. Additionally, participants were asked if the questions were clear and relevant to their condition, and whether they would like to add or change the wording of the asked questions.

3.2.4 Patient recruitment

A purposive sampling technique was used to sample eligible participants and the sample size determination used in this study was guided by the criterion of information redundancy (data saturation) which is a widely acceptable sample size criterion in qualitative research (Vasileiou et al., 2018). Participants of this study were recruited from a single secondary care facility in the UK between August 2019 and March 2020. Potential participants were identified from the patient admissions list of the hospital respiratory ward. To be eligible for the study, the participant needed to have the following criteria; 1) admitted to the hospital with an exacerbation of COPD, defined as requiring a change in treatment (e.g. bronchodilators, steroids, antibiotics), 2) ability to provide informed consent, 3) prior diagnosis of COPD (clinical diagnosis), 4) suffer from one or more acute COPD exacerbation attacks in the past year, 5) smoking history >10 pack years 6) level of dyspnoea, 3-5 as measured by the extended medical research council dyspnoea scale, and

finally, 7) aged more than 40 years old. Participants were excluded if they were eligible for palliative care and if they were non-English speakers.

3.2.5 Method of data collection and reporting

A female researcher (BA) with a background in respiratory care and clinical rehabilitation conducted detailed, face-to-face, semi-structured interviews (interview guide attached in the appendices) either at the patient's bedside if the patients were comfortable or in a nearby ward day room. The research lead (BA) has previous training in conducting interviews and qualitative research. Interviews were audio-recorded, and the data were then prepared and transcribed by an external authorised transcription service. Before and after each interview, the researcher completed field notes, which helped to form a comprehensive conceptual picture of the research findings in each patient's case. Data collection was continued until the dataset was deemed to reach saturation (Fusch and Ness, 2015). To determine this, a preliminary analysis of seven patients' transcripts was conducted, wherein the transcripts were coded, and base themes were generated, followed by further analysis which was conducted on the remaining five patients to enable the investigation of data saturation. Finally, this qualitative study was reported according to COREQ guidelines (Consolidated Criteria for Reporting Qualitative Research) (Booth et al., 2014).

3.2.6 Analysis

Two researchers (BA and AB) analysed the textual data via thematic analysis (TA), which is defined as "a method of identifying themes and pattern of meaning across the dataset in relation to a research question" (Clarke et al., 2015). TA has a six-stages process which was applied during this analysis. These stages are as follows: 1) data familiarization; 2) generating initial codes; 3) searching for themes; 4) reviewing themes; 5) defining and naming themes; 6) producing the analysis report (Clarke et al., 2015). During the coding

process, deductive coding was applied with a top-down approach to explore the pre-identified research concepts (mentioned in the designing the study guide section). NVivo qualitative data analysis software was used to handle the textual data (Ltd, 2018).

3.3 Results

Twelve patients (nine males and three females) were recruited during their admission to an acute respiratory ward (Glenfield hospital Leicester, UK) following a COPD exacerbation event. The mean age of the participants was 65.8 (SD 8.3) years, with COPD severity classification based on the Global Initiative for Chronic Obstructive Lung Disease (GOLD, 2019) ranging from moderate to very severe COPD (25% Moderate COPD, 33% Severe COPD, 33%). The overall collected demographics are found in Table 3.1.

Table 3.1 Semi-structured interviews participants' demographics

Participant ID	Age	Gender	COPD severity classification*	eMRCD*	Ethnicity	Frequency of exacerbation events in the past year*
1	58	Male	-	4	White	3
2	73	Male	Moderate	5a	White	4
3	58	Female	Very Severe	5a	White	3
4	66	Male	Very severe	4	White	2
5	49	Female	Severe	4	White	5
6	78	Male	Very Severe	5b	White	2
7	68	Male	Severe	5b	White	5
8	62	Female	Very Severe	4	White	10
9	64	Male	Severe	4	White	3
10	66	Male	Moderate	4	White	2
11	74	Male	Severe	5a	White	2
12	74	Male	Moderate	5a	White	4

Footnote- COPD Severity Classification*= COPD severity classified according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD, 2019), (the information presented are the historical lung function measurement retrieved from the latest test found in the patient file), eMRCD*=Extended Medical Research Council Dyspnoea Scale (Steer et al., 2012).

3.3.1 Semi-structured interviews findings

Six overarching themes were generated. They are: 1) health deterioration phase, 2) hospitalisation phase, 3) recovery phase, 4) returning home experience, 5) care received, and 6) patients' perceived therapy options. The comprehensive thematic map which shows the generated overarching themes, themes, and sub-themes is found in figure 3.1.

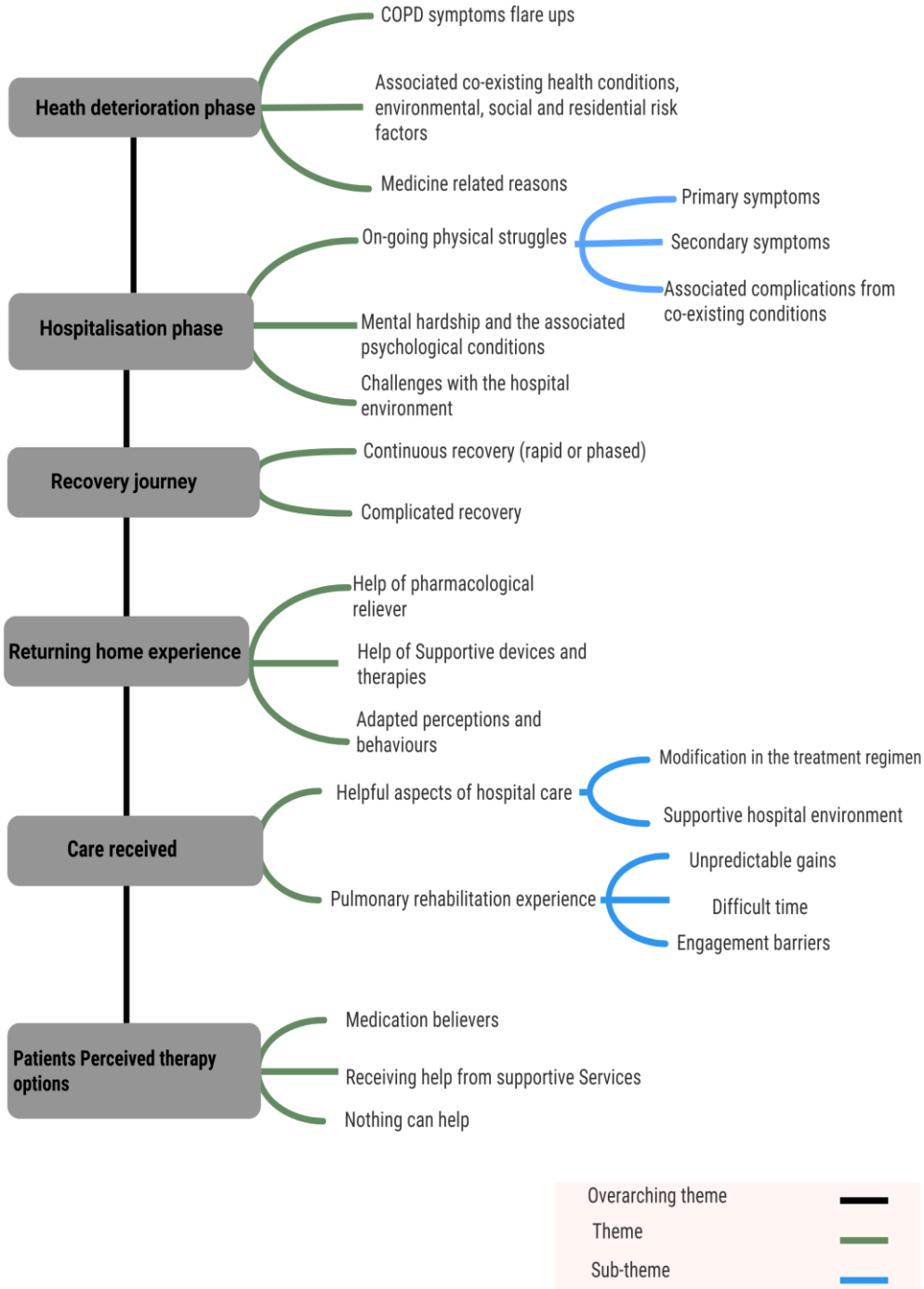

Figure 3.1 Thematic map

Overarching theme 1. Health deterioration phase

This overarching theme encompasses information about the patient's health deterioration which led to the patient seeking care from secondary health care services. This generated overarching theme included three themes:

Theme A) COPD symptoms flare ups

The majority of patients explained that issues with breathing was one of the initial and main struggles that led most of them to seek medical attention.

"I had to call paramedics out because my airways closed and I couldn't get them open. I couldn't breathe" (Participant ID 8)

" I suffered an exacerbation in my COPD on Wednesday morning: couldn't breathe. I did use the nebuliser at home and that made very little difference. I couldn't string more than two or three words together. And I think most of the time they didn't make a lot of sense even to my wife let alone anybody else. It was obviously time to call an ambulance" (Participant ID 11)

"Suffering with breathing, I couldn't breathe really, what do you call it, exacerbation of COPD" (Participant ID 7)

It was seemingly evident in many of the participant cases that patients were more drawn to giving breathless as the first priority to be mentioned as the first sign of their health deterioration before mentioning any other COPD related respiratory symptom that might have co-existed during the exacerbation event, whenever they were asked about the perceived cause behind their hospital admission.

Moreover, patients perceived other flare up respiratory and non-respiratory symptoms as the reason behind their hospital admission. However, in multiple accounts these symptoms were mentioned as a secondary result of the breathlessness symptom itself, such as decrease in mobility and suffering from panic attacks, or as a standalone exacerbated symptom that happened to co-exist during the exacerbation event such as, for example, constant cough and mucus build up in the chest.

" Because I was poorly for a few days. And could not breath and I got to the point where I could not move and I could not seem to get any air in, usually when I have a panic attack I phone the ambulance that when every time I come to the hospital on average, I don't know because I get poorlier and poorlier and I know I am weak and that when I start panic, you feel like you are drowning. It's a horrible sensation" (Participant ID 3)

"I came down with a cold Monday night. Woke up Tuesday, chest was full of mucus, coughing like mad. And went to see the GP, and was told I had a viral exacerbation. They weren't happy with my sats, put me on a nebuliser and oxygen, and then they phoned me an ambulance" (Participant ID 5)

"I started getting very breathless…I had a bad cough" (Participant ID 6)

Theme B) Associated co-existing health conditions, environmental, social and residential risk factors

Analysing the patients' narratives showed that the flare-up of other co-existing health conditions such as asthma and cardiac diseases was among the reasons that contributed to their current exacerbation state:

"Shortness of breath, I've got asthma, COPD attack. And it's just shortness of breath" (Participant ID 9)

"Well, because I suffer from angina, heart attack, but I had AF this time which you can't clear. And I couldn't clear it myself so I called 999" (Participant ID 2)

Additionally, the weather was considered by patients as a reason behind their AE event. *"It started at the weekend. I went into the local town, did some shopping and I felt really terrible, out of breath….Came back, I didn't feel too clever. Monday I felt really dreadful, I thought, put it down to weather" (Participant ID 10)*

"Shortness of breath, It works out about every 12 months, when the weather changes" (Participant ID 9)

Not being able to live in a smoke free environment and living with an unsupportive partner were mentioned as reasons for health deterioration and hospitalisation.

"Well, where I live everyone smokes, I've had to change bedrooms, I don't sleep in with the missus no more, she smokes in bed and it's just no good for me. She won't give up. So that's why I keep getting these flare-ups, because everyone around me is smoking" (Participant ID 1)

Theme C) Medicine-related reasons

In this theme participants articulated experiences related to complications resulting from the prolonged use of inhaled corticosteroid drugs, lack of availability of rescue medicine, or the need to seek modification of their prescribed medicine as reasons that led them to seek care from secondary care services.

"I have several health problems, one of which is I have osteoporosis, which is sometimes triggered by steroids I've been using for my illness. And I have a habit of breaking bones. I've broken ribs on first left- and right-hand side of my front rib cage. Then the next day at about 9.30, when I was just waking up after a fairly sleepless night, I was changing my position and gave a short cough, and I heard something go snap in my back, and I had agonies of pain. So I rang the ambulance" (Participant ID 4)

"I try and give it a couple of days before I do ring the ambulance, you know what I mean, to see if my breathing goes back to normal. But normally I would run out of inhaler or I run out of medication and I can't get any medication because it's normally at the weekend" (Participant ID 1)

"My inhalers were working overtime. I thought you've got enough for one more week and that isn't going to last long. So, I rang up 111, and they sent three ambulance drivers out" (Participant ID 10)

"Well, I had a re-occurrence of my breathing problems. Last year I was in the hospital 10 times. It started with pneumonia. And it took me months to get over the pneumonia and it's left me with breathing problems. Someone of my age, your oxygen intake should be 88 to 92, which I mentioned to you. But now and again you get, something happens, and you're breathing heavy and your levels go down. And I've come into hospital to help put it right. And I've found out putting me on steroids and things like that helps" (Participant ID 12)

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Overarching theme 2. Hospitalisation phase

This overarching theme encompasses information about the associated physical and psychological struggles experienced during the early phase of hospitalisation for an acute exacerbation of COPD event, and how patients experienced the hospitalisation period. This theme has three identified themes.

Theme A) On-going physical struggles: This theme grouped the experienced physical struggles during hospitalization into **three distinct categories.**

I) Primary symptoms

This category included the symptoms that were very prominent in causing an ongoing physical struggle for the patients on its own and were continuously given first priority when

mentioned by the participants. Those dominants were exacerbated breathlessness and chest tightness.

"My breathing, that's what I'm here for really" (Participant ID 8)

"I think the breathlessness, which comes and goes really. Thursday and Friday I felt reasonably well. And up to lunchtime on Saturday. For instance I could get from here to the bathroom and back without stopping. You know, I had to use the walker, which I've never used before. But since then just making that short trip, I've lost my breath altogether and need to use the, my reliever inhaler, about six times to try to stabilise it" (Participant ID 11)

"But now and again you get, something happens and you're breathing heavy, and your levels go down. And I've come into hospital to help put it right. And I've found out putting me on steroids and things like that helps" (Participant ID 12)

II) <u>Secondary symptoms</u>

This category included the symptoms that were expressed or linked by the participants as a consequence of suffering from the primary symptom (breathlessness), e.g., balance issues, decrease in mobility, pain, fatigue, mucus build-up and cough.

"I just can't breathe, I just can't move ..... No, just can't breathe. Everything you do is very painful" (Participant ID 9)

"It's hard work to keep breathing, so you get very, very tired" (Participant ID 3)

"When you start to get lack of breath, you start to get dizzy. You can be walking out somewhere, you can be keeling over. You can fall down a ditch and nobody's going to see you fall, anything like that" (Participant ID 10)

" I had a reoccurrence of my breathing problems, not being able to clear my throat. What it is, it's phlegm. Now they gave me tablets for it, which helped a lot" (Participant ID12)

"I had a bad cough, sometimes it was green, sometimes it would be brown, and that I was really in a bad way" (Participant ID 6)

III) <u>Associated complications from co-existing conditions</u>

This category included comorbidities and undiagnosed co-conditions that existed during the acute exacerbation event and influenced the patient's overall health or extended their physical struggles e.g. abdominal aneurysm, hernia, and sleep disturbance.

"Breathlessness, coughing, … because I've got a hernia, and when I cough that really hurts" (Participant ID 7)

" I can't breathe, because that's what makes me come in in the first place. I've got an aneurysm in my belly, you see, and that's what kicked it all off because I get a real bad pain in my belly" (Participant ID 1)

" I have tremendous problems with sleep disturbance at home. I can stay for two or three days without actually falling asleep. What I do is I just take no notice of it, and listen to the radio, TV, late night stuff, and just go right the way through. I have been known to not sleep for two or three days. It sounds impossible but it is possible with me. The only problem I do have is that I sleep walk after the third day. And I was sleep walking on the ward and they weren't best pleased with me ..... .it's always particularly pronounced when I am in hospital, not being able to sleep" (Participant ID 4)

Theme B) Mental hardship and its associated psychological conditions

In this theme, participants discussed various mixtures of feelings and psychological symptoms that were presented during the acute COPD exacerbation event and hospitalisation. For example, some participants understandably reported a progressive build-up of pessimistic attitude about their recovery and prognosis due to the continuous deterioration of their health and running out of therapy options.

"I mean I've suffered with COPD now since 2011 I think I was diagnosed. And I've always kept a very positive attitude; in fact friends and people have said they can't understand, even when I'm at my lowest, how positive I am. But that's beginning to wear a bit thin, particularly this time. I'm not lying here worrying myself sick about it,

but it's there. Because I know for myself I'm getting worse, it's inevitable really. I had the lung volume reduction surgery in 2013, and that gave me two good years really. Last year the consultant looked at doing the left lung. But that's out the question now, I'd never survive the operation. So we've run out of options really, which again doesn't help the mental state" (Participant ID 11)

Participants also reported experiences that highlighted dismal feelings of uselessness, losing the sense of self-independence and feelings of vulnerability due to the patient current health state.

"The breathlessness, that's the feeling that you can't walk, and you just feel useless really" (Participant ID 3)

"I can't walk very far, I haven't been able to for some time now. And at the moment while I'm here (the hospital), I can't walk at all without the walker. Now I've never needed one before. I've now got two at home that the hospital have supplied. And I can't stand unaided, which I find quite hard because I've been able to do that. I've got to hold onto something if I stand up" (Participant ID 11)

"When you start to get lack of breath you start to get dizzy. You can be walking out somewhere; you can be keeling over. You can fall down a ditch and nobody's going to see you fall, anything like that" (Participant ID 10)

Additionally, panic and fear sensations were reported. It is important to highlight the context where these were mentioned, namely as a result of not being able to breathe as normally as the patient was used to (a physical trigger), rather than as a result of a build-up of anxiety due to a psychological trigger.

"I tend to panic a lot when I can't breathe, because that's what makes me come in in the first place" (Participant ID 1)

Anxiety was also present in the participant extracts and highlighted as a result of the awareness of their current health state and their understanding of the inevitable deterioration that come with the AE event.

"I get a bit anxious sometimes. I'm naturally optimistic, always have been, which helped. But, as I say, that is wearing a little bit thin now. I can't walk very far; I haven't been able to for some time now. And at the moment, while I'm here (at the hospital) I can't walk at all without the walker" (Participant ID 11)

Theme C) Challenges with the hospital environment

In this theme, participants discussed how they experienced the hospital environment, e.g., they indicated their stay in the hospital caused some agitation, where they reported uncomfortable experiences with the dryness in the hospital atmosphere.

"I think the heat and the dryness of the atmosphere in the hospital's not helping, because my throat feels really dry. My mouth and my lips are really dry, so that's not helping" (Participant ID 5)

Additionally, another participant highlighted those problems with sleep disturbance became more pronounced during hospitalisation.

"That's the third day without sleep ..... but it's always particularly pronounced when I am in the hospital, not being able to sleep" (Participant ID 4)

Moreover, difficulty in carrying out the newly given advice received from their attending physicians about ways to help manage their current condition were mentioned.

"I have been taught to breathe from my nose and out from my mouth and sometimes this is painful" (Participant ID 3)

Some participants reported facing conflict with hospital staff and other residing patients for various reasons.

"I was sleep walking on the ward and they weren't best pleased with me" (Participant ID 4)

"I had a doctor come to me, you can put it on tape as well, and he kept saying to me, it's all right dear, I know how you feel. And then I said to him, get out of my room, get away from me, you don't know how I feel. And I was that cross with him the tears were streaming down my face, because I'm not a violent person, so I couldn't hit him, because I don't believe in violence. And I was so mad. He was telling me he understood, I said you don't understand how I feel. I said you do not understand at all how I feel" (Participant ID 8)

Overarching theme 3. Recovery journey

Within this overarching theme, participants explain how they experienced the recovery process post their acute COPD exacerbation phase. From this overarching theme, two distinct themes were generated: a) continuous recovery (rapid or phased recovery) and b) complicated recovery.

Theme A) Continuous recovery (rapid or phased)

This participant cohort discussed achieving full, rapid or phased recovery largely due to the pharmacological intervention given to them during their hospitalisation period.

"I mean I can still talk, I'm holding this interview. If I was very bad, I wouldn't be able to continue without taking short bursts to speak, and just a little bit wheezy.

It is getting a lot better than it was. Another day on steroids and I'll be completely clear" (Participant ID 4)

"I would say the day when I finish my course of antibiotics, I will feel more myself on average" (Participant ID 3)

Another participant expressed that their recovery process happened in phases during the hospitalisation phase, and continuously progressed post the hospitalisation phase.

"I think most times I've been in hospital I've obviously felt better and gone home and I've felt a lot better" (Participant ID 5)

Theme B) Complicated recovery

Another participant cohort discussed that they could achieve full recovery from other related respiratory symptoms such as cough, but they continuously confirmed that breathlessness was always going to be present and viewed as a never-ending struggle.

"Well the longest I've stopped out of hospital is about six weeks, and then I'm usually back in ... Cough usually goes away, but the breathing doesn't. The breathing's always going to be poor" (Participant ID 7)

"Some days I breathe easier than other days. And some days I'm really gasping for breath, I really struggle, really, really bad to breathe. Because my saturation levels,

my oxygen levels drop right down. That's all part and parcel of the COPD" (Participant ID 8)

"It'll be ongoing. This COPD, it'll never go away"(Participant ID 10)

Additionally, another patient highlighted that if breathlessness was to improve it was going to be improved regarding its severity. However, it would not disappear completely. An element of uncertainty about prognosis and anticipation of another relapse of the symptoms was also evident in the patients' extracts.

"Well, I would hope the severe breathlessness will have largely altered before I leave, which is what happened last time. It won't disappear altogether. And I hope the walking will improve but I don't know" (Participant ID 11)

"It'll come back again but you can't, you can't prognose when it's coming back" (Participant ID 2)

Participant articulated that his recovery depends largely on his ability to successfully control his exposure to passive smoking, otherwise he thinks his current residential arrangements with actively smoking partner will lead him to experience another further COPD exacerbation event in the future.

"I'm all right for about a month, you know what I mean? Well, it depends on the situation, where I am. If I'm around smokers .... unless I've got the right tools to cope with it, then I'll be all right. But if I haven't then that's when I start going downhill again" (Participant ID 1)

Overarching theme 4. Returning home experience

This overarching theme encompasses the ways participants coped and dealt with their symptoms at home. Three themes were identified.

A) Help of pharmacological reliever

Participants mostly tended to use medication as a way to get relief from exacerbated symptoms (breathlessness) at home.

"Well, all I can do is take what they give me, the medicine" (Participant ID 9)

"Well, hopefully the breathlessness I'll be able to manage with inhalers and the nebuliser" (Participant ID 11)

B) Help of Supportive devices and therapies

In this theme, participants discussed using various non-pharmacological methods such as fans, a respiratory muscle training device (Aerosure), air filters, practising breathing techniques, using walkers and activity-basing techniques.

"*Well, take my meds, and sometimes I go and lie down in my room. I've always got the window open at home, and I've got the fan on, so that usually helps, especially with the warmer weather we've been having*" *(Participant ID 5)*

"I've got a walker, I have to stop so far, and sit on the seat and take my time, and then go again (Participant ID 6)

"*I used the Aerosure device ..... bought an air filter for about £250, top of the range model, and it has an ultraviolet light that kills everything that's sucked into it*" *(Participant ID 4)*

"*If you're starting to feel yourself, like a panic level attached. You sit down on a hard chair, not on a soft chair, not say on the settee chair. And then just take deep breaths through your nose, through your mouth. Get your inhaler with you by all means, but only use that if necessary in my opinion. Try and bring your breathing*

down, just try and bring your breathing under control. Once you've done that, you feel right as rain" (Participant ID 10)

"In a couple of days, I'm going to ask for a stroller, four-wheeler where you can put your oxygen on it and go for a little walk. But I can't at the minute because my breathing's not good enough yet. But once I'm a bit better I'll ask for a stroller, and then I'll go for a walk" (participant ID 7)

C) Adapted perceptions and behaviours

These were the assumed perceptions and adopted behaviours patients acquired or realized while going through the experience of self-managing their symptoms such as avoiding exertion, social reliance, the perception of incapability or struggling with self-managing the exacerbated condition.

"I try to take my time, I try to slow down. I am not as active as I used to be, but when I am well I make the most of those days" (Participant ID 3)

"Well, all I can do is take what they give me, the medicine. This medicine and just take my time, just don't work which is a problem – because if you're working outside or inside, you're making yourself bad " (Participant ID 9)

"The wife helps me, she's my rock. She does everything for me, everything" (Participant ID 7)

"Struggle, that's the only word I can really use, struggle" (Participant ID 8)

"Well, you can't manage it because you can't prognose it, when it's going to happen. You can't manage it yourself I think, because it could come back for two hours after you've had it again, two days, two weeks, two months, you don't know when" (Participant ID 2)

Overarching theme 5. Care received

This overarching theme encompasses the participants' views on aspects of hospital care or therapy that helped them the most, and it provides a holistic exploration of the patient's pulmonary rehabilitation experiences. This overarching theme identified two themes labelled as a) helpful aspects of hospital care and b) pulmonary rehabilitation experience.

Theme A) Helpful aspects of hospital care

This theme included information about the patient's views about the various aspects of hospital services, for example, their views about the care received from their attending physicians, nurses or allied health professionals or about the pharmaco and supportive therapies that helped them the most during hospitalisation. This theme identified two subsequent themes:

I**) Modification of the treatment regimen**

Participants in this theme indicated that the change in their treatment doses or the modification of their treatment regimen was the most helpful intervention given to them during their hospitalisation following an AE-COPD event.

"*Well, the combination of the steroids and the heavy-duty nebulisers, and the antibiotics helped me*" *(Participant ID 4)*

"*Just medicine, the different things they've given me*" *Participant ID 9)*

"*The mask thing has helped me breathe a lot better*" *(Participant ID1)*

II) The supportive hospital environment

Participants expressed that the health advice and the supportive therapies they received from the attending staff was a helpful factor during their hospitalisation period.

"I've had the physio come round and see me a couple of times, but it's just trying to put into practice what he's telling me. I've got to learn to breathe again. In through the nose, and out through the mouth. It's a lot easier said than done" *(Participant ID 5)*

"The COPD nurse, they come and give me advice ... it's just controlling breathing and calming measures, so umm like this little thing that helped" (Participant ID 3)

Additionally, some participants mentioned that the hospital environment itself with its supportive, healthy atmosphere, and the nearby attending staff was identified a crucial factor that helped them the most during their hospitalisation period.

"Well, I'm going to say forceful doctors who seem to know exactly what they're doing, and put you on the right track" (Participant ID 4)

"Well, like helping me to do my medication, taking my medication and nebulisers and that ... Well, the nurses are good, which helps you, well, you can have a laugh and that with them, you know what I mean, which makes you a bit better. If you came into a ward where they were all miserable and what have you, and didn't have a laugh and that, you'd be the same wouldn't you? Miserable" (Participant ID 7)

"I wouldn't say it was care. Everybody's been nice along the way" (Participant ID 10)

"It's the satisfaction of knowing if anything else goes off, there's people on hand to sort me out" (Participant ID 12)

Theme B) Pulmonary rehabilitation experience

Within this theme patients discussed their views about pulmonary rehabilitation, their perceptions and engagement barriers. Analysis of the patient extracts identified the following subsequent themes.

I) Unpredictable gains

Participants articulated finding unpredictable positive gains after engaging in PR courses.

"*You get to the point where you believe that you can do things and it sort of showed you that you can do more than you realised … that is really, really good, that is worth being in there" (Participant ID 3)*

"The exercise, surprisingly I enjoy, even though, like everybody else on the very first time, they're sitting there on the Monday morning thinking I can't breathe, why I am going to be doing exercise? … M: But I enjoyed that. And I've always carried on after the course" (Participant ID 11)

II) Difficult time

Some participants expressed that their PR experience was challenging such as when they faced falling ill during their PR course, being overworked, or being identified by the PR staff as being unsuitable for PR due to frailty.

"*Well, I suppose it was. Near the end I wasn't very well at all. So I got ever so groggy like I was going to fall over. He said (the staff) I don't think you'll be able to carry on. So then I stopped it*" *(Participant ID 6)*

"I didn't do a lot of exercises because like I say I did not have the energy. I was really poorly, really, really poorly ... because I couldn't walk, I couldn't stand, it was awful. I thought I'd lost the use of my legs (Participant ID 8)

"So I got ever so groggy like I was going to fall over. So [unclear 0:20:12] with my walking and the breathing. He said I don't think you'll be able to carry on [unclear 0:20:22]. So then I stopped it" (Participant ID 6)

"*You see the problem is that I've had to cancel a couple of times, because there's really no point in going down there just to sit in a room with a COPD attack, because I can't do the exercises. To do the weight exercises sometimes. I take the view that you go all the way down there, because it's quite a long way for me to go, it's*

two buses and a lot of discomfort, not to be able to do the class. And I have to call in and say no, because it's doing me more harm than good" (Participant ID 4)

Another participant mentioned that the PR staff expected some level of achievement from her, that she felt it was unrealistic and refused to meet those expectations.

"*Yeah, it was bloody hard as well ... They expect you to jump on a bloody bike as well. I've never understood that ... I'm not going to jump on a bike in my life" (Participant ID 10)*

III) Engagement barriers

Many participants declined referral or dropped out of a pulmonary rehabilitation course due to co-morbidities that prevent them from participating, travel issues and having a busy lifestyle.

"Yeah. But I couldn't do it because of my heart condition" (Participant ID 2)

"No, because [unclear 0:12:40] I haven't got the time and I can't afford it. "Because I have to have a taxi here all the while, because I live the other side of Leicester... it costs me £20 to get up here, and £20 to get back" (Participant ID 12)

"I have been enrolled in one but I didn't go ... because I couldn't travel" (Participant ID 1)

However, interestingly, one patient reported that there was no need for them to participate in such a program because they felt they were fitter than the people in their age group.

"Because I'm usually quite fit-ish for my age. And it's just this, the winter weather, but when it comes from summer to winter it always takes me out. Where

people catch the flu, I catch pneumonia. So that's why I know I shall be in again this year. I come in every year" (Participant ID 9)

Overarching theme 6. Patients' perceived therapy options

This overarching theme encompasses information about the patient's care needs following discharge and it includes the following three branched sub-themes:

Theme A) Medication believers

Some participants in this theme showed over-reliance on pharmacological therapy in that they believed drugs were the only thing that could help with their condition.

" The only thing is now my medication" (Participant ID 6)

"With breathing, not a lot. It doesn't help. I've got a catheter. I've got half a foot, so I'm disabled. Well, I get medication, and that's about it" (Participant ID 12)

"No, I can't really think of anything. As long as I don't run out of my inhalers and that, I'm all right" (Participant ID 1)

Theme B) Receiving help from supportive services

This theme captured information about the patients' need for supportive therapies such as pulmonary rehabilitation (PR) and other post-discharge services such as having a carer or receiving help from Voluntary Services.

"Probably trying to keep on top of my physio, and do things slowly, and try not to overdo things again" (Participant ID 5)

" I think the pulmonary rehabilitation will be most helpful, if we can get to the point where I'm well enough to go on it. I've been before and it's always helpful" (Participant ID 11)

"Yeah, probably carer" (Participant ID 10)

"The Voluntary services are very good, women's voluntary service .... Well, they come and see you, see that you're OK when you come out of hospital, that you've got a cup of tea and that because when you've been in hospital for a week your milk's gone off, your bread's gone off and that. They're very, very good. I can't praise them enough" (Participant ID 2)

Theme C) Nothing can help

Some participants reported negative perceptions about any possibility of improving their lung condition, as they believed nothing could improve their progressed and deteriorated lung condition.

" I've got to the stage as well, I don't want to do anything in case I start gagging and I can't breathe, because it's scary. Imagine you can't breathe, it is very scary ... I've got no idea. Do you know that I've past caring to be honest?" (Participant ID 8)

"My lungs are pretty badly damaged, so I wouldn't think there are any other therapies available" (Participant ID 4)

3.4 Discussion

3.4.1 COPD exacerbation experience

Individuals experiencing an AECOPD mostly identify the symptom of breathlessness as the primary reason behind their health deterioration, which then leads them to seek help from secondary health care services. This could give healthcare professionals a much clearer idea about how patients might prioritise therapy that is structured around managing breathlessness first, before considering any other treatment option. Thus, a comprehensive patient's therapy plan should always be established and linked around this central and very important therapeutic aspect (managing breathlessness) to enable stimulating the patient's interest and engagement and facilitate attaining further therapeutic outcomes.

In a previous qualitative study that looked into the patients' experiences in identifying exacerbation in COPD, patients revealed similar findings to participants in this study, in that patients identified an increased level of breathing problems such as experiencing heaviness and tightness in the chest, labelled as the "invisible symptom" when

a sign of developing COPD exacerbation (Williams et al., 2014). Additionally, the latter qualitative study highlighted similar further findings as our current study with regard to the presence of other burdensome exacerbated symptoms called "the visible symptoms" that patients usually experience during an exacerbation attack, such as increased in sputum production, severity of cough and limited mobility.

Interestingly, in our study, some participants reported that the lack of availability of rescue medication during their attack was a driving reason for them to seek help from secondary healthcare services. This could explain some of the more frequent and short hospital admissions that certain groups of acute exacerbators exhibit during their COPD exacerbation event. In a previous study that investigated some of the primary and secondary care views from multiple European countries about self-treatment of AE-COPD, many respiratory clinicians were open about the use of rescue packs that included steroids only or accompanied by antibiotics as a way to self-manage exacerbation attacks. However, clinicians also suggested that this option should only be available to selected patients, with proper patient education about risk management (Davies et al., 2014).

Mental hardship was also one of the critical identified sub-themes where participants reported suffering from various psychological symptoms and emotions during the acute exacerbation of COPD phase, such as suffering from panic attacks as a result of experiencing a physical trigger (dyspnoea) with a heightened state of anxiety arousal which mostly leads to panic sensation (Barrera et al., 2014), ongoing anxiety about future recurrence of dyspnoea episodes and feeling vulnerable as a result of an AE-COPD event. This burdensome psychological impact has evolved further pessimistic attitudes about never attaining full recovery and feelings of being useless. This confirms similar findings of pessimistic attitudes and dismissal feelings that were also reported in the Harrison et al 2015 study, which investigated similar patient populations (Harrison et al., 2015b). Additionally, these pessimistic attitudes can also be explained as a product of the complicated recovery journey that some patients might have experienced in the past. This past experimental knowledge that the patients have formed about never attaining full recovery might also be the driving force behind declining a new treatment option that could be provided to them in

the future. This latter finding can also give a different perspective about the discharge services uptake barriers than the traditional reported ones do, e.g. accessibility issues, comorbidities, and patients being unwell (Jones et al., 2018, Benzo et al., 2015). This gives a new outlook that could explain the low participation rates within the acute exacerbation patients group.

3.4.2 Returning home

Returning home post-AECOPD showed participants' increased need to use supportive aids and therapies to help them manage their symptoms at home. This use of supportive aids and therapies was highly prominent with patients suffering from an increase in disease severity, which indicate a need to ensure educating this patient group about all the existing non-pharmacological aids and supportive therapies that are available to them for their home use. Another patient cohort demonstrated adopting negative perceptions and behaviours that were gained through their past experiential knowledge about managing exacerbation events. For example, patients tended to avoid exertion by being less active, depended on receiving care from others or struggled to know the best course of action to self-manage their exacerbated disease condition. In an observational mixed methods study that explored the patients' perceptions about what could make their life easier post-AECOPD, 20% of the participants suggested knowing more information about the provision of oxygen therapy, 12% suggested having a carer at home, 8% needed more visits from healthcare professionals and 4% needed advice on what to do when symptoms flare-ups happen (Gruffydd-Jones et al.). Additionally, the qualitative component of this study revealed an educational need expressed by the participants about how to react when their symptoms deteriorated and when was it appropriate for them to use their standby medications such as steroids, antibiotics and home oxygen (Gruffydd-Jones et al.).

The findings from this presented study, where participants showed maladaptive behaviours such as being less active to avoid exertion which will eventually cause physical deconditioning and a series of health consequences (Hurst et al., 2020b), highlighted some

level of cognitive distortion which, in psychology is defined as "the result of processing information in ways that predictably resulted in identifiable errors in thinking" (Yurica and DiTomasso, 2005). Such a condition could benefit from widely known effective psychotherapy e.g. Cognitive behavioural therapy (CBT) (von Leupoldt and Janssens, 2016, Livermore et al., 2015) or acceptance and commitment therapy (ACT) (Fernandes-James et al., 2019). Moreover, the study findings regarding participants not knowing the best course of action when they experience COPD exacerbation signify a knowledge gap that needs to be augmented in future related interventions designed for individuals with COPD exacerbation.

3.4.3 Care received

Participants in this study displayed uncertainty about the benefits of PR, which then changed to positive attitudes when a favourable outcome was accomplished at the end of their PR programme. This could never be the case for some patients, and being uncertain about the benefits of rehabilitation might play a role in them dropping out of PR before completing their rehabilitation course. Participants also found PR a difficult task due to feeling overworked, experiencing significant exertion, and feeling unable to understand the rehabilitation staff's requests. These observations highlighted a need to ensure finding time to properly administer detailed education about the expected benefits of rehabilitation before the start of the PR journey. Moreover, patients should also know that the sensation of dyspnoea will be manifested during the exercise sessions, and feelings of being overworked during the PR sessions might result in an improvement in exercise endurance, capacity, and dyspnoea outside PR. Our study findings mirrored previous study findings conducted by Janaudis-Ferriera et al. (2019) where a need for proper education for all (healthcare professionals and patients) about PR benefits was also reported to inform the faces of an acceptable form of PR for AE-COPD individuals (Janaudis-Ferreira et al., 2019a).

3.4.4 Therapy options

In this study, interestingly, many patients believe that medication is the only option for them following AE. This being so convinced that only one method of therapeutic intervention is worthy at their stage of the disease might lead to difficulty in accepting new forms of therapeutic intervention. A finding of previous study that investigated patients' self-management strategies for managing COPD exacerbation events also reported overreliance among acute exacerbators on pharmacotherapy to self-manage their condition at home (Williams et al., 2014). This highlights a future burden on health care professionals to disseminate the evidence behind new effective therapeutic interventions that can effectively manage certain disease severities or disease conditions.

Upon deeper exploration within the patient group that chose a need for another course of rehabilitation, were the ones who had experienced PR in the past and found a favourable outcome by engaging in it. Therefore, efforts to disseminate the benefits of PR through sharing the experiences of such individuals with the wider COPD exacerbation population might help eligible prospective participants consider PR and could boost individual motivation and engagement throughout the PR journey.

It is evident from the generated findings mentioned above that education is an important aspect to consider within the COPD exacerbation population. However, a health educator should consciously consider the elements of the delivered educational session and the traits of the receiver of this learning session (Blackstock and Evans, 2019). For example, as these educational sessions will target an adult learner, it is essential to consider that such a learner mostly forms his or her knowledge from previous experimental life experiences. Such a thing might play a significant role in shaping their understanding, perceptions of their illness and their future health decisions. Thus, there is a significant need to develop novel psychoeducational interventions that could help target and modify any negative illness perceptions or false disease knowledge. For example, adopting a transformative learning theory, which is defined as the process by which we transform problematic frames of references (mindsets, habits of mind, meaning perspectives), sets of assumptions and expectations, to make them more inclusive, discriminating, open, reflective and emotionally

able to change (Mezirow, 2018), might be an option with acute and post-acute exacerbation of COPD population as it targets all elements that can shape and modify barriers to engage in healthy behaviours arises from past experiential knowledge (Mezirow, 2018). In the field of physical rehabilitation, an interesting learning model has been developed and used in the occupational therapy discipline called 'The Model of Meaning Perspective Transformation in Adult Physical Rehabilitation'. This model was developed based on transformative learning theory and is characterised by three important steps that guide the transforming process: 1) the trigger phase, 2) the change phase and 3) the outcome phase (Dubouloz-Wilner, 2020). Applying this learning model and other similar transformative models in the past with patients who suffer from chronic illnesses such as stroke and diabetes has shown some benefits in improving patient acceptance and transitions into treatment (Smith-Miller et al., 2020) (Kessler et al., 2009). This latter observation could suggest another possible applicability, that needs to be evaluated by future research within the field of pulmonary rehabilitation for individuals with AE COPD (Dubouloz and King, 2016).

3.4.5 Study strengths and limitations

This study's main strengths are due to the following reasons: 1) it provides comprehensive insights into AECOPD experience at different time points pre, acute (hospitalisation) and post-COPD exacerbation, and 2) the study recruited hospitalised individuals with AECOPD to capture the true experience of COPD exacerbation while still fresh in the patients' minds rather than asking participants to recall their experiences. This is because, in older adults, one of the most common memory complaints is related to "episodic memory", which is defined as the long-term explicit memory that comprises a person's unique recollection of experiences and events and the associated context in which the event took place (Tulving, 2002). In the literature, impairments in episodic memory have been shown to improve with the provision of environmental support, such as using cues or instructions (de Lima et al., 2019). Therefore, in our study, we decided to interview individuals with AECOPD during hospitalisation to allow them to use their current

experience as a cue or stimulus to evoke their episodic memory. This also allowed patients to compare and gauge their symptoms across the phases of their experience (pre, during and post), which added authenticity to the patients' captured experience. However, it is important to mention that although the captured experiences observed within this study (as discussed above) were highly relevant and consistent with previously published research, our findings cannot be generalised over the whole COPD exacerbation population for the following reasons: 1) the recruitment of this study was stopped prematurely due to the coronavirus pandemic in 2020, which hindered our ability to reach data saturation in some explored areas of the study (care received), 2) all of the study participants are from a single centre and all are from a white ethnic group 3). Therefore, due to these limitations, our study's findings cannot be generalised to the whole COPD exacerbation population.

3.5 Conclusion

In this study, it was evident that breathlessness was considered by participants as the most burdensome symptom throughout their COPD exacerbation experience. Thus, it is suggested that healthcare professionals should use dyspnoea-related topics and therapeutic interventions as the central focus that integrate within every aspect of COPD exacerbation disease management. Additionally, results showed a great need for education sessions that are formed based on psychoeducation to improve participants' disease knowledge and modify negative illness perceptions and maladaptive behaviours that patients have formed throughout the years.

3.6 Reflexivity Statement

3.6.1 Team data analysis and reliability of coding

At the early phase of the data analysis process, the study lead (BS) who conducted the analysis process and the senior researchers (SS and THW) who have expertise in clinical

and qualitative research collaboratively discussed the key texts and gathered different insights as to whether the texts were appropriately interpreted, coded and linked to the themes. Additionally, the team reviewed the outlying emerged codes and the possibility of establishing new categories other than the initial categories identified by the literature.

3.6.2 Comparison of data within and across cases in the dataset

This was facilitated by adapting the Clarke et al., (2015) thematic analysis process which allows themes to be checked in relation to the coded extract (level 1), and against the whole data set (level 2). This created the thematic map that links the whole data set.

3.6.3 Use of field notes

The careful use of field notes (by the study's analysts) during the initial stages of analysis provided an in-depth insight and enabled a comprehensive conceptual understanding for each individual case, particularly by using the written visual observations which helped with furthering understanding of the findings within each individual case.

3.6.4 Attention to 'negative' cases

Different versions of the coding book had been generated during different stages of the analysis process. This enabled the team to continuously assess the progression of the coding tree and its linkage to the designated categories. Additionally, this iterative process provided a second opportunity to rethink outlier cases and further highlight their existence.

3.6.5 Reflexivity

Prior assumptions and experience

In qualitative research, it is believed that value assumptions are always evident and are only problematic if researchers are unaware of how their assumptions might cause bias or influence their research (Probst and Berenson, 2014). Therefore, in this study, the research team were highly reflexive and attempted to challenge their own bias and assumption during each stage of the study.

A good example of this was found in the explicit intention of the research chief investigator (SS) to create a research team that involved all the relevant study stakeholders in all the key stages of the study's design process. This research team consisted of the chief investigator (SS) and clinical Physiotherapists who have an extensive background in the care of COPD patients and the delivery of pulmonary rehabilitation (SS & THD), a respiratory physician (NG), a clinical health psychologist (CB) and the doctoral research student (BS), who collaboratively formulated the interview guide and revised the questions to eliminate adding any leading questions or prompts that might introduce bias within the patients' answers. Additionally, in order to gain broader views and feedback about the questions in terms of how relevant and clear they were, patients' input was sought during the interview questions piloting process. This enabled the research team to consider all views and edit the questions accordingly before the commencement of the data collection.

Moreover, in an attempt to reduce the interviewer's unconscious personal bias during the data collection, the interviewer (who is also the prime data analyst (BS)) attended formal training in qualitative research and interviewing skills.

Finally, during the analysis process, additional help was sought from the broader research team at the biomedical research office at Glenfield Hospital to look at the key extracted text from the interview transcripts in order to gain a broader interpretation of the data and its linkage to designated categories and themes. In order to prompt fair dealing and include the full range of the different patient perspectives and views, the study's analyst

ensured an equal interpretation, and expression of the major and minor themes, and all of the deviant cases as well.

Awareness of the patient's environment, privacy, researcher's background and the potential psychological harm.

Patients were asked before the beginning of the interview if they wished to leave their bedside to go to a nearby rest room in the ward if they felt uncomfortable conducting the study at their bedside. Additionally, throughout the interview patients were told that if they felt uncomfortable discussing certain aspects, they were always welcome to point this out, choose not to answer or end the interview altogether.

Chapter 4 . Acute Exacerbation of Chronic Obstructive Pulmonary Disease (AECOPD) Bothersome Impact and Patients Non-Pharmacological Care Priorities: A Patient Survey Study

4.1 Introduction

An acute exacerbation of chronic obstructive pulmonary disease (AECOPD) is defined as significant worsening or "flare-ups" of the disease symptoms and the physiological parameters from the baseline measures to the peak, either suddenly or a short gradual onset, which requires an adjustment in the regular patient treatment (Aaron et al., 2012, Kim and Aaron, 2018). In a large Canadian population-based cohort study that investigated the long-term profile of severe COPD exacerbation, results showed that during the mean follow-up period of 3.6 years (range from 1 day to 17 years), around 33166 individuals with COPD had at least one subsequent severe exacerbation that requires hospitalisation with a mean rate of 37.8 per 100 per year and the risk of next severe exacerbation was estimated to increase by 30-40 severe exacerbation per 10,000 per day particularly within the first trimester following hospital discharge (Suissa et al., 2012).

Additionally, data about the frequency of COPD exacerbation reported from a United Kingdom (UK) multi-centre primary care trial revealed a mean frequency of COPD exacerbation of more than three times a year occurs in 9% of mild and moderate COPD patients, 19% with severe COPD patients and 29% with very severe COPD patients (Thomas et al., 2014). The increase in the number of exacerbations within this patient population has led to a ten-fold increase in the cost of COPD treatment, which is believed to cost the National health services (NHS) an estimated £982 million annually (Directorate, 2012a).

The current recommended COPD care strategies that can provide effective, comprehensive COPD management around the time of exacerbation and help target dual

outcomes (the patient and the health care system) include integrating individualised non-pharmacological treatment interventions such as pulmonary rehabilitation (Global Initiative for Chronic Obstructive Lung Disease, 2020, NICE, 2018). However, recent national audit data showed indicators of poor PR uptake among the referred individuals post-AECOPD who started PR within 30 days of referral (17.3%) compared to individuals with stable COPD who usually undertake PR within 90 days of their receiving a referral (58%) (Singh S, 2020).

Patients' reported reasons for poor PR uptake varied from co-existing psychological conditions, transport issues, lifestyle limitations, lack of interest, motivation or knowledge about the PR benefits (Benzo et al., 2015, Jones et al., 2018).

In the literature, the reported symptomatic burden in people with advanced COPD, who usually make up most of the frequently exacerbated individuals, included symptoms such as breathlessness (94%), lack of energy (71%), dry mouth (60%), cough (56%), worrying (51%), drowsiness (41%), irritability (42%), non-chest pain (41%), chest pain (37%) and wheezing (40%) (Blinderman et al., 2009). Additionally, suffering from a COPD exacerbation event can cause health deteriorations in the individual lung function, physical activity, mental health, and quality of life (Hurst et al., 2020b). Although these data gave a good glimpse into the complex health implications and burden around the time of COPD exacerbation, to date there is no available data about the patients' perceived most bothersome disease implications at the time of exacerbation. Exploring such an aspect aligns with the proposals of interested scholars, who have suggested that patients, around the time of COPD exacerbation, could have more problems than breathlessness and exercise limitation, which might require supplemental treatment strategies other than what is currently given in conventional PR programmes (Evans and Steiner, 2017). Furthermore, among the interested scholars suggested strategies to help stimulate the exacerbated individuals' better engagement in PR post acutely was by gaining input from patients about their therapy prioritises not only retrospectively (post-discharge) but also during the actual time of exacerbation (at hospitalisation) (Rochester and Singh, 2020).

Thus, this study's primary aim is to explore the patients' non-pharmacological care priorities, and the reported most bothersome COPD exacerbation symptom or disease implications throughout the exacerbation phase (at hospitalisation and post-discharge). The study's secondary aims are: I) to explore how patients deal with their bothersome symptoms or disease implications (the disease implications are defined as the psychological, functional conditions or behaviours that are associated with the experience of COPD exacerbation), II) to explore the patients' perceived optimal timing to receive the non-pharmacological care priorities post-discharge from the hospital and III) to explore patient views about the strategies that could enhance uptake of the conventional PR programme.

4.2 Methods

4.2.1 Collection of validated outcomes

To assess the AECOPD disease implications at hospitalisation, the following validated measures were evaluated with the help of the study lead:

1) Multi-Dimensional Dyspnea Profile (MDP). This questionnaire is divided into an immediate perception domain (include 5 choices of breathing descriptions and intensity scales; 0 describe the intensity of unpleasant breathing as none to 10 describe the intensity of breathing as most intense), and an emotional response domain (include five emotions ratings and breathing sensation scale with 10 scores started with 0 for neutral to 10 unbearable unpleasant breathing)(Meek et al., 2012). (See Appendix F for the questionnaire sample)

2) Patient Activation Measure (PAM-13). This is a self-administered questionnaire which has 13 items that describe the knowledge, skills, and confidence a patient has in managing their health and care. The patient uses a 5 points Likert scale to score the answers (Hibbard et al., 2005). The question answers range from strongly disagree, disagree, agree, strongly agree and non-applicable. The total activation score can range from 0-100 points. The total scores lead the individual to be ‘categorized within four levels of patient activation’. Participants in level one are described as being disengaged and overwhelmed. Level 2 is

becoming aware but still struggling. Level 3 is taking action. Level four is 'maintaining behaviours and pushing further' (A questionnaire sample and a full description of the patient activation characteristics by level is found in Appendix G).

3) Montreal Cognitive Assessment (MOCA), which is a screening instrument for cognitive dysfunction. It evaluates attention and concentration, executive functions, memory, language, visuoconstructional skills, conceptual thinking, calculations, and orientation. The maximum score is 30, and if patients score 26 or above, they are considered to have a normal cognitive function (Freitas et al., 2012). (See Appendix H for a sample of the MOCA test)

4) Fatigue measured using the Centre for Epidemiological Studies Depression Scale revised version (CESD-R), whereby two questions related to fatigue were extracted (questions 7 and 16). Answers were rated from 0 to 4, with the higher the number denoting the higher the occurrence of the event (Eaton et al., 2004). (See Appendix I for a sample of the CESD-R scale)

5) The Support Needs Approach for Patients (SNAP), which is a tool that comprises 15 items (broad areas of support need) which patients with progressive disease commonly report they need support with. In this survey participants can indicate a need for support by choosing from three choices; no need for support, a little more support, or quite a bit more support(M Farquhar, 2018). (See Appendix J for the SNAP tool sample)

Finally, the following patient-related outcomes were routinely collected by the attending wards COPD nurses' team, namely: 1) COPD assessment collected via the COPD Assessment Test (CAT), which is a self-administered questionnaire developed to assess COPD patients' breathlessness, chest tightness, cough, sputum, confidence, activity, sleep, and energy levels. This questionnaire has eight questions rated on a 0 to 5 scale (Tsiligianni et al., 2012). 2) The anxiety outcome was collected through the Generalized Anxiety Disorder assessment (GAD-7), which is a self-reported scale that has seven items which measure different aspects of anxiety; worry, tension, restlessness, muscle pain, fatigue, difficulty concentrating and irritability. The GAD scale is scored by adding up the score for

each of the seven items. The total score can range from 0 to 21, with higher scores indicating more severe anxiety symptoms (Spitzer et al., 2006). 3) The depression outcome was measured via the patient health questionnaire (PHQ-9), which is a nine items self-reported scale that measures individual depression severity. Scores can range from 5,10,15, and 20 representing mild, moderate, moderately severe, and severe depression respectively (Kroenke et al., 2001).

4.2.2 Survey Design

To address the study's primary objective, a survey was designed to collect data regarding the most bothersome impacts of COPD exacerbation and the patients' non-pharmacological care priorities during hospitalisation and post-discharge after suffering from AECOPD. The survey questions were designed by using two initial approaches: 1) the involvement of healthcare professionals (the study authors and a health psychologist) who have previous experience in managing individuals with acute and sub-acute COPD exacerbation, and 2) a literature search to identify the research gaps and candidate research questions. To identify possible problems with the survey, we elected to use the 'Conventional Pretesting Method' (Presser and Blair, 1994), whereby the survey was administered to the Patient and Public Involvement Group (PPI), followed by a guided discussion to explore the following with the participant: what each question meant to the respondent, how clear the questions were, the difficulties respondents experienced while taking the survey and, finally, whether the respondents had any additional ideas for or concerns about the survey. A total of eight respondents participated in the survey pretesting (two rounds of piloting process). After the piloting process was completed, the survey was then revised and edited accordingly. Finally, a further attempt was made to check the face validity of the survey items through face-to-face semi-structured interviews in which the same questions were modified to be asked in a different format appropriate for the interview guide. A summary of the piloting process is reported in the appendices section of this thesis (appendix D).

4.2.3 Survey procedures and measurement

To address the survey's primary objective in relation to patients' bothersome symptomatic impact, the survey included questions about how bothersome each exacerbated symptom for the patient during hospitalisation and post-discharge from COPD exacerbation event. To answer these questions, the participants had to choose from the seven points bothersome Likert item where symptoms were rated from 0 to 6. The descriptive anchors for the Likert item questions were the following: 0-2 (not bothersome), 3-4 (somewhat bothersome) and 5-6 (extremely bothersome). It is important to mention that the survey's face validity was established through the piloting process and through the content analysis of the qualitative interviews. However, the complete psychometric properties were not investigated.

