Newcastle Chronic Obstructive Pulmonary Disease (COPD) Cognitive Behavioural Therapy (CBT) Care Study: A Randomised Controlled Trial

(Funded by the National Institute for Health Research)

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Abstract

Title - Randomised controlled trial (RCT) to identify if cognitive behavioural therapy (CBT) with respiratory nurses reduces anxiety in patients with chronic obstructive pulmonary disease (COPD). (Trial Registration - ISCRCTN55206395).

Introduction

Anxiety and depression are common comorbidities in COPD. The aim of this research is to identify if CBT delivered by respiratory nurses reduces anxiety in a large COPD population.

Methods

Study Design – Prospective RCT.

Sample Size - 112 for each arm were required.

Approach – 1,518 patients were approached: 279 were recruited.

Randomisation –Electronic randomisation was used.

Intervention – CBT with a respiratory nurse plus self-help leaflets.

Comparison – Self- help leaflets.

Main Outcomes -Primary outcome was symptoms of anxiety. Secondary outcomes were depression and quality of life.

Data collection – was undertaken by nurses blinded to treatment allocation.

Results

The groups were well matched at baseline. The CBT intervention achieved clinical and statistically significant change for all outcomes: HADS-Anxiety group mean change of 3.4 (SD 4.20) p=<0.001 CI 2.62- 4.17; HADS-Depression 2.20 (SD 3.62) p=<001, CI 1.53 – 2.87; CAT 2.7 (SD 6.36) p=< 0.001, CI 1.49 – 3.88 and EQ-5D utility group mean change of 0.08 (SD 0.31) p=0.007, CI -0.14 - -0.02 at 3 months. The leaflet group achieved a clinical and significant reduction in group mean change of 1.9 (SD 3.80) p= <0.001, CI 1.19 - 2.55 in HADS-Anxiety and CAT 2.06 (SD 5.34) p=<0.001, CI 1.09 – 3.04. The HADS-Depression group mean change was only statistically significant 1.07 (SD 3.55) p=0.001, CI 0.44 – 1.71. The EQ-5D utility scores group mean change of -0.003 (SD 0.31) p= 0.09 CI -0.06 – 0.05 which did not reach statistical or clinical significance.

Conclusion

Overall the CBT intervention was superior to the leaflet intervention.

Funded by: National Institute for Health Research (NIHR).

Declaration

I hereby declare that this submission is my own work. To the best of my knowledge and belief, it contains no material previously published or written by another person except where due acknowledgment has been made in the text. It does not contain material which has been accepted for the award of any other degree or diploma of the university or other institute of higher learning.

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Contents

Glossary of Abbreviations

ADL	Activities of Daily Living
ADIS-IV	Anxiety Disorders Interview Schedule (Version 4)
AIDS	Acquired immune deficiency syndrome
ANCOVA	Analysis of covariance
BAI	Beck Anxiety Inventory
BDI	Beck Depression Inventory
BLF	British Lung Foundation
BMI	Body mass index
CAT	COPD Assessment Test
CBT	Cognitive behavioural therapy
CES-D	Center for Epidemiologic Studies Depression Scale
CI	Confidence interval
COPD	Chronic Obstructive Pulmonary Disease
COPD-CEQ	COPD-Cognitive Error Questionnaire
CRQ	Chronic Respiratory Questionnaire
CTs	Controlled trials
DALY	Disability adjusted life years
DARE	Database of Abstracts of Reviews of Effects
EQ-5D	EuroQol -5D Questionnaire
EU	European Union
FEV1	Forced expiratory volume in 1 second
FVC	Forced Vital Capacity
GCP	Good clinical practice
GCSE	General Certificate of Education
GHQ	General Health Questionnaire
GOLD	Global Initiative for Chronic Lung Disease
GP	General Practitioner
HADS	Hospital Anxiety & Depression Scale
HNC	Higher National Certificate
HND	Higher National Diploma

HRQOL	Health Related Quality of Life
HSRS	Health Sickness Rating Scale
IAPT	Improving Access to Psychological Therapies
ICMJE	International Committee of Medical Journal Editors
ICS	Inhaled Corticosteroids
ILD	Interstitial Lung Disease
IMD	Index of Multiple Deprivation
IPBQ	Illness Specific Catastrophic Cognitions
IQR	Interquartile range
ISRCTN	International Standard of RCT Number
KSQ	Kellner's Symptom Questionnaire
LAMA	Long Acting Muscarinic Antagonist
MCID	Minimal clinical important difference
MMSE	Mini Mental State Examination
MRC	Medical Research Council
MRCQ	Medical Research Council Questionnaire
Muco	Mucolytics
N	Number
Nebs	Nebuliser
NHS	National Health Service
NICE	National Institute for Health and Clinical Excellence
NIHR	National Institute for Health Research
NVQ	Non-Vocational Qualification
O2 Sats	Oxygen Saturations
QOF	Quality Outcome Framework
QOL	Quality of life
P	Probability
PD4	Phoshodiesterase 4 Inhibitors
PhD	Doctor of Philosophy
PPI	Patient and Public Involvement
PR	Pulmonary Rehabilitation

PROMS	Patient-reported outcome measures
PSQI	Pittsburgh Sleep Quality Index
RCT	Randomised Controlled Trial
RDS	Research Design Service
RVI	Royal Victoria Infirmary
SABA	Short-Acting Beta Agonist
SAMA	Short-Acting Muscarinic Antagonist
SCL-90	Symptom Checklist-90
SD	Standard Deviation
SF-36	Short form 36
SGRQ	St Georges Respiratory Questionnaire
SIP	Sickness Impact Profile
STAI	Stait Trait Anxiety Inventory
TLCO	Transfer Factor
TSC	Trial Steering Committee
UK	United Kingdom
VAR 36	Short Form 36 for Veterans
VAS-A	Visual Analogue Scale – anxiety
VAS- D	Visual Analogue Scale – Depression
WHO	World Health Organisation

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Thesis Overview

This thesis describes research undertaken to address symptoms of anxiety and depression in patients with COPD. The first chapter provides an introduction to COPD to set the scene. The impact of COPD is considerable. Not only does COPD lead to debilitating physical symptoms, but it also has a significant impact on psychological well-being and symptoms of anxiety and depression are common. Chapter two explores the important psychological impact of this progressive disease. A literature review was completed on the psychological treatment of anxiety and depression in COPD and is shown in chapter three. Conclusions of previous research clearly suggests there is a need for a well powered randomised controlled trial (RCT) to evaluate the effectiveness and acceptability of CBT among patients with COPD. The aim of this research is to address the gap in the literature by conducting an appropriately designed RCT. In chapter four I have described the development of a novel CBT based intervention used in this study to address symptoms of anxiety. The development of the CBT model was underpinned with theoretical and clinical insight into the psychological impact of COPD and experience using CBT with COPD patients. The CBT model used was developed and refined over many years before funding from the National Institute for Health Research was awarded to embark on this research.

Chapter five describes the research methods used to conduct this study and is followed by the results and discussion. This research is unique in that respiratory nurses have been trained to deliver the CBT intervention rather than mental health practitioners. Respiratory nurses have expertise in COPD from a physical perspective. Combining additional skills in psychological care may be a better model of care for patients with complex physical health needs. As with most non-drug interventions the CBT intervention is inherently complex. CBT has a number of components, the intensity of the intervention will vary depending on patient needs, a number of nurses' deliver the CBT and importantly it is commonly difficult to identify which interventions are the most effective. The final chapter proposes implications for practice and future recommendations for further research. A number of appen-

dices are located at the back of the thesis and will be referred to in the text. Appendix 11 includes a summary of publications, presentations and webinar's completed since commencing this PhD.

Chapter 1 - COPD

1.1 Introduction

In the United Kingdom (UK) life expectancy is increasing and continues to improve (1). However, as people are living longer the prevalence of health problems is growing. Already 30% of the population with long term conditions accounts for 70% of National Health Service (NHS) spending (2). A term used to describe ill-health or disease burden is 'disability adjusted life years' (DALYs). DALYs reflect the number of years lost due to ill health, disability or early death (3). The UK has poor rankings in terms of DALYs in five out of 30 disease areas assessed including heart disease, breast cancer, lung cancer, respiratory infections and COPD (1). COPD is a very common long term respiratory condition and a major public health issue causing significant disability and mortality worldwide (4). Poor physical health increases the risk of mental illness (5). Increasing evidence indicates that there is a close relationship with obstructive lung diseases such as asthma, chronic bronchitis and emphysema with mental health problems (6). One large Canadian study suggests that adults from a general population with COPD have an increased risk of major anxiety and depression disorders compared to those without COPD with odds ranging from 1.9 to 3.8 (7). The risk may well be higher in the North East due to a high prevalence of smoking which is a major cause of COPD.

For many years there has been poor integration of physical and mental health which it is argued merely reinforces stigma, constrains physical health outcomes, and impairs broader economic performance (5). There is increasing evidence that integrating mental and physical care for people with long-term conditions can improve both physical and mental health and reduce costs (5). The aim of this research is to identify if an intervention delivered by respiratory nurses can help reduce symptoms of anxiety and depression in a large COPD population.

1.2 Definition of COPD

COPD is a preventable disease characterised by persistent airflow limitation and is associated with chronic inflammatory changes (8). Chronic bronchitis results from inflammation which causes structural changes and narrowing of the large airways. Emphysema involves destruction of lung tissue causing alveoli to lose their elasticity. This reduces the support of

the airways and results in obstruction. Physiologically, emphysema is characterised by a reduction in the transfer of carbon monoxide and oxygen within the lungs (8). These pathological changes lead to air trapping and progressive airflow problems resulting in breathlessness and other characteristic symptoms of COPD (8). With chronic bronchitis and emphysema the work of breathing is increased and ventilatory capacity is reduced (9).

Airflow limitation is best measured by spirometry, as this is the most widely available reproducible test of lung function (8). Spirometry measures how much air can be exhaled in one second (forced expiratory volume in one second or FEV_1) and how much air can be exhaled fully in one breath (forced vital capacity or FVC). Airway obstruction has to be established by measuring the FEV_1/FVC ratio (8). A FEV_1/FVC ratio of <70% is indicative of COPD (8). Unfortunately, significant airflow obstruction is often present before the patient is aware of it (10).

1.3 Classification of COPD

There are a variety of classification systems for COPD; many are based on lung function criteria. At the onset of this study one of the best known scoring systems for COPD in the UK was the National Institute of Clinical Excellence (NICE) COPD Guidelines which were updated in 2010 (10). The NICE criteria for severity of COPD is presented in table 1.

Table 1 NICE Spirometric Classification of COPD (10).

COPD Classification	FEV1	FEV1/FVC Ratio
Mild	≥ 80% predicted	<0.70
Moderate	≥50 - <80 predicted	<0.70
Severe	30 - <50% predicted	<0.70
Very Severe	<30 or >50% predicted with chronic respiratory failure	<0.70

A major drawback of using spirometric classifications is that FEV_1 is a poor descriptor of disease status (8). More recently classifications have encompassed spirometric and clinical phenotypes. Newer classification systems are recommended by The Global Initiative For Chronic Obstructive Lung Disease (GOLD) which include symptom burden, exacerbation frequency, activity limitation, future risk of disease progression and a combined assessment (8). The GOLD classification system can be found in table 2 (8).

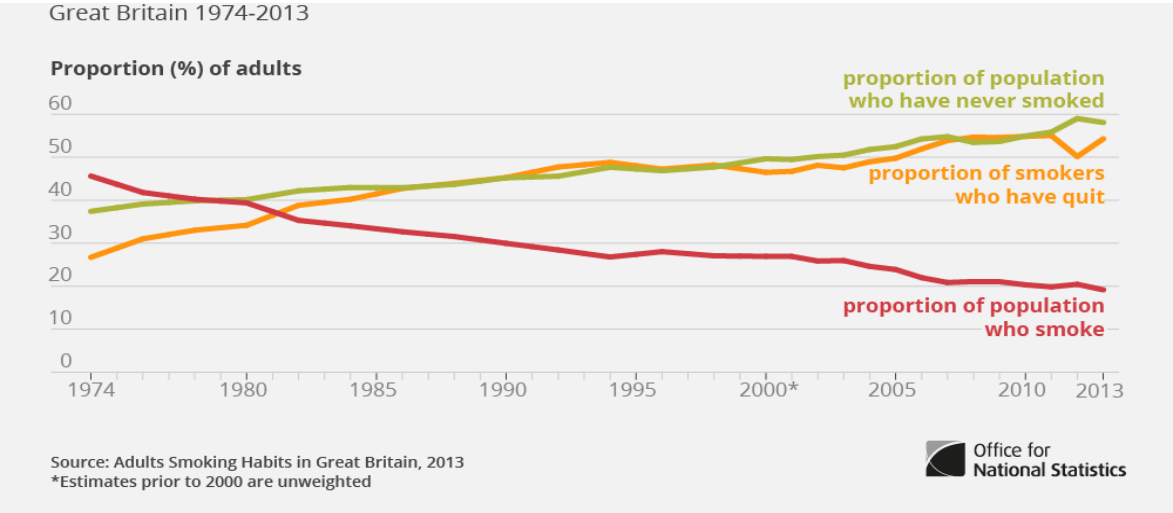
Table 2 – GOLD Classification system of COPD (8).

Patient	Characteristics	Spirometric Classification	Exacerbations a year	Medical Research Council Breathlessness Score	CAT Score
A	Low risk.				
	Less symptoms	FEV1 ≥ 80% predicted	≤ 1	0-1	<10
B	Low risk.				
	More symptoms	FEV1 ≥ 50 - <80%	≤ 1	≥ 2	≥10
C	High risk.				
	Less symptoms	FEV1 ≥ 30 - <50%	≥ 2	0-1	<10
D	High risk.				
	High symptoms	FEV1 < 30%	≥ 2	≥ 2	≥10

1.4 Causes of COPD

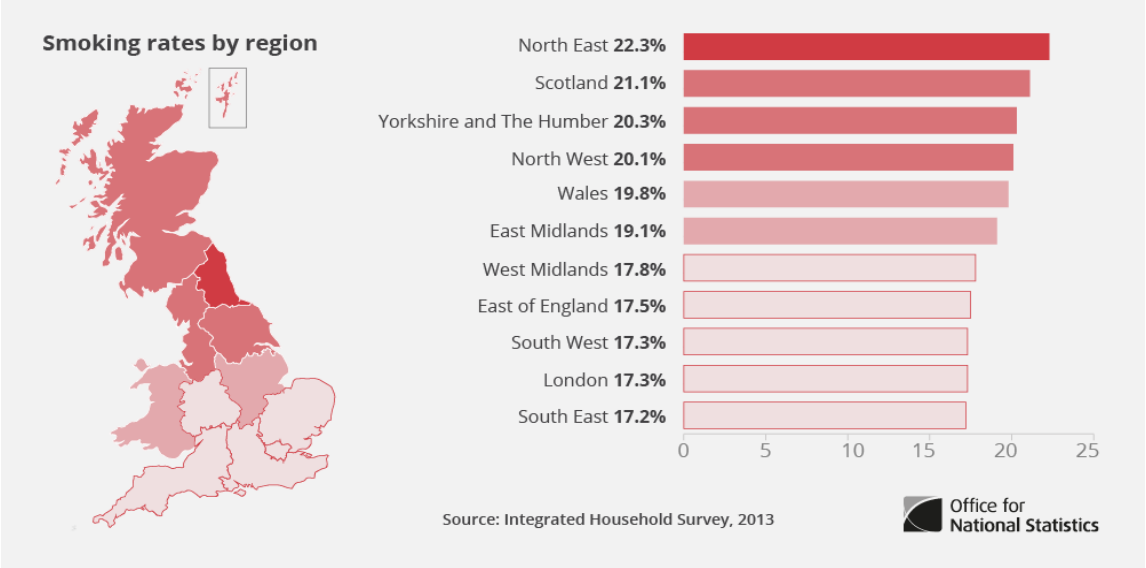
The main cause of COPD is smoking (10). In 1974, just under 50% of adults in the UK smoked (1). Thankfully the prevalence has decreased over the years. The change in smoking habits is presented in figure 1 from data from the Office for National Statistics (11).

Figure 1 - Change in cigarette smoking habits from 1974 – 2013 from Office of National Statistics (11).



In the North East the prevalence of smoking has reduced to 22.3% but it remains higher than the national average of 19.5% (12). Data from the office for National Statistics highlights the smoking rates by region can be seen in figure 2 (11).

Figure 2 - North East prevalence of adult cigarette smokers (11).



Source: Office of National Statistics (11)

In routine and manual workers in the North East, the prevalence of smoking is as high as 31% which is the second highest in the country (13). Stopping smoking can prevent further deterioration of lung function but it cannot repair the damage that has already occurred (14). As a result it is imperative to help patients to stop smoking (15). In clinical practice smoking is often recorded in terms of 'pack years'. One pack year is equivalent to smoking twenty cigarettes a day for one year. So for example, if a patient smoked 20 cigarettes a day for one year this is documented as one pack year (16). If a patient smokes 20 cigarettes for 20 years that is documented as 20 pack years.

There are other causes of COPD including exposure to biomass fuels, workplace exposure to dust and fumes, history of repeated lower respiratory-tract infections during childhood, chronic asthma, and history of pulmonary tuberculosis, intrauterine growth problems, and poor nutrition. Whilst the mining industry is no longer in existence in the North East, occupational dust such as coal dust (17) and pollution are said to be particularly relevant causes of COPD in the North East region (13). In a minority of patients deficiency of anti-protease enzymes can also cause the development of COPD (18).

1.5 Socioeconomic status and COPD

There is strong evidence that the risk of developing COPD is inversely related to socioeconomic status (19). This may be due to more smokers coming from lower socioeconomic and disadvantaged groups (20). When reviewing the literature there are several definitions of socioeconomic status. In general, the term socioeconomic status encompasses several elements including income, education, occupation (including employment status), location of residence, housing (including home amenities), an individual's social standing and may also include participation in social organisations (21). Whilst socioeconomic status is often associated with poverty it is closely linked to health as it is an important determinant of health and premature death (21). There are a number of studies that have demonstrated a positive relationship between socioeconomic status and pulmonary function. Both spirometry measures (FEV_1 and FVC) and measurements of other lung function tests such as transfer factor are reduced with low socioeconomic status (21, 22).

Smoking contributes to the adverse effects of poverty but other factors may contribute (21). What is not clear is whether the risk of COPD reflects exposure to pollutants, crowding, poor nutrition, infections or other factors that are related to low socioeconomic status (8). In reality, the link between socioeconomic status and COPD is complex (23), likely to be multifactorial and includes several factors including smoking, prenatal exposures, more frequent lower respiratory tract illness in childhood, housing conditions, air pollution, environmental tobacco smoke, diet, genetic factors and occupation (19).

COPD is closely associated with deprivation and higher rates are seen in deprived urban communities (24). In a large cross-sectional study involving 422 general practices in England, COPD was found in the most deprived people (31.1 per 1000 patients; 95% CI=28.4 to 30.1) and those living in the North East of England had the highest prevalence (25). Locally the health of people in Newcastle upon Tyne is varied compared to the England average and deprivation is higher than the national average (26). Younger patients with COPD tend to live in the most deprived areas (24).

A large national audit of COPD admissions across England calculated deprivation using the Index of Multiple Deprivation (IMD). The results showed that COPD patients admitted to

hospital were notably deprived in respect to income, employment, health deprivation/disability, education, skills and training (24). Prescott and Vestbo (1999) highlight that the risk of admission to hospital for COPD was threefold higher for people of the lowest socioeconomic group compared to the highest even when adjusted for smoking (19).

1.6 Symptoms of COPD

Many people are unaware they have COPD as they may not experience symptoms in the early stages of the disease. Chronic cough and sputum production may precede the development of airflow limitation by many years. The chronic cough may be intermittent and may be unproductive (8). Conversely, significant airflow limitation may develop without chronic cough and sputum production (8). However, as the disease progresses the cardinal symptoms of COPD are cough, sputum production, and breathlessness (8). These symptoms are progressive in nature. Breathlessness is an important feature of cardio-respiratory disease. (27). Breathlessness is not simply an automatic physiological function but a complex interaction between physiological, psychological, social and environmental factors (28). The mind has the power to alter breathing patterns temporarily and dysfunctional breathing patterns can develop (9). If patients focus on their breathing this can make matters worse. Breathlessness has much in common with pain; both are highly subjective sensations (29). Typical COPD patients describe their breathlessness as a sense of increased effort to breathe, heaviness, air hunger or gasping (30). Breathlessness is a major cause of disability and anxiety (8) and managing breathlessness is a fundamental goal of treatment in COPD (28).

Assessing breathlessness can be challenging. One method of assessing breathlessness is to use the Medical Research Council (MRC) Breathlessness scale (presented in table 3) originally developed by Fletcher in 1952 (31). The MRC breathlessness scale is a self-reported scale that quantifies the disability associated with breathlessness rather than the severity of breathlessness (27). The scale has been used for many years and is recommended by the National Institute of Clinical Excellence in the Quality Standards for COPD (32). The scale does not quantify breathlessness, instead it provides a range of respiratory disability from none (grade 1) to almost complete incapacity (grade 5) (27). The scale is also not sensitive to changes in breathlessness (33). However, a recent report has found that the MRC score is only being recorded in 60% of patients admitted to hospital (24).

Table 3– MRC Breathlessness Scale (31)

Grade	Degree of breathlessness related to activities
1	Not troubled by breathlessness except on strenuous exercise
2	Short of breath when hurrying on the level or walking up a slight hill
3	Walks slower than most people on the level, stops after a mile or so or stops after 15 minutes at own pace
4	Stops for breath after walking about 100 yards or a few minutes on level ground
5	Too breathless to leave the house, or breathless when undressing

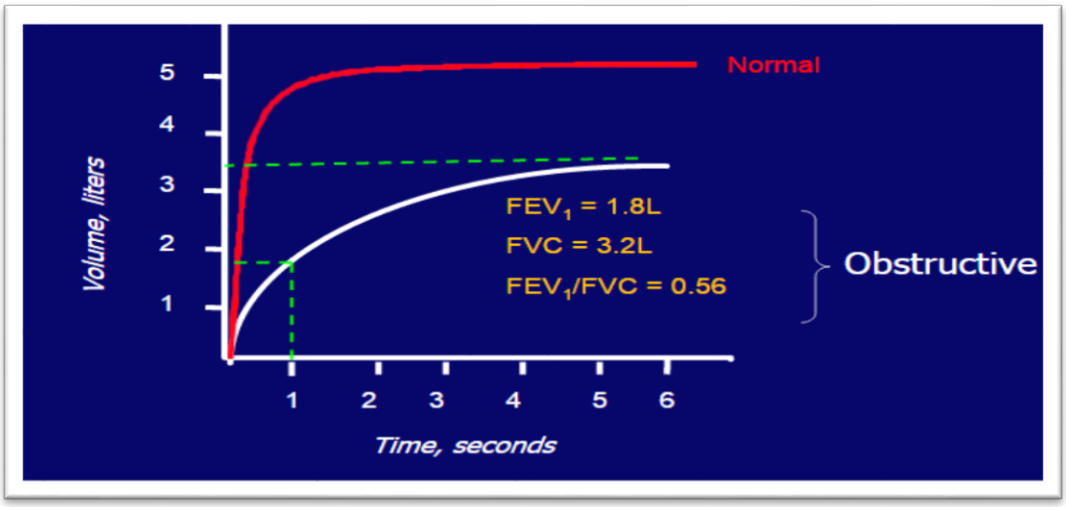
In addition to breathlessness, systemic effects can occur. COPD is a multi-system condition and other symptoms include fatigue, effort intolerance (10), skeletal muscle weakness and weight loss (34). COPD may also initiate or worsen comorbidities such as ischaemic heart disease, osteoporosis, normocytic anaemia, diabetes, metabolic syndrome and depression (8). Patients are also prone to respiratory failure, often resulting in admission to hospital (35).

1.7 Diagnosis of COPD

There is no single diagnostic test for COPD. The diagnosis is made on the basis of symptoms, clinical history, risk factors and lung function tests (8, 10, 36). Spirometry is required to make the diagnosis (8). The presence of a post-bronchodilator FEV_1/FVC ratio less than 70% confirms the presence of persistent airflow limitation found in COPD. This criterion has been used in numerous clinical trials and is routinely accepted in clinical practice. However, the use of airflow limitation will result in more frequent diagnosis of COPD in the elderly and less frequent diagnosis in adults younger than 45 years of age (37). Although COPD is defined on the basis of airflow limitation, in practice the decision to seek medical help is usually determined by the impact of a symptom on a patient's life. A person may seek attention because of a chronic symptom or because of a first exacerbation or worsening of COPD (8). An exam-

ple of spirometry from a patient with COPD can be seen in figure 3 (8). According to the Department of Health, one in eight people over 35 has COPD that has not yet been identified or diagnosed, and over 15% are only diagnosed when they present to hospital as an emergency (38). Notably there are some variants of emphysema where there is significant lung destruction but little or no airflow limitation. Such patients would not be deemed as having COPD within all COPD classification systems.

Figure 3– Example of obstructive spirometry from Global Initiative for Chronic Obstructive Lung Disease (8)



Source: Global Initiative for Obstructive Lung Disease (8).

1.8 Prevalence

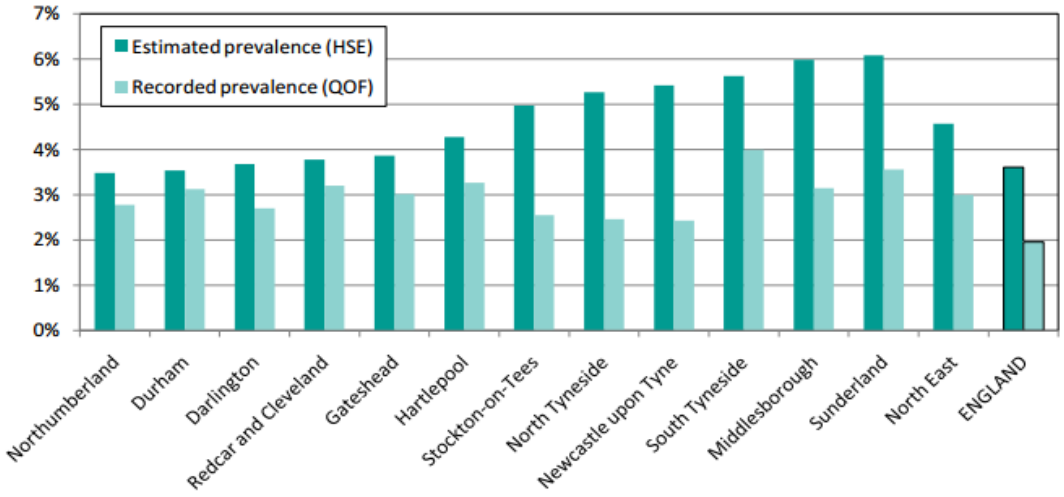
It is well established that smoking is the single most important cause of COPD. Whilst the incidence of smoking is well documented, surprisingly little is known about the true prevalence of COPD (39) although more studies are emerging. It is estimated that approximately 64 million people are affected by COPD globally (3). There is a linear increase in the prevalence of COPD with age, irrespective of smoking status (26). As a result of the aging population, the prevalence and mortality rates will increase in the coming decades (3). Prevalence rates in men have reached a plateau but are increasing in women (40). Approximately 974,999 patients were recorded on General Practitioner (GP) COPD registers for 2008 (41). It is estimated that approximately 2,000,000 people remain undiagnosed (42). This is equivalent to 13% of the population of England aged 35 and over (39). The figures on prevalence in the UK need to be interpreted with caution as the accuracy of data depends on clinical

case finding and recording by general practices which is often poor (42). This is certainly the experience locally. Under diagnosis may be due to a number of factors such as:

- People not recognising the symptoms which may have developed gradually over a long period of time (42). This is particularly likely for patients with mild COPD, who may not realise their cough or breathlessness is a sign of something more serious (43).
- People consider symptoms are due to smoking and think nothing can be done to help (37).
- Health care professionals treat symptoms but fail to diagnose an underlying lung disease (37). It has been suggested that some patients may attend their general practice but not receive a diagnosis due to the testing and clinical interpretation required (43).
- Primary care may lack resources to undertake opportunistic case finding which can be cost effective (44).

The North of England has the highest prevalence of COPD in England with a prevalence rate of 4.6% (43). Recorded prevalence by local authorities in the North East can be found in figure 4. One contributing factor will undoubtedly be the low socioeconomic status of the area.

Figure 4- Recorded COPD prevalence in 2010 based on (Quality Outcome Framework (QOF) data from 2009/2010) compared with estimated prevalence (Health Survey of England, 2001) for 16 + populations in Local Authorities in the North East of England from North East Public Observatory (43).



Source: North East Public Observatory (43).

1.9 Mortality

There is increasing evidence suggesting that COPD increases the risk of mortality (45). Data from the World health Organisation (WHO) suggests that death rates from respiratory disease in the UK are almost double the European Union (EU) average (3). For the first time there were over half a million deaths registered in England and Wales in 2013 (41). In 2013 there were 27,000 deaths in England and Wales attributable to COPD (11). Mortality from COPD is expected to be the third leading cause of death by the year 2030 (3). Premature death from respiratory disease is a problem in the North East Region with the main cause of mortality reflecting its industrial legacy of mining and ship-building and high smoking rates (12). In the North East life expectancy for men is 77.5 and women is 81.4, both of which are lower than the average in England which is 79.2 for men and 83 for women (26).

With very severe disease five year survival is 30% in men and 24% in women (10). If you are admitted to hospital with an exacerbation of COPD your mortality can be affected. Of those patients who are admitted, 15% will die within three months (42), 25% will die within one year (10) and following an exacerbation the five-year mortality is approximately 50% (46). The place of death is also important. Research indicates that patients with COPD are less

likely to engage in end of life care planning (47). In addition, it has been suggested that people dying from respiratory diseases were much more likely to die in hospital than at home or in a hospice (48).

1.10 Management of COPD

Once COPD has been diagnosed, effective management should be based on an individualised assessment of their symptoms and future risks (8). COPD is treatable but not curable. The management of COPD has improved over the last twenty years. COPD treatment has traditionally focused on lung function but it is now recognised that FEV_1 alone is a poor descriptor of disease status (8). The Outcomes Strategy for COPD and Asthma set out bold objectives to improve the quality and outcomes for people with COPD and Asthma (38). In the strategy a key objective is to enhance quality of life (QOL) for people with COPD by providing early identification, diagnosis, treatment with proactive care and management of all stages of the disease (38). Achieving this objective may be very difficult given the limited resources in the NHS. The goals of effective management of patients with COPD have recently been revised in the GOLD Strategy (8). Two fundamental objectives of treatment have been identified. The first objective is relieving and reducing the short term impact of symptoms. The second is reducing the long-term impact of COPD such as exacerbations (8).

1.10.1 Pharmacological treatment

Pharmacological therapy in COPD is used to reduce symptoms, reduce the frequency and severity of exacerbations, and improve health status and QOL (8). Recommendations for suitable models for pharmacological management have been produced by a number of organisations including the NICE (10) and the recently updated GOLD Strategy (8). Nowadays there are significantly more pharmacological and non-pharmacological treatments available. A step-wise approach is generally used. Bronchodilators are recommended and include beta-agonists and anti-cholinergic therapies which may be long or short-acting depending on the patient's symptoms (8). Based on efficacy and side effects, inhaled treatments are preferred over oral preparations (8). Long term treatment with inhaled corticosteroids is recommended for patients with severe and very severe airflow limitation and for patients with frequent exacerbations (or worsening of COPD) that are not adequately controlled by long-acting bronchodilators (8). Pharmacological treatments commonly used to treat exacerbations

of COPD are short-acting bronchodilators, oral corticosteroids and antibiotics. Depending on the clinical condition of the patient respiratory support may be required including oxygen therapy, ventilator support may be provided using either noninvasive ventilation (with a nasal or facial mask) or invasive ventilation (by oro-tracheal tube or tracheostomy) (8). In addition, appropriate fluid balance with attention to the use of diuretics, anticoagulants, nutrition and the treatment of comorbidities is also recommended (8).

1.10.2 Pulmonary rehabilitation

A vast amount of research has been undertaken into pulmonary rehabilitation over the years with the bulk of evidence based on patients with COPD (49). Pulmonary rehabilitation is an evidence based treatment recommended as a key management strategy for patients with COPD (8, 10, 42). One of the main aims of rehabilitation is to improve patient symptoms (49). Patients who are most likely to benefit from pulmonary rehabilitation are those who are limited by breathlessness or muscle fatigue (49). Pulmonary rehabilitation programmes include individualised exercise and disease-related educational sessions (49). A key component of pulmonary rehabilitation is physical activity. Physical activity is extremely important as inactivity has been linked with reduced survival, poorer QOL and increased healthcare utilisation (50). However, there are also psychosocial benefits of pulmonary rehabilitation (49). Given the complex nature of pulmonary rehabilitation, numerous outcome measures are used to capture changes in exercise capacity, QOL, symptoms and more recently levels of anxiety and depression (49). These outcome measures are important to monitor patients' progress before and after pulmonary rehabilitation.

Unfortunately many patients decline to attend pulmonary rehabilitation. This may be for a number of reasons including transport or acute illness. However, some patients have difficulty understanding the rationale or benefits behind the referral for pulmonary rehabilitation. Others may have strong beliefs about their ability to exercise given their physical problems or lack the motivation to attend (49). Anxiety and depression co-morbidity in patients with COPD predicts poor adherence to pulmonary rehabilitation (51). In 2011 the results of a large study demonstrated that anxiety and depression were related to worse outcomes not only at the start of pulmonary rehabilitation, but also at the end (52). It has been suggested that CBT may improve uptake and completion of this important treatment (49) and a

large Health Technology Assessment multi-center randomised controlled trial is planned to start 2015/2016, of which I am co-applicant.

1.11 Exacerbations and Hospital Admissions

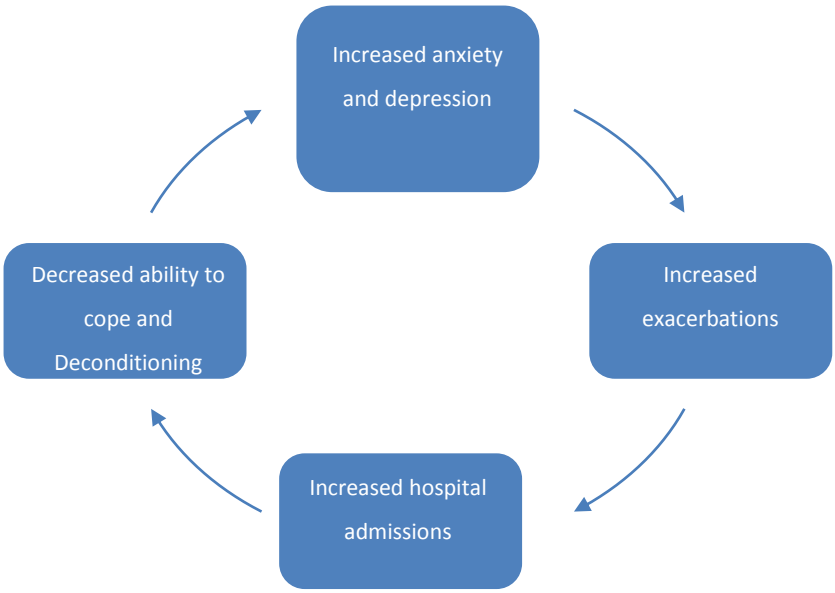
An exacerbation of COPD is defined as an acute event characterised by a worsening of the patient's respiratory symptoms that is beyond normal day-to-day variations and leads to a change in medication (8). Exacerbations are common, particularly those with severe disease (38). Exacerbations become more frequent (two or more) and more severe as the severity of COPD increases (53) resulting in reduced physical activity (54), poorer QOL (55) and increased risk of death (56). Unfortunately exacerbations contribute to further deterioration of lung function. The more frequent the exacerbations the greater the decline (57). The best predictor of having frequent exacerbations is a history of previous treated exacerbations and the risk also increases as airflow limitation worsens (8). There appears to be an independent COPD phenotype of patients who exacerbate frequently and this has significant implications for targeting exacerbation prevention strategies (53).

Exacerbations are a common cause of hospital admissions. COPD is responsible for approximately 10% of all medical admissions (38), the second most common cause of emergency admissions to hospital and one of the most costly inpatient conditions to be treated by the NHS (38). Reducing emergency admissions is a national and local priority as resources within the NHS are very limited (42). Over the last few years there has been an increasing number of community services tasked to prevent hospital admissions. Despite these services COPD admissions continue to increase. It is estimated that COPD admissions have increased 13% between 2008 and 2014 (24). Whilst the number of hospital admissions in Newcastle upon Tyne NHS Hospitals Foundation Trust is decreasing, there were 263.4 admissions per 100,000 of the population (58). A proactive Community Chest Outreach Team in Newcastle may account for the fall. However, it is entirely appropriate for some patients with COPD to be admitted, for example, with severe exacerbations, pneumonia or other complications. Patients are also prone to respiratory failure, requiring admission to hospital (35). The percentage of females admitted with COPD exacerbations has risen slowly since 2003 with 51% of admitted cases in an audit completed in 2014 (24).

Long term conditions such as COPD are amongst the most common reasons for readmissions in the North East Region (12). In 2011/2012 the 30 day emergency readmission rate for patients in the North East region was higher than that of any other health region in the country (12). Readmissions may be clinically appropriate but some admissions are considered to reflect ineffective patient management (12). A variety of factors may contribute to avoidable readmissions including inappropriate discharge and lack of care within the community. However, a study in 2003 identified that a low FEV_1, low levels of physical activity and passive smoking (or indeed actual smoking) were risk factors of readmission (59).

However, there are some admissions where the main cause of admission is anxiety and panic. It has been suggested that there may be a relationship between anxiety and depression and exacerbations of COPD (60, 61). Whilst the literature was not conclusive, a recent systematic review in 2014, suggested that anxiety and depression increased the likelihood of hospitalisation, prolonged the length of stay and resulted in a greater risk of mortality post discharge (57). A vicious cycle can develop (figure 5).

Figure 5 – Diagrammatic representation of the theoretical relationship between anxiety and depression and acute exacerbations of COPD that result in hospital admissions or readmission (57).



It is important to remember that many patients have transitory mood symptoms during exacerbations that improve spontaneously as their physical state improves (57). The challenge

is to identify those who have more permanent and sustained anxiety and depression; to develop ways of screening and implementing effective management strategies to alleviate the impact of these comorbidities; and enable patients to cope better with their COPD (57).

1.12 Impact on QOL

As COPD cannot be cured, treatment has focused on managing symptoms and improving QOL (8). QOL is a term used to describe 'the standard of health, comfort, and happiness experienced by an individual' (62). The term 'health related QOL' (HRQOL) or health status as it is often referred to, is also used and is more specific to health (63). As improving HRQOL is an important goal in COPD management assessing health status is now established to assess therapy for patients with chronic lung disease (64). More recently patient-reported outcome measures (PROMS) have been used to determine outcome for healthcare. PROMS are intended to reflect outcomes relevant to patients and are increasingly being used for healthcare quality improvement. Essentially, PROMS are health questionnaires asking patients to report on their symptoms and QOL (65).

In COPD, QOL and health status are determined by factors including gender, disease severity, lung function, body mass index, smoking, symptoms, comorbidity, anxiety, depression and exacerbations (63). Two of the most common and least treated comorbidities of COPD are anxiety and depression (66). The impact of pulmonary disease on activities of daily life is adversely affected by anxiety and depression even after controlling for the effects of breathlessness (67). Anxiety and depression has a significant impact on QOL and affects outcomes such as pain, physical function and general health (68). Disease specific outcomes such as mastery of their illness and symptoms of breathlessness are also affected (68). As a result of physical symptoms of COPD patients become less active. For some patients activity levels can reduce but often patients actually avoid activities that induce breathlessness resulting in physically deconditioned and a vicious cycle develops.

Symptoms of COPD lead to a gradual progression of disability over many years that may be accelerated in a stepwise fashion after exacerbations or hospitalisation. As a consequence day to day functioning is affected and QOL is reduced. Patients focus on feeling unwell and their inability to perform activities of daily living. Feelings of frustration, anxiety and depres-

sion can follow. It is clear that patients cope with COPD in many ways. Some people perceive that their lives are almost untouched by COPD, yet others are significantly disabled (63).

1.13 Compliance with medication and self-management

Each year millions of pounds are spent on drug treatment for COPD. Untreated anxiety and depression has been shown to have major implications for compliance with medical treatment, due to the effects on cognitive functioning and the decreased effectiveness of self-management activities (69, 70). An increasing number of people with COPD living with significant disability have to 'self- manage' their conditions on a daily basis. It has been suggested that helping people to care for themselves more effectively can improve their physical and mental well-being (2). There appears to be evidence that supporting self-management can have a positive impact on people's clinical symptoms, attitudes, behaviours, QOL and patterns of healthcare resource use (2). In COPD, 'self-management' often refers to the use of rescue packs to manage exacerbations of the disease. However, this is a simplistic view of self-management which encompasses much more than that.

A recent review and meta-analysis on the effectiveness of self-management interventions on QOL and healthcare utilisation in people with COPD identified 22 RCTs included in five systematic reviews categorised as 'self-management and education' for COPD from the Cochrane Library. The results suggest that self-management interventions can improve HRQOL and reduce the number of emergency department visits but there is wide variation in effect (71). Furthermore, interventions that tackle mental health and promote physical activity are more effective than those aimed directly at respiratory health (71). However, this is a simplistic view of self-management. Recommendations for future interventions should focus on tackling mental health and promoting physical activity not just taking rescue packs for exacerbations (71). It was also suggested that brief, simple self-management interventions may be as effective as more complex interventions (71). This is an important finding for clinical practice as brief interventions are easier to deliver and potentially of lower cost (71).

There are a number of ways to support self-management including providing information leaflets, peer support, one to one counselling, group education, telemedicine and psychological behaviour change interventions (2). In COPD the use of self-management plans is less well characterised compared with other long term conditions (72). Self-management support is not a new concept and has been around for many years. Whilst research is growing in the area of self-management more research is needed. De Silva (2011) suggests that more ways of developing the effectiveness of behavioural change are necessary (2). For some long term conditions there has been a focus on 'giving information' in a structured way to facilitate self- management e.g. diabetic patients may receive technical information about diet, medication, exercise, eye and foot care. It is argued that the focus of care for anxiety and depression should be on cognitive and behavioural interventions (2).

1.14 Economic Burden of COPD

COPD is a very costly condition and is associated with significant economic burden (8). The total annual cost of COPD to the NHS is estimated to be over £800 million for direct healthcare costs, which equates to £1.3 million per 100,000 (73). COPD exacerbations account for the greatest proportion of the total COPD burden on the health care system (8). In this country, COPD causes 115,000 emergency admissions per year (74) with an estimated cost of around £2,000 each (73).

However, any estimates of the cost of COPD are likely to under-represent the economic value of home care provided by family members (8). It is argued that COPD may force individuals to leave the workplace as a result of their illness or perhaps care for a family member who has the disease. The Department of Health (2011) suggest that 40% of people with lung diseases are below retirement age and are unable to work as a result of their illness (42). It has been suggested that the indirect costs of COPD may represent a serious threat to national economies (8).

1.15 Summary

COPD is one of the most important chronic diseases of both developing and developed countries. In the UK millions of people are believed to have the disease – many of whom will not yet be diagnosed. The principal features of COPD are airflow obstruction with associated cough, sputum production and breathlessness. It is a progressive incurable illness with

worsening symptoms such breathlessness and gradual disability. Whilst smoking is the main cause of COPD in the majority of cases there are other causes of the disease. Exacerbations are common, particularly for those with severe disease. Comprehensive guidelines for the management of COPD exist, using pharmacological and non-pharmacological treatments such as pulmonary rehabilitation to manage symptoms.

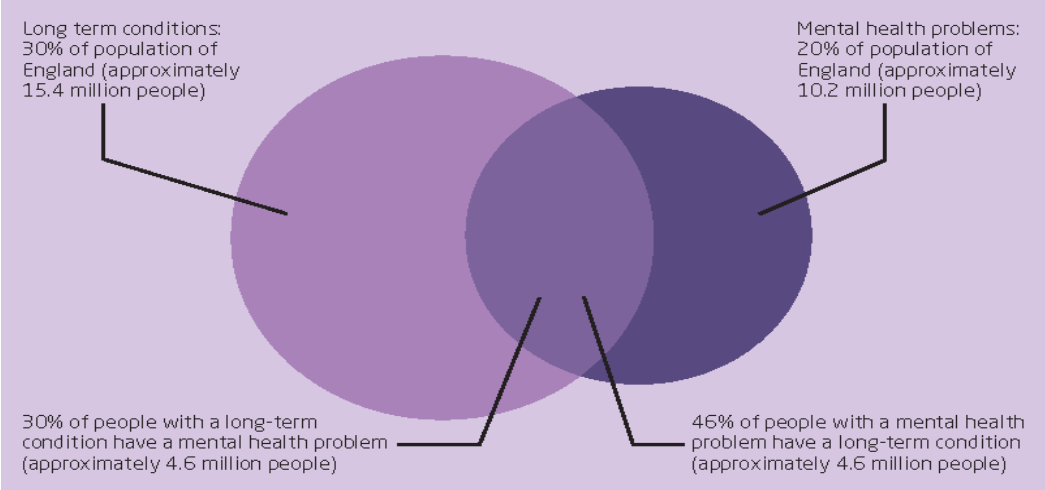
COPD has a significant impact on morbidity and mortality and for those who survive the illness their QOL can be severely affected. As COPD cannot be cured the focus of care is on improving the patient's QOL. The following chapter will explore the emotional consequences of COPD and the role of anxiety and depression in this debilitating disease.

Chapter 2 - Psychological Comorbidity in COPD

2.1 Introduction

Physical health and mental health are inextricably linked (75). It is estimated that around 30% of people with a long term physical health problem also have a mental health problem (76). Not surprisingly there has been an increasing awareness of the psychological morbidity of medical problems for a number of years. Figure 6 below illustrates the overlap between long term conditions and mental health problems (77). The mechanisms underlying the relationship between mental and physical health are complex (77). Evidence suggests a combination of biological, psychosocial, environmental and behavioural factors may all be involved (78).

Figure 6 – The overlap between long-term conditions and mental health problems (77).



Source: Kings Fund Report (77).

It is difficult to determine whether the chronic medical problem causes anxiety and depression or the psychological disorder increases the risk of developing physical health problems (79). People who are anxious or depressed are more likely to smoke and it is estimated that approximately three million smokers in the UK have a mental health disorder (80). Smoking is around twice as common among people with mental disorders, and more so with severe mental health problems (80). Whilst smoking is a well-known cause of COPD it is also associated with an increased risk of onset of anxiety disorders and depression (80). On the other hand, high levels of anxiety have been identified as a risk factor for starting smoking in the first instance (81). Whatever the direction of causality, it is clear that mental health

problems have a major impact on symptoms and outcomes for people with COPD (77). Independent of COPD severity, comorbid mental health problems are associated with worse health status and breathlessness (82) which are both important factors for treatment of COPD.

The prevalence of anxiety in COPD is generally considered to be high (83). Prevalence figures are difficult to interpret as reviews of studies suggest prevalence ranges from 2- 96% (83). A systematic review and meta-analysis reported the prevalence of clinically significant symptoms of anxiety as 36%, and 40% for depression in patients with COPD. Screening for symptoms of anxiety and depression are recommended by strategies such as GOLD Strategy (8) and the NICE COPD Guidelines (10). However, in clinical practice this is rarely undertaken despite the fact that these psychological conditions are potentially treatable.

For patients who have recently recovered from an acute exacerbation of COPD, the prevalence of depression and anxiety is reported to be as high as 50% for depression and 58% for anxiety (66). For some patients symptoms may be transient and improve spontaneously as the patients physical condition improves but for others the symptoms may persist (66). A number of variables have been associated with anxiety and depression in patients with COPD (66). These variables are listed in table 4.

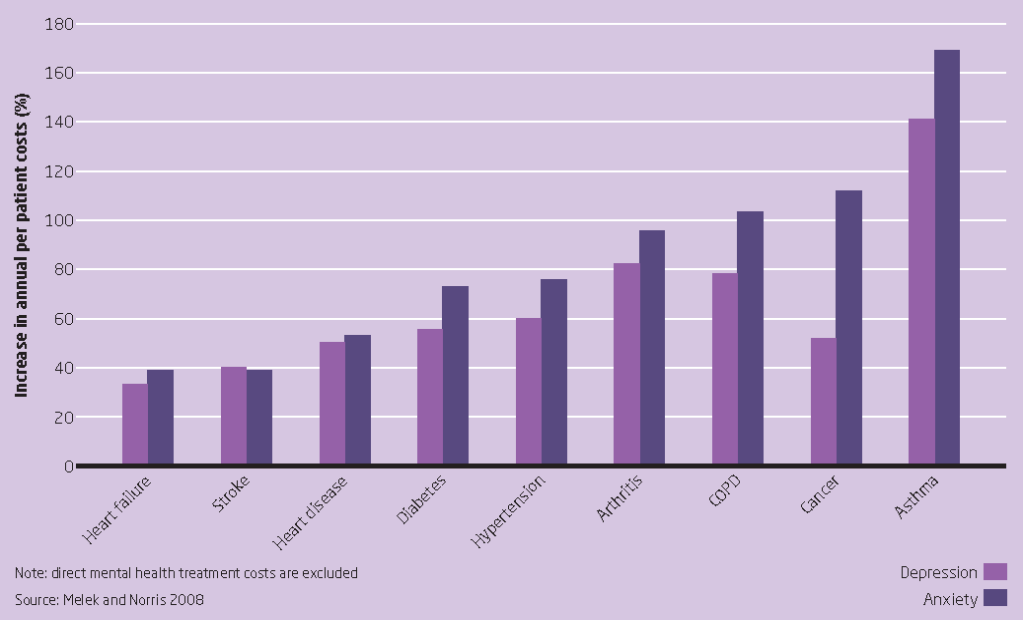
Table 4 – Variables associated with anxiety and depression in patients with COPD (66)

Physical disability
Severe disability
Presence of co-morbidity
Percentage of predicted FEV1 <50%
Low body mass index
Poor QOL
Living alone
Female gender
Current smoking
Low socioeconomic status
Long term oxygen therapy

The implications for people with COPD and comorbid anxiety and depression are serious. Patients have poorer clinical outcomes, lower QOL, reduced ability to manage physical symptoms effectively, increased risk of hospitalisation and re-hospitalisation and furthermore an increased risk of mortality (66, 84) . It is apparent that one of the most important interventions to prevent COPD, or to stop further deterioration of the disease is smoking cessation. Patients who may be anxious or depressed are more likely to be associated with unhealthy behaviours such as smoking (77, 80, 85). It has been claimed that patients with mental illness are less likely to be successful quitting (86). However, in contrast, it has been argued that whilst people with mental health problems are twice as likely to smoke, they have substantially greater quit rates (87).

The economic impact of COPD has attracted much attention over the last few years. It is only recently that the additional costs of mental health problems and physical illness have been highlighted. By interacting with and exacerbating physical illness, co-morbid mental health problems raise total health care costs by at least 45 per cent (77). Melek and Norris (2008) suggest that patients with chronic medical conditions and comorbid anxiety and depression incur considerably higher healthcare costs than those without psychological problems (79). Data from Melek and Norris's research was presented in a recent report by the King's Fund highlighting the important issue of mental health for patients with COPD and other medical conditions (figure 7) (77). In 2007, the estimated cost of anxiety was £8.94 billion and £7.5 billion for depression. The projected costs for 2026 are £14.2 billion for anxiety and £12.2 billion for depression (88).

Figure 7 – Costs associated with anxiety and depression and chronic conditions -data cited from Melek and Norris (2008) (77).



Source: Kings Fund Report (77).

Our physical, social and economic environments all have important effects on our physical and mental health (1). Certain psychosocial factors have been investigated in COPD patients. As early as 1999, Prescott et al found that socioeconomic inequalities in education and income are also associated with a threefold increase in hospital admission (19). Coventry et al (2011) also found that patients who owned and occupied their own homes had fewer readmissions to hospital compared with patients who did not (61). In the same study, the authors state that depression was found to be a significant predictor for initial hospital readmissions (61). Anxiety is a significant predictor of the frequency of hospital admissions and re-admissions for acute exacerbations of COPD (61).

2.2 Anxiety

Anxiety is an unpleasant emotional feeling associated with a state of 'threat' or not being able to cope. Anxiety has been defined as a future orientated emotion, characterised by perceptions of frightening and uncontrollable events or situations (89). Excessive levels of anxiety and stress have been shown to negatively impact on the functioning of many systems. The brain is the key organ of the stress response as it determines what is threatening and therefore controls the behavioural and physiological responses (90). Many of the symptoms of anxiety are physiological in nature reflecting activation of the sympathetic and para-

sympathetic nervous system (89). Common symptoms of anxiety can be seen in table 5 (89).

Table 5- Common symptoms of anxiety (89).

Physical	Behavioural	Cognitive/affective symptoms
Shortness of breath/rapid breathing	Avoidance	Frightening thoughts/images or memories
Choking sensation	Escape (flight response)	Fear of losing control or being unable to cope
Sweating	Hyperventilation	Catastrophising
Increased heart rate/palpitations	Pursuit of safety or reassurance	Worry
Chest pain/pressure	Difficulty speaking	Poor concentration
Muscle tension	Freezing	Apprehension
Dizziness/lightheaded/headaches	Restlessness	Difficulty in reasoning
Increased BP	Insomnia	Poor memory
Tingling in arms/legs		Narrowing of attention
Dry mouth		
Nausea/diarrhea		
Trembling/shaking		

Symptoms triggered by anxiety clearly overlap with the symptoms of COPD (91) and as a result can be more complex to identify and manage. It has been hypothesised that a patient's fear leads to misinterpretation of bodily experiences such as breathlessness and hyperventilation and this can lead to intense feelings of panic (92). Greater levels of anxiety have been associated with poor satisfaction with marital relationships in COPD patients (93), are more common in women than men and in current smokers compared to ex-smokers (70). It is unclear whether the prevalence or magnitude of anxiety-related symptoms differ according to the severity of obstruction; with some studies but not all reporting no relationship between these (83). Not surprisingly, anxiety has been shown to lead to impaired health status, poorer treatment outcomes and reduced survival (84). In male patients, low levels of perceived self-efficacy in symptom management, poorly adapted coping strategies and low levels of social support have been associated with higher levels of anxiety (85).

It is understandable that patients experiencing extreme breathlessness find it difficult to attribute the symptoms correctly to anxiety and panic when they have a genuine respiratory

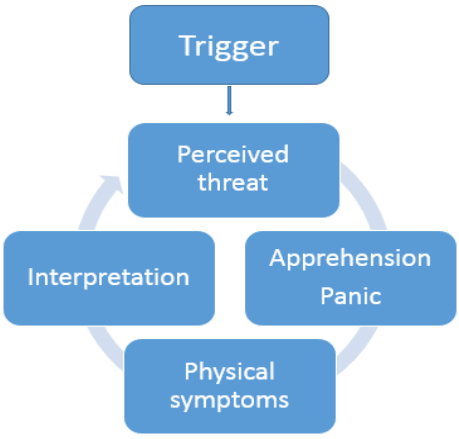
problem. Indeed, sometimes health care professionals do not recognise the impact of anxiety on breathlessness and may well initiate treatment for an infective exacerbation of COPD. However, a link between COPD and anxiety is highly plausible. In extreme cases, anxiety may develop into panic attacks.

2.3 Panic

The term 'panic' is derived from the name of the Greek God Pan (94). According to Greek mythology, Pan would frighten people and the acute terror felt came to be called 'panic' (94). A 'panic' is now defined as an episode of intense fear of sudden onset and is accompanied by a surge of strong unpleasant physiological symptoms (hyper arousal) (95). When danger is perceived, the automatic fear response occurs faster than conscious thought. Surges of adrenaline are released which subside quickly once the perceived or actual threat has passed (96). During panic attacks there is an intense feeling of 'air hunger' (97) and often a fear of suffocation. Some panic attacks are very sudden and unexpected. For some people, however, the panic attack may be provoked by exposure to an identified trigger and can be anticipated (94). Attacks usually peak within a few minutes (98). Panic is also associated with difficulty reasoning, and a feeling of imminent catastrophe (98). Therefore, the experience of panic can be so distressing that many people develop a strong apprehension about having another attack. Individuals will often avoid situations that may trigger the panic (95).

A leading theoretical model for panic is Clark's cognitive model (99). In Clark's model a panic attack results when ambiguous bodily sensations are interpreted as imminently catastrophic, increasing arousal and so creating a vicious cycle (Figure 8) (92). Of interest, within the COPD population with similar disease severity, catastrophic over-interpretation of the immediate danger of breathlessness occurs in some individuals but not all (99). Indeed, it has been proposed that elevated anxiety sensitivity, a trait variable, may increase symptoms in vulnerable people exposed to the stressful life events associated with living with COPD (99).

Figure 8 – Clark's Model of Panic (92).



Critical features of panic attacks can be seen in table 6. It is noticeable that many of the features described in table six are similar to the physiology of COPD. What may be different is the disproportionate responses that can occur during panic attacks. The prevalence of panic disorder in patients with COPD is 10 times greater than the overall population (100). There is evidence that untreated panic attacks in COPD do not resolve but may instead increase the risk of panic disorder developing (101).

Table 6 – Critical features of panic attacks in COPD - Adapted from Clark and Beck (95)

Situations which trigger symptoms e.g. exertion
An abrupt onset of physiological arousal including breathlessness and fast heart rate
Heightened self-focus
Hypervigilance of bodily sensations e.g. increased focus on breathing
Perceived physical, mental or behavioural catastrophe (I can't breathe and I am going to die)
Apprehension and fear of future panic attacks (I will have another attack and die)
Extensive safety seeking behaviours (such as avoidance of activities or exertion; calling 999 for an ambulance for reassurance or having numerous admissions to hospital where it is perceived to be safe)
Perceived lack of control (patients feel that they cannot do anything themselves)
Is distinct from anxiety (it is an intense form of anxiety)

In contrast to Clark's model of panic is the notion that psychological processes underlying pathological anxiety are mainly automatic (102). Anxiety and panic are part of our 'natural wiring'. It could be argued that panic should not be seen as an extreme form of anxiety but rather it is a natural 'fight or flight' response to perceived imminent danger. This natural response can be helpful when we need to respond quickly to danger but becomes unhelpful if it is persistent, and can be very distressing.

A link has been found with mental health problems such as panic, generalised anxiety and low FEV_1/FVC ratio in numerous studies (6). Spitzer et al (2011) suggest a possible explanation for the association between mental health and lung function is that airflow limitation may induce panic, or conversely, that panic may decrease airflow, but not to a clinical and diagnostic threshold (6). A number of theories have been proposed to explain the links between anxiety and obstructive lung disease. From a pathophysiological perspective it has been argued that hypercapnia and acid-base disturbances accompanying obstructive lung disease may induce anxiety (103). A psychological explanation would suggest illness perceptions, beliefs and misinterpretations of respiratory symptoms (e.g. breathlessness) have a role to play (6). It has also been suggested that patients with prominent respiratory symptoms show greater fluctuations in end-tidal CO2 and brain lactate (97).

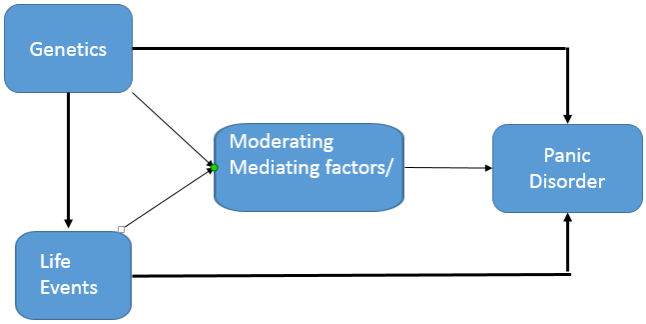
Whether COPD or anxiety causes breathlessness or indeed whether it is a combination of the two, there is no doubt that breathlessness can be a distressing and frightening symptom which can lead to catastrophic interpretation of what is happening (e.g. a patient may think that they cannot breathe and death is imminent). A key feature of panic episodes is the tendency to interpret the certain bodily sensations in terms of an impending biological disaster (95). In individuals who have normal lung function physical symptoms such as increased respiratory rate and heart rate can be alarming. However, for patients with respiratory problems an increase in respiratory rate can be terrifying. Patients become anxious about becoming breathless and avoid exertion which may trigger unpleasant symptoms occurring, leading to physical deconditioning which then exacerbates the panic cycle. Panic symptoms are most prevalent in people with low perceived control over symptoms and the disease; pa-

tients having negative beliefs about the life-limiting consequences of unpredictable breathlessness attacks and by people using emotional coping strategies such as denial and avoidance (104).