To explore the patients' care priorities during the acute versus the post-acute phase of the AECOPD, a therapy list was used with 'check all that apply' instructions to collect the data. The survey's secondary objectives were collected through a mixture of single and multiple-choice questions, open-ended questions and through administering the collection of validated questionnaires. Additionally, this study used several validated questionnaires and scales to measure various patient-related outcomes, which are all described below (for a sample of the patient survey and validated questionnaire, please refer to Appendix E-J).

4.2.4 Sampling, Participants and Recruitment

A purposive sampling technique was used in that the study lead (BA) used the hospital admission list to identify potential eligible patients according to the set eligibility criteria (Campbell et al., 2020). For the study purpose, the following eligibility and exclusion criteria were used.

Inclusion criteria

- COPD patients admitted to the Glenfield General Hospital Respiratory Ward following acute exacerbation
- ability to read and write in English

Exclusion criteria

- patients suffering from end-stage COPD (To identify individuals eligible for palliative care a surprise question was used (Noppe et al., 2018), in conjunction with the Clinical Frailty Scale (Pal and Manning, 2014). As documented in their medical notes, any individual who have a recorded no answer to the surprise question and a score of six or more on the clinical frailty scale was excluded.
- inability to read and write in English
- cognitively impaired patients (if they had been diagnosed with Dementia and/or Alzheimer's disease)
- significant speech or hearing impairment
- inability to secure informed consent

4.2.5 Survey sample calculation and recruitment

To estimate the survey population size, a search was conducted through England's Public Health Profiles website to explore the number of hospital admissions due to COPD exacerbation in the Leicester city area. The search revealed that in Leicester City the emergency hospital admissions for COPD for the year of 2018/19 was 985 cases (PHP, 2020). Therefore, with a confidence level of 95% and a margin error of 10%, which is

considered acceptable for exploratory studies (Habib et al., 2014), the survey target sample size was identified to be 88 survey participants.

The study was set to be conducted for 18 months (Aug 2019-Feb 2021) and consisted of two patient visits (see figure 4.1 for the description of each visit). Eligible participants admitted to the Respiratory Ward at Glenfield General Hospital, Leicester, were approached about the study within 48 hours of admission, since patients with COPD exacerbations tend to be discharged promptly from the wards. The aim was to gather consent on the same day the questionnaires were distributed and, thus, patients were given a window of up to 5 hours to decide if they want to participate in our study (patient consent and ethical approval letter are attached in appendix K). After screening the eligible patients from the admission lists, the study lead (BA) performed two visits; the first visit took about 10 minutes to brief eligible participants about the study and if participants agreed to enrol in the study, a second visit was performed for 45 minutes to complete the survey and the questionnaires. The patient survey and validated questionnaires were all delivered at the bedside. Before the COVID-19 pandemic started, participants were undertaking the survey and questionnaires in a paper format. However, following the start of the COVID-19 pandemic, this was shifted to an electronic version to eliminate infection cross-contamination.

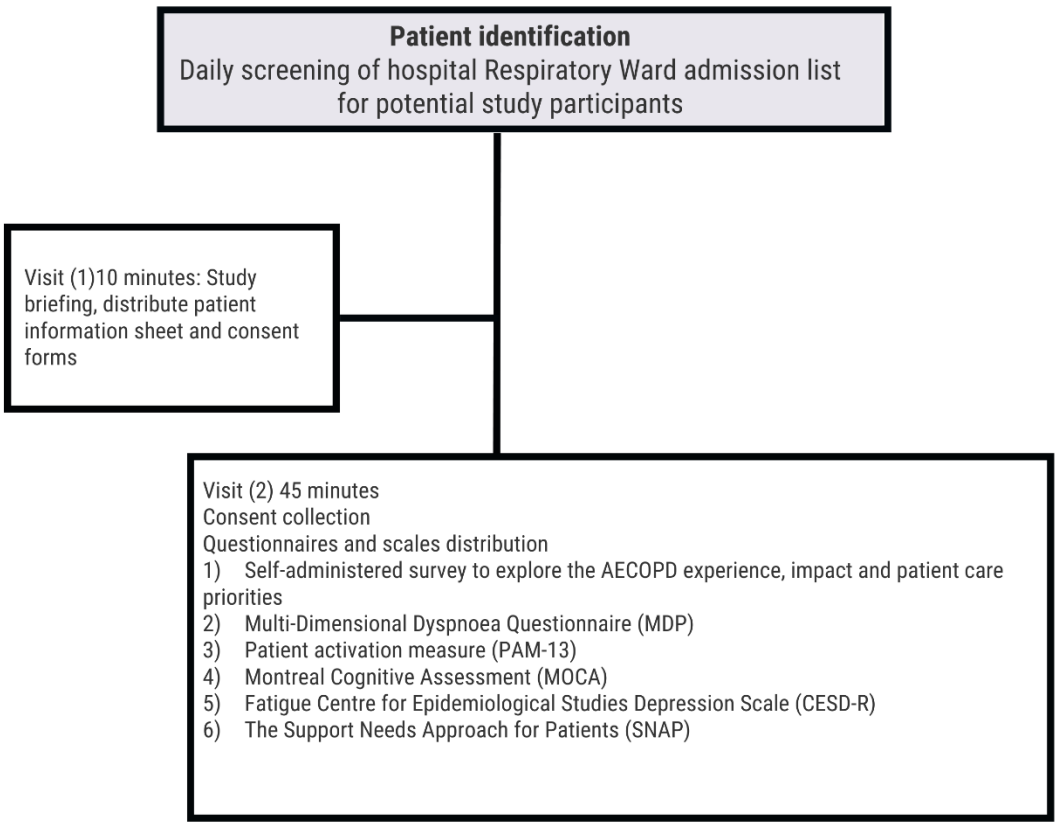


Figure 4.1 Patient survey study flow

4.2.6 Data analysis

Descriptive statistics, numbers and percentages were used to show the distribution of the results. To measure continuous data central tendency, the mean and standard deviation was used for the normally distributed variables. For the ordinal data and non-normally distributed data, mode, median and inter-quartile range (IQR) were used. Responses variability will be investigated through IQR (IQR ≤1 means complete consensuses). For data handling, an SPSS advanced statistical software was used (IBM, Released 2019). To handle missing data, pattern and proportion of missingness was investigated through SPSS software and data imputations were conducted where applicable.

4.3 Results

4.3.1 Handling missing data

The pattern of missing data was explored through advanced statistical analysis software SPSS (IBM, Released 2019). The missing data were thought to be missing completely at random (MCAR), which means that there was no relationship between the missingness of the data and any values observed or missing. The proportion of missing variables was 10%, and therefore data imputations were conducted (Jakobsen et al., 2017). To estimate missing values, Multiple Imputations (MI) were undertaken by using a linear regression model for the continuous variables and, for ordinal data, the logistic regression model was used (Jia and Wu, 2019). One variable, the 'Dizziness' symptom, was dropped from the analysis before conducting the imputations due to more than 40% of the variable values being missing at not random (this variable was introduced to the survey following a midway amendment process, and only a few participants had the chance to take this version of the survey before the termination of the study due to the coronavirus (COVID-19) pandemic. Finally, midway into the recruitment process, some of the routinely collected validated questionnaires (the ones that measured anxiety and depression) were changed to different measures. This eventually resulted in eliminating these parameters from the analysis due to insufficient data collected on both measures.

4.3.2 Survey, validated questionnaires and scales findings

A total of 50 individuals (57%) of the targeted sample size (21 males, 29 females) participated in the survey. The participants' mean age score and the standard deviation (SD) were 68.6 (9.4) years. The majority of the participants were ex-smokers (67%), held a college degree (42%), had COPD severity classification (GOLD) of severe (50%), had 1-3 hospital admissions due to COPD exacerbation in the last year (57%), and had a previous experience with PR (70%). The overall description of the survey participants' characteristics is found in table 4.1.

In the survey exploring the patients' perceived factors that contributed to their hospital admissions, reasons were mostly attributed to the following: infection (72%), weather (38%), exhaustion (28%), and because of their previously prescribed medication not working very well (24%). A complete list of the patients' perceived contributing reasons behind their hospital admission is found in Figure 4.2.

Table 4.1 Survey participants' characteristics

Participants completing the survey (n=50)	
Gender, n male/female	21/29
Age, mean (SD) years	68.6 (9.4)
Smoking Status, n (%)	
Active smoker	15 (31%)
Ex-smoker	32 (67%)
Passive smoker	1 (2%)
Education level, n (%)	
University	5 (12%)
College*	17 (42%)
Senior school	16 (37%)
Primary school	2 (5%)
No education	1 (3%)
COPD, severity classification, *n (%)***	
Mild	2 (4%)
Moderate	17 (36%)
Severe	23 (50%)
Very severe	5 (11%)
FVC (L) Mean (SD)	2.3 (0.85)
FEV_1 (L) Mean (SD)	1.19 (0.69)
FEV_1/FVC (%) Mean (SD)	47.7 (14.0)
Admissions to the hospital in the last 12 months	
1-3 admissions	31 (63%)
>3 admissions	16 (32%)
Living status, *n (%)*	
Alone	23 (46%)
Family	8 (16%)
Partner	5 (10%)
Spouse	14 (28%)

Received education about self-management	
Yes	32 (70%)
No	14 (30%)
Have prior experience of PR	
Yes	32 (70%)
No	14 (30%)
Total CAT scores mean (SD)	22.4 (5.4)
MOCA Test, Median and (IQR)	
Visiospatial/ executive function sub-score (maximum 5 points)	5 (5-4)
Naming sub-score (maximum 3 points)	3 (3-3)
Attention sub-score (maximum 6 points)	5 (6-4)
Language sub-score (maximum 3 points)	3 (3-1)
Abstraction sub-score (maximum 2 points)	2 (0)
Delayed recall sub-score (maximum 5 points)	4 (5-2)
Orientation sub-sore (maximum 6 points)	6 (0)
MOCA Total score mean (SD)	26 (5)

Footnote. Gaussian data are presented as mean ± SD, and non-Gaussian data are presented as median (IQR), * College= this category denotes the level of education completed after A levels but did not reach a bachelor's level e.g., diplomas, and associate degrees, ** COPD severity was classified according to the GOLD 2019 guidelines for COPD disease classification (the data represented in this table is historical data retrieved from latest pulmonary function test found in the patient file).

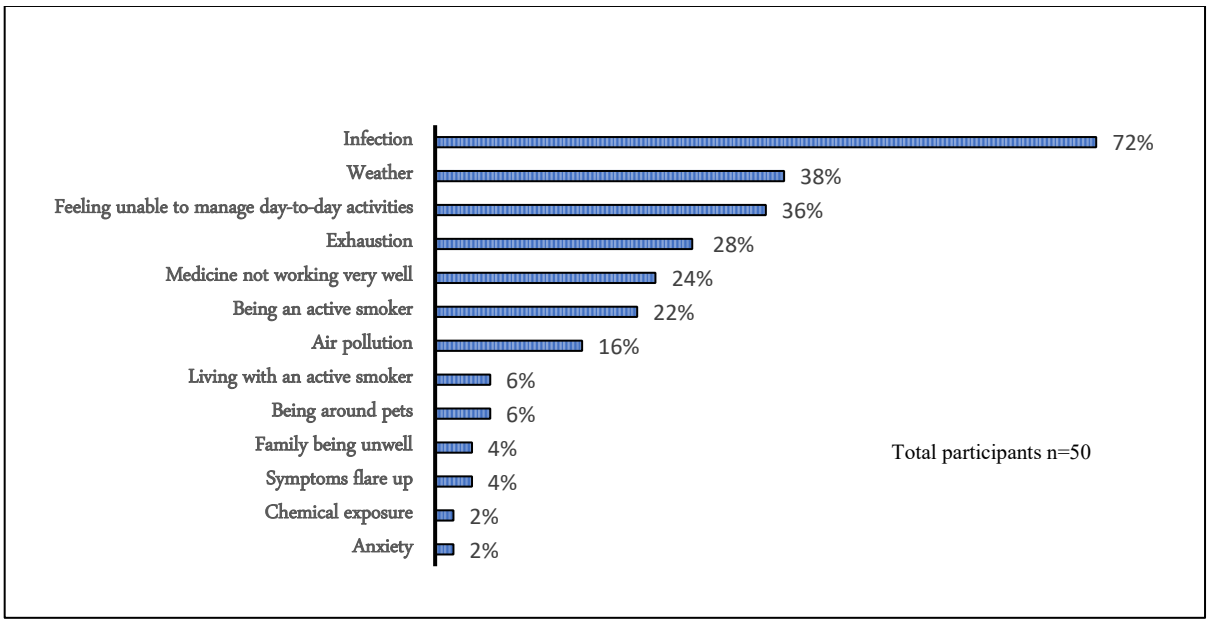


Figure 4.2 The AECOPD individuals' perceived reasons behind their hospital admission

Descriptive outcome measures

- **COPD Assessment Test (CAT)**

The mean total score of CAT results was 22.4 (SD 5.4). This mean total score is categorised within the high impact level of COPD, whereby the disease can stop the affected patients from performing most of their daily activities. Patients within this impact level tend to exhibit breathlessness while performing physical activity such as walking, or while they talk. Cough is also problematic within this patient category, as it can introduce tiredness and affect sleep. Additionally, patients within this level (high) tend to avoid exercise for safety issues and exhibit episodes of anxiety and panic attacks (Jones et al., 2011b).

- **Multi-Dimensional Dyspnea profile (MDP)**

Forty-six of the 50 (92%) survey participants completed the MDP questionnaire during admission. The median (IQR) for the immediate unpleasantness scale (A1) was 4 (3-5) (see figure 4.3). Out of the listed sensory descriptors (SQ Choice) majority, 70% of the participants chose the "I am breathing a lot" choice to describe their breathing. This descriptor was also selected as the most accurate description of their breathing at hospitalisation (46%) (see figures 4.4 and 4.5). The median (IQR) scores for the sensory descriptors (SQ scale) which described how patients felt about their breathing (immediate sensation) were as follows: breathing work effort 3.5 (3-4), air hunger 3 (6.75-2), chest tightness 3 (5-2), mental effort 3 (5.75-1) and breathing a lot 4 (6-2) (see figure 4.6). On the other hand, the median and IQR scores of the emotional descriptors (A2 Scales) which patients used to describe and score how their disturbed breathing made them feel during the hospitalisation time were as follows: depressed 3 (5-0), anxious 3 (5.75-0.25), frustrated 3.5 (6-1), angry 0.5 (4-0) and afraid 2.5 (5.75-0) (see Figure 4.7). Finally, the total scores of the immediate perception domain and the emotional domain during the time of hospitalisation for half of the participants were scored within the lower range of the total scores for both domains (see figure 4.8).

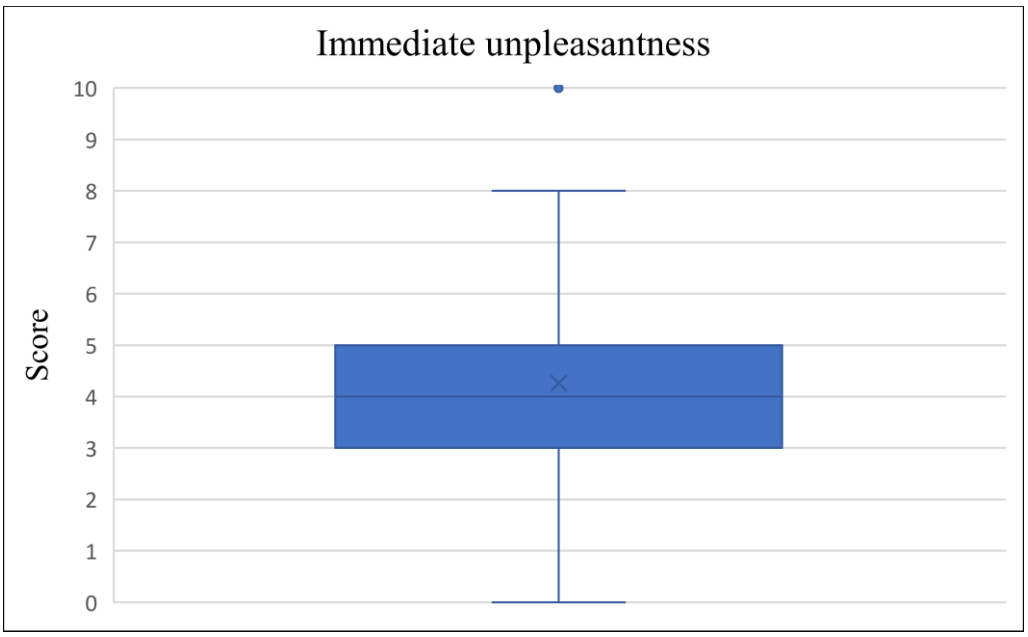


Figure 4.3 AECOPD individuals' immediate unpleasantness scale. The boxes represent the interquartile range, with indication of the median (horizontal line). Outliers are represented by circles.

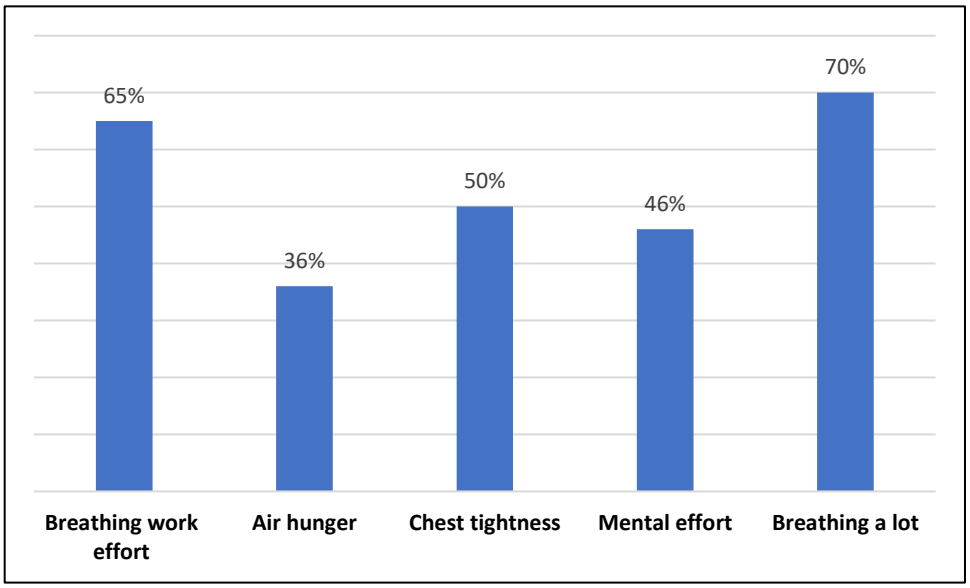


Figure 4.4 AECOPD individuals' immediate sensation about how breathing feels

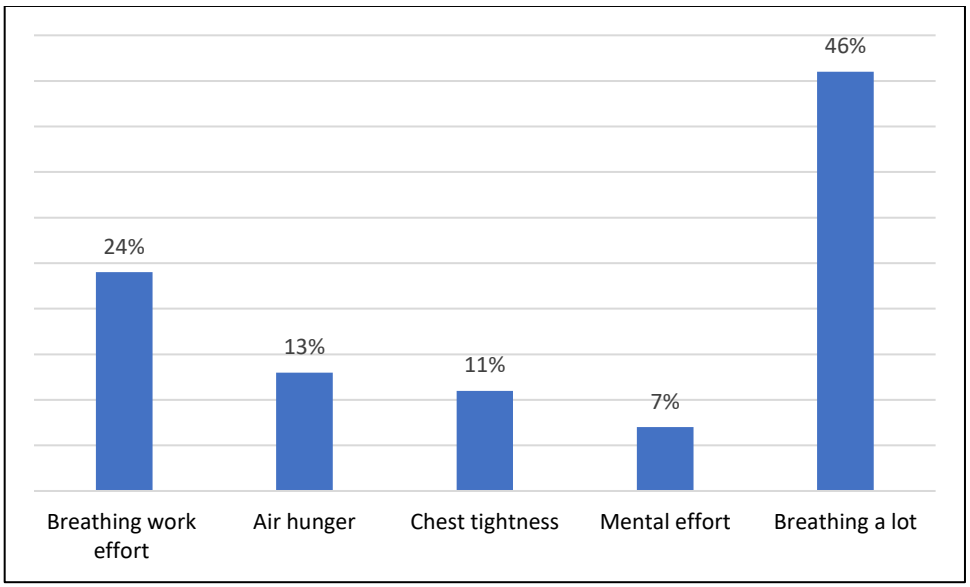


Figure 4.5 AECOPD individuals' most accurate breathing descriptor

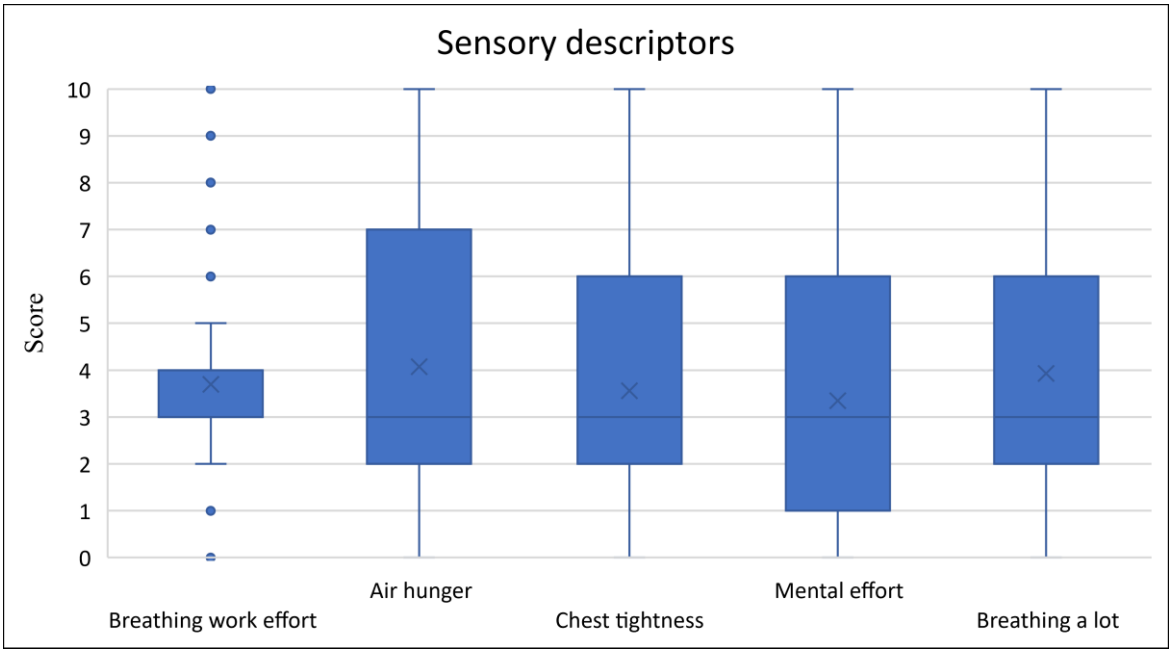


Figure 4.6 Breathing sensory descriptors scale. The boxes represent the interquartile range, with indication of the median (horizontal line). Outliers are represented by circles.

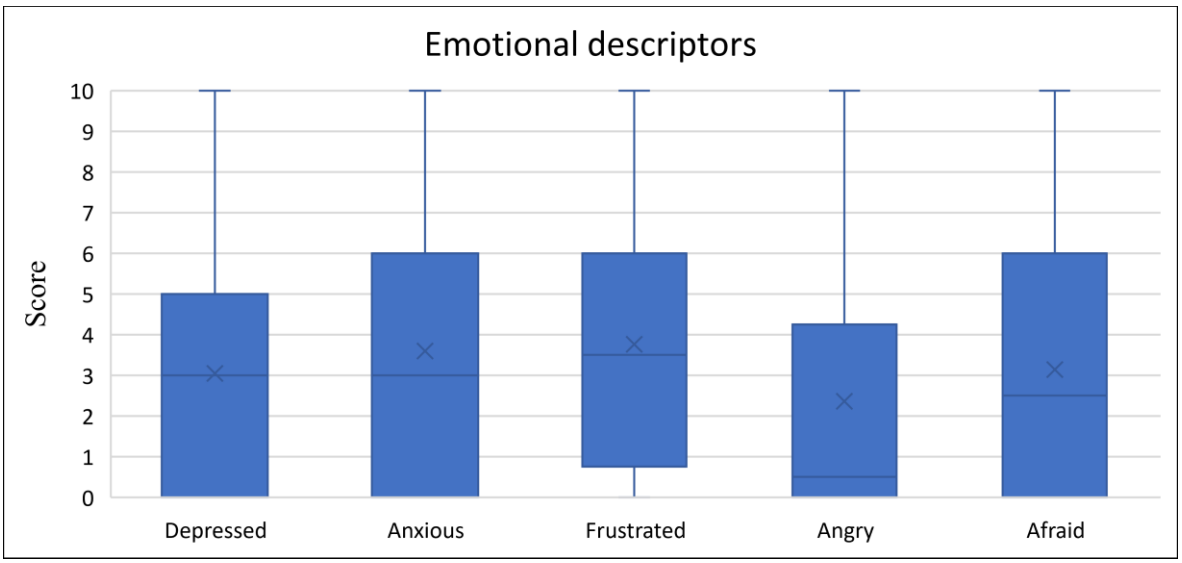


Figure 4.7 Emotional descriptors. The boxes represent the interquartile range, with indication of the median (horizontal line).

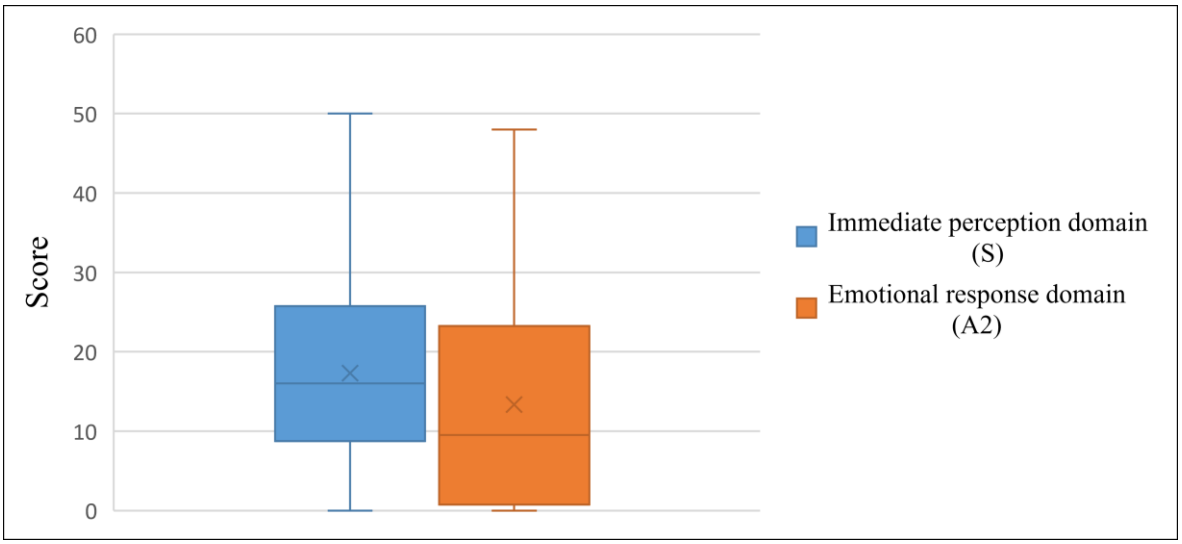


Figure 4.8 Total score of the immediate perception and emotional response domains. To calculate the total scores for the immediate perception domain (S), the sum of A1 intensity and the intensities of the five sensory descriptors were used and for the "emotional response domain" score (A2) the sum of the five emotional descriptors were calculated.

- **Patient activation measure (PAM-13)**

Thirty-eight participants (76%) out of the 50 completed the PAM-13 questionnaire, with the median (IQR) of the PAM-13 total score being 51 points (60-47) (see figure 4.9). Most of the participants (14, 37%), were categorised within level two (low activation) of the patient activation scale. At this level, individuals are described as they have some knowledge, but large knowledge gaps remain. They believe health is largely out of their control but they can still set simple goals (Insignia®, 2017). This participant category can adapt the following perspective "I could be doing more" (Insignia®, 2017).

The second most reported patient activation level was level one (low activation) where 12 (32%) survey participants were categorised within this level. At this level, participants are labelled as 'disengaged and overwhelmed' and described as passive individuals who lack confidence, whose knowledge is low, their goal orientation is weak, and adherence is poor. This participant category adapts the following perspective "my doctor is in charge of my own health" (See figure 4.10) (Insignia®, 2017). Additionally, 11 (29%) participants were categorised in level three (higher activation). At this level, individuals are characterised as having positive emotional balance, being goal-oriented, understanding their role, having sufficient knowledge about their disease and having good self-management skills (Insignia®, 2017).

One participant (3%) was categorised within level four (the highest activation level) which labels individuals as being able to 'maintain behaviours and pushing further'. At this level, individuals exhibit stronger positive emotional balance, strong orientation, understand their role regarding their health, have strong knowledge about their disease, and hold very good self-management skills (Insignia®, 2017).

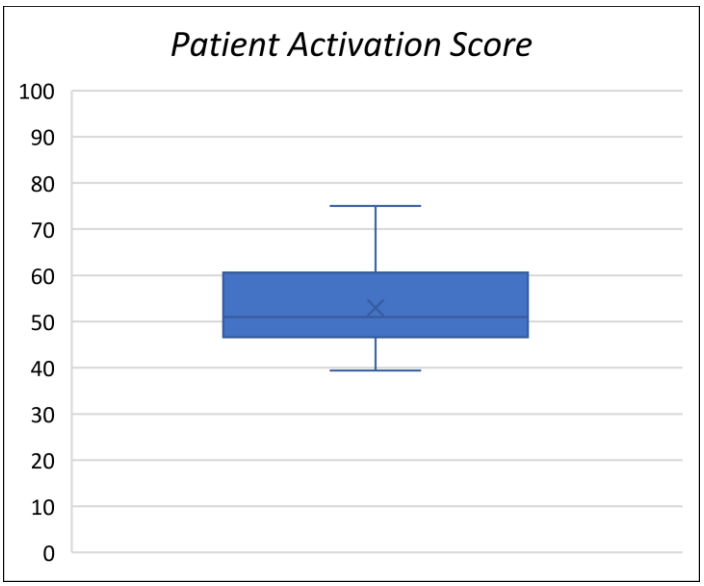


Figure 4.9 Participants' activation score. The boxes represent the interquartile range, with indication of the median (horizontal line).

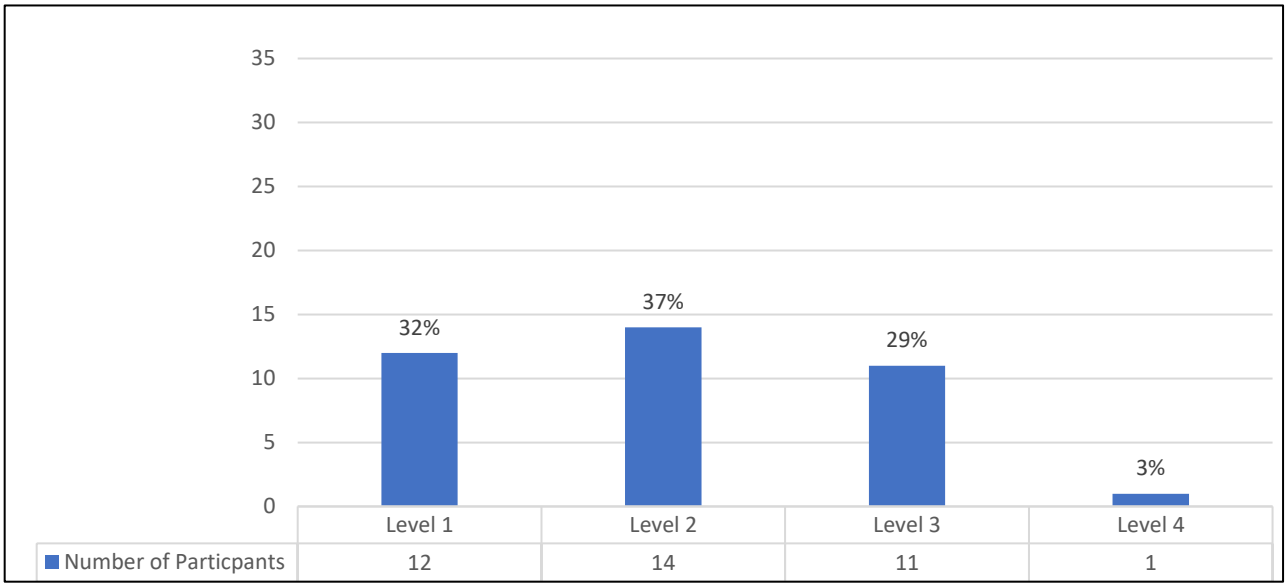


Figure 4.10 Participants' activation level (PAM-13)

- **Montreal Cognitive Assessment (MOCA)**

All 50 participants of the survey cohort (100%) undertook the MOCA test. The MOCA test total score mean and standard deviation was 26 (SD 5). This mean score suggests that, on average, participants have no cognitive impairment. Investigating the MOCA subscales of this cohort showed that participants performed well across all MOCA domains (see table 4.1).

- **Fatigue Assessment Measured by Centre for Epidemiological Studies Depression Scale Revised Version (CESD-R)**

In this study, forty participants (80%) completed the fatigue questions extracted from the CESD-R scale. Following the analysis, the results showed a higher percentage (40%) of the participants reported they could not get going for 3-4 days of the week. In addition, a higher proportion of the participants (33%) reported frequently being tired nearly every day for two weeks (see figure 4.11). Only a few participants reported no experienced fatigue within this survey cohort (3% for the 'I could not get going question', and 'I was tired all the time question' 5%).

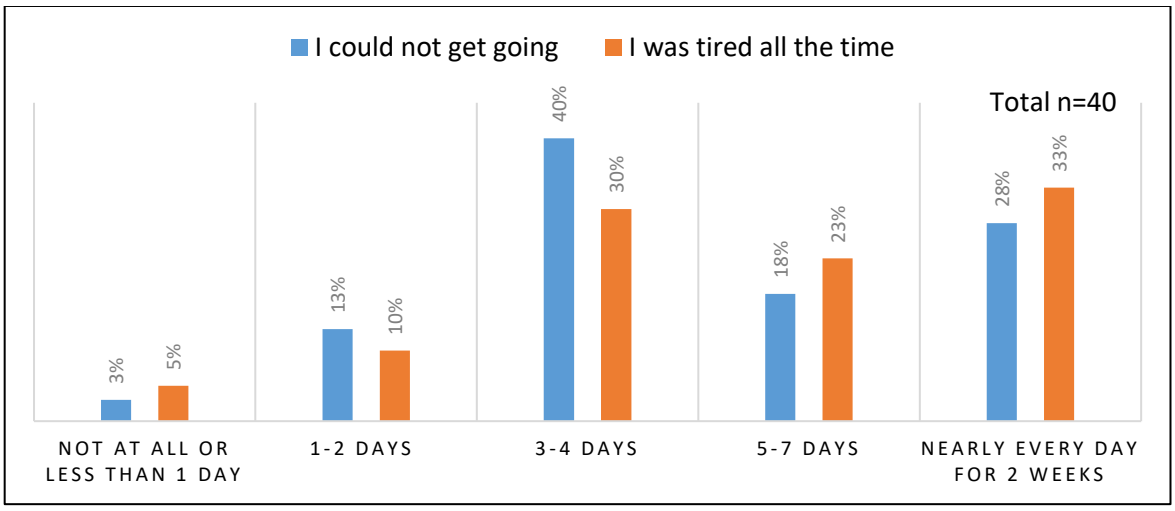


Figure 4.11 Distribution of the answers for the fatigue questions extracted from the CESD-R)

- **The Support Needs Approach for Patients (SNAP)**

Thirty-eight participants (76%) completed the SNAP tool (see appendix J). Figure 4.12 shows the distributions of the AECOPD participants' expressed needs captured by the SNAP tool. The results showed that the majority of the participants indicated a little more support was needed with understating their illness (55%), managing symptoms (47%), dealing with feelings and worries (50%). Additionally, approximately half of the cohort indicated either no support needed or a need for a little more support in looking after any other physical health problems they had (42% for both answer choices). In practising a healthier lifestyle option, 50% of the participants indicated no need for support, and 45% of participants needed a little more support.

Conflicting results were found regarding a need for having support within the aids and equipment option, where almost half of the participants' cohort selected no need for support (47%), and a little more support was chosen by 45% of the participants. The participants indicated a support need in knowing what to expect in the future (45% stated a little more support needed) and accessing or using services (42% indicated a little more need for support).

Interestingly, the only area where a high number of the participants indicated a need to have quite a bit more support was getting out and about (29%). Most AECOPD participants identified no need for support within the following SNAP items: overcoming boredom and loneliness 58%, financial and legal support 76%, family relationships 84%, practical help with the home and garden 66% and carer support 79%.

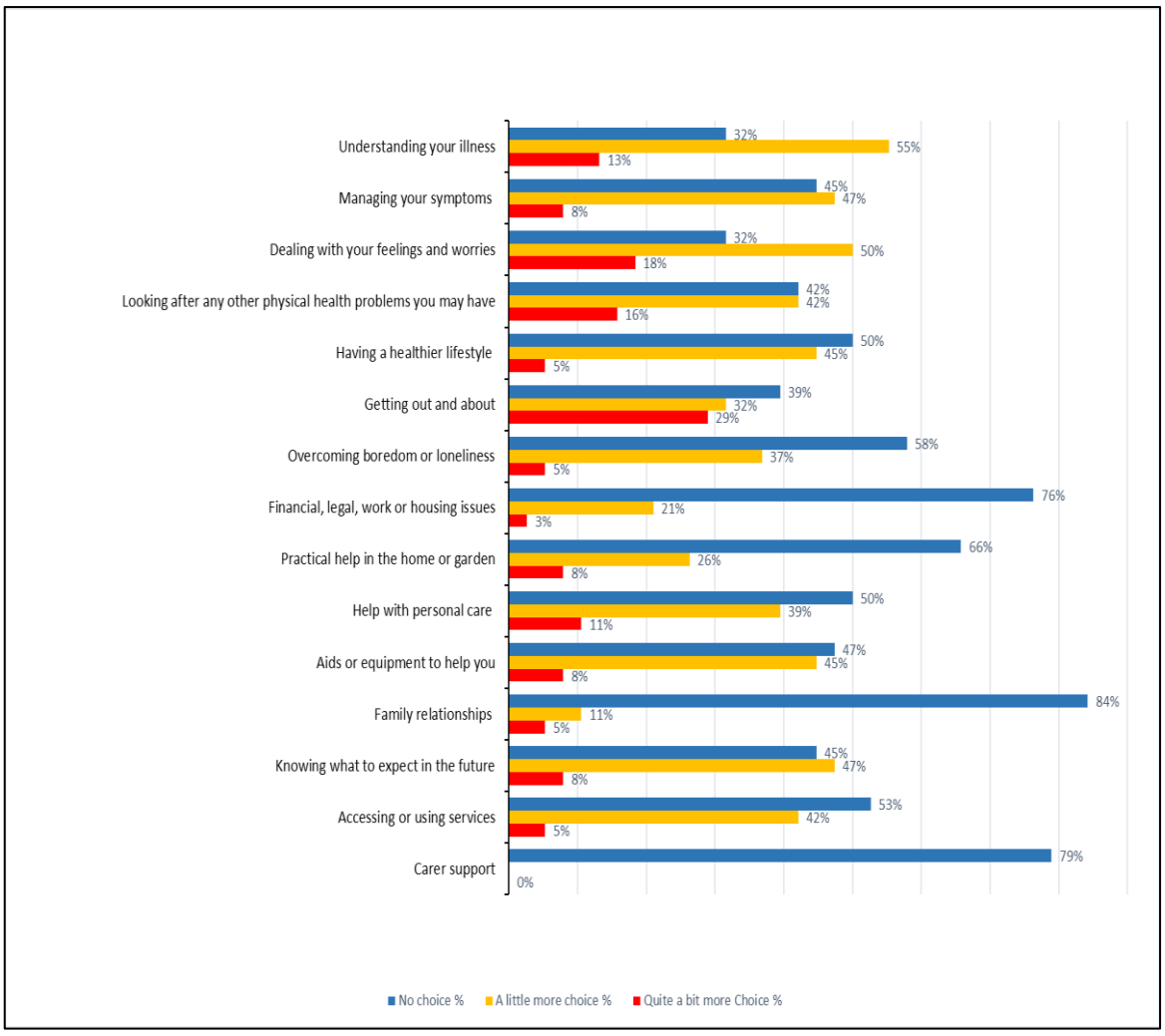


Figure 4.12 The AECOPD expressed needs captured by the SNAP tool

4.3.3 Bothersome AECOPD implications or symptoms during the hospitalisation phase

Survey results showed that during the AECOPD phase, only 16% of patients regarded breathlessness as not bothersome during the hospitalisation phase. When the central tendency of the scores was measured, the results showed, on average, that patients perceived breathlessness as a 'somewhat bothersome' symptom during hospitalisation, with a median score of 4. Additionally, when the response variability was explored through the interquartile range (IQR), results confirmed that the variability of the participants' responses were not far apart from the median score (IQR of 2) (see figure 4.13). However, the results did not suggest complete consensus as few survey participants (16%) perceived breathlessness as a non-bothersome symptom during the hospitalisation phase (see figure 4.14), with the other majority perceiving it as 'extremely bothersome' (40%).

Moreover, on average, cough was also perceived as 'somewhat bothersome' by respondents during hospitalisation, with a median score of 3 and a relatively narrow variability in the responses with an IQR of 2 (See figure 4.14 for the distribution of responses). Other symptoms, such as chest tightness/ wheezes and limited mobility, were, on average, perceived as 'somewhat bothersome' during hospitalisation (Median 4). It is also important to mention that the calculated IQR of 3 suggests that perceptions were highly polarized among the participants' selected responses (see figure 4.14 for the distribution of the responses)

Exhaustion and tiredness (median 3.5), leg weakness (median 3) and sleep disturbance (median 3) were all perceived as 'somewhat bothersome' by the survey participants. However, perceptions were also highly polarised, with an IQR of 3, 5 and 3, respectively (see figure 4.14 for the distribution of the responses).

Finally, the results have shown that participants, on average, perceived low mood, fear and panic attacks and pain as 'not-bothersome' symptoms during the hospitalisation phase. However, the IQR 4 for low mood, 4 for fear and panic attacks, and 3 for pain

symptoms indicated divided perceptions among the survey participants as 42%, 42% and 28%, respectively, rated these symptoms as 'bothersome' (see figure 4.15).

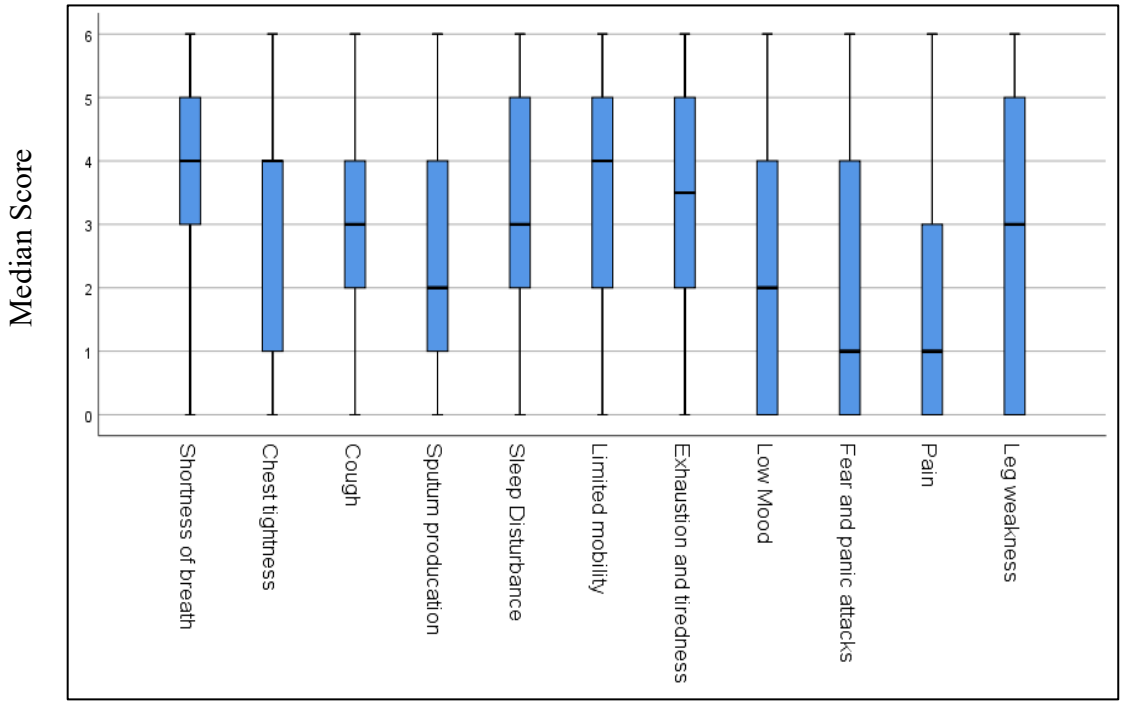


Figure 4.13 AECOPD individuals' reported level of bothersome symptoms and disease implications during the hospitalisation phase. The boxes represent the interquartile range, with indication of the median (horizontal line).

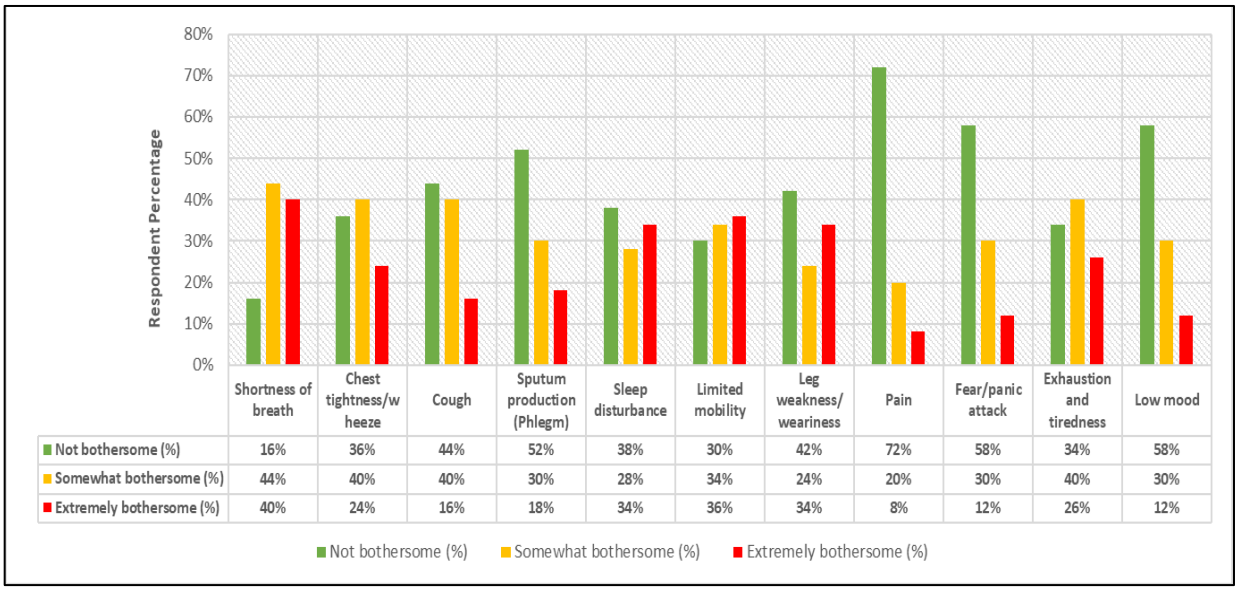


Figure 4.14 Patients' reported bothersome AECOPD symptoms and disease implications during the hospitalisation phase

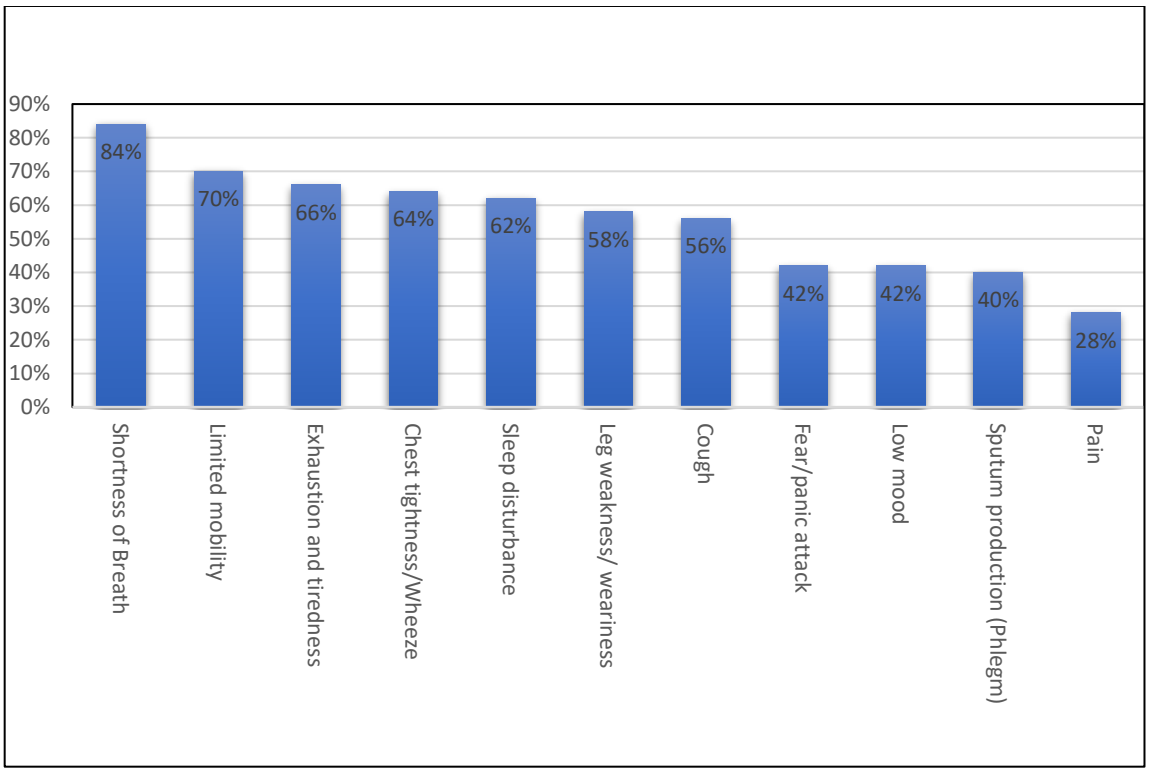


Figure 4.15 Proportions of the AECOPD patients' reported bothersome symptoms and disease implications during the hospitalisation phase

4.3.4 Bothersome AECOPD implications or symptoms during the post-discharge phase

In this section of the survey, participants were asked to rate how bothersome their symptoms 'usually' were (post-discharge phase). Results showed that respondents, on average, perceived shortness of breath (median 4) as 'somewhat bothersome' with a relatively narrow variability of the responses (IQR of 2) (see figure 4.16). The existing variability was due to 10% of the survey participants perceiving breathlessness as 'not bothersome' during the post-discharge phase, in contrast to the majority of the participants (90%), who perceived breathlessness symptoms as 'bothersome' (see figure 4.17).

Limited mobility and exhaustion and tiredness scored a median of 4 (somewhat bothersome) with an IQR of 3 for both symptoms. Leg weakness and weariness were also

rated, on average, as ‘somewhat bothersome’ (median 3; IQR 2). The percentages distribution shows that the majority of the survey participants rated these symptoms with some degree of bothersome, either somewhat or extremely bothersome symptoms (see figure 4.18)

Furthermore, chest tightness/wheezing (median 3; IQR 2), cough (median 3; IQR 3) and sleep disturbance (median 3; IQR 3) were, on average, perceived by the respondents as ‘somewhat bothersome’ during the post-discharge phase, with IQR indicating the wide variability of the responses (see figure 4.16).

On the other hand, sputum production (median 2), fear and panic attacks (median 1), low mood (median 2) and pain (median 2) were, on average, rated as ‘not-bothersome’ with significant variability in the IQR: 3, 4, 4, 4 respectively (see figure 4.16). However, the percentage trends of these disease implications less support the bothersome nature of these implications during the post-discharge phase (see figure 4.18).