Patients with COPD who experience panic attacks solely in relation to their COPD symptoms would not be diagnosed with panic disorder (105). Panic disorder consists of recurring, unforeseen panic attacks which are unrelated to COPD. Which, as discussed, is followed by persistent worry and distress about having further attacks (105). Patients often begin to avoid situations they associate with an increase in unpleasant physiological sensations, such as physical exercise. Behavioural avoidance is seen in approximately one-third of individuals with co-morbid COPD and panic disorder (106).

A newer model has emerged proposing a diathesis (vulnerability)-stress explanation. Diathesis-stress models of panic suggest that specific psychological disorders develop as the result of an interaction between vulnerability factors and stressful events (99). Examples of stressors include physical activity leading to breathlessness. Research into the relationships between cognitive diathesis for the development of panic-spectrum pathology is growing (99). Genetic factors, personality, behavioural characteristics, stressful life events (such as medical illness) may have a role in moderating or mediating the influence of life events on the development of panic disorder (107). In addition, socio-demographic variables and functional impairment may also have a role to play in panic in biologically vulnerable individuals supporting a possibly gene-environment interaction (107). It is thought that genetic make-up sets the biological vulnerability to anxiety. A hypothetical model of genetic factors, life events and moderating/mediating factors in the etiology of panic can be seen in figure 9 (107).

Figure 9 – A modified hypothetical model of genetic factors, life events and moderating/mediating factors in the etiology of panic (107).



Whatever the mechanism responsible for the development of anxiety and panic, the impact on patients' lives is considerable. The literature suggests the negative effects of anxiety lead to poor functional status (108), increased in the likelihood of admission and readmission to hospital (109), longer length of stay, greater risk of mortality post discharge (57), impaired HRQOL and risk for suicide attempts (110). Patients who have COPD and panic disorder often admit to 'feeling safe' when ambulance services are called, when they are admitted to hospital and often refuse to go home following an admission. This increased reliance on the safety of health services can further exacerbate the panic cycle. Inappropriate escalation of medical treatment can undermine patient confidence and have limited use on preventing admissions as a result of panic attacks. Another important consideration is that patients with panic have a higher level of depressive symptoms further compounding their distress (99). Given the impact of psychological symptoms outlined above, it seems reasonable to argue that the treatment of anxiety and panic among patients with COPD is imperative to improve patients QOL given there is no cure for their condition.

2.4 Depression

Depression refers to a wide range of mental health problems characterised by a loss of interest and enjoyment in ordinary things and experiences (sometimes referred to as a loss of positive affect) (111). A number of symptoms of depression are reported. Physical, behavioural and cognitive symptoms of depression are presented in table 7 (111).

Table 7– Common physical, behavioural and cognitive symptoms of depression (111).

Physical	Behavioural	Cognitive
Insomnia	Reduced activity	Anxious thoughts
Increased symptoms e.g. pain	Social withdrawal	Loss of interest/enjoyment
Muscle tension	Irritability	Low self-esteem
Altered appetite	Tearfulness	Poor concentration
Possible weight loss	Agitation	Feelings of guilt/helplessness
Fatigue	Self-harm/suicide attempts	Mental slowing
Lack of libido		Negative thinking
		Loss of confidence
		Rumination
		Unmotivated
		Suicidal ideation

Symptoms of depression must be present for at least two weeks and be associated with marked impairment of daily functioning (111). Whilst individuals will vary in their experience of depression usually a diagnosis requires assessment of the severity, duration and course of the symptoms (111). Four severity groups are provided in national guidelines (111):

- Subthreshold depressive symptoms (fewer than five) with minor functional impairment.
- Mild depression with at least five symptoms or functional impairment.
- Moderate depression with symptoms and functional impairment.
- Severe depression with most symptoms and significant functional impairment.

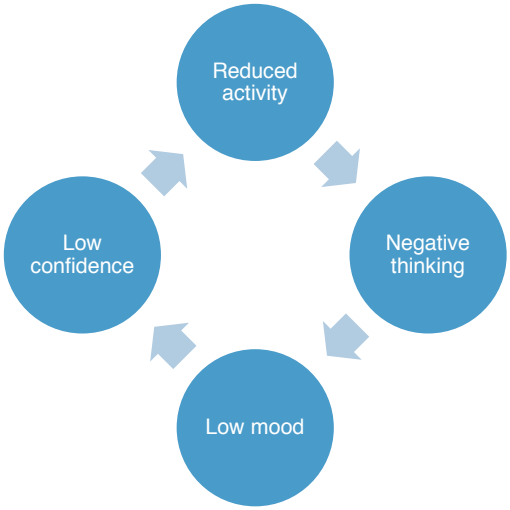
Increasingly, it is recognised that subthreshold or minor symptoms of depression can cause significant morbidity (111). Ideally, early intervention to treat mild symptoms would be the goal of treatment to prevent the progression to severe depression, which is more difficult to

treat. Unfortunately there does not seem to be a distinctive 'cut-off' between 'clinically significant' degrees of depression (111). When patients have chronic physical health problems there is an added complexity distinguishing the somatic symptoms of the physical health problem from those associated with depression (111).

People with depression vary in the pattern of symptoms they experience, due to a number of factors including gender, personality, family history, premorbid difficulties (e.g. trauma such as sexual abuse), social circumstances and psychological mindedness (111). COPD can cause and exacerbate depression (111). As a result of breathlessness patients may not be able to participate in normal activities of daily living. This reduced activity leads to feelings of hopelessness, impacts on fatigue and perceived energy levels which ultimately affects mood (see figure 10) (111). It is thought that depression is a time-limiting condition lasting up to six months before complete recovery (111). Contradicting this view is data from the World Health Organisation which found that depression was present at 12 months (112). However, in my clinical experience patients commonly report symptoms of depression lasting years.

Depression is two to three times more common in patients with chronic physical health conditions such as COPD (111). Chronic physical health problems can both cause and exacerbate depression, but the reverse can also occur. Depression is associated with risk factors such as smoking, sedentary lifestyle and obesity, which are also risk factors for physical health problems (113). Patients with COPD may have a spectrum of symptom severity ranging from short term depression symptoms, to dysthymia (longer term low mood that is not yet disabling) to clinical depression (66).

Figure 10 – Vicious cycle of depression



Depression can exacerbate distress and physical symptoms such as pain and there may be a dose-response relationship between illness severity and the extent of disability (111). However, this has not been the experience in respiratory clinics in Newcastle where anecdotal evidence suggests that patients with mild COPD can have at least as many if not more symptoms of depression than patients with very severe COPD. What is clear is that symptoms of depression have a negative impact on a number of important patient outcomes.

In a large prospective cohort study, Ng et al (2007) found that comorbid depressive symptoms in patients with COPD are associated with poorer survival, longer hospitalisation stay, persistent smoking, increased symptom burden, and poorer physical functioning (84). The authors found that patients commonly feel hopeless and helpless about changing their life circumstances; lack the drive and motivation to seek help and may succumb to early death instead (84). Clearly this is something which must be addressed. A recent systematic review found that symptoms of depression also led to increased likelihood of being admitted to hospital, longer hospital stays and increased risk of death post discharge (4). Worryingly, the systematic review also found that only about one third of COPD patients with depression were being treated for it (4).

2.5 Screening for Anxiety and Depression

Detecting symptoms of anxiety and depression is the first step in providing effective support for patients (77). In research, symptoms of anxiety and depression are usually detected us-

ing one of three types of measures: self-report questionnaires, checklist based structured interviews and clinical assessment by a psychiatrist (114). A number of validated measures could be employed to assess COPD patients' symptoms of psychological distress. The most common measures used in previous COPD studies are the Beck Anxiety Inventory (BAI) (115), the Beck Depression Inventory (BDI) (116) and the Hospital Anxiety and Depression Scale (HADS) (117). The Beck Anxiety Inventory can over-estimate symptoms of anxiety in patients who have respiratory problems as it includes a question about breathlessness. The HADS scale has fewer items to complete compared to the Beck Questionnaires and this is an important consideration for elderly patients. The HADS scale is a brief self-reported questionnaire comprising of two scales with seven questions each. One scale is for anxiety and another for depression (See Appendix 1). Each item on the scale is rated on a four point Likert scale (zero to four). Scores range from 0 -21 for each subscale. A higher score indicates worse symptoms and is indicative of clinically significant emotional distress (61). The questionnaire assesses emotional symptoms over the preceding seven days (118) and takes a few minutes to complete (119).

The classification of patients as being anxious or depressed according to HADS is controversial (118). In a large cross-sectional study of stable COPD patients, the authors concluded that the HADS questionnaire had a low diagnostic accuracy of depression but was an appropriate scale to evaluate psychological distress. This is in keeping with other recommendations that the HADS is used as both a screening tool and to monitor changes over time (61). The HADS has been found to be reliable and validated for hospital medical out-patient setting (117). Nowak et al have suggested that a range of cut-offs have been used, for example, HADS-Depression >4 in coronary heart disease, HADS-Depression >7 in cancer and HADS-Depression >11 in end-stage renal disease (118). An updated analysis of the HADS in 2002 found similar results in general medical, psychosomatic and psychiatric patients with an optimal cut-off of ≥8 for both subscales to define patients with probable diagnosis of depression or anxiety (118). With the above cut off, the HADS is reported to have high sensitivity (80%) and specificity (90%) (84). Dowson et al found that more severe COPD (FEV_1 predicted) correlated with higher HADS-Anxiety ($r=0.39$, $p=0.001$) and depression ($r=0.34$, $p=0.005$) scores (120). In a Dutch population the HADS has the advantage of being insensitive to age (121).

When using measurement scales it is useful to understand what the 'minimal clinical important difference' (MCID) to assess improvements in clinical settings. The MCID is concerned with methods of estimating the threshold of clinical significance of a measurement such as HRQOL or symptoms e.g. HADS scores (64). The MCID for the HADS Questionnaire in COPD has been reported to be a reduction of 1.5 or a change of 20% on either sub-scale or the total score (122). However, there has been no agreed definition of what 'the clinically significant threshold' is (123).

2.6 Treatment of anxiety and depression in COPD

Once symptoms of anxiety and depression are identified, appropriate treatment should be given (10). However, in clinical practice screening and management of psychological symptoms in COPD patients remains extremely poor and is not done to a consistently high level (77). A number of reasons may include the fact that health care professionals focus on physical symptoms (124). Very little attention is generally given to the patient's psychological well-being, in spite of its impact in predicting disability and other outcomes. It may also be more difficult to identify the cause of symptoms such as breathlessness or fatigue which often overlap with COPD and psychological problems such as anxiety and depression.

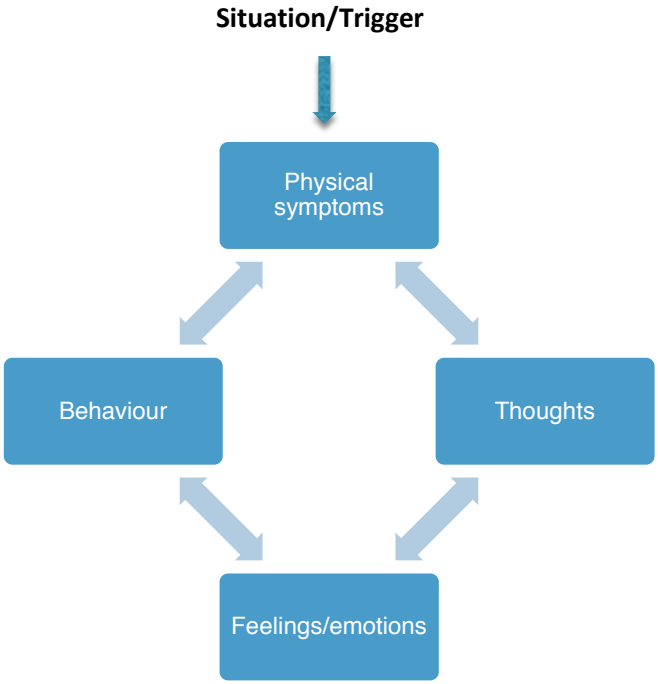
In addition, health care professionals working in the physical health setting have varying levels of training in psychological well-being and may feel ill-equipped to deal with emotional difficulties. It has frequently been suggested that professionals feel that they will 'open a can of worms' by discussing psychological issues with patients. More worryingly, there remains stigma relating to psychological problems and the use of psychiatric or psychological services. Patients may interpret the suggestion of referral as a lack of understanding regarding the validity of their symptoms. Guidelines for the management of anxiety and depression recommend psychological treatment, pharmacological treatment or both in combination (111, 125) . Psychological interventions include CBT, counselling and self-help approaches.

2.7 CBT

CBT is a psychological therapy that represents a combination of behavioural and cognitive theories of behavior (126). In CBT, the term 'cognitive' relates to people's thoughts (words or images), emotions, feelings, ideas, beliefs and values. The term 'behaviour' relates to

what a person does or chooses not to do. The core idea of therapy is that a person's emotional reactions are influenced by what they 'think' (cognitions) or indeed what they 'do' (behaviour). A diagram of the model can be found in figure 11. Part of the inheritance from behavioural therapy is the notion that our behaviour is crucial in maintaining or changing psychological states (127). CBT is a treatment that focuses on understanding how experiences are developed, interpreted and explores the interaction between physical symptoms, thoughts, mood, behaviour and environment which are intricately linked. A core component of CBT is that it is not the event that is important but what an individual makes of that event. Patients may all experience the same physical illness but interpret the experience in different ways. One patient may feel anxious and depressed about their situation and feel they have no control in managing their symptoms, others may feel the opposite.

Figure 11 – The CBT Model (127)



A fundamental part of cognitive therapy is the role of our cognitions or thoughts. Negative automatic thoughts are particularly important in CBT. Negative automatic thoughts are negative appraisals or interpretation of life events. These thoughts pop into our minds, are usually unchallenged and impact on our mood and behaviour. The CBT model helps therapists try to identify unhelpful thoughts and behaviour. Central to the CBT model is the use of a 'formulation' sometimes referred to as a 'case conceptualisation' or 'the hot cross bun'

(128). The formulation is a summary of the patient's problems, helps the patient and therapist make sense of the current difficulties, can help identify factors that may be maintaining the problem and acts as a bridge to identify potential areas for change or interventions that may be useful. A core skill for any cognitive therapist is to be able to understand the patient's problems and collaboratively identify ways of tackling or adapting to the difficulties. By making sense of the problem new skills can be developed to change or reconsider unhelpful thoughts and behavior leading to improved emotional health.

The focus of treatment is on the 'here and now' rather than exploring difficulties from the past. The rationale for dealing with the present is to tackle current problems and what is maintaining them. However, it may be necessary to work at a deeper level if the patient's problems affecting the present are rooted in past events or experiences. In such cases experiences, beliefs, values and precipitating events would be explored and addressed.

Treatment is generally described as brief therapy, typically involving up to six sessions (brief intervention). However, longer therapy sessions may be needed and up to 20 sessions may be provided (high intensity intervention). CBT is structured and collaborative. Patents are experts in what they are experiencing and therapists can help guide the patient to identify their problems and CBT techniques that might be helpful to them. A cornerstone of cognitive therapy is a technique called 'socratic' questioning. Socratic questioning encourages patients to build on their problems, strengths, identify important goals for them and develop their own ideas or solutions to their problems. This technique is different to the traditional questioning style used by many healthcare professionals who engage in 'advice giving'. A gifted therapist can make this look deceptively easy but it is a great skill. Therapists tend to develop their own repertoire of questions that have been beneficial in clinical practice.

Whilst CBT will certainly not cure an individual's medical condition, it may well be a means of helping manage comorbidities such as anxiety and depression. Importantly, it may also influence physical symptoms such as breathlessness (128). Patients may be reluctant to change their behaviour to avoid the unpleasant feeling they experience when they become breathless. In such circumstances, the patient may lack confidence because they fear the consequences (what if I get breathless), they have had previous experience of failure (I always get breathless when I do anything), or because their emotional state (i.e. depressed,

anxious or stressed) Techniques that can improve patients' knowledge or skills (mastery) to be able to cope may help them take small steps to overcome obstacles to behavioural change (129) and support the potential role of cognitive and behavioural approaches.

Measuring progress is an important aspect of CBT therapy. A number of methods are used ranging from psychometric questionnaires, Likert scales and diaries. The ultimate aim of therapy is to enable patients to learn useful skills to manage their own difficulties. There are numerous cognitive and behavioural techniques. These techniques will be discussed in Chapter 4 when the CBT model for COPD patients is discussed.

2.8 Psychological Therapy in the physical health setting

It is argued that people with long term physical health conditions and mental health needs often receive fragmented care. Health and social care services are not currently organised to provide an integrated response to dual physical and mental health needs (77). Naylor suggests that the institutional and professional separation of care leads to missed opportunities to improve the quality and efficiency of care (77). Increasing specialisation and the decline of generalism in hospital settings can create a lack of co-ordination and oversight of patients' multiple needs (130). The government's mental health strategy 'No Health Without Mental Health' places considerable emphasis on the connections between mental and physical health (77). The King's Fund has previously argued that developing more integrated forms of care for people with co-morbid mental and physical health problems should be one of the top ten priorities for clinical commissioning groups (131).

Over the last ten to fifteen years the delivery of psychological care in the physical health setting has changed considerably. In particular, cancer services have made significant steps to improve psychological care for cancer patients. In 2004 the National Institute for Clinical Excellence published excellent guidance for Cancer Services to improve supportive and palliative care for adults with cancer (132). A four-level model of professional psychological assessment and intervention was recommended (see table 8). Psychological support at levels one and two are provided by health professionals directly responsible for the care of people with cancer. More severe psychological distress (levels three and four) should be managed by a variety of specialists included counsellors, nurses, psychologists, psychotherapists and

liaison psychiatrists (132). It was recommended that staff providing psychological care were adequately trained and supervised.

Table 8– Recommended model of professional psychological assessment and support from NICE. Improving supportive and palliative care for adults with cancer (132).

Level	Group	Assessment	Intervention
1	All health and social care professionals.	Recognition of psychological needs.	Effective information giving, compassionate communication and general psychological support.
2	Health and social care professionals with additional expertise.	Screening for psychological distress.	Psychological techniques such as problem solving.
3	Trained and accredited professionals.	Assess for psychological distress and diagnosis of some psychopathology.	Counselling and specific psychological interventions such as anxiety management and solution-focused therapy, delivered according to explicit theoretical framework.
4	Mental health specialists.	Diagnosis of psychopathology.	Specialist psychological and psychiatric interventions such as CBT.

In 2007 The Improving Access to Psychological Therapy (IAPT) programme was launched in the UK. This programme was a large scale initiative which focuses on delivering psychological therapy for adults with a particular emphasis on depression and anxiety disorders within the English NHS (133). The overall purpose of IAPT is to implement NICE Guidance for the treatment of anxiety and depression. The evidence in NICE Guidance prioritised CBT as it is the therapy with the widest application for anxiety and depression and the most evidence supporting its effectiveness (134). NICE systematically reviewed the evidence for the effectiveness of a variety of interventions for depression and anxiety disorders which led to the publication of a series of clinical guidelines (133). Other therapies (interpersonal psychotherapy, behavioural couple's therapy, counselling and brief dynamic therapy) is recommended for depression but not anxiety (133).

The IAPT model of care for the delivery of CBT interventions is 'stepped care' in line with Nice Guidelines (134). Stepped care means assisted self-help or signposting being the focus at step two and face to face therapy at step three (133). Patients may be offered the least intrusive, most effective intervention first such as low intensity therapy. For some patients low intensity interventions such as guided self-help delivered through books and leaflets, structured exercise, computerised forms of CBT or brief face to face interventions can help patients retain a sense of self-worth when working with a professional trained in CBT skills (134). For patients with long standing or severe symptoms face to face high intensity interventions delivered by a specialist practitioner may be more appropriate. Practitioners providing step two treatment are typically NHS band four to five staff and band six or seven for staff providing high intensity therapy (135). However, even with the introduction of IAPT it has been recommended that ways of embracing the use of psychological therapies should be developed for physical health conditions than its current medical and diagnostically based approach (135).

2.9 Summary

It is well known that COPD is a serious illness with physical and psychological effects. Whilst guidelines on COPD recognise the psychological impact of COPD, there has been little research beyond prevalence studies. It is now widely accepted that anxiety and depression are common comorbidities experienced by patients with COPD. Unfortunately, many patients will not benefit from the treatments recommended in the guidelines suggested above as their symptoms may not even be identified in the first place (79). There is a significant opportunity to explore the use of cognitive and behavior strategies to address anxiety and depression and new ways to deliver CBT within the National Health Service. Complex psychological interventions such as CBT may well be effective in treating debilitating comorbidities such as anxiety and depression.

Identifying symptoms of anxiety and depression is a key step to providing appropriate support and treatment. CBT is a psychological intervention which is recommended for the treatment of many mental health problems including anxiety and depression (111). Firstly, CBT is a treatment that helps develop an understanding of the patient's current problems and explore the patient's thoughts and behaviour to deal with the difficulties. Secondly,

having a clearer understanding of problems can then lead to identifying ways to overcome these difficulties and identify strategies that can help improve the patient's QOL. Thirdly, many cognitive and behavioural techniques could potentially enhance medical care to manage difficult symptoms such as breathlessness e.g. behavioural techniques such as planning and pacing activities can help breathlessness alongside inhaled therapy. CBT is evidence based psychological 'talking' treatment, which explores the links between situations thoughts, feelings, physical symptoms and behaviour. By developing new skills, patients can then become their own therapist and use the techniques they have learnt in similar situations. This empowers patients and is thus a good fit with the move towards greater inclusion of patients in their care and supporting self-management.

With the increasing awareness of psychological issues in long term conditions and the scale of the problem facing COPD patients it is becoming increasingly difficult to ignore the fact that CBT is a potentially useful treatment for COPD patients in improving symptoms of anxiety, depression and improving self-management of the condition. New ways of addressing physical and mental health needs are needed as current health and social services in England are not currently organised in a way which supports an integral response to the physical and mental health needs of patients (77). The next chapter presents a literature review undertaken to identify the effectiveness of psychological interventions in COPD.

Chapter 3 - Literature Review

A comprehensive literature review was undertaken to identify previous research on the use of psychological based therapy in the management of anxiety and depression in the COPD population. The initial search in 2011 has been updated in preparation for this thesis and all relevant papers are discussed in this chapter. The chapter begins with details on the literature search strategy. A critique of the literature from the 1980's to the current date follows and important recommendations for future research are identified in section 3.3. The chapter concludes with a final summary.

3.1 Literature Search Strategy

At the start of this PhD I attended seminars on conducting robust literature searches before developing my research strategy. An initial search of health and psychology databases identified a prior systematic review and meta-analysis of the efficacy of psychologically based interventions to improve anxiety, depression and QOL (136). The review analysed published research from 1983 to September 2009. The authors were contacted to gain permission to use the terms to extend their literature review from 2009. I then used these search terms to undertake the initial literature search. I also consulted with a senior librarian to check the search strategy for robustness and no amendments to the search terms were deemed necessary.

3.1.1 Literature review Search terms

A wide range of free-text terms for each of the concepts were selected in order to be as comprehensive as possible. Synonyms were identified. Truncation was used for variations of words e.g. Anxi* which would capture anxiety or anxious. Controlled vocabulary terms, text words, synonyms and related terms for each concept at a time were joined together with the Boolean 'OR' operator. Search terms were formulated using population, intervention, and comparison and outcome format (Table 9).

Table 9 – Literature review search terms.

Population	Intervention	Comparison	Outcome
COPD COAD Chronic obstructive pulmonary disease Chronic obstructive airways disease Chronic bronchitis Emphysema Respiratory disease Depress* Anxi* Panic	Cognitive behavioural therapy Cognitive behave* therapy CBT Psychotherapy Stress management Relax* Psychological intervention	Education Usual Care	Anxiety Depression Health related quality of life (HRQOL) Quality of Life (QOL)

For the purpose of this review the working definition of 'psychological intervention' was studies which aimed to address and modify cognitions, behaviour and mood in order to reduce symptoms of anxiety and depression.

3.1.2 Language

The search was limited to English language.

3.1.3 Databases

Databases can be searched using standardised subject terms assigned by indexers. Standardised subject terms (as part of a controlled vocabulary or thesaurus) are useful because they provide a way of retrieving articles that may use different words to describe the same concept. Each database was searched separately depending on the terms used within thesaurus/sub headings or mesh. Databases searched can be found in table 10.

Table 10 – Databases used for literature search.

Medline (medical studies)
Psychinfo (psychological studies)
Web of Science
Cinahl and BNI (nursing studies)
Cochrane Central Register of Controlled Trials (CENTRAL)
Google Scholar
AMED

3.1.4 Search Results

The results of the Medline search has been included in this thesis as an example of the search strategy results.

Search History

1. Medline; "chronic obstructive pulmonary disease".ti,ab [Limit to: (Language English)]; 27041 results.
2. Medline; COPD.ti,ab [Limit to: (Language English)]; 24546 results.
3. Medline; COAD.ti,ab [Limit to: (Language English)]; 190 results.
4. Medline; PULMONARY DISEASE, CHRONIC OBSTRUCTIVE/ [Limit to: (Language English)]; 21078 results.
5. Medline; 1 OR 2 [Limit to: (Language English)]; 38159 results.
6. Medline; 1 OR 2 OR 4 [Limit to: (Language English)]; 43447 results.
7. Medline; 1 OR 2 OR 3 OR 4 [Limit to: (Language English)]; 43636 results.
8. Medline; 3 OR 5 [Limit to: (Language English)]; 34874 results.
9. Medline; 3 OR 6 [Limit to: (Language English)]; 38310 results.
10. Medline; "chronic obstructive pulmonary disease".ti,ab; 30527 results.
11. Medline; COPD.ti,ab; 28523 results.
12. Medline; COAD.ti,ab; 202 results.
13. Medline; PULMONARY DISEASE, CHRONIC OBSTRUCTIVE/; 25022 results.
14. Medline; 10 OR 11; 40001 results.
15. Medline; 14 [Limit to: (Language English)]; 34673 results.
16. Medline; 10 OR 11 OR 13; 44375 results.
17. Medline; 16 [Limit to: (Language English)]; 38119 results.
18. Medline; 10 OR 11 OR 12 OR 13; 44563 results.
19. Medline; 18 [Limit to: (Language English)]; 38298 results.
20. Medline; emphysema.ti,ab; 18985 results.
21. Medline; EMPHYSEMA/; 4793 results.
22. Medline; 20 OR 21; 21345 results.
23. Medline; "respiratory disease".ti,ab; 12231 results.
24. Medline; RESPIRATORY TRACT DISEASES/; 19119 results.
25. Medline; "respiratory disease*".ti,ab; 20729 results.
26. Medline; 10 OR 11 OR 12 OR 13 OR 20 OR 21 OR 23 OR 24 OR 25; 97088 results.
27. Medline; CBT.ti,ab; 5837 results.
28. Medline; "cognitive behav* therapy".ti,ab; 8885 results.
29. Medline; "stress management".ti,ab; 3015 results.
30. Medline; relax*.ti,ab; 129825 results.
31. Medline; RELAXATION/ OR RELAXATION THERAPY/; 7570 results.
32. Medline; "psychological intervention*".ti,ab; 2850 results.
33. Medline; psychotherapy.ti,ab; 26524 results.
34. Medline; PSYCHOTHERAPY/; 41820 results.
35. Medline; 27 OR 28 OR 29 OR 30 OR 31 OR 32 OR 33 OR 34; 200626 results.
36. Medline; 26 AND 35; 573 results.
37. Medline; "quality of life".ti,ab; 161832 results.
38. Medline; QUALITY OF LIFE/; 127634 results.
39. Medline; QOL.ti,ab; 22231 results.
40. Medline; HRQOL.ti,ab; 8795 results.
41. Medline; 37 OR 38 OR 39 OR 40; 208854 results.
42. Medline; 36 AND 41; 74 results.
43. Medline; 42 [Limit to: (Language English)]; 62 results.

The abstracts from the papers identified from database searches were reviewed to identify pertinent papers. From all of the studies identified from electronic and hand searches 16 papers were included in this review and a number of methodological factors were assessed for quality.

3.1.5 Alerts

The search strategy was saved and an alerts system was set up to capture newly published papers. This strategy proved to be successful as one paper was found from a google scholar alert. Alerts also identify abstracts from conferences and can highlight important developments in the field early.

3.1.6 Reference lists

Once relevant articles were identified reference lists were checked for additional papers.

3.1.7 Author contact

Authors of published research in the field were contacted and asked if they had any other current research that could be included in the review. No further unpublished research was identified.

3.1.8 Literature searches

A search was undertaken from September 2009 to February 2012 to capture any studies published after the systematic review by Baraniak and Sheffield (136). Dr. De Soyza and I independently reviewed the abstracts and met to confirm agreement of the inclusion or exclusion of abstracts. Papers were obtained if it was not clear from the abstract if the paper should be included. Five new papers were identified which had been published after 2009. To ensure the literature search was as up to date as possible, a further search was repeated in September 2015. A systematic review was conducted by Coventry et al on the effect of complex psychological or lifestyle interventions for depression and anxiety in COPD had been published (137). The authors concluded that complex interventions that include an exercise component significantly improve symptoms of depression and anxiety in people with COPD and highlighted the importance of promotion physical activity in this population (137). However the effect of physical activity was less for anxiety than depression (137). The last systematic review to date was published in 2014 (4) and two papers had been published (138, 139). Table 11 shows the studies identified in each systematic review. In total 16 papers including psychological interventions were identified.

In addition, Dr De Soyza and I were invited to assist in a Cochrane Review of psychological interventions for the treatment of anxiety in COPD. The protocol for the review has since

been published (140). For the Cochrane review I screened over 500 abstracts and no studies were identified that had not been included in this systematic review confirming that the literature search strategy used for this PhD was robust. A summary of the papers included in the five systematic reviews can be found in table 11.

Table 11 – Summary of papers included in five systematic reviews on psychological interventions for anxiety and depression in COPD.