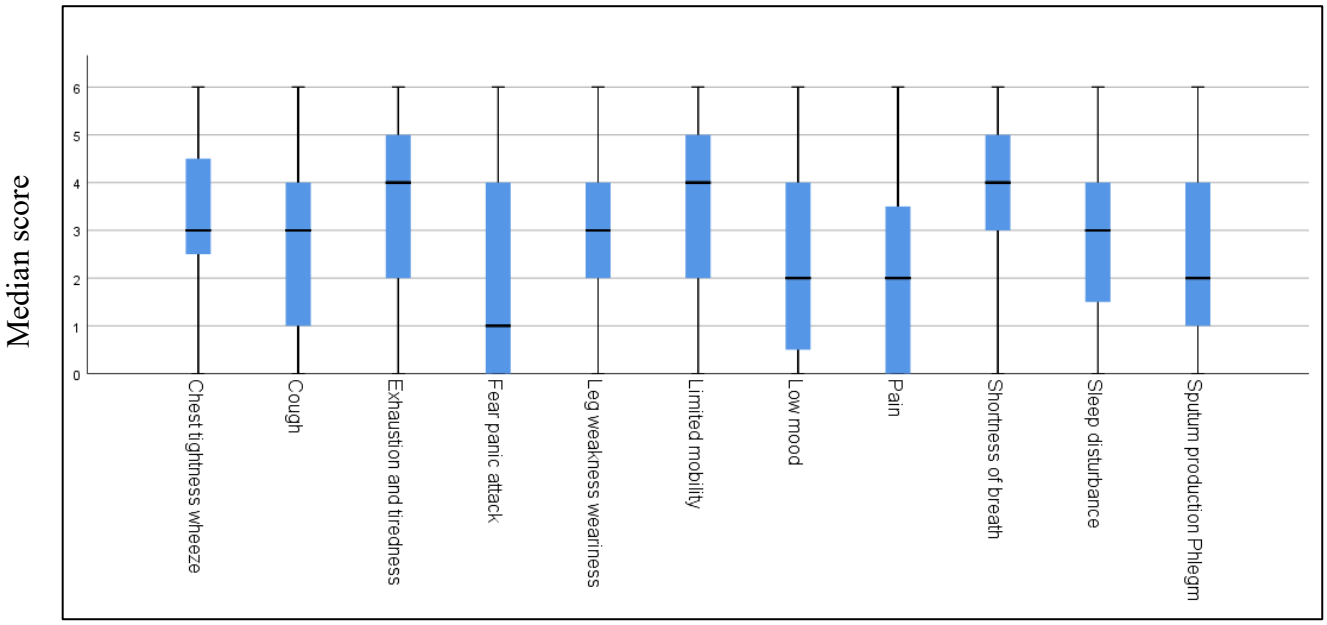
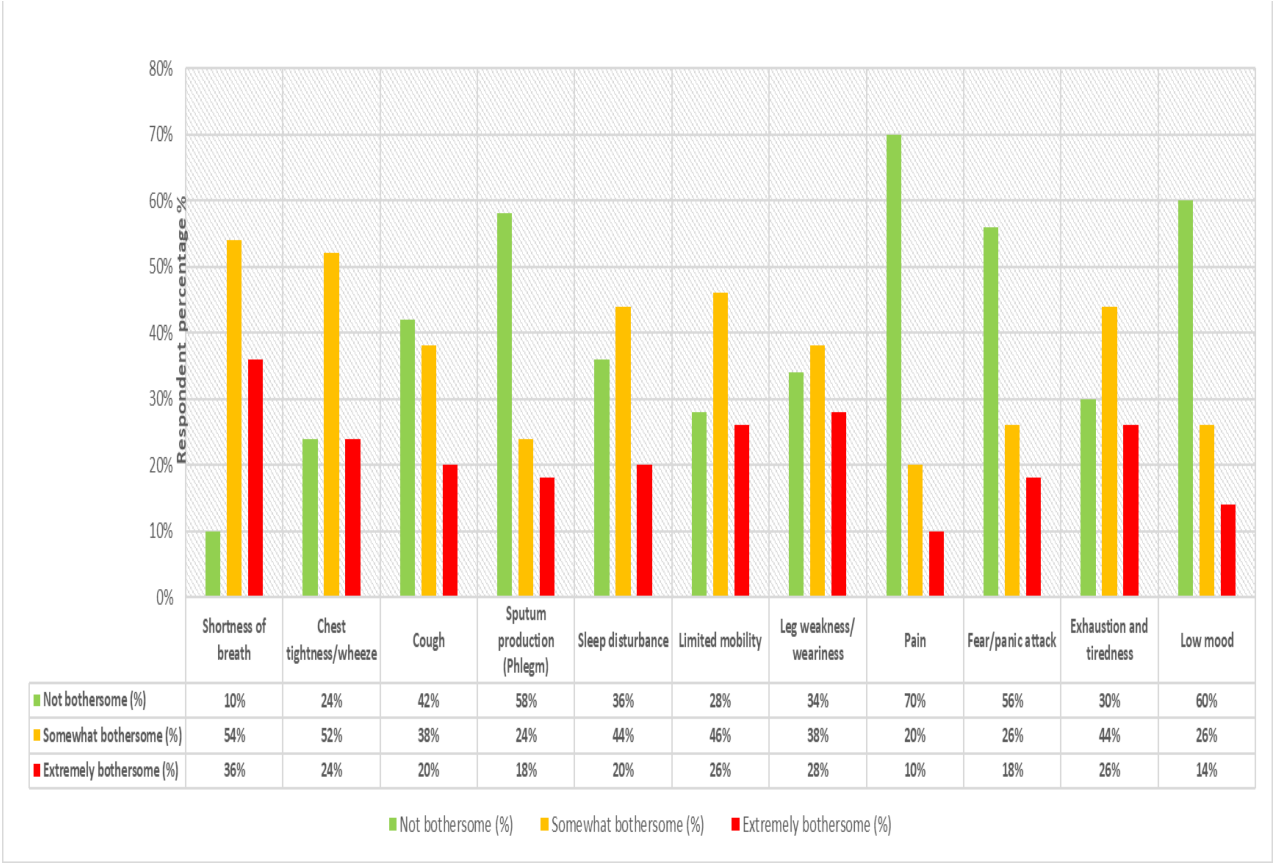


Figure 4.16. AECOPD individuals reported level of bothersome symptoms and disease implications during the post-discharge phase. The boxes represent the interquartile range, with indication of the median (horizontal line).



	Shortness of breath	Chest tightness/wheeze	Cough	Sputum production (Phlegm)	Sleep disturbance	Limited mobility	Leg weakness/ weariness	Pain	Fear/panic attack	Exhaustion and tiredness	Low mood
Not bothersome (%)	10%	24%	42%	58%	36%	28%	34%	70%	56%	30%	60%
Somewhat bothersome (%)	54%	52%	38%	24%	44%	46%	38%	20%	26%	44%	26%
Extremely bothersome (%)	36%	24%	20%	18%	20%	26%	28%	10%	18%	26%	14%

Figure 4.17. Patients reported bothersome AECOPD symptoms and disease implications during the post-discharge phase

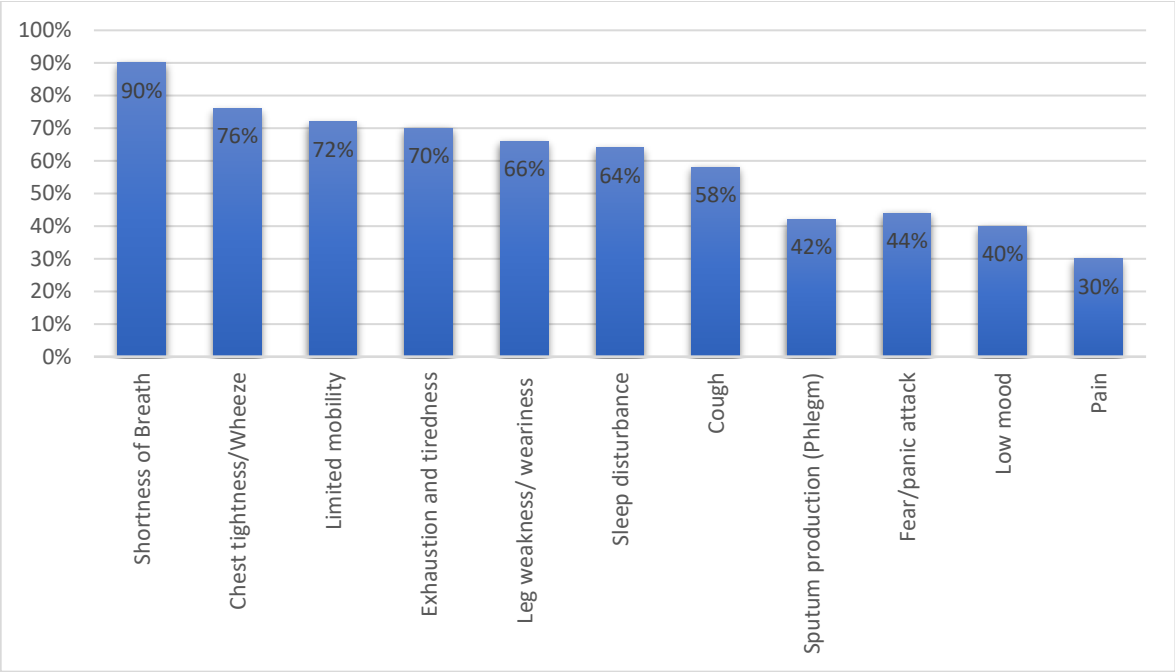


Figure 4.18. Proportions of the AECOPD patient reported bothersome symptoms and disease implications during the post-discharge phase

4.3.5 How individuals with AECOPD deal with bothersome disease implications and symptoms

Participants mostly avoid activities to prevent symptom deterioration n=25 (50%). Additionally, a proportion of participants n=14 (28%) expressed that they tended to ignore the symptoms or indicated they did not know how to deal with their bothersome symptoms n=6 (12%).

Few participants elected to take different approaches, such as n=2 (4%) doing what their health care professionals advised them to do, self-managing n=1 (2%) and trying to live with bothersome symptoms or seeking medical intervention n=2 (4%).

4.3.6 AECOPD non-pharmacological patient care priorities during the hospitalisation phase

Exploring the patients' non-pharmacological care priorities during the hospitalisation phase revealed that, as a whole, the AECOPD individuals prioritised various care interventions according to their diverse needs (see figure 4.19). However, upon closer exploration, results showed that respondents mostly prioritised less active therapeutic approaches during the hospitalisation phase. For example, the top three prioritised non-pharmacological patient care interventions during hospitalisation were receiving: advice on breathing exercises (58%), education about self-pacing techniques (48%) and help with exhaustion and tiredness by providing equipment to help with day-to-day activities such as walking aids and electronic gadgets or assistive appliances around the house (46%) (see figure 4.19). Lower percentage trends were reported within the prioritised non-pharmacological patient care intervention that required more active participation from the patient's side during the hospitalisation phase. For example, the reported percentages of the prioritised exercise interventions were as follows: receiving exercises to improve strength all over the body (12%), receiving specific exercises to improve strength in the lower body (12%), and strength in the upper body (6%).

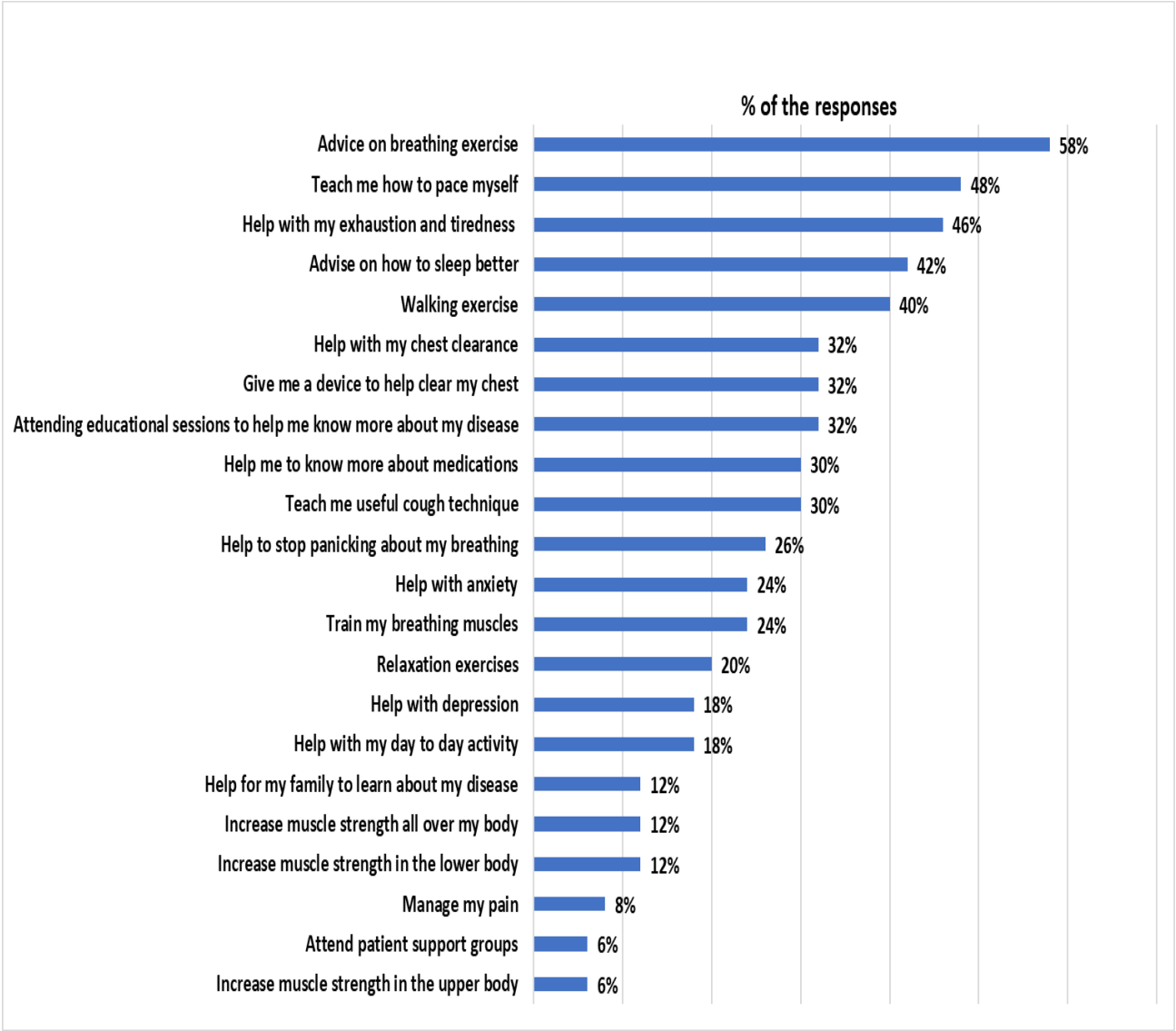


Figure 4.19. AECOPD non-pharmacological patient care priorities during the hospitalisation phase

4.3.7 AECOPD non-pharmacological patient care priorities during the post-hospital discharge phase

Similar to the hospitalisation phase, individuals with AECOPD seemed to have various non-pharmacological care priorities during the post-discharge phase (see figure 4.20). However, the top three prioritised non-pharmacological patient care interventions indicated a higher percentage of the survey participants prioritised interventions that required more active participation from the patient side, such as breathing muscle training (50%), increased muscle strength and tolerance all over the body (40%) and help with exhaustion and tiredness (38%) (figure 4.20).

Conversely, managing pain (8%), attending educational sessions to improve disease knowledge (6%) and carer educational sessions were among the least prioritised non-pharmacological patient care interventions during the post-hospitalisation phase (6%).

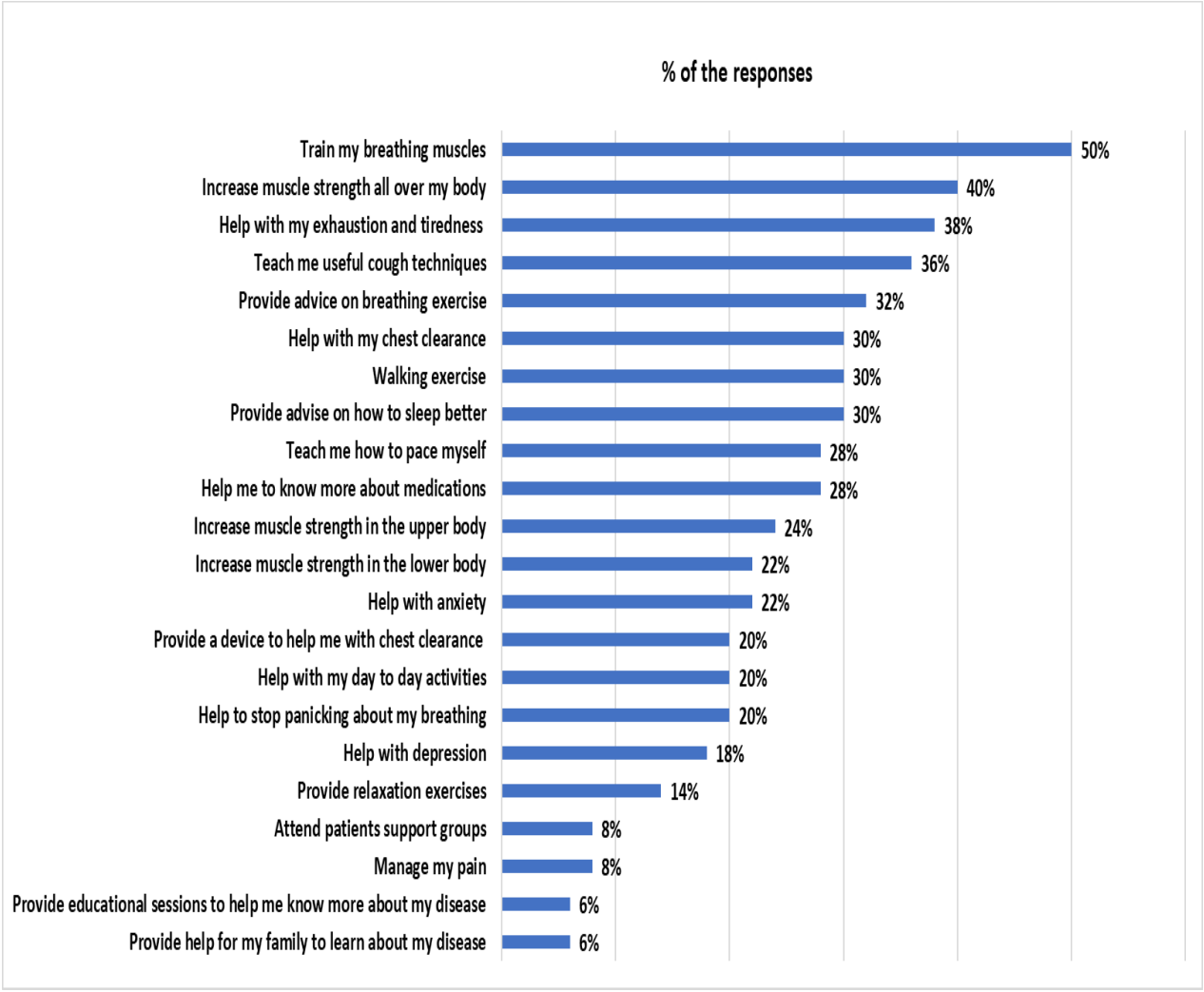


Figure 4.20. AECOPD non-pharmacological patient care priorities post-hospital discharge

4.3.8 Timing to administer the non-pharmacological patient care priorities post-hospital discharge

Exploring the survey participants' preferences about the best time frame to administer their prioritised non-pharmacological patient care needs post-discharge, the results showed the following: with regard to managing breathlessness, the majority of the patients' selections were between two options, namely immediately n=16 (32%) and in a few days post-discharge n=12 (24%). Additionally, with regard to help with cough, the majority of respondents seemed to give almost equal preference to three choices: n=10 (20%) immediately; n=10 (20%) in a week time; n=12 (24%) chose within a month's time.

For exercise to increase muscle strength and tolerance, the majority of the patients selected to start this therapy within a month of discharge n=24 (48%). Moreover, in relation to exhaustion and tiredness management, most participants preferred the non-pharmacological intervention to be delivered in a few days n=20 (40%) post-discharge. Administering help with regard to helping with mood (anxiety and depression management), patients' selections were more diverse as the data distribution looked as follows: n=18 (36%) selected not at all; within a month, n=17 (34%); in few days n=5 (10%); in a week n=5 (10%).

Regarding improving knowledge about the disease, the majority of the survey participants chose the 'in a few days option' n=16 (32%). For help with sleep disturbance, the top two preferred options were in a few days n=12 (24%) and in a month n=12 (24%). Finally, with regard to managing pain post-discharge, the vast majority of the survey patients selected the 'not at all option' n=32 (64%).

4.3.9 Strategies to enhance uptake to conventional pulmonary rehabilitation programme

Participants selected various suggestions that could enhance their ability to attend a pulmonary rehabilitation (PR) programme within the period of one month of post-AECOPD hospitalisation. The majority of respondents preferred to make physical exercises easier to do (43%), some chose to start with education before starting any physical exercises (36%), some to concentrate on only exercises that make them less breathless (36%) and some chose the option to provide transport (32%). The other selected options, however less favourable, were the following: wait until the patient completely healed before enrolling in the PR programme (28%), provide more interactive educational sessions (18%), start when the weather was better (18%) and, finally, allow their carer to engage in the programme (14%).

4.3.10 The participants perceived importance of receiving non-pharmacological care intervention for the AECOPD symptoms and disease implications

The majority of the participants gave the highest level of importance (very important) to receiving non-pharmacological care interventions to deal with breathlessness (79%), and just over half of the cohort indicated a high level of importance to receiving non-pharmacological care intervention for chest tightness (52%). Additionally, 39% to 40% of the participants indicated a high level of importance (‘very important’) to receiving non-pharmacological care intervention to deal with limited mobility and muscle weakness. A highly polarised level of importance was selected within the receiving non-pharmacological care intervention to deal with the cough symptom, sputum production, sleep disturbance, exhaustion and tiredness (see figure 4.21 for distribution of the responses). However, a larger number of the survey participants indicated that it was not at all important to receive non-pharmacological care for pain (41%) and disease implications such as fear and panic attacks (46%) and low mood (40%).

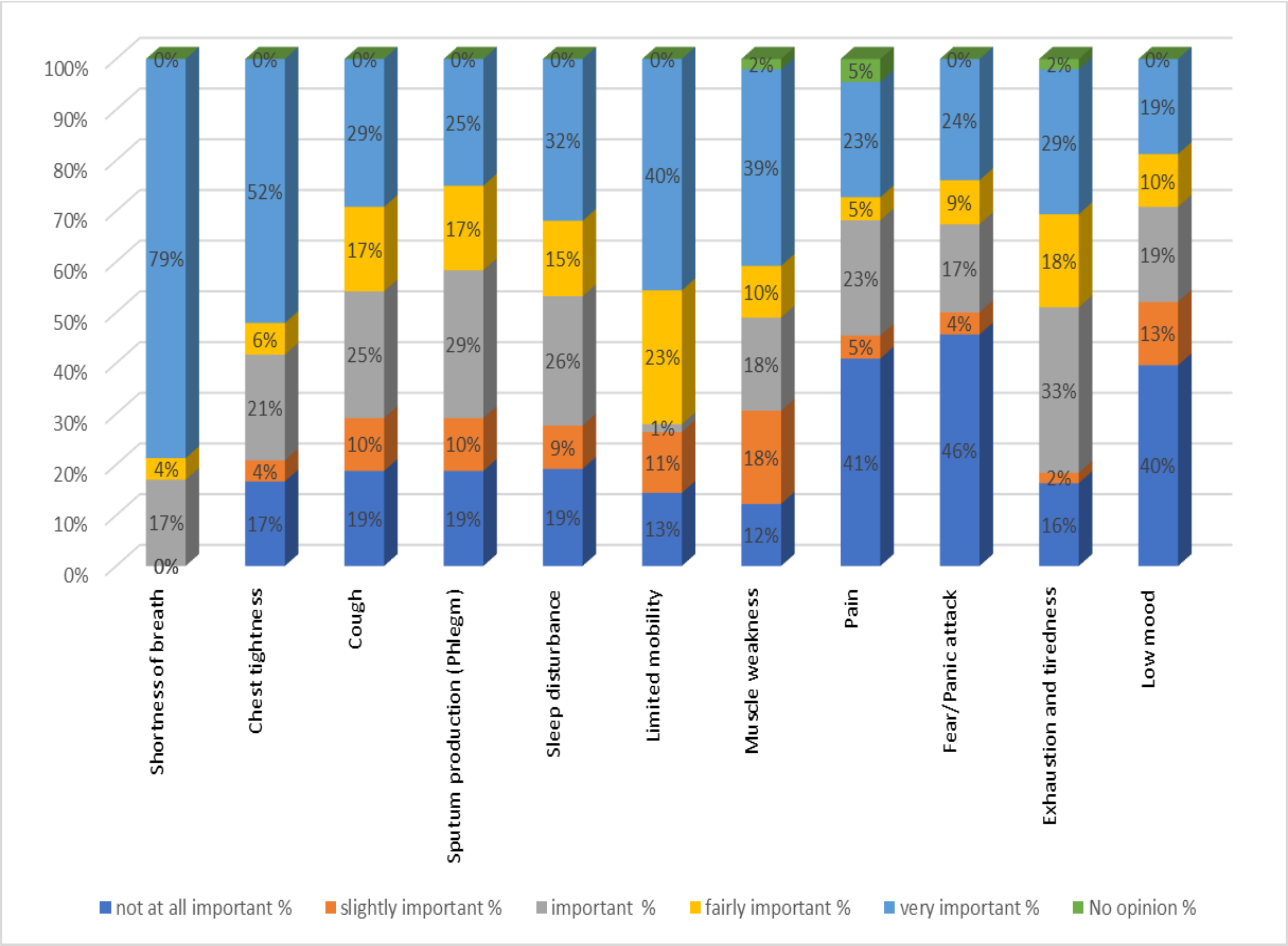


Figure 4.21. Participants perceived level of importance to receive therapy for the AECOPD disease implications

4.4 Discussion

To our knowledge, this is the first study that has explored individuals' care priorities during both phases of AECOPD (at hospitalisation and post-discharge). In addition, the multifaceted exploration conducted within this study has provided a very useful insight into the most bothersome AECOPD symptoms and disease implications for the patients. The present study key results in relation to the assessed validated measures at hospitalisation showed, a median score closer to the mid-point of the MDP breathing unpleasantness sub-scale and a breathing descriptor that is closely related to the presence of increased work of breathing within this population. The captured patient activation levels within our study population were low. However, the investigated participants' cognitive function were on a normal level. The survey key findings showed various identified bothersome symptoms and patient care needs (patient care priorities), however, the highest identified median scores of bothersome disease implications or symptoms and the highest selected proportions of prioritised patient care needs were all seemed to be interlinked with either the results generated from this study designed survey or from the results of the validated tool of identifying patients care or support needs (SNAP tool) used in this study.

In this present study, the multi-dimensions of dyspnoea symptom measured by the MDP dyspnoea scale showed a median score of 4 (IQR 3-5) on the immediate sensation of unpleasantness subscale which measures the difficulty in breathing that individuals usually experience with COPD disease. Comparing our study's AECOPD hospitalised individuals' median score of breathing unpleasantness subscale 4 (IQR3-5) to the out patients COPD individuals reported in Morélot-Panzini et al. (2016) who have not had exacerbation within the last six weeks prior to their assessment, the results showed a higher median score at 6.0 (IQR 3.5-7.0)(Morélot-Panzini et al., 2016). The lower reported median score of our study cohort (4; IQR 3-5), which is located closer to the middle part of the 10-point pleasantness sub-scale, could be interpreted as a result of the pharmacological management usually provided to individuals during their hospitalisation phase, which could provide better control of their exacerbated dyspnoea and thus lower the median score of the patients reported unpleasant breathing sensation at hospitalisation. Moreover, results of the MDP

dyspnoea scale showed that the majority of the AECOPD individuals in this study chose the 'I am breathing a lot' descriptor as the most accurate representation of their breathing. Exhibiting this kind of breathing sensation can be closely related to the rapid shallow breathing pattern exacerbated COPDers develop due to the inflammatory manifestations that occur in the lungs, such as bronchospasm, mucosal oedema and increase in sputum production (O'Donnell and Parker, 2006).

In contrast, the most accurate breathing descriptor reported in the Morélot-Panzini et al. (2016) study of participants with stable COPD (out patients) to describe their breathing was "air hunger"(Morélot-Panzini et al., 2016). This finding was also consistent with the reported MDP results of another recent study conducted on stable COPD individuals (Daynes et al., 2022). This variability in the reported scores of unpleasantness sensation of the dyspnoea symptom subscale and within its most accurate reported description between the AECOPD and the stable or out-patient COPD individuals could show the complex nature of the breathlessness profile and the variability of its presentations during the different COPD time points (during the acute and stable phases).

Moreover, in our study, emotions induced by the breathlessness sensation reported in the MDP scale showed a similar anxiety median score (median 3) to the one found in a stable population, which seems to indicate that anxious emotions related to breathlessness sensation can be a long-standing problem for COPD individuals (Morélot-Panzini et al., 2016, Daynes et al., 2022). Frustration and depression sensations (median score of 3.5, 3 respectively) as a reaction to breathing difficulties were also among the emotional responses with the highest median levels in our study. However, lower median scores were reported within these emotions in the Morélot-Panzini et al. (2016) study conducted on stable COPD individuals. These findings could signify that a greater level of the psychological burden induced by breathlessness can be more pronounced during the hospitalisation phase.

The PAM-13 results in this study showed that the majority of the study participants were classified within the lowest level of activation (the first or second level of the PAM-13 scale). At these levels, individuals are described as overwhelmed, disengaged, believing the health care professional is in charge of their health, having limited disease knowledge,

having poor self-management skills, holding a negative emotional experience, poor goal orientation and problem-solving skills and having a weaker support system (Insignia®, 2017). Such findings are consistent with the data reported in an international survey with a large sample size (n=4,343) where the multivariate analysis showed that the increased level of breathlessness found in exacerbated population is an independent factor associated with the low levels of patients' activation measures (levels one and two) (Müllerová et al., 2016). This lack of patients' intrinsic activation levels suggests a need to incorporate a component of a psychotherapy element in any future designed intervention for the AECOPD population, in order to help facilitate their transitioning to higher activation levels where individuals are ready to take action and participate in activities that can improve their health such as PR (Greene et al., 2016, Kearns et al., 2020).

In contrast, to the impaired cognitive function reported in other studies that investigated the exacerbated COPD individuals (López-Torres et al., 2016, Dodd et al., 2013), on average the participants in our study showed no signs of cognitive impairment as the reported mean and standard deviation (SD) of the total MOCA test score was 26 (5). This could be for reasons, such as our study's limited sample size and the nature of our study, in that the probability of participants who might agree to take part in a survey study that includes a large number of questionnaires and written material are more likely to have better cognitive ability than those who decline participation. Moreover, this finding could also suggest that the mean total MOCA score of this study cohort which falls within the normal cognitive function range could rule out that the insights produced from this survey could have been impacted by the limited cognitive function usually found in the exacerbated population (Dodd et al., 2013). Nevertheless, given that proportion of our study participants fall within the impaired cognitive function range, it is important for future health interventions to consider the application of validated clinical instruments such as the Addenbrooke's Cognitive Examination (ACE)-III tool (Morris et al., 2019) during the pre-hospital discharge phase to help with assessing and identifying individuals with impaired cognitive function who might need additional help with information assimilation. This is because in the literature it has been reported AECOPD individuals can suffer from impairments in recalling memory, planning, organisation, manipulation and information

processing (Dodd et al., 2013). Such impairments might hinder the individual ability to process health-related information largely given to them at the time of admission with AECOPD. Therefore, it is recommended for future health interventions designed for this population to consider using a phased or a step-based approach incorporated within a model of a complex intervention that allows the re-introduction of the health related information throughout different time points of the exacerbation journey and via different methods e.eg, written information, viewed visually, or facilitated by the a healthcare professional in order to help the exacerbated individuals with assimilating the knowledge delivered to them.

A key finding of this survey showed that, overall, hospitalised exacerbated COPD individuals suffer from various bothersome symptoms and disease implications during the acute phase of COPD exacerbation. However, about 50% of the data set suggested higher bothersome median scores (4, somewhat bothersome) were reported within three bothersome disease implications or symptoms mostly related to breathing and mobility problems during the hospitalisation phase. These three were shortness of breath, chest tightness, and limited mobility. Post hospitalisation, the following disease implications and symptoms scored the highest median scores on the bothersome scale (4, somewhat bothersome) and were related to breathing, physical ability, and fatigue, namely shortness of breath, limited mobility, exhaustion, and tiredness. These prominent issues reported by the AECOPD individuals in our study concur with the downward spiral of the heath deterioration that usually happens with COPD exacerbation occurrence as it starts first with deterioration in lung function, which could lead patients to exhibit bothersome shortness of breath, chest tightness and the decrease in physical activity which usually immediately follow the decline in lung function (Hurst et al., 2020b).

Moreover, despite the MDP scale in this study captured indications of anxiety and depression emotions related to the breathlessness sensation, the survey findings, on average, found that the patients' level of bothersome related to the psychological implications (such as low mood and fear and panic attacks) did not seem to be considered as bothersome by the patients during the hospitalisation or the discharge phase of the AECOPD. This could be due to several reasons: I) the progressed severity of the disease led participants to focus

more on the tangible limitations as these are more pronounced during the increased severity of the disease (Jones et al., 2011), II) the stigma related to mental health and mental health literacy could all play a role in patients not identifying those psychological disease implications as bothersome (Golberstein et al., 2008, Conner et al., 2010) and, importantly, III) the questions in this survey asked participants to rate how bothersome these disease implications were to them, not whether they experienced these psychological incidents. Therefore, the survey result might reflect the true level of participants' perceived bothersome level with regard to psychological elements of the disease implication, rather than the existence of these psychological disease implications.

In this study, it was evident that the breathlessness symptom was prevalent during both phases of the COPD exacerbation and the majority of the participants indicated a high level of importance to receiving intervention to manage this symptom (79%). This finding is consistent with the results of a previous systematic review of the care needs of advanced COPD individuals, where breathlessness was considered as the central feature of COPD, and is contrary to the lung cancer individuals, who reported higher levels of pain (Gardiner et al., 2010). This highlights a need for health care professionals to use breathlessness management as a fundamental aspect of any health care intervention designed for COPD exacerbation management.

To our knowledge, this is the first time the SNAP tool (M Farquhar, 2018) has been used to assess the support needs of individuals at the time of an AECOPD since its development within the context of care for individuals with advanced COPD. One of the interesting results of our implementation was that the highest percentage of the AECOPD individuals (29%) indicated a need for the highest level of support (selecting the ‘quite a bit’ choice) for receiving support within the ’getting out and about’ patient care need. This could highlight the pronounced need for help with AECOPD disease implications related to limited mobility and fatigue as this later finding is in harmony with our study survey finding, where individuals with AECOPD showed higher median scores of bothersome level in relation to AECOPD symptoms and disease implications that broadly cover breathing problems, limited mobility and fatigue. A greater need for support was clear again, as a

higher percentage of individuals with AECOPD prioritised non-pharmacological patient care interventions that required less active participation from the patients' side in hospitalisation. And prioritised interventions that particularly target their highly bothersome symptoms and disease implications related to breathing and limited mobility and provide help with fatigue such as; receiving advice on breathing exercises (58%), receiving educational sessions on how to pace themselves (48%) and help with exhaustion and tiredness via providing mobility equipment and household appliances or gadget (46%).

In contrast, the individuals' with AECOPD non-pharmacological care priorities during the post-discharge phase adopted more active participation intentions from the patients' side. Participants prioritising non-pharmacological care interventions were also closely related to their identified highest median scored bothersome symptoms (e.g., breathlessness, limited mobility and fatigue). Therefore, train my breathing muscle (50%), increase muscle strength all over the body (40%), helping with exhaustion and tiredness (38%), and receiving advice about useful cough techniques were all among the prioritised non-pharmacological patient care interventions that recorded the highest responses rate within the post-discharge phase.

Results from a recent Delphi survey, which included 25 COPD experts and looked at the standardisation of the clinical management of acute hospitalised exacerbation of COPD in Europe, showed that among the consensus list (of the expert agreed symptoms that must be captured and evaluated at hospitalisation time) was dyspnoea and reduced exercise tolerance. However, the COPD experts in that study only agreed to consider the evaluation of fatigue symptoms at the time of hospitalisation (Ramakrishnan et al., 2021). This could mean that, although our survey results showed the patients pronounced desire to receive fatigue management across all phases of the AECOPD experience, the chances that this symptom would be evaluated and managed might not always be guaranteed in light of the Ramakrishnan et al. (2021) expert survey results.

Last but not least, exploring the previous PR attenders' perspectives on how to improve conventional PR programmes, the majority of the participant selected a preference to make the exercise easier to do (43%). This could mean a need for more support from the

healthcare professionals in charge of the delivery of exercise sessions for AECOPD individuals in providing extra coaching and ensuring properly informing this patient population about the benefits of the progressive exercise prescription and expected exhibited dyspnoea following engaging in strenuous exercise sessions.

4.5 Strengths and Limitations

This study has several strengths. For example, this is the first study to explore the most bothersome impact of COPD exacerbation during different time points (during hospitalisation and at discharge) and the exacerbated individuals' detailed non-pharmacological care priorities. This unique exploration has provided new insight into the patient's symptomatic experience and care needs. This study can be used to inform the development process of future interventions related to the COPD exacerbation population. Notwithstanding, limitations also exist within this exploratory study: I) the limited sample size of the survey limited our ability to generalise our findings, II) the fact that this is a single-centre study and the sampling technique used in this study may be a limitation on our ability to capture the full spectrum of the COPD exacerbation populations. Therefore, random sampling might be more appropriate, III) identifying the patient's non-pharmacological care priorities via using ranking questions might give a better reflection of patient priority levels. However, we thought hospitalised individuals might find it difficult to rank a lengthy care priorities list in a paper format and, therefore, we opted to use a multiple-choice question format.

4.6 Conclusion

Breathlessness and limited mobility were among the highest reported bothersome AECOPD impacts during both phases of the exacerbation phase (at hospitalisation and post-discharge). Moreover, on average, in the post-hospital discharge phase, exhaustion and tiredness (fatigue) were perceived among the highest medians score of bothersome AECOPD disease impacts. This study's results suggested that individuals with AECOPD broadly had variable non-pharmacological patient care priorities. However, individuals

were more prone to priorities non-pharmacological patient care interventions that required passive participation during the hospitalization phase and a more active participation approach during the post-hospital discharge phase.

4.7 Impact of COVID-19 on this Research Study

Recruitment for this study started in November 2019. Most of the time the recruitment process was very challenging, even before the COVID-19 pandemic began, due to participants perceiving the number of survey questions and validated questionnaires delivered within this study as burdensome and time-consuming at the time of hospitalisation. This caused us to submit a protocol amendment to remove some of the initially approved questionnaires. Furthermore, at the time of the COVID-19 pandemic, which started in March 2020, this study was still in its early recruitment process stage and the pandemic caused additional challenges due to the respiratory nature of the disease. Most of the respiratory wards were impacted, and restrictions were applied, which prevented unnecessary interactions with ward residents. This resulted in approximately four months of pause for our research activities. After this period, protocol amendments were submitted to allow this research study to collect data via using a tablet to minimise infection cross-contamination that might happen with the paper format and enable us to continue collecting data for questionnaires that require face-to-face interaction with the participants. After the protocol amendment approval, we were able to recruit ten more individuals for this study. However, due to the local outbreak that happened in Leicester, we were again prevented from being able to collect any further data. Thus, in December 2020, we elected to halt further recruitment attempts, perform an analysis of the 50 already recruited individuals and carry on with our research steps to address the overarching thesis aim.

Chapter 5 . Building Healthcare Professionals Consensus on Non-pharmacological Patient Care Priorities during the Hospitalisation and Post-Discharge Phases of Acute exacerbation of Chronic Obstructive Pulmonary Disease: A Delphi survey

5.1 Background

The recommended management of stable COPD in the clinical guidelines includes a long and comprehensive list of a variety of interventions such as administration of pharmacotherapy, smoking cessation advice, offering pulmonary rehabilitation and, in some cases, offering lung surgery and lung volume reduction procedures and alpha-1 antitrypsin replacement therapy, managing the nutritional factors, providing education about COPD disease, self-management plans and offering palliative care for eligible individuals (NICE, 2019, GOLD, 2019). However, in the acute COPD exacerbation phase, the focus of these clinical guidelines is prominently focused on the pharmacological side of its management, with less details provided regarding the non-pharmacological interventions that can be included to provide holistic care for the acute exacerbators.

Investigating clinicians' adherence to the clinical COPD guidelines pharmacotherapy pertaining to the stable COPD population from primary care records has been reported to be sub-optimal (Yii et al., 2019, Bertella et al., 2013, Sehl et al., 2018). And similar poor adherence rates to the clinically recommended non-pharmacological interventions by COPD guidelines have also been reported. For example, results from Kaufman et al. (2015) study revealed an underutilization of the non-pharmacological COPD guidance within their 14 investigated primary care practices as only 49% of the patients' records reported documented advice about vaccination, 53% received motivation advice about engaging in physical activity, and only 24% of the patients received an exacerbation action plans (Kaufmann et al., 2015).

Moreover, within the hospitalised COPD population, clinicians' adherence rate to COPD management guidelines revealed from a study that included 245 hospital-based COPD individuals, an overall poor adherence rate of 29.8 % to the COPD treatment guidelines. Among the lowest reported low adherence to the clinical COPD management guidelines reported in that study (Jouleh et al., 2018) were in relation to pharmacological treatment (35.5%) and pulmonary rehabilitation (16.7%), in contrast to other COPD management interventions delivered during hospitalisation such as influenza vaccine (70.6%), COPD awareness (86.5%) and smoking cessation advice (96%) (Jouleh et al., 2018).

Barriers to COPD guidelines adherence in primary care has been investigated in a recent systemic review, with data showing that general practitioners (GPs) find the clinical guidance not always clear enough to be applied in everyday practice because of the GPs' unfamiliarity with the guidelines recommendations, time constraints, or due to the complexity of the treatment algorithms (Sehl et al., 2018). Although no such data that investigated the barriers to clinical adherence to COPD guidelines in hospitalisation exists, one can expect a greater barrier to guidelines adherence due to the high COPD exacerbation burden to the patient and health care systems as these present additional challenges that could prevent the transition of the guidelines' recommended interventions into daily clinical practice (Hurst et al., 2020a).

To help provide standardised, evidence-based care for AECOPD individuals at the hospital and post-discharge phases, researchers in the field have carried out several standardisation initiatives such as developing COPD care bundles at admission and discharge, care pathways, coordinated case management and clinical decision support system interventions (MacDonell et al., 2020, Epstein et al., 2019). Although all of these interventions have provided various degrees of positive outcomes in reducing healthcare utilisation and in short-term outcomes such as length of hospital stay and readmission rates (MacDonell et al., 2020), the impact of these interventions on the patients' related clinical outcomes is still unclear (Epstein et al., 2019, MacDonell et al., 2020). In addition, the implementation of these interventions in the real world within various healthcare systems

still faces some challenges due to staffing issues and a lack of having dedicated trained teams to successfully deliver these interventions (Shaw et al., 2020).

A European Delphi study investigated the COPD experts' agreement over performing evaluation on various collections of clinical characteristics and outcome measures during the time of hospitalisation for an AECOPD. In this research attempt, the results of the consensus process, which included opinions of 25 COPD experts who undertook the Delphi survey process, recommended with a 'must' evaluation of dyspnoea, wheezes, sputum production, cough, reduced exercise tolerance, increased inhaler use, confusion and loss of consciousness (Ramakrishnan et al., 2021). However, the same COPD expert group had a consensus agreement to only consider evaluating patients for chest tightness, chest pain, fatigue and loss of balance. Although fatigue (Ebadi et al., 2021), chest tightness and chest pain (Jones et al., 2011) can be highly prevalent within frequent exacerbators. Moreover, in this study, experts recommended that pharmacological treatments at hospitalisation included oxygen, nebulised bronchodilators, systemic corticosteroids, antibiotics, opiates and diuretics. Among the only recommended non-pharmacological treatments were chest physiotherapy and assisted mobilisation. Although this study reported valuable information about the COPD experts' opinions of the recommended treatments at the time of hospitalisation, most of which included pharmacological interventions, it did not indicate the level of expert consensus (level of agreement). Nor did it provide clear information about all the interventions (pharmacological and non-pharmacological) included in their survey treatment lists to reveal how inclusive this list was.

The benefits of delivering non-pharmacological interventions around the time of COPD exacerbation, such as pulmonary rehabilitation, smoking cessation and self-management plans, can provide optimal care and help reduce readmissions, improve symptoms management and improve patient knowledge about the disease (Harrison et al., 2014c). However, access and uptake to many of these non-pharmacological interventions remain challenging and have been identified as multi-factorial, e.g., reasons were related to

patients, healthcare professionals and healthcare systems (NACAP, 2021, Jones et al., 2018).

As prioritising a given treatment could give it the best chance of being delivered, this present study aims to build consensus among healthcare professionals about their agreement regarding prioritising patient care interventions, particularly the non-pharmacological interventions during the hospitalisation and post-discharge phases of an AECOPD. In addition, this research study has been conducted in response to a recently recommended strategy to promote the uptake of an important non-pharmacological intervention (PR) which suggests that gaining input from the service stakeholders (the patients and healthcare professionals) about their therapy priorities could help with enhancing uptake (Rochester and Singh, 2020). Therefore, in this Delphi survey, to broaden our exploration, we aimed to include healthcare professionals (HCPs) from four high-income countries (United Kingdom, United States, Australia and Canada) to allow including perspectives of HCPs who serve in various developed healthcare systems. The results of the collaborative decision-making process (building consensus process) undertaken within this study will inform the development of a complex intervention to promote PR uptake for COPD individuals post suffering from acute exacerbation of COPD.

5.2 Objectives

To build consensus among healthcare professionals (HCPs) involved in the care of individuals with acute and post-acute COPD exacerbation on their agreement regarding prioritising non-pharmacological patient care interventions based on their expertise, experience and the potential therapeutic benefits.

Scope of the study and context of the use:

Health condition: acute and post-acute COPD exacerbation.

Population:

Healthcare professionals caring for acute and post-acute COPD exacerbation patients with clinical experience of ≥ five years.

Intervention:

Three rounds of the Delphi survey.

Context of use:

Primarily for adaptation within the development process of stakeholders' co-designed complex intervention to promote PR uptake post-AECOPD.

5.3 Methods

5.3.1 Survey design and recruitment

The collaborative decision-making process (the consensus process) of this survey study was conducted through the Delphi method. This is defined as a survey technique used to facilitate an efficient group dynamic process and is done in the form of an anonymously written and multi-stage survey process, with feedback of group opinion being provided after each round (Heiko, 2012). The development of this Delphi survey was based upon a patient

survey where patient care priorities were identified during both phases of COPD exacerbation (at hospitalisation and post-hospital discharge), which can be found in chapter 4 of this thesis.

The survey initially consisted of three rounds of the Delphi method online. Healthcare professionals from high-income countries such as the United Kingdom, United States, Australia and Canada were identified and invited to participate in the survey through the relevant international healthcare societies (e.g., British and American thoracic societies), via search on social media and then through our own personal email contact list if they met the following criteria: health care professional with ≥ five years of clinical experience and who is involved in the care of acute or post-acute exacerbation of COPD patients.

The eligible international panellists who met the eligibility criteria were sent a personal online invitation and asked to nominate other local healthcare professionals who could meet the study's eligibility criteria. The study aimed to recruit 10 to 50 panellists as this number falls within the recommended range from the literature for Delphi studies (Turoff and Linstone, 2002, Ogbeifun et al., 2016). Following the identification of panellists (74 individuals), each study participant received an introductory email that provided information about the study, the completion time for the survey (both surveys took about 10 minutes to complete), participant privacy information, the data handling procedures, the consent obtaining procedure and a unique survey link which participants were able to use to access the online survey. In addition, the introductory email included information about the number of survey rounds and a statement that ensured participants were reminded about their responsibility toward completing at least two survey rounds. Participants were initially given two weeks to complete the survey, although extensions were applied when needed. To ensure survey retention, reminders about participation were sent out at the beginning of the second week of each survey cycle. The participants remained anonymous to each other throughout all the survey rounds.

5.3.2 *Information source.*

An initial patient survey study was designed with the help of a group of experts in the field (SS, NG, and THD), through a search of the literature, the Patient and Public Involvement (PPI) Group and the help of actual AECOPD patients, who undertook a qualitative interview (Figure 5.1). Following the survey analysis, the patient-identified care priorities items were then arranged in random order and incorporated within two patient care priorities lists that targeted the management of the acute and post-acute phases of COPD exacerbation (at hospitalisation and post-hospital discharge). Finally, the resulting designed survey was pretested internally for feedback and enhancement with seven HCPs before the commencement of the Delphi first survey round.

5.3.3 *Delphi consensus process*

Round one

In this survey iteration, the HCPs were asked to rate their level of agreement on the patients' chosen care priorities during the hospitalisation and post-hospital discharge phases of the AECOPD based on their expertise, experience and potential therapeutic benefits. This was done via using five-point Likert item questions with the following anchors; 1= strongly disagree, 2=disagree, 3= neither agree nor disagree, 4= agree, and 5= strongly agree. Additionally, within the Delphi first round, the following participants' demographics were collected: region, professional experience (in years) and clinical role. Finally, in this survey iteration, HCP were able to provide additional comments or suggest that new patient care interventions be added to the patient care interventions lists (Figure 5.1).

Rounds two and three

Following the initial survey round analysis, a consensus was deemed reached if an item's interquartile range (IQR) was ≤1, as this value of the IQR is reported as a suitable indicator to measure consensus within a 5-point Likert item (Heiko, 2012). If the analysed items achieved consensus (either positive or negative agreement), it was then reported as such and removed from the second survey round. However, if the patient care priority item

did not achieve consensus, the item was then added to the second survey round to be evaluated by the panel, together with the newly suggested items generated from the initial survey participant feedback. Additionally, after the completion of each survey round, a subjective analysis was also conducted adjacent to the previously mentioned quantitative consensus criteria (IQR ≤1 for the 5-point Liker item) to aid the decision about the need and value of either continuation or termination of the survey cycle (Figure 5.2) (Heiko, 2012).

Following analysis of the survey results of the consecutive round (round two), items that achieved consensus were removed and reported with their classification within the consensus list (either positive or negative agreement). For the items that were still in dissensus and had not achieved consensus, the Wilcoxon signed-rank test was performed on paired results from both rounds (one and two) of that item to assess the stability of the dissensus status between the two rounds. If the responses were not statistically significantly different (p-value ≥ 0.05), then responses were considered stable, and the patient care priority item was removed from any subsequent round and reported as stable 'disagreement'. Following analysis of the quantitative paired results generated from the dual survey rounds, a continuation or termination of the survey cycle was discussed at the end of each consecutive round, with the study's authors subjectively reviewing the survey results to aid the decision about whether survey continuation or termination was needed. This was based on the following criteria: 1) whether all items achieved consensus or dissensus status, 2) if continuation of the rounds was worthwhile in terms of adding more value to the analysis process, 3) consideration of recruitment, financial and time constraints.

5.3.4 Data analysis

Participants' characteristics distribution was reported in numbers and percentages. As stated above, interquartile range (IQR) was used to measure consensus. Median and mode were used as measures of central tendency to help summarize opinions within all the patient care priority items. The Wilcoxon signed-rank test was used to measure the dissensus stability status. If the P-value ≥ 0.05 was not statistically significantly different, then

responses were considered stable and reported as such. To handle and analyse the data, the SPSS statistical package version 26.0 was used (IBM, Released 2019).

5.3.5 Ethics approval

The Medicine and Biological Sciences Research Ethics Committee at the University of Leicester reviewed and approved the research study. The Ethics reference is: 29960-bsaa5-ls:respiratorysciences

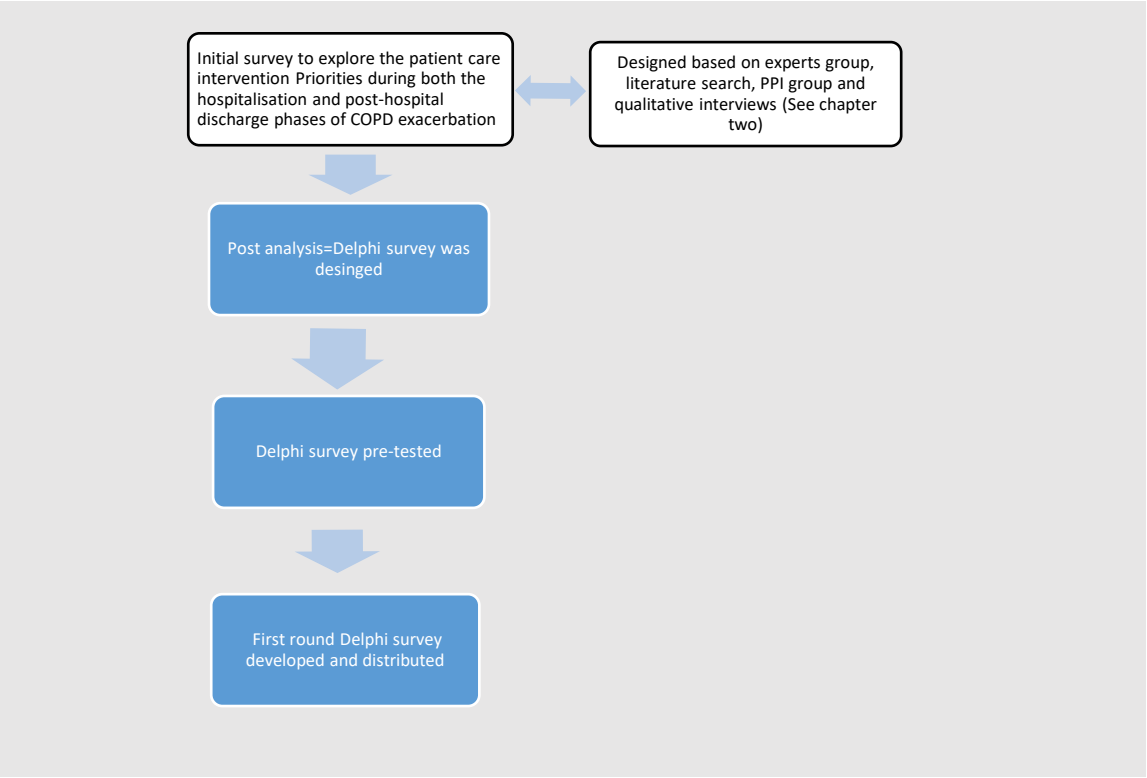


Figure 5.1 Delphi survey design process

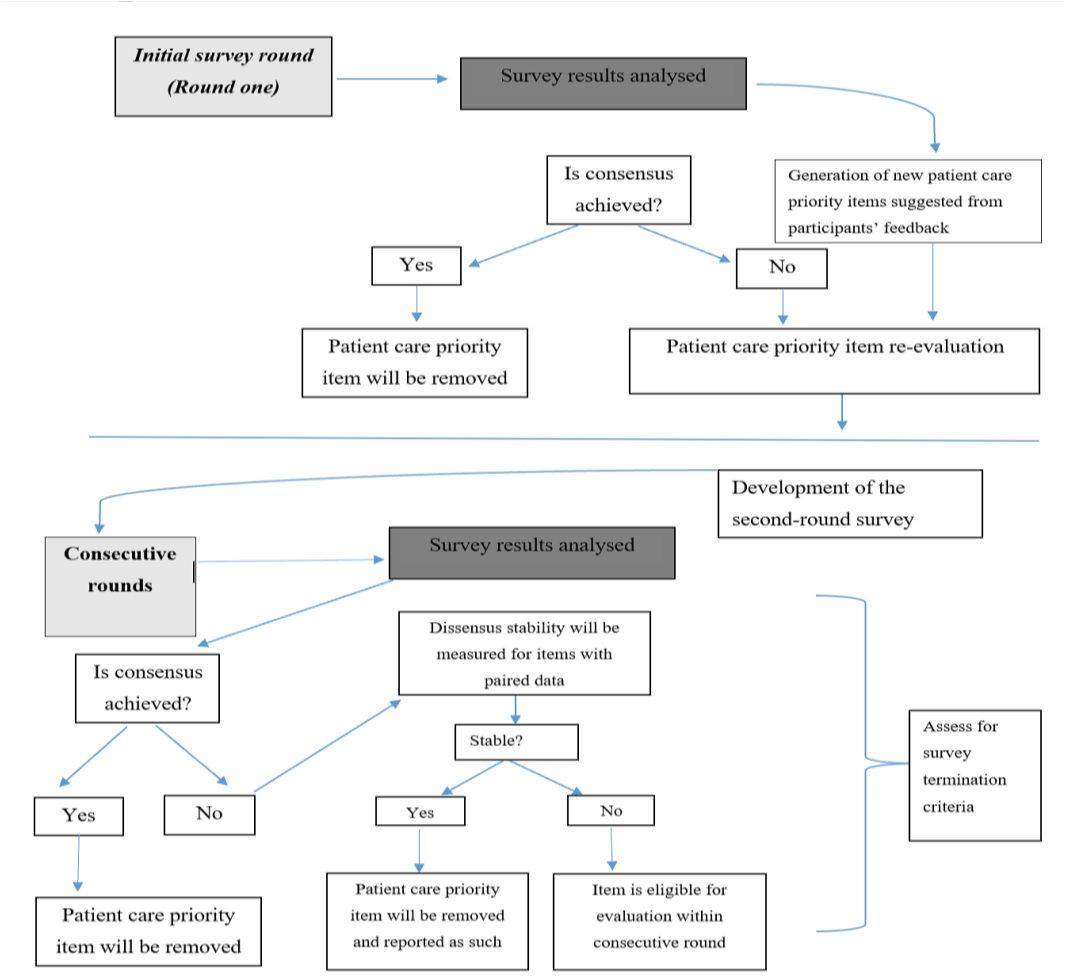


Figure 5.2 Delphi consensus process

5.4 Results

The study was conducted during a three-month period (October to December 2021). Of 74 potentially eligible healthcare professionals (HCP) who were approached via email, 46 (62%) completed the initial Delphi round (round one), and 45 (60%) completed the consecutive round (round two) (see table 5.1 below for participants' characteristics). The participating countries in the survey were the United Kingdom, where twenty (43.5%) panellists completed round one and 29 (64.4%) completed round two. Three (6.5%) panellists were from the United States and completed rounds one and two. Nine (19.6%)

panellists in round one were from Australia, with eight (17%) completing round two. Fourteen (30.4%) panellists were from Canada and completed round one, with five (11%) completing round two. Most of the participating panellists had more than 20 years of professional experience (41% in round one and 44% in round two). In this study, the professional role of the panellists was mostly allied healthcare professionals (56% in round one and 64% in round two) and medical doctors (22% in round one and 8% in round two). After round one, no further new items were recommended to gain consensus on. This Delphi survey was terminated after the completion of round two as the Delphi process reached the pre-defined survey termination criteria (details can be found within the results of round two).