Study	Rose et al,2002 (129)	Coventry and Gellatly,2008 (141)	Baraniak and Sheffield, 2011 (136)	Coventry et al, 2013 (137)	Smith et al, 2014 (4)	Heslop-Marshall, 2015
Howard & Dupont, 2014 (139)						√
Jiang & He, 2012 (138)					√	√
Hynninen, 2010 (142)				√	√	√
Cully, 2010 (143)						√
Lamers, 2010 (144)				√	√	√
Howard, 2010 (145)						√
Livermore, 2010 (101)				√	√	√
Heslop, 2009 (146)			√			√
De Godoy, 2003 (147)		√	√	√	√	√
Kunik, 2008 (148)			√	√	√	√
Kunik, 2001 (149)		√	√	√	√	√
Emery, 1998 (150)	√	√	√	√		√
Eiser,1997 (151)		√	√			√
Lisansky and Clough, 1996 (152)			√			√
Gift et al, 1992 (153)	√		√	√		√
Rosser, 1983 (154)	√		√			√

3.1.8 Data Extraction

Data was extracted from the papers using standardised data extraction sheets from The Cochrane Collaboration.

3.2 Critique of Literature

Over the past 35 years there has been a slow and steady development of psychological research in patients with COPD (155). Previously, psychoanalysis was the dominant psychological approach (155). Psychological factors were viewed as the primary causes of physical symptomatology in diseases such as asthma. COPD tended to be an exception, most notably because smoking was clearly seen as a non-psychological determinant of the disease (155). The psychoanalytical approach aimed to help professionals understand and help their patients in managing their illness (155). However, over time the psychoanalytic approach was criticised for being over reliant on subjective clinical judgment and speculation (155). Researchers also sought to establish whether COPD could be linked to psychological personality states and traits rather than deep psychic conflicts (155). Traits such as hypersensitivity, marked passivity and emotional immaturity were identified (156). In 1977, other researchers explored the psychosocial consequences of COPD and found 'disturbingly high prevalence of anxiety, depression, alcoholism, sexual dysfunction, and various psychiatric psychopathologies (e.g. paranoid states)' (157).

In the 1980's there were several developments in psychological research. Psychologists specialising in neuropsychology collaborated with respiratory physicians and psychiatrists to investigate whether the chronic and progressive airway obstruction seen in COPD causes hypoxaemia and affects cognitive function (155). Researchers established how COPD could lead to neuropsychological impairments (158). It is argued that cognitive impairment may compromise patients' capacity to engage with medical advice so this may be an important consideration (155). Clinicians also began to recognise that there was a disparity between objective measurements of treatment effects and subjective measures reported by patients so began to focus on QOL (155). Standardised questionnaires such as the Chronic Respiratory Disease Questionnaire (CRQ) (159) and St Georges's Respiratory Questionnaire (SGRQ) were developed to assess QOL (160). This was an important change as 'QOL' was seen as a 'soft', 'subjective' secondary outcome measure (155).

Researchers also began to focus on illness behaviour and experiences. The Bronchitis and Emphysema Symptom Checklist was developed and used to assess symptoms, attitudes, personality factors and clinical characteristics (161). The investigation of such variables has led

researchers to consider how psychological and behavioural factors maintain and increase both perceived severity and medical intractability of the illness once it has already developed (155). Kaptein suggests that interventions designed to modify illness behaviour may exert an impact on outcome variables (155). Researchers also explored the role of patient education as a potential intervention that could help modify behaviour. The results suggested that patient education has a minor effect on health perception (i.e. locus of control) but no significant gains in terms of physical function, mental health or social function (162).

3.2.1 Research in the 1980's

The first serious discussions and analysis of psychological treatment for COPD were published in the early eighties (154). The first study was undertaken in the UK and investigated the use of psychotherapy for psychiatric comorbidity in COPD patients who were disabled by breathlessness. The authors rightly identified that breathlessness is a common, distressing and frequently untreated symptom from a psychological perspective (154). This is certainly still the case thirty years later. Details of the study characteristics can be found in table 12.

Table 12 – Main characteristics of the study published in the 1980's.

Author/ Country	Study Design and sampling	Number of patients	Intervention	Comparator	Characteristics of participants and follow –up	Psychological outcomes and measures
Rosser et al, 1983 (154) UK	Randomised Trial Recruited from patients attending clinic Blinding not reported	65 total: 16 -analytic or supportive psychotherapy 16- Nurse support 16- Control (weekly lab tests)	8 sessions Weekly 45 minute For analytic or supportive psychotherapy or Nurse administered sessions (practicalities of living with COPD)	Weekly lab tests	Mean age 66 68% male Mild-severe COPD Mean FEV_1 0.9	Anxiety (GHQ and VAS) Depression (GHQ and VAS) HSRS

Abbreviations: General Health Questionnaire (GHQ), Health sickness rating scale (HSRS), Visual Analogue Scale (VAS).

As with many studies of complex interventions, it is unclear from the paper exactly what the therapy entailed. It states that three types of psychotherapy were used and only two groups of psychotherapy could be identified (supportive psychotherapy and analytic psychotherapy). One group was seen by a nurse 'without any psychotherapy training' and sessions included management of 'practical realities in patients' lives. It is unclear that this would be classified as psychotherapy. Furthermore, it would certainly be difficult to replicate this study from the details provided in the paper. The results are also confusing and no firm conclusions can be made. However, one useful point identified in the paper is that the authors did suggest that 'nurse therapists would have an advantage of being cheap'. The authors also commented that patients had not sought psychological help so this was a limitation of their study. Indeed, in clinical practice most patients with COPD do not actively seek help for symptoms of anxiety and depression.

3.2.2 Research in the 1990's

Research into the efficacy of psychological interventions into anxiety and depression in COPD patients continued to grow in the 1990's. Four studies were published. The main characteristics of the studies can be found in table 13. Three studies involved CBT and one used progressive muscle relaxation (often used by CBT therapists to aid relaxation). Two studies were RCT's (150, 153). Gift et al (1992) conducted a small RCT on the effectiveness of progressive muscle relaxation (153). The results reported that the use of relaxation techniques decreased anxiety, dyspnoea and 'airway obstruction' (153). The authors concluded that relaxation techniques needed to be tested on a larger sample of COPD patients (153). In 1997, Eiser et al conducted a small pilot study consisting of a six week course of group CBT. The authors suggest the intervention produced a modest improvement in exercise tolerance in anxious and breathless patients with moderate to severe COPD, without alleviating their anxiety or improving their QOL (151). However, there was a high risk of bias in this study (see Table 15).

In 1996, Lisansky and Clough investigated the effectiveness of an eight week self-help educational program for patients in a very small study (152). The authors suggest a positive treatment response but acknowledged that additional studies were warranted for more intensive evaluations. The findings of this study need to be viewed with caution as there was a high

risk of bias when assessed. The final study published in 1998 was Emery's study which was the largest with 75 patients in total (150). Exercise, education and stress management were the interventions assessed in this study. The authors found that the education and stress management group experienced decreased symptomatology as a result of social support and better knowledge of the disease process (150). Interestingly, the authors state that greater knowledge may have been associated with increased distress in the education and stress management group. The results indicate that minimum psychological changes were observed among patients in the exercise only group. This study also has a high risk of bias (see Table 15).

A major limitation of studies into psychological interventions in COPD is the fact that there was a lack of high quality research up to the end of the 1990's. Trials were small and none of the studies had a power calculation.

Table 13– Main characteristics of studies published in the 1990's.

Author/ Country	Study Design and Sampling	Number of patients	Intervention	Comparator	Characteristics of participants and follow –up	Psychological outcomes and measures
Emery et al, 1998 (150) USA	RCT Recruited from local better breathing clubs, advertising (TV and papers), work of mouth and physician referral	79 total: 3 groups:- 29 - exercise, education and stress management (EXESM) 25 - Education and stress management (ESM) 25 - Control	1 week course of 16 education sessions & and 10 stress management classes over 10 week course. One group received 37 sessions of exercise in addition to above.	Waiting list controls	Mean age 66.6 53% female FEV_1/FVC <70% Clinical symptoms of COPD >6 months	Anxiety (STAI; SCL subscale) Depression (CES-D affect-balance scale; SCL-90 depression subscale) QOL (SIP)
Eiser et al, 1997 (154) UK	Controlled Trial Recruited from hospital outpatients	18 total: 12 Group CBT * 8 Matched controls	6 x 90 minute sessions of Group CBT Delivered by psychiatrist	Control group received no treatment	Mean age 72 55% female Moderate –severe COPD	Anxiety (HADS) QOL (MRCQ)

		*(2 patients dropped out)	(replaced after 3 sessions)		Pre-trial HADS score higher in CBT group than controls.	
Lisansky & Clough, 1996 (152) USA	Quasi-experimental Study Pre-post test No information on patient recruitment	8 total: CBT 13 initially (5 dropped out)	8 weekly 90 minute sessions of 45 minutes education, 15 min break followed by group CBT. Not specified who delivered treatment	No comparator	Mean age 69.5 Mean FEV_1/FVC ratio only (0.68) 62.5% female 20% Hispanic 80% Anglo Moderate – severe COPD	Anxiety (KSQ) Disability (SIP) Cognitions (COPD-CEQ)
Gift et al, 1992 (153) USA	RCT Recruited from patient list of 3 private physicians	26 Total: 13 PMR 13 Controls	4 weekly sessions of progressive muscle relaxation. Delivered by Venue: physician's office	Control – sat quietly in room for same time Venue: physician's office	Mean age 67 69.2% female 100% Caucasian Confirmed COPD by spirometry	Anxiety (STAI)

Abbreviations: Centre for Epidemiologic Studies -Depression (CES-D), COPD- Cognitive Error Scale (COPD-CEQ), Hospital Anxiety and Depression Scale (HADS), Kellner's Symptoms Questionnaire (KSQ), Medical Research Council Questionnaire (MRCQ), Symptom Check List (SCL), Sickness Impact Profile (SIP), State Trait Anxiety Inventory (STAI).

3.2.3 Research in the 2000's

Research grew at a significant pace in the 2000's with the publication of 11 studies. The majority of the studies were RCTs or controlled trials (CTs). CBT was used in all 11 studies. Characteristics of the studies can be found in table 14. From all of the studies published so far the format varied between individual treatment (101, 144, 146, 153) group therapy (142, 145, 148, 149, 150-152) and in the most recent trials CBT self-help manuals have been used (with booster sessions organised by telephone) (138, 139). It is not clear from two papers if the intervention was individual or group therapy (147, 154).

The first study published in 2001 investigated the effect of a two hour single session of CBT on anxiety, depression, QOL and satisfaction with treatment (149). The results demonstrated that anxiety and depression decreased with the brief intervention but there was no change in physical functioning of the patients (149). De Godoy et al then published a study of pulmonary rehabilitation with 10 psychotherapy sessions (147). The paper contained an

extremely vague description of 'CBT and logotherapy' to the extent it is unclear what the intervention entailed. This will be discussed in further detail in section 3.3. In addition, the sample size was small and the control group improved more than the treatment group. This is not surprising as it appeared that the control group did in fact receive information on 'coping with illness' which appeared to include CBT techniques which may have affected the outcome of the study. Finally, the study was also assessed as high risk of bias (see Table 15).

In 2008, Kunik et al completed a further study involving group CBT and COPD education (148). The results suggested improvements in QOL for COPD patients. However, the study was deemed high risk of bias (see Table 15). In 2009, a small case series was published involving 10 patients with CBT (146). This study was the first to use respiratory nurses to deliver the CBT intervention which showed potential. The study has a high risk of bias (see Table 15). The author concluded that further evaluation of CBT delivered by respiratory nurses was needed (146). As part of a PhD, Lamer's (2010) investigated the use of a CBT minimal psychological intervention for elderly patients with COPD (144). The main focus for the study was depression, but data on anxiety was collected. The study was of higher quality than previous studies and the results suggest the brief nurse led intervention in the patients' home, reduced depressive symptoms and anxiety in elderly patients with minor to moderate depression. It was concluded that adding the minimal psychological intervention to standard care is likely to improve the care for elderly COPD patients (144).

An Australian study used another brief CBT intervention specifically to treat panic attacks and prevent the development of panic spectrum psychopathology and anxiety symptoms (101). As with many studies, anxiety was not an entry criteria for the study. The authors found a decrease in hospital admissions following the intervention but suggested that larger scale trials were needed to supplement the findings of their study. Another small study of group CBT was published in 2010 (142). The authors investigated an intervention consisting of seven weekly sessions lasting two hours. The paper was very well presented and evaluated well when assessed for bias. There was a significant reduction in symptoms of anxiety and depression and the authors concluded that the results underline the need for integrating mental healthcare into the overall medical regime for COPD (142).

A further paper from the USA was published in 2010 (143). The study was a very small 'open trial' of poor quality. There was no comparison group in the study. The findings were that further research is needed and suggested that highly trained CBT therapists may not be required to improve patient outcomes. In 2010, an interventional controlled study of group CBT was published (145). The results suggested that the intervention had potential and a future RCT was planned. The definitive RCT followed in 2014 using a CBT self-help manual. The trial was the largest study to be undertaken to date and suggested that the manual improved self-management and reduced costs to the NHS. The authors concluded the treatment should be considered as an option for the majority of patients as a preventative measure and develop coping strategies (139).

The first study from China was published in 2012. This study used CBT to address uncertainty, anxiety, depression and QOL. As with many of the other studies the paper was assessed as high risk of bias (see Table 15). The study suggests that uncertainty management can improve emotional status but further studies were needed. Despite the fact the intervention lasted 10 months the authors suggested a longer intervention may be beneficial. A summary of the main characteristics of studies published in the 2000's can be found in table 14.

Table 14 – Main characteristics of the studies published in the 2000's.

Author/ Country	Study Design and sampling	Number of patients	Intervention	Comparator	Characteristics of participants and follow -up	Psychological outcomes and measures
Howard and Dupont, 2014 (145) UK	RCT Recruited from 10 GP practices and invited to participate. Computer block randomisation.	222 total 112 CBT 110 Control	CBT Breathlessness manual with two telephone booster sessions plus Relaxation CD	British Lung Foundation information booklets.	Mean age – 72.2 52% Females FEV_1/FVC ratio	Anxiety (HADS) Depression (HADS) HRQOL (CRQ-5R)

Jiang and He, 2012 (138) China	RCT Recruited from hospital outpatients.	99 Total: 50 CBT 49 Control	CBT uncertainty management using Self-Help Manual and audio CD. Weekly telephone calls for 4 weeks then monthly calls for 10 months	Usual Care	Mean age 65 63% Males	Anxiety (SSAI and STAI) Depression (HADS) QOL (SF-36)
Lamer's et al, 2010 (144) Holland	RCT (anxiety was secondary outcome) Recruited from 89 general practices Computerised Block randomisation	187 Total: 96 CBT intervention (only 71 patients received intervention). 91 usual care	Minimal Psychological Intervention (MPI) 2-10 individualised visits over 3 months Nurse administered with psychiatric/GP support	Usual care	Mean age 71 years 60% Males No details of lung function given Mild- moderate depression (anxiety not stated) Follow up varied - 1 week, 3 and 9 months after intervention Control group – 6 weeks	Anxiety (SCL) Depression (BDI) HRQOL (SGRQ)
Livermore et all, 2010 (101) Australia	RCT Recruited from outpatient clinics (consecutive patients who met criteria) or in-patients invited to participate. Patients volunteered for the study. Excel computer package was used to generate a random sequence of numbers.	41 total: 21 CBT 20 usual care	4 individualised hour long sessions of CBT following PR Administered by psychologist. Patient manual used.	Routine care following PR	Mean age 73.2 56% Females FEV_1/FVC ratio <70% FEV_1 <60% Moderate – severe COPD Follow up at 6, 12 and 18 months	Anxiety (HADS) Depression (HADS) Panic attacks and panic disorder (ADIS-IV) HRQOL (SGRQ) Illness specific catastrophic cognitions (IPBQ)
Howard et al, 2010 (145) UK	Interventional control study	48 total	4 weekly 2 hours Group with a carer (average 6 participants per group) CBT sessions. Patients received a handbook and relaxation tape. A 6 week telephone follow-	Patients were own controls (from retrospective data)	Mean age 71 60% males 54% were married 85% ex-smokers Average pack 39 pack years Mean FEV_1 % was 33% No record of FEV_1/FVC ratio 33% have long term oxygen Therapy (LTOT)	Anxiety (HADS) HRQOL (SGRQ) Hospital admissions

			up was undertaken.		Follow up 4 weeks and 10 weeks	
Hynninen et al, 2010 (142) Norway	RCT Recruitment from outpatient pulmonary clinic and by newspaper advert Randomisation by matched pairs (according to their FEV1 predicted), one participant was randomly assigned to CBT.	51 total: 25 CBT 26 standard care	7 weekly 2 hour group session at university outpatient clinic 5 patients on average). Phone follow-up. Administered by Masters-level psychology student.	Standard care with 5-10 minute telephone contact every 2 weeks.	Mean age 61 51% female FEV_1/FVC ratio <70% FEV_1 % predicted <80% Mean education years 12.1 25% current smokers Follow up 2 and 8 months from baseline.	Anxiety (BAI) Depression (BDI-II) HRQOL (SGRQ) Sleep Quality (PSQI)
Cully et al, 2010 (143) USA	Open trial CHF and COPD patients recruited from electronic medical records (10 COPD, 6 CHF and 7 both)	23 CBT	6 x 50 minute sessions of CBT (ACCESS). 2 face to face sessions followed by 4 core modules either face to face or telephone. Administered by 5 providers advanced psychology trainees)	No comparison	Mean age 100% male Follow up at 8 weeks and 3 month	Anxiety (STAI-Trait) Depression (BDI-II) HRQOL (CRQ)
Heslop et al, 2009 (146) UK	Pre-Post observational study. Recruited from hospital out-patients clinic.	10 CBT	CBT 2-6 individual sessions depending on need.	No comparator	Mean age 80% severe COPD 10% Moderate 10% Mild	Anxiety (HADS-A) Depression (HADS-D) Hospital Admissions

Kunik et al, 2008 (148) USA	RCT (single blind) Recruited from veterans hospital and advertising	238 total: 120 education 118 CBT	CBT 8 x 1 hourly sessions per week Delivered by psychological interns and post-doctoral fellows	Group COPD education 8 sessions (1 hour) Delivered by psychological interns and post-doctoral fellows	Mean age 66.3 96.2% males 81% Caucasian FEV1/FVC ratio <70% FEV1 <70% Moderate anxiety or depression Follow-up 4,8 and 12 months 48% attrition rate	Anxiety (BAI) Depression (BDI) HRQOL (CRQ) QOL (SF-36)
De Godoy et al, 2003 (147) Brazil	RCT (single blind) Consecutive patients attending outpatients referred for PR	30 total: 14 PR and psychotherapy 16 PR only	12 week PR programme: 24 sessions of physical exercise, physiotherapy; 12 psychological sessions *does not state if group or individual sessions (Cognitive & logotherapy) and 3 educational sessions. Delivered by psychologist	12 week PR programme: 24 sessions of physical exercise, physiotherapy & 3 educational sessions only	Mean age 60.33 73% Male FEV1/FVC ratio not stated Mild-moderate anxiety and depression Follow-up 3 months	Anxiety (BAI) Depression (BDI) HRQOL (SGRQ)
Kunik et al, 2001 (149) USA	RCT (single blind) Recruited from veterans hospital and advertising	48 total: 24 CBT 29 education	Single 2 hour Group CBT (6-10) 6 weekly phone call Delivered geropsychiatrist	Group Education and 6 weekly phone calls Delivered by internist	Mean age 71.3 83% male 90% Caucasian FEV1/FVC <70% Mild anxiety and depression Follow-up 3 months	Anxiety (BAI) Depression (GDS) QOL (SF-36)

Abbreviations: Anxiety Disorder Interview Schedule (ADIS-IV), Beck Anxiety Inventory (BAI), Beck Depression Inventory (BDI), Chronic Respiratory Questionnaire (CRQ), Geriatric Depression Scale (GDS), Hospital Anxiety and Depression Scale (HADS), Illness Specific Catastrophic Cognitions (IPBQ), Pittsburgh Sleep Quality Index (PSQI), Pulmonary Rehabilitation, Symptom Checklist (SCL), Short-Form 36 (SF-36) ST Georges Respiratory Questionnaire (SGRQ), Short State Anxiety Inventory (SSAI), State Trait Anxiety Inventory (STAI).

3.2.4 Relevant Systematic Reviews

In 2002 the first systematic review of the efficacy of psychological treatment to reduce anxiety and panic in patients with COPD was published (129). Systematic reviews aim to iden-

tify, evaluate and summarise the findings of all relevant studies. However, flaws in the design of the review can introduce bias (163). A limitation of the review by Rose et al (2002) is the inclusion of the term 'pulmonary rehabilitation' in their search strategy (129). Pulmonary rehabilitation is a very important exercise based intervention rather than a psychological intervention. Whilst the benefits may well affect psychological well- being, its primary focus is improving exercise capacity. There were many articles on the topic of pulmonary rehabilitation which were not included in their review. In addition, several papers of psychological interventions in COPD were missed and could have been included e.g. Emery et al (150), Eiser (151) and Lisansky and Clough (152). It may be that the literature search terms were flawed which can miss pertinent papers or the design of the review introduced bias (163). Rose's review rightly concluded that there was insufficient research of sufficient quality on which to base recommendations for effective interventions for anxiety and panic in COPD.

A second systematic review was conducted by Coventry and Gellatly in 2008 and focused on CBT for the treatment of mild to moderate anxiety and depression (141). The author's question was focused and the PICO format was used to identify an appropriate population, intervention, comparison and outcomes. The authors state that the search terms were broad to capture the maximum number of studies but this paper did not include studies which were identified in a third review which followed in 2011. Again this may be due to the search terms or criteria used. This review identified a study by De Godoy in 2003 (147). However, I found two papers from the authors of the same study. The first paper in 2003 reported on 39 patients and the second paper in 2005 included 49 patients (147, 164). Coventry included four papers in their final review and concluded that there was scant evidence for the use of CBT to reduce symptoms of anxiety and depression (141). The authors suggested that there was only limited evidence that CBT, when used with exercise and education, can contribute to significant reductions in anxiety and depression in COPD patients and suggested there was scope for a well powered RCT to evaluate the effectiveness of CBT in a COPD population (141).

A third systematic review on the efficacy of psychologically based interventions to improve anxiety, depression and QOL in COPD was published in 2011 (136). A clearly focused question was identified in terms of population studied, intervention given and the outcomes considered. The authors conducted extensive searches to identify appropriate research from 1983 up to 2009. In addition reference lists were scrutinised to identify additional studies. Key authors were contacted to obtain details of additional studies in an attempt to address publication bias. Data were extracted using a standardised extraction sheet. A second reviewer independently extracted data from 50% of included studies to ensure accuracy and reliability. It is recommended that a second researcher should independently check all of the forms for accuracy and detail to ensure data extraction is unbiased and reliable (163).

A final review and meta-analysis was published in 2014 (4). As with previous reviews, the search was restricted to English language studies only which may result in the exclusion of appropriate research in other languages. The review included papers published between 2000 and 2013. A clearly focused question was identified and PICO format was used to determine eligibility criteria. Study selection and data extraction was undertaken by two independent reviewers. A study from China was identified (138). Four studies were included in the meta-analysis and the results of the review concluded that there was a small effect of CBT interventions.

3.2.5 Assessment of Bias

It is important to assess the risk of bias in all studies in a review (165). The task of assessing the risk of bias in studies is part of assessing the strength of a body of evidence (166). Biases can result in an overestimation or underestimation of the true effect of an intervention (165). The Cochrane Collaboration recommend using judgements when assessing bias and discourage the use of scales (165). It is argued that common scales emphasise reporting rather than the conduct of the research and does not cover allocation concealment, one of the most important potential biases in trials (165). The outcome of bias assessment is recorded as low, medium or high risk (165). The papers identified in this review were judged for risk of bias and the results are presented in table 15.

Table 15 – Assessment of bias.

	Random sequence generation	Allocation concealment	Blinding of outcome assessment	Losses to follow up >20%	Adequate statistical handling of missing data	ITT Analysis
Howard & Dupont, 2014	Low	Low	High	Low	Low	Low
Jiang & He, 2012	High	High	High	Low	Moderate	High
Lamer's et al, 2010	Low	Low	High	High	Low	Low
Livermore et all, 2010	Low	Moderate	Moderate	High	Low	Low
Howard et al, 2010	High	High	High	Low	Low	Low
Hynninen et al, 2010	Low	Low	High	Low	Low	Low
Cully et al, 2010	High	High	High	Low	High	High
Heslop et al, 2009	High	High	High	Low	Low	High
Kunik et al, 2008	High	High	High	High	Low	Low
De Godoy et al, 2003	High	High	High	Low	Low	High
Kunik et al, 2001	High	High	High	Low	Low	High`
Emery et al, 1998	Moderate	High	High	Low	Low	High
Eiser et al, 1997	High	High	High	Low	Low	High
Lisansky & Clough, 1996	High	High	High	Low	High	High
Gift et al, 1992	Low	High	High	High	Low	Low
Rosser et al, 1983	Moderate	High	High	Low	High	High

When assessed for bias all studies were assessed as high risk and therefore the results must be viewed with caution. There is a clear need to develop a RCT which address bias.

3.2.6 Recruitment and attrition

Recruitment was a problem in some studies. A host of complex and inter-related factors, including patient, provider and health care systems, affects accessibility of medical treatment (167). Patients with COPD are at high risk of poor mental health treatment and underuse services for a variety of reasons including stigma, access to care, or do not recognise mental health needs (167). Causes highlighted by patients in the studies identified for this

review included lack of transportation (142), patients believing they are not anxious or depressed, being too busy or feeling fatigued (142) , illness or death (144). It is also likely that patients who are anxious would rather avoid anything that may increase their anxiety such as participating in research. Patients may also lack motivation, especially if they are depressed (84). Careful consideration must be given to engage and support patients to ensure adequate participate rates are achieved (142).

3.2.7 COPD Severity

A range of COPD severity was found across the studies. A recommendation of one of the reviews suggested including all severities of COPD (136). It was noted that a number of methods were used to ascertain the severity of airways obstruction. This ranged from spirometry and peak flow measurements (153), spirometry (151, 152, 154) , no measurements at all (144) or it is not mentioned in the paper (143). Only five studies reported the gold standard FEV_1/FVC ratio <70%. Two studies reported mean FEV_1 (145, 154). The main disadvantage of not recording the FEV_1/FVC ratio is the diagnosis of COPD cannot be confirmed. One study relied on general practitioner (GP) opinion for the diagnosis or verification merely being made based from the GP practice COPD register (144). Relying on a diagnosis from primary care may result in patients without COPD being inappropriately included in studies as primary care databases have a 20% misdiagnosis of COPD (168).

3.2.8 Age

The ages of patients were similar in all of the studies. The mean age ranged from 60 – 73.

3.2.9 Setting

The studies were undertaken in a number of different countries with a variety of healthcare systems (see Table 16). It is therefore difficult to identify the impact of cultural or environmental differences (4).

Table 16 - Summary of countries where studies were conducted.

Country	Number of Studies (n=16)
United States of America	6
Australia	1
Holland	1
New Zealand	1
UK	4
Norway	1
China	1
Brazil	1

3.2.10 Psychological Morbidity

You would expect studies investigating the effectiveness of an intervention to reduce symptoms of anxiety or depression to include psychological morbidity as a necessary entry criteria (unless it is a preventative study). The level of psychological morbidity within studies identified in this review varied. Some studies did not report baseline psychological morbidity at all. This is important data which should be clearly documented. Table 17 outlines which studies included symptoms of anxiety as an inclusion criteria.

Table 17 – Studies with anxiety in inclusion criteria.

Study	Anxiety Symptoms in inclusion criteria
Howard & Dupont, 2014 (145)	No
Jiang & e, 2012 (138)	No
Hynninen, 2010 (142)	No
Cully, 2010 (143)	Yes – STAI-S or STAI-T >39
Lamers, 2010 (144)	No
Howard, 2010 (145)	No
Livermore, 2010 (101)	No – preventative study. Excluded patients with panic disorder.
Heslop, 2009 (146)	Yes – HADS-Anxiety score ≥8
De Godoy, 2003 (147)	No
Kunik, 2008 (148)	Yes – BAI >16
Kunik, 2001 (149)	No
Emery, 1998 (150)	No
Eiser, 1997 (151)	Yes – HADS-Anxiety score ≥8
Lisansky & Clough, 1996 (152)	No
Gift et al, 1992 (153)	No
Rosser, 1983 (154)	No

3.2.11 Study design

RCTs are the gold standard study design for evaluation of health care interventions (169). Randomisation is key to ensure the intervention and control groups do not differ and biased results can be minimised (169). Ten of the studies were RCTs. The remainder were non-randomised experimental designs which have been shown to be prone to bias (169). However, as there is a lack of high quality RCT's all papers have been included in this review.

3.2.12 Power Analysis

A significant problem with a number of studies on CBT in COPD was the low sample sizes and lack of power calculation. From the 16 studies only five reported a power calculation. Two studies failed to recruit sufficient patients suggested in the power calculation which is a significant weakness (101, 142).

3.2.13 Outcome Measures

A major problem with the studies was that numerous outcome measures were used to evaluate the efficacy of the interventions. It is therefore difficult to compare the outcomes of the studies. For anxiety several measures were used: Visual Analogue Scale, Spielberger Anxiety Inventory, Kellner's Symptom Questionnaire, Symptom Check List, Beck Anxiety Inventory and the HADS-Anxiety questionnaire. The authors of one study acknowledged that the measures were defective and yielded such variable results that it is difficult to draw any conclusions from their small sample (170). The most common measure used to assess symptoms of anxiety was the HADS-Anxiety subscale and this questionnaire was used in five studies. The HADS has fewer items than the other measures which reduces patient burden, has been extensively validated in medical out-patient settings and validated in COPD patients. Similarly QOL was measured by generic measures in some studies and HRQOL measures in others including the CRQ, SF36, SGRQ, IPBQ, MRCQ and SIP. The most common measures used were the CRQ and the SGRQ.

3.2.14 Blinding

Blinding is recommended to minimise bias (165). Double blinding ensures that preconceived views of subjects and clinicians cannot systematically bias the assessment of outcomes (171). Due to the nature of the interventions used in the papers included in this review, it is difficult to blind patients to the intervention they received. In De Godoy's paper it is suggested that 'both groups were blinded in relation to activities of the other group' (page 155). It is difficult to comprehend how patients could give informed consent if they were not aware of the activities entailed in each group. Some studies tried to minimise bias and data collection was undertaken by individuals blinded to the group assignment.

3.2.15 Type of Interventions

Interventions to change behaviour are typically complex, involving many interacting components (172). The CONSORT statement for randomised trials of 'non-pharmacological' interventions recommends precise specification of trial processes, including specific detail of the delivery of interventions and description of the different components of the interventions (173). Studies describe interventions in protocols and publications in different ways but may mean the same thing (e.g. self-monitoring may be labelled daily diaries or behavioural counselling may involve educating patients, providing feedback, self-monitoring and reinforcement) (174). This may lead to uncertainty and confusion (174). The CONSORT Guidelines provide an excellent structure for reporting RCTs. However, it is argued that behavioural scientists should provide additional information in published reports (175). The following information has been proposed:

a) The content or elements of the intervention

b) The characteristics of those delivering the intervention

c) The characteristics of the recipients

d) The setting

e) The mode of delivery (e.g. face to face)

f) The intensity (e.g. contact time) and duration (number of sessions)

g) Checks on adherence to delivery protocols

The studies identified in this review were assessed for the above categories and a summary can be found in table 18.

Table 18 – Description of interventions used in studies.

Study	Characteristics of those delivering intervention	Characteristics of recipients de-	Setting	Mode of delivery	Intensity and duration	Adherence to delivery protocols
Howard and Dupont 2014 (139)	Psychologists	Yes	Home	Self-Help Manual with two 30 min booster sessions by phone	Patients were encourage to use manual for 1 hour daily during 5 week programme	Not stated
Jiang & He, 2012 (138)	Nurses (no further information given)	Yes	Home	Self-Help Manual and audio CD	Weekly telephone calls (35 minutes) for 4 weeks then monthly calls for 10 months	Not documented
Lamer's et al, 2010 (144)	Nurses	Yes	Home	One to One sessions	Maximum of ten visits over three months. 1 hour each visit. (Range 2-10 hours. Mean 4 visits).	Checklists were used to check adherence to protocol
Livermore et all, 2010 (101)	Psychologists	Yes	Hospital out-patient Department	One to One sessions	1 hour sessions over 4 weeks. 4 hours in total.	Not stated
Howard et al, 2010 (145)	Psychologists (although this is not explicit in the paper)	Yes	Hospital out-patients Department	Group sessions plus handbook and relaxation tape. Telephone call at 5 weeks	2 hour weekly sessions over 4 weeks. 8 hours in total.	Not stated
Hynninen et al, 2010 (142)	Two masters level Psychology students	Yes	University Out-patient clinic	Group sessions	1 hour weekly sessions over 7 weeks	Sessions were videotaped for adherence and competence
Cully et al, 2010 (143)	Five psychology interns, post-doctoral fellows, pre-doctoral interns.	Yes	Large Medical Centre	One to one sessions plus 3 booster telephone or one to one sessions	50 minute sessions (6 in total) plus 3 booster telephone or one to one sessions of 10-15 minutes. 5-6 hours.	Yes
Heslop et al, 2009 (146)	Respiratory Nurse	Yes	Hospital Out-patients Department or home visit	One to one sessions	30 minute sessions. Every two weeks. Number of sessions ranged 2-13 (mean 4)	No

Kunik et al, 2008 (148)	Psychology interns and post-doctoral fellows	Yes	Large Medical Centre	Group sessions	8 hourly sessions held weekly	Yes
De Godoy et al, 2003 (147)	Not stated	Yes	Hospital out-patients department	? One to one sessions	12 hourly sessions held weekly	Not stated
Kunik et al, 2001 (149)	Gero-psychiatrist	Yes	Hospital out-patients department	Group sessions	Single 2 hour session	Not stated
Emery et al, 1998 (150)	Psychologist	Yes	Hospital out-patients	Group sessions	1 hour weekly sessions over 10 weeks (in addition to PR). 10 hours in total.	Not stated
Eiser et al, 1997 (151)	Psychiatrist	Yes	Hospital out-patients department	Group sessions	90 minute sessions at weekly intervals. Total number 6.	Not stated
Lisansky and Clough, 1996 (152)	Psychiatrist & nurse	Yes	Hospital out-patients department	Group sessions	8 weekly sessions. No further information given.	Not stated
Gift et al, 1992 (176)	Pre-recorded tape	Yes	Physician's office	Individual sessions	4 weekly sessions for 20 minutes.	Not applicable
Rosser et al, 1983 (154)	Psychoanalyst	Yes	Hospital Out-patients	?One to one (not clear from paper)	45 minute sessions over 2 months. 8 sessions in total.	Yes

A major challenge with complex interventions is identifying the effective components within them. Some of the papers in this review were difficult to read and identify what the intervention involved, who undertook the intervention and what the intensity and duration of the sessions were. This makes replication and implementation of the most effective interventions difficult (174). A number of interventions were used including group and individual CBT, CBT based education, taped progressive muscle relaxation and individual analytical therapy. It has been suggested that group CBT may not be appropriate for patients with more severe disability and/or psychological distress (142). Whilst group therapy may be more cost effective, it may not be acceptable to patients and lessens individualised goal setting opportunities (142). Key components of the interventions used in previous research were clearly presented in some studies (139, 144, 145, 146, 148, 149). Hynninen et al (2010)

provided a very comprehensive table of techniques used, the aim of the technique and an example to aid the reader (142). Table 19 summarises the main cognitive and behavioural change techniques used across all studies based on the Taxonomy of behavioural techniques (174).

Table 19 - Taxonomy of techniques used in studies.

Study	Formulation	Goals setting and planning	Feedback and monitoring (e.g. verbal, homework, diaries)	Shaping knowledge/psychoeducation	Relaxation	Cognitive therapy(e.g. changing unhelpful cognitions)	Behavioural activation (e.g. activity, exercises)	Breathing control	Adaptive behaviours (e.g. pacing, planning,)	Written information/Manual/CD	Sleep Management	Psychoanalysis
Howard & Dupont, 2014	√	√	√	√	√	√	√	√	√	√		
Jiang and He, 2012					√	√				√		
Lamer's et al, 2010		√	√	√		√			√			
Livermore et all, 2010				√		√	√	√	√			
Howard et al, 2010				√	√	√		√	√			
Hynninen et al, 2010				√	√	√	√					√
Cully et al, 2010				√	√	√	√		√			
Heslop et al, 2009	√	√	√	√	√	√	√	√	√	√		
Kunik et al, 2008			√	√	√	√	√		√		√	
De Godoy et al, 2003						√						
Kunik et al, 2001				√	√	√	√				√	
Emery et al, 1998				√	√	√						
Eiser et al, 1997				√	√	√						
Lisansky and Clough, 1996			√			√					√	
Gift et al, 1992					√							
Rosser et al, 1983												√

Older studies tended to use less techniques (or report less). Almost all of the studies reported using shaping knowledge or psychoeducation, relaxation and cognitive therapy.

3.2.16 Delivery of the intervention

In previous research a variety of professionals delivered the CBT intervention. This ranged from nurses, psychology students, psychoanalysts, internist, psychiatrist, psychologist and post-doctoral fellows. One study involved a number of professionals including a nurse, psychologist, physiotherapist and occupational therapist. Each profession will have varying levels of training and expertise in psychological care. No studies have established if CBT delivered by respiratory nurses reduces anxiety, depression and healthcare utilisation/ hospital admissions.

3.3 Recommendations for future research

A number of methodological weaknesses of current research has been proposed and need to be addressed in future research including:

- Small sample sizes and underpowered studies (4, 129, 141)
- Failure to measure or report lung function to ensure only COPD patients recruited (129).
- A need to include patients with all COPD disease severity (141, 136).
- More rigorous inclusion and exclusion criteria for clinical samples (129)
- Short duration of studies (129).
- Lack of standardisation of outcome measures (4, 129). Rose et al (2002) suggest the use of the HADS (129).
- The need to use theories of the relationship between dyspnoea and anxiety to develop the most appropriate treatment including interventions for panic (129).
- Heterogeneity of interventions (4).
- Identify suitable settings for the intervention including primary care, community settings and even home visits (141).
- Interventions should target QOL and evaluate their efficacy (136).

- There may be alternative methods of using CBT such as telephone or computerised CBT models (141).
- Lack of blinding in assessment of treatment outcomes (129).
- Finally, there is a need to for a well-developed RCT to investigate the use of CBT for patients with COPD (141).

3.4 Summary

There are a growing number of studies evaluating the efficacy of psychological interventions to improve the psychological well-being of patients with COPD. Most of the studies published in the last twenty years have used CBT. In total 16 studies were included in this review incorporating research involving 612 patients. However, despite the valuable contributions of prior research, a number of methodological limitations leave the role of CBT in question. Most studies of CBT in COPD patients include very small numbers of patients from a variety of different health care settings with a variety of health care professionals undertaking the CBT. Mixed results were found in these studies. It is noteworthy that studies that have been conducted more recently are of a higher standard. However, it is difficult to interpret and combine the results as the studies are so different in terms of design, setting, focus, interventions and outcome measures. There is some evidence that psychological interventions impact on anxiety and depression but further research is needed. What is not clear is if CBT is effective in the COPD population where complex physical health symptoms compound symptoms of anxiety and depression or what the best model is to support patients.

In a comprehensive systematic review, Baraniak and Sheffield (2011) concluded that there is some evidence that psychological interventions such as cognitive behavioural therapy impact on anxiety (136). However, a meta-analysis revealed a small effect for anxiety only. Previous reviews have highlighted that there is a need for high-quality research of CBT in the routine management of patients with COPD (129, 136). Future studies should develop robust methodology (4, 129, 177) be adequately powered (4) and include a clearly defined population (129). It has also been recommended that the treatment of psychological difficulties in COPD should be developed from existing models of care e.g. panic (129) and evaluate health outcomes such as QOL and cost effectiveness (136). In addition, future studies should use robust outcomes measures of anxiety, depression and QOL suitable for a COPD

population (4, 129). However, it is of course critical to identify an intervention that is acceptable to patients (141). The recommendations from previous researchers have been carefully considered to develop an appropriately robust RCT for this research.

The following chapter provides the background of the development of the novel CBT intervention used in this study. The research methods for the study will then be presented in chapter 5.

Chapter 4 – Development of a Novel CBT Intervention for people with COPD and anxiety

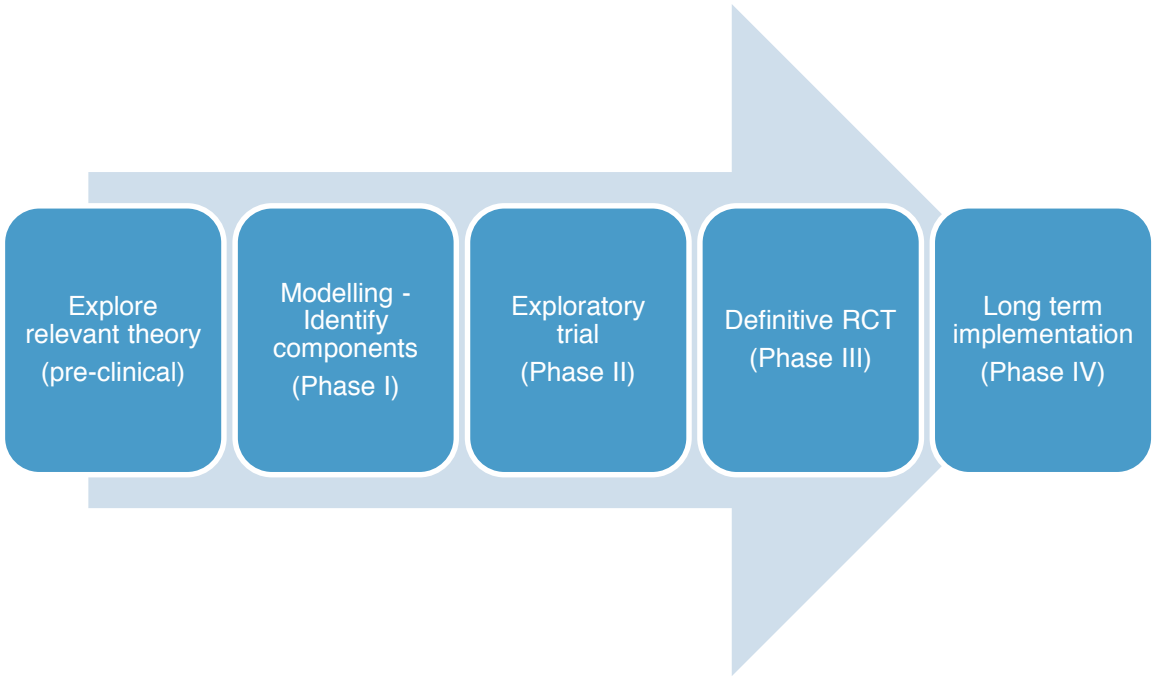
The previous chapters of this thesis have outlined the theoretical basis of using CBT for symptoms of anxiety and depression in patients with COPD and a summary of previous research has been given. The aim of this chapter is to describe how the complex CBT intervention used in this study evolved and developed and provide a description of the CBT intervention itself to enable future researchers to replicate the intervention if needed.

4.1 Complex interventions in healthcare

Complex interventions are increasingly being used in health care. Conventionally complex interventions are described as having several interacting components (172). Whilst it could be argued that few interventions are simple, there are inevitably some that are more complex than others (172). Examples of complex interventions include treatments that are not drugs or surgical procedures, but may have many potential 'active ingredients' (178). It can be difficult to precisely define the 'active ingredients' that makes development and evaluation even more difficult (178). On a continuum, we may consider a RCT of a drug versus a placebo is at the simplest end of a spectrum (178) and a comparison of psychological therapy as being at the most complex end of the spectrum.

In 2000, the MRC published guidance for developing and evaluating RCTs for complex interventions to improve health (178). The MRC originally proposed a sequential framework that might help researchers and set out objectives to be met at each stage prior to moving forward to the next stage. These stages are outlined in figure 12. However, it was suggested that these stages may not be a stepwise process, but rather a flexible approach depending on the quality of existing evidence and nature of the intervention (172).

Figure 12 – The original MRC Framework for the development and evaluation of RCTs of complex interventions to improve health (178).



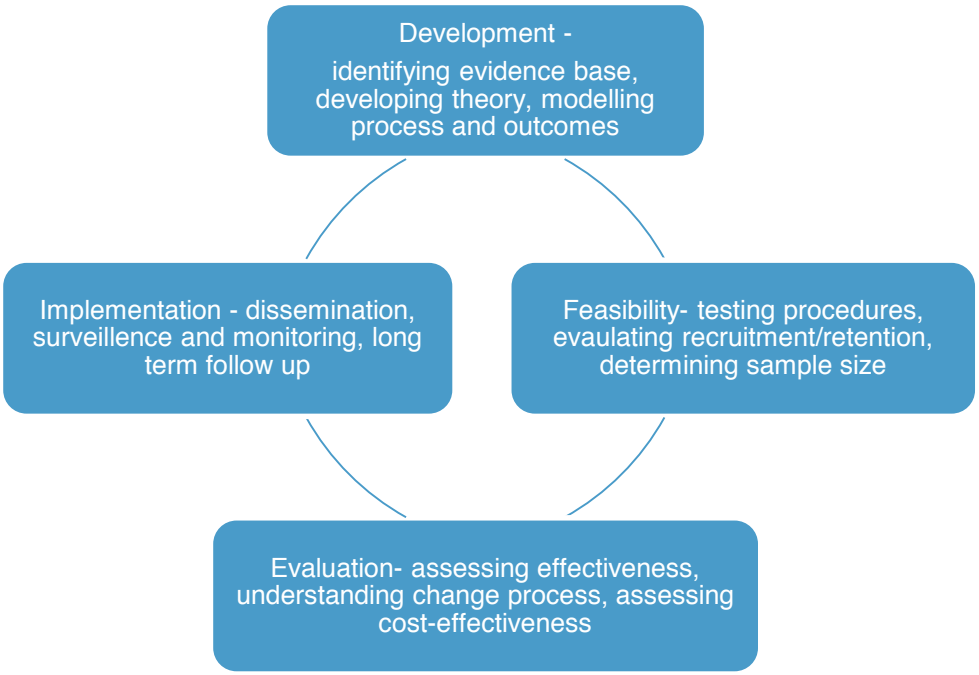
In 2008, an update of the MRC guidance reinforced these key messages and addressed the limitations identified in the original document. The MRC rightly highlight a number of dimensions add to the complexity of an intervention (172). These are presented in table 20.

Table 20 – Dimensions of Complexity of CBT Interventions (172).

The intervention itself – the content, mode of delivery, number of sessions, duration, intensity, context.
Adaptability/flexibility– the extent to which the intervention can be modified and on what basis, for example: participant assessment and therapeutic progress based on clinical judgment.
Location - clinic, home setting or other venue.
Psychological therapist - number of therapists involved, therapist professional training, knowledge and skills, therapeutic relationship with patients and compliance with the treatment protocol.
Patient – preference, physical disability and comorbidities, cognitive ability, motivation, confidence, perceptions of self-efficacy and compliance.

The MRC updated the framework as it had been recognised that the development of a complex intervention may take a wide range of different forms, and addressed the linear framework with a cyclical model (Figure 13) (172). This acknowledges the experimental approach that incorporates learning at each stage of development of a complex intervention.

Figure 13 – Diagram of the revised MRC Framework for the development and evaluation of RCTs for complex interventions to improve health (172).



4.2 Background to the development of the complex CBT intervention for this study.

The development of the CBT model used in this study evolved over many years and was conceived from work within the field of palliative care and physical health. Dr. Kathryn Mannix, a Consultant in Palliative Care, pioneered the development of CBT in palliative care. Dr. Mannix recognised that specialist nurses working in palliative care commonly encountered patients with emotional problems and frequently offered psychological support to patients and their families. There was evidence that CBT was an effective psychological treatment for anxiety, panic and depression in physical health although no formal studies had been undertaken within palliative care settings. Traditionally CBT was undertaken by highly trained CBT therapists. However, within the palliative care setting this model was thought not be desira-

ble or practical for very ill people with advanced or end-stage illness on account of the limited access to this level of psychological therapist and the high level of need (179). Indeed, many patients in the physical health setting have complex physical and emotional health needs, reduced energy reserves and possibly a limited capacity for new therapeutic relationships (179). Dr. Mannix's novel idea was to identify if non-mental health professionals who worked in palliative care could be trained in 'basic CBT skills or first aid' (179).

A basic introductory course in CBT skills for nurses working with palliative care patients was developed (179). A RCT was designed to assess the effect of the training using a before and after design without any controls. Sixteen experienced nurses, two hospice social workers and two palliative care occupational therapists volunteered to enter a study to evaluate the effectiveness of the CBT training. The training consisted of the equivalent of nine days taught sessions over a twelve week period. The course included basic theory of CBT; models of anxiety, depression, panic, adjustment to serious illness and training and supervision in relevant cognitive and behavioural techniques (179). The course involved observing tutors modeling CBT skills, practicing skills using role play, and all trainees completed a reflective diary (179).

An integral part of the study for all participants was supervision with an experienced CBT trainer who was familiar with delivering CBT in a physical health setting. Supervision was structured to build skills and trainers modeled CBT techniques (179). Trainees were assigned to groups of four and attended for two hours fortnightly over three months. Trainees were asked to supply audiotapes of interviews with patients and bring to supervision for reflection and comment (179). After twelve weeks basic training half of the nurses were randomised to continue supervision or a control group of no ongoing CBT supervision to identify if the CBT skills were enhanced or diminished. I had volunteered for the study and following the initial training was randomised to ongoing supervision with Dr. Chris Baker.

The primary outcome measure for the study was the change in the trainee's level of competency in the application of CBT techniques over time. Audiotapes of actual clinical sessions with patients were assessed using a ten-item scale called the Cognitive First Aid Rating Scale (CFARS) which had been developed by the research team specifically to assess CBT skills of non-mental health practitioners (179) (Appendix 2). In addition all trainees participated in a

structured clinical interview detailing their experiences of learning CBT and their use of CBT skills. The results of the study demonstrated that the brief, focused training in CBT techniques supported by supervision, produces a significant improvement in the ability of palliative care professionals to recognise emotional distress, select appropriate CBT techniques, enable patients to gain insight, change their behaviour and regain control (179). A further RCT was published in 2009 which also demonstrated a significant impact on common mental disorders in patients with advanced cancer (180).

In cancer services it was identified that patients' psychological symptoms were not recognised and this resulted in patients not being offered access to the services they needed (179). Respiratory patients face the same problem as many health care professionals lack appropriate assessment skills and may underestimate the benefits of psychological support. Health and social care professionals offering day-to-day care are in a position to provide general psychological support to patients and carers and can play a key role in psychological assessment, prevention and amelioration of distress (132). I identified that there was a strong argument to develop awareness of psychological needs and skills in delivering psychological care into the field of respiratory medicine considering the psychological burden encountered by patients.

My initial idea to deliver CBT to COPD patients with symptoms of anxiety and depression first developed in 2001 during my participation in the study for palliative care professionals. The aim of CBT for patients with COPD was to address psychological needs and to compliment medical management. My experience suggested that CBT might be effective in addressing breathlessness, dysfunctional breathing, related anxiety, reduced activity levels and avoidance of activities (that induce breathlessness and lead to deconditioning) and break the panic cycle. Evidenced based CBT models for depression and anxiety were drawn upon to develop a treatment for patients with COPD (92).

I continued to apply my basic CBT skills and applied to complete a post graduate diploma in CBT at the Newcastle Regional CBT Centre and Durham University. Most of the professionals training at diploma level were from a mental health background including psychiatrists, mental health nurses and social workers. Very few professionals from the physical health background applied for training at diploma level and I was the only professional from a physical

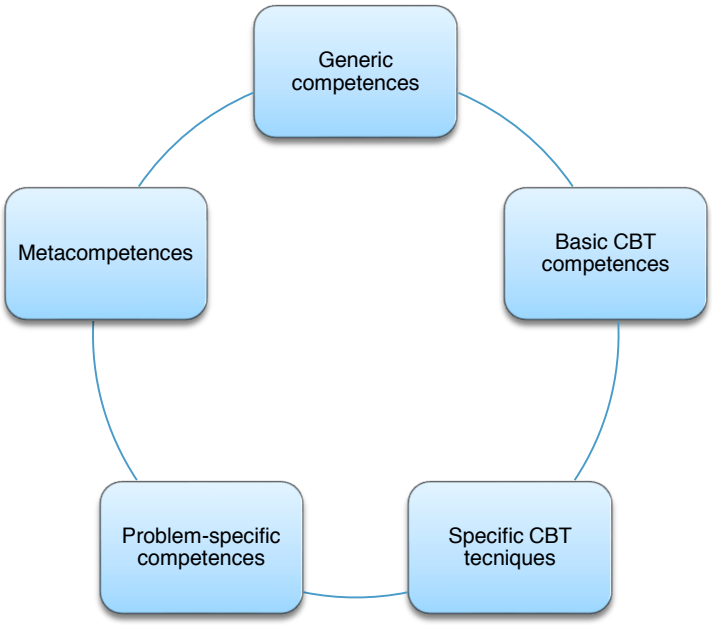
health background to undertake the course in 2003. Reflecting on the impact of my therapy work enabled me to identify the potential benefits of this approach for people with COPD. A key stage in the revised MRC framework for complex interventions is identifying the evidence base to develop the model to be used. As part of the course I completed a dissertation on the use of CBT for patients with respiratory disease, looked at the literature relating to psychological distress in COPD and the rationale for using CBT skills and techniques for anxiety, panic and depression. It was clear at the time that there was limited research on the effects of CBT with COPD patients and there were no studies with respiratory nurses delivering the intervention.

4.3 CBT Competencies

Developing, piloting, evaluating and implementing a complex intervention can be a lengthy process (172). During my training as CBT therapist I was assessed through academic assignments and practical assessments to ensure I had achieved the necessary competencies. It is essential that individuals have the right skills to deliver CBT to a good and coherent standard (134). It took several years to consolidate my knowledge and skills. However, this experience enabled me to develop and refine a model of CBT that could be used for patients with COPD as suggested in the new MRC Framework.

Within the NHS a number of professionals may deliver psychological therapies and their training will vary considerably. In 2007, a report was published by the Department of Health identifying competences that are needed to deliver good-quality CBT, rather than simply relying on job titles to indicate proficiency (134). The evidence to support the competencies was identified by a group of leading experts in the field drawing on descriptions given in clinical controlled trials (which usually use 'manuals' describing the treatment model and associated techniques) (134). They suggested a range of competencies that a therapist should have in order to adhere to evidence based models of treatment delivery to achieve the best outcomes for the patient (134). Figure 14 shows the key therapeutic competences identified in 2007 (134).

Figure 14- Competency Framework for CBT skills (134).



Generic competences such as building a therapeutic alliance, knowledge, assessment skills and ability to use supervision are applicable to all forms of psychological therapy (134). CBT needs to be undertaken by knowledgeable healthcare professionals who understand mental health problems, are able to elicit and understand the patient's history (or story), identify suitable interventions to be effective in their treatment and understand the rationale for using them. However, I would argue that it is crucial to understand the role of physical health problems on psychological well-being. The patient's physical health will almost certainly be relevant to the patients presenting problems. Key competencies identified by the MRC include the ability to explain and demonstrate the rationale for CBT to the patient, structuring therapy sessions appropriately, the use of problem solving skills, agreeing goals for interventions, and using measures to guide therapy and monitor outcome (134).

A vital role of any therapeutic intervention is the ability to build a good therapist-patient relationship by relating to patients in a warm, encouraging and accepting manner. One might expect that due to the nature of the work, most health care professionals within the heath care setting have some therapeutic skills in psychological and emotional care. However, it is clear that some people do not have a natural ability to develop therapeutic relationships sufficiently to deal with emotional distress. A common way of coping with distressed patients is to offer 'a cup of tea' to diffuse the situation. This may be a kind gesture but may

not address the patient's difficulties. Undertaking CBT with physically ill patients is challenging in that patients may not understand the link between physical and psychological symptoms, may not be able to sit or concentrate for a traditional mental health-style one hour consultation and may not be able to attend a clinic for treatment.

As time progressed I gained a good insight into specific mental health problems experienced by patients with COPD and consolidated my competencies in generic therapeutic and CBT skills in line with the MRC Framework. Specific CBT techniques were used and were evaluated well by patients. According to the MRC Competency Framework 'meta-competencies' involve reaching the stage where you develop abstract knowledge, incorporating theory and practice and can skillfully adapt therapy to the individual needs of the patient (172). With limited time and resources I adapted CBT therapy to suit the needs of patients presenting with COPD within the constraints of my working environment. Sessions were shorter than traditional therapy but remained structured. Having a structure for therapy is advantageous for busy clinics when time is limited. It is argued that the structured nature of CBT is often misunderstood and is not merely a set of techniques, delivered in a didactic manner by a directive therapist (134). If CBT were implemented in this manner it is highly unlikely it would be successful (134). A fundamental characteristic of CBT is to work collaboratively with the patient. Within my clinical setting patients are not used to such structured sessions, determining an agenda or indeed being actively involved in the session so care was taken to develop a model that they would be acceptable to patients.

There are a number of competency frameworks and there is no consensus about the methods of developing these frameworks (181). Roth and Pilling (2007) appropriately acknowledge that the combination of knowledge, skills and attitude defines competency and without the ability to integrate these areas, practice is likely to be poor (134). Having said that, on the whole, the structure of the competency model proposed by the Department of Health is excellent, is applicable to anyone who delivers CBT and is not too prescriptive that it is set in stone.

4.4 Identifying appropriate CBT techniques for patients with COPD

When developing an intervention it is important to have a coherent theoretical basis for the intervention, be clear about what you are aiming for and how you will bring about that

change (172). Key theoretical models were used to identify appropriate CBT techniques as the CBT therapy evolved for patients with COPD. Addressing symptoms of anxiety requires specific techniques depending on the severity and complexity of the patient's difficulties (125). Techniques commonly used for anxiety include those that help the patient identify and modify unhelpful thoughts or emotions which can trigger the 'fight or flight response', and tackle unhelpful behaviours (such as avoidance or safety behaviours). Techniques used for COPD patients who were troubled with symptoms of depression predominantly included behavioural activation.

As I developed my own competencies and model I began to think about other staff developing their CBT skills. Developing competencies in specific CBT techniques, ensuring fidelity to treatment and enabling replication of therapy involves identifying and carefully describing the techniques used. The CONSORT statement for RCTs of non-pharmacological interventions recommends including a 'description of the different components of the intervention' (178). Mitchie et al (2013) would argue that the absence of standardised definition of behavioural techniques is likely to lead to duplication of effort and undermines the potential to accumulate evidence across reviews (174). Common CBT techniques that I have found helpful during my own training, supervision and reflection on CBT practice with patients with COPD patients, as well as in training and supervising others can be found in table 21.

Table 21- Key Components of techniques used in the COPD CBT Intervention

Component techniques	**Aim**	**Examples**
Education /increasing awareness	Increase awareness about COPD, anxiety, panic and depression. Help patient understand the link between physical and psychological symptoms.	Explaining how anxiety can exacerbate breathlessness and the link between frightening thoughts, role of adrenaline and identifying vicious cycles that can develop.
Cognitive therapy	Identifying, challenge and reconsidering unhelpful thinking and behaviour and identify more helpful ways of thinking or behaving.	Identifying patients own unhelpful thoughts about their breathing which may lead to panic e.g. I'm going to die.
Goal setting	Set or agree goals important to the patient. Goals would be reviewed, modified to smaller or new goals set if needed.	Agree a goal such as practice a technique to manage breathless or an activity each day that may help patient feel a sense of achievement. Goals would be reviewed and further adapted.
Graded tasks and Behavioural Activation	Reduce avoidance and increase levels of activity especially activities which provide a sense of achievement or pleasure, increase confidence and help improve mood.	Patients complete a simple activity diary and rate activities for achievement or pleasure. Patients are encouraged to break tasks down into small manageable bite size activities and pace themselves.
Breathing Control	Instruction (written, verbal and practical) of techniques that might help control breathing more effectively.	Instruction (written, verbal and practical) of breathing exercises. This may involve a demonstration.
Relaxation/mindfulness	Help the patient to learn to relax and cope with their physical symptoms. Techniques can reduce tension and help develop coping skills.	Practicing progressive muscle relaxation or mindfulness techniques especially when feeling breathless or anxious.
Distraction	To help shift attention away from breathing to an alternative focus for attention to avoid triggers for panic.	Patient to focus on something e.g. count backwards from a hundred in seven's, to take mind off breathing when they have exerted themselves.
Comparing outcomes	Help patient identify and compare the advantages and disadvantages of their thinking or behaviour.	Patients discuss the advantages and disadvantages of avoiding exertion in case they become breathless.
Biofeedback	Providing feedback about physiological measurements as part of a behavioural change strategy.	Breathing tests would be discussed and expectations of what might be achieved given their level of lung function.