Table 5.1 Delphi survey participants' characteristics

Round one (n=46)		Round two (n=45)
Region, *n (%)*		
United Kingdom	20 (44%)	29 (64%)
United States	3 (7%)	3 (7%)
Australia	9 (20%)	8 (17%)
Canada	14 (30%)	5 (11%)
Professional experience (in years), *n (%)*		
5-10 years	11 (24%)	11 (24%)
11-15 years	9 (20%)	5 (11%)
15-20 years	7 (15%)	9 (20%)
>20 years	19 (41%)	20 (44%)
Professional role, *n (%)*		
Medical doctor	10 (22%)	8 (18%)
Respiratory nurse	6 (13 %)	4 (9%)
Allied health care practitioner	25 (56%)	29 (64%)
Advanced critical care practitioner	0 (0%)	1 (2%)
Other	4 (9%)	3 (7%)

5.4.1 Results of the initial round (round one)

In round one, the 46 international panellists were asked to rate their agreement with the non-pharmacological patient care priority items that had been identified by AECOPD individuals in a previous patient survey as prioritised non-pharmacological care interventions to be received either in the hospitalisation or post-discharge phase of AECOPD (see chapter 4). Additionally, in this survey iteration, the HCPs were asked to

suggest any non-pharmacological prioritised items to them to be added to the original patient list in the subsequent rounds to build consensus on (round two).

Analysis of the first-round items that achieved consensus is reported in detail in table 5.2. Upon reviewing the consensus list, results showed that breathing control advice and anxiety management (median 5) were the only two items that, on average, scored the highest level of prioritisation (strongly agree prioritised patient care intervention) for being delivered during the hospitalisation phase of COPD exacerbation.

Fatigue management achieved the highest level of consensus (perfect level of consensus; IQR 0), which means that the polarised opinions were close to none and, on average, results of this therapy priority item favoured a positive agreement (agreed prioritised patient care item; median score 4). It was apparent from the results that healthcare professionals strongly prioritised interventions with the least physical strain during the hospitalisation phase (see table 5.2).

The results of the initial round resulted in seven non-pharmacological patient care priorities being in dissensus (which means the IQR range was more than ≥1; see table 5.3) for the delivery during the hospitalisation phase. These were: 1) respiratory muscle training, 2) cough management, 3) administering airway clearance devices, 4) body exercises to increase muscle strength and tolerance in the lower limb, 5) depression management, 6) delivering COPD disease education to carers, and 7) pain management advice.

In the post-discharge phase, HCPs reached a consensus on prioritising the delivery of several non-pharmacological patient care priorities (see table 5.4). Upon evaluation of the HCPs consensus list, it was revealed that HCPs strongly prioritised, with perfect consensus (IQR 0), physically active non-pharmacological approaches such as delivering walking exercises (median 5; strongly prioritised item). In addition, other strongly agreed (median score 5) prioritised non-pharmacological patient care priorities but with a lower level of consensus (IQR 1) to be delivered during the post-discharge phase of AECOPD exacerbation were: activity pacing advice, body exercises to increase muscle strength and tolerance in upper and lower limbs, breathing control advice, anxiety, depression and panic

attack management, delivery of education sessions about diseases to the patient and carers, education sessions about medication use and adherence and facilitating attendance to support groups. A detailed list of all the items that reached consensus in round one for the delivery during the post-discharge phase of AECOPD can be found in table 5.4.

The panellist feedback generated from the round one survey was also reviewed by the study team, and it was agreed that the following items be included for evaluation with the consecutive round (round two): 1) delivering education sessions regarding home oxygen use, safety and adherence, 2) individualised therapeutic goal setting, 3) smoking cessation advice, 4) advice on vaccination, 5) nutritional advice, 6) advice on attending pulmonary rehabilitation program, 7) advice on returning to work and 8) providing self-management and action plans.

Finally, for the consecutive round (round two), all patient care priority items that had achieved consensus from the hospitalisation and post-discharge phases were removed and reported as such within the participant feedback report. Additionally, in the consecutive round (round two), respondents received a survey that included items that were in dissensus status (see tables 5.3 & 5.5) for a second chance of re-evaluation together with the group median and range scores resulting from the first-round rating for all items except one, namely cough management. This item was considered to be covered within the airway clearance therapy item, and adding it separately was deemed unnecessary and, therefore, was eliminated from the survey. Furthermore, in the consecutive survey round, the newly generated items which resulted from the respondents' feedback in round one were also included for evaluation within survey round two.

Table 5.2 HCPs consensus list of the non-pharmacological patient care priorities to be delivered during the hospitalisation phase of AECOPD exacerbation (round one)

Items achieved consensus	IQR	Agreement type	Median score	Mode score	Level of prioritisation
Fatigue management	*0 (perfect consensus)*	*Positive*	*4 (Agree)*	*4*	*Agreed prioritised intervention*
Breathing control advice	*1 (Consensus)*	*Positive*	*5 (Strongly Agree)*	*5*	*Strongly agreed prioritised intervention*
Anxiety management	*1 (Consensus)*	*Positive*	*5 (Strongly agree)*	*5*	*Strongly agreed prioritised intervention*
Delivering walking exercises	*1 (Consensus)*	*Positive*	*4 (Agree)*	*5*	*Agreed prioritised intervention*
Panic attack management	*1 (Consensus)*	*Positive*	*4 (Agree)*	*5*	*Agreed prioritised intervention*
Delivering education session about medication use and adherence	*1 (Consensus)*	*Positive*	*4 (Agree)*	*5*	*Agreed prioritised intervention*
Airway clearance therapy	*1 (Consensus)*	*Positive*	*4 (Agree)*	*4*	*Agreed prioritised intervention*
Activity pacing advice	*1 (Consensus)*	*Positive*	*4 (Agree)*	*4*	*Agreed prioritised intervention*
Body exercises to increase muscle strength and tolerance in the upper limbs	*1 (Consensus)*	*Positive*	*4 (Agree)*	*4*	*Agreed prioritised intervention*
Facilitating attendance at patients' support groups	*1 (Consensus)*	*Positive*	*4 (Agree)*	*4*	*Agreed prioritised intervention*
Delivering education session about the COPD disease	*1 (Consensus)*	*Positive*	*4 (Agree)*	*4*	*Agreed Prioritised intervention*
Sleep disturbance management	*1 (Consensus)*	*Positive*	*4 (Agree)*	*4*	*Agreed prioritised intervention*
Delivering relaxation sessions	*1 (Consensus)*	*Positive*	*4 (Agree)*	*3*	*Agreed prioritised intervention*

Table 5.3 Non-pharmacological patient care priority items that did not achieve consensus to be delivered during the hospitalisation phase of AECOPD exacerbation (round one)

Items in dissensus status	IQR	Median	Mode	Range
Respiratory muscle training	2	3	2	1-5
Cough management	2	4	5	2-5
Administering airway clearance devices	2	4	4	1-5
Body exercises to increase muscle strength and tolerance in the lower limbs	2	4	4	2-5
Depression management	2	4	5	5-2
Delivering COPD disease education to carers	2	4	4	1-5
Pain management advice	2	4	4	2-5

Footnote. Scores definition: 1= Strongly disagree, 2=disagree, 3=neither agree nor disagree, 4=agree, 4= strongly agree

Table 5.4 HCPs consensus list of the non-pharmacological patient care priorities to be delivered during the post-discharge phase of AECOPD (round one)

Items achieved consensus	IQR	Agreement type	Median score	Mode score	Level of prioritisation
Delivering walking exercises	*0 (Perfect consensus)*	*Positive agreement*	*5 (Strongly agree)*	*5*	*Strongly agreed prioritised intervention*
Activity pacing advice	*1 (Consensus)*	*Positive agreement*	*5 (Strongly agree)*	*5*	*Strongly agreed prioritised intervention*
Body exercises to increase muscle strength and tolerance in the upper limbs	*1 (Consensus)*	*Positive agreement*	*5 (Strongly agree)*	*5*	*Strongly agreed prioritised intervention*
Body exercises to increase muscle strength and tolerance in the lower limbs	*1 (Consensus)*	*Positive agreement*	*5 (Strongly agree)*	*5*	*Strongly agreed prioritised intervention*
Breathing control advice	*1 (Consensus)*	*Positive agreement*	*5 (Strongly agree)*	*5*	*Strongly agreed prioritised intervention*
Anxiety management	*1 (Consensus)*	*Positive agreement*	*5 (Strongly agree)*	*5*	*Strongly agreed prioritised intervention*
Depression management	*1 (Consensus)*	*Positive agreement*	*5 (Strongly agree)*	*5*	*Strongly agreed prioritised intervention*
Panic attacks management	*1 (Consensus)*	*Positive agreement*	*5 (Strongly agree)*	*5*	*Strongly agreed prioritised intervention*
Facilitating attendance to patients' support groups	*1 (Consensus)*	*Positive agreement*	*5 (Strongly agree)*	*5*	*Strongly agreed prioritised intervention*
Delivering education session about the COPD disease	*1 (Consensus)*	*Positive agreement*	*5 (Strongly agree)*	*5*	*Strongly agreed prioritised intervention*
Delivering education session about medication use and adherence	*1 (Consensus)*	*Positive agreement*	*5 (Strongly agree)*	*5*	*Strongly agreed prioritised intervention*
Delivering COPD disease education to carers	*1 (Consensus)*	*Positive agreement*	*5 (Strongly agree)*	*5*	*Strongly agreed prioritised intervention*
Relaxation sessions	*1 (Consensus)*	*Positive agreement*	*4 (Agree)*	*5*	*Agreed prioritised intervention*

Fatigue management	*1 (Consensus)*	*Positive agreement*	*4 (Agree)*	*5*	*Agreed prioritised intervention*
Sleep disturbance management	*1 (Consensus)*	*Positive agreement*	*4 (Agree)*	*4*	*Agreed prioritised intervention*

Table 5.5 Non-pharmacological patient care priority items that did not achieve consensus to be delivered during the post-discharge phase of AECOPD (round one)

Items in dissensus status	IQR	Median	Mode	Range
Respiratory muscle training	2	3	3	2-5
Airway clearance therapy	2	4	5	3-5
Administering airway clearance devices	2	4	4	3-5
Pain Management	2	4	4	2-5

Footnote. Scores definition: 1= Strongly disagree, 2=disagree, 3=neither agree nor disagree, 4=agree, 4= strongly agree

5.4.2 Consecutive round (round two)

In this round (round two), all non-pharmacological prioritised patient care items that existed within the hospitalisation phase of the AECOPD intervention list had achieved consensus except for two items, which are: 1) delivering education sessions regarding home oxygen use, safety and adherence and 2) providing nutritional advice (IQR 2, median score is 4; agree for both items). Additionally, the results of the consensus list showed that HCPs disagreed on prioritising the delivery of respiratory muscle training (IQR1; median score 2; disagree) during the hospitalisation of AECOPD exacerbation. Furthermore, HCPs neutrally agreed on prioritising the delivery of advice on returning to work during the hospitalisation phase of the exacerbation event (median score 3; neither agree nor disagree). On the other hand, providing advice on smoking

cessation, vaccination and attending pulmonary rehabilitation programs were all among the highly prioritised interventions for delivery in the hospitalisation phase of AECOPD (for the detailed consensus list, see table 5.6). Only two items that were generated from the participants' feedback did not achieve group consensus. They were 1) delivering education sessions regarding home oxygen use, safety, and adherence (IQR 2; median score 4) and 2) providing nutritional advice (IQR 2; median score 4).

For the post-discharge phase list, all patient care prioritised items reached consensus. Consensus results showed that HCPs strongly agreed on prioritising the delivery of the following items during the post-discharge phase of AECOPD: 1) providing advice on attending pulmonary rehabilitation programme (IQR 0; median 5), 2) providing smoking cessation advice (IQR 1; median 5), 3) providing vaccination advice (IQR 1; median 5) and provide self-management action plans (IQR 0; Median 5) and 4) offering individualised therapeutic goal setting (IQR 1; median 5). The consensus analysis also showed that respiratory muscle training (IQR 1; median 3; neither agree nor disagree) received consensus as a neutral prioritised therapy by HCPs during its second round of the re-evaluation process. A detailed list of the non-pharmacologic patient care priorities can be found in table 5.7.

Finally, upon comprehensive reviewing of the consensus results generated from this survey round (round two), only two items did not achieve consensus: delivering education sessions regarding home oxygen use, safety and adherence and providing nutritional advice. Thus, the decision was made to report the two outstanding items that did not reach consensus in the hospitalisation phase priority list in round two within the analysis report as 'items that did not achieve consensus'. This means that polarised opinions were evident within the respondents' group. However, this cannot be proven as stable dissensus because the stability criteria were not tested by the Wilcoxon signed-rank test because further re-evaluation needs to be carried out on these two items in a third Delphi survey round to determine the stability of the group disagreement. This decision was taken based on the reasons that follow. Firstly, the two dissensus items were not originally listed in the initial survey list as these items were generated through

previous research which applied mixed methods (patient survey, qualitative interview and literature search). Secondly, it was thought that conducting further evaluation on these two items might not generate significant benefit to the already acquired results and further recruitment efforts, extending the study's duration and funding, were not thought justifiable. Therefore, the decision about survey termination was then deemed to be appropriate.

Table 5.6 HCPs consensus list of the non-pharmacological patient care priorities to be delivered during the hospitalisation phase of AECOPD (round two)

Items achieved consensus	IQR	Agreement type	Median score	Mode score	Level of prioritisation
Delivering COPD disease education to carers*	*0 (Perfect consensus)*	*Positive*	*4 (Agree)*	*4*	*Agreed prioritised intervention*
Providing smoking cessation advice	*1 (Consensus)*	*Positive*	*5 (Strongly agree)*	*5*	*Strongly agreed prioritised intervention*
Providing advice on vaccination	*1 (Consensus)*	*Positive*	*5 (Strongly agree)*	*5*	*Strongly agreed prioritised intervention*
Providing advice on attending pulmonary rehabilitation program	*1 (Consensus)*	*positive*	*5(Strongly agree)*	*5*	*Strongly agreed prioritised intervention*
Providing self-management and action plans	*1 (Consensus)*	*Positive*	*4 (Agree)*	*5*	*Agreed prioritised intervention*
Administering airway clearance devices*	*1 (Consensus)*	*Positive*	*4 (Agree)*	*4*	*Agreed prioritised intervention*
Body exercises to increase muscle strength and tolerance in the lower limbs *	*1 (Consensus)*	*Positive*	*4 (Agree)*	*4*	*Agreed prioritised therapy*
Depression management*	*1 (Consensus)*	*Positive*	*4 (Agree)*	*4*	*Agreed prioritised therapy*
Pain management*	*1 (Consensus)*	*Positive*	*4 (Agree)*	*4*	*Agreed prioritised therapy*
Providing advice on returning to work	*1 (Consensus)*	*Neutral*	*3 (Neither agree nor disagree)*	*3*	*Neutral prioritised intervention*
Respiratory muscle training*	*1 (Consensus)*	*Negative*	*2 (Disagree)*	*2*	*Disagreed prioritisation/ denied prioritisation*

*Footnote. * Items re-evaluated from the initial round (round one); table is organised from the highest level of consensus to the lowest.*

Table 5.7 HCPs consensus list of the non-pharmacological patient care priorities to be delivered during the post-discharge phase of AECOPD (round two)

Items achieved consensus	IQR	Agreement type	Median score	Mode score	Level of prioritisation
Providing advice on attending Pulmonary Rehabilitation Program	0 (Perfect consensus)	Positive	5 (Strongly agree)	5	Strongly agreed prioritised intervention
Providing self-management and action plans	0 (Perfect consensus)	Positive	5 (Strongly agree)	5	Strongly agreed prioritised intervention
Airway clearance therapy*	0 (perfect consensus)	Positive	4 (Agree)	4	Agreed prioritised therapy
Providing individualised therapeutic goal setting	1 (Consensus)	Positive	5 (Strongly agree)	5	Strongly agreed prioritised intervention
Providing smoking cessation advice	1 (Consensus)	Positive	5 (Strongly agree)	5	Strongly agreed prioritised intervention
Providing advice on vaccination	1 (Consensus)	Positive	5 (Strongly agree)	5	Strongly agreed prioritised intervention
Delivering education sessions regarding home oxygen use, safety, and adherence	1 (Consensus)	Positive	4 (Agree)	5	Agreed prioritised intervention
Providing nutritional advice	1 (Consensus)	Positive	4 (Agree)	4	Agreed prioritised intervention
Pain management*	1 (Consensus)	Positive	4 (Agree)	4	Agreed prioritised therapy
Administering airway clearance device*	1 (Consensus)	Positive	4 (Agree)	4	Agreed prioritised intervention
Respiratory muscle training*	1 (Consensus)	Neutral	3 (Neither agree nor disagree)	3	Neural prioritised therapy

Footnote. * *Items re-evaluated from the initial round (round one); table is organised from the highest level of consensus to the lowest*

5.4.3 The overall HCPs highly prioritised non-pharmacological patient care priorities to be delivered during both the hospitalisation and post-discharge phases of AECOPD

In the hospitalisation phase of COPD exacerbation, HCPs strongly agreed on prioritising the delivery of non-pharmacological patient care interventions that specifically targeted and modified patients' knowledge by providing medical advice regarding various topics such as breathing control, attending pulmonary rehabilitation programs, smoking cessation and vaccination. The only other aspect of patient care where HCPs achieved consensus in strongly prioritising during the hospitalisation phase of an AECOPD was with regard to improving the AECOPD individual's psychological wellbeing, mainly by providing psychological therapy that targeted anxiety (See figure 5.3).

During the post-hospitalisation phase of an AECOPD, HCPs had consensus and strongly agreed on prioritising the delivery of several patient care interventions that targeted four core patient management elements: 1) physical ability, 2) psychological wellbeing, 3) knowledge, 4) chronic illness management (see figure 5.4 for more details).

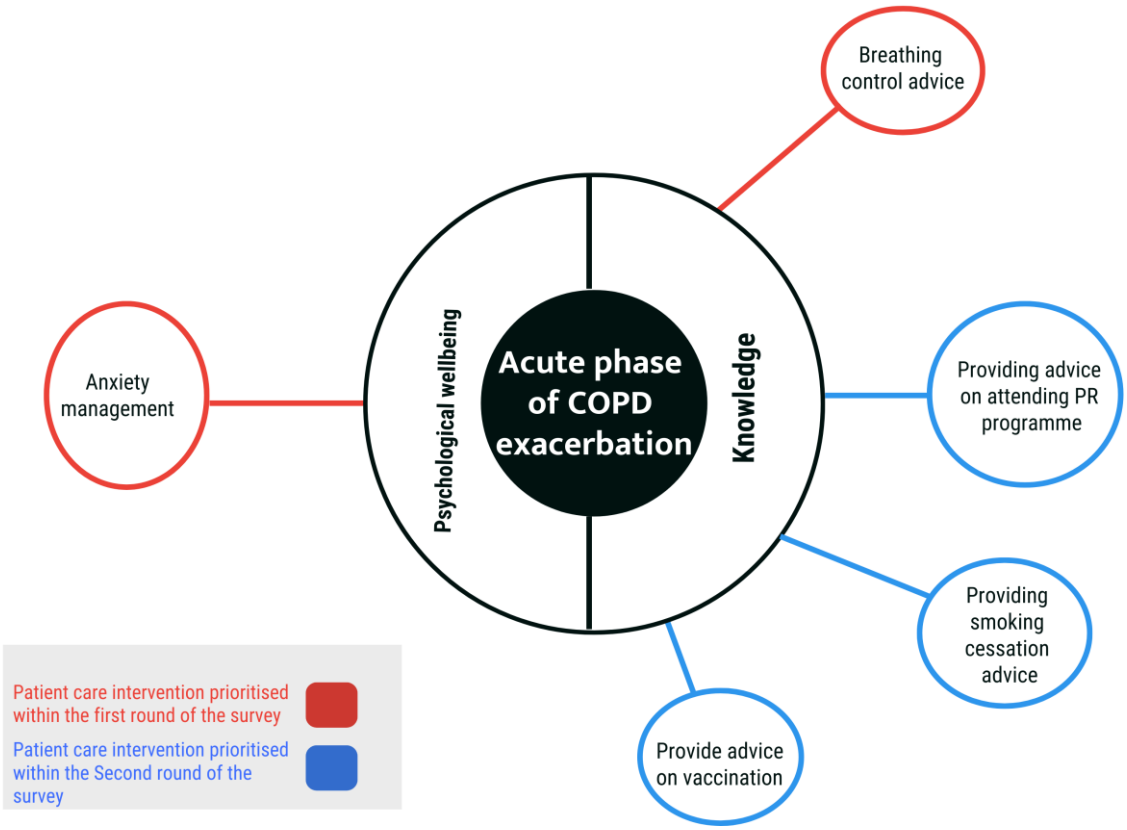


Figure 5.3 HCPs strongly agreed prioritised non-pharmacological patient care priorities to be delivered during the hospitalisation phase of AECOPD

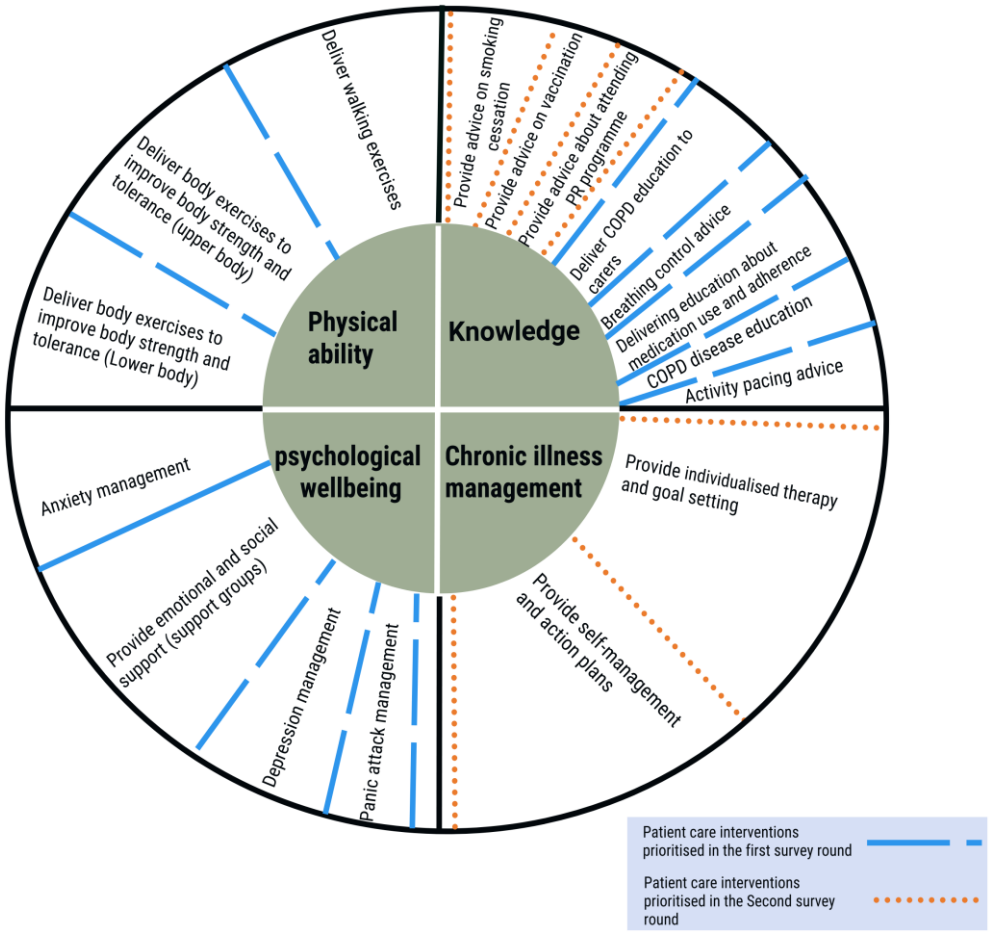


Figure 5.4 HCPs strongly agreed prioritised non-pharmacological patient care priorities to be delivered during the post-acute phase of COPD exacerbation

5.5 Discussion

This is the first study to report the consensus of healthcare professionals (HCPs) on non-pharmacological patient care priorities for managing acute and post-acute COPD exacerbation individuals. It is crucial to mention that the effectiveness and importance of many of the non-pharmacological patient care interventions listed in this study's survey are already established in the literature (Crisafulli et al., 2018, Puhan et al., 2016, Shen et al.,

2020, Abonie et al., 2020, Harrison et al., 2015a). Additionally, many of the included non-pharmacological patient care interventions in the survey lists are currently recommended in the clinical guidelines for the management of COPD exacerbation (GOLD, 2019, NICE, 2019). Therefore, it is essential to emphasise that the aim of this study was not to establish consensus about the importance of these non-pharmacological patient care interventions but, rather, to establish consensus on whether healthcare professionals agree on prioritising the delivery of these therapies or interventions when managing COPD exacerbation individuals during the hospitalisation and post-discharge phases COPD exacerbation and how HCPs might potentially prioritise these interventions.

The key results of the consensus process showed that in the hospitalisation phase, HCPs had a limited number of prioritised non-pharmacological patient care interventions in comparison to the post-hospitalisation phase. For example, on average, HCPs strongly agreed on prioritising non-pharmacological patient care interventions in the hospitalisation phase that produced less physical strain on the acute exacerbated individuals and mostly aid in modifying patient knowledge by providing advice regarding aspects that could help patients primarily with improving control on breathing and avoid future COPD exacerbation attacks. This was evident via them reaching consensus with strongly agreeing on prioritising patient care items that provide advice with regard to the benefits of attending a pulmonary rehabilitation programme (PR), smoking cessation, and having the vaccination. Prioritising improving patients' knowledge in these areas is considered justifiable during the acute phase of the disease as patient education can increase patients' disease coping skills and aid the patient's understanding of their condition, which can positively impact the patient's adherence to treatment plans, and help introduce proactive measures that can assist avoidance of future exacerbation attacks (Schäfer et al., 2015, Wedzicha et al., 2017).

HCPs strongly prioritising advice about breathing control in hospitalisation could be mainly driven by their understanding of the AECOPD condition, where deterioration of dyspnoea is predominantly considered a prominent feature of exacerbation events (Harrison et al., 2014b). As the majority of the participating HCPs in this survey are based in the UK (43.5% in round one and 64.4% in round two), and the provision of COPD bundles is

integrated within a good number of the NHS hospitals (NACAP, 2021), this could influence HCP opinion regarding identifying these two non-pharmacological interventions (advice about enrolment in PR and smoking cessation programmes), because the eligibility assessments of these two highly prioritised interventions as (PR and smoking cessation) are currently conducted as part of the bundle delivery in hospitalisation while preparing for patient discharge. In addition, the high prioritisation of the encouraging advice to enrol in PR among the HCPS could also be attributed to the fact that nowadays, PR is considered the most appropriate setting in which to advance patients' disease knowledge, as it provides a combination of patient education topics and exercise training which leads to comprehensive positive health-related outcomes (Smith et al., 2020). Furthermore, due to the widely recognised PR benefits post exacerbation of COPD, such benefits include a significant positive impact on an individual's quality of life and exercise capacity (high-quality evidence) and reduced hospital admission post-acute exacerbation of COPD (pooled odds ratio (OR) 0.44; 95% confidence interval (CI 0.21 to 0.91) (moderate quality evidence) (Puhan et al., 2016).

Anxiety management in this study gained panellist consensus as the only strongly prioritised psychological intervention to be delivered during the acute phase of COPD exacerbation. The high level of prioritisation within this specific psychological condition could be linked to the HCPs' recognition of the impact of the unpredictable dyspnoea episodes, which are predominantly present within the acute exacerbation event and which, when experienced, can lead patients to develop a strong sense of loss of control that could provoke anxiety attacks and amplify the perception of dyspnoea among exacerbators (Tan et al., 2019). Additionally, data from a large cohort study showed that anxious COPD patients experienced more symptoms based exacerbations (≥2 hospitalizations, 14 vs 8%; P = 0.03) and longer hospital stays compared to the non-anxious patients (mean days ± SD, 49 ± 48 vs 27 ± 21; P = 0.03) (Xu et al., 2008). A suggested non-pharmacological approach to managing anxiety and dyspnoea within the acute phase could be in the form of a controlled breathing intervention which has been previously tested in a randomised control trial conducted on 46 acute COPD exacerbation individuals (Valenza et al., 2014). The application of this intervention, which consisted of relaxation exercises, pursed-lip

breathing and active expiration, was found to make a statistically significant improvement on the intervention group's anxiety, measured by the hospital anxiety and depression scale (change in the anxiety sub-scale mean value was 6.314 ; SD ± 0.712 (95% CI -18.36 to 2.014; P <.001) and in dyspnoea scores the mean value was 2.917; SD ± 3.21 (95% CI -1.228 to 0.28; (P= <.001) measured by the modified medical research council dyspnoea scale (Valenza et al., 2014). Other utilised psychotherapy approaches to manage disease-specific anxiety and fear in either the acute or general COPD population, which yield positive results, could include cognitive behavioural therapy (Thew et al., 2017) and acceptance and commitment therapy (Graham et al., 2016).

In the post-acute phase, HCPs strongly prioritised various non-pharmacological interventions that targeted four fundamental patients care elements, namely knowledge, physical therapy, psychological wellbeing and chronic illness management. Further exploration of the HCPs' highly prioritised non-pharmacological interventions to improve physical ability showed that HCPs strongly prioritised expanding the selection of physical therapy interventions such as walking and all over the body strength and endurance exercises. The existence of this high level of prioritisation within this element of patient care (physical ability or function) post the acute phase of COPD exacerbation could be due to the widely known negative impact of the acute exacerbation of COPD on the patient's muscle mass and function within the respiratory and peripheral skeletal muscles, which inversely correlates with an increased risk of hospital readmission and exacerbation frequency (Gosker et al., 2021). Additionally, HCPs strongly prioritised the benefits of the delivery of physical exercise interventions during the post-acute phase of COPD exacerbation event, which could be due to the proven benefits of such intervention. For example, in a study done by Bruna et al. (2020), muscle exercise training impeded in early home-based PR that consists of aerobic exercises and resistance training done by using walking exercises, free weights and sit-to-stand exercises following acute exacerbation of COPD showed a meaningful clinical improvement in the functional exercise capacity measured by six minutes walking test mean (SD) change 76 (60) m and quality of life measured by the Chronic Respiratory Questionnaire (CRQ) total score 15 (21) units (Wageck et al., 2020). Moreover, physiotherapy interventions during the post-acute stage

of COPD exacerbation are well-established in the literature and are widely recommended within the current healthcare guidelines (NICE, 2019, GOLD, 2019).

Understandably, HCPs strongly agreed on prioritising interventions related to effectively managing the chronic nature of COPD disease via providing patient-focused therapy and future care planning, for example, by providing individualised goal setting, self-management and action plans. Such interventions yielded positive results in improving patient health-related quality of life and respiratory-related hospital admissions: For example, results from a meta-analysis showed that at the 12-month follow-up period, the mean of the total score of the health-related quality of life outcome (measured by St. George's Respiratory Questionnaire) was lower by -2.69 points compared to the usual care groups (95% CI-4.49 to -0.90; 10 studies; high-quality evidence) and intervention participants were at lower risk for at least one respiratory-related hospital admission in comparison to the usual care (OR 0.69, 95% CI 0.51 to 0.94; 14 studies; moderate quality evidence) (Lenferink et al., 2017).

In the literature, there are some proven benefits of respiratory muscle training (breathing exercises) to the general COPD in relation to reducing dyspnoea, improving thoracic and abdominal muscle coordination, and improving functional capacity (Holland, 2014). Despite this, HCPs in our study collaboratively disagreed with prioritising respiratory muscle training during the acute phase of COPD exacerbation and had an undecided opinion about prioritising the delivery of this intervention during the post-acute stage of COPD. This could be due to certain types of respiratory exercises, such as pursed-lip breathing, having shown a beneficial effect in managing breathlessness, improving ventilation and individual functional performance in the general COPD population (Hillegass, 2009, Nield et al., 2007). However, other types of respiratory training, such as the deep diaphragmatic breathing technique, which primarily focuses on augmenting lung volume, might not be considered to be the best option during acute exacerbations as patients increasingly suffer from airflow obstruction, hyperinflation and expiratory flow limitation and, therefore, attempts to further increase lung volumes could produce an adverse effect on the patients (Holland, 2014, Mendes et al., 2019).

Another type of breathing exercise, known as Inspiratory Muscle Training (IMT), is performed by using handheld devices that provide inspiratory flow resistance and a pre-set inspiratory effort to achieve airflow through the device has to be reached by the patient. The effectiveness of IMT has been reported in a recent meta-analysis of studies that employed IMT on stable COPD patients, with results showing a clinically relevant reduction in dyspnoea by 0.5 points, as measured by the Chronic Respiratory Questionnaire (CRQ), improvement of quality of life by a reduction of at least four points in the St George's Respiratory Questionnaire (SGRQ), significant improvement in the exercise capacity (+ 43m) measured by the Six-Minute Walk Test (6MWT) and significant improvement in the inspiratory muscle strength measured by the Maximal Inspiratory Pressure (PImax) (Beaumont et al., 2018). However, in the studies that used IMT in conjunction with PR, results showed that IMT did not provide extra benefits for dyspnoea and exercise capacity compared to when PR alone was delivered (Beaumont et al., 2018, Nolan and Rochester, 2019). Thus, due to IMT's limited benefits compared to the more holistic benefits COPD patients usually acquire from PR attendance, IMT is still not considered a standardised intervention within COPD management. This evidence might explain the HCPs' disagreement or undecided opinion in this study regarding prioritising the delivery of this non-pharmacological intervention within the COPD exacerbation population. Further to this, the benefits of IMT within the AECOPD population are still unclear due to trials investigating such interventions being predominantly conducted on stable COPD populations and finding collective evidence that back up the benefits of such intervention within the acute or post-acute COPD population is currently limited.

Overall, the patient care management elements that reached the study group consensus and he highest level of HCPs prioritisation (Strongly agree) during both stages of COPD exacerbation (at hospitalisation and post-discharge) seemed broadly consistent with clinical guidelines recommendations (NICE, 2019, GOLD, 2019), and it tackled many of the most prevalent features of COPD exacerbation such as, for example, breathlessness, limited mobility, anxiety and fatigue (Kessler et al., 2006, Hurst et al., 2020b). Mapping the present study finding with the patients' findings can be found in chapter eight of this thesis (from page 254-255).

5.6 Strengths and limitations of this study

This study has several strengths: 1) it is the first study to explore the HCPs' non-pharmacological patient priorities in managing COPD exacerbation, 2) it is an international study as it included HCPs from major high-income countries such as the United Kingdom, the United States, Australia and Canada which helped in gaining the perspectives of HCPs from various health care systems, 3) the study panellist group size and retention rate are considered as within the higher range of the recommended group sizes in Delphi studies, 4) the majority of the HCPs participating in the Delphi survey hold more than 20 years of experience, which qualifies them as experts in the field of COPD management.

Notwithstanding, in this study, stability testing was only applied to the items that did not achieve consensus. Thus, Delphi methodologists might consider this a limitation because less rigour was used to investigate the stability of items that reached consensus (Heiko, 2012). However, doing so is common practice within currently conducted healthcare Delphi studies and, in addition, not applying stability testing does not eliminate the validity of the acquired consensus as it only adds less rigour to the consensus process (Ramakrishnan et al., 2021, Holland et al., 2021). Moreover, another limitation of this study arose from the method used to collect the HCPs' patient care priorities (which was by scoring the HCPs' agreement level with each proposed patient care item). Such a method might not be considered the best approach for scoring priorities, and a ranking system of the priority level might be a better approach to serve the study purpose.

5.7 Conclusion

In the acute phase of COPD exacerbation, HCPs strongly agreed on prioritising interventions that introduce proactive measures to prevent future exacerbation attacks, which modify and manage two core elements of patient care, namely knowledge and psychological well-being (specifically anxiety management). However, post acutely, HCPs expanded their

highly prioritised interventions to cover various fundamental elements of a patient's care to include knowledge, physical ability, psychological wellbeing and chronic illness management.

Chapter 6 . Interventions to Improve Conventional Pulmonary Rehabilitation Referral, Uptake and Completion Post-Acute Exacerbation of COPD Event: A Systematic Review

6.1 Introduction

Pulmonary rehabilitation (PR) following post-acute COPD exacerbation (AECOPD) is nowadays considered a cornerstone standardised therapy pathway for exacerbated COPD individuals (NICE, 2019), and the introduction of such therapy can have a positive dual impact on patients and healthcare systems (Jenkins et al., 2018). In a recent meta-analysis that studied the impact of PR following AE-COPD and included 20 randomised control trials, results showed that PR led to a large improvement above the threshold of minimal important difference in both health-related quality of life (measured by the Chronic Respiratory Questionnaire [CRQ]) and the St. George's Respiratory Questionnaire [SGRQ] and exercise capacity, measured by the Six-Minute Walking Test [6MWT]) (Puhan et al., 2016). Additionally, the review found that these benefits can be extended to positively impact the healthcare system by reducing the number of unplanned hospital re-admissions (Puhan et al., 2016), which currently account for a large proportion of the cost of managing COPD worldwide (Punekar et al., 2014, Oostenbrink and Rutten-van Mölken, 2004).

Despite these documented benefits of PR, the uptake of such treatment post-acute exacerbation events is still perceived as far less than ideal as the reported PR rates of referral, participation and completion by a clinical audit conducted within multiple rehabilitation centres in northwest London showed that only 32% of all eligible PR participants (n=286) received a referral, about 67% of the referred (n=60) started PR post hospitalisation (21% out of all eligible post-AECOPD PR participants) and only 72% of

those who started the PR programme (n=60) actually completed it, which still accounts for only 47% of all referrals (n=90), (Jones et al., 2014). Similar poor post-AECOPD PR referral and uptake numbers were reported on a larger national scale (this UK audit included n=201 PR services with n=6.056 records), in which only 6.3% of post-AECOPD individuals were referred to PR from secondary care services and 4.1% referred from primary and community care services after treatment for AECOPD. The audit also reported that the PR uptake was around 17.3% when the referred AECOPD post-hospitalisation individuals started PR within 30 days of referral (Singh S, 2020).

Poor rehabilitation uptake post-AECOPD has been extensively investigated in the literature (Jones et al., 2018, Janaudis-Ferreira et al., 2019b, Benzo et al., 2015). In addition, recently PR uptake barriers have been grouped into three distinct reason-related categories: a) referrers, b) patients and c) healthcare systems (Jones et al., 2018). The reported barriers within the referrers category included referrers' poor knowledge about PR benefits or the centres that were accessible to patients, which might ultimately have a direct causative impact on patients' initial decisions about accepting or rejecting PR referrals (Jones et al., 2018). In a recent qualitative study by Janaudis-Ferreira et al. (2019), one of the study themes indicated the need to spread knowledge among patients and healthcare practitioners about PR benefits and also highlighted the need for the referring practitioners to be more informed about PR programmes located close to patients' residences (Janaudis-Ferreira et al., 2019b). Moreover, among the documented PR barriers exclusively related to the second category (the patients) were issues with transport, patients being unwell, suffering from other comorbidities and co-existing physiological conditions such as depression (Jones et al., 2018, Benzo et al., 2015).

Attempts to improve the uptake of conventional PR for the stable or acute exacerbation of COPD population remain limited despite the wealth of literature regarding PR barriers. For example, in a systematic review of the effectiveness of interventions promoting PR uptake and completion in the general COPD population, results showed that insufficient evidence was found due to only one randomised control trial being eligible to be included in the review (Jones et al., 2017). Therefore, the review results were

considered insufficient for guiding clinical practice, and the review authors suggested that further research attempts should be made to tackle the PR uptake problem (Jones et al., 2017). Further, efforts were made to cover this topic in another systematic review published in 2018, which included only 14 studies of interventions to promote PR referral and uptake designed for the stable and post-acute exacerbation of the COPD population (Early et al., 2018). However, this review is now considered outdated as more than four years have passed since the Early et al. (2018) publication, and we believe there might be other research attempts that have been explicitly conducted within the exacerbation of the COPD population to promote PR referral, uptake and completion. For this reason, we aimed to review and synthesise the available evidence that has emerged during recent years of interventions designed to improve conventional PR referral, uptake and completion around the time of exacerbation of COPD. The result of this review will also help with fulfiling the urgent need to explore the effectiveness of studies that have employed such interventions on this challenging population (acute or post-acute COPD exacerbation) to aid the designing process of future complex interventions that aim to improve conventional PR uptake post-AECOPD events.

6.2 Objectives

To determine the effectiveness of interventions that aim to improve referral, uptake and completion of the conventional pulmonary rehabilitation programme, structured exercise therapy programme or physical activity programme during or after post-acute exacerbation of COPD.

6.3 Participants

Adults (at least 18 years of age) with a primary diagnosis of COPD confirmed by the Spirometry test in line with national and international guidelines (The National Institute for Health and Care Excellence [NICE] and Global Initiative for Chronic Obstructive Lung Disease [GOLD]), and who are in admission or post hospitalisation after suffering from AECOPD.

6.4 Intervention

Any intervention with the specific aim of improving referral, uptake, completion of conventional pulmonary rehabilitation, exercise therapy, physical activity program and/ or to enhance disease knowledge and patient readiness to commence PR during hospitalisation or post-hospitalisation from acute exacerbation of a COPD event.

6.5 Comparison

Any concurrent control group receiving only standard care or referred to or enrolled in pulmonary rehabilitation, physical activity or exercise programme but not receiving an intervention aimed at improving PR referral, uptake or completion, patient disease knowledge, patient activation and readiness to engage in PR, physical activity, or exercise therapy programmes (e.g., not beyond usual care).

6.6 Outcomes

6.6.1 Primary outcomes

- uptake of conventional pulmonary rehabilitation, structured exercise, or physical activity programme (received baseline assessment)
- referred or accepted a referral to pulmonary rehabilitation
- adherence or completion of pulmonary rehabilitation (total number of sessions attended, received discharge assessment, or as specified by study reports)

6.6.2 Secondary outcomes

- change in disease knowledge (any validated measures)
- patient activation and readiness to commence PR, exercise therapy, or physical activity programme (any validated measures)

6.7 Methods

The protocol of this review was constructed according to Prisma Guidelines for reporting systematic reviews (Page et al., 2021). The review protocol was registered on PROSPERO (2021 CRD42021235607) (Bedor Alkhathlan, 2021).

6.7.1 Eligibility

Studies were included if they reported one of the review outcomes of interest: data about the referral, uptake and completion of the conventional pulmonary rehabilitation programme, structured exercise or physical activity programme following acute exacerbation of COPD. For this review, PR programmes were defined as multicomponent

interventions that included exercise training, education, and behavioural interventions to help improve the physical and psychological well-being of COPD individuals (Spruit et al., 2013). Exercise or physical activity programmes were defined as any structured programme that included planned, structured and repetitive body movements for the purpose of body conditioning (Huge, 2022). Uptake was defined as having attended the first appointment with a PR practitioner where an initial assessment was conducted. The eligible studies needed to include the following participants: I) healthcare professionals who referred patients with AECOPD to PR or any structured exercise or physical activity programme in a primary, secondary or community care setting, II) studies in which the population were adult participants (at least 18 years +) with either acute exacerbation of COPD or post-acute exacerbator, III) any intervention with the specific aim of improving patient uptake, completion, changes in patient's knowledge and readiness to commence conventional pulmonary rehabilitation or any structured exercise therapy or physical activity programs during or post-acute exacerbation of COPD, e.g., discharge bundles, taster sessions, video-based interventions, written material (manuals) and clinician delivered interventions and, finally, IV) the intervention must have been delivered during the secondary care setting or up three months post-hospital discharge from the AECOPD event.

Finally, studies were excluded if they had the following characteristics: I) mixed group results where sub-group data of the acute or post-acute COPD population were not described and could not be separated, II) intervention was designed to improve physical activity or exercise training in general but not within a structured programme. The following search restrictions were applied: I) only peer-reviewed articles, II) in English language and III) full-text articles.

6.7.2 Data sources and search strategy

Various core databases were used to conduct the search. These were the Cochrane Central Register of Controlled Trials (CENTRAL) to identify any existing relevant systematic reviews, MEDLINE, EMBASE (Ovid SP), PsycINFO (Ovid), CINAHL EBSCO

(Cumulative Index to Nursing and Allied Health Literature), AMED EBSCO (Allied and Complementary Medicine), hand searches of the proceedings of major respiratory conferences. We also searched Google Scholar for any previously known papers that did not appear through other database searches. Finally, we aimed to search the reference list of any identified and included study. All information sources searched for were from 1946 to July 2023. The language was set to English, and only peer-review articles were included. Key search terms were structured around four search strategy concepts: 1) population (e.g. Lung Diseases, Obstructive, COPD, Disease Exacerbation, Acute Disease, AE-COPD/ 'AECOPD'), 2) intervention (e.g. 'exercise therapy', 'rehabilitat*'), 3) outcomes (e.g. 'adherence', 'attendance', 'complet*', 'knowledge', 'readiness', 'commence', 'education', 'patient-activation') and 4) study setting e.g. hospital care, centre based, hospital-based, home care (see supplementary attached for complete search strategy mesh terms and keywords).

A continuous search within the core databases, e.g., Medline, Central, CINAHL, EMBASE, AMED and PsycINFO for relevant articles was repeated weekly from April 2022 onwards. The search results were compiled using Rayyan Software developed by Qatar Computing Research Institute (QCRI) (Mourad Ouzzani, 2016).

6.7.3 Study selection and data extraction

The search results were entered into Rayyan software, and two independent reviewers (BA and MA) who were blinded to each other's decisions screened the article titles and abstracts and then performed a full-text review of the identified eligible studies. Following the screening process, decisions were reviewed, and conflicts were resolved by a third review (SS). Data extraction followed the screening process whereby the two independent reviewers (BA and MA) piloted an extraction form and implemented it into Covidence software (Innovation), where the data extraction happened. The two reviewers performed data extraction independently, and the following data were extracted: population (type, size and demographics), intervention, comparison, and outcomes (PICO). In addition,

the following data, funding and conflict of interests, were also extracted. The study authors were contacted to enquire about missing data or the availability of the full text of a publication. The extracted data were then assessed for eligibility for a meta-analysis. If a meta-analysis was appropriate, statistical analysis was performed using Review Manager Software (RevMan5) (Collaboration, 2020). However, if narrative synthesis was more relevant, the data was then tabulated.

6.7.4 Quality assessment

Reviewers (BA and MA) independently assessed the risk of bias in individual studies using the Cochrane risk-of-bias tool for randomised trials (RoB 2) (Sterne JAC, 2019) for the randomised control trials. In the non-randomised studies of intervention (NRSI), the ROBINS-I tool for assessing the risk of bias was used (Sterne JAC, 2016).

6.7.5 Data analysis

Data from studies that overlap in terms of intervention and measured outcomes were planned to be pooled for meta-analysis. Additionally, inverse variance random effects will be used to describe the findings, and the heterogeneity will be identified by I^2 Test. If there were enough studies that overlapped in terms of outcome measures, we planned to pool these data together (with the participant as the unit of analysis) in a meta-analysis using a generic inverse variance random-effects method and explore any sources (e.g., clinical and/ or methodological diversity) of heterogeneity identified by the I2-test statistic. If there was an insufficient amount of evidence, we provided a narrative synthesis of our findings where applicable, according to the general framework for narrative synthesis by applying the following elements: I) developing a preliminary synthesis via using the tabulation method, II) exploring relationships in the data via using visual graphics, and III) assessing the robustness of the synthesis via reflecting critically on the synthesis process (Popay et al., 2006).

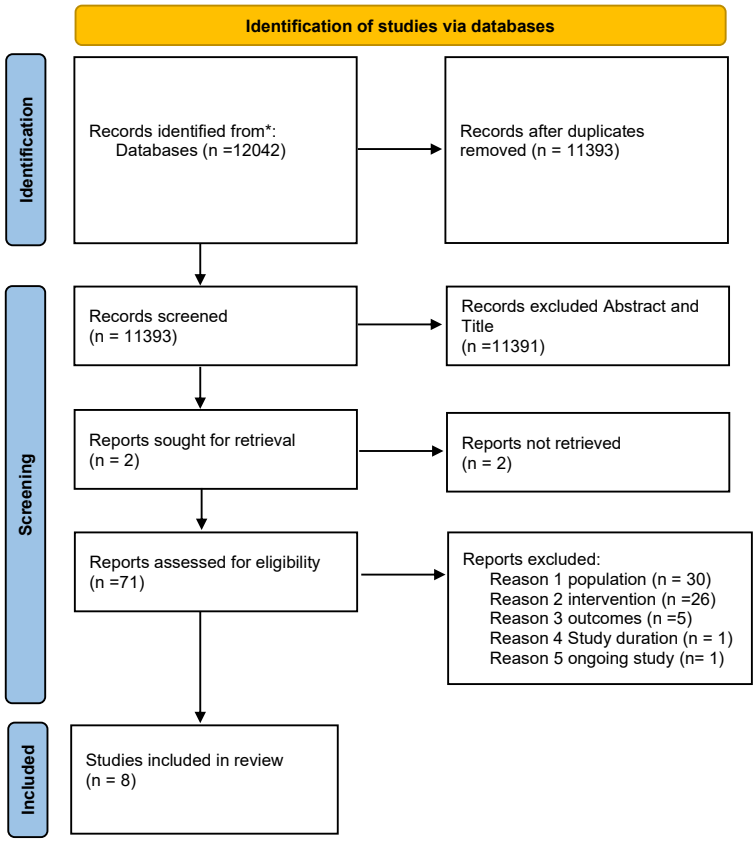
6.7.6 Study design

It was anticipated that there would be a limited number of trials available. Thus, we aimed to include a wide range of study designs, e.g. Randomised Control Trials (RCTs), individual and cluster level) and observational studies (cohort, cross-sectional, longitudinal, prospective, or retrospective studies). We only included studies that were reported in full text and published in peer-reviewed journals. Case studies were excluded.

6.8 Results

The search identified 12,042 potentially relevant articles, of which eight met the inclusion criteria (Figure 6.1). All the studies were written in the English language. Six studies were conducted in the United Kingdom (Barker et al., 2020, Barker et al., 2021, Sewell et al., 2017, Revitt et al., 2018, Houchen-Wolloff et al., 2021, Hopkinson et al., 2012). Two were in Canada (Milner et al., 2019, Janaudis-Ferreira et al., 2018). The study characteristics are described in table 6.1. Five studies included data about a referral to PR as an outcome and included 1851 participants in total. Two reported referral numbers, percentages and level of significance (P-value) (Barker et al., 2020, Barker et al., 2021), and three studies reported only numbers and percentages (Sewell et al., 2017, Hopkinson et al., 2012, Houchen-Wolloff et al., 2021). The largest number of participants came from Sewell et al. 2017 (an audit data), with 1170 participants (Sewell et al., 2017). Three studies reported outcome measures related to PR referral, uptake and completion (Barker et al., 2020, Barker et al., 2021, Houchen-Wolloff et al., 2021). However, Revitt et al. (2018) only reported PR uptake and completion, and those outcome data were extracted from the study recruitment flow chart. The other two studies, Sewell et al. (2017) and Hopkinson et al. (2012) reported only one outcome measure, which was PR referral. PR adherence was only reported in one study by Barker et al. (2020). Disease knowledge was reported by only two studies, namely Ferreira et al. (2018) and Houchen-Wolloff et al. (2021). Lastly, two studies

reported patient activation measures captured by evaluating the patient's readiness to commence PR, and were those by Ferreira et al. (2018) and Milner et al. (2019).