Re-attribution	Identify perceived cause of an experience or behaviour and suggesting alternative explanations.	Acknowledging that COPD causes breathlessness but exploring how the patient thinks anxiety may affect breathing and how techniques for anxiety can help.
Positive self-talk	Positive self- talk (aloud or silently) for encouragement or reassurance.	Patient may tell themselves their breathing will settle down when they use distraction and breathing control.
Problem solving	Learning to analyse situations and identify strategies to overcome difficulties or any barriers.	Identify ways to achieve one of their goals e.g. organising a wheelchair may help patients achieve their goal of going out more.
Fear-based exposure	Replace avoidance with graded exposure to situations or activities which are associated with anxiety.	If a patient has avoided going out of the house they may agree to walk to the garden gate and then increase the distance gradually.
Behavioural Experiments	To test hypotheses about a particular belief or behaviour.	A patient may be believe they will not be able to walk to the garden gate. An experiment could be developed to try it and test out their hypothesis.

Written information can also be provided during CBT sessions as an adjunct to therapy to reinforce discussions. Written self-help leaflets have come to be seen both as psychological interventions in their own right and also as an adjunct to therapist-delivered care. Such interventions have been referred to as 'psychoeducation' or 'bibliotherapy' (182). Psychoeducation is a more general approach involving the provision of therapeutic information, which could include written materials, support and advice. Providing unsupported written materials is bibliotherapy (182).

4.5 Field testing

Having identified the key components of CBT for patients with COPD and competencies for delivery of this in a Chest Clinic setting, the next stage was to test or evaluate the therapy (172). It is also important to adequately pilot the intervention so field testing was undertaken (172). Modelling a complex intervention prior to a full scale evaluation can provide important information about the design of both the intervention and the evaluation of it (172).

Once I had qualified as a CBT therapist I developed a CBT clinic dedicated to respiratory patients and began field testing this approach. At the Chest Clinic at the RVI I introduced routine screening for symptoms of anxiety and depression using the HADS questionnaire. The majority of patients referred to the CBT Clinic had a diagnosis of COPD but a minority had other respiratory conditions such as interstitial lung disease (ILD), lung cancer, bronchiectasis, tuberculosis and asthma. At the time I had no intention of developing the CBT intervention to conduct a RCT or undertaking a PhD. However, I had developed a good theoretical understanding of how CBT could be adapted for patients with COPD. According to the MRC it is key to understand what changes are expected and how change is to be achieved when a novel treatment package is being developed (172). As time progressed I began to standardise the therapy which again is recommended before a complex intervention such as CBT can be evaluated and is expected to have a worthwhile effect (172).

With encouragement from Dr. Baker I completed a case series involving ten patients with COPD who had symptoms of anxiety or depression. Hospital admissions were noted before and after CBT. Although this was a very small sample, the results demonstrated clinical and statistical improvements in anxiety and depression scores and a statistically significant reduction in hospital admissions following CBT (183). This encouraging pilot study led to me to refine the treatment as I gained experience.

Following a teaching session for medical students I was approached by a fourth year student (Tom Foley) who expressed an interest in CBT in COPD and he arranged to work in the Chest Clinic for an elective placement. The student completed a small non-randomised retrospective controlled study of 42 patients: 21 who had completed CBT were matched with 21 historical matched controls. The same techniques were used for managing anxiety and depression as the case series. The study design was not ideal but the results again suggested that CBT significantly reduced anxiety and depression and also had a significant reduction on hospital admissions. The average number of COPD related admissions in the six months before CBT treatment was 1.48 compared with 0.42 after treatment. This suggested that treatment may influence hospital admissions, which had not been demonstrated previously. The results were published (183) and the medical student has since qualified and is now specialising in psychiatry.

4.6 Development of the CBT Lung Manual

My training, supervision, experience and CBT treatment outcome evaluation lead me to develop a CBT guide for working with patients with respiratory illness (Appendix 3 – CD provided). Manuals are commonly written to guide CBT therapy for particular psychological problems. In essence a manual is basically a package of techniques, to use for a particular problem. What is not known is which components in manuals actually help patients, and by exactly what process (134). Manuals are similar to guidelines and clinicians can use their clinical judgement to decide which elements of an intervention to include and which to ignore depending on the patients individual needs. However, a criticism of the 'manual approach' is that it does not do justice to the complexity and individuality of the patient (184). Furthermore, rigorous adherence to a manual may discourage clinical judgement, innovation and adaption to the individual patient's needs (184). With this in mind, the Lung Manual was developed to provide a framework of CBT techniques to support nurses delivering this complex intervention in this study. The manual provides a structure of key components but also allows flexibility depending on patient's individual needs. An advantage of producing a manual is to aid the standardisation of the CBT intervention and clarification of the competencies required to effectively and safely deliver it. This is critical to address issues of clinical governance and ensure safe practice.

4.7 CBT Foundation Training Course

After I completed my CBT training I observed there were very few courses in CBT foundation skills for health care professionals working in the physical health setting. Building on from the original training I had completed, I decided to develop a training course to help other nurses working in the general physical health setting to learn how to undertake CBT for respiratory patients. Dr. Sanjay Rao (Consultant Psychiatrist) was working at Newcastle upon Tyne Hospitals and also provided supervision and support during CBT training. We developed a foundation CBT program. The training programme was built upon the four tier model of professional psychological assessment and support recommended for cancer patients, with an emphasis for the training level one and two. The primary aim of the course was to help health care professionals working in the physical health setting develop a basic understanding of CBT and develop CBT skills and techniques that could be used in their daily work. The course would not enable staff to be 'qualified CBT therapists' but would provide

additional skills to enable them to deal more effectively with emotional distress in their clinical setting. Dr. Rao left Newcastle Hospital Trust in 2005 and Consultant Clinical Psychologist Dr. Christine Baker volunteered to take over. As the course evolved and improved we decided to consolidate the course into three days. The content of the course is presented in table 22.

Table 22 – Content of Basic CBT Foundation Course.

Day 1	**Day 2**	**Day 3**
Course aims	Revision	Feedback from homework
Basic introduction to CBT	Feedback from homework	Case presentations (from participants)
Using CBT in physical health setting	Goal setting	What next
Anxiety	Cognitive techniques	Evaluation
Panic	Behavioural techniques	
Depression	Case study	
Screening for anxiety and depression symptoms	Practice	
Formulation of patients difficulties	Summary	
Socratic Questioning and guided discovery	Homework	
Unhelpful thinking		
Practice		
Homework		

This training has been delivered, evaluated and refined over 12 years and provides foundation level 2 CBT training for qualified and experienced health care professionals, developing the understanding of the CBT approach and an introduction to the techniques outlined above. A workbook was also developed to encourage participants of the training course to continue to practice CBT skills once the course had been completed (Appendix 4). The aim of the booklet was to learn CBT techniques and practice on themselves which would hopefully consolidate some of the techniques used during their training.

4.8 Clinical Supervision

Throughout my training I had clinical supervision. This is expected for any sort of psychological treatment. Clinical supervision within the context of CBT has two aims. The first is to improve outcomes for patients and the second is to improve the performance of practitioners (134). Without effective supervision and clinical governance procedures, there remains the potential for a minority of practitioners to provide ineffective therapy (135). Supervision provides an excellent means to reflect on practice, be open to constructive criticism, develop knowledge and skills further and identify any gaps in competence which supervision reveals (134). Without supervision CBT skills are likely to diminish (179). Clinical supervision helped me develop a better understanding of 'what' I was doing and 'why' in addition to reflecting on individual cases.

An integral part of undertaking CBT for this study was to participate in clinical supervision with Dr. Christine Baker. Dr. Baker works within the physical health setting and is a very experienced supervisor, providing supervision for post graduate and Masters students undertaking CBT training. Monthly supervision sessions for one hour are scheduled as standard practice within the Chest Clinic. Supervision is structured to build skills and to model CBT skills. Video-taped sessions are used to reflect on the nurses skills and provide support for further skill development.

4.9 Evaluation of competency and internal validity of the treatment

The effectiveness of individual practitioners and their routine clinical outcomes vary considerably (135). To reduce the amount of therapist variance, clinicians and researchers provide concrete treatment manuals in which the principles and techniques of the therapy are detailed with varying degrees of specificity (185). However, merely reading manuals is not sufficient to ensure that therapists do conduct treatment according to the manual (185). Usually therapists are given rigorous training, and their performance is assessed by supervisors using adherence and competence scales (186). Adherence is the degree to which a particular treatment has been delivered, whereas competence involves the quality of the particular treatment provided (185).

For the purpose of this study, I planned to address the effectiveness of CBT delivered by clinic nurses trained in CBT and drawing on The Lung Manual. It was not the intention to

achieve the level of competency expected from highly experienced mental health practitioners such as those involved in delivery of IAPT. As previous studies within the physical health setting, the aim were to enable the nurses to apply 'CBT first aid' to patients who may be distressed (179). Permission was obtained to use the CFARS to assess the nurses' competency providing CBT. It was therefore envisaged to record a random selection of clinical sessions and use the CFARS to rate the skills of the nurses conducting the CBT. Clinical sessions using CBT are commonly video recorded at regular intervals and used to assess competency of CBT skills. The benefits of recording actual sessions is invaluable for clinical supervision and enables practitioners and supervisors to assess skills and integrity to treatment manuals. This was an important part of the intervention for this trial and the results are presented in chapter 6.

4.10 Summary

The overall aim of this chapter was to provide an insight into the background of the development of the CBT intervention used in this study. A number of people were key to the development of the CBT intervention. Experienced clinicians and cognitive therapists such as Dr. Kath Mannix, Dr. Sanjay Rao and Dr. Christine Baker working in the physical health setting have supported me in the development of this CBT intervention. I have followed the steps recommended in the revised MRC Framework for the development and evaluation of complex intervention by naturally progressing through each stage. Over the years the CBT intervention has been refined to the point where a substantial evaluation was possible. Field work was invaluable to evaluate and finalise the intervention so it could be used in this study.

The addition of the training course, The Lung Manual and the CBT workbook evolved to support health care professionals working in respiratory disease develop their skills and expertise when dealing with emotional distress. An eclectic model has been specially developed for patients with respiratory conditions from the stepped care approaches of psychological care used within cancer care and IAPT. This study is the first to identify if a brief CBT intervention developed and delivered by respiratory nurses can reduce symptoms of anxiety and depression and improve patient's QOL. Details of the CBT intervention have been described to provide future researchers sufficient information to replicate this research. The next

chapter describes the research methods used for this study. The research methods, aims and objectives, hypothesis and outcomes are outlined followed by details of the study.

Chapter 5 – Research Methods

5.1 Introduction

The methodology used for this research has been peer reviewed and funded by the National Institute for Clinical Research (NIHR) as part of a clinical academic fellowship. The NIHR is committed to funding studies if they are likely to improve patient care.

5.2 Research methodology

The most common research methodology used in medical sciences is quantitative research methods such as RCTs. Quantitative researchers use scientific techniques that are likely to produce quantified, and if possible, generalisable conclusions (187). It is well recognised that some research designs are more powerful than others in their ability to answer research questions on the effectiveness of interventions (188). Within quantitative methods, RCTs are considered the 'gold standard' methodology for evaluation of health care interventions in terms of being the most scientifically rigorous method of hypothesis testing and evaluating the effectiveness of interventions (188, 189) . RCTs aim to determine whether a cause and effect relationship exists between treatment and outcomes (171).

As highlighted in the literature review RCTs can lack methodological rigor. It is therefore important that RCTs should be appropriately designed, conducted and reported (190). A properly designed study optimises the chances of accurately estimating the effectiveness of treatment avoiding potential sources of bias and controlling for confounding variables (189). If a trial is conducted correctly the results should be sufficiently precise and allow application in clinical practice (191). A RCT was used for this research as the efficacy of CBT could only properly be assessed by comparing it against an appropriate control group.

5.3 Study Design

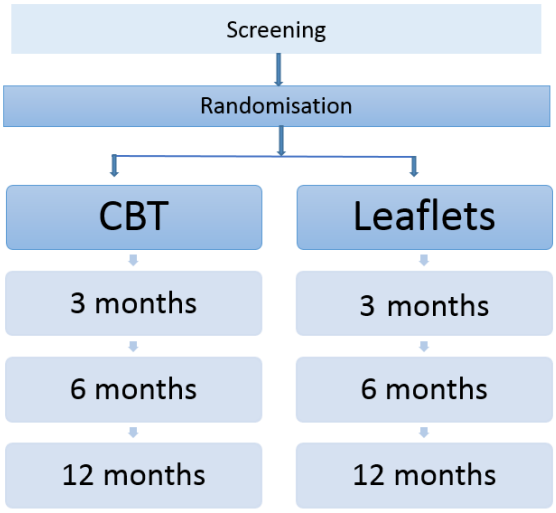
This research was carefully planned over many months to maximise the opportunity to develop a useful and credible study. At the initial stages of preparing an application to the NIHR I consulted the local NIHR North East Research Design Service (RDS) to gain advice on the most appropriate study design. The RDS support researchers to develop and submit high quality applied health and social care studies for national peer-reviewed funding programs. I

also met with my potential supervisory team on a number of occasions to discuss study design options. Previous studies of CBT in COPD have included control groups with 'standard care', group education, waiting list controls, weekly laboratory visits and even sitting quietly in a room for the same amount of time (as opposed to interventions such as progressive muscle relaxation).

Following discussions it was clear that several options were possible. One option considered was to have a treatment group of CBT compared with a control group receiving 'standard care'. Standard care in other respiratory departments across the UK did not include addressing psychological symptoms. Therefore standard care would be a control of 'no intervention'. However at the time of developing the research proposal, standard care within the Trust was to provide self-help CBT leaflets or individual CBT depending on the patient's preference in accordance with NICE guidance on psychological symptoms. It was deemed to be unethical to conduct a trial with care below the prevailing 'standard practice'. As CBT is a proven treatment for anxiety recommended by the National Institute of Clinical excellence, it would also be poor practice to deny this established treatment from the control group.

It was also expected that patients with COPD are likely to deteriorate physically during the trial so offering an active control intervention which could potentially help reduce symptoms of anxiety was considered important. A prospective randomised parallel controlled trial was therefore designed with two arms. One arm was respiratory nurse led CBT with an active control arm of self-help leaflets. At the start of the study it was not known if the interventions were equivalent of if one was superior to the other. Participants in the self-help leaflets were made aware of the potential to have CBT at the end of the trial should this intervention be better than the self-help leaflets. No other studies have used a design with these interventions. The study design flowchart can be found below in figure 15.

Figure 15 – Flowchart of the study design and follow up time points.



5.4 Aim of the study

The aim of the study was to assess the effectiveness of CBT delivered by respiratory nurses compared to an active control of self-help leaflets.

5.5 Objectives

The objectives of this study were to address the impact, feasibility and efficacy of teaching CBT skills to non-mental health professionals (such as respiratory nurses), to treat anxiety and depression in a clinical population of COPD patients. This is particularly important as there is a national shortage of therapists. In reality, the most realistic cost effective and pragmatic model to be able to provide rapidly scalable psychological care for patients with COPD may well be trained respiratory nurses. Respiratory nurses are front line staff who work with high volumes of COPD patients and are ideally placed to assess patients' physical and psychological needs. Having respiratory problems can be life threatening so having dual physical and psychological skills would be invaluable assessing patients' symptoms and defining if they needed physical therapies or psychological support (or both).

5.6 Hypothesis

The hypothesis was that CBT delivered by respiratory nurses in addition to self-help leaflets was superior to providing self- help CBT leaflets alone.

5.7 Primary outcome

Whilst CBT is an evidence based intervention for the treatment of psychological problems there is no research into the effects of an individual CBT based intervention on hospital admissions in this patient group. This study builds upon and extends prior work of Lamer's et al (2010) that applied a psychological intervention in Dutch primary care COPD patients with depression (144). The study extends clinical observations from Newcastle Respiratory Clinics that anxious patients with COPD appear to be admitted most frequently and this may prove a key target sub-group to study for healthcare utilisation and cost effectiveness studies. The findings will hopefully inform future clinical care, services and research.

I discussed the possibility of having two primary outcomes (anxiety and depression) within my supervisory team. As a single primary outcome and a small number of secondary outcomes are the most straightforward for statistical analysis it was agreed that anxiety would be the primary outcome. The primary objective was to identify if CBT delivered in a standardised manner by respiratory nurses reduced anxiety in patients with COPD. This would be measured by a fall in group mean HADS-Anxiety score of 1.5 points at 3 months post-therapy compared to standard care of self-help CBT leaflets. As discussed in chapter 2, this value has been deemed an appropriate MCID (122).

5.8 Secondary Outcomes:-

Five secondary objectives were developed:-

A. To identify if CBT delivered by respiratory nurses reduced anxiety at six and 12 months compared to standard care (self-help leaflets).

B. To investigate if CBT delivered by respiratory nurses reduce depression as measured by the HADS-Depression Scale at three, six and 12 months compared to standard care (self-help leaflets).

C. To investigate if CBT delivered by respiratory nurses improves patient QOL at three, six and 12 months as measured by a reduction in COPD Assessment Tool (CAT) (192) and EuroQol 5 Dimension questionnaire (EQ5D) utility scores.

D. To identify if CBT delivered by respiratory nurses reduces hospital admissions in the 12 months following randomisation (compared to 12 months pre-randomisation).

E. To ascertain if CBT is more effectively delivered by respiratory nurses with advanced CBT training (post -graduate diploma) compared to foundation level training (three day short course).

For the purpose of this PhD only the results from the primary and secondary outcome data for the three month follow up point will be presented.

5.9 Patient and Public Involvement

It was important to involve patients and relatives when developing the study design. A face to face meeting was organised with COPD patients, carers and the regional manager of the British Lung Foundation (BLF) prior to applying for funding from the NIHR for this research. Representatives from the BLF were useful to understand their standpoint or priorities as a charity representing people with lung conditions from a national perspective. The regional manager for the Northern and Yorkshire Region (Mrs. Bev Wears) was approached and agreed to be involved in the research. For practical reasons the meeting was held at the RVI Hospital in an area easily accessible for wheelchair patients and refreshments were provided. The aim of the meeting was to explain the rational for the research in the first instance, present a draft research proposal and discuss the relevance of the research to patients and family. It was also important to assess if the research matched the views and ideas from a personal perspective of patients with COPD and their family members. Care was taken to keep the discussions simple and understandable by using 'plain english' and avoiding unnecessary jargon.

An important consideration when involving the public is any ethical implications (193). Discussing the psychological implications of an illness such as COPD may be upsetting so care was also taken to present psychological difficulties within COPD in a sensitive and supportive manner. Patients were encouraged to offer their personal experience of having COPD and comment on the research proposal. A crucial element of PPI is that the involvement of people who use services can lead to research that is more relevant to their needs and hence is more likely to encourage people to take part (193).

One of the suggestions from the meeting highlighted the importance of providing assistance with transport (e.g. providing taxis) or providing home visits for housebound patients especially as car parking is particularly difficult and expensive at the RVI site. The groups views

on the proposed questionnaires were sought to ensure the use of the HADS (Appendix 1, COPD CAT (Appendix 5) and EQ5D (Appendix 6) would not over burden patients who may be physically unwell.

5.10 Institution

Newcastle upon Tyne NHS Hospitals Foundation Trust was the main institution undertaking this study. The Trust provides secondary and tertiary services at two main hospital sites. The Royal Victoria Infirmary (RVI) is situated in the West of the city, and has been providing healthcare to communities in the North East for over 250 years (194). The Freeman Hospital is situation in the North of the city. The majority of respiratory services offered by the Freeman Hospital are elective and specialist services such as lung transplantation, pulmonary hypertension, bronchiectasis and sleep disorders. Approximately 30% of patients attending Newcastle upon Tyne NHS Hospital Foundation Trust are patients from outside Tyne and Wear. Patients attend the Trust from surrounding areas including Northumberland, Gateshead, South Tyneside, North Tyneside, Sunderland and Cumbria (194).

A number of in-patient and out-patient Chest Clinics are available at both hospital sites. Each site has a dedicated Respiratory Consultant lead for COPD Dr. Burns is the lead consultant at the RVI site and Dr. De Soyza is the lead consultant at the Freeman site. Most but not necessarily all COPD patients attend these consultants specialist COPD clinics. Initially two study sites within The Newcastle Upon Tyne Hospitals NHS Foundation Trust were used:

- The Chest Clinic at the Royal Victoria Infirmary Hospital.
- The Respiratory outpatient clinic at the Freeman Hospital.

Two further study sites were added towards the end of the study after gaining ethical approval to increase recruitment. These included:

- South Tyneside District General Hospital.
- Queen Elizabeth Hospital, Gateshead.

Only two patients were recruited from South Tyneside and Gateshead Hospitals.

5.11 Study Population

The ideal study sample represents the total population from which the sample is drawn (195). Sampling simply means studying a proportion of the population rather than the whole population which can be expensive and time consuming (195). Quantitative studies usually use sampling techniques based on probability theory. Probability sampling involves attempts to minimise sampling error in that they give the highest chance of the sample being representative of the total population (195). For this study it was important to recruit a sample representative to the COPD population in secondary care. The population of interest was all patients attending secondary care out-patient departments with a confirmed diagnosis of COPD (mild, moderate, severe or very severe as defined by NICE, 2010) with a HADS-Anxiety score ≥8. Attempts were made to include all patients with COPD attending Chest Clinics to ensure they had an equal chance of being recruited into the study to minimise the risk of bias and random sampling was used. However, like all probability samples no sample can ever be totally represent the population (195).

To capture as many COPD patients as possible I attended respiratory department meetings at the Royal Victoria Infirmary and Freeman Hospital to disseminate information about the trial at the outset and gain their assistance in setting up an appropriate method of recruitment for both sites that was convenient to their service. Dr. De Soyza is the lead consultant for COPD at the Freeman Hospital and ensured all COPD patients attending his clinics were screened and offered information about the study. Similarly Dr. Burns is the COPD lead at the Royal Victoria Infirmary and the majority of recruitment from the RVI site was from his clinic.

5.12 Governance

5.12.1 Ethics

The Department of Health requires that research involving patients is reviewed independently to ensure it meets ethical standards (196). An appointment was made to attend the Sunderland Ethics committee on 21/02/2011. A favourable opinion was granted (Reference 11/NE/0025).

5.12.2 Research and Development Approval

Within NHS organisations Research and Development Departments facilitate the local management of all research within that organisation (197). An application was made for approval to undertake the study within Newcastle upon Tyne Hospitals Foundation Trust. Approval was granted (Reference 5473).

5.12.3 Caldicott

Information governance is a key process to consider when conducting research. Patient information is an exceptionally valuable resource for researchers, with great potential to improve healthcare, both for individuals and populations (198). However, every patient should feel confident that personal and health information is held safely and securely. Information governance ensures necessary safeguards are in place for the appropriate use of patient information which would be collected during the study. Caldicott approval was requested and obtained (Reference 1527). All personal data were held on a database at the RVI site. For purposes of data analysis, only completely anonymised data sets were sent to Newcastle University via email. This included data relating to gender, age, ethnic group, lung function, smoking status, education, MRC dyspnoea scores, hospital anxiety and depression scores, medication and body mass index (BMI).

5.12.4 NIHR Clinical Research Network Portfolio

The NIHR Clinical Research Network (CRN) is a government funded organisation. The aim of the NIHR CRN is to support late phase clinical trials and other well-designed studies (199). The NIHR CRN Portfolio is part of the UK Clinical Research Network Portfolio, which comprises the network portfolios for England, Northern Ireland, Scotland and Wales. These four portfolios are held on a single information system: the UKCRN Portfolio Database (200). As this study was funded by the NIHR Clinical Academic Training Fellowship and the NHS agreed to meet the support costs for the study it was eligible to be entered on the NIHR CRN Portfolio (Reference CRN Study ID: 10519).

5.12.5 Trial registration

The ISRCTN registry was launched in 2000 in response to the growing body of opinion in favour of prospective registration of randomised controlled trials (RCTs) (201). The registry

website states that the scope of the registry has widened beyond RCTs to include any study designed to assess the efficacy of health interventions in a human population (201). The registry is recognised by WHO and International Committee of Medical Journal Editors (ICMJE) and accepts all clinical research studies (whether proposed, ongoing or completed), providing content validation and the unique identification number necessary for publication (201). All study records in the database are freely accessible and searchable. ISRCTN supports transparency in clinical research, helps reduce selective reporting of results and ensures an unbiased and complete evidence base (201). This includes both observational and interventional trials (201). This study was registered with International Standard of RCT Number (ISRCTN reference 55206395).

5.12.6 Trial Protocol and amendements

A trial protocol was developed at the start of the study to describe the objectives, design, methodology, statistical considerations and organisation of the clinical trial (197). During this study the recruitment rate was significantly lower than for respiratory pharmaceutical clinical trials in Newcastle and was slower than anticipated. This will be discussed further in chapter 7. Advice was sought from the Trial Steering Committee (TSC) (see section 5.12.7) and it was agreed to open recruitment to two local hospitals in an attempt to achieve the required sample size. The trial protocol was amended accordingly to recruit from local hospitals in Gateshead and South Tyneside Hospitals. A trial amendment application was made and favourable ethical approval was obtained. The protocol was published in 2013.

5.12.7 Trial Steering Committee

TSCs provide the overall supervision of clinical trials (203) and to monitor the progress and conduct of the research and advise on scientific credibility (204). Their role is to monitor the progress and conduct of the study and advise on scientific credibility (203). It is recommended that at least two people who have experience of using services are involved in a TSC (193). A patient, carer and BLF representative were invited and agreed to assist with the management of the research by joining the TSC. In this trial specific funding for patient travel was in place to avoid any financial or logistic barriers to participation. A list of members can be found in table 23. Those involved in the TSC were not participants of the trial as this can be compromising for the participant and research team (193).

Table 23 - Members of the COPD CBT CARE Trial Steering Committee.

Name	Position
Dr. Graham Burns (Chair)	Consultant Respiratory Physician
Mrs. Violet Knowles	Carer Representative
Mrs. Pamela McGregor	Patient Representative and carer representative
Mrs. Bev Wears	British Lung Foundation Manager Northern and Yorkshire Region
Mrs. Susan Leach	Research Nurse (Mental Health Clinical Network)
Dr. Anthony De Soyza	Senior Lecturer and Consultant Respiratory Physician
Dr. Chris Baker	Consultant Psychologist
Dr. Debbie Carrick-Sen	Head of Nursing and Midwifery Research
Dr. Nick Steen	Principle Research Associate (Institute of Health and Society)
Professor Elaine McColl	Director NIHR Newcastle Clinical Trials Service

The TSC for this study met on 13 occasions throughout the study.

5.12.8 Good Clinical Practice (GCP)

NIHR CRN GCP training was completed locally as this is a key requirement for anyone involved in the conduct of clinical research is Good Clinical Practice (GCP). GCP is the ethical and practical standard to which all clinical research is conducted (205).

5.13 Study Duration

The duration of the study was 12 months from randomisation. The rationale was to identify if CBT was effective and if the effect was sustained up to 12 months post randomisation.

5.14 Sample Size and Power Analysis

For scientific and ethical reasons, the sample size for a trial needs to be planned carefully with a balance between clinical and statistical considerations (189). The power of a study is its ability or sensitivity to detect a statistical difference when one actually exists. The best way to reduce the possibility of overlooking a finding (type II error) is to conduct a power analysis to determine the number of subjects needed to detect a clinically important difference when one exists (206). Calculating sample sizes can help to take into account variability in individual level outcomes (172). Elements of the sample size calculation include:

- The estimated outcomes in each group (which implies the clinically important target difference between the intervention groups).
- The α (type I) error level.
- The statistical power or the β (type II) error level and
- For continuous outcomes, the standard deviation of the measurements (207).

The sample size for this study was calculated by Dr. Nick Steen a senior statistician from Newcastle University Medical Statistics and affiliated with the NIHR North East-Research Design Service (RDS). The COPD patient group is complex. It was anticipated that patients would experience disease progression. It was estimated that up to 10% patients may die within 3 months of commencement of the study and up to 30% may die during the 12 month follow up. We anticipated a 30% approach decline rate and 20% data collection attrition. Taking into account expected mortality and data attrition we initially estimated that 312 patients would be required to be consented for the study. Complete outcome data on 224 patients (112 patients per group) was therefore required. This would give 80% power at 95% significance to detect a standardised difference of 0.375 (equivalent to a change in HADS-Anxiety of at least 1.5 when SD 4) assuming a type 1 error rate of 5%. The intended mean difference was in line with prior estimates of clinical significance 1.32-1.5 (122).

5.15 Eligibility criteria for participants

Research studies should have strict criteria for including and excluding patients to reduce the risk of bias and the possibility of preferentially admitting subjects who may help to support a hypothesis and prove a point (206). Eligibility criteria for this study were chosen based on recommendation from previous research and agreed by the supervisory team who had extensive expertise in COPD, psychological interventions and research methods. The inclusion criteria and exclusion criteria are outlined in 5.13.1 and 5.13.2.

5.15.1 Inclusion Criteria

- Patient with a confirmed diagnosis of COPD FEV_1 ratio <70%.
- All disease severity will be eligible including mild to moderate (FEV_1 >50% predicted) and severe to very severe (<50% predicted).
- Patients with symptoms of anxiety as defined by HADS-Anxiety scores ≥8.

- Willing to participate in the study and provide written informed consent.
- Agreed to have CBT treatment session video recorded if randomly selected for validation.
- Agreed to attend a minimum of 2 and maximum of 6 CBT sessions.

5.15.2 Exclusion Criteria

- Patients with HADS-Anxiety score <8 (within normal range).
- Patients with known psychiatric history such as psychosis.
- Patients receiving psychological talk therapy including CBT treatment.
- Patients with cognitive impairment (e.g. dementia).
- Patients involved in any other clinical trial.

5.16 Screening of participants

Potential patients were identified through routine clinic outpatient appointments by their treating physician or nurse from 22nd of August 2011 to 28th of October 2014. Spirometry and psychological screening using the Hospital Anxiety and Depression Scale is routinely completed for all patients at each clinic visit. All patients with a HAD-anxiety score ≥8 who fulfilled the entry criteria were given a participant information leaflet by the health professional providing direct care in the respiratory clinics (Appendix 7). Patients were encouraged to take the patient information leaflet to read and discuss with their family or friends prior to any contact regarding consent. The patient information leaflet contained contact details if they needed more information or if they had any questions about the research. In addition the clinical staff asked the patient if they consented to being contacted within two to seven days following the clinic appointment. The patients contact details were written onto the HADS Questionnaire if consent was given. All of the HAD questionnaires were collected from respiratory clinics. If the patient agreed to being contacted they were approached by telephone or in writing.

5.17 Screening Log

A log of all patients who were screened was maintained and held securely in a password protected file at the Royal Victoria Infirmary site on a Microsoft Excel Database. The screening log contained the following details:-

- Hospital number
- HADS anxiety score
- HADS depression scores
- Outcome of screening (e.g. recruited, declined, HADS-anxiety <8).

5.18 Recruitment procedures

Patients were given a minimum of 24 hours to consider taking part in the study. All patients who had agreed were contacted by telephone. Any questions the patients had were answered and further information provided if needed. All patients interested in participating in the study were then offered a home visit or hospital out-patient appointment to gain consent.

5.18.1 Consent

Informed consent is at the heart of all research (196). Written informed consent was obtained once the patient agreed to proceed with the study (Appendix 8). The original signed consent form was retained in the Investigator Site File. Every patient was provided with a copy of the patient information leaflet and consent for their records. The GP and hospital consultant were notified of the patient's participation in the study and which group they had been allocated (See Appendix 9).

5.18.2 Recruitment

It was originally anticipated that 312 patients would be required for this research. Over the course of the study the recruitment rate was much slower than anticipated but the dropout rate was less than expected. It was agreed by the TSC to stop recruiting once 112 patients in each treatment arm had completed three month follow up.

5.18.3 Recruitment database

Data management is extremely important. In this current study an appropriate database was integral to the research from the onset.

5.18.4 Clinic Posters

Following ethical approval posters were displayed in clinics at the Royal Victoria Infirmary and Freeman Hospital to increase awareness of the research in the area and further contact

details provided if patients would like further information. Very few enquiries were made as a result of the posters.

5.19 Randomisation of patients

Randomisation refers to the process of assigning participants to study groups at random. Randomisation has several important features. Firstly, it allows each participant having an equal probability of being assigned to any given group (188). Randomisation eliminates selection bias and balances possible known and unknown confounding factors in order to create a control group that is as similar as possible to the treatment group (188). Without randomisation treatment comparisons may be prejudiced (189). To ensure all patients had an equal chance of being randomised to either group and avoid selection bias a computerised randomisation program was used in conjunction with Newcastle University. Equal randomisation was used as in standard parallel group trials power is maximized by using 1:1 allocation ratio.

Whilst randomisation may help remove selection bias, it does not always guarantee that the groups will be similar with regard to important patient characteristics (208). One way of trying to ensure that the groups are well matched is to identify important prognostic factors and use stratification during the randomisation process (188). For this study patients were stratified at randomisation by disease severity namely FEV1 >50% predicted (mild to moderate COPD) and <50% predicted (severe to very severe) and age to control for these potential confounding variables. Patients were informed that their initials, date of birth and severity of COPD would be entered into a web-based system, which returned the allocation status. Wherever possible patients were present during the randomisation procedure for further transparency and ensure patients understood how their treatment had been allocated.

5.20 Allocation Concealment

Successful randomisation in practice depends on two interrelated aspects (189). Firstly, adequate generation of an unpredictable allocation sequence and secondly, concealment of that sequence until assignment occurs (189). Allocation concealment is a technique that is used to help prevent selection bias by concealing the allocation sequence from those assigning participants to intervention groups. The technique prevents researchers from consciously or unconsciously influencing which participants are assigned to a given intervention group

(188). Ideally, RCTs should be double-blind (i.e. patient and staff responsible for the trial are blinded to the treatment allocation until the study is completed) if appropriate (171). It was not possible for participants or the nurses involved in this study to be blinded to their intervention. Patients knew at the outset which group they had been allocated to once they had been randomised. However, to reduce interviewer bias nurses involved in the outcome data collection were blinded to the allocated intervention. Finally, the data analysis was validated by a statistician who was blinded to the intervention.

5.21 Data Collection

Demographic and clinical data was collected at baseline (see Table 24). To minimise inconvenience to patients and optimise data collection data was collected at the patient's preferred location. This was either in the patient's home or a taxi was provided to transport the patient to the hospital if this was preferred by the patient. It was agreed to collect data two weeks before or after the required follow up date from randomisation. The rationale for this was to allow data to be collected for patients who may be unwell and unable to complete the questionnaires, on holiday or for those who were difficult to contact. Data was collected at three, six and 12 months using validated and non-validated questionnaires. Data collection forms were developed for three month, six month and 12 month endpoints to record primary data (Appendix 10). Data collected were then entered onto the database. All data entered was double checked by a trials data manager. The dataset was checked visually for errors e.g. obvious errors, outliers or values out of expected range which can distort the results during data analysis. Any errors identified were corrected.

Table 24 - Baseline Data Collection Template.

Data	Baseline	Time point 1- Three months	Time point 2- Six months	Time point 3- 12 Months
Demographic Data	√			
Gender	√			
Age	√			
Smoking Status and pack years	√			
Ethnic Group	√			
Marital Status	√			
Education	√			
Inhaler Technique	√			
Spirometry and oxygen saturations	√			
MRC Dyspnoea Score	√			
Comorbidities	√			
BMI	√			
Medication	√			
Health care utilisation	√	√	√	√
Participation in pulmonary rehabilitation	√	√	√	√
HADS/CAT/EQ-5D	√	√	√	√

5.22 Study Interventions

All patients received standard medical care which included:

- Normal Chest Clinic visits with recording of weight, smoking status, spirometry, oxygen saturation levels and inhaler technique monitoring.
- Standard screening for symptoms of anxiety and depression using the HADS questionnaire at each clinic visit.
- Attending pulmonary rehabilitation.

Patients also received either CBT or self-help leaflets depending on their treatment allocation.

5.22.1 Group 1 – Self-Help CBT Leaflets

Patients randomised to the self-help leaflets were provided with unsupported written information on anxiety and depression (if needed) (209, 210) and the Self-Help Toolkit (211). Patients were advised to work through the leaflets and contact their primary care team should further help be required. As this was a pragmatic trial it was accepted that treatment in primary care may include psychotherapy, counselling, antidepressants and/or anxiolytics or indeed no treatment at all. Information on primary care directed interventions was recorded at each study follow up visit.

5.22.2 Group 2 - CBT Arm (CBT based treatment with a respiratory nurse).

Patients randomised to the CBT arm of the trial were provided with the same self-help leaflets provided in group one but received individualised CBT on a one to one basis. The CBT intervention involved the standardised CBT based programme described in chapter four. The ability to standardise interventions is a cornerstone of RCTs (212). For this study a manualised treatment protocol (The Lung Manual) was developed and used in an attempt to standardise the CBT treatment as much as possible and to ensure the CBT based treatment could be replicated. An initial assessment was undertaken at the patient's first visit. The CBT nurse therapist assessed the patient's current difficulties to develop an individualised treatment plan at the first session. A standardised format was used (see Table 25).

Table 25 - Patient Assessment at Initial CBT Visit.

Medical History
Medication
Allergies
Social History
Presenting Problem/Difficulties
HADS Score
Formulation using 'Hot Cross Bun Model' (see appendix 4 page 225)
Goals
Change Techniques
Negotiate Homework
Patient feedback and review of session
Arrange follow up

An individualised treatment plan would be developed depending on the patients presenting problem. Key techniques outlined in table 20 were drawn upon. The techniques were based on the those recommended in NICE Guidelines (125). The purpose of the techniques were to aid the development of coping strategies, help the patient learn effective ways to respond appropriately to symptoms and reduce avoidance behaviours that maintain anxiety and low mood.

Delivery of CBT

The CBT was delivered by four respiratory nurses. Two nurses were trained CBT therapists after completing a Post Graduate Diploma in CBT. One nurse was an experienced therapist and had been qualified 10 years. The second nurse had been qualified in CBT for two years. In comparison two nurses had completed brief training in CBT basic foundation skills and techniques within the last two years. All four nurses had supervision to develop their skills and expertise. Unfortunately, three of the respiratory nurses left the Trust during the study. The provision of the intervention was continued by the most experienced CBT therapist until the end of the study. The intervention was delivered in the Chest Clinic at the Royal Victoria Infirmary, Newcastle upon Tyne or within the patients' home.

Training of Respiratory Nurses

A half day training session was developed to familiarise the nurses involved in the study with the Lung Manual Treatment Programme. A presentation was given explaining the manual and how to use it. Practical exercises were undertaken to reinforce the use of the Manual and ensure the nurses were confident when using it. Mrs. Violet Knowles from the TSC also attended the session and gave positive feedback on her experience.

Number and duration of CBT sessions

Between two and six sessions of CBT therapy were offered depending on clinical need. Sessions were held every two weeks. The first session was scheduled for 30 - 60 minutes. This included ten minutes for administration at the end of the session to complete notes and dictate a letter for the consultant and GP when required. Letters were sent after the second and final CBT session. Subsequent follow up sessions were up to 30 minutes every two weeks over a three month period.

CBT Clinical Supervision

Psychological clinical supervision was provided to the four CBT nurse therapists on a monthly basis by Consultant Clinical Psychologist (Dr. Christine Baker) as per standard practice. A standard template was used to record supervision sessions (See Appendix 11).

Quality control of manualised CBT programme

In previous research studies attempts have been made to validate the quality of the CBT intervention. For this study data was collected to assess consistency of the CBT intervention delivered in the treatment arm. Twenty two CBT sessions were video recorded to validate adherence to the CBT manual and the quality of the CBT intervention. All the videos were assessed by a CBT therapist independent of the study delivery team using the CFARS rating scale.

5.23 Outcome Measures for Anxiety and depression

It was important to use well validated outcome measures to assess psychological symptoms and QOL. As stated in chapter two a number of validated measures could have been employed to assess symptoms of psychological distress. The most common measures used in

previous studies are the Beck Anxiety Inventory, the Beck Depression Inventory and the Hospital Anxiety and Depression Scale (117). The HADS questionnaire has been used extensively in studies on the psychological management of anxiety and depression in COPD. The HADS questionnaire was selected as the most appropriate outcome measure for this study for the following reasons:

- To reduce the burden of completing long questionnaires for patients.
- The HADS was recommended for future research in a systematic review (129) and allowed comparability to other studies which have used the questionnaire.
- A power calculation could be undertaken using published recommendations for the MCID for the HADS (122).
- The clinical teams in the respiratory departments were already familiar with the HADS questionnaire and it seemed reasonable to use this for the study.

5.24 Outcome Measures for QOL

The patient burden of completing questionnaires was an important consideration when designing the research. Several disease specific QOL questionnaires were considered for ease of completion, sensitivity to change and validated in the COPD population. Two outcome measures were chosen to measure QOL. The first was the CAT Questionnaire, a newly validated disease specific health status (192). The advantage of the CAT Questionnaire is that it is readily available, easy to complete and interpret and practical for clinical use (213). For research purposes the CAT is significantly shorter than the St Georges Respiratory Questionnaire (SGRQ) which is commonly used to assess QOL. The CAT contains eight items with strong correlation between CAT and it is considerably shorter than the longer 51 item SGRQ which preceded it (192). A difference or change of two or more units suggests a clinically significant difference or change in COPD health status (214). The CAT test takes approximately five minutes to administer and is clearly less cumbersome for patients to complete than the SGRQ.

The EuroQol 5 Dimension Questionnaire (EQ5D) was also used to assess generic QOL. The EQ-5D is a brief (five item) well utilised, self-administered, generic, QOL questionnaire, yielding a preference value (215). The EQ5D takes about five to ten minutes to administer and assists in cost effectiveness analysis of an intervention using quality adjusted life years.

The quality-adjusted life year (QALY) is a measure of disease burden, including the quality and quantity of life lived. It is used to assess the value for money of a medical intervention. A cost effectiveness analysis is planned once 12 month data is collected.

5.25 Statistical Methods

Many RCTs aim to identify whether a treatment can reduce pre-existing levels of symptoms (such as anxiety) and obtain measurements at baseline and follow up (216). When this study was first planned the NIHR North East RDS based in Newcastle were consulted and Dr. Nick Steen formulated a brief analysis plan prior to the commencement of the study. This was important as the method of data analysis should be specified in the trial protocol (216). Prior to analysing the data a detailed analysis plan was circulated to all supervisors for comments. For the purposes of this thesis "completer" analysis is presented for patients who completed 3 months follow up. An "Intention to treat" analysis is planned for the final publication when data collection is complete.

As stipulated in the sample size calculation, the groups were compared using independent t-tests (the primary outcome variable being the HADS-Anxiety score at 3 months). Future analyses by a statistical collaborator are underway using imputation analysis to derive the "intention to treat analysis". A longitudinal analysis will be undertaken on data collected at multiple points in time, comparing the changes in HAD scores over time in the different trial arms using repeated measures analysis of variance. This will allow us to make use of all the observed data for a patient even if they missed one or more time points. A Consort Diagram was produced.

5.25.1 Statistical Software

Data analyses were conducted using Minitab Version 17, Minitab Incorporated.

5.25.2 Tests for Normality

Many statistical procedures including student *t*-tests, correlation, regression, analysis of variance, namely parametric tests, are based on the assumption that the data follows a normal distribution (217). The term 'normal distribution' assumes that the population of interest from which the samples are taken may not be 'normal' but rather the samples should be

compatible with the population (which they represent) (218). Normality and other assumptions should be taken seriously, for when the assumptions are not correct, it is said to be impossible to draw accurate and reliable conclusions about the results. Several tests can be undertaken to test distribution of data (217). Visual inspection of the distribution may be used, although this approach is usually unreliable and does not guarantee that the distribution is normal (217). A visual inspection can be made using dot plots (for small samples), histogram, stem –and-leaf-plot or normal plot. Kolmogorov-Smirnov and Shapiro-Wilk computer tests are sometimes used to assess normality more objectively. For this study assessment of normality was undertaken for continuous variables by visual inspection using histograms. An assessment was made to identify if the data was symmetrical, skewed to the right (positively skewed) or skewed to the left (negatively skewed).

5.24.3 Population Description

Descriptive statistics were used to describe characteristics of the patient population using means with standard deviations and percentages.

5.24.4 Statistical Tests used for data analysis

Statistical comparisons of trials comparing variables at different time points can be undertaken in several ways (216). One method is to compare the groups post treatment (216). Alternatively a change score can be calculated by subtracting the follow up score from the baseline score. Using the change score approach leads to a statement such as 'anxiety reductions were 1.5 points greater on treatment A compared to treatment B'. Using change scores takes into account imbalances at baseline between treatment groups (216). However, if the average baseline scores are the same in each group the estimated treatment effect will be the same using these two approaches (216). Vickers and Altman highlight an important point, if the treatment is effective the statistical significance of the treatment effect by the two methods described above, will depend on the correlation between the baseline and follow up scores (216). If the correlation is low using the change score will add variation and the follow up score is more likely to show a significant result (216). Conversely, if the correlation is high using only follow up scores will lose information and the change score is more likely to be significant (216). Whichever method is used should be specified in the trial protocol in advance (216).

For the primary outcome in this study the change score was calculated for continuous numerical data to take account of chance imbalances at baseline between the treatment groups (216). To calculate the change score the HADS-Anxiety scores at three months follow up were subtracted from baseline to identify the individual change in scores (216). Unpaired student *t*-test were then used to analyse the data from the two groups. Assumptions for paired tests include the data from the population of interest are normally distributed and the sample size is reasonable (219). However, as this study had a large sample size i.e. over 30-40, it is argued that the sampling distribution tends to be normal, regardless of the shape of the data hence the violation of the normality assumption should not cause major problems (217).

Unpaired student *t*-tests were also used to compare secondary outcome variables for HADS-Depression and CAT scores at three months. Paired student *t*-tests were used to analyse numerical data from related groups (CBT group) at baseline and three months and self-help leaflet group at baseline and three months. Unpaired student *t*-tests were conducted to see if there were any differences between baseline mean HADS-Anxiety and HADs-Depression scores of patients who completed the study compared to those who were recruited but either did not receive the CBT intervention or patients who did not complete the three months follow up period. Non-parametric tests were used where data were not normally distributed.

Chi-squared tests were used to compare categorical data. Logistic regression analysis was undertaken to assess the impact of a number of factors to predict who would respond to treatment. Several continuous variables including HADS-Anxiety scores, HADS-Depression scores, age, gender, CAT score, EQ-5D utility scores and FEV_1 were used. The categorical variable gender was also assessed. In the CBT group, logistic regression analysis was undertaken and included the variables outlined above plus the nurse therapists delivering the intervention. Pearson correlation was used to explore the relationship between several variables including HADS-Anxiety, HADS-Depression, CAT, EQ-5D utility scores, Age and FEV_1. Where applicable, tests were two tailed and significance was set at a level of 0.05. Pearson correlation was used to identify the strength and correlation between two variables (such as FEV_1 and HADS-Anxiety).

Further analysis is planned to use analysis of covariance (ANCOVA) for data collected from baseline and all time points thereafter. This method is a better approach as it addresses baseline imbalance because of regression to the mean (216). In effect ANCOVA adjusts each patients follow up score for his or her baseline score, but has the advantage of being unaffected by baseline differences (216). An additional advantage of ANCOVA is that it generally has greater statistical power to detect a treatment effect than other methods (220). In addition ANCOVA can be seen as a type of multiple regression and can be expanded to include additional prognostic variable such as age and diagnostic group (216). However, as with all analysis of continuous data, ANCOVA depends on some assumptions. Assumptions include that the groups are defined by the levels of a single factor, in the population of interest, the variable (e.g. HADS-Anxiety score) is normally distributed in each group, the variance in the groups is the same and the sample size is reasonable {Petrie, 2009 #1601}. If these assumptions are not achieved data transformation may be indicated (221).

5.26 Summary

A critical analysis of the literature has highlighted the need for a well powered and designed RCT to identify if CBT is effective in reducing psychological distress. This study builds upon and extends previous research evaluating the efficacy of psychological interventions for anxiety and depression in COPD. This study has been carefully planned to address weaknesses and recommendations of previous studies. It is unique in that it utilises respiratory nurses who work closely with COPD patients. Respiratory nurses have knowledge, skills and expertise in caring for patients' physical well-being. Additional training in addressing psychological skills is possible. CBT is an evidence based intervention that enhances respiratory nurses' skills to managing frightening symptoms of breathlessness, anxiety and depression. The most appropriate method to identify if CBT undertaken by respiratory nurses is effective for patients with COPD is a RCT was developed to address the research questions and test the hypothesis.

This chapter has detailed the research methods used for the study. In the next chapter the results will be presented. Results are broken down into the following sections:

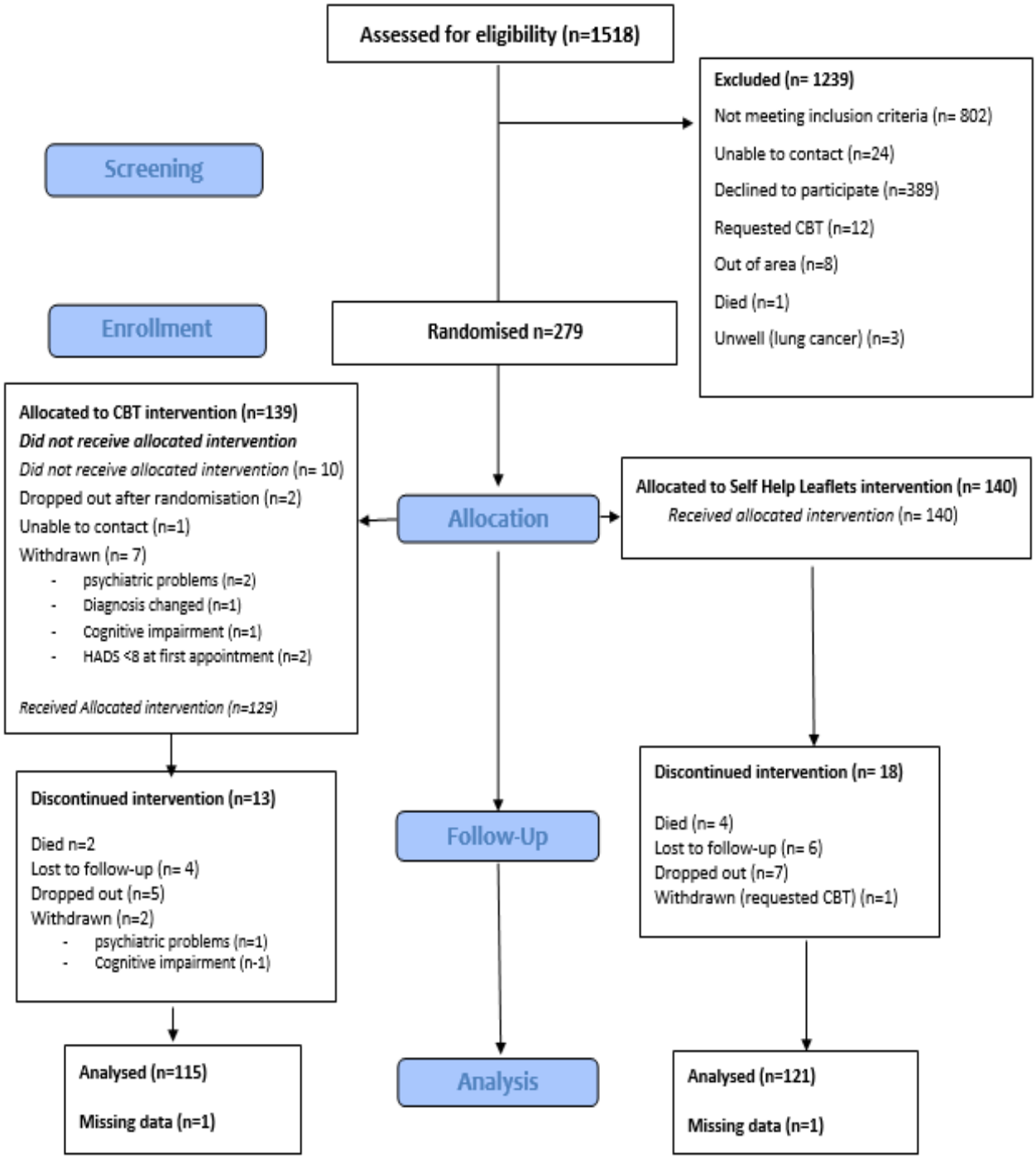
1. Patient screening
2. Recruitment

3. Population description
4. Anxiety (primary outcome)
5. Depression (secondary outcome)
6. CAT HRQOL (secondary outcome)
7. EQ-5D Generic QOL (secondary outcome)
8. Correlation between variables at baseline
9. Level of training to deliver intervention (secondary outcome)
10. Patient feedback
11. Summary

Chapter 6 – Results

The results for the study will now be presented. A Consort Diagram detailing the patient flow can be found below (Figure 16).

Figure 16 – Consort Diagram of Patient Flow.



6.1 Patients Screened

From June 2011 to October 2014 1518 patients were screened. In total 620 (41%) patients recorded a HADS-Anxiety score <8, so were not eligible for the study. There were 898 (59%) patients who were eligible with HADS-Anxiety score ≥8, of which 389 (43%) declined to participate in the research. Depression scores were collected from 1515 patients (data was incomplete from three patients when the forms were collected). Table 26 provides a summary of the outcome from screening patients for this study.

Table 26- Summary of outcome from patients screened for eligibility.

Description	Number /(percent) (n=1518)	Mean HADS-Anxiety/(SD)	Number /(percent) (n=1515)	Mean HAS-Depression/(SD)
Recruited	279 (18)	12.1 (3.1)	279 (18)	9.2 (3.9)
Declined	389 (26)	11.7 (3.02)	388 (26)	8.7 (4.10)
HADS-Anxiety <8 & HADS-Depression <8	620 (41)	3.9 (2.35)	848 (56)	3.7 (2.22)
Previous psychological problems	86 (6)	13.0 (3.2)	86 6)	11.0 (4.30)
'COPD' but FEV_1/VC Ratio >70	41 (3)	12.9 (3.56)	41 (3)	9.7 (4.74)
Unable to contact	24 (2)	11.9 (3.17)	24 (2)	8.5 (4.79)
Not COPD	27 (2)	11.5 (2.97)	27 (2)	7.7 (3.28)
In other study	4 (<1)	9.3 (0.50)	4 (<1)	6 (4.76)
Cognitive impairment	24 (2)	13.0 (2.71)	24 (2)	9.6 (4.44)
Out of area	8 (<1)	10.9 (2.10)	8 (<1)	9.1 (3.76)
Prognosis less than 1 year (cancer)	3 (<1)	14 (3.0)	3 (<1)	10 (6.0)
Requested CBT now	12 (<1)	12.6 (2.69)	12 (<1)	10.3 (3.31)
Died	1(<1)	13	1 (<1)	10

The mean HADS-anxiety scores for the 1518 patients screened was 8.70 (SD 4.91). As expected the scores were normally distributed and are shown in a histogram (Figure 17). The median was 9 and IQR was 5-12. The arrow in figure 17 marks the entry criteria for this and previous research of CBT in COPD when the HADS Questionnaire was used.

Figure 17 – Histogram of the distribution of HADS-Anxiety scores for 1518 patients screened for eligibility for the study.

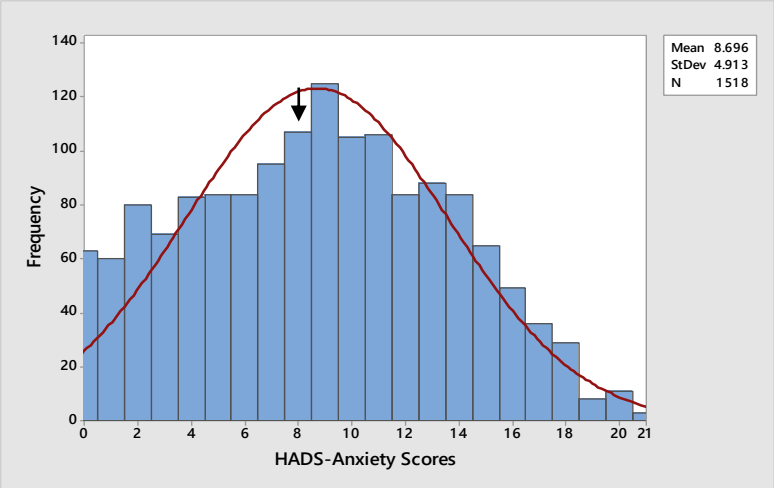
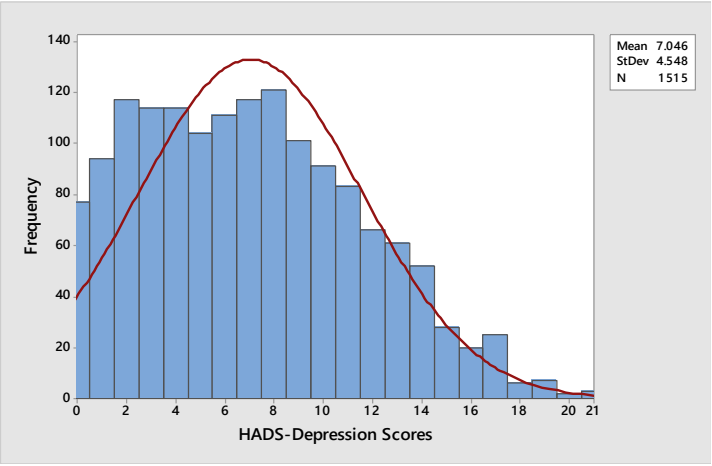


Figure 18 below shows the HADS-Depression scores for 1515 patients screened. The distribution of the scores does not appear to be normally distributed. In this cohort, symptoms of depression were lower than symptoms of anxiety with the mean HADS-Depression score of 7.0 (SD 4.55). The median HADS-Depression score was 7 and IQR 3-10.

Figure 18 – Histogram of the distribution of HADS-Depression scores for 1515 patients screened for eligibility for the study.



6.2 Baseline Characteristics of patients recruited

In total, 279 patients were recruited: 139 patients were randomised to the CBT group and 140 to the Leaflet group. Baseline characteristics can be found in table 27.

Table 27 – Baseline characteristics of patients recruited at baseline.

	CBT Group (n=139)	**Leaflet Group (n=140)**	**Total Patients (n=279)**
	Total /(Percent)	**Total /(Percent)**	**Total /(Percent)**
Age (years)	66	67	66.5
Gender			
Male	61 (44)	67 (48)	128 (46)
Female	78 (56)	73 (52)	151 (54)
Ethnic Group			
White British	139 (100)	140 (100)	279 (100)
Educational Level			
No higher educational qualifications (e.g. GCSE and above)	100 (75)	103 (77)	203 (73)
BTS Severity of airflow obstruction			
Mild	16 (11)	13 (9)	29 (10)
Moderate	44 (32)	47 (34)	91 (33)
Severe	50 (36)	49 (35)	99 (35)
Very Severe	29 (21)	31 (22)	60 (22)
MRC Breathlessness Score			
0- 2	8 (6)	12 (9)	20 (7)
3	26 (19)	18 (13)	44 (16)
4	39 (28)	44 (31)	83 (30)
5	67 (48)	65 (46)	132 (47)
Employment Status			
Employed	8 (6)	76 (4)	15 (5)
Retired	60 (42)	56 (40)	115 (41)
Unemployed	7 (5)	5 (4)	12 (4)
Retired early due to ill health	65 (47)	72 (51)	137 (49)
Married or Co-habiting	68 (49)	63 (45)	132 (47)
Current smoker	39 (28)	40 (29)	79 (28)
Mean pack years	46	49	47
BMI (kg/M2)	26	27	26.5

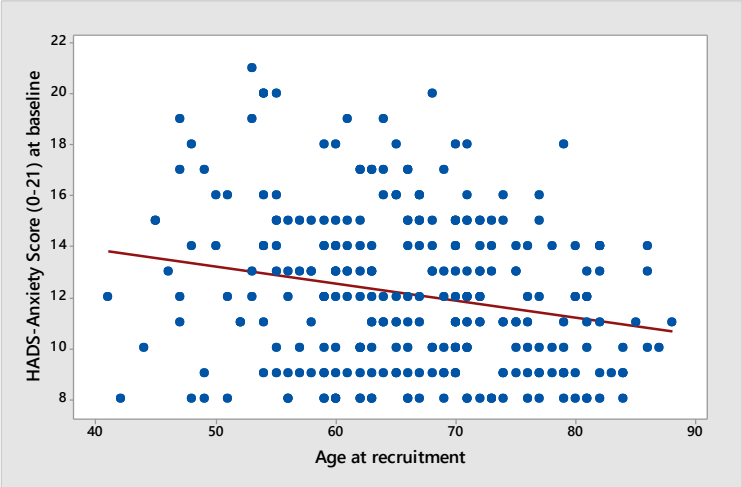
Abbreviations: BMI -Body Mass Index, GCSE -General Certificate of Education, MRC- Medical Research Council.