From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71.For more information, visit: http://www.prisma-statement.org/

Figure 6.1 Systemic review flow diagram (PRISMA 2020 flow diagram)

Table 6.1 Included studies' characteristics

Study ID and Setting	Sample Size	Demographics	Source of Participants	Study design	Intervention	Comparison	Outcome measures	Findings relevant to this review
Barker et al. (2020) (United Kingdom)/ Secondary care	Recruited 200 Randomised 196 (intervention group n=98) Usual Care Group (n=98)	Intervention: Sex M, n (%) 49 (50) Age, yr. 70 (11) FEV1/FVC 0.53 (0.16) FEV1 % Predicted 38 (28–49) MRC, dyspnoea scale score 4 (3–5) Pack-years history, yr 40 (26–55) COPD Assessment test 23 (8) Hospital length of stay, d 3 (2–7) Previous experience of PR, n (%) 50 (51) 4MGS, <0.60 m/s, n (%) 50 (51) Control: Sex M, n (%) 46 (47) Age, yr 68 (11) FEV1/FVC 0.53 (0.17) FEV1 % Predicted 34 (26–47) MRC, dyspnea scale score 4 (3–5) Pack-years history, yr 40 (28–60) COPD Assessment test 23 (8) Hospital length of stay, d 2 (1–5) Previous experience of PR, n (%) 51 (52) 4MGS, <0.60 m/s, n (%) 49 (50)	Hospitalised patients with AECOPD	Randomised control trial (RCT)	Intervention group received COPD discharge bundle delivered by Respiratory specialist +verbal information about PR and a patient co-designed education Video	Usual care (which they received COPD Discharge bundle (it included verbal information about PR program).	Primary outcome Uptake percentage uptake of PR within 28 days of hospital discharge within each treatment arm Secondary Referral, Completion, adherence, uptake to PR within 90 days, change in CAT, and Change in 4MGS from discharge to 90 days (M/S)	**PR uptake** within 28 days of hospital discharge d,(n%), intervention 33 (34), Control 40 (41) P value 0370, The Kaplan-Meier curve demonstrated no significant between-group difference in time to uptake of PR log rank test P = 0.490). **PR Referral** within 28 days of discharge n(%), Intervention 70 (71) versus 68 (69) P value 0.754 **PR Completion** n (%) 15 (46) versus 23 (58) p value 0.305 **PR Adherence**, PR sessions completed by those taking up PR n (%) Intervention mean (SD) 8 (6) versus 10 (6) P value 0.268 Complection intervention n=15 (46%) versus n=23 (58%) p value 0.305 **Uptake to PR within 90 days** intervention n (%) intervention 52 (53) versus 55 (56) p value 0.911
Barker et al. (2021) United Kingdom	Data of Hospitalised patients with AECOPD episodes Study included 291 episodes **(no bundle received** (n=63) **Bundle received from a hospital practitioner involved in the delivery of PR** (n=25), **Bundle received from a hospital practitioner with no involvement in PR** (n=203)	**No bundle received (n=63)** Age (years) 72 (9) Male (n (%)) 29 (46) FEV1 % predicted 42 (26 to 62) Smoking status: Never / former / current (n (%)) 2 (3) / 42 (67) / 18 (29) Median (IQR) duration of inpatient stay (days) 4 (2 to 9) **Bundle received from a hospital practitioner involved in PR delivery (n=25)** Age (years) 72 (11) Male (n (%)) 12 (48) FEV1 % predicted 41 (30 to 63) Smoking status: Never / former / current (n (%))1 (4) / 17 (68) / 7 (28) Median (IQR) duration of inpatient stay (days) 3 (2 to 8) **Bundle received from a hospital practitioner with no involvement in PR (n=203)** Age (years) 72 (9) Male (n (%))105 (52) FEV1 % predicted:37 (26 to 48) Smoking status: Never / former / current (n (%))1 (1) / 132 (65) / 70 (34) Median (IQR) duration of inpatient stay (days) 3 (1 to 6)	Data from records of hospitalised patients with AECOPD episodes	Prospective cohort study	Three exposures (No COPD discharge bundle received versus COPD discharge bundle form a practitioner with involvement in PR versus COPD discharge bundle received from practitioner with no involvement in PR) Followed up for 4 weeks after hospital discharge.	Three arm comparison	1) Referral for PR (defined as a referral received by PR service) within 4 weeks of hospital discharge 2) Uptake of PR (defined as the proportion of those referred attending a PR assessment) within 4weeks of hospital discharge.	**Referral for PR**:Of the 63 episodes where the COPD discharge bundle was not used, none were referred for PR. COPD discharge bundles delivered by PR practitioners compared with non-PR practitioners were associated with increased PR referral (n=15 (60%) vs n= 25 (12%), p<0.001; adjusted OR: 14.46, 95% CI: 5.28 to 39.57 **Uptake of PR** (n=6 (40%) vs n=8 (32%), p=0.001; adjusted OR: 8.60, 95% CI: 2.51 to 29.50 **PR Completion** between groups who received the COPD discharge bundle in the group who received the bundle from PR practitioner n=2 (33%) complected PR programme versus n=3 (36%) in the group who received the bundle from practitioner with no involvement in PR

Study ID and Setting	Sample Size	Demographics	Source of Participants	Study design	Intervention	Comparison	Outcomes measures	Findings relevant to this review
Hopkinson et al. (2012) (United Kingdom)/ Secondary care	94 patients on the respiratory ward	Age: mean 74.6 SD (11.2) years Sex: 64% male Median length of stay: 6 days	Hospitalised patients with COPD	Before and after study of process indicators	1) ward based staff education 2) discharge care bundle with referral for PR assessment 3) patients offered phone call 48-72 hours post discharge to check if they were improving, if not then community input is expected 4) PDSA cycle to refine process 5) prize draw for staff completing checklist 6) ward staff attended hospital PR session 7) PR patient information leaflet versus usual care (historical)	Usual care (historical)	Compliance with smoking cessation advice PR referral Self-management plan administered Inhaler technique reviewed Follow-up arrangements documented	**PR referrals:** 31 referrals to pulmonary rehabilitation for Chelsea and Westminster patients compared with 81 in the year post initiation. An increase of 158%
Sewell et al. (2017) (United Kingdom)/ Secondary care	From April 2012 to March 2013, a total of 1,742 patients were discharged with a primary diagnosis of COPD Of these, 1,170 (67.2%) patients received the COPD discharge bundle over the 12-month project duration	Not reported	Hospital records of patients discharged with primary diagnosis of COPD	Before and after audit data for operational improvement activities	1) COPD discharge care bundle comprising of referral to smoking cessation and pulmonary rehabilitation services 2) introduction of a self-management manual 3) assessment of inhaler technique + follow-up phone calls at 2 working days and 15 days post discharge.	Only one outcome - length of stay (LOS), was compared with the mean LOS for the 3 years previous to the implementation of the care bundle project	1) recorded total number of patients discharged with a primary diagnosis of COPD 2) referral rates to smoking cessation and pulmonary rehabilitation services 3) mean LOS for those patients receiving the care bundle was also recorded and compared to mean LOS for all COPD discharges from the hospital for the years 2012-2013 and 2011-12 4) 30- day readmission data for the patient who received the COPD care bunde	**PR Referral** rate to PR rose from 39.7% in Q1 to 55.9% in Q4

Study ID and Setting	Sample Size	Demographics	Source of Participants	Study design	Intervention	Comparison	Outcomes measures	Findings relevant to this review
Revitt et al. (2018) (United Kingdom)/ Post discharge	Post AECOPD patients (n=56) referred to PR, (n=36) consented and randomised intervention group PEPR (n=24), D-PEPR (n-=12)	Intervention Group PEPR Age (years) mean 64.32, SD (7.37) FEV1 (l) 1.10, SD (0.44) FEV1 (% pred) 51.04, SD (20.46) FEV1/FVC ratio 46.52, SD (12.99) Intervention Group D-PEPR Age (years) mean 65.8, SD (7.24) FEV1 (l) , 1.34 SD (0.54) FEV1 (% pred) 52.33, SD (17.53) FEV1/FVC ratio 45.45, SD (9.48)	Following admission of AECOPD out patient asessment clinic	Randomised controlled trial (RCT)	Early post exacerbation pulmonary rehabilitation (PEPR) occurred within 4 weeks of hospital discharge PR components were the same for both groups; PR sessions were delivered twice a week for 6 weeks and each session lasted for 2 hours. Sessions contained individualised aerobic and resistance exercises and education sessions that covered chest clearance and energy conservation	Delayed PEPR (D-PEPR) which commenced 7 weeks after a control period of no intervention.	The incremental shuttle walking test (ISWT) and the endurance shuttle walk test (ESWT). PR uptake and completion was not listed within the primary or secondary measures/data were extracted from the study flow diagram.	**PR uptake** but not stated as primary or secondary measure. However, data were excreted from the study flow diagram Received allocated intervention PEPR (n=22) versus DPER (n=6) PEPR- commenced within 4 weeks of hospital discharge (n=14) D-PEPR-control period of 7 weeks (no intervention), then commenced PR (n=3) **PR Complection** PEPR (n=14) versus D-PEPR (n=3)
Houchen-Wolloff et al. (2021) (United Kingdom)/Post discharge	n=2080 patients were screened for eligibility n=100 patients were recruited (4.8% of those screened)	Age (years) mean 71.2 SD (9.3) FEV1/FVC mean 46.2 (13.9) FEV1 (% predicted) mean 44.8, SD (18.3 Pack-years 50.2 (31.0)	Hospitalised patient with AECOPD	Single-centre, non-randomised feasibility study	SPACE for COPD is an interactive web-based programme that offers a comprehensive package of exercise and self-management education. The programme has four stages, each of which has specific tasks that the user needs to achieve before progressing to the next stage Tasks included: 1) creating and updating their own short-term goals, 2) completing knowledge tests on COPD and exercising safely 3) reading or watching videos on specific topics, such as inhaler techniques or healthy eating. In stage 2, patients were encoraged to do aerobic and strength training and were asked to record their progress. The intervention included a symptom diary that linked to the patient's individual exacerbation action plan. The web-based programme usually takes approximately 11 weeks to complete. This patient cohort had access for 1 year to promote long-term behaviour change and maintenance.	Usual Care	1) feasibility of the intervention 2) COPD Knowledge Questionnaire [BCKQ]) 3) the acceptability of the intervention and trial (qualitative interviews) 4) intervention engagement (web usage statistics; number of log-ins and use of web features captured directly from the administrator section of the website) 5) uptake to outpatient PR (uptake and completion rates for those referred)	**PR referral:** 57 accepted a referral for rehabilitation **PR uptake:** 47 were assessed and 35 started a program; **PR completion:** 19% (19/100) of the total population completed either a hospital or community outpatient rehabilitation programme **COPD Knowlege Questionnaire [BCKQ]): This was done with 42 patients who returned the questionnaires at 6 months. The change in the BCKQ score was 7.8 (SD 10.2) points, an increase of 21% (prescreening score: mean 37.1, SD 9.5; postscreening score: mean 44.9, SD 9.4).**

Study ID and Setting	Sample Size	Demographics	Source of Participants	Study design	Intervention	Comparison	Outcomes measures	Findings relevant to this review
Milner et al. (2019) Canada / secondary care	n=54 COPD excerbation admitted n= 44 eligible individuals n=6 individuals accepted the intervention	Age 71 (66–86) Female, % (n) 66.7 (4) FEV1% pred., median (range) 37 (22–61) MMRC score, median (range) 3.5 (2–4) CAT score, median (range) - 30 (26–35) Current/former smoker, % (n) 66.7 (4) Hospital LOS in days, median (range) 5 (1–56) 7 (2–41)	Hospitalised patients with AECOPD	Non-randomised Interventional study (study pre–post)	Deliver a PR 'taster' session to patients hospitalized with AECOPD. The intervention was estimated to take 30–40 minutes and delivered individually. The taster session included patients accompanying the researcher to one of the hospital gyms and the researcher planned to show and/or involve patients in typical aerobic and resistance exercise with no focus on intensity, explaining the general components of a PR programme, and provided the participants with a handout that introduced PR and its benefits and covered the general education topics. At the end of the 'taster', patients were given a 'menu' of the PR programmes available in the Greater Montreal area, showcasing all options available to them in terms of timing, location and delivery format. To ensure the intervention was delivered uniformly, a script was drafted for the researcher to use as a reference	None	Acceptability 1) acceptability, 2) feasibility, 3) safety of delivering a PR 'taster' session, 4) Evaluating the changes in patient knowledge of and readiness to commence PR (changes in motivation to commence PR and confidence to commence PR, 5) make recommendations for the refinement of future iterations of the intervention based on the findings of this study	**Readiness to commence PR measured via:** **1) a modified version of the Readiness to Change Exercise Questionnaire;** 3 of the patients were already in the action phase pre-intervention, post-intervention, 5 but 1 were in the action phase and 1 participant was unable to be categorized into a stage both pre- and post-intervention **2) two Likert-type scales which assessed motivation and confidence; n**o median change was observed post-intervention within both scales **3) a modified version of the Treatment Self-Regulation Questionnaire (TSRQ) for exercise to measure motivation to enrol in PR: s**light positive change (median change +0.67) in relative autonomous motivation index (RAMI) (indicating how self-determined the decision to commence PR was) was observed post-intervention **4) verbally capturing the participants willingness to accept a PR referral: f**ive out of the six included participants reported that they intended to enrol in PR
Janaudis-Ferreira et al. (2018) Canada/ secondary care	n=102 patients were approached to participate in the study 31 patients were randomised to either intervention (n =15) or control (n =16) groups	Intervention: Age, y 71 ± 11 Sex, M/F, No 8/7 FEV1, % predicted 45.25 ± 7.36 FEV1/FVC 0.45 ± 0.09 MRC 4 ± 0.8 Pack years 52.4 ± 32 Time since COPD diagnosis y 5.36 ± 3.5 Control: Age, y 74 ± 10 Sex, M/F, No 4/9 FEV1, % predicted 34.7 ± 23.8 FEV1/FVC 0.46 ± 0.09 MRC 4 ±0.8 Pack years 39.7 ± 11 Time since COPD diagnosis, y 7.31 ± 7.9 Data are presented as mean ± SD	Hospitalised patients with AECOPD	Randomised Controlled Trial (pilot)	The intervention group received two one-to-one 30 min education sessions via a manual (the first session was delivered 7 days after hospital admission either in hospital or at the patient's home after their discharge. The second was delivered within 2 weeks of admission). The following topics were addressed: 1) normal lung function 2) how COPD affects the lungs, symptoms and aggravating factors 3) the importance of smoking cessation and strategies for smoking cessation 4) respiratory medication and how to use it 5) the identification of symptoms of an acute exacerbation 6) the role of pulmonary rehabilitation, and the importance of maintaining an active lifestyle.	Usual care	**1) d**isease-specific knowledge and informational needs measured using the Bristol COPD Knowledge Questionnaire (BCKQ) 2) program feasibility measures 3) Lung Information Needs Questionnaire (LINQ) 4) patient satisfaction 5) willingness to participate in pulmonary rehabilitation	**1) disease-specific knowledge was** measured using the Bristol COPD Knowledge Questionnaire (BCKQ) - compared with the changes observed in the control group (mean change, 3.4 ± 4.9), the magnitude of change in the intervention group was greater for the BCKQ (mean change 8 ± 5.14; P = .018) **2) willingness to participate in pulmonary rehabilitation** - 13 of 15 patients in the intervention group indicated that it was “too soon” to consider PR

6.8.1 Populations and settings

The descriptions of patients' populations were variable. However, age and gender were mainly reported across studies by Barker et al. (2020), Barker et al. (2021), Hopkinsons et al. (2012), Milner et al. (2019) and Ferreira et al. (2018). In contrast, Revitt et al. (2018) and Houchen-Wolloff et al. (2021) only reported age alongside other study outcomes. No study reported ethnicity, socioeconomic status, patients' educational level or frailty measures. Only one study, Sewell et al. (2017), reported no participant demographics. All the studies included interventions that targeted only patients. Overall, the mean age of the study participants was ≥ 64 years, and 33%-64% of the samples were male.

All the studies recruited or used records data of patients hospitalised with AECOPD (secondary care setting), namely Barker et al. (2020), Barker et al. (2021), Hopkinsons et al. (2012), Sewell et al. (2017), Houchen-Wolloff et al. (2021), Milner et al. (2019) and Ferreira et al. (2018). Only Revitt et al. (2018) recruited participants post-AECOPD discharge.

6.8.2 Study designs

Study designs were heterogenous, and most of the included studies were Non-Randomised Studies of Interventions (NRSI) such as; prospective cohort study (Barker et al., 2021), pre and post-interventional study (Milner et al., 2019), non-randomised feasibility study (Houchen-Wolloff et al., 2021), two audit data of evaluation of process indicators (Hopkinson et al., 2012) and service improvement activities (Sewell et al., 2017). The remaining studies used Randomised Control Trial (RCT) as a main study (Barker et al., 2020, Revitt et al., 2018), and one used a preliminary RCT study (Pilot study) (Janaudis-Ferreira et al., 2018).

6.8.3 Interventions

Most studies reported one of the main PR programme-related outcomes, namely Barker et al. (2020), Barker et al. (2021), Sewell et al. (2017), Hopkinson et al. (2012) and Houchen-Wolloff et al. (2021). The majority of the studies that reported the referral outcome used interventions already implemented in the clinical practice (usual care) either on its own e.g. the COPD discharge bundle (Barker et al.,(2021); Sewell et al. (2017); Hopkinson et al. (2012)) or by supplementing the implementation of the COPD discharge bundle with additional interventions such as a patient co-designed video that included information about the benefits and shared personal experiences of PR from indiviuals with COPD (Barker et al., 2020), or by using novel interventions such as the COPD interactive web-based programme that offered a comprehensive package of exercise and self-management education (Houchen-Wolloff et al., 2021). Referral was reported at the level of individual patients or clinical departments (Barker et al., (2020); Barker et al. (2021); Houchen-Wolloff et al. (2021)) and at system level (National Health Service) (Hopkinson et al., 2012, Sewell et al., 2017). Studies measuring uptake and completion included interventions similar to the ones mentioned earlier within the referral outcome with an addition of intervention that was already established within the clinical practice (pulmonary rehabilitation). However, it was administered in two study arms at two different time points (either early, which occurred within four weeks of discharge from post-exacerbation of COPD or delayed, which started seven weeks of post exacerbation of COPD) (Revitt et al., 2018). Moreover, in the Revitt et al. (2018) study, the PR components were identical for both groups, and included exercise and education sessions delivered twice a week for 2 hours. The only study that measured PR adherence used a COPD discharge bundle supplemented with a patient co-designed video intervention (Barker et al., 2020).

In the studies that measured COPD disease knowledge, interventions included either an interactive web-based program (Houchen-Wolloff et al., 2021) or one-to-one 30-minute educational sessions (Janaudis-Ferreira et al., 2018). The educational components included in the Houchen-Wolloff et al. (2021) study requested completing two tests regarding COPD knowledge and exercise safety, as well as reading or watching videos about topics that covered inhaler techniques and healthy eating. In the Houchen-Wolloff et al. (2021) study,

participants gained access to the web programme as soon as they consented to participate during their inpatient stay. However, in the Ferreira et al. (2018) study, the educational session covered much more varied educational topics which were delivered in a manual format, such as normal lung function, how COPD affects the lungs, symptoms and exacerbation aggravating factors, highlighting the importance of smoking cessation, PR and maintaining an active lifestyle and, lastly, information about respiratory medication and how to use it. The educational intervention for this study was delivered within seven days of hospital admission, either in the hospital or at the patient's home (Janaudis-Ferreira et al., 2018).

Intervention that measured patients' readiness to commence PR used one-to-one 30-minute educational sessions provided by a physiotherapist with expertise in COPD, as previously mentioned in Ferreira et al. (2018). Another study used a novel approach which was designing a PR taster session to measure the patient's readiness to commence PR. In the taster session, the participants accompanied the researcher to the hospital gym to get an overview of the PR programme and what it involved and tried out or observed some of the exercises usually included in PR classes. This session lasted for up to 40 minutes and was delivered individually.

Many of the included clinician-led interventions did not report measures to confirm intervention fidelity (Barker et al., 2020, Barker et al., 2021, Sewell et al., 2017, Revitt et al., 2018, Janaudis-Ferreira et al., 2018). However, in one study by Hopkinsons et al. (2012), intervention fidelity was measured and maintained by assigning members of the clinical team to teach via a drop-in approach in order to help the clinician in charge of the intervention delivery with improving their knowledge about smoking cessation and inhaler techniques. In addition, pharmacists involved in the study designed laminated pictorial charts attached to the wards' drug trolleys to help reinforce the proper inhaler techniques. Furthermore, an administrative team was involved in monitoring the returns of the discharge bundles and helped with encouraging ward nurses' engagement by allowing them to enter a prize draw upon completion of the bundle. However, it was unclear whether the ward nurses received any formal training or an education session, especially pertaining to pulmonary

rehabilitation. Finally, in the Milner et al. (2019) study, to make the delivery of the intervention uniform, a written script was provided for the researchers.

In the studies included in the systematic review, comparison groups were only found in five studies out of the eight included (Barker et al., 2020, Barker et al., 2021, Hopkinson et al., 2012, Revitt et al., 2018, Janaudis-Ferreira et al., 2018), with only three of the studies reporting statistical significance with P-values (Barker et al., 2020, Barker et al., 2021, Janaudis-Ferreira et al., 2018).

6.8.4 Outcomes

Referral to PR was listed as the primary outcome in Barker et al. (2020) and Barker et al. (2021), and mostly defined in the remaining included studies as a referral received by a PR team. Additionally, PR referral was collected as part of the audit data reported by Hopkinson et al. (2012) and Sewell et al. (2017). PR uptake was one of the primary outcome measures in Barker et al. (2020) and Barker et al. (2021), with uptake defined as the proportion of those referred attending a PR assessment or a documented attendance at the PR programme within four weeks of hospital discharge. COPD disease knowledge was one of the primary outcome measures reported by Houchen-Wolloff et al. (2021). To measure the COPD disease knowledge outcome in Houchen-Wolloff et al. (2021), they used the Bristol COPD Knowledge Questionnaire (BCKQ), which is designed to assess a patient's knowledge and the results of patient education. The BCKQ questionnaire covered 13 topics ranging from disease epidemiology, aetiology, symptoms, breathlessness, phlegm, infections, exercises, smoking, vaccination, inhaled bronchodilators, antibiotics, oral steroids and inhaled steroids. The BCKQ questionnaire has been previously tested for its suitability to be used with the COPD population for clinical and research purposes, and is considered a valid and reliable questionnaire (White et al., 2006). In the Milner et al. (2019) study, readiness to commence PR was reported within the study's primary outcomes, and was measured by multiple questionnaires and scales such as, for example, a modified version of the Readiness to Change Exercise Questionnaire, which is defined as a 12-item instrument for measuring the patients' state of change describing the stages the individual undergoes within the behavioural change process. This process has four stages: 1) pre-

contemplation, 2) contemplation, 3) preparation and 4) action stage (Kheawwan et al., 2016).

In addition, Milner and his colleagues (2019) used two Likert-type scales which assessed the patient's motivation and confidence both adapted from the Bourbeau et al. (2016) behaviour-change intervention study in patients with COPD. However, which questions they used were not precisely specified within the study manuscript nor within the supplementary material. Furthermore, in the Milner et al. (2019) study, a modified version of the Treatment Self-Regulation Questionnaire (TSRQ) for exercise was used to measure the participant's motivation to enrol in the PR programme (this questionnaire uses a scale from 1-7 (anchors spread as the following: not at all true, somewhat true to very true) The questionnaire is structured to ask a question, with the responses representing the individual external, introjected and identified regulations, and intrinsic motivation. The scale scores can be used individually, or can be used as a Relative Autonomy Index (RAI) which can identify if the motivation is self-determined (Levesque et al., 2007). Finally, in the Milner et al. (2019) study, patients were verbally asked whether they had the intention of accepting a referral to PR.

Lastly, in Revitt et al. (2018), despite their intervention aims to improve the uptake of PR, the study primarily focused on measures that assess patients' functional capacity as a primary outcome measure and data about PR uptake within both arms of the intervention were only extracted through the study flow diagram.

6.8.5 Conflicts of interest

In all studies, no potential conflicts of interest were reported with respect to the research, authorship, and/or publication of the journal articles included in this review.

6.8.6 Assessment of methodological quality of included studies

The included randomised control trials (Barker et al., 2020, Janaudis-Ferreira et al., 2018) had a low risk of bias. However, the Revitt et al. (2018) RCT had an overall high risk of bias (see figures 6.2 and 6.3) because randomisation was not equal due to problems with recruitment and a subsequent high withdrawal rate. The authors speculated this was potentially due to patients' unstable condition post suffering from acute exacerbation of COPD and patients' reluctance to partake in a structured programme after hospitalisation. Moreover, within the study report, there was no mention of whether the outcome assessors were blinded, as this could have introduced some conscious or unconscious bias in measuring the study outcomes. There was also a considerably high level of drop-out in both arms of the study, which could also have caused attrition bias. Finally, due to the nature of the intervention, participants in all trials were aware of their assignment to the intervention, which might have influenced the study outcomes, even though this is unavoidable for this type of study.

The risk of bias within the non-randomised studies of intervention (NRSI) was mainly serious (75%), due to both the confounding factors associated with the study designs (see figures 6.4 and 6.5) and the overall risk of bias being mostly serious.

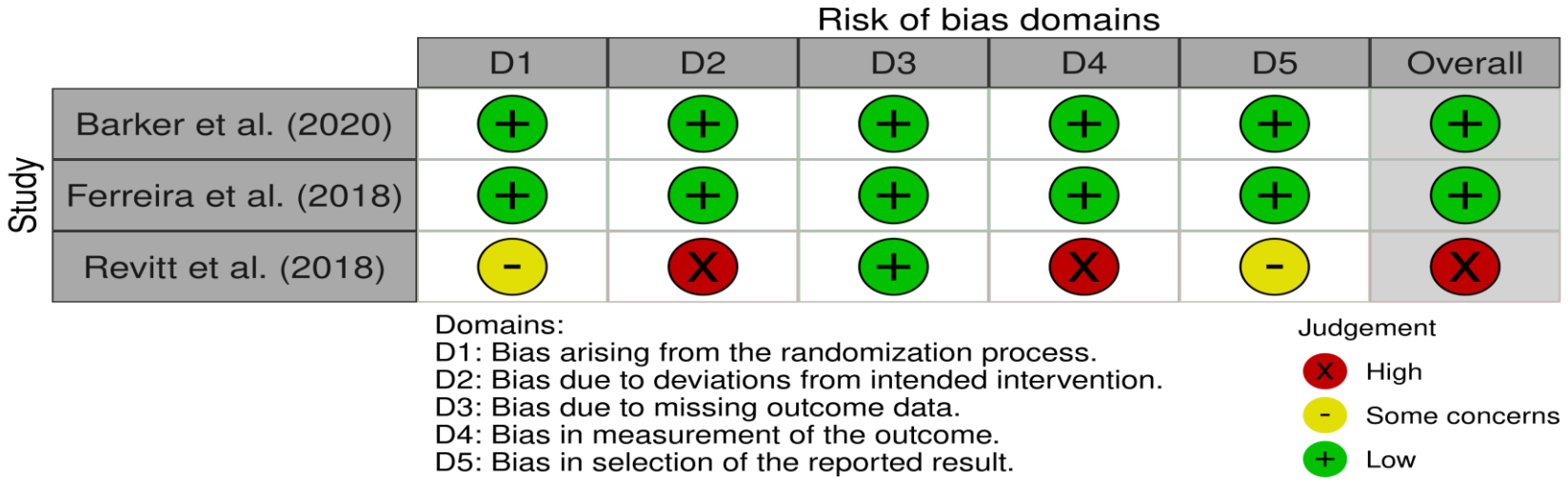


Figure 6.2 Risk of bias assessment for randomised control trials (traffic plot)

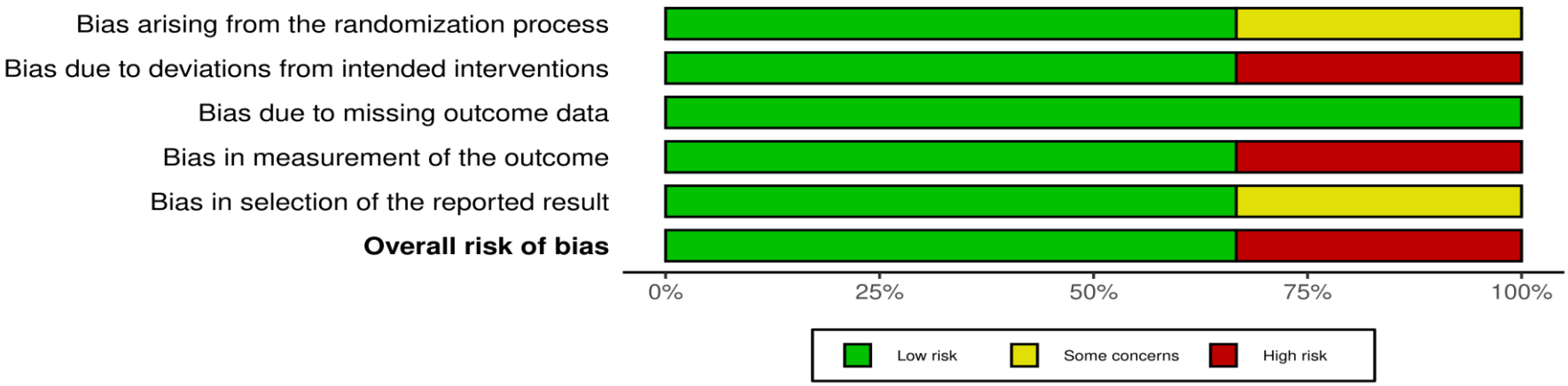


Figure 6.3 Summary plot for included randomised control trials (RCTs)

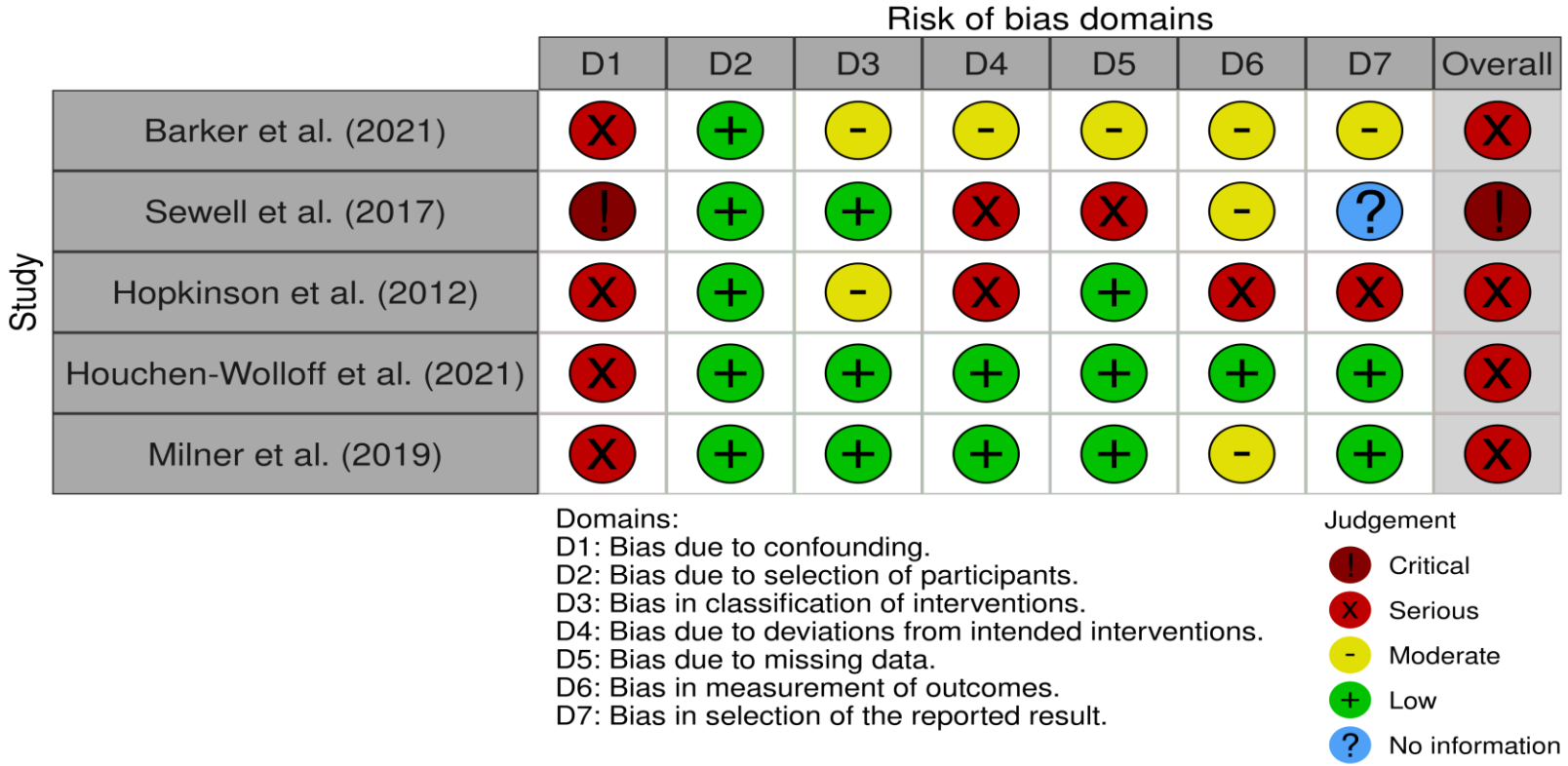


Figure 6.4 Risk of bias Assessment of non-randomised study of intervention (traffic plot)

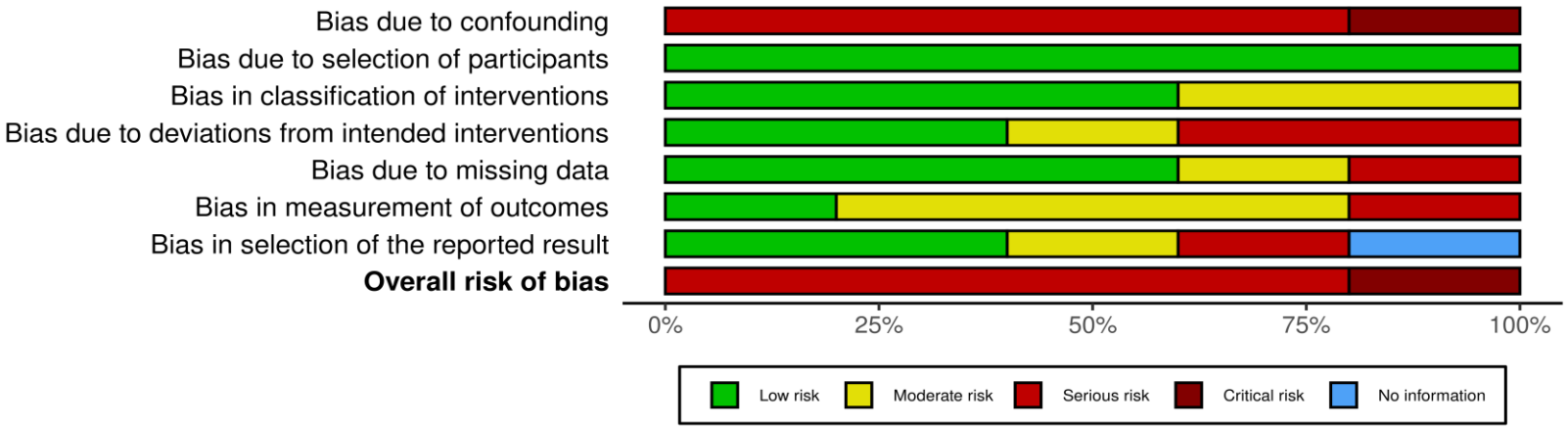


Figure 6.5 Summary plot for Non-randomised Study of intervention (NRSI)

6.8.7 Study Findings

We concluded that a meta-analysis was not possible due to several reasons: A) the studies that generated overlapping outcomes have heterogeneity in the studies (methodological and clinical variations) which can limit our ability to generate meaningful combined evidence of the intervention effectiveness, B) there were only two RCTs included in this review that measured similar outcomes (see table 6.2). Notwithstanding, one of the studies (Revitt et al., 2018) has high risk of bias and was prematurely terminated due to study failure. Such a study is usually excluded in systematic reviews. However, we chose to include this study in our review (due to limited available evidence) and only perform narrative synthesis to be able to show all the current available evidence pertaining to our review objectives. The reported outcomes in this review should only be understood in the context of each included study. Table 6.2 provides a summary of all the characteristics and effects of the interventions.

Table 6.2 Summary of intervention characteristics and effect

Review outcome/ PR Referral post-AECOPD					
Study ID*	***Intervention type***	***Study design***	***Sample size***	***Intervention Effect***	***Risk of bias***
Barker et al. (2020)	Discharge bundle+ patient co-designed video	RCT	Intervention n=98 Control n=98	*No significant effect (intervention n=70 (71%) versus n=68 (69%) p-value 0.754*	*Low*
Barker et al. (2021)	Discharge bundle	Prospective cohort study	n=291 episodes	*Positive significant effect (for those who received the bundle from current PR practitioners versus bundles from practitioners without involvement in PR (referral: 60% vs 12%, p<0.001)*	*Serious*
Hopkinson et al. (2012)	Discharge bundle	Before and after observational study	n=94 patients on the Respiratory ward	31 referrals to pulmonary rehabilitation with 81 in the year post initiation (an increase of 158%)	*Serious*
Houchen-Wolloff et al. (2021)	Space for COPD interactive web-based programme	Feasibility study	n=100 participants	57 (57%) accepted a referral	*Serious*
Sewell et al. (2017)	Discharge bundle	Before and after audit data for operational improvement activities	n= 1,170 participants	Referral to PR n= 627 (54%)	*Critical*
Review outcome/ PR Uptake post-AECOPD					
Barker et al. (2020)	Discharge bundle+ Video	RCT	Intervention n=98 Control n=98	*No significant effect on uptake (within 28 days of hospital discharge) intervention 33 (34%) versus 40 (41%) p=0.370 No significant effect on uptake (within 90 days of hospital discharge) intervention 52 (53%) versus 55 (56%) p-value= 0.911*	*Low*
Barker et al. (2021)	Discharge bundle	Prospective cohort study	n=291 episodes	*Positive Significant effect (on uptake within the group who received discharge bundle from current PR practitioner 40% (P<0.001))*	*Serious*
Houchen-Wolloff et al. (2021)	Space for COPD interactive web-based program	Feasibility study	n=100 participants	*35 (61.4%) started a PR programme out of those who accepted a referral*	*Serious*
Revitt et al. (2018)	Early PEPR versus D-PEPR	RCT	n=24 PEPR arm n=12 D-PEPR	*PEPR n= 22 (92%) versus D-PEPR n=6 (50%) Results favour the intervention group*	*High*
Review outocme/ PR completion post-AECOPD					

Barker et al. (2020)	Discharge bundle+ patient co-designed video	RCT	Intervention n=98 Control n=98	*No significant effect (intervention group 15 (46%) versus control group 23 (58%) p-value 0.305)*	*Low*
Barker et al. (2021)	Discharge bundle	Prospective cohort study	n=291 episodes	*Out of the 6 who commenced PR within 28 days of hospital discharge in the bundle group delivered from PR practitioner n=2 (33.3%) complected PR, out of the 8 who commenced PR from the bundle group delivered from practitioner with no involvement in PR n=3 (37.5%) complected PR programme.*	*Serious*
Houchen-Wolloff et al. (2021)	Space for COPD interactive web-based programme	Feasibility study	n=100 participants	*n=19 (54.2%) of the 35 who started the PR programme (completed either a hospital or community outpatient rehabilitation programme*	*Serious*
Revitt et al. (2018)	Early PEPR versus D-PEPR	RCT	Intervention n=98 Control n=98	*PEPR n=14 (63%) Completers versus D-PEPR n=3 (50%)*	*High*
Review outcome / PR sessions adherence post-AECOPD					
Barker et al. (2020)	Discharge bundle+ patient co-designed video	RCT	Intervention n=98 Control n=98	*No significant effect (intervention mean 8 SD (6) Control mean 10 SD (6) P-value 0.268)*	*Low*
Review outcome/ Disease Knowledge post-AECOPD					
Houchen-Wolloff et al. (2021)	Space for COPD interactive web-based programme	Non-randomised study of interventions (NRSI) (feasibility study)	n=100 participants	*The change in the BCKQ score was 7.8 (SD 10.2) points, an increase of 21% (pre-screening score: mean 37.1, SD 9.5; post-screening score: mean 44.9, SD 9.4).*	*Serious*
Janaudis-Ferreira et al. (2018)	One-to-one 30-min educational sessions via manual	Pilot RCT	Intervention n =15 Control (n =16) groups	*Positive significant effect with* BCKQ score (*the intervention group (mean change, 8 ± 5.14 versus control group 3.4 ±4.9); P = .018)*	*Low*
Review outcome/ readiness to commence PR post-AECOPD					
Janaudis-Ferreira et al. (2018)	One-on-one 30-min educational sessions via manual	Pilot RCT	Intervention n =15 Control n =16	***Reported willingness to attend PR** post intervention 13 of 15 patients in the intervention group reported it was too soon to consider*	*Low*

Milner et al. (2019)	PR "taster" session	Pre and post interventional study	n=6	***Reported willingness to attend PR** post intervention 5 out of the six (83%) participants reported intentions to participate in PR* **No change** *was reported within the* motivation to commence PR and confidence to commence PR in the pre and post scores median change 0 reported by a modified version of the readiness to change questionnaire. ***RAMI*: relative autonomous motivation index reported within TSRQ Questionnaire modified version to include items about PR showed** a slight median change +0.67	 *Sersious*
Footnote. Grey shading represents the studies that measured all PR programme-related outcomes (PR Referral, Up-take, and Completion). Studies are organised in alphabetical order					

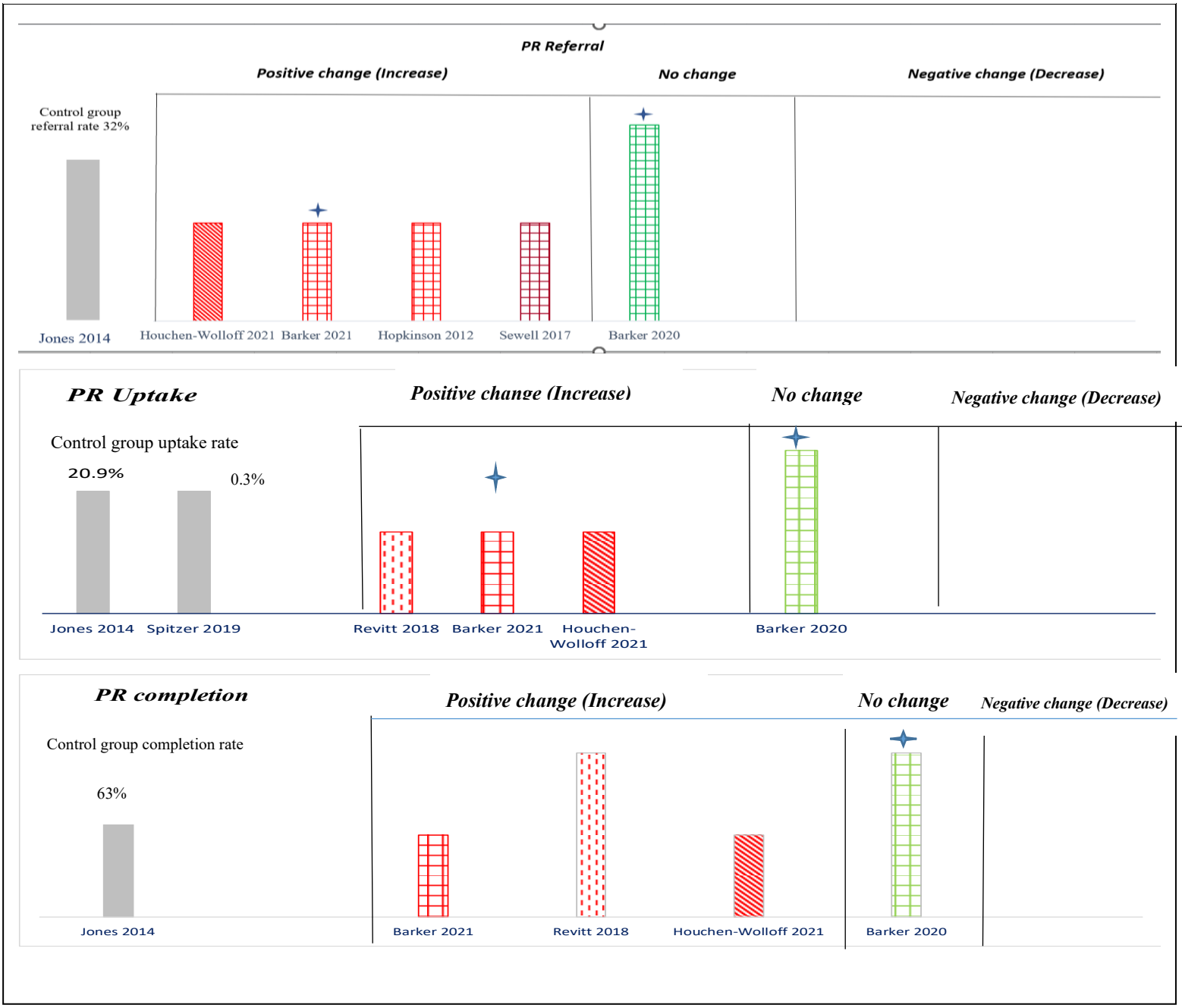
6.8.8 Referral to PR

Four studies reported a positive change (an increase) in referrals following the intervention (see harvest plot in figure 6.6). In the study by Barker et al. (2021), there was a substantial increase in referral rate in the group who received the COPD discharge bundle from a practitioner involved in the delivery of PR 60% versus 12% (p-value <0.001) compared to the group who received a referral from a practitioner with no involvement in PR delivery. Additionally, in the Barker et al. (2021) study, the multivariate logics regression analysis results showed an adjusted odds ratio (adjusted for possible confounders such as patient demographic and hospitalisation factors) of PR referral within 28 days post-hospital discharge was 14.46 times higher (95% CI (5.28 to 39.57); P-value <0.001) in the group who received the discharge bundle from practitioners involved in PR service delivery.

Following the introduction of the COPD discharge bundle on n=94 patients hospitalised with AECOPD in the Hopkinson et al. (2012) study, there was an increase in the number of referrals post initiation of the COPD bundle with 81 referrals compared to 31 win the previous year, representing a 158% increase in PR referral rate. Another introduction of the COPD discharge bundle in the Sewell et al. (2017) audit study, which has the highest population size (n=1170 AECOPD post-discharge individuals) of all the included studies in this review, showed an upward trend in referral rates from 39.7% in the first quarter of the study duration, to 55.9% in the fourth quarter of the study. However, the authors in this study did not report referral rates prior to the initiation of the COPD discharge bundle within their study report. Moreover, PR referral rates in the Barker et al. (2020) study, where authors used a COPD discharge bundle and verbal information about PR in both arms of the study and only supplemented the intervention group with a patient co-designed video (showcasing former patients sharing their experiences with PR services), showed a promising increase in referral rate within 28 days of hospital discharge across all study groups (n=138;70%), compared to the reported numbers from observational studies with no intervention (Jones et al. 2014 audit data reported referral rate of 32% of all eligible PR participants to post-AECOPD hospitalisation). However, the supplementation of this video did not provide a significant statistical change when compared with the control group (Intervention n=70 (71%) versus Control n=68 (69%); P =0.754).

Finally, PR referral rates reported in the Houchen-Wolloff et al. (2021) study, where patients received a novel intervention in the form of a web-based programme (SPACE for COPD) which includes a comprehensive package of exercise training and self-education material (containing educational elements that encouraged patients to participate in aerobic and strength training), resulted in more than half of the participants (57%) who took part in the online web-based programme accepting a subsequent PR referral. However, within the study report there was no clear indication of the specific timeline within which these individuals accepted the PR referral.

Figure 6.6 Harvest plot of interventions and their influence on PR referral, uptake, and completion



Footnote 2. Bar colour represent risk of bias (green= low risk, red= serious risk, dark red =critical risk), bar pattern represent intervention used intervention included web-based programme intervention included COPD discharge bundle intervention included PR delivered at two time points the level statistical change pertain to the intervention group who received intervention more than what is included in usual care, the star over barker 2021 and Barker 2020 bars represent the level of comparative significant between the two study groups (either intervention versus control in Barker 2020 or between two intervention groups with practitioners involved in PR delivery versus no involvement in PR delivery in Barker 2021), bars without star represents studies that only included descriptive statistics within its reported outcomes. Bar height represent the study design, high= RCT, medium= Audit data, Low=NRSI. Note the control studies found within the left side of the plot is to provide a reference number of outcome results reported within observational studies of no intervention (control studies). Additionally control study data can help with contextualize the descriptive statistical change reported in non-comparative studies. In the control groups all outcomes' data are reported within month of discharge. The sole purpose of this harvest plot is to provide a graphical representation of the available data.

6.8.9 Uptake of PR

Two studies that used COPD discharge bundles, Barker et al. (2020) and Barker et al. (2021), collected information about PR programme uptake post introduction of the bundles. In both studies, the intervention group received the COPD discharge bundle either supplemented with other intervention components such as patient co-designed video (Barker et al., 2020) or by involving a PR practitioner to deliver the bundles (Barker et al., 2021)). Results from the Barker et al. (2020) study showed low PR uptake rates within 28 days of hospital discharge (Intervention n=33 (34%) versus Control n=40 (41%)) with intervention resulting in an insignificant effect (no change) within the group comparison P=0.370. On the other hand, the PR program uptake within 90 days of hospital discharge in the Barker et al. (2020) study was comparatively higher across both groups (Intervention n=52 (53%) versus Control n=55 (56%)) if compared to the national and international observational studies of no intervention conducted previously (reported PR uptake rate of 20.9 % in the Jones et al. (2014) UK study and 0.3% in the Spitzer et al. (2019) USA study). However, the higher PR uptake rate across both study groups in Barker et al. (2020) was reported to be statistically insignificant in the comparison between study groups (P value =0.911). In Barker et al. (2021), PR programme uptake proportions within 28 days of hospital discharge were less than half of the participants in both study exposure groups (intervention group 40% versus 32% in the control group). However, group comparison showed a significant change (p-value <0.001), favouring the intervention group who received the COPD bundle from the current PR practitioner (Barker et al., 2021).

In the Houchen-Wolloff et al. (2021) study, the conventional PR programme uptake rates of those who initially accepted a PR referral following the introduction of the study intervention (a web-based interactive programme that offers a comprehensive package of exercise and self-management education) was around 47% (n=47) of the overall study participants (n=100) and, out of the ones who actually started the PR programme post the intervention the uptake rate was around 35% (n=35). The conventional PR uptake reported

in Houchen- Wolloff et al. (2021) following the intervention could be considered relatively higher compared to the reported international PR programme uptake rate post-AECOPD (Jones et al., 2014, Spitzer et al., 2019). However, the authors in Houchen-Wolloff et al. (2021) study did not specify within their study manuscript the timeline for which these study individuals commenced their conventional PR programme. Finally, PR uptake numbers extracted from the Revitt et al. (2018) study report showed that out of the total study participants (n=36) who consented and randomised (n=24 in the PEPR and n=12 in the D-PEPR), n=22 (91%) participants started early post exacerbation PR (PEPR) administered within four weeks of hospital discharge and only n=6 (50%) individuals out of the 12 who were randomised within the second study arm (delayed post exacerbation PR) commenced seven weeks after a control period of no intervention.

6.8.10 Adherence and completion of pulmonary rehabilitation

Only one study, Barker et al. (2020), reported data about PR adherence in their study report, adherence was defined by the mean number of PR sessions attended by patients starting the PR programme (Barker et al., 2020). The results showed that across the whole study group, the mean PR session adherences were nine sessions (SD 6) out of the studies' 16 total sessions. In addition, results from this study's comparative statistics (between the study groups) revealed a statistically insignificant change between the intervention and control groups with regard to PR adherence (Intervention mean 8 sessions SD (6) versus Control mean 10 sessions SD (6); P value =0.268) (Barker et al., 2020). These reported adherence numbers were lower than the reported median and IQR adherence numbers (median 14 IQR 10-16) of observational studies with no intervention in the post-exacerbation of COPD population (Jones et al., 2014).

PR completion, on the other hand, was reported in four studies (see table 6.2), and results showed the following: in the only included randomised control trial (Barker et al., 2020) the proportion of PR completion in the intervention group was 46% (n=15) PR compared to 58% (n=23) in the control group. Also in Barker et al. (2020), across both study arms, the proportions of PR completion were among the highest reported within the studies included in this review. However, the reported PR completion numbers did not reach

statistical significance (P-value =0.305) between the study's groups. In Barker et al. (2021), PR completion rates were almost similar and fairly low across both COPD bundle exposure groups (in the group who received the bundle from a current PR practitioner n=2 (33.3%) compared to the group who received the bundle from a practitioner with no involvement in PR n=3 (37.5%), and no statistical significances were reported within the study report.

In Houchen-Wolloff et al. (2021) study PR completion rate of those who started a PR programme was n=19 (54%), which constituted only 19% (n=100) of the whole study cohort. Finally, in the Revitt et al. (2018) study, where PR was administered within two different time points post COPD exacerbation (early at four weeks post-discharge and delayed at seven weeks of the control period with no intervention) PR completion rate was reported to be as follows: out of the n=22 who received intervention allocation n=8 participants dropped out and 64% (n=14) completed the early PR intervention post exacerbation (PEPR). In the second study arm, at the start of the study only 6 participants received the allocation for the delayed PR intervention and n=3 dropped out after the start of the intervention. Finally, only half of the participants in the group who started the delayed intervention (D-PEPR), 50% (n=3), completed the study (Revitt et al., 2018).

6.8.11 Change in knowledge

Change in COPD knowledge was reported in a pilot RCT study by Ferreira et al. (2018), in which a comprehensive 30-minute educational package was delivered, firstly within seven days of the AECOPD hospitalisation period or immediately following discharge (at home) and secondly within two weeks of admission (Janaudis-Ferreira et al., 2018). The educational sessions included elements of PR programme education, and resulted in a greater and statistically significant change in COPD knowledge observed in the intervention group measured by the BCKQ assessment questionnaire (Intervention mean change 8 ± SD 5.14 points; versus 3.4 ± SD 4.9 points in Control; P-value=0.018). Additionally, in the Houchen-Wolloff et al. (2021) study, following analysis of the returned

BCKQ questionnaires at six months, results showed that the online educational package delivered within the study intervention led to an increase in patients' COPD knowledge in around 21% of the pre-screening score (mean change 7.8; SD 10.2) points post-intervention (prescreening score mean 37.1, SD9.5; post-screening score mean 44.9, SD 9.4). This 21% of the BCKQ change is considered above the clinically meaningful change reported in the literature post outpatient PR, which is reported to be around18% (White et al., 2006).

6.8.12 Patient activation and readiness to commence PR

Outcomes related to readiness to commence PR were captured by patients verbally reporting their intentions to attend PR programme in a pilot RCT study by Janaudis-Ferreira et al. (2018). This study's results showed a greater proportion of the approached participants in the study were not intending to consider PR because they felt it was too soon for them (86%) (n=13 out of n=15 approached participants). In addition, outcomes related to readiness to commence PR were reported by a fesability study with a small sample size (Milner et al., 2019), using multiple measures to capture readiness. Results from this study (Milner et al., 2019) captured the participants' intentions about attending PR verbally, where 83% of the study participants (n=5 out of the total study cohort n=6) reported intentions to participate in PR programme post receiving the PR taster session and four out of the five participants (80%) reported that a home-based programme was the programme of choice for them. In the Milner et al. (2019) study, the modified readiness to change questionnaire (which places participants into four stages: pre-contemplation, contemplation, preparation or action phases (Bourbeau et al., 2016)), was also used, with results showing that half of the participants (3 out of 6) were already in the action phase before the intervention (PR taster session) started, and all but one (n=5, 83%) were in the action phase post the intervention. One questionnaire respondent was not categorised because they selected neither agree nor disagree category for all question items within both questionnaire administration times. The final two measures used in the Milner 2019 study were Likert-

type questions that investigated patient motivation and confidence to commence PR (pre- and post-intervention), which resulted in no observed median score change (median score change of 0 in the motivation and confidence domains). However, there was a slight change in the median score within the autonomous motivation index (RAMI) reported within the PR modifiable version of the TSRQ Questionnaire of +0.67.

6.9 Discussion

This review has shown that attempts to design AECOPD-dedicated interventions to help with improving PR programme referral and uptake as primary or secondary outcomes for this subset of the COPD population are limited and such research attempts only had started in 2012 with the introduction of the COPD discharge bundle in Hopkinsons et al. (2012). This review has also shown that this gap in the literature is currently widely acknowledged, and more exploratory and interventional studies had been introduced and tested during 2017-2021 (Sewell et al., 2017, Revitt et al. 2018, Janaudis-Ferreira et al., 2018, Milner et al., 2019, Barker et al., 2020, Barker et al., 2021, Houchen-Wolloff et al., 2021). Additionally, in this review, interventions to improve referral largely used COPD discharge bundles either as a standalone intervention or alongside other co-interventions (Barker et al., 2020, Barker et al., 2021, Hopkinson et al., 2012, Sewell et al., 2017). Such intervention (COPD discharge bundles) consistently yielded promising positive results, as reported within the reviewed studies on the referral outcome (in the studies included in this review who had used such interventions). For example, in the Barker et al. (2020) RCT study, where they used COPD discharge bundles in both arms of the study (control and intervention arm) supplemented with the addition of the patient co-designed video in the intervention arm, results showed a substantial rise in referral rate in both groups to around 71% in the intervention group and 69% in the control group compared to the reported audit data numbers of no intervention reported in Jones (2014) (31% referral rate). However, comparing the significance between the study arms resulted in a no significant change between both interventions p-value =0.754. This statistically non-significant finding

suggested the additional component of the patient-co-designed video added no superior value to the efficacy of the COPD discharge bundles. However, the authors of this study also highlighted that this finding could also signify that the delivery of the co-designed video about the PR benefits might not be suitable during the hospitalisation phase due to six out of the 15 patients included in the qualitative sub-study by Barker et al. (2020) reporting an inability to recall seeing the video at the hospital discharge. In the later NRSI study carried out by Barker et al. (2021), in which COPD discharge bundles were also used, results showed that within the study's three cohorts, the cohort who did not receive the bundle (n=63) had received no PR referrals whereas, for the second cohort, who received the discharge bundle from the practitioner involved in the delivery of PR services, the referral rate was found to be significantly higher (referral received from PR practitioner 60% versus 12% from a practitioner with no involvement in PR 12%; P-value 0.001). Moreover, following the introduction of the COPD discharge bundle, the referral rate increased in the Sewell et al. (2017) study, as more than half of the PR-eligible participants received a referral to PR. In Sewell et al. (2017), the study authors recommended the need to involve a designated team with sufficient knowledge about PR to ensure efficient and appropriate delivery of the bundles, a recommendation which then showed its effectiveness in the Barker et al. (2021) study results as this integration of PR dedicated healthcare professionals resulted in an increase of the adjusted OR to 14,46 times; a 95% CI 5.28 to 39.57 increase in referral within 28 days of hospital discharge compared to the referral numbers of the study's group who received the discharge bundle from healthcare professionals not involved in the PR delivery. Although the integration of COPD discharge bundles seemed to cause a positive impact by standardising the referral process, it is important to mention that such evidence is still far from being conclusive, and there remains a need to adapt and optimise these interventions within multiple high-quality RCTs in order to draw firm conclusions about their effectiveness.

In relation to the PR programme uptake outcome, two previous studies conducted in high-income countries, such as the United Kingdom (Jones et al., 2014) and the United States (Spitzer et al., 2019), reported the prevalence of PR uptake post-AECOPD hospitalisation. Results showed that the PR uptake rates of those eligible were around 20.9%

and 0.3%, respectively. Thus, we can say that PR Uptake rates reported within this review of interventional studies resulted in an acceptable and higher change (although in some instances not significant) to previous data of no intervention (Jones et al., 2014, Spitzer et al., 2019). This review also showed that interventions with an integrated educational element that is appropriately phased to allow individuals with AECOPD sufficient time to attain recovery and with PR delivery options readily available (hospital-based, community, remote or face-to-face options), the interventions seemed to produce promising results in relation to PR uptake post-acute exacerbation of COPD. For example, in Barker et al. (2020), PR uptake rate within 28 days of hospital discharge in the intervention groups was 34% compared to 53% within 90 days of hospital discharge which could signify a patient's preference to delay participation in PR until their exacerbated condition improved. Additionally, in the Houchen-Wolloff et al. (2021) study, 35% of those who accepted a referral started either a hospital or an outpatient PR programme. Although the availability of various modes of PR delivery could be a reason for this improved PR uptake (35%) (Houchen-Wolloff et al., 2021), compared to the previously reported numbers of PR uptake coming from observational studies conducted on this population (post-acute exacerbation of COPD) (Jones et al., 2014), it is important to mention that in the Houchen-Wolloff et al. (2021) study, there was no reported data in the study manuscript regarding the specific time frame in which these participants undertook their PR programme. In addition to this, a high proportion (n=1366, 68.98%) of possible eligible participants in the Houchen- Wolloff et al. (2021) study declined participation because they were not web literate, which could signfy that web-based intervetions could only work with a subset of the post-AECOPD population and should always be offered as an addtional PR option besides face-to-face PR strategy.

Moreover, the modest yet significant increase (40%) in PR uptake found in Barker et al. (2021) exposure group, where they received the COPD discharge bundle from practitioners with involvement in PR service delivery, might be attributed to various co-founding reasons such as the small number of the PR practitioners involved in the delivery of the bundle (six members), possibly as a result of lack of standardisation between the healthcare provider/patient exposure time, or as result of pre-existing patient knowledge,

attitudes and beliefs which had not been collected as part of the study outcome data. Thus, drawing a meaningful and firm conclusion about the effectiveness of such intervention cannot currently be established until such intervention is enhanced and such co-founders are better controlled within subsequent RCT studies. Within this narrative review, the only study that showed an excellent PR uptake results in contrast to the widely sub-optimal PR uptake rates reported in individuals post-AECOPD was found in Revitt et al. (2018), where early post-exacerbation rehabilitation resulted in a 91% uptake rate versus 50% within the delayed PR group who started the delayed PR seven weeks after an AECOPD event. However, due to the fact that the study was considered a failed study, it is important not to overinterpret these results.

Overall, the intervention strategies included in this review that addressed promoting conventional PR uptake post- AECOPD hospitalisation might only have targeted some of the commonly reported uptake barriers, such as lack of perceived benefits or knowledge of PR, accessibility and transport issues. However, this might not address the broader spectrum of all other possible PR uptake barriers, such as the existence of patients' co-morbidities, the patient's behavioural and psychological issues, pre-existing negative patients' experiences of physical exertion induced by exercise and its related dyspnoea (Cox et al., 2017, Harrison et al., 2015b, Jones et al., 2018). Therefore, it is recommended that future interventions abstain from stating a general aim within the PR uptake outcome and, instead, aim to provide focused intervention objectives that clearly state the exclusively targeted PR uptake barriers within their designed interventions. This would help future systematic reviews provide better and more focused guidance about the effectiveness of the interventions that are designed to improve PR uptake and effectively address the complexity of the PR barriers currently found in the literature.

In this review, there was only one study that reported data about PR adherence (Barker et al., 2020), and few of the other studies included data about PR programme completion (Barker et al., 2019, Houchen-Wolloff et al., 2021, Revitt et al., 2018). This highlights the importance for future studies to include such intervention outcome measures to facilitate in assessing intervention strategy efficacy and effectiveness throughout the

complete pulmonary rehabilitation process (from referral to graduation from the PR programme).

It was interesting to see that the intervention designed in the Millner et al. (2019) study, where a PR taster session was used with individuals with AECOPD before discharge, did not collect any data about the patients' actual PR attendance numbers and only opted to assess the patients' readiness to engage in the PR programme. Additionally, in the Millner et al. (2019) study, the authors used several modified assessment tools to evaluate the patient's readiness to participate in PR, whose validity is not yet established within the COPD population or within the PR research field. This could highlight the lack of readily available assessment tools that can measure such outcomes in the context of PR and also highlights the importance for researchers in the field to strive to establish the validity of such PR-related outcome measures. Due to the above limitations, we highly recommend future optimisation of the Millner et al. (2019) intervention within a rigorous study design, larger sample size and with an expanded selection of PR-programmed related and validated outcomes. This is because a similar intervention reported in Graves et al. (2010) study, where a group opt-in session was used in stable COPD individuals delivered by a physiotherapist and a clinical psychologist, yielded positive results with PR uptake and completion. In the Graves et al. (2010) intervention, the study's healthcare professionals (a physiotherapist and a clinical psychologist) presented a case study of a patient with COPD and asked patients to share and contextualise the feelings and symptoms that might have been experienced by the individual presented in the case study. This was done through collaborative work with the patients to enable the patients themselves to find ways to reverse the effect of the negative symptoms and feelings by introducing self-management strategies and PR. Following the application of this intervention, there were reported positive results in PR uptake and completion rate as 51.7% of their large sample size (400 individuals) entered a PR programme and, of those who entered, 87.9% completed their PR course. (Graves et al., 2010).

COPD knowledge outcomes reported in this review were statistically positive within the educational interventions used in the studies by Janaudis-Ferreira et al. (2018) and Houchen-Wolloff et al. (2021). These positive findings suggest that individuals who suffer

from COPD exacerbation could successfully assimilate knowledge about their disease. However, it was difficult to judge when the best time was to deliver such interventions to exhibit this positive change within both interventions. This was due to the fact that in Janaudis-Ferreira et al. (2018), the 30-minute education sessions were delivered at two different time points; the first on the seventh day of hospital admission and the second 14 days after, and yet COPD knowledge was only evaluated at a single time point, which happened at 28 days of discharge. Furthermore, in the Houchen-Wolloff et al. (2021) study, COPD knowledge measure was collected at six months post the exacerbation event, which suggests that such positive change may have happened due to the enhanced cognitive state of the individual during the natural course of recovery and might not reflect the actual COPD knowledge state during the immediate stage of AECOPD. This is an important aspect to consider as studies have shown individuals who suffer from AECOPD are more likely to suffer from cognitive impairment, specifically within their orientation, compared to stable COPD individuals (France et al., 2021, Crişan et al., 2014). Therefore, it is recommended that future studies further investigate the ideal time to deliver educational packages to individuals with COPD exacerbation to help ensure the appropriateness of the intervention delivery time and maximise the benefits of the delivered educational interventions.

6.9.1 Strengths and limitations

The strength of this review is attributed to the following reasons: I) the recognised strength of the systematic review methods, II) to date, this review is the first review that has evaluated interventions to promote PR programme specific outcomes in the AECOPD population, III) this review has contributed to providing an insight into all the available types of evidence that currently exist in the literature within the interventions designed to promote referral, engagement and completion of conventional PR post-AECOPD and IV) this review can help researchers in the field to identify research gaps that exist in the field and provide useful future research incentives. On the other hand, limitations of the review can be related to the heterogeneity of the intervention strategies, insufficient and poor

quality of the evidence found within the currently existing literature. Therefore, it is difficult to generalise the findings of this review or make firm conclusions to guide clinical practice.

6.9.2 Implications for practice and research

COPD discharge bundles to enhance PR referral are cost-effective and are considered as familiar interventions for clinical teams compared to other interventions (Dixon et al., 2020). However, having a dedicated trained staff was highlighted in the literature as an important aspect to ensure the proper delivery of the bundles (Barker et al., 2021, Sewell et al., 2017). No intervention used in the studies included in this review yielded a positive comprehensive impact on the whole PR programme outcomes (referral, uptake, adherence and completion), which might suggest a need to incorporate more complex interventions to target each individual point of the PR process. In this review, we found several studies that developed interventions to improve the AECOPD functional and quality of life outcome measures. However, no PR programme-related outcomes were collected within those studies (Greening et al., 2014, Jang et al., 2021, Ramon Maria, 2017, Sloots et al., 2021). This highlights the need for the researchers in the field to ensure including such outcomes in their future designed trials to enable cumulative review of the effectiveness of their designed interventions within those outcomes. Moreover, national clinical audit data provide information and set quality standards about PR programme referral, uptake, and completion are easily found and reported for the general COPD population (Singh S, 2020). However, there is a cuurent lack of national audit data that set the quality standards dedicated to this this subset of the COPD population (post-AECOPD) which imposes a current limitation on what data could be used to define successful PR uptake and completion.

Finally, most of the reported interventions found in this review were developed and evaluated in high-income countries, which might not be readily transferable for testing and use in other healthcare systems with differences in the referral pathways and levels of

service integration. Thus, this could highlight the greater burden on the interested researchers in the field who are based in middle and low-income countries where 90% of deaths happen from COPD globally, as they cannot easily build upon this existing knowledge (WHO, May, 2022).

6.10 Conclusion

The review was unable to provide conclusive cumulative evidence as regards the effectiveness of the interventions currently found in the field. Nor was it able to provide a clear clinical recommendation regarding the effectiveness of the interventions found within any of this review's evaluated outcomes. However, the adaptation of COPD discharge bundles, either as standalone or with supplementary interventions, might provide a promising positive result with the AECOPD population with regard to PR referral outcome, although this finding needs to be confirmed with high-quality RCTs in the future. Finally, the evidence found in relation to the remaining outcomes of this systematic review was found to be heterogeneous and insufficient to draw any meaningful conclusions about the effectiveness of the tested interventions within the current reviewed evidence. Therefore high-quality research is needed to help guide clinical practice.

Chapter 7 . Thesis results, data synthesis and complex intervention development

Four research steps were undertaken in this thesis to address the MRC framework steps presented in the methods section (section 1.4) of this thesis. These steps resulted in the following: 12 hospitalised individuals with AECOPD were recruited in the qualitative interview-based study, 50 hospitalised individuals with AECOPD were recruited in a patient cross-sectional survey study, 46 HCPs recruited in round one and 45 in round two of the Delphi international study and, finally, eight studies were included in the systemic review of the effectiveness of interventions designed to promote uptake of conventional PR post-AECOPD conducted within this thesis.

A detailed summary of the key findings generated from conducting this thesis' research steps which helped with guiding and informing the development phase of the complex intervention, is found in Appendix P. The findings from the qualitative and quantitative research conducted on the AECOPD population revealed a collection of disorienting dilemmas due to the experienced physical limitations, flare-ups of their symptoms and identification of barriers to personal change resulting from past experiential knowledge, negative illness perceptions, knowledge deficiency and psychological and behavioural issues (See Appendix P for a detailed description of the findings, resulted interpretation and recommendations for intervention components). Consequently, following the synthesis of the thesis's key findings, multiple theories were identified as the grounded theories of the complex intervention proposed components to help promote PR programme uptake post-AECOPD. The first identified theory was related to the field of adult education, known as Transformative Learning Theory (Mezirow, 1997). The principles of this theory guided the development process of the Meaning and Perspective Transformation (MPT) model cited in (Dubouloz-Wilner, 2020). The MPT model is

identified as an intervention needed to transfer the individual's meanings and perspectives to help promote transformative learning and change in the individual's behaviour to facilitate the initial elements of a successful rehabilitation process. In addition, the data synthesis process identified a need for a second intervention component guided by the grounded theory related to the field of psychology, which is known as the Relational Frame Theory (Hayes et al., 2001). The principles of this theory guide the Acceptance and Commitment Therapy (ACT) component of the complex intervention (Harris, 2019).

The stakeholders' input (patients) about the most bothersome impact of exacerbation resulted in identifying problems with breathing (breathlessness, chest tightness) as the most bothersome disease impact on the patient during hospitalisation and post-discharge. Fatigue was an added bothersome exacerbation burden highlighted by the patients' post-discharge from AECOPD (see Appendix P, patient survey section). This highlighted a need to have the patients' identified most bothersome impact of exacerbation as the focal point of any proposed intervention in order to enhance patient interest and engagement in the proposed therapies. Patient care priorities identified by the individuals with AECOPD at hospitalisation showed a patient desire for interventions that are mainly delivered by HCPs without the need for their active physical involvement. In addition, the thesis results showed that individuals with AECOPD were more prone to prioritise interventions that required active involvement only during the post-hospitalisation phase, which highlighted a need for delaying the introduction of exercise therapy until after the hospitalisation period. Furthermore, the participated HCPs prioritised patient care during both phases of AECOPD (at hospitalisation and post-discharge) revealed that the second stakeholder group (HCPs) prioritised interventions that tackled knowledge deficiency and prevented future exacerbation attacks at hospitalisation, and, during the post-discharge phase many of their prioritised patient care interventions looked very similar to the elements of the conventional PR programme. Therefore, the data synthesis of the input from these key stakeholders highlighted a need to modify the conventional PR programme to include a designated PR pathway for the post-AECOPD population that uses these identified needs as the focal points of the proposed pathway.

Results from this thesis' narrative synthesis of the systemic review revealed inconclusive findings due to the nature of the included evidence (see Chapter 6 for systematic review and Appendix P (Systematic review section) for the extracted evidence). However, the results highlighted the worthiness of adapting the Barker et al. (2021) intervention and the optimisation of the Barker et al. (2020) video intervention within a second evaluation attempt.

Finally, the generation of the above results helped with addressing the fifth step of the MRC framework, namely articulating the proposed Complex Intervention Programme Theory. Figure 7.1 includes the aspects of the programme theory in a logic model, where research input, activities, output, intervention core components, outcomes, assumptions, and external factors are all presented.

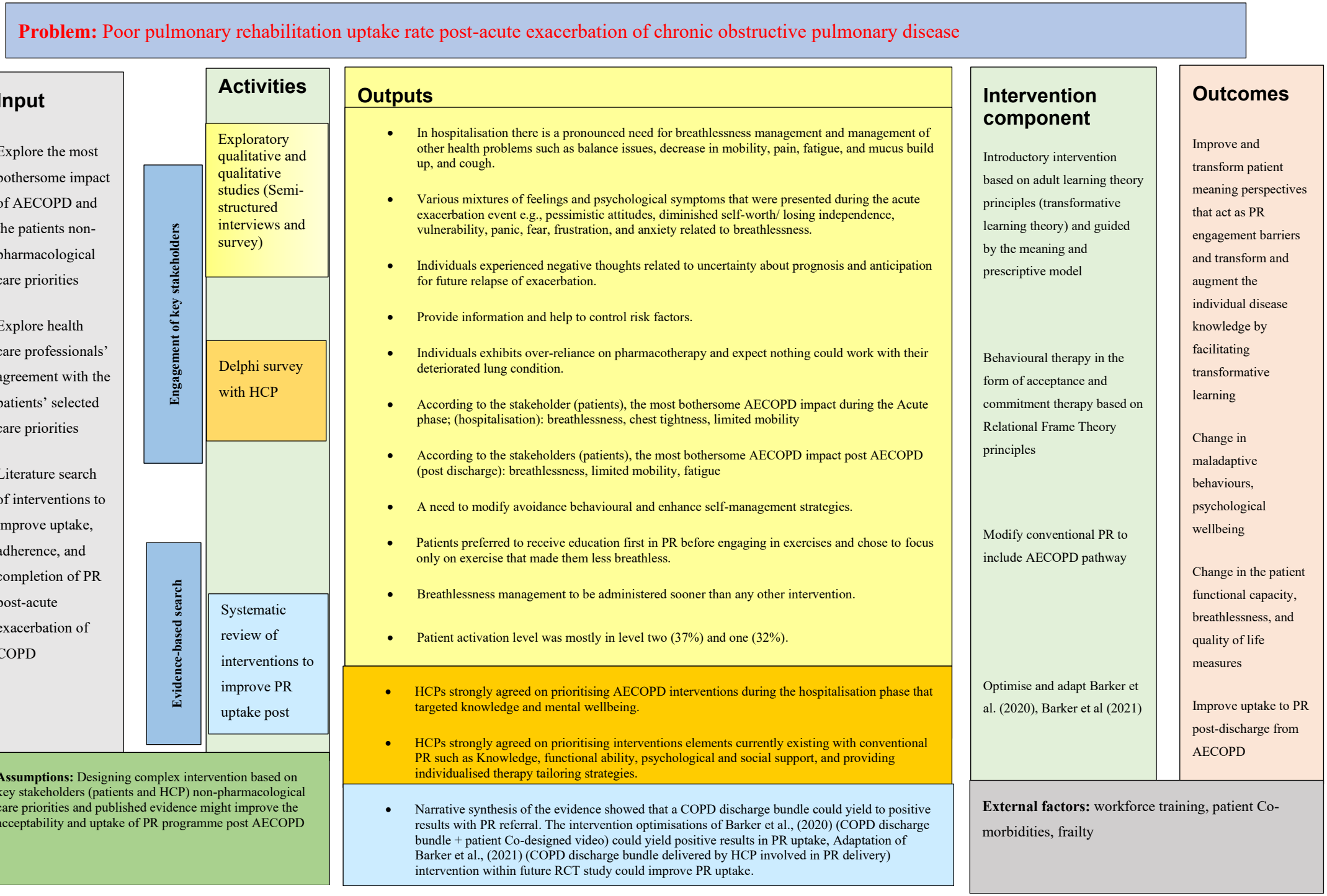


Figure 7.1 Programme theory logic model

7.1 Complex intervention development and its core components

This thesis chapter includes the final step incorporated from the MRC framework to develop the early design of this novel complex intervention (prototype) to promote PR uptake post-AECOPD. Figure 7.2 (the prototype design) shows the intervention to be delivered through a phased approach (three phases): level one (introduction phase) which includes the MPT component, level two (preparation phase) includes the ACT component, and level three (action phase) includes a post-AECOPD PR pathway. Each level or phase will appropriately target barriers that could hinder the post-AECOPD individuals' ability to engage in PR and take an active role in their health.

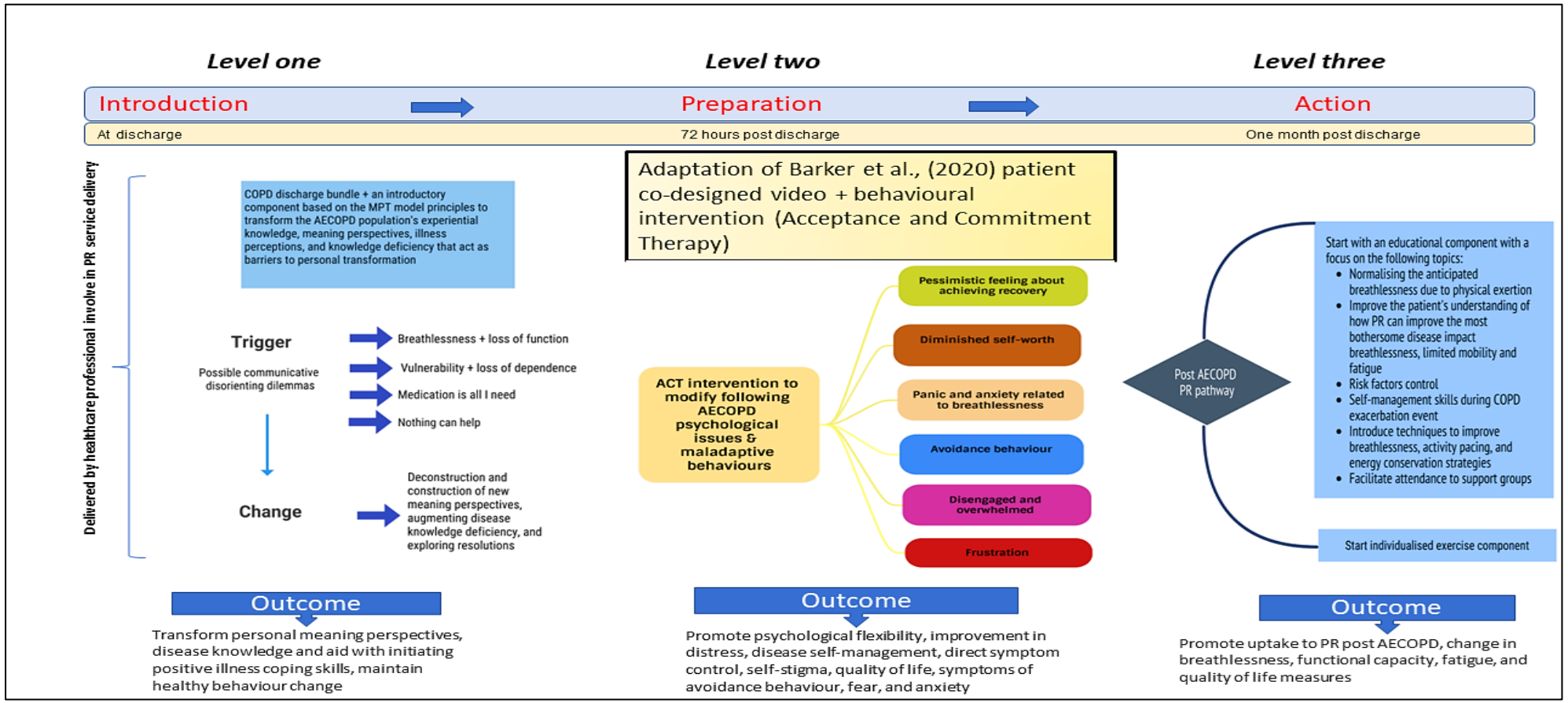


Figure 7.2 Complex intervention preliminary version (prototype)

7.1.1 Level one of the intervention (introduction phase)

Level one of the complex intervention (the introduction phase) will include two components. The first component is adaptation of certain elements of the Barker et al. (2021) intervention and the second is a novel Meaning Perspective Transformation (MPT) learning component. This level of the intervention (level one) will be set to be delivered as soon as the individual with AECOPD is ready for discharge. The adapted elements of the Barker et al. (2021) intervention include delivering a COPD discharge bundle via a health care professional involved in the PR service delivery (Barker et al., 2021).

In this level, the second component of the intervention will include a supplementation of the MPT model that aims to detect and modify the patient's knowledge deficiency and negative illness perceptions by identifying distortions and help with transforming the individual meaning perceptive to help eliminate barriers to behavioural change. Distortions, in this case are defined as habitual meanings of beliefs, values, feelings and knowledge that the individual holds and expresses (as words or phrases) that no longer fit the individual's new reality and can act as a strong barrier to change (Dubouloz-Wilner, 2020; Cranton, 1998). The supplemented learning intervention is built based on the meaning and perspective transformation (MPT) model cited in Dubouloz-Wilner's 2020 publication, which is generated from the outcome of three updated meta-analysis (meta-data analysis, meta-method analysis and meta-theory analysis) of 8 qualitative adult physical rehabilitation studies (which included a total of 150 interviews), conducted on the following chronic conditions: rheumatoid arthritis (Dubouloz et al., 2008, Dubouloz et al., 2004, Ashe et al., 2005), spinal cord injury (Carpenter, 1994, Dubouloz et al., 1999), myocardial infarction (Dubouloz et al., 2001), cerebral stroke (Kessler et al., 2009) and multiple sclerosis (Dubouloz et al., 2002). The Meaning Perspective Transformation model (MPT) that exists in adult rehabilitation science (Dubouloz-Wilner, 2020), is guided by the principles of the Transformative Learning Theory (TLT) found in adult education which was developed by Jack Mezirow in 1991(Mezirow, 1991). In Mezirow's definition of TLT,

he describes the theory as the “process of effecting change in a frame of reference” (cited in Mezirow, 1997, p.5). Mezirow gave a detailed description of the transformative learning process in his publication and explained that throughout the years adults will form a coherent body of experiences, associations, concepts, values, feelings and formulate frame of structured assumptions through which they understand their experiences and set their line of action (Mezirow, 1997).

In one of the studies conducted on spinal cord injury individuals that contributed to the formulation of the MPT model (Carpenter, 1994), the concept of change in the meaning perspectives showed itself in the rehabilitation process through three core elements: rediscovering self (establishing the connection between how the person knew themselves to be and external self-post suffering from thy physical limitation), redefining disability (redefine the concept of independence and challenging the individual’s stereotypes and attitudes towards their limited functional ability and helping them to rediscover their potential by exploring options and build their confidence), establishing a new identity (by understanding the reality of their new reality after suffering from their condition). In this study, the author suggested that in order for the individual to be successfully rehabilitated they needed to go through transforming (deconstruction and reconstruction) the meaning perspectives related to these identified core elements that might act as barriers to taking an action and achieving the long-term benefits of rehabilitation (Carpenter, 1994).

Another qualitative study by Dubouloz et al. (2008) conducted on ten rheumatoid arthritis individuals to identify and describe the process of meaning and perspective transformation while going through physical rehabilitation, showed that individuals who experienced an acute onset of their disease that progressed with intermittent remissions report more difficulties engaging in the modification of their occupational performance and undergo what they called a complex adaptation process for their illness. This complex adaptation happened due to the challenges of a personal change that originated from the nature of their illness (the fluctuating nature of the symptoms with occasional remission resulting in participants hoping for cure without requirement to change their ways). The addition of the pharmacological medicine which led in most cases to providing control of the flare up symptoms for a while also delayed the patient’s recognition of the need for a

change in their occupational performance (Dubouloz et al., 2008). Furthermore, receiving help from a care giver or a healthcare professional evoked feelings of being useless among the study participants. Losing independence and having to use assistive devices for mobilisation also resulted in many distortions that were regarded by the participants as giving in to the disease. In this study (Dubouloz et al. 2008), the change in meaning perspectives in eight out of the ten study participants resulted in resolving conflicts between participants meaning perspective and the recommended occupational intervention and induced change to adapt strategies to help with their functional ability which in turn helped the participants to effectively cope with their illness.

In a study conducted on stroke patients to investigate whether the change following stroke follows a process similar to the one found in the meaning perspective model. Results showed that within this population two triggers were identified that guided the process of meaning perspective change in those patients: 1) experiencing limitations in the individuals' physical ability and 2) the presence of feelings of vulnerability (Kessler et al., 2009). These triggers acted as disorienting dilemmas that can be transformed with the presence of three supporting factors to enable effective change in the meaning perspectives that could act as barriers to a successful rehabilitation process such as, factor 1) environment support (support from HCPs, family and friends), factor 2) knowledge (information to facilitate understanding of their condition, learn about possibilities of recovery, coping with their condition, explore resolutions) and factor 3) choice of action (making decisions to facilitate regaining more control of their condition) (Kessler et al., 2009).

The illness meaning perspective and the disorienting dilemmas found in the above population of chronic illnesses who underwent a rehabilitation process looked very similar to the data generated from the individuals with AECOPD in this thesis. For example, the disorienting dilemmas related to individuals' feelings of uselessness, vulnerability, physical limitations, fluctuation of the symptoms, over-reliance on medications and loss of independence were all very evident within this thesis population (AECOPD). Therefore, an attempt to apply the MPT model could help with achieving long term positive outcomes with regards to improving the individual's knowledge, understanding of themselves and their condition, prompting and maintaining a healthy behavioural change, and help with

inducing positive coping skills that can promote a successful rehabilitation process, which makes the MPT model a worthwhile intervention to be tested and evaluated with the AECOPD population.

The adaptation of the MPT model used in the introductory component of this thesis complex intervention is considered a novel attempt for it use in pulmonary rehabilitation. This MPT model will include three phases to allow transformative change in patient negative meanings and perspectives (distortions) and modify barriers to change: A) the trigger phase, B) the change phase and C) the outcome phase. This introductory component of the complex intervention is set to be delivered during the hospitalisation phase (specifically within the period closer to discharge as usually within this period patients perform decisions about up-taking discharge services).

In the MPT model the first phase, which is **A) the trigger phase**, the HCP will ask the individual to critically reflect on their chronic illness and how they experience their flare ups to gain insight about how the individuals define themselves, their beliefs and values (to understand their meaning perspectives) in order to aid the HCP to identify "disorienting dilemmas". These dilemmas occur when individuals become ill and are no longer able to function the way desired, or when they go through various experiences that fail to meet their expectations. In this phase the individuals might express having deteriorating symptoms. In AECOPD, for example, this refers to an increase in their level of breathlessness, loss of function, running out of treatment options, being vulnerable or dependent on others, dissociation between their old self and their new reality and exhibiting over-reliance on pharmacotherapy. Identifying the meanings perspectives and disorienting dilemmas will help with identifying barriers or in some instances enable facilitators to initiate a transformative change that can be carried out within the second phase of this model. In the second phase of the MPT model is **B) the change phase**. In this phase the identified meaning and perspectives and distorting dilemmas that appeared within the first phase of this model will go through deconstruction or reconstruction of new meaning perspectives, the individual disease knowledge deficiency will be augmented and exploring resolutions will be introduced (exploring the PR options in all forms such as centre, community-based and remote versions, and focusing the communicated health benefits on dealing with the

AECOPD most bothersome impacts such as breathing problems, mobility and fatigue). In this phase, the transformation in meaning perspective will happen and the individual's readiness to change will be initiated. The final phase of this intervention is **C) the outcome phase**, which is where the individuals will show readiness to change by making modifications to his or her lifestyle to accommodate the newly formulated new perspectives (in the case of our population, individuals will consider accepting referral and engagement in PR programme post hospitalisation). The resulting outcomes of this component of the complex interventions are to transform negative illness perceptions, initiate a proper connection between the individual old self and new reality, improve knowledge about the disease and treatment options, help with maintaining healthy behavioural change and help with inducing positive illness coping skills.

7.1.2 Level two of the intervention (preparation phase)

The second level (preparation) of this complex intervention will target psychological issues and maladaptive behaviours. The magnitude of the impact of these problems, as discussed in chapter 8 of this thesis, warranted including a behavioural therapy component to help positively modify the deeper psychological issues that potentially cannot be modified by the MPT model alone, for example avoidance behaviour (agoraphobia), pessimistic feelings about achieving recovery, panic, anxiety, being disengaged and overwhelmed, to help eliminate them from becoming another potential barrier to PR. Thus, in this component of the complex intervention, Acceptance and Commitment Therapy (ACT) intervention was selected to be delivered within the preparation component of the complex intervention. The definition of Acceptance and Commitment Therapy (ACT), as the acronym states is about acceptance of the new reality of individuals who live with chronic conditions and promote taking action about it (Hayes et al., 2006).

In a study undertaken by Fernandes-James et al (2019), the association between psychological flexibility (acceptance) and engagement in pulmonary rehabilitation within eight weeks post-hospitalisation has been investigated through quantitative means with the

delivery of acceptance and action questionnaire-II (AAQ-II), engaged living scale (ELS) and with the recorded engagement in post-AECOPD PR. The AAQ-II questionnaire consists of seven items to measure psychological inflexibility and experiential avoidance (items are anchored with the seven-point Likert scale ranging from score of 1= for never true to a score of 7= for always true). the scale is scored by totalising the seven items and higher scores indicate greater psychological inflexibility (Bond et al., 2011). The ELS scale, on the other hand, can be used to evaluate the individual's valued life activities. The scale includes 16 items that are rated on a 5-point Likert scale (1= completely disagree to 5= completely agree). The ELS scale includes two subscales (value living, which includes 10 items, and life fulfilment which has 6 items), with the higher the score indicating greater clarity and engagement with personal values and an increase in life fulfilment (Trompetter et al., 2013). The result of this study showed that among the n=41 individuals who undertook the AAQ-II questionnaire and the n=40 individuals who completed that ELS scale an AAQ-II total score of 11 indicated 60% probability of psychological flexibility, which was associated with a greater chance of accepting PR referral. The ELS total score of 73 was associated with 68% of probability of accepting PR referral. In this study (Fernandes- James et al, 2019), the authors suggested that ACT therapy might help AECOPD individuals to develop their psychological flexibility, which might then support engagement in PR post-AECOPD. The authors also stated that the suggested ACT therapy intervention appears to be sensitive to the main psychological and behavioural issues that individuals with AECOPD suffer from, such as limited physical ability and its related emotions, and adding ACT approach to any intervention targeted at this population might maximise the effectiveness of intervention.

To our knowledge, ACT has not been yet tested for its effectiveness with individuals experiencing AECOPD. However, in the past ACT has been used within many other chronic illnesses such as cardiac conditions, diabetes, brain injury, cancer and epilepsy (Graham et al., 2016). The systematic review of Graham et al (2016) revealed that the application of ACT intervention showed not only significant results in psychological flexibility but also resulted in significant improvement in distress reduction, disease self-management and lifestyle, direct symptom control, self-stigma and quality of life (Graham et al., 2016).

Additionally, another systemic review revealed the effectiveness of ACT intervention in managing symptoms of avoidance behaviour, fear and anxiety (Ruiz, 2010) .

Therefore, it is thought that the application of the introductory intervention guided by the MDT model together with ACT intervention that is specifically sensitive to the AECOPD population's arising problems (details about these issues and emotions are found in section 7 of this thesis) would provide a comprehensive attempt to combat many of the possible barriers to PR uptake.

ACT therapy is guided by the Relational Frame Theory (RFT), and has six core steps (Harris, 2019) which are applied within the preparation phase of this complex intervention during the follow-up period (usually 72-hour post-discharge). The six steps of the ACT intervention are: **1) Contacting the present moment**. In this step, the patient will consciously pay attention to their present moment in a physical and mental manner such as, for example, identifying struggles with worries, fears, frustration, avoidance behaviour and negative thoughts about disease progression and being overwhelmed by the physical limitations imposed by their condition. **2) Defusion,** whereby the patients will allow their emotions and thoughts to come to realisation and they will become aware of their thoughts instead of suppressing them. This allows them to focus on doing what is important to those individuals instead of struggling with the thoughts (allowing the thought to pass; for example, saying "thank you, mind"). **3) Acceptance**. This step allows the individual to open up and make room for the painful feelings, sensations and emotions and encourages the individuals to accept them instead of fighting them. **4) Self as context**. In this step the individual will get in touch with their deep sense of self (as an observant) as distinct from their thoughts, memories and feelings, which allows for adjustment to their long term conditions and the challenges that comes with it. **5) Values**. In this step individuals will recognise what matters to them the most and what the individuals truly want their life to be about. **6) Committed action**, which is taking an effective action towards their health guided by the individuals' values.

In this component of the complex intervention, there will be an adaption and optimisation of the Barker et al. (2020) patient co-designed education video. The Barker et

al. (2020) video intervention includes experiences of real PR graduates telling their experienced benefits of PR and act as role models (Barker et al., 2020). Although the change in PR uptake rate post the Barker et al. (2020) intervention between the control and intervention groups were insignificant within 28 days and 90 days of the discharge from the hospital, the results of the sub-qualitative study showed that out of the 15 participants who engaged in the interviews, 40% of the participants did not recall receiving the educational video, which suggested the inappropriateness of the timing of the video administration. However, others in the interviews who recalled seeing the video reported positive feedback about it. The authors suggested that the reason behind the insignificant results could have been not only due to inappropriate timing of the intervention delivery, but also the lack of additional counselling due to their efforts to avoid adding extra cost to the intervention. Therefore, optimisation of such an intervention within a different time frame. For example, in this thesis proposed intervention during the follow-up period, which usually happens within 72 hours of hospital discharge, together with the additional interventions presented in levels one (MPT model educational intervention) and two (ACT intervention) of this complex intervention, could yield significant results towards PR uptake which is a worthwhile research attempt.

7.1.3 Level three of the intervention (action phase)

The third level (action) of this complex intervention will include a modification of the conventional PR programme to incorporate the post-acute exacerbation of COPD pathway that encompasses additional topics and focus points which broadly resulted from this thesis's exploratory work (details are found in Appendix P, matrix synthesis of the key findings). This component of the complex intervention will be delivered at one-month post-AECOPD hospitalisation. The pathway will start by initiating the educational component first, before engaging in exercise. This educational component includes the following focal points: normalising the anticipated breathlessness due to physical exertion to allow the patient not to view the resulting breathlessness from engaging in exercise as a harmful body sensation, applying more emphasis by improving the patient's understanding of the benefits of PR towards the most bothersome exacerbation impact (breathlessness, limited mobility, and fatigue), introducing exacerbation risk factors control and self-management skills during COPD exacerbation, providing advice about the therapeutic techniques for breathlessness, activity pacing and energy conservation strategies, and facilitating attendance to patient support groups. The final step of this phase will allow individuals post-AECOPD to engage in an individualised exercise component.

Chapter 8 . Thesis Discussion

In this intervention development process, the key stakeholders (patients and healthcare professionals) and the non-pharmacological patient care priorities that target the most bothersome implications of exacerbation of COPD during two time frames (at hospitalisation and post-discharge) have been integrated within the formation of this proposed complex intervention model that primarily aims to improve PR programme uptake post-AECOPD. The integration of intervention stakeholders into the intervention development process has been recommended by the current literature as a possible way that can foster participation in non-pharmacological interventions and, most importantly, pulmonary rehabilitation (Rochester and Singh, 2020, Cheng et al., 2017). In this thesis, the updated version of the MRC framework has been used to build the intervention model, as this approach allows the involvement of the stakeholders, reviews published evidence, draws on existing theories and enables an iterative process of refining and redesigning the intervention, which can then produce interventions with a higher chance of being successful (Skivington et al., 2021). In addition, the MRC framework has been applied extensively in the past when designing health care complex interventions due to its fundamental strengths arising from the framework's ability to combine evidence and theory to produce rigorous complex intervention (O'Cathain et al., 2019, Heron, 2019, Lakshman et al., 2014).

The synthesis process of the key research findings produced from this thesis' research steps conducted in phases one and two (chapters 3 and 4) provided an in-depth insight into the patient COPD exacerbation experience within two important touchpoints of the patient exacerbation journey (the acute and post-acute phases). Such insight has shown breathlessness as an ongoing pronounced struggle that consequently produces various mental and physical implications for the individual with exacerbation such as feelings of frustration, panic, fear, diminished self-worth, pessimistic feelings towards recovery,

limited mobility, balance and fatigue issues. The complexity of breathlessness and its consequences has been explained through an evidence-based breathlessness model named as the Breathing, Thinking and Functioning Clinical Model of Breathlessness (Spathis et al., 2017). This model describes the complexity of the breathlessness symptom as a vicious cyclic relationship, where the dysfunctional breathing pattern manifested in acute exacerbations can evoke negative emotions, misconceptions, memories and past experiences, which then lead to a reduction in the functional ability of the individual and, in turn, cause worsening or maintaining the breathlessness symptom.

Similar findings to this thesis research output have been found in multiple publications that have explored the experiences of individuals with acute exacerbation, whereby the pronounced burden of breathlessness was found to be extremely dominating and resulted in intense emotions such as fear of death and anxiety related to dyspnoea, and individuals with AECOPD being labelled as consumed by the process of breathing (Harrison et al., 2014b). Additionally, the feelings of tiredness and diminished self-worth patients expressed within this thesis's qualitative interviews mirrored recent qualitative study findings where individuals with AECOPD experienced self-stigma due to the self-inflicted nature of the disease, which consequently led to a decrease in the individuals' self-esteem (Jørgensen et al., 2021). Participants in this qualitative study also articulated being tired due to the mental and physical burden that the acute exacerbation of a COPD attack imposes on them (Jørgensen et al., 2021).

Within this thesis's qualitative theme that captured the recovery journey of the participants post the acute exacerbation phase, many participants perceived breathlessness as part and parcel of COPD and assumed their breathing was always going to be poor. This finding poses more emphasis on the previous scholars' recommendation highlighting the importance of integrating other forms of non-pharmacological management strategies other than the pharmacological interventions universally given during hospitalisation to help better control and provide additional support with the breathlessness symptom (Hassali et al., 2020). Uncertainty about the future in terms of the disease prognosis and anticipation of future relapse was also among the captured experiences reported during the post-hospital discharge phase. These findings match similar results reported in a recent phenomenological

study conducted on elderly individuals recently recovering from AECOPD, in which uncertainty and fear about the future were also reported among the study's themes (Rosa et al., 2018). In health psychology, feelings of uncertainty can be the product of "individual inability to determine the meaning of illness-related situations", which can, as a result, contribute to the individual's negative mood and intensify their stress levels (Small and Graydon, 1993). This finding could signify a knowledge gap among exacerbated individuals that needs to be augmented to help improve individuals' understanding of their disease progression which could ultimately enhance the individuals with COPD exacerbation coping strategies.

An AECOPD is defined in the literature as an acute sustained worsening of the individual COPD symptom from beyond the day-to-day variations that require a change in the individual's medication (NICE, 2019, GOLD, 2019). The commonly reported symptoms that accompany this definition are primarily respiratory symptoms such as breathlessness, cough, increase in sputum production and change in its colour (NICE, 2019, GOLD, 2019). Thus, someone can assume that this could be the only or the most bothersome disease impact for the individual, whereby he or she might need a targeted therapy that can help treat these arising problems. However, in the quantitative survey study conducted in this thesis, when individuals with AECOPD were specifically asked to rate how bothersome the exacerbation symptoms were for them during the hospitalisation and post-discharge phases, the reported bothersome symptoms with the highest median bothersome scores during the hospitalisation phase included not only respiratory symptoms and the results were, breathlessness, chest tightness and limited mobility. On the other hand, the reported bothersome symptoms with the highest median score during the post discharge phase were reported to be breathlessness, limited mobility and exhaustion and tiredness. While it is ideal and essential for HCPs to provide holistic management plans that tackle all the individual's problems, having a management plan that target the most bothersome disease impact first might pave the way for the exacerbated individual to accept and engage with any other proposed heath care interventions that could improve their overall health and could help them to attain long term health benefits.

Interestingly participants in this thesis survey study rated breathlessness symptom with the highest median scores during not only the hospitalisation but also during the post-discharge phase, which shows the long-standing bothersome impact of this symptom even after receiving pharmacological therapy during the admission phase. In the literature, dealing with breathlessness in outpatient setting have been reported to be prevalent as a large population-based retrospective cross-sectional study conducted on 3642 individuals with severe COPD, showed that 72.5% of the study participants reported having breathlessness within seven days prior to their telephone interview. Moreover, among those who reported breathlessness, a large proportion of the participants (70%), reported experiencing other symptoms such as fatigue due to their breathlessness (Kessler et al., 2011).

Accordingly, these findings highlight the importance of ensuring that the communicated health language (either spoken, written or visual) of the interventions that target individuals with exacerbation of COPD to have a core focus on the most bothersome symptomatic impact, which has been identified in this thesis to be dominantly breathing problems (breathlessness and chest tightness), limited mobility and fatigue. The health focus language of the interventions should communicate clearly to the patient how any proposed health care interventions can improve the bothersome exacerbation implications, how they are supposed to work to produce their impact, and what are the expected obstacles of engaging with the intervention.

Recently, scholars in the field have started to acknowledge the complexity of breathlessness symptoms and how one single intervention might not be able to palliate the breathlessness effectively. Among their suggestions has been a need for a complex intervention delivered by a team with a diverse set of professional skills as this could be the ideal way to help with managing breathlessness effectively (Bausewein et al., 2018). As much as the complexity of the intervention and designing it to tackle the most bothersome disease impact to the intended population are important factors. In this thesis, we hypothesised that designing a complex intervention based on individuals with COPD exacerbation health care priorities might promote uptake of the non-pharmacological intervention (PR) post-AECOPD. Therefore, part of the exploratory research conducted in

this thesis allowed an investigation of this aspect. Exploring the exacerbated individual's health care priorities enabled us to identify whether what has been provided currently matches the therapy or care priorities of the exacerbated population, and also allowed us to capture any existing gaps in the currently provided health care services. The generated results of these research steps showed that within the qualitative part of this research step (semi-structured interviews, found in Chapter 3), the majority of the participants exhibited an over-reliance on medication and identified it as the only health care intervention needed. Others stated that nothing could help with their condition and only a small cohort identified a need for PR post-discharge. However, when participants were given a list of all the possible non-pharmacological health care interventions within the quantitative study (the survey study, chapter 4), they seemed to respond to it, and thus they were able to choose a mixture of various non-pharmacological interventions during hospitalisation and post-discharge phases.

Although exploring the patient-identified non-pharmacological care priorities during the hospitalisation and post-discharge phases showed varying selected patient care priorities, this might be due to the complexity of the condition's health implications, which then translated to various therapy needs. However, the highest resulting response trends from the patient survey study showed that participants were prioritising interventions that require a passive participation approach from the patient side in the hospitalisation phase that mostly targeted improving their knowledge, for example, prioritising a need to receive advice on breathing exercises, teaching them activity pacing techniques, and receiving help with exhaustion and tiredness. However, exploring the highest response trends related to the post-discharge phase, participants seemed to prioritise non-pharmacological health care interventions that support an active participation approach, such as training their breathing muscles, providing exercises to improve muscle strength and endurance all over their body and receiving help with exhaustion and tiredness. This finding could suggest that, in theory, exacerbated individuals might have intrinsic readiness to participate in physically active therapeutic approaches if they were appropriately phased within a suitable time frame and if the barriers related to the specific behavioural and psychological attributes found in individuals with AECOPD (discussed later) have been modified.

The discrepancies between the participants' lack of ability to identify non-pharmacological care/therapy options post discharge from the hospital exhibited in the qualitative part of the research steps in this thesis and their exhibited adjusted ability when presented with the comprehensive therapy list in the survey research step could signify a knowledge gap where individuals with exacerbation might not be fully aware of the existence of their disease-related non-pharmacological health care interventions. A support needs approach for patients (SNAP) tool, which was developed to help identify needs for the patient with advanced COPD, can help tackle this problem by initiating a dialogue between the HCP and patient to identify non-pharmacological needs that the exacerbated individual might require more support with and match them with existing therapeutic interventions currently used within the clinical practice (M Farquhar, 2018). In this thesis, the application of the SNAP tool within the survey study revealed, the majority of the AECOPD participants indicated a need for a little more support with; understating their illness (55%), managing symptoms (47%), dealing with feelings and worries (50%), and the area with the highest proportion of participants indicated a need for quite a bit support with was getting out and about (29%).

Opinions of HCPs regarding the patients' identified non-pharmacological health care priorities were explored in this thesis using the international Delphi study. In this Delphi study, many of the participating HCPs were considered experts in the field of caring for individuals with acute and post-acute COPD exacerbation, as about 44% of the participating HCPs held more than 20 years of professional experience. In this study, the HCPs' highest level of consensus (strongly agree) were drawn towards prioritising improving the patients' knowledge by introducing breathing control topics and proactive measures that prevent future exacerbation events, as well as promoting mental wellbeing by providing anxiety management during the hospitalisation phase. However, during the post-discharge phase, HCPs' highest level of consensus (strongly agree) about the non-pharmacological health care priorities seemed more expanded and included various elements that currently manifested in the conventional PR model (see Figure 5.4 in Chapter 5). The HCPs' prioritisation of non-pharmacological health care interventions that target anxiety in the acute stage could be attributed to their awareness of the multi-dimensional aspect of

dyspnoea and how the heightened level of patient anxiety triggered by the feeling of suffocation, panic about breathing and approaching a near-death situation might cause the debilitating consequences of such symptoms on the exacerbated individual, which might affect patients health-related outcomes (Hayen et al., 2013, Sigurgeirsdottir et al., 2019, Janssens et al., 2011).

HCPs' non-pharmacological patient care priorities in hospitalisation were considerably consistent with COPD discharge bundle elements with regards to introducing information and arranging referrals to PR and smoking cessation programmes, and providing self-management plans that include flare-up action plans and mood and symptoms diaries (Hopkinson et al., 2012). However, other important patient care elements specifically related to providing fatigue management was not found among the HCPs' highest prioritisation (strongly agreed) patient care list.

Although a high number of individuals with AECOPD in our survey identified receiving help with fatigue symptom and activity pacing intervention as a prioritised non-pharmacological intervention to be received during the hospitalisation phase. In clinical practice, pharmacological therapy to treat cardinal AECOPD symptoms such as breathlessness, cough and increase sputum production often receive the most attention during hospitalisation. Whereas symptoms that require the delivery of non-pharmacological interventions, such as fatigue, are often neglected, despite being highly prevalent in the COPD population (Spruit et al., 2017). Suffering from fatigue has been associated with worsened health status, dysfunctional illness beliefs, low mood and reduced exercise tolerance (Spruit et al., 2017), and it could prevent individuals with COPD from performing important daily life activities (Kapella et al., 2006, Spruit et al., 2017). Therefore, neglecting to offer help with this symptom early on in the management process can likely provoke the individual's feelings of being limited regarding what he or she can achieve and, therefore, refuse engagement in post-discharge therapies that require active engagement, such as PR. Additionally, providing information about energy conservation and activity pacing technique discussions about the benefits of PR, in particular with the fatigue symptom, could match the individuals with AECOPD to their care priorities and, therefore might yield attaining positive overall treatment outcomes post-AECOPD exacerbation.

The insights arising from the generated sub-themes of the qualitative research step conducted in the thesis, in which individuals showed over-reliance on medication or believed that nothing could help with their exacerbated condition, as well as the uncertainty about prognosis, could not only highlight a knowledge gap but also could be due to accumulated past experiential knowledge and illness perceptions that the individual has formed throughout the years due to the chronic nature of the disease (Kaptein et al., 2008).

Examination of illness perceptions has been investigated in a number of publications within the general COPD population. In these publications, the meaning and perspectives formulated by individuals about their illness experience in terms of how accepting they were of the new reality of their health and its associated disability, their negative expectations about the future, and the individual functional status were found to dictate a direct relationship whereby an associated emotional burden and negative thoughts followed (Pozzar et al., 2020). This negative impact could cause a series of health implications related to behavioural, mental, and physical health outcomes (Sawyer et al., 2019), and could eventually lead the individuals to acquire maladaptive coping strategies (Vaske et al., 2017).

In studies conducted exclusively on the AECOPD population to examine their illness perceptions and psychological attitudes, it was revealed that individuals with AECOPD were likely to be grouped within three distinct clusters: in control, disengaged and distressed. The latter two clusters showed lower illness coherence, more associated symptoms and weaker emotional response (disengaged group). In the distressed group, individuals had higher illness coherence, perceived their symptoms to be a result of their disease and had greater consequences such as statistically significant more severe anxiety and depression, lower self-efficacy and health status in all four domains of the chronic respiratory questionnaire-self reported (CRQ-SR) than the ones in the control group (Harrison et al., 2014d). Moreover, in a recent study that aimed to investigate the type of attitudes in response to chronic diseases among hospitalised patients via using the Type of Attitude Towards Disease Questionnaire, the results revealed that patients with COPD appeared to be associated with the intrapsychically and interpsychically maladaptive type of attitudes, whereby individuals with these types of attitudes can display obsessive fears, irritable weakness, pessimistic assessment of their condition and their prognosis and, finally,

show paranoid and dysphoric characteristics which can impose a heightened burden on the affected individual (Zarishnyak et al., 2020). The presence of these maladaptive attitudes among individuals with AECOPD could work as barriers that might prevent engagement in post-discharge therapies that require active participation from the patient's side.

In addition to the maladaptive attitudes or behaviours mentioned above, in the research results generated from the quantitative research step (chapter 4) in this thesis, the participants showed poor self-management skills, as 50% of the participants tried to avoid activities, and 28% tried to ignore the symptoms. Previously, the avoidance behaviour that individuals with COPD in general display has been explained as being a result of dyspnoea-related fear. To explain this relationship effectively, scholars in the field have used both the cognitive model of panic and the anxiety sensitivity construct in order to explain how the mechanism of avoidance behaviour is formed. In such a mechanism, COPD individuals catastrophically misinterpret their bodily sensations, for example, the dyspnoea resulting from engaging in physical activity or being in an unpleasant social environment as harmful consequences to their health, which then leads them to avoid arousing this harmful bodily sensation which, in turn, causes them to experience physical deconditioning and social isolation (Clark, 1986). The anxiety sensitivity aspect of this model can be due to the individual's expectation of being anxious or stressed due to being in an uncomfortable situation (Reiss, 1991). In COPD, individuals who present with panic symptoms could also exhibit higher anxiety sensitivity, with both observations being found to predict a panic spectrum in the COPD population (Livermore et al., 2012; Holas et al., 2017). In the literature, it has been reported that individuals with a panic spectrum could suffer from a common complication of panic called "agoraphobic avoidance", which is the refusal to encounter phobic situations. Individuals can experience this agoraphobic avoidance while, for example, driving, or in the circumstance of COPD individuals, while avoiding engaging in physical exercise to prevent the bodily consequences of such an encounter or as a result of fearing the outcome. In a study that used multiple regression analysis to assess if anxiety and depression are predictors for the severity of the agoraphobic avoidance behaviours (measured by the Mobility Inventory (MI) scale) in hospitalised COPD individuals, the results revealed that the Hospital Anxiety and Depression Scale (HADS) (anxiety scores)

significantly predicted avoidance behaviour for both MI alone and MI accompanied. Additionally, the Anxiety Sensitivity Index-3 (ASI) physical concerns scores, the ASI total and HADS depression scores for both independent variables were at a near significant level (Holas et al., 2017). Therefore, any proposed intervention to promote PR or any exercise therapy uptake targeted at post-AECOPD should include elements that can modify this barrier (agoraphobic avoidance) to facilitate engagement in the intervention.

Moreover, patient activation levels measured by the PAM-13 questionnaire revealed that the majority of the participants in this thesis survey were categorised within lower levels of activation (levels one and two). In such levels, individuals can display disease knowledge deficiency, low goal orientation and low self-management skills (Insignia®, 2017). This finding could highlight a need to evaluate such parameters in the future within the clinical practice to enable the identification of those individuals and help them to improve their activation levels by providing interventions that target improving their disease-related knowledge and enhance their self-management behaviours, which would then allow these individuals to take an active role towards their health, adapt and maintain healthy behaviours. In the literature, a change in patient activation levels showed to induce a positive change in illness self-management behaviours of individuals who suffer from chronic diseases (Hibbard et al., 2007). However, the exact effect of patient activation levels on the AECOPD population's self-management behaviours is an area that still needs to be investigated.

All of the above findings generated from this thesis research output or in conjunction with the evidence currently found in the literature revealed a prominent burden of breathlessness on the exacerbated individuals that is ongoing, complex and requires additional support beyond what is provided during the hospitalisation phase. The non-pharmacological health care interventions prioritised by patients supported a less active participation approach during the hospitalisation phase and more active participation from the patient side post-discharge phase. This shows an intrinsic readiness that the exacerbated individuals have towards improving their body strength and breathing that requires additional support to help a patient develop this readiness towards taking a more active role in their health. Conversely, in the HCP's strongly agreed consensus list of the non-

pharmacological health care priorities were shown to be drawn towards targeting and improving the knowledge of individuals with AECOPD by introducing proactive measures to prevent future repetition of an exacerbation event and improve the anxiety levels of the individuals with AECOPD.

Towards the post-discharge phase, the HCPs' highest level of prioritisation (strongly agreed) of non-pharmacological patient care interventions were expanded, which mirrors what is currently included in the conventional PR programmes. The research steps of this thesis showed the barriers to change that those exacerbated individuals hold require targeted interventions to aid positive modification of those barriers. The identified barriers include complex issues related to knowledge deficiency and illness perceptions (meanings and perspectives), which scholars in the field suggest augmenting by introducing education components developed based on adult learning theories that match the recipients' learning needs and can help with guiding the behavioural transformation process (Blackstock and Evans, 2019, Pozzar et al., 2020). This thesis research output also identified additional priorities for non-pharmacological health care interventions to modify the barriers to change that these exacerbated individuals hold, for example, barriers related to the disease-associated illness meaning perspectives and psychological conditions, avoidance and maladaptive behaviours, and low patient activation levels, which could hinder the patients' abilities to engage and maintain healthy behaviours (a description of the suggested intervention can be found in chapter 7, section 7.1.1 to 7.1.3).

Moreover, this thesis research output highlighted a need for modification of current PR services to include a designated pathway for individuals with an exacerbation that uses a health-focused language based on the stakeholder (patient) identified therapy priorities and most bothersome impact as an opportunity to promote engagement in a PR post-acute exacerbation event (a detailed description of the suggested pathway can be found in section 7.1.3). The in-depth exploration conducted in this thesis (chapters 3, 4, and 5) and its linkage to the existing literature allowed further incorporation of interested scholars' therapeutic approach recommendations. For example, using a phased care approach that can appropriately stage the various component of complex interventions used with individuals with COPD exacerbation to facilitate continuum of the patient treatment plans, which could

then allow attaining long-term treatment outcomes (Evans and Steiner, 2017, Harrison et al., 2014c). Lastly, a narrative synthesis of the systematic review of the limited literature conducted in this thesis (chapter 6), showed a promising opportunity for intervention adaption and optimisation of the patient PR experience video found in Barker et al. (2020) and for the application of the COPD discharge bundle delivered by HCP involved in the PR service delivery found in Barker et al. (2021) (a detailed description of the adaption and optimisation of the interventions can be found in section 7.1.3).

8.1 Thesis strengths and limitations

The strengths of this thesis lie in the mixed methods utilised to collect this thesis's desired data, the novelty of some areas of exploration and the chosen framework to guide the development process of the complex intervention. For example, the application of the well-cited Medical Research Council (MRC) framework, which was used to develop this thesis's complex intervention as it allows developers to systematically incorporate published evidence, stakeholders' perspectives and theories to produce complex intervention models that have a good chance of being effective, adding strength to the development process of this complex intervention (O'Cathain et al., 2019). Additionally, the patient and HCP surveys conducted in this thesis were the first to explore the patient's non-pharmacological health care priorities during hospitalisation and post-discharge following AECOPD. The data generated from the qualitative part of the research steps provided a holistic insight into the COPD exacerbation experience within three distinct phases before, during and post the AECOPD event. The systematic review conducted in this thesis was the first to review the effectiveness of interventions aimed at improving PR uptake within this dedicated population (post-AECOPD) and therefore provides a much-needed synthesis of the available evidence.

In the thesis, patient and public involvement were integrated in the interview guide and survey development and piloting process, which allowed for further refinement of the

survey and interview guide. Additionally, the qualitative interviews were initially used to provide face validity to the patient survey, which added extra strength to the survey construction process. In the international Delphi survey, the majority of the participating HCPs have substantial years of experience (41% of participating HCPs in round one of the surveys have more than 20 years of experience engaged, with 44% in round two). The perspectives of HCP across different healthcare systems (United Kingdom, United States, Australia and Canada) were also captured, adding strength to the findings of this research step output.

Notwithstanding, the research conducted in this thesis has several limitations. One of the main limitations occurred as a consequence of the Coronavirus disease (COVID-19) pandemic, which resulted in stopping the recruitment process prematurely before reaching data saturation within the qualitative study (in the care received part of the exploration) and prevented reaching the desired sample size of the survey study. In addition, the purposive sampling technique used in the qualitative and quantitative part of the research steps and the fact that patient interviews and survey were conducted in a single centre hindered our ability to generalise the findings of the research output generated from these research steps. Furthermore, in the process of providing face validity to the survey content, a survey amendment request was submitted to ethics to enable the inclusion of additional bothersome symptom captured within the qualitative interviews (dizziness) and that its related non-pharmacological therapy (balance therapy) be added to the bothersome symptom and therapy lists used within the patient survey. This was subsequently approved by the ethics research committee. However, due to a limited number of participants who undertook this version of the survey (because of the impact of the COVID-19 pandemic on the recruitment process of the patient survey), the decision was made to exclude this symptom from the analysis and list it as a limitation to the inclusivity of bothersome symptom and therapy lists used in this thesis' patient survey.

In an effort to lessen the survey burden on the participants by reducing the survey study administration time and its related health outcome assessments, it was decided that two questions pertaining to the fatigue subscale from the Centre of Epidemiological Studies Depression Scale revised version (CESD-R) be extracted to enable quantifying the fatigue

events. This attempt might not be the best option to assess the impact of fatigue symptoms, and other validated instruments, such as the Brief Fatigue Inventory (BFI), might provide an enhanced, valid and rapid way of assessing fatigue in the COPD population (Chen et al., 2016). The inability to assess the clinical impact of anxiety, depression and frailty via dedicated validated measures might be also considered an added limitation to the patient survey study conducted within this thesis. Finally, the limited number of interventional studies included in this thesis systematic review and the heterogeneity in its methods and study designs yielded only narrative synthesis of the literature, which prevented performing meta-analysis to evaluate the effectiveness of the modelled interventions and thus hindered the ability to evaluate the cumulative evidence and provide clear guidance to current clinical practice.

8.2 Contributions to literature

The exploratory research conducted within this thesis offers a broader insight into the patient's COPD exacerbation experience, its impact and the key stakeholders' care priorities. Such exploration and its generated information can help in the development process of future interventions designed to tackle issues found in this population, for example, interventions aimed at improving knowledge and dealing with psychological, functional, or symptomatic problems. Moreover, the results of the systematic review conducted in this thesis have shown that attempts to create interventions to improve PR uptake only started in 2018, despite earlier published data about the poor uptake of PR post-AECOPD (Jones et al., 2014) and only three studies included PR programme outcome measures that captured the whole pulmonary rehabilitation process, namely referral, uptake, and completion (Barker et al., 2020, Barker et al., 2021, Houchen-Wolloff et al., 2021), and of those studies that reported data about PR uptake, only a single study was a randomised control trial (Barker 2020). Additionally, information about how limited these attempts were was also reported in a systematic review published in 2017 that reviewed the effectiveness of an intervention to promote PR uptake and completion in the general COPD population only included one randomised control trial (Jones et al., 2017). Therefore, it is important for

interested researchers in the field to develop and evaluate high-quality randomised control trials of interventions to help promote the uptake of PR post-AECOPD that ensures including PR programme outcomes across the whole rehabilitation process to enable future meta-analyses of the evidence that can provide clear guidance to policymakers and clinical practice.

8.3 Future research

The conducted research steps in this thesis specifically addressed the development phase of the updated MRC framework (Skivington et al., 2021). Therefore, the produced preliminary version of the complex intervention (prototype of the intervention) presented in this thesis should continue to undergo further future research steps presented in the updated MRC framework to ensure the completeness of the process before implementing this complex intervention in the real world. The remaining steps of the MRC framework process for developing complex interventions include identifying uncertainties in terms of identifying problems, limitations or the need for additional exploratory research and economic considerations and workforce training via consultation with the stakeholders involved in the funding and service delivery to refine the deigned intervention. A proposed research method that can easily address the later aims within a structured and clearly detailed process is found in the multi-method approach by Hawkins et al. (2017). As incorporating different approaches is considered acceptable within the complex intervention development process of the updated MRC framework (O'Cathain et al., 2019, Skivington et al., 2021). Hawkins et al. (2017) multi-method approach can be considered a useful additional approach as it effectively allows the engagement of service stakeholders and policymakers to co-produce the final version of the intervention through three structured steps that include a) evidence review and stakeholder consultation, b) co-production and c) prototyping of the final intervention (Hawkins et al., 2017). In such multi-method approach, the evidence generated from this thesis can be easily incorporated within the initial step of this approach to seek feedback from the service users and policy makers about the acceptability feasibility, possible limitations, economic and workforce considerations.

Additionally, to further support the evidence generated from this thesis that can be utilised within the Hawkins et al. (2017) multi-method approach, small-size feasibility studies can be undertaken for each individual component of this thesis prototype complex intervention to evaluate the proposed component in relation to outcomes such as acceptability, recruitment, adherence and its effectiveness toward its proposed clinical measures (reported within the initial porotype version of the complex intervention in figure 7.2). All the data generated from these proposed research steps or actions will ultimately help with addressing the complete updated MRC framework steps to inform decisions about evaluating the intervention within a future definitive randomised control trial and subsequently aid with decisions about its broader implementations in the clinical practice.

List of Appendices

Appendix A.

Participant #: _____

Date: _____

Interview Start Time: _____

Understanding the Effects of Hospital-associated Disability in Exacerbations of Chronic Obstructive Pulmonary Disease: Patient Experience, Impact of Hospital-Associated Disability and COPD Exacerbation

Interview Guide

Gain consent and introduction

Introduce you, name and role

You have consented to take part in an interview as part of the Hospital-associated Disability in Exacerbations of Chronic Obstructive Pulmonary Disease study. During the interview I would like to discuss your hospital experience and the associated symptoms that comes with your COPD exacerbation. It is an opportunity for you to tell me anything that you think is relevant. The results of this study will also inform a larger project investigating the patient care priorities after suffering from your recent lung problem.

Do you have any questions?

Are you happy for me turn on the audio recorder to record the interview as it takes place?

For the benefit of the tape it is …day…time.

Withdrawal

If anything we speak about today makes you feel uncomfortable you are free to not answer a particular question, request for the recorder to be switched off to resume the interview after a short break, or you can ask to stop the interview altogether at any point.

Hospital admissions and returning home

1. So, to get us started, can you tell me a little bit about why you have been admitted to hospital on this occasion?

2. Have you ever been in hospital for the same reason as you are now?

3. Since you have been admitted, what symptoms have bothered you the most? Have these changed while you have been in hospital? If yes, how?

4. a) Thinking about all the symptoms you have been experiencing, how long do you think these symptoms will last once you leave hospital?

b) Do you think any symptoms will continue for longer than others?

c) How do you think you might manage these symptoms when you are at home?

Care received and therapy options

5. a) While you have been in the hospital, which aspects of care have helped you the most? Is there anything else that you think could improve the care you receive in hospital?

b) What do you think might help you the most once you leave hospital?

c) Has anything been discussed with you so far about your care when you leave hospital?

d) For anything you have mentioned, when would be the best time for you to start to engage with this care?

6. Do you know what pulmonary rehabilitation is? If **yes**, what do you know about it? Have you ever been referred to pulmonary rehabilitation? What do you think of your previous experience with it?

If NO, (Pulmonary rehabilitation is a programme designed to help with your recovery to restore your physical and psychological well-being. It typically involves walking, exercise and talks).

b) If no, why? Is there anything that would make you more likely to attend?

6. a) Have you experienced any leg weakness while you have been in hospital?

If yes…this is not uncommon. We know that many people experience muscle weakness in hospital due to what we call muscle wasting which just means loss of muscle and results in weakness for example in the legs/arms. This can make things like walking a lot harder.

If no….we know that many people experience muscle weakness in hospital due to what we call muscle wasting which just means loss of muscle and results in weakness for example in the legs/arms. This can make things like walking a lot harder.

b) How would you feel about being offered a drug that could help build up the muscles?

c) Some of these drugs are similar to testosterone, how would you feel about being asked to take something like this? (Prompt if participant doesn't know much about testosterone: Some people may worry that long term use may cause hair growth, or affect the prostate in men).

7. Are you feeling ok after everything I have asked you today? Is there anything else you would like to add? Do you have any questions for me?

3. Demographics Component

1. Age: _____

2. Gender: _____

3. COPD severity _____

Interview End Time: _____

Length of interview: _____

Interviewer's Name: _____

Appendix B.

UNIVERSITY OF LEICESTER
INSTITUTE FOR LUNG HEALTH LEICESTER
National Institute for Health Research
Leicester Biomedical Research Centre- Respiratory
Glenfield Hospital
Groby Road
Leicester
LE3 9QP

Tel: 0116 258 3370
Fax: 0116 258 3494
Email: leics.respiratorybru@nhs.net
www.leicsrespiratorybru.nihr.ac.uk

Patient Identification number for this study:

CONSENT FORM

Title: **Patient experience and understanding of hospital-associated disability**

A nested sub-study of: Understanding the effects of hospital-associated disability in exacerbations of Chronic Obstructive Pulmonary Disease

Name of Investigator: Dr Neil Greening

Please initial box

1. I confirm that I have read and understand the additional participant information sheet dated 24/04/2018, version 2 for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐
2. I understand that my participation in this sub-study is voluntary and I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. I understand that if I withdraw then information collected so far may still be used in the project analysis. ☐
3. I consent to the interview to being audio recorded ☐
4. I agree to my GP being informed that I am taking part in this study. ☐
5. I agree to take part in this additional sub-study. ☐

Name of Patient	**Date**	**Signature**
Name of Person taking consent	Date	Signature

Appendix C

FW: Amendment Approval EDGE 105207 SA 01

AB Alkhathlan, Bedor S.A.
To Greening, Neil J. (Dr.)

Reply | Reply All | Forward

Thu 04/07/2019 11:00

From: Wann Lisa - Research and Innovation Manager <lisa.wann@uhl-tr.nhs.uk>
Sent: 04 July 2019 09:50
To: Greening Neil - Honorary Consultant <Neil.Greening@uhl-tr.nhs.uk>
Cc: Research & Innovation Admin Mailbox <RIAdmin@uhl-tr.nhs.uk>; Alkhathlan, Bedor S.A. <bsaa5@leicester.ac.uk>; Finney Selina A - Ethics and Regulatory Officer <Selina.A.Finney@uhl-tr.nhs.uk>; Terry Sarah - Research Governance Lead <sarah.terry@uhl-tr.nhs.uk>; UOLSPONSOR <UOLSPONSOR@leicester.ac.uk>
Subject: Amendment Approval EDGE 105207 SA 01

Dear Dr Neil Greening

Ref: EDGE ID 105207 PROJECT_ID 239167
Title: Understanding the effects of hospital-associated disability in exacerbations of Chronic Obstructive Pulmonary Disease
Project Status: Open
End Date: 31/10/2022

Thank you for submitting documentation for Substantial Amendment 01 04th June 2019 for the above study. The amendment has been classed as a Category C amendment.

I confirm that all the documentation and relevant regulatory approvals relating to this amendment have been received by the University Hospitals of Leicester NHS Trust R&I Department. We acknowledge that the Sponsor was able to implement this amendment as soon as any relevant regulatory approvals were in place.

Please ensure that all documentation and correspondence relating to this amendment are filed appropriately in the relevant site file.

Documents received:

Document	Version	Date
Interview schedules or topic guides for participants [Interview Schedule Guide]	2	15-May-19

Undertaking research in the NHS comes with a range of regulatory responsibilities. Please ensure that you and your research team are familiar with, and understand the roles and responsibilities both collectively and individually.

Documents listing the roles and responsibilities for all individuals involved in research can be found on the R&I pages of the Public Website. It is important that you familiarise yourself with the Standard Operating Procedures, Policies and all other relevant documents which can be located by visiting http://www.leicestersresearch.nhs.uk/standard-operating-procedures/

The R&I Office is keen to support and facilitate research where ever possible. If you have any questions regarding this or other research you wish to undertake in the Trust, please contact this office.

Please note that a letter confirming authorisation will not be sent. Please retain a copy of this email in your site file.

Appendix D.

Survey piloting Summary

Pilot Round 1- Post-Acute COPD exacerbation

Patients were recruited from the respiratory ward at Glenfield Hospital. Two patients agreed to participate in the piloting process. Participant completed all the survey questions within a reasonable time (approximately 14 minutes). Participant one stated that all of the questions were relevant and there is no need to add additional questions or items to the answers. However, the participant suggested adding instructions to the questions that ask the patients specifically to pick only the symptoms that apply to them.

The second participant required approximately 15 minutes to finish the survey. The participant said the questions were conclusive and relevant; however, they suggested leaving the choice for question one open. Therefore, the question's answer style was changed to allow for continuous data entry. Moreover, the Participant suggested adding borders to the tables to facilitate picking the relevant answers from the list and also suggested adding an additional possible choice to question eight that state" I manage myself" which was considered and added to the questions. Finally, the participant stated that the survey was long and therefore, the last question that asked about barriers for attending pulmonary rehabilitation was removed to reduce the questions numbers and it was thought that the question was well investigated by the existing literature.

Pilot Round 2- PPI date 25/06/2019 and time (11:45 am).

The meeting included 6 chronic patients with three out of the six patients had COPD. The meeting lasted approximately 40 minutes and it included a brief presentation that

explained the study aims to the patients. Hard copies of the survey were distributed to the patients to give the participant a chance to look at the questions and write their feedback on the questions. Below is the detailed feedback from every participant.

Participant One

Aged 78 year old, female. She required 13 minutes to complete the survey. The participant stated the questions were relevant. However, she would like the survey to be simplified in terms of the layout.

Participant Two

Aged 69-year-old, Male. He required 12 minutes to complete the survey. The patient did not highlight any particular issue with survey while completing.

Participant Three

Aged 73 year old, female. She required 13 minutes to fill out the survey. When filling out the survey, the participant thought that the same question was asked twice (Q8and Q9) therefore, did not fill out the question correctly. A decision has been reached that these questions needed no further amendments and it was thought that this issue will be avoided in the future because the survey will be filled during the presence of the researcher B.S, which will hopefully limit any confusion during the process of filling out the survey.

Participant Four

Female and did not provide her age. However, she stated that she holds a master degree. The participant required 6 minutes to complete the survey, which was the shortest time compared to the other participant. The participant suggested adding an item to question 7, stating if patients are living with an active smoker have contributed to their current admission. Their feedback is considered and the question is amended accordingly.

Additionally, according to the participant feedback, it was decided to move question 6 to the last page before question number 16 and depending on the patient's answer to the

question they will be prompted to continue or stop filling the survey. Also, the participant suggested adding an extra item to question number 16 allow carer/ partner to be involved in the patients' chronic care process. The valuable suggestion was accepted and the question was amended accordingly. Lastly, the participant suggested that we add an extra box to the therapy priorities choices that allow patients to pick "not sure" choices. However, we disregarded this suggestion because we wanted the patients to give us a definitive answer whether or not any of the therapies would be a priority to them to help us to draw a clear conclusion during the analysis process of our survey questions.

Participant Five

Aged 70 year old, female. The patient has experienced a similar problem to participant 3 with regard not being able to distinguish that the questions asked during different timelines, and though it was the same question repeated twice. As mentioned above, it was thought that the question by itself and how it is written was not an issue, and this problem can be solved by the researcher explaining every question to the patients before they start filing the survey.

Participant Six

Aged 71 year old, female. The participant filled the survey within 13 minutes and did not specify any issues with the survey.

Overall discussion during the session

During the overall discussion, the participants suggested reducing the number of questions because the survey was thought to be too long to fill by acute patients. Participants also noted that question number 15 was a significant and interesting question to ask.

Survey content face validity from qualitative interviews

The analysed interviews transcripts did not identify any new emerging survey items that can be manged with non-pharmacological interventions other than the ones listed in the current version #2 of the survey except for the following items;

Dizziness was captured by the interviews as a troublesome symptom patients suffer within both the acute and sub-acute phase and it was added to the troublesome symptoms checklist.

"When you start to get lack of breath you start to get dizzy. You can be walking out somewhere, you can be keeling over. You can fall down a ditch and nobody's going to see you fall, anything like that" (Participant ID10).

"yeah you feel a bit unstable on your feet"(Participant ID 3)

"bit dizzy, I get dizziness" (Participant ID 6).

Therefore, a balance therapy has been added to the therapy priorities checklist. Additionally, some patients has identified walking aids as a need and therefore a walking aids item has been added to the therapy priorities checklist.

"In a couple of days I'm going to ask for a stroller, four wheeler where you can put your oxygen on it and go for a little walk. But I can't at the minute because my breathing's not good enough yet. But once I'm a bit better I'll ask for a stroller, and then I'll go for a walk" (Participant ID7).

Appendix E

NHS University Hospitals of Leicester NHS Trust

UNIVERSITY OF LEICESTER

COPD-INTRO CRF V 3.0 07/10/2020

Participant ID: ☐☐☐☐☐ - Use **Black pen** only

Date Of visit: ☐☐/☐☐ / ☐☐☐☐ (dd/mm/yyyy)

Glenfield General Hospital

TIDe: Training to Improve Dyspnoea

Sub-study:

acute COPD exacerbation experience, Impact, aNd Therapy pRiOrities (COPD-INTRO)

CONFIDENTIAL
Patient Basic Characteristics and Questionnaires

Section 1: Patient Demographic and Clinical History

Gender	○ **Male**	○ **Female**	○ **Other**
Age			

The highest level of education completed?

COPD severity

CAT Total score=

FEV1 (L)	**Q1=**	**Q4=**
FVC (%)	**Q2=**	**Q5=**
FEV1/FVC (%)	**Q3=**	**Q6=**
	Q7=	**Q8=**

GAD-7 Score

GAD-7

Over the last 2 weeks, how often have you been bothered by the following problems? *(Use "✓" to indicate your answer)*	Not at all	Several days	More than half the days	Nearly every day
1. Feeling nervous, anxious or on edge	0	1	2	3
2. Not being able to stop or control worrying	0	1	2	3
3. Worrying too much about different things	0	1	2	3
4. Trouble relaxing	0	1	2	3
5. Being so restless that it is hard to sit still	0	1	2	3
6. Becoming easily annoyed or irritable	0	1	2	3
7. Feeling afraid as if something awful might happen	0	1	2	3

(For office coding: Total Score T____ = ____ + ____ + ____)

PHQ-9 Score

Over the last 2 weeks, how often have you been bothered by any of the following problems?	Not at all	Several days	More than half the days	Nearly every day
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, or hopeless	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself — or that you are a failure or have let yourself or your family down	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed? Or the opposite — being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
9. Thoughts that you would be better off dead or of hurting yourself in some way	0	1	2	3

PHQ-9 total score: ☐

Clinical Frailty Index		
Supersize Q	Yes	NO

Section 2: Questionnaire 1

Q1. How many times have you been admitted to the hospital about your chest in the last 12 months?

☐

Q2. How many days have you had symptoms worsening, leading to your admission?

☐ Days

Q3.Do you live alone?

○ Yes	○ No

If you answer NO, please specify who you live with?

○ Spouse
○ partner
○ Family
○ Others, please specify……

Q4. Smoking status

○ None smoker
○ Passive smoker
○ Ex-smoker
○ Active smoker, please specify how many pack per-day……

Q5. If you are an active smoker, have you ever received advice on how to quit smoking?

○ **Yes**	○ **No**	○ **N/A**

Q6.In your opinion, what is/are the factors that contributed to your current admission?

Please check all that apply;

○ Infection	○ Living with an active smoker
○ Feeling unable to manage day to day activities	○ Air pollution
○ Exhaustion	○ Weather
○ Medicine not working very well	○ Being around pets
○ Family being unwell	○ Other, please specify……
○ Being an active smoker	

Q7. Could you rate the following symptoms according to how bothersome they are for you NOW?

Symptom	Not bothersome			Somewhat bothersome		Extremely bothersome	
Shortness of breath	0	1	2	3	4	5	6
Chest tightness/Wheeze	0	1	2	3	4	5	6
Cough	0	1	2	3	4	5	6
Sputum production (Phlegm)	0	1	2	3	4	5	6
Sleep disturbance	0	1	2	3	4	5	6
Limited mobility	0	1	2	3	4	5	6
leg weakness/ weariness	0	1	2	3	4	5	6
Dizziness	0	1	2	3	4	5	6
Pain, please specify where.....	0	1	2	3	4	5	6
Fear/panic attack	0	1	2	3	4	5	6
Exhaustion and tiredness	0	1	2	3	4	5	6
Low mood	0	1	2	3	4	5	6
Other, please specify and rate.....	0	1	2	3	4	5	6

Q8. Could you rate the following symptoms according to how bothersome they are for you <u>USUALLY</u>?

Symptom	Not bothersome			Somewhat bothersome		Extremely bothersome	
Shortness of breath	0	1	2	3	4	5	6
Chest tightness/Wheeze	0	1	2	3	4	5	6
Cough	0	1	2	3	4	5	6
Sputum production (Phlegm)	0	1	2	3	4	5	6
Sleep disturbance	0	1	2	3	4	5	6
Limited mobility	0	1	2	3	4	5	6
leg weakness/ weariness	0	1	2	3	4	5	6
Dizziness	0	1	2	3	4	5	6
Pain, please specify where……	0	1	2	3	4	5	6
Fear/panic attack	0	1	2	3	4	5	6
Exhaustion and tiredness	0	1	2	3	4	5	6
Low mood	0	1	2	3	4	5	6
Other, please specify and rate……	0	1	2	3	4	5	6

Q9.Please rate how important it is for you to treat this symptom(s)

Symptom	Not at all important	Slightly important	Important	Fairly important	Very important	No opinion
Shortness of breath	○	○	○	○	○	○
Chest tightness	○	○	○	○	○	○
Cough	○	○	○	○	○	○
Sputum production (Phlegm)	○	○	○	○	○	○
Sleep disturbance	○	○	○	○	○	○
Limited mobility	○	○	○	○	○	○
Muscle weakness	○	○	○	○	○	○
Dizziness	○	○	○	○	○	○
Pain, please specify where.....	○	○	○	○	○	○
Fear/panic attack	○	○	○	○	○	○
Exhaustion and tiredness	○	○	○	○	○	○
Low mood	○	○	○	○	○	○
Other, please specify and rate.....	○	○	○	○	○	○

Q10.How do you deal with symptom(s)? You could choose from the following or explain more within the other choice.

○ I try to ignore it/them
○ I don't know how to deal with it/them
○ I try not do as much so I used to do to avoid aggravating the symptom
○ I do what my doctor/nurse advise me to do
○ I manage myself
○ Other, please explain, ……

Q11. Have you received any education/ training about ways to manage your symptom(s) effectively?

○ **Yes** ○ **No**

If you answer <u>YES</u>, please tell us how?

……

Q12. What therapy do you think might help you the most while you are at HOSPITAL?

Please check all that apply and/ or specify other therapy priority within the (other) choice.

Help With My Breathlessness	
	Advise on Breathing exercise
	Train my breathing muscles
	Teach me how to pace my self

Help With My Cough	
	Help with my chest clearance
	Teach me useful cough technique
	Give me a device to help clear my chest

Increase My Muscles Strength and Tolerance	
	walking exercise
	Increase muscle strength in the upper body
	Increase muscle strength in the lower body
	Increase muscle strength all over my body
	Help with my day to day activity, e.g. (gadget, appliances, walking aids)
	Balance therapy

Help With My Mood	
	Relaxation sessions
	Help with anxiety
	Help with depression
	Help to stop panicking about my breathing
	Attend patients support groups

Help With Learning About My Disease	
	Attending educational sessions help me know more about my disease, symptoms
	Help me to know about Medications
	Help for my family to learn about my disease

Help with my Sleeping	
	Advice on how to sleep better

Help with my exhaustion and tiredness	
	Help with my day to day activities, e.g. (gadget, appliances)

Manage my pain

Other,.....

Q13.What therapy do you think might help you the most after your DISCHARGE?

Please check all that apply and/ or specify other therapy priority within the (other) choice.

Help With My Breathlessness	
	Advise on Breathing exercise
	Train my breathing muscles
	Teach me how to pace my self

Help With My Cough	
	Help with my chest clearance
	Teach me useful cough technique
	Give me a device to help clear my chest

Increase My Muscles Strength and Tolerance	
	walking exercise
	Increase muscle strength in the upper body
	Increase muscle strength in the lower body
	Increase muscle strength all over my body
	Help with my day to day activity, e.g. (gadget, appliances, Walking aids)
	Balance therapy

Help With My Mood	
	Relaxation sessions
	Help with anxiety
	Help with depression
	Help to stop panicking about my breathing
	Attend patients support groups

Help With Learning About My Disease	
	Attending educational sessions help me know more about my disease, symptoms
	Help me to know about Medications
	Help for my family to learn about my disease

Help with my Sleeping	
	Advice on how to sleep better

Help with my exhaustion and tiredness	
	Help with my day to day activities, e.g. (gadget, appliances, walking aids)

Manage my pain

Other,.....

Q14. If we were to deliver therapy upon your discharge, when would you like it to be delivered?

Please check that apply

Therapy	When to deliver the therapy					
	Immediately	**In a Few days**	**1 week**	**In 1 month**	**3 months**	**Not at all**
Help with my Breathlessness						
Help with my Cough						
Increase my muscle strength and tolerance						
Help with my balance issues						
Help With My Mood						
Help with learning about my disease						
Help with my Sleep problems						
Help with my exhaustion and tiredness						
Manage my pain						

Pulmonary rehabilitation is a programme designed to help with your recovery to restore your physical and psychological wellbeing

Q15.Have you ever been to a pulmonary rehabilitation programme?

- ○ **Yes**
- ○ **NO**

If you answer Yes, please specify where?

.....

.....

*If you answered **No** to the above question please stop here, if you answered **Yes** please continue to the following question* ⬇

We recommend pulmonary rehabilitation within a month of being in the hospital.

16. What would make you <u>more likely</u> to come to pulmonary rehabilitation in the <u>next month?</u>

○ More education to start with before exercise therapy
○ Concentrate on exercises (e.g., strength) that make me less breathless.
○ Make the exercises easier to do
○ Change the way the sessions provided (make educational sessions more interactive)
○ Give me the ability to set my own session schedule (programme provided during several days of the week)
○ More different time slots where sessions provided
○ Having the option to do it away from the center. E.g. (home, manuals, web-based)
○ Allow me to start the programme at home and then come to the center
○ Provide transport
○ Wait for a few more weeks until I am completely better
○ Start whenever the weather is better
○ Inform my carer/partner/other about the programme
○ Other, please specify.....

Appendix F

Multidimensional Dyspnea Profile page 1 of 4 name/code_____date&time

MULTIDIMENSIONAL DYSPNEA PROFILE

Script for first time use:

The purpose of this questionnaire is to help us understand how your breathing feels.
There are no right or wrong answers. We want to know what you tell us about your own breathing.

On this page we ask you to tell us how unpleasant your breathing feels. On a later page we will ask you about the intensity or strength of your breathing sensations. The distinction between these two aspects of breathing sensation might be made clearer if you think of listening to a sound, such as a radio. As the volume of the sound increases, I can ask you how loud it sounds or how unpleasant it is to hear it. For example, music that you hate can be unpleasant even when the volume is low, and will become more unpleasant as the volume increases; music that you like will not be unpleasant, even when the volume increases.

A1 Scale

Use this scale to rate the **unpleasantness or discomfort** of your breathing sensations, how **bad** your breathing feels [felt].

Please focus on the period Right now _____

← ←	0	1	2	3	4	5	6	7	8	9	10
PLEASANT	NEUTRAL										UNBEARABLE

SQ choice

Below are phrases or terms arranged in groups of similar meaning.

Step 1: Check each group that describes how your breathing feels [felt] _____right now_____(indicate focus period).

Step 2: Please also mark *one* group that most accurately describes how your breathing feels [felt].

	Step 1		Step 2
If *ANY* term in the group applies, choose that group.	DOES NOT APPLY	DOES APPLY	MOST ACCURATELY DESCRIBES
My breathing requires muscle work ***or*** effort			
I am not getting enough air ***or*** I am smothering ***or*** I feel hunger for air			
My chest and lungs feel tight ***or*** constricted			
My breathing requires mental effort ***or*** concentration			
I am breathing a lot			

Multidimensional Dyspnea Profile page 3 of 4 name/code_____date&time

SQ Scales

Use these scales to rate the intensity of the breathing sensations you feel [felt] (like the loudness of sound, regardless of whether the sensation is pleasant or unpleasant; for example a sensation could be intense without being unpleasant.)

Please focus on the period right now_____

If ANY term in the group applies, rate that group.	NONE										AS INTENSE AS I CAN IMAGINE
My breathing requires muscle work ***or*** effort	0	1	2	3	4	5	6	7	8	9	10
I am not getting enough air ***or*** I am smothering ***or*** I feel hunger for air	0	1	2	3	4	5	6	7	8	9	10
My chest and lungs feel tight ***or*** constricted	0	1	2	3	4	5	6	7	8	9	10
My breathing requires mental effort ***or*** concentration	0	1	2	3	4	5	6	7	8	9	10
I am breathing a lot	0	1	2	3	4	5	6	7	8	9	10
Other*	0	1	2	3	4	5	6	7	8	9	10

*If you need to, you can add additional descriptions of your breathing sensations.

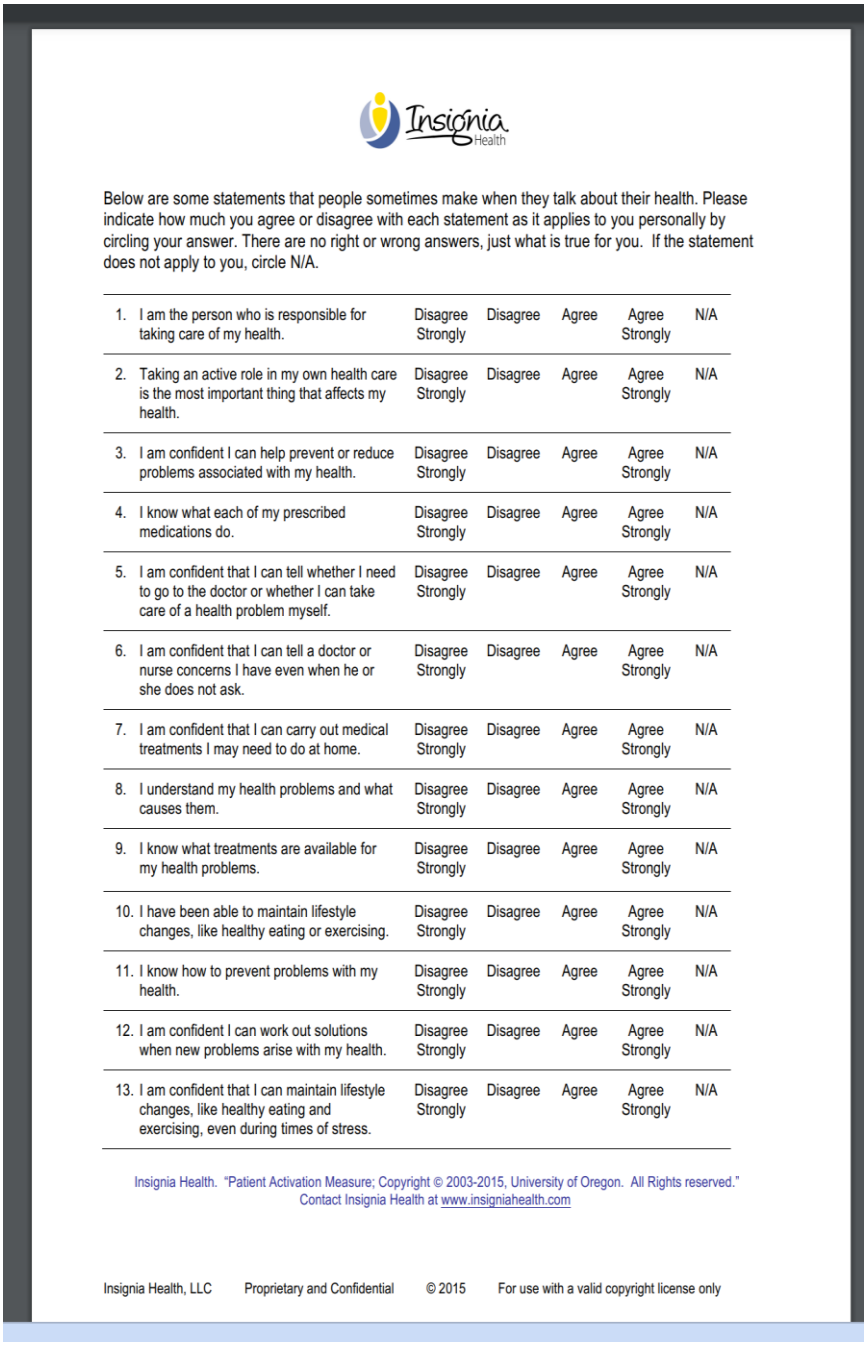
A2 Scales

When your breathing doesn't feel normal, you may experience emotions or 'feelings'. Using the scales below, please tell us about how your breathing sensations made you feel – rate zero for any emotion you did not feel.

Please focus on feelings during the period right now_____.

	NONE										THE MOST I CAN IMAGINE
Depressed	0	1	2	3	4	5	6	7	8	9	10
Anxious	0	1	2	3	4	5	6	7	8	9	10
Frustrated	0	1	2	3	4	5	6	7	8	9	10
Angry	0	1	2	3	4	5	6	7	8	9	10
Afraid	0	1	2	3	4	5	6	7	8	9	10
Other?	0	1	2	3	4	5	6	7	8	9	10

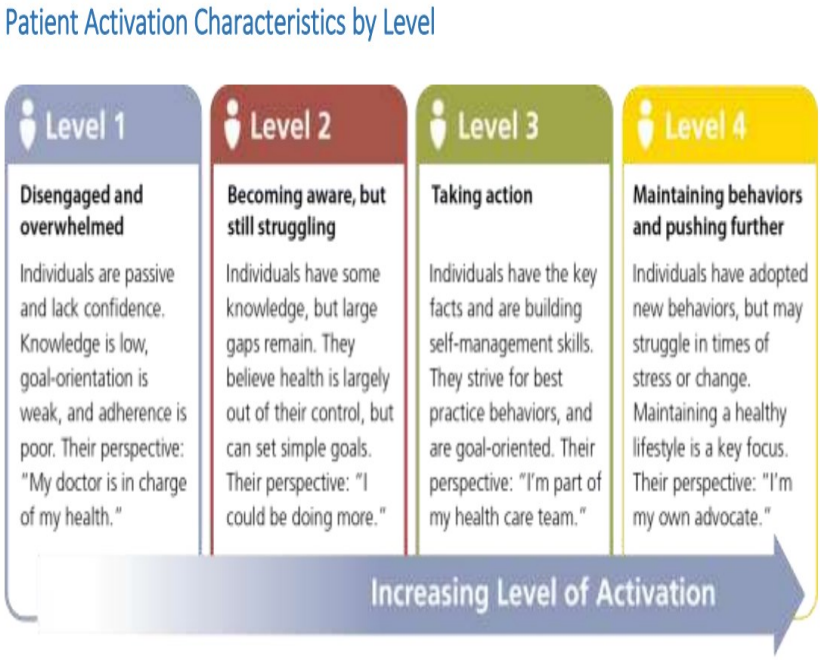
Appendix G



Insignia Health

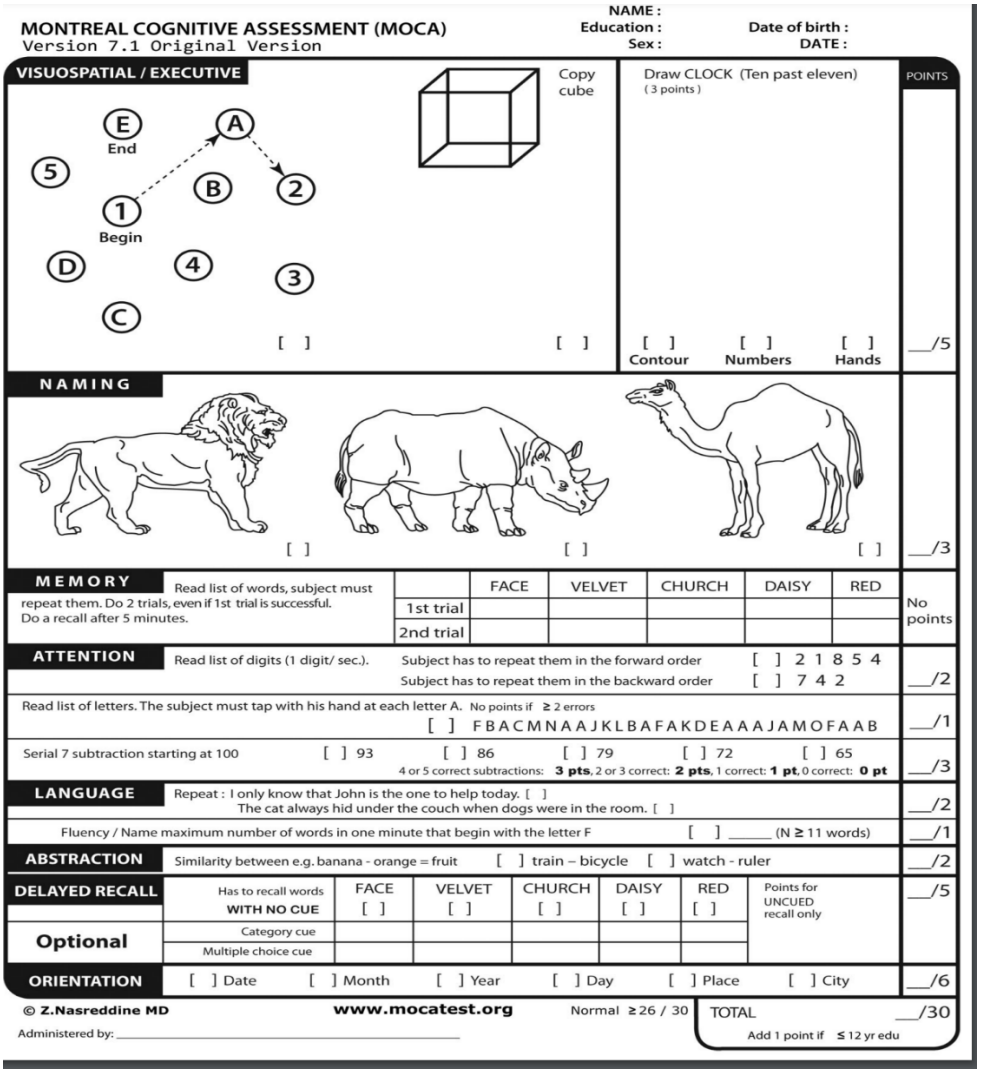
Below are some statements that people sometimes make when they talk about their health. Please indicate how much you agree or disagree with each statement as it applies to you personally by circling your answer. There are no right or wrong answers, just what is true for you. If the statement does not apply to you, circle N/A.

1. I am the person who is responsible for taking care of my health.	Disagree Strongly	Disagree	Agree	Agree Strongly	N/A
2. Taking an active role in my own health care is the most important thing that affects my health.	Disagree Strongly	Disagree	Agree	Agree Strongly	N/A
3. I am confident I can help prevent or reduce problems associated with my health.	Disagree Strongly	Disagree	Agree	Agree Strongly	N/A
4. I know what each of my prescribed medications do.	Disagree Strongly	Disagree	Agree	Agree Strongly	N/A
5. I am confident that I can tell whether I need to go to the doctor or whether I can take care of a health problem myself.	Disagree Strongly	Disagree	Agree	Agree Strongly	N/A
6. I am confident that I can tell a doctor or nurse concerns I have even when he or she does not ask.	Disagree Strongly	Disagree	Agree	Agree Strongly	N/A
7. I am confident that I can carry out medical treatments I may need to do at home.	Disagree Strongly	Disagree	Agree	Agree Strongly	N/A
8. I understand my health problems and what causes them.	Disagree Strongly	Disagree	Agree	Agree Strongly	N/A
9. I know what treatments are available for my health problems.	Disagree Strongly	Disagree	Agree	Agree Strongly	N/A
10. I have been able to maintain lifestyle changes, like healthy eating or exercising.	Disagree Strongly	Disagree	Agree	Agree Strongly	N/A
11. I know how to prevent problems with my health.	Disagree Strongly	Disagree	Agree	Agree Strongly	N/A
12. I am confident I can work out solutions when new problems arise with my health.	Disagree Strongly	Disagree	Agree	Agree Strongly	N/A
13. I am confident that I can maintain lifestyle changes, like healthy eating and exercising, even during times of stress.	Disagree Strongly	Disagree	Agree	Agree Strongly	N/A



Footnote 8.1. Source: Insignia® 2017.

Appendix H



MONTREAL COGNITIVE ASSESSMENT (MOCA)
Version 7.1 Original Version

NAME :
Education :
Sex :
Date of birth :
DATE :

VISUOSPATIAL / EXECUTIVE

Copy cube

E End, A, 5, B, 2, 1 Begin, D, 4, 3, C

[ ] [ ]

Draw CLOCK (Ten past eleven) (3 points)

[ ] Contour [ ] Numbers [ ] Hands

POINTS ___/5

NAMING

[ ] [ ] [ ]

___/3

MEMORY Read list of words, subject must repeat them. Do 2 trials, even if 1st trial is successful. Do a recall after 5 minutes.

	FACE	VELVET	CHURCH	DAISY	RED
1st trial					
2nd trial					

No points

ATTENTION Read list of digits (1 digit/ sec.).

Subject has to repeat them in the forward order [ ] 2 1 8 5 4

Subject has to repeat them in the backward order [ ] 7 4 2

___/2

Read list of letters. The subject must tap with his hand at each letter A. No points if ≥ 2 errors

[ ] F B A C M N A A J K L B A F A K D E A A A J A M O F A A B

___/1

Serial 7 subtraction starting at 100 [ ] 93 [ ] 86 [ ] 79 [ ] 72 [ ] 65

4 or 5 correct subtractions: **3 pts**, 2 or 3 correct: **2 pts**, 1 correct: **1 pt**, 0 correct: **0 pt**

___/3

LANGUAGE Repeat : I only know that John is the one to help today. [ ]

The cat always hid under the couch when dogs were in the room. [ ]

___/2

Fluency / Name maximum number of words in one minute that begin with the letter F [ ] _____ (N ≥ 11 words)

___/1

ABSTRACTION Similarity between e.g. banana - orange = fruit [ ] train – bicycle [ ] watch - ruler

___/2

DELAYED RECALL

	FACE	VELVET	CHURCH	DAISY	RED	Points for UNCUED recall only
Has to recall words WITH NO CUE	[ ]	[ ]	[ ]	[ ]	[ ]	
Optional Category cue						
Optional Multiple choice cue						

___/5

ORIENTATION [ ] Date [ ] Month [ ] Year [ ] Day [ ] Place [ ] City

___/6

© Z.Nasreddine MD www.mocatest.org Normal ≥ 26 / 30

TOTAL ___/30

Add 1 point if ≤ 12 yr edu

Administered by: _____

Appendix I

Center for Epidemiologic Studies Depression Scale – Revised (CESD-R)
Fatigue Questions

Below is a list of the ways you might have felt or behaved. Please check the boxes to tell me how often you have felt this way in the past week or so.	Last Week				Nearly every day for 2 weeks
	Not at all *or* Less than 1 day	1 - 2 days	3 - 4 days	5 - 7 days	
I could not get going.	0	1	2	3	4
I was tired all the time.	0	1	2	3	4

REFERENCE: Eaton, W. W., Smith, C., Ybarra, M., Muntaner, C., Tien, A. (2004). Center for Epidemiologic Studies Depression Scale: review and revision (CESD and CESD-R). In ME Maruish (Ed.). *The Use of Psychological Testing for Treatment Planning and Outcomes Assessment* (3rd Ed.), Volume 3: Instruments for Adults, pp. 363-377. Mahwah, NJ: Lawrence Erlbaum.

Appendix J

How are you?

We would like to know what support you need. Please tick the box that best represents your needs now, for each statement below.

Do you need **more support** with...	No	A little more	Quite a bit more	Do you need **more support** with...	No	A little more	Quite a bit more
...understanding your illness				...practical help in the home or garden			
...managing your symptoms (including medication and oxygen)				...your personal care (e.g. dressing, washing)			
...dealing with your feelings and worries				...aids or equipment to help you			
...looking after any other physical health problems you may have				...family relationships (including talking to your relatives about your illness)			
...having a healthier lifestyle (e.g. keeping active or eating well)				...knowing what to expect in the future			
...getting out and about				...accessing or using services			
...overcoming boredom or loneliness				...anything else - please write in:			
...financial, legal, work or housing issues				**Does a family member or friend who helps you need more support?**			

Appendix K

Dear Professor Singh

Ref: EDGE ID 91082 PROJECT_ID 220947
Title: A Randomised Controlled Trial to Investigate the Use of High Frequency Airway Oscillations as Training to Relieve Dyspnoea in COPD.
Project Status: Open
End Date: 30/09/2021

Thank you for submitting documentation for Non-Substantial Amendment 04 15th October 2020 for the above study. This amendment is classed as a Category A amendment.

I confirm that the amendment has the authorisation of the University Hospitals of Leicester NHS Trust R&I Department and may be implemented with immediate effect. Also as the UHL is also the Sponsor of this research, please regard this email as the Sponsor Green Light for the UHL Sites.

Please ensure that all documentation and correspondence relating to this amendment are filed appropriately in the relevant site file.

Documents Approved:

- Protocol v5.0 08/10/2020
- CRF VERSION v3.0 07/10/2020
- PIS with Consent-version v4.0 19/11/2020

Undertaking research in the NHS comes with a range of regulatory responsibilities. Please ensure that you and your research team are familiar with, and understand the roles and responsibilities both collectively and individually.

Documents listing the roles and responsibilities for all individuals involved in research can be found on the R&I pages of the Public Website. It is important that you familiarise yourself with the Standard Operating Procedures, Policies and all other relevant documents which can be located by visiting http://www.leicestersresearch.nhs.uk/standard-operating-procedures/

The R&I Office is keen to support and facilitate research where ever possible. If you have any questions regarding this or other research you wish to undertake in the Trust, please contact this office.
Please note that a letter confirming authorisation will not be sent. Please retain a copy of this email in your site file.

We wish you every success with your research.

Should you have any queries or require further information please do not hesitate to contact me.

#hello my name is…

Lisa Wann
R&I Manager
University Hospitals of Leicester NHS Trust
Research & Innovation, Leicester General Hospital, Gwendolen Road, Leicester, LE5 4PW.

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NHS Trust

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Groby Road
Leicester
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Tel: 01162502758
Fax: 0116 258 3950

PATIENT INFORMATION SHEET

TIDe: Training to **I**mprove **D**yspno**e**a
Sub-study:

acute **COPD** exacerbation experience, **I**mpact, a**n**d
Therapy P**rio**rities (COPD-INTRO)

A Qualitative exploratory study to understand the experience, impact and therapy priorities of Acute COPD exacerbation patients

Principle Investigator: Professor Sally Singh
Study Lead: Bedor Alkhathlan MSc , RRT
Contact number: 01162502758
Email: Bsaa5@leicester.ac.uk

Leicester Biomedical Research Centre

CERS Centre for Exercise and Rehabilitation Science

Supported by NIHR

Invitation

You are being invited to take part in the above research study conducted by the respiratory research team. We are inviting COPD patients who are admitted to the hospital with Acute COPD exacerbation (flare-ups). Before agreeing to the research, please take time to read the following information carefully and discuss it with friends, relatives, and your Respiratory Consultant if you wish. Ask a member of the research team if you have any questions or need further Information. Take time to decide whether or not you wish to take part. This research will be contributing to an educational qualification. Thank you for reading this information sheet.

What is the purpose of this study?

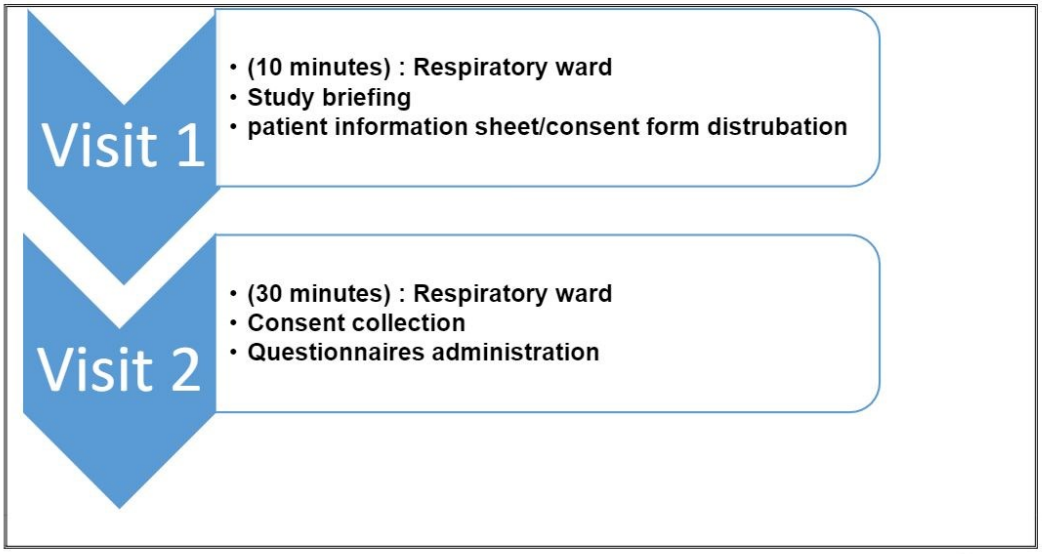
Patients with Chronic Obstructive Pulmonary Disease (COPD) often experience flare ups which result worsening of their breathlessness, cough, sputum production, physical ability, mood, anxiety and memory. This study will investigate the Patient's COPD flare up's experience and its impact and what are your therapy priorities might be during and after your hospital stay..

Do I have to take part?

No, it is up to you to decide whether or not to take part. If you decide to take part you will be given this information sheet to keep and asked to sign a consent form. If you decide to take part you are still free to withdraw at any time and without giving a reason. A decision to withdraw, or a decision not to take part, will not affect the standard of care you receive. The data collected to the point of withdrawal may still be used.

What will happen if I take part?

The study lead at the Respiratory Biomedical Research Unit at Glenfield Hospital will visit you first to explain the study and answer any questions that you may have and ask you whether or not you would like to take part in the study. You will receive a patient information sheet and a consent form either in a paper copy or electronic version, and you will be given up to 5 hours to discuss your decisions with members of your health care providers or with your family. Afterwards, the research lead will make a second visit to collect the consent form. If you agree to participate the research lead will ask you to complete a number questionnaires at your bedside. This can be done independently or with the support of the research lead.



Questionnaires and survey. During the Second visit, you will be asked to do a number of questionnaires and a survey in a paper or electronically. Most of these are short and take only a few minutes to complete. The Questionnaires will ask about your symptoms, assess your memory, and ability of taking charge of your own health. Finally, you will be given a survey that will ask about your COPD exacerbation personal experience, your therapy priorities during and after your hospital stay. The research lead will be there to answer any questions and help you where needed.

What are the possible disadvantages and risks?

There are no anticipated risks with you participating in the study.

What are the possible benefits of taking part?

There will be no benefits to the participants other than Participants involved in the study will be providing valuable information that may help healthcare professionals understand your post COPD exacerbation experience and tailor the provided health care services to meet your most important needs.

Will my taking part be kept confidential?

All information which is collected about you during the course of the study will be kept strictly confidential. Only authorised members of the research and clinical teams will access to your medical records and personal data. By signing the consent form, you will acknowledge and authorise these procedures.

What happens to the results of the study?

Procedures for handling, processing, storage and destruction of your data are compliant with General Data Protection Regulation (GDPR) applied from 25 May 2018. Therefore, if you agree to take part in a research study, the sponsor University of Leicester will collect the minimum personally-identifiable information needed for the purposes of the research project. Information about you will be used in the ways needed to conduct and analyse the research study. NHS organisations and Insignia health ® may keep a copy of the information collected about you. Depending on the needs of the study, the information that is passed to the research sponsor may include personal data that could identify you. You can find out more about the use of patient information for the study you are taking part in from the research team or the study sponsor

University of Leicester is the sponsor for this study based in Leicester city/ England. We will be using information from you and/or your medical records in order to undertake this study and will act as the data controller for this study. This means that we are responsible for looking after your information and using it properly. University of Leicester will keep identifiable information about you for 5 years after the study has finished. And the results of this study will be used by Mrs Bedor Alkhathlan for her PhD project by Leicester University.
Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible.
You can find out more about how we use your information by contacting Tel: 0116 2502758 . if you would wish to complain, or have any concerns about any aspect of the way have been treated during the study you can contact the NHS patient and information Liaison Services (PILS) by telephone:08081788337 or email:pils@uhl-tr,nhs.uk

Who reviewed this study?

All research that involves NHS patients and staff, information from medical records or uses NHS premises must be granted a favourable opinion from the NHS research ethics committee prior to commencement. A favourable opinion does not mean that you will not come into harm during the study, however it does mean that the committee is satisfied that your rights will be respected and that the risks are reduced to a minimum. This study has been reviewed and given favourable opinion by the Leicester South Research Ethics Committee.

Contact details for further information:

For further information please contact:
Professor Sally Singh or Bedor Alkhathlan MSC, RRT
Centre of Exercise Rehabilitation Science (CERS), University Hospitals of Leicester, Glenfield Hospital, Groby Road, Leicester, LE3 9QP.
Tel: 0116 250 2758
E-mail:Bsaa5@leicester.ac.uk

Thank you very much for considering taking part in this project.

Patient Identification number:

Patient Consent Form

A Qualitative exploratory study to understand the experience, impact and therapy priorities of Acute COPD exacerbation patients.

Principal Investigator: Professor Sally Singh

	Patient to initial
1. I confirm that I have read and understood the patient information sheet dated 19/112020 version 4.0 for the above study and have the opportunity to ask questions.	☐
2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected and all data collected up until withdrawal will be retained.	☐
3. I understand the relevant sections of my medical notes and/or study data maybe looked at by individuals from the study team, the sponsor, NHS trust or form regulatory authorities where relevant by taking part in the research. I give permission for these individuals to have access to my records.	☐
4. I agree to complete the questionnaires and the scales either with a paper copy version or electronically that will evaluate my symptoms, memory, COPD exacerbation personal experience, and my therapy priorities	☐
5. I agree to take part in the above study.	☐

Name of the patient	Date	signature
Researcher	**Date**	**Signature**

Appendix L

Medicine and Biological Sciences Research Ethics Committee

12/10/2021

Ethics Reference: 29960-bsaa5-ls:respiratorysciences

TO:
Name of Researcher Applicant: Bedor Alkhathlan
Department: Respiratory Sciences
Research Project Title: Title: Building Health Care Professional Consensus on Patients' Non-pharmacological Therapy Priorities During Both the Acute and Post-acute Phases of Chronic Obstructive Pulmonary Disease (COPD) Exacerbation

Dear Bedor Alkhathlan,

RE: Ethics review of Research Study application

The Medicine and Biological Sciences Research Ethics Committee has reviewed and discussed the above application.

1. Ethical opinion

The Committee grants ethical approval to the above research project on the basis described in the application form and supporting documentation, subject to the conditions specified below.

2. Summary of ethics review discussion

The Committee noted the following issues:
An interesting application and there are no concerns with this. If you do wish to alter your protocol or questionnaire at any point please remember to submit an amendment through the UoL ethics app.
Good luck with the study!

3. General conditions of the ethical approval

The ethics approval is subject to the following general conditions being met prior to the start of the project:

As the Principal Investigator, you are expected to deliver the research project in accordance with the University's policies and procedures, which includes the University's Research Code of Conduct and the University's Research Ethics Policy.

If relevant, management permission or approval (gate keeper role) must be obtained from host organisation prior to the start of the study at the site concerned.

4. Reporting requirements after ethical approval

You are expected to notify the Committee about:

- Significant amendments to the project
- Serious breaches of the protocol
- Annual progress reports
- Notifying the end of the study

5. Use of application information

Details from your ethics application will be stored on the University Ethics Online System. With your permission, the Committee may wish to use parts of the application in an anonymised format for training or sharing best practice. Please let me know if you do not want the application details to be used in this manner.

Best wishes for the success of this research project.

Yours sincerely,

Dr. Chris Talbot
Chair

Appendix M

UNIVERSITY OF LEICESTER

Title: Building Health Care Professional Consensus on Patients' Non-pharmacological Therapy Priorities During Both the Acute and Post-acute Phases of Chronic Obstructive Pulmonary Disease (COPD) Exacerbation

Participant's Information Sheet

You are invited to participate in this Delphi process, which aims to build health care professional consensus on the Chronic Obstructive Pulmonary Disease (COPD) (non-pharmacological) therapy priorities during both the acute and post-acute stages of COPD Exacerbation.

What is the purpose of this research?

Conducting this survey will help inform the development of Stakeholders co-designed complex Pulmonary rehabilitation (PR) approach to promote uptake of PR therapy post-Acute exacerbation of COPD. The survey process will be conducted within three consecutive rounds (two weeks apart). Please note that we appreciate your involvement within the three rounds of this survey, where each survey round will take a maximum of 10 minutes to complete. The survey will remain open for two consecutive weeks. However, if you need an extension, please contact the study lead to help with this.

Am I eligible to take part in this study?

You are eligible to take part in the survey if you have any of the following eligibility criteria;

A Health care professional with ≥ five years of clinical experience who are involved in the care of acute or post-acute exacerbation of Chronic Obstructive pulmonary disease patients

What do I have to do?

If you wish to participate, please use the link below to log into the survey platform.

Please note your completion of this survey will represent your consent to participate in this study.

Will what I say in this research project be kept confidential?

Yes, your responses are anonymous and completely confidential

How my information will be kept?

Data will be stored on a secure server in a folder to which only the study researchers have access.

At all times this project will comply with the General Data Protection Regulations (GDPR, 2018) approved by the EU parliament on 14 April 2016 and passing into UK law with effect from 25 May.

Who is organising and funding the research project?

This research study is part of a PhD project funded by the University of leicester

What if something goes wrong?

In the very unlikely event of you being harmed by taking part in this research project, there are no special compensation arrangements. If you are harmed due to someone's negligence, then you may have grounds for legal action but you may have to pay for it.

Who has reviewed the research project?

This project and associated documents have been approved by the University of Leicester Research Ethics Committee

Please don't hesitate to contact the study lead (Bedor Alkhathlan, bsaa5@le.ac.uk) if you have any further questions about this study.

If you have any concerns or queries about the way in which this project has been conducted, then you should contact the Chair of the University Research Ethics Committee on ethics@le.ac.uk.

If you require more GDPR data protection information then you can access this via the University's Information Assurance Services.

Principle investigator

Professor Sally Singh
ss1119@le.ac.uk

Study lead
Bedor Alkhathlan
Bsaa5@le.ac.uk

Appendix N

Delphi survey sample (Round one)

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Building Healthcare Professionals Consensus on Patients' Non-pharmacological Therapy Priorities During Both the Acute and Post-acute Phases of Chronic Obstructive Pulmonary Disease (COPD) Exacerbation

Introduction

Thank you for participating in this Delphi process, which aims to build healthcare professional consensus on non-pharmacological **therapy priorities** of patients with chronic obstructive pulmonary disease (COPD) identified during both the acute and post-acute stages of COPD exacerbation.

This Delphi survey was developed based on a previous research study that recruited patients during the acute stage of COPD exacerbation to explore their perceived non-pharmacological therapy priorities during both the acute and the post-acute stages of COPD exacerbation.

This survey process will be conducted over three consecutive rounds (two weeks apart). Each survey round will take approximately 10 minutes to complete. The survey will remain open for two consecutive weeks. Please note that you will find an "Other" box under each section, please use it if you would like to suggest a therapy item to be included in the subsequent survey round or if you would like to provide feedback. This will help us to modify the survey items for the next round.

Your responses are anonymous and completely confidential. The completion of this survey will represent your consent to participate in this project.

Please do not hesitate to contact the study lead if you have any questions about this study.

Kind Regards,

Study lead

Bedor Alkhathlan

PhD student in the Department of Respiratory Sciences, University of Leicester, United Kingdom

Bsaa5@leicester.ac.uk

Principle investigator

Professor Sally Singh

University of Leicester, Department Respiratory Sciences

ss1119@leicester.ac.uk

This study has been reviewed and approved by the University of research committee, country, with ethics approval r**eference:** 29960-bsaa5-ls:respiratorysciences.

Demographic data

What is your professional role?

- Medical Doctor
- Respiratory Nurse

Allied Health Care Practitioner, e.g., Physiotherapist, Respiratory Therapist, Occupational Therapist...

Advanced Critical Care Practitioner

Other

If other, please specify

How long is your Professional experience?

5-10 years

11-15 years

15-20 years

>20 years

What is your Geographic Region?

United Kingdom

United States

Australia

Canada

Other

- Next

Building Healthcare Professionals Consensus on Patients' Non-pharmacological Therapy Priorities During Both the Acute and Post-acute Phases of Chronic Obstructive Pulmonary Disease (COPD) Exacerbation

25%

25% completeSection 1: The Acute Phase Therapy List

This part of the survey uses a table of questions, view as separate questions instead?

The acute-phase therapy list (non-pharmacological). In this section, you will see several therapy priorities selected by individuals during hospitalisation for an AECOPD (without a particular order) to be administered during hospitalisation. Please indicate your level of agreement about these therapy priorities based on your expertise, experience, and potential therapeutic benefits.

	Strongly disagree	Disagree	Neither agree nor disagree	Agree	Strongly Agree
Respiratory muscle training	○	○	○	○	○
Breathing control advice	○	○	○	○	○
Activity pacing advice	○	○	○	○	○
Airway clearance therapy	○	○	○	○	○
Cough management	○	○	○	○	○
Administering airway clearance devices	○	○	○	○	○
Walking exercises	○	○	○	○	○
Body exercises to increase muscle strength and tolerance in the upper limbs	○	○	○	○	○

Body exercises to increase muscle strength and tolerance in the lower limbs	○	○	○	○	○
Relaxation sessions	○	○	○	○	○
Anxiety management	○	○	○	○	○
Depression management	○	○	○	○	○
Panic attacks management	○	○	○	○	○
Facilitate attendance to patients support groups	○	○	○	○	○
Delivering education sessions about the COPD disease	○	○	○	○	○
Delivering education sessions about medication use and adherence	○	○	○	○	○
Delivering COPD disease education to carers	○	○	○	○	○
Fatigue management	○	○	○	○	○
Sleep disturbance management	○	○	○	○	○
Pain management	○	○	○	○	○

Please, provide any other therapy priority item or comments here:

Building Healthcare Professionals' Consensus on Patients' Non-pharmacological Therapy Priorities During Both the Acute and Post-acute Phases of Chronic Obstructive Pulmonary Disease (COPD) Exacerbation

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Section 2: The Post-Acute Phase Therapy List

This part of the survey uses a table of questions, view as separate questions instead?

The post-acute phase therapy list (non-pharmacological). In this section, you will see several therapy priorities selected by individuals during hospitalisation for an AECOPD (without a particular order) to be administered after their hospital discharge. Please indicate your level of agreement about these therapy priorities based on your expertise, experience, and potential therapeutic benefits.

	Strongly disagree	Disagree	Neither agree nor disagree	Agree	Strongly Agree
Respiratory muscle training	○	○	○	○	○
Breathing control advice	○	○	○	○	○
Activity pacing advice	○	○	○	○	○
Airway clearance therapy	○	○	○	○	○
Cough management	○	○	○	○	○

Administering airway clearance devices	○	○	○	○	○
Walking exercises	○	○	○	○	○
Body exercises to increase muscle strength and tolerance in the upper limbs	○	○	○	○	○
Body exercises to increase muscle strength and tolerance in the lower limbs	○	○	○	○	○
Relaxation sessions	○	○	○	○	○
Anxiety management	○	○	○	○	○
Depression management	○	○	○	○	○
Panic attacks management	○	○	○	○	○
Facilitate attendance to patients support groups	○	○	○	○	○
Delivering education sessions about the COPD disease	○	○	○	○	○
Delivering education sessions about medication use and adherence	○	○	○	○	○
Delivering COPD disease education to carers	○	○	○	○	○
Fatigue management	○	○	○	○	○
Sleep disturbance management	○	○	○	○	○
Pain management	○	○	○	○	○

Please, provide any other therapy priority item or comments here:

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Building Healthcare Professionals Consensus on Patients' Non-pharmacological Therapy Priorities During Both the Acute and Post-acute Phases of Chronic Obstructive Pulmonary Disease (COPD) Exacerbation

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Results dissemination

For survey results dissemination, please provide your email below

Building Healthcare Professionals Consensus on Patients' Non-pharmacological Therapy Priorities During Both the Acute and Post-acute Phases of Chronic Obstructive Pulmonary Disease (COPD) Exacerbation

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100% complete

Final page

Thank you for your participation in the survey

Appendix O

Delphi survey sample (Round two)

Building Healthcare Professionals Consensus on Patients' Non-pharmacological Therapy Priorities During Both the Acute and Post-acute Phases of Chronic Obstructive Pulmonary Disease (COPD) Exacerbation (Second Delphi Round)

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Introduction

Thank you very much for participating in this Delphi study which aims to build healthcare professional consensus on the non-pharmacological therapy priorities of patients with chronic obstructive pulmonary disease (COPD) identified during both the acute and post-acute stages of COPD exacerbation.

This Delphi survey was developed based on a previous research study on patients experiencing acute COPD exacerbation to explore their perceived non-pharmacological therapy priorities during both the acute and post-acute stages of COPD exacerbation.

During the first round of the survey, we achieved consensus on prioritising the delivery of the following non-pharmacological interventions during the acute phase of the COPD exacerbation event:

Items achieved consensus in the first round - (The Acute-phase therapy priorities)
Fatigue management
Breathing control advice
Activity pacing advice
Airway clearance therapy
Walking exercises
Body exercises to increase muscle strength and tolerance in the upper limbs
Relaxation sessions
Anxiety management

Panic attack management
Facilitate attendance to patients support groups
Delivering education session about the COPD disease
Delivering education session about medication use and adherence
Sleep disturbance management

Items achieved consensus in the first round – (The post-acute phase therapy priorities)
Walking exercises
Breathing control advice
Activity pacing advice
Body exercises to increase muscle strength and tolerance in the upper limbs
Body exercises to increase muscle strength and tolerance in the lower limbs
Relaxation sessions
Anxiety management
Depression management
Panic attacks management
Facilitate attendance to patients support groups
Delivering education session about the COPD disease
Delivering education session about medication use and adherence
Delivering COPD disease education to carers
Fatigue management
Sleep disturbance management

Additionally, the survey respondents provided useful suggestions about the delivery of other prioritised therapy items, which were included in the second survey round. The items on which we achieved consensus were not included in the second round.

This survey round will take a maximum of 10 minutes to complete. You do not need to have completed Round 1 of the survey in order to take part in Round 2. The survey will remain open for two consecutive weeks.

Please note that in this survey round, we are not asking you to change your opinion if you strongly believe in it. The intention of this round is to give you the chance to re-evaluate your decisions about your previously ratings of items for which group consensus has not been achieved. This could be considered an opportunity to either confirm your initial opinion or modify the rating of an item that you were not sure about. Finally, it is a chance to evaluate the newly incorporated items that emerged from the first round of participants' feedback.

Additionally, please use the "Other" box under each section if you would like to suggest an extra therapy item to be included in the subsequent survey round or if you would like to provide feedback. This will help us to modify the survey items for the next round.

Your responses are anonymous to the group, and any identifiable information will be completely confidential and secured within our password-protected server. The completion of this survey will represent your consent to participate in this project.

Please do not hesitate to contact the study lead if you have any questions about this study.

Kind Regards,

Study lead

Bedor Alkhathlan

PhD student in the Department of Respiratory Sciences, University of Leicester, United Kingdom

Bsaa5@leicester.ac.uk

Principle investigator

Professor Sally Singh

Department of Respiratory Sciences, University of Leicester, United Kingdom

ss1119@leicester.ac.uk

This study has been reviewed and approved by the University of research committee, country, with ethics approval reference: 29960-bsaa5-ls:respiratorysciences.

Demographic data

What is your professional role?

- Medical Doctor
- Respiratory Nurse
- Allied Health Care Practitioner, e.g. Physiotherapist, Respiratory Therapist, Occupational Therapist...
- Advanced Critical Care Practitioner
- Other

How long is your Professional experience?

- 5-10 years
- 11-15 years
- 15-20 years
- >20 years

What is your Geographic Region?

- United Kingdom
- United States
- Australia
- Canada
- Other

HealthCare Professionals Consensus on Patients' Non-pharmacological Therapy Priorities During Both the Acute and Post-acute Phases of Chronic Obstructive Pulmonary Disease (COPD) Exacerbation (Second Delphi Round))

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25% complete

Section 1: The acute phase of COPD exacerbation therapy priorities list (non-pharmacological interventions)

In this section, you will see a list of several non-pharmacological priority interventions to be delivered during **the acute phase of COPD exacerbation** for which consensus has not been reached among healthcare professionals during Round 1. We now present these therapy priority interventions once again for re-evaluation together with newly incorporated therapy priority interventions generated from the respondent feedback from the first round.

Please note that next to each therapy priority intervention, you will see the first-round median score and the score range for the responses of the whole group. Additionally, interventions that do not include a median score or score range mean that they are newly incorporated.

Kindly follow the instructions for Task 1.

This part of the survey uses a table of questions, view as separate questions instead?

Task 1. Please indicate your level of agreement about prioritising the delivery of these non-pharmacological therapeutic interventions during the **acute phase of COPD exacerbation** based on your expertise, experience, and potential therapeutic benefits.

	1= Strongly disagree	2= Disagree	3= Neither agree nor disagree	4= Agree	5= Strongly Agree
Respiratory muscle training (Rd 1: Median 3 (Neither agree nor disagree), range 1-5)	○	○	○	○	○
Administering airway clearance devices (Rd 1: Median 4 (Agree), range 1-5)	○	○	○	○	○
Body exercises to increase muscle strength and tolerance in the lower limbs (Rd 1: Median 4 (Agree), range 2-5)	○	○	○	○	○
Depression management (Rd 1: Median 4 (Agree), range 2-5)	○	○	○	○	○

Delivering COPD disease education to carers (Rd 1: Median 4 (Agree), range 1-5)	○	○	○	○	○
Pain management (Rd 1: Median 4 (Agree), range 2-5)	○	○	○	○	○
Delivering education sessions regarding home oxygen use, safety, and adherence	○	○	○	○	○
Provide individualised therapeutic goal setting	○	○	○	○	○
Provide smoking cessation advice	○	○	○	○	○
Provide advice on vaccination	○	○	○	○	○
Provide nutritional advice	○	○	○	○	○
Provide advice on attending Pulmonary Rehabilitation Program	○	○	○	○	○
Provide advice on returning to work	○	○	○	○	○
Provide self-management and action plans	○	○	○	○	○

Please, provide any other therapy priority item or comments here:

Building Healthcare Professionals Consensus on Patients' Non-pharmacological Therapy Priorities During Both the Acute and Post-acute Phases of Chronic Obstructive Pulmonary Disease (COPD) Exacerbation (Second Delphi Round))

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50% complete

Section 2: The post-acute phase of COPD exacerbation therapy priorities list (non-pharmacological interventions)

In this section, you will see a list of several non-pharmacological priority interventions to be delivered during **the post-acute phase of COPD exacerbation** for which consensus has not been reached among healthcare professionals during Round 1. We now present these therapy priority interventions once again for re-evaluation together with newly incorporated therapy priority interventions generated from the respondent feedback from the first round.

Please note that next to each therapy priority intervention, you will see the first-round median score and the score range for the responses of the whole group. Additionally, interventions that do not include a median score or score range mean that they are newly incorporated.

Kindly follow the instructions for Task 2.

This part of the survey uses a table of questions, view as separate questions instead?

Task 2. Please indicate your level of agreement about prioritising the delivery of these non-pharmacological therapeutic interventions during the post-acute phase of COPD exacerbation based on your expertise, experience, and potential therapeutic benefits.

	Strongly disagree	Disagree	Neither agree nor disagree	Agree	Strongly Agree
Respiratory muscle training (Rd 1: median 3 (neither agree nor disagree, range 2-5)	○	○	○	○	○
Airway clearance therapy (Rd 1: median 4 (Agree), range 3-5)	○	○	○	○	○
Administering airway clearance device (Rd 1: 4 (Agree), range 3-5)	○	○	○	○	○
Pain management (Rd 1: median 4 (Agree), range 2-5)	○	○	○	○	○
Delivering education sessions regarding home oxygen use, safety, and adherence	○	○	○	○	○
Provide individualised therapeutic goal setting	○	○	○	○	○
Provide smoking cessation advice	○	○	○	○	○
Provide advice on vaccination	○	○	○	○	○
Provide nutritional advice	○	○	○	○	○
Provide advice on attending Pulmonary Rehabilitation Program	○	○	○	○	○

Provide self-management and action plans					

Please, provide any other therapy priority item or comments here:

Building HealthCare Professionals Consensus on Patients' Non-pharmacological Therapy Priorities During Both the Acute and Post-acute Phases of Chronic Obstructive Pulmonary Disease (COPD) Exacerbation (Second Delphi Round))

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75% complete

Results dissemination

For survey results dissemination, please provide your email below

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100% complete

Final page

Thank you for your participation in the survey

Appendix O

Delphi survey sample (Round two)

Building Health Care Professionals Consensus on Patients' Non-pharmacological Therapy Priorities During Both the Acute and Post-acute Phases of Chronic Obstructive Pulmonary Disease (COPD) Exacerbation (Second Delphi Round)

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Introduction

Thank you very much for participating in this Delphi study which aims to build healthcare professional consensus on the non-pharmacological therapy priorities of patients with chronic obstructive pulmonary disease (COPD) identified during both the acute and post-acute stages of COPD exacerbation.

This Delphi survey was developed based on a previous research study on patients experiencing acute COPD exacerbation to explore their perceived non-pharmacological therapy priorities during both the acute and post-acute stages of COPD exacerbation.

During the first round of the survey, we achieved consensus on prioritising the delivery of the following non-pharmacological interventions during the acute phase of the COPD exacerbation event:

Items achieved consensus in the first round - (The Acute-phase therapy priorities)
Fatigue management
Breathing control advice
Activity pacing advice
Airway clearance therapy

Walking exercises

Body exercises to increase muscle strength and tolerance in the upper limbs

Relaxation sessions

Anxiety management

Panic attack management

Facilitate attendance to patients support groups

Delivering education session about the COPD disease

Delivering education session about medication use and adherence

Sleep disturbance management

Items achieved consensus in the first round – (The post-acute phase therapy priorities)

Walking exercises

Breathing control advice

Activity pacing advice

Body exercises to increase muscle strength and tolerance in the upper limbs

Body exercises to increase muscle strength and tolerance in the lower limbs

Relaxation sessions

Anxiety management

Depression management

Panic attacks management

Facilitate attendance to patients support groups

Delivering education session about the COPD disease

Delivering education session about medication use and adherence

Delivering COPD disease education to carers

Fatigue management

Sleep disturbance management

Additionally, the survey respondents provided useful suggestions about the delivery of other prioritised therapy items, which were included in the second survey round. The items on which we achieved consensus were not included in the second round.

This survey round will take a maximum of 10 minutes to complete. You do not need to have completed Round 1 of the survey in order to take part in Round 2. The survey will remain open for two consecutive weeks.

Please note that in this survey round, we are not asking you to change your opinion if you strongly believe in it. The intention of this round is to give you the chance to re-evaluate your decisions about your previously ratings of items for which group consensus has not been achieved. This could be considered an opportunity to either confirm your initial opinion or modify the rating of an item that you were not sure about. Finally, it is a chance to evaluate the newly incorporated items that emerged from the first round of participants' feedback.

Additionally, please use the "Other" box under each section if you would like to suggest an extra therapy item to be included in the subsequent survey round or if you would like to provide feedback. This will help us to modify the survey items for the next round.

Your responses are anonymous to the group, and any identifiable information will be completely confidential and secured within our password-protected server. The completion of this survey will represent your consent to participate in this project.

Please do not hesitate to contact the study lead if you have any questions about this study.

Kind Regards,

Study lead

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This study has been reviewed and approved by the University of research committee, country, with ethics approval reference: 29960-bsaa5-ls:respiratorysciences.

Demographic data

What is your professional role?

- Medical Doctor
- Respiratory Nurse
- Allied Health Care Practitioner, e.g. Physiotherapist, Respiratory Therapist, Occupational Therapist...
- Advanced Critical Care Practitioner
- Other

How long is your Professional experience?

- 5-10 years
- 11-15 years
- 15-20 years
- >20 years

What is your Geographic Region?

- United Kingdom
- United States
- Australia
- Canada
- Other

Care Professionals Consensus on Patients' Non-pharmacological Therapy Priorities During Both the Acute and Post-acute Phases of Chronic Obstructive Pulmonary Disease (COPD) Exacerbation (Second Delphi Round))

25%

25% complete

Section 1: The acute phase of COPD exacerbation therapy priorities list (non-pharmacological interventions)

In this section, you will see a list of several non-pharmacological priority interventions to be delivered during **the acute phase of COPD exacerbation** for which consensus has not been reached among healthcare professionals during Round 1. We now present these therapy priority interventions once again for re-evaluation together with newly incorporated therapy priority interventions generated from the respondent feedback from the first round.

Please note that next to each therapy priority intervention, you will see the first-round median score and the score range for the responses of the whole group. Additionally, interventions that do not include a median score or score range mean that they are newly incorporated.

Kindly follow the instructions for Task 1.

This part of the survey uses a table of questions, view as separate questions instead?

Task 1. Please indicate your level of agreement about prioritising the delivery of these non-pharmacological therapeutic interventions during the **acute phase of COPD exacerbation** based on your expertise, experience, and potential therapeutic benefits.

	1= Strongly disagree	2= Disagree	3= Neither agree nor disagree	4= Agree	5= Strongly Agree
Respiratory muscle training (Rd 1: Median 3 (Neither agree nor disagree), range 1-5)	○	○	○	○	○
Administering airway clearance devices (Rd 1: Median 4 (Agree), range 1-5)	○	○	○	○	○
Body exercises to increase muscle strength and tolerance in the lower limbs (Rd 1: Median 4 (Agree), range 2-5)	○	○	○	○	○
Depression management (Rd 1: Median 4 (Agree), range 2-5)	○	○	○	○	○

Delivering COPD disease education to carers (Rd 1: Median 4 (Agree), range 1-5)	○	○	○	○	○
Pain management (Rd 1: Median 4 (Agree), range 2-5)	○	○	○	○	○
Delivering education sessions regarding home oxygen use, safety, and adherence	○	○	○	○	○
Provide individualised therapeutic goal setting	○	○	○	○	○
Provide smoking cessation advice	○	○	○	○	○
Provide advice on vaccination	○	○	○	○	○
Provide nutritional advice	○	○	○	○	○
Provide advice on attending Pulmonary Rehabilitation Program	○	○	○	○	○
Provide advice on returning to work	○	○	○	○	○
Provide self-management and action plans	○	○	○	○	○

Please, provide any other therapy priority item or comments here:

Building Health Care Professionals Consensus on Patients' Non-pharmacological Therapy Priorities During Both the Acute and Post-acute Phases of Chronic Obstructive Pulmonary Disease (COPD) Exacerbation (Second Delphi Round))

50%

50% complete

Section 2: The post-acute phase of COPD exacerbation therapy priorities list (non-pharmacological interventions)

In this section, you will see a list of several non-pharmacological priority interventions to be delivered during **the post-acute phase of COPD exacerbation** for which consensus has not been reached among healthcare professionals during Round 1. We now present these therapy priority interventions once again for re-evaluation together with newly incorporated therapy priority interventions generated from the respondent feedback from the first round.

Please note that next to each therapy priority intervention, you will see the first-round median score and the score range for the responses of the whole group. Additionally, interventions that do not include a median score or score range mean that they are newly incorporated.

Kindly follow the instructions for Task 2.

This part of the survey uses a table of questions, view as separate questions instead?

Task 2. Please indicate your level of agreement about prioritising the delivery of these non-pharmacological therapeutic interventions during the post-acute phase of COPD exacerbation based on your expertise, experience, and potential therapeutic benefits.

	Strongly disagree	Disagree	Neither agree nor disagree	Agree	Strongly Agree
Respiratory muscle training (Rd 1: median 3 (neither agree nor disagree, range 2-5)	○	○	○	○	○
Airway clearance therapy (Rd 1: median 4 (Agree), range 3-5)	○	○	○	○	○
Administering airway clearance device (Rd 1: 4 (Agree), range 3-5)	○	○	○	○	○
Pain management (Rd 1: median 4 (Agree), range 2-5)	○	○	○	○	○
Delivering education sessions regarding home oxygen use, safety, and adherence	○	○	○	○	○
Provide individualised therapeutic goal setting	○	○	○	○	○
Provide smoking cessation advice	○	○	○	○	○
Provide advice on vaccination	○	○	○	○	○
Provide nutritional advice	○	○	○	○	○
Provide advice on attending Pulmonary Rehabilitation Program	○	○	○	○	○

Provide self-management and action plans					

Please, provide any other therapy priority item or comments here:

Building Health Care Professionals Consensus on Patients' Non-pharmacological Therapy Priorities During Both the Acute and Post-acute Phases of Chronic Obstructive Pulmonary Disease (COPD) Exacerbation (Second Delphi Round))

75%

75% complete

Results dissemination

For survey results dissemination, please provide your email below

100%

100% complete

Final page

Thank you for your participation in the survey

Appendix P

Matrix synthesis of the key findings of the thesis research steps

Key stakeholders		Activity	Input	Output	Interpretation and recommendations
	Individuals with AECOPD	Semi-structured interviews	Provide deeper insight into the patients' AECOPD experience and explore the patients' perceived therapy options	**<u>Theme 2. Hospitalisation phase</u>** This theme encompasses information about the associated physical and psychological struggles experienced during the early phase of hospitalisation for an acute exacerbation of COPD event, and how patients experienced the hospitalisation period. This theme has three identified sub-themes.	In hospitalisation, there is a pronounced need for breathlessness management and management of other health problems such as balance issues, decreased mobility, pain, fatigue, mucus build-up and cough.
				<u>Sub-theme A) on-going physical struggles</u>	MPT model to target the disorienting dilemmas (physical limitations, flare-up symptoms) +ACT therapy (to target distress reduction, direct symptom control,

				This sub-theme grouped the experienced physical struggles during hospitalisation into three distinct categories. **I. <u>Primary symptoms</u>** This category included the symptoms that were very prominent in causing an ongoing physical struggle for the patients on their own and were continuously given first priority when mentioned by the participants. Those dominants were exacerbated breathlessness and chest tightness. *"My breathing, that's what I'm here for really" (participant ID8)* *"I think the breathlessness, which comes and goes really. Thursday and Friday I felt reasonably well. And up to lunchtime on Saturday. For instance, I could get from here to the bathroom and back without stopping. You know, I had to use the walker, which I've never used before. But since then, just making that short trip, I've lost my breath altogether and I need to use the, my reliever*	and improve disease management skills).

				inhaler about six times to try to stabilise it" (participant ID11). *“But now and again you get, something happens and you’re breathing heavy, and your levels go down. And I’ve come into hospital to help put it right. And I’ve found out putting me on steroids and things like that helps” (participant ID12).* **II. <u>Secondary symptoms</u>** This category included the symptoms that were expressed or linked by the participants as a consequence of suffering from the primary symptom (breathlessness) e.g., balance issues, decrease in mobility, pain, fatigue, mucus build-up and cough *"I just can't breathe, I just can't move.....No, just can't breathe. Everything you do is very painful" (participant ID9).*	

				“It’s hard work to keep breathing so you get very, very tired" (participant ID3). *"When you start to get lack of breath you start to get dizzy. You can be walking out somewhere, you can be keeling over. You can fall down a ditch and nobody's going to see you fall, anything like that" (participant ID10).* *"I had a reoccurrence of my breathing problems, Not being able to clear my throat. What it is, it's phlegm. Now they gave me tablets for it which helped a lot" (participant ID12).* *“I had a bad cough, sometimes it was green, sometimes it would be brown, and that I was really in a bad way” (participant ID 6).*	

				<u>Sub-theme B) Mental hardship and its associated psychological symptoms</u> In this sub-theme, participants discussed various mixtures of feelings and psychological symptoms that were presented during the acute COPD exacerbation event and hospitalisation. For example, some participants understandably reported a progressive build-up of pessimistic attitude about their recovery and prognosis due to the continuous deterioration of their health and running out of therapy options. *"I mean, I've suffered with COPD now since 2011, I think I was diagnosed. And I've always kept a very positive attitude; in fact friends and people have said they can't understand, even when I'm at my*	MPT + to target sense of vulnerability, loss of independence, loss of function. In addition, ACT therapy to manage the following: pessimistic attitudes, diminished self-worth, fear and anxiety related to breathlessness.

				lowest how positive I am. But that's beginning to wear a bit thin, particularly this time. I'm not lying here worrying myself sick about it, but it's there. Because I know for myself I'm getting worse, it's inevitable really. I had the lung volume reduction surgery in 2013, and that gave me two good years really. Last year the consultant looked at doing the left lung. But that's out the question now, I'd never survive the operation. So we've run out of options really, which again doesn't help the mental state" (participant ID11). Participants reported experiences that highlighted dismal feelings of uselessness. *"… the breathlessness, that's the feeling that you can't walk and you just feel useless really" (participant ID3).* Losing the sense of self independence	

				"I can't walk very far; I haven't been able to for some time now. And at the moment while I'm here (the hospital), I can't walk at all without the walker. Now I've never needed one before. I've now got two at home that the hospital have supplied. And I can't stand unaided, which I find quite hard because I've been able to do that. I've got to hold onto something if I stand up" (participant ID11). Feelings of vulnerability were also expressed due to the patient's current health state. *"You can be walking out somewhere, you can be keeling over. You can fall down a ditch and nobody's going to see you fall, anything like that" (participant ID10).* **<u>Panic and fear sensations</u>** Panic and fear sensations were mentioned as a result of not being able to breath as normally as the patient used to (a physical trigger).	Post discharge there is a need to manage the following: breathlessness, limited mobility. ACT therapy to address the associated negative thoughts related to uncertainty about prognosis and anticipation for future relapse of exacerbation. There is also a need to provide information as well as a need to provide help to control risk factors within a dedicated post-AECOPD PR pathway.

				“I tend to panic a lot when I can't breathe because that's what makes me come in in the first place" (participant ID1). *“I’ve got to the stage as well, I don’t want to do anything in case I start gagging, and I can’t breathe because it’s scary. Imagine you can’t breathe, it is very scary” (participant ID8)* **<u>Anxiety</u>** Anxiety was also present in the participant extracts and highlighted as a result of the awareness of their current health state and their understanding of the inevitable deterioration that come with the AE event. *"I get a bit anxious sometimes. I'm naturally optimistic and always have been, which helped. But as I say that is wearing a little bit thin now. I can't walk very far, I haven't been able to for some time now. And at the moment, while I'm here I can't walk at all without the walker" (participant ID11).*	

				<u>Overarching theme 3. Recovery journey</u> Within this theme, participants explained how they experienced the recovery process post their acute COPD exacerbation phase. From this, two distinct subsequent themes were identified a) continuous recovery (rapid or phased recovery) and b) complicated recovery. **Sub-theme B) Complicated recovery** Participants in this sub-theme articulated they could achieve full recovery from other related respiratory symptoms such as cough, but they continuously confirmed that breathlessness was always going to be present and viewed it as a never-ending struggle. *"Well, the longest I've stopped out of the hospital is about six weeks, and then I'm usually back in...Cough usually goes away, but the breathing doesn't. The breathing's always going to be poor" (participant ID7).* *"Some days I breathe easier than other days. And some days I'm really gasping for breath, I really*	

				struggle, really, really bad to breathe. Because my saturation levels, my oxygen levels drop right down. That's all part and parcel of the COPD" (participant ID8). *"It'll be ongoing. This COPD, it'll never go away" (participant ID10).* Uncertainty about prognosis and anticipation of another relapse of the symptoms was also evident within the patients' extracts. *"Well, I would hope the severe breathlessness will have largely altered before I leave, which is what happened last time. It won't disappear altogether. And I hope the walking will improve but I don't know" (participant ID11).* *"It'll come back again but you can't, you can't prognose when it's coming back" (participant ID2).*	

				Inability to control AECOPD risk factors (passive smoking) was identified as a determinant of complicated recovery. *"I'm all right for about a month, you know what I mean? Well it depends on the situation, where I am. If I'm round smokers.... unless I've got the right tools to cope with it, then I'll be all right. But if I haven't then that's when I start going downhill again" (participant ID1).* **<u>Overarching theme 6. Patients' perceived therapy options</u>** This overarching theme encompasses information about the patients care needs following discharge, and includes the following three branched sub-themes: **<u>Medication believers</u>**	Apply MPT model to transform and improve knowledge related to over-reliance on medications and modify negative perceptions resulting from previously formed experiential knowledge (meaning perspectives) to aid transformative learning and improve disease knowledge and awareness about all the therapeutic options.

				Some participants in this theme showed over-reliance on pharmacological therapy in that they believed drugs were the only thing that could help with their condition. *"The only thing is now my medication" (participant ID6)*. *"No, I can't really think of anything. As long as I don't run out of my inhalers and that I'm all right" (participant ID1).* *"With breathing, not a lot. It doesn't help I've got a catheter. I've got half a foot, so I'm disabled. Well, I get medication, and that's about it" (participant ID12).* **<u>Nothing can help</u>**	

				Some participants reported negative perceptions about any possibility of improving their lung condition, as they believed nothing could improve their progressed and deteriorated lung condition. *"My lungs are pretty badly damaged, so I wouldn't think there's any other therapies available (participant ID4).* *" I've got to the stage as well I don't want to do anything in case I start gagging and I can't breathe, because it's scary. Imagine you can't breathe, it is very scary.... I've got no idea. Do you know that I've past caring to be honest?" (participant ID8).*	

		Patient Survey	Exploring the most bothersome impact of AECOPD during the hospitalisation phase	The most bothersome AECOPD impact during hospitalisation were: **breathlessness, chest tightness, limited mobility** All of these exacerbation impact scored the highest median score (4) on the Likert scale	According to the stakeholders (patients), the most bothersome AECOPD impact during the acute phase (hospitalisation): **breathlessness**, chest tightness, **limited mobility**.
			Exploring the most bothersome impact of AECOPD post-discharge phase	The most bothersome AECOPD impact post-discharge were: breathlessness, limited mobility, exhaustion and tiredness. All of these impact of exacerbation scored the highest median score (4) on the Likert scale.	According to the stakeholders (patients) the most bothersome AECOPD impact during the post-hospital discharge phase: **breathlessness, limited mobility,** exhaustion, and tiredness (fatigue). AECOPD PR pathway with a focus on breathlessness, limited mobility and fatigue management.

			Patients' self-management for bothersome symptoms	The majority of the survey participants tried to avoid activities to prevent symptom deterioration (50%), and the second highest majority tended to ignore the symptoms (28%).	ACT therapy to modify avoidance behavioural and enhance self-management strategies.
			Exploring patients' activation levels Measured by PAM-13 Questionnaire	The majority of the participants were categorised within level two n=14 (37%). This level describes individuals as "have some knowledge, but large gaps remain". They believe health is largely out of their control but can set simple goals. This participant category adopted the following perspective "I could be doing more". The second highest proportion of the participants were categorised within level one n=12 (32%). In this level, participants are labelled as "disengaged and overwhelmed" and described as "individuals are passive and lack confidence, knowledge is low, goal orientation is weak, and adherence is poor. This participant category adopted the following perspective: "my doctor is in charge of my own health".	ACT therapy to transform from level one to action level.
			Multi-Dimensional Dyspnoea Profile (MDP) scale	During hospitalisation, out of the listed sensory descriptors the majority (70%) of the participants chose the "I am breathing a lot" choice to describe their breathing.	Breathlessness and feelings of frustration, anxiety.

				The highest median (IQR) of the sensory descriptor was for breathing a lot descriptor 4 (6-2), the highest median for the emotional descriptor frustrated was 3.5 (6-1). In our quantitative study, emotions induced by the breathlessness sensation reported from the MDP scale showed a similar anxiety median score (median 3) to the one found in a stable population, which could indicate that anxious emotions related to breathlessness sensation can be a long-standing problem for COPD individuals (Morélot-Panzini et al., 2016, Daynes et al., 2022).	
			AECOPD non-pharmacological therapy priorities during the hospitalisation phase	There were mixed results, but the highest proportion of the participants picked the following as therapy priorities: advice on breathing exercises, teach me how to pace myself, help with exhaustion and tiredness.	Introduce learning topics related to breathing, fatigue management through MPT (by detecting disorienting dilemmas and exploring therapeutic options to initiate meaning and perspective transformation, and augmenting knowledge by exploring therapeutic options.
			AECOPD non-pharmacological therapy priorities	There were mixed results, but the highest proportion of the participants picked the following as therapy priorities: train my breathing muscles, increase muscle	PR with topics concentrated on breathlessness management,

			post-discharge phase	strength all over my body, help with exhaustion and tiredness.	improving functional capacity and managing fatigue.
			Patients suggested strategies to enhance conventional pulmonary rehabilitation programme	(43%) preferred to make physical exercises easier to do. (36%) chose to start with education before joining any physical exercises. (36%) chose to concentrate only on exercises that made them less breathless.	Education first, easier exercises, breathlessness management as the driving force for the AECOPD PR pathway (as a core component).
			The patients' perceptions of the best timeframe to deliver therapy to their bothersome symptoms	The majority of the survey participant chose the following timing for the delivery of therapy: Breathlessness (32%) - immediately. Increase muscle strength and tolerance (48%) - in a month. Exhaustion and tiredness (40%) - few days. Psychotherapy (36%) - not at all. Knowledge (32%) - few days.	Breathlessness management and administered sooner than any other intervention.

	Healthcare professionals (HCP)	Delphi international survey	Explore the health care professionals' consensus about the patients' identified care priorities during hospitalisation phase	The highest HCPs level of agreement was given to prioritising non-pharmacological patient care interventions that focused on two core elements of patient care: **a) Improve patients' knowledge** with regard to the following aspects: breathing control advice, providing advice on attending PR, providing smoking cessation advice, providing advice on vaccination, **b) Mental wellbeing** by providing anxiety management.	Key stakeholders (HCPs) strongly agreed on prioritising AECOPD interventions during the hospitalisation phase that targeted knowledge and mental wellbeing (recommended intervention is MPT and ACT).
			Explore the healthcare professionals' consensus about the patients' identified care priorities post-discharge phase	The highest HCPs level of agreement was given to prioritising non-pharmacological patient care interventions that focus on four elements: **a) Knowledge,** e.g. activity pacing advice, delivering an educational session about COPD disease, medication use and adherence, breathing control advice, carer education, advice on PR and vaccinations. **b) Physical ability,** e.g., delivering walking exercises / all over body exercises to improve body strength and tolerance. **c) Psychological wellbeing,** e.g., anxiety, depression, panic attack management, patient support groups.	Key stakeholders (HCPs) strongly agreed on prioritising intervention elements that currently exist within conventional PR (these elements shaped the focus points of the AECOPD PR pathway).

				d) <u>Chronic illness management,</u> e.g., self-management and action plans, individualised goal setting.	
	Literature search	Systematic review	Review the effectiveness of interventions designed to increase PR uptake, adherence, and completion	The limited amount of evidence and the methodological and clinical heterogeneity of the studies prevented drawing firm conclusions. However, the narrative synthesis of the available evidence shows the following. **<u>PR Referral</u>** In Barker et al. (2021), there was a substantial increase in referral rate in the group who received the COPD discharge bundle from a practitioner involved in the delivery of PR, 60% versus 12% (p-value <0.001), compared to the group who received a referral from a practitioner with no involvement in PR delivery. In the Hopkinson et al. (2012) study, an increase in the number of referrals post initiation of the COPD bundle	COPD discharge bundle could yield positive results with PR referral.

				was 81 compared to 31 within the previous year, which represents a 158% increase in the PR referral rate. In Sewell et al. (2017), an audit study, which has the highest population size (1170 AECOPD post-discharge individuals) included in this review, showed an upward trend in referral rate from 39.7% in the first quarter of the study duration to 55.9% in the fourth quarter of the study. In the Barker et al. (2020) study, the authors used discharge bundle and verbal information about PR in both arms of the study, and only supplemented the intervention group with a patient co-designed video. This video showed that patients sharing their experiences with PR services resulted in a promising increase in referral rate within 28 days of hospital discharge with the whole groups included in the study n=138 (70%). However, the supplementation of this video did not add superior change when compared with the control group (Intervention n=70 (71%) versus Control n=68 (69%); P =0.754)	

				PR Uptake Results in the Barker et al. (2020) study showed that uptake rates within 28 days of hospital discharge were considered higher (Intervention n=33 (34%) VS Control n=40 (41%)) than what has been reported in observational studies without intervention: 21% in Jones et al. (2014) and 0.3% in Spitzer et al. (2019). However, in Barker et al. (2020), the intervention resulted in no significant effect (no change) between the groups P=0.370. Better PR uptake numbers were reported within 90 days of hospital discharge by Barker et al. (2020). The authors suggested adapting the intervention with further enhancement with regard to delaying the exposure to co-designed intervention until post-discharge as "6 of 15 of those interviewed had no recall of seeing the video" and provide additional counselling when delivering the video intervention to the patients. In Barker et al. (2021), the study authors suggested that the discharge bundle delivered via HCP involve PR delivery improved uptake to PR. The authors also suggested confirming the finding with RCT.	Intervention optimisations of Barker et al. (2020) (COPD discharge bundle + patient co-designed video) could yield positive results in PR uptake. In addition, results from the Cox et al. (2019) study of video testimonials portraying patients' experiences of PR within the stable COPD population improved patients understanding of PR, as 79% of participants expected PR would be beneficial to them and felt that they would be able to physically manage PR (Cox et al., 2019). This adds to the incentive to optimise the Barker et al. (2020) intervention and test it with subsequent studies. ********** Adaptation of Barker et al. (2021) (COPD discharge bundle delivered

				In Houchen-Wolloff et al. (2021), conventional PR uptake numbers were higher when compared to previously reported audit data from the same setting (Jones et al. (2014) and Spitzer et al. (2019)). The authors (Houchen-Wolloff et al., 2021), suggested that their intervention has helped in improving the participants' disease knowledge, and certain AECOPD sub-groups (who prefer and are willing to engage in a web-based programme) could benefit from using such intervention as a bridge intervention to the conventional Post exacerbation PR. **PR Adherence** Only one study reported adherence, namely Barker et al. (2020), and showed no significant results with adherence outcome. **PR Completion** High completion rates in both groups were in Barker et al. (2020). However, there was no significant change between the two groups (intervention group n=15 (46%) compared to 23 (58%) in control).	by HCP involved in PR delivery) intervention within future RCT study could improve PR uptake. ********** Web-based Space COPD could work as a bridge intervention to promote post-exacerbation PR uptake to a subset of the population who are willing to engage in web-based interventions.

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