There were no significant differences for any demographic or clinical parameters at baseline.

6.2.1 Age

The mean age for all patients was 66 (range 41 to 88). There was no difference between the two groups (p=0.40, 95% CI -3.31 - 1.34). There were 157 (56%) of patients over 65 years of age and 61 (22%) of patients over 75 years. Prior observations have suggested that anxiety may be more commonly associated with certain age groups. Pearson product-moment correlation was performed to identify if there was a relationship between the severities of anxiety (as measured by the HADS-Anxiety scale) in the recruited population and age. Figure 19 shows a scatterplot of the correlation between HADS-Anxiety scores and age at baseline.

Figure 19 – Scatterplot of the correlation between HADS-Anxiety scores and age at baseline.



There was a negative correlation indicating that anxiety decreases with age (-0.218, p=<0.001). Pearson product-moment correlation was also performed to identify if there was a relationship between HADS-Depression and age. Figure 20 shows the relationship between HADS-Depression scores and age at baseline.

Figure 20 – Scatterplot of the correlation between HADS-Depression scores and age at baseline.

The results indicate that depression decreases with age (-0.32, p=<0.001).

6.2.2 Gender

From the 279 patients recruited 151 patients (54%) were female and 128 (46 %) male. There was no difference between the groups regarding gender at baseline.

6.2.3 Ethnicity

All of the patients recruited were white British. From the patients screened there was only one patient from an ethnic minority group, who politely declined to participate in the study. There are no statistics on the prevalence of COPD in ethnic groups in the North East. The low numbers of patients screened from ethnic groups other than white British may be unusual to other areas in the country.

6.2.4 Smoking Status

Patients had a significant smoking history of 47 pack years. From the patients recruited 79 (28%) patients continued to smoke.

6.2.5 Severity of Obstruction

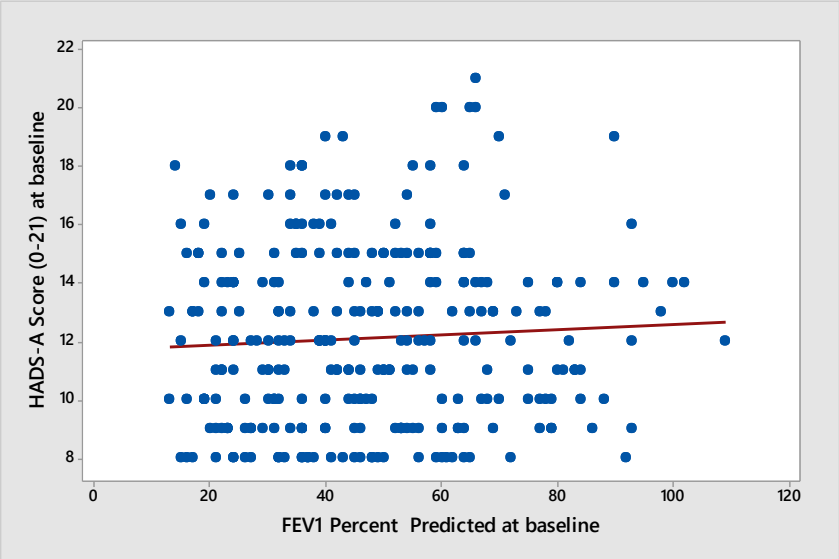
As expected for a secondary care population 159 (57%) patients recruited had severe to very severe COPD. The severity of COPD for patients recruited into the study is shown below in table 28 using NICE Criteria (10).

Table 28 – Breakdown of severity of obstruction at baseline using NICE Criteria (n=279).

Severity of Obstruction	All patients n=279/(percent)	CBT n=139 / (percent)	Leaflets n=140 /(percent)
Mild	29 (10)	16 (11)	13 (9)
Moderate	91 (33)	44 (32)	47 (34)
Severe	99 (35)	50 (36)	49 (35)
Very Severe	60 (22)	29 (21)	31 (22)

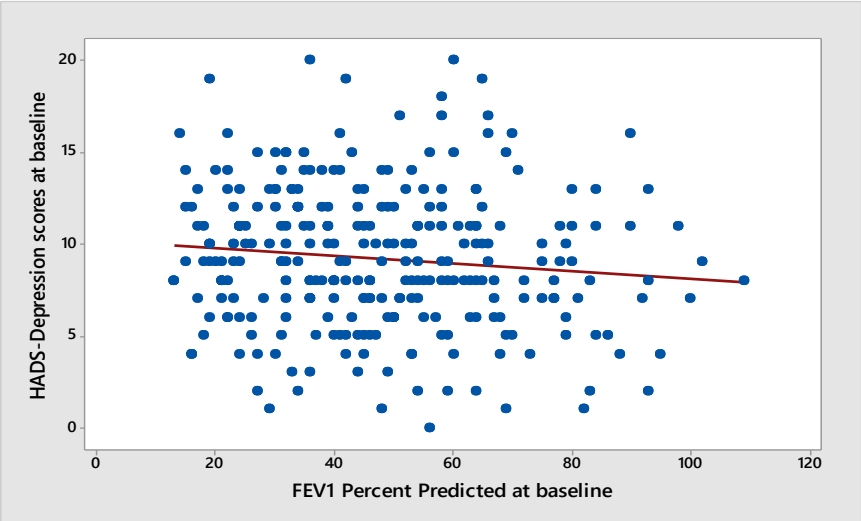
Pearson product-moment correlation was used to identify if there was a correlation between FEV_1 and HADS-Anxiety. Figure 22 shows a scatterplot of HADS-Anxiety scores and FEV_1 at baseline of study entry.

Figure 22 – Scatterplot of the correlation between HADS-Anxiety scores and FEV_1 at baseline (n=279).



Unlike previous studies there was no correlation between HADS-Anxiety scores at baseline and actual FEV_1 recorded at baseline when analysed using Pearson Product-Moment Correlation (-0.009, p=0.89), or HADS-Anxiety scores and FEV_1 percentage predicted (0.06, p=0.32). Similarly, Pearson product-moment correlation was used to identify if there was a correlation between FEV_1 and HADS-Depression (Figure 23).

Figure 23 – Scatterplot of the correlation between HADS-Depression scores and FEV1 at baseline (n=279).



The results indicate that there was no correlation between HADS-Depression scores and actual FEV1 recorded at baseline when analysed using Pearson Product-Moment Correlation (0.01, p=0.82), or HADS-Depression scores and FEV1 percentage predicted (-0.11, p=0.07).

6.2.6 Medical Research Council (MRC) Breathlessness scores

In total 259 (92%) recruited reported MRC scores of 3 or above indicating significant disability associated with breathlessness affecting QOL with 132 (47%) reporting MRC 5. A summary of the scores can be found in table 29.

Table 29- MRC Breathlessness scores of patients recruited at baseline (n=279).

MRC Dyspnoea Score	CBT Group n=139 /(percent)	Leaflets n=140 /(Percent)	Total n=279 /(percent)
0-unable to answer	0	1 (<1)	1 (<1)
1	0	0	0
2	8 (6)	11 (8)	19 (6)
3	25 (18)	19 (14)	44 (16)
4	39 (28)	44 (31)	83 (30)
5	67 (48)	65 (47)	132 (48)
Median/mean MRC	4	4	4

6.2.7 Marital Status

Just under half of patients were married or co-habiting. There was no significant difference between the mean HADS-Anxiety or HADS-Depression scores for patients who were married or co-habiting compared to those who were not (Anxiety p=0.55 95% CI -0.951- 0.505; Depression p=0.11 95% CI -1.654 – 0.158).

6.2.8 Mortality

From 279 patients recruited only six patients died before reaching the primary endpoint at three months. Two patients died in the CBT group and four patients from the Leaflet group. Table 30 provides information on the cause of death for each patient.

Table 30 – Summary of cause of death for CBT and Leaflet groups (n=6)

	CBT Group		
Patient	**Cause of Death**	**Age**	**Expected**
1	Infective exacerbation of COPD and bronchiectasis	84	Yes
2	VF Cardiac Arrest	59	Yes
	Leaflet Group		
1	Pneumonia/cor pulmonale/renal failure	82	Yes
2	Pneumonia/Chronic lymph	76	Yes
3	Pneumonia/Severe COPD/Type 2 respiratory failure	60	Yes
4	Pneumonia	67	Yes

6.2.9 Educational Status

The majority of patients recruited in this study did not have any formal educational qualifications. In total 203 (73%) patients did not have any educational qualifications. Only six (2%) patients had qualifications at A-level or above.

6.2.10 Employment Status

Very few patients were employed with only 15 (5%) stating they were working. From the 279 patients recruited, 137 (49%) stated they had to retire early due to ill health. Out of the

patients who retired early 49 (36%) were under the age of 60 with 13 (9.5 %) of these patients under the age of 50. A breakdown of employment status can be found in table 31.

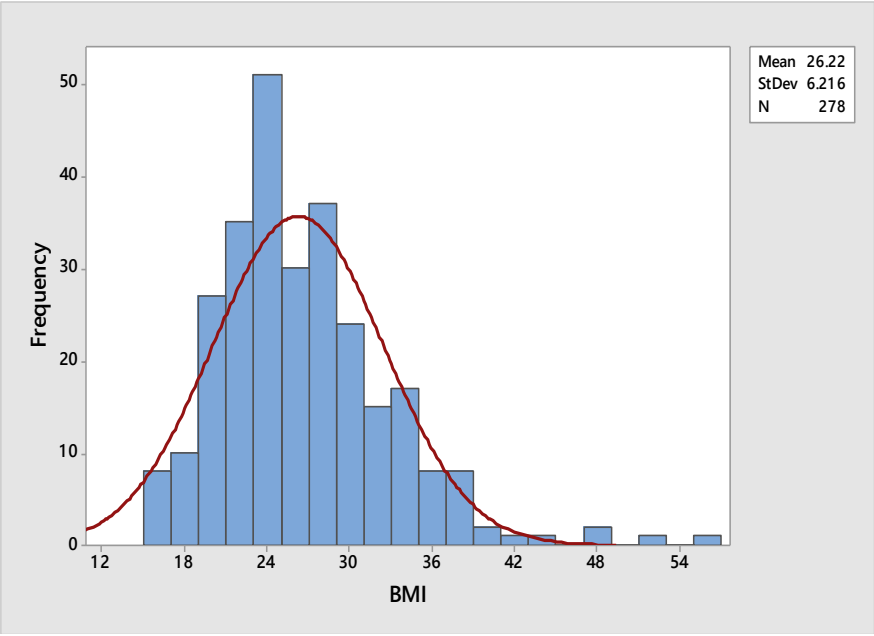
Table 31- Employment status of patients recruited at baseline (n=279).

Occupational Group	CBT Group n=139 Number /(percent)	Leaflet Group n=140 Number /(percent)	Total n=279 Number/(percent)
Employed	9 (7)	6 (4)	15 (5.4)
Retired	58 (42)	57 (40)	115 (41.2)
Unemployed	7 (5)	5 (4)	12 (4.3)
Retired early due to ill health	65 (47)	73 (52)	137 (49.1)

6.2.11 BMI

BMI ranged from 15 - 55. The mean BMI scores for 278 patients was 26 (27 in CBT group and 26.5 in Leaflet group). In total, 45 (16%) of patients had a BMI scores ranging from 15 to 20 which is a poor prognostic indicator (222) (223). A histogram of BMI scores from all patients recruited can be found in figure 24 and was normally distributed.

Figure 24 – Histogram of the distribution of BMI scores for patients recruited (n=279).



6.2.12 Pulmonary Rehabilitation (PR)

At the point of entry only a third of patients had completed PR despite the fact that PR is a key treatment for patients with COPD. A breakdown of rehabilitation can be found in table 32. In total, 102 patients had not completed PR. It is likely that PR had been offered but this could not be confirmed. A number of patients (56 patients) had been referred for PR. During the study, 23 patients completed pulmonary rehabilitation (13 from the CBT group and 10 from the leaflet group). By the end of the 12 months study period only 120 patients (43%) had completed pulmonary rehabilitation. The other 33 (59 %) patients who had been referred either declined, dropped out or the re-habilitation team were unable to contact them.

Table 32-Breakdown of participation in pulmonary rehabilitation at baseline (n=279)

	Number/ (percent) CBT Group	Number/ (percent) Leaflet Group	Total/ (percent)
Completed at baseline	46 (33)	51 (36)	97 (35)
No	54 (39)	48 (34)	102 (36)
Declined	9 (7)	5 (4)	14 (5)
Dropped out	3 (2)	5 (4)	8 (3)
Unable to contact	0	2 (1)	2 (1)
Referred	27 (19)	29 (21)	56 (20)

6.2.13 Respiratory Medication

At baseline patients were asked to report respiratory medication used. The results are provided in table 33.

Table 33- Self-reported respiratory medication used by patients at baseline (n=279)

Self-Report Respiratory Medication	CBT Group (n-139)- Number/ (percent)	Leaflet Group (n=140) Number / (percent)	Total (n=279) Number / (percent)
Short acting beta agonists	138 (99)	139 (99)	277 (99)
Short acting anticholinergics	1 (1)	2 (1)	3 (1)
Long acting beta agonists	2 (1)	1 (1)	3 (1)
Long acting anticholinergics	128 (93)	132 (94)	187 (67)
Corticosteroids/Long acting beta agonists	133 (96)	134 (96)	267 (96)
Mucolytics	55 (40)	59 (42)	114 (41)
Nebulised short acting bronchodilators	18 (13)	21 (15)	39 (14)
Diuretics	36 (26)	39 (28)	75 (27)
Prepacks (steroids/antibiotics)	48 (35)	53 (38)	101 (36)
Oxygen (short burst)	4 (3)	2 (1)	6 (2)
Oxygen (Long term oxygen therapy)	15 (11)	9 (6)	24 (9)
Oxygen (Ambulatory oxygen)	2 (1)	4 (3)	6 (2)

6.2.14 Medication for anxiety and depression

Self-reported data was also collected on the use of pharmacological therapy for anxiety and depression. The results are provided in table 34. In this study 35% of patients reported receiving treatment for depression which is slightly higher than the 30% quoted in a recent systematic review (4).

Table 34– Self-reported medication used for anxiety and depression at baseline (n=279)

Self-Report Psychiatric Medication	CBT Group (N=139) Number / (percent)	Leaflet Group (n=140) Number/(percent)	Total / (percent)
Anti-depressants	52 (37)	47 (34)	99 (35)
Anxiolytics	14 (10)	6 (4)	20 (7)

6.3 Outcome of CBT group following randomisation

In the CBT group, 11 (8%) patients did not receive the allocated treatment (Table 35). Data collection was missed for one patient at three months.

Table 35 – Summary of randomised patients who did not receive CBT intervention.

Number of patients	Reason
3	Dropped out (reasons stated: two patients withdrew consent; one patient's husband was ill).
2	Withdrawn (incorrectly completed HADS. Scores <8 on re-screen so were not eligible).
2	Withdrawn due to unrecognised cognitive impairment.
2	Withdrawn due to psychiatric problems which clinical team were not aware of.
1	Diagnosis changed from COPD to asthma.
1	Lost to follow up. Did not respond to telephone calls or letter to organise CBT. This was reported to GP and hospital consultant.

In total 129 patients received the allocated intervention. At three months, 13 (10%) patients discontinued the intervention. The reasons for discontinuing the CBT intervention can be found in table 36.

Table 36 – Summary of patients who discontinued CBT intervention (n=13).

Number of patients	Reason
2	Died.
4	Lost to follow up but known to be still alive
5	Withdrew consent (reasons stated: ill health, too busy, 'could not be bothered' and 'not her cup of tea').
2	Found to be ineligible; one patient had psychiatric problems which clinical team were not aware of and another had cognitive impairment.

Patients from both groups who did not complete the three month follow up are not included in the 'per-protocol' analysis. Data collection was missed for one patient in the CBT group at three months.

6.4 Outcome of Leaflet group following randomisation

In the leaflet group, all of the randomised patients received the allocated intervention (140 in total). At three months, 18 (13%) patients discontinued the intervention (see Table 37).

Data collection was missed for one patient in the leaflet group at three months (which was the same as the CBT group).

Table 37 – Summary of patients who discontinued Leaflet intervention.

Number of patients	Reason
4	Died.
6	Lost to follow up.
7	Dropped out (reasons stated: social problems, too busy, ill health, three patients requested CBT).
1	Withdrawn as clinician requested CBT for patients who was in palliative phases of COPD.

Across both treatment arms six (2%) patients died before the three months follow up time point which was lower than the 10% at 3 months and 15% over the year anticipated at the start of the study. Data attrition was 15% overall which was lower than the anticipated 20% at the start of the study.

6.5 Comparison of patients completing study to 3 months (completers) and patients who did not (non-completers).

When the non-completers were grouped irrespective of treatment allocation there were no difference between those who completed the three month follow up compared to patients who did not for the following: age, FEV_1, HADS-Anxiety, HADS-Depression, CAT or EQ-5D utility scores (Table 38).

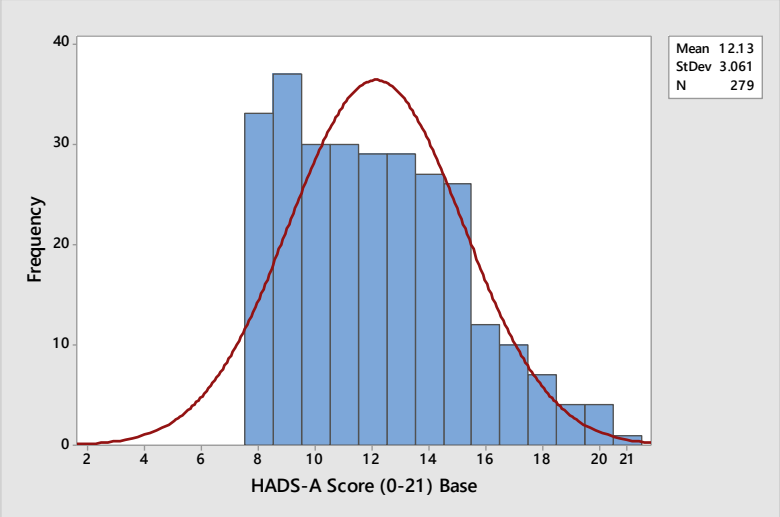
Table 38 – Comparison of variables between patients completing three month follow up and those who did not.

Variable	Completers (number= 236)	Non-Completers (number=43)		
	Mean (SD)	**Mean (SD)**	**p-value**	**95% CI**
Age	66 (9.58)	65 (SD 11.5)	0.59	-2.71-4.74
FEV1	1.33 (2.65)	1.11 (0.66)	0.27	-0.17-0.61
HADS-Anxiety	12.1 (3.02)	12.3 (3.33)	0.68	-1.32-0.86
HADS-Depression	9.0 (3.84)	10.3 (3.79)	0.05	-2.51-0.01
CAT	28.3 (6.36)	29.3 (5.33)	0.27	-2.84-0.81
EQ-5D Utility	0.41 (0.27)	0.38 (0.29)	0.48	-0.06-0.13

6.6 Anxiety

The HADS-Anxiety scores ranged from eight (which was the minimum entry criteria) to 21 for the 279 patients recruited. The distribution of HADS-Anxiety scores would be expected to be normally distributed in the general population. However, in this study the distribution of the scores were skewed as the entry criteria into the study was ≥8 using HADS-Anxiety scale (figure 25).

Figure 25– Histogram of the distribution of HADS-Anxiety Scores for patients recruited at baseline.



The mean HADS-Anxiety score for 279 patients was 12.1 (SD 3.1), median 12 and IQR 9 – 14. Mann-Whitney Test was used to analyse the data. There was no difference between the groups for HADS-Anxiety scores at baseline using Mann-Whitney Test (Table 39).

Table 39 – Comparison of HADS-Anxiety scores for CBT and Leaflet groups at baseline (n=279).

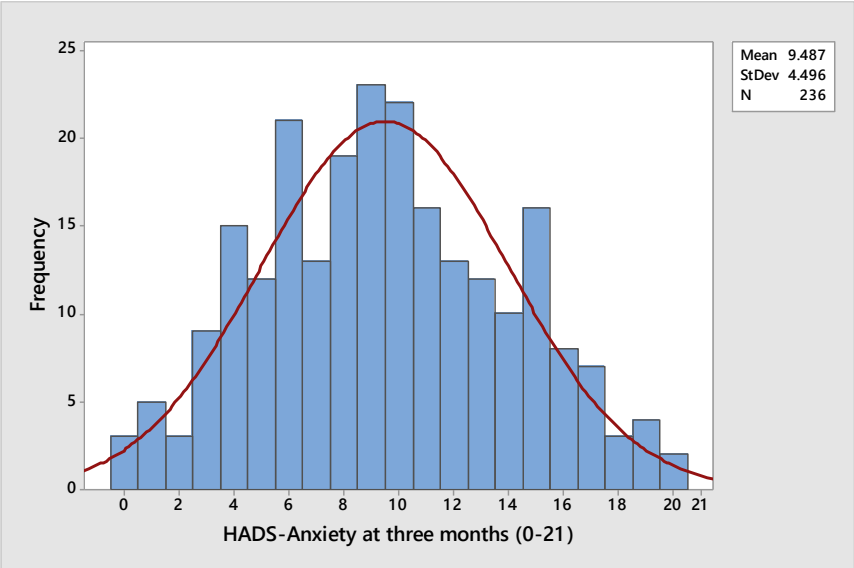
	CBT Group (n=139) Median Baseline	Leaflet Group (n=140) Median Baseline	p-value	(95% CI)
HADS-Anxiety Score	12.0	12.0	0.55	(-0.000-1.000)

6.6.1 HADS-Anxiety Scores at three months

The primary outcome for this study was a change in group mean HADS-Anxiety scores at three months. A clinically meaningful reduction is defined as ≥1.5 points on the HADS-Anxiety scale (122). In total 236 patients completed the primary endpoint of three months (85% completion rate). Data was normally distributed (Figure 26). The HADS-Anxiety scores

ranged from 0 -20 at three months. The mean HADS-Anxiety score was 9.5 (SD 4.5), median 9 and IQR 6-13.

Figure 26 – Histogram of distribution of HADS-Anxiety scores for patients completing three months.



Of the 236 patients completing the primary endpoint, 132 (56%) improved over ≥1.5 on the HADS-Anxiety scale (termed responders). Logistic regression analysis was performed on all patients completing the primary outcome at three months. The aim was to assess the impact of a number of factors to predict who would respond to either CBT or Leaflets (≥1.5 on the HADS-Anxiety scale). Baseline continuous variables assessed included age, HADS-Anxiety, HADS-Depression, CAT and EQ-5D utility scores at baseline. Categorical variables included gender. Three variables made a unique contribution to the model (responding ≥1.5 on HADS-Anxiety scale). The strongest predictor was a HADS-Anxiety score at baseline with an odds ratio of 1.20 (p= 0.001 95% CI 1.07 – 1.34). The second strongest was age with an odds ratio of 1.04 (p=0.005 95% CI 1.01 – 1.08). The third strongest was the CAT score at baseline with an odds ratio of 0.94 (p=0.008 95% CI 0.89 – 0.98).

6.6.2 HADS-Anxiety Scores for patients in the CBT group at three months.

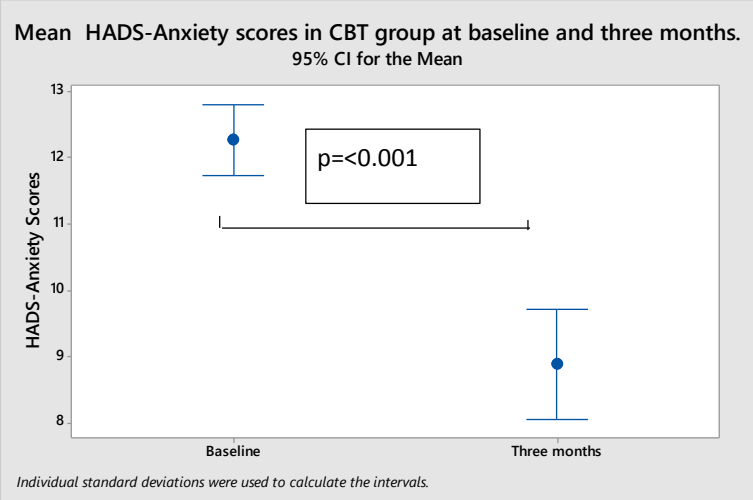
In the CBT arm the HADS-Anxiety scores ranged from 0 – 20. The mean HADS-Anxiety score reduced from 12.3 (SD 3.19) at baseline to 8.9 (SD 4.50), at three months (Table 40). The group mean change was 3.40 (SD 4.2; 95% CI 2.62 - 4.17 p=<0.001) reaching the suggested MCID of 1.5 (122).

Table 40 – Change in mean HADS-Anxiety scores for patients in the CBT group at baseline and three months.

	CBT Group (n=115) Mean (SD) Baseline	CBT Group (n=115) Mean (SD) Three months	p-value	(95% CI)
HADS-Anxiety Score	12.3 (3.19)	8.9 (4.50)	<0.001	2.62-4.17

The interval plot in figure 27 shows mean change in HADS-Anxiety scores for the CBT group at baseline and three months.

Figure 27- Interval plot of the mean HADS-Anxiety scores for the CBT groups at baseline and three months.



The results indicate there is a statistically and clinically significant improvement in mean HADS-Anxiety score at the three month primary end point in the CBT group.

6.6.3 Comparison of responders compared to non-responders in CBT group.

From the 115 patients, 69 (60%) patients achieved a decrease of ≥1.5 in HADS-Anxiety scores (responders) reaching the MCID for their individual scores suggested by Puhan (122) compared to 46 (40%) who did not (non-responders). Patients who achieved a fall of HADS-Anxiety scores by ≥1.5 in the CBT group were compared with those patients who did not respond (Table 41).

Table 41 – Comparison of baseline data in responder patients in CBT group compared to those who did not. (Responder was defined as a fall in MCID ≥1.5 on HADS-Anxiety Scale).

Variable	Responders (n=69) Mean (SD)	Non-responders (n=46) Mean (SD)	p-value	95% CI
Age	68.1 (8.54)	62 (10.9)	0.002	2.33 – 9.91
FEV_1	1.15 (0.60)	1.29 (0.52)	0.19	-0.351 – 0.07
HADS-Anxiety	12.5 (2.94)	12.0 (3.42)	0.42	-0.73 – 1.73
HADS-Depression	8.64 (3.75)	10.0 (4.28)	0.08	-2.91 – 0.18
CAT	27.0 (6.53)	29.11 (6.27)	0.09	-4.52 – 0.30
EQ-5D Utility	0.48 (0.27)	0.35 (0.28)	0.02	0.02 – 0.23

There was a significant difference between responders and non-responders for age and EQ-5D utility scores. This suggests older patients and those with better QOL (as measure by the EQ-5D utility scores) responded better than younger patients reporting poorer QOL.

6.6.4 HADS-Anxiety for patients in the Leaflet group at three months.

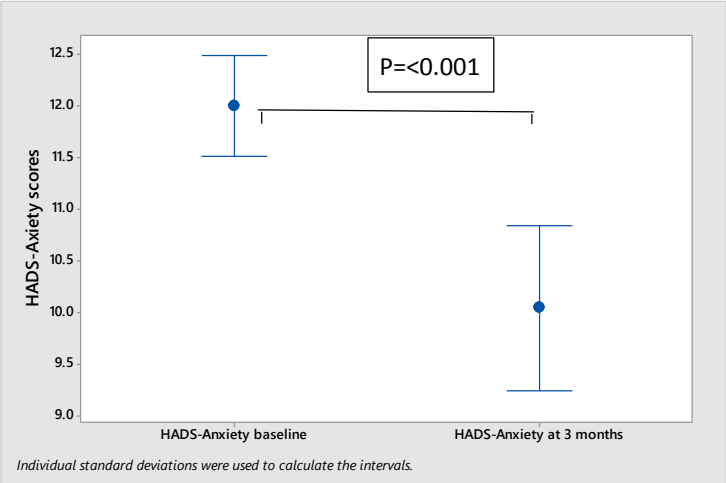
The HADS-Anxiety scores in the leaflet group ranged from 0-19. The mean HADS-Anxiety score reduced from 12.0 (SD 2.93) at baseline to 10.1 (SD 4.44) (Table 42).

Table 42 – Mean HADS-Anxiety scores for patients in the Leaflet group at baseline and three months.

	Leaflet Group (n=121) Mean (SD) Baseline	Leaflet Group (n=121) Mean (SD) Three months	p-value	(95% CI)
HADS-Anxiety Score	12.0 (2.93)	10.1 (4.44)	<0.001	1.19 - 2.55

An interval plot of the mean HADS-Anxiety scores for the Leaflet group at baseline and three months is presented in figure 28.

Figure 28 – interval plot of mean HADS-Anxiety scores for Leaflet group at baseline and three months.



The group mean change from baseline to three months was 1.9 (SD 3.8) 95% CI 1.19 – 2.55 p=<0.001 reaching the suggested MCID of ≥1.5 (122).

6.6.5 HADS-Anxiety Scores comparison of mean change between the CBT and Leaflet groups at three months.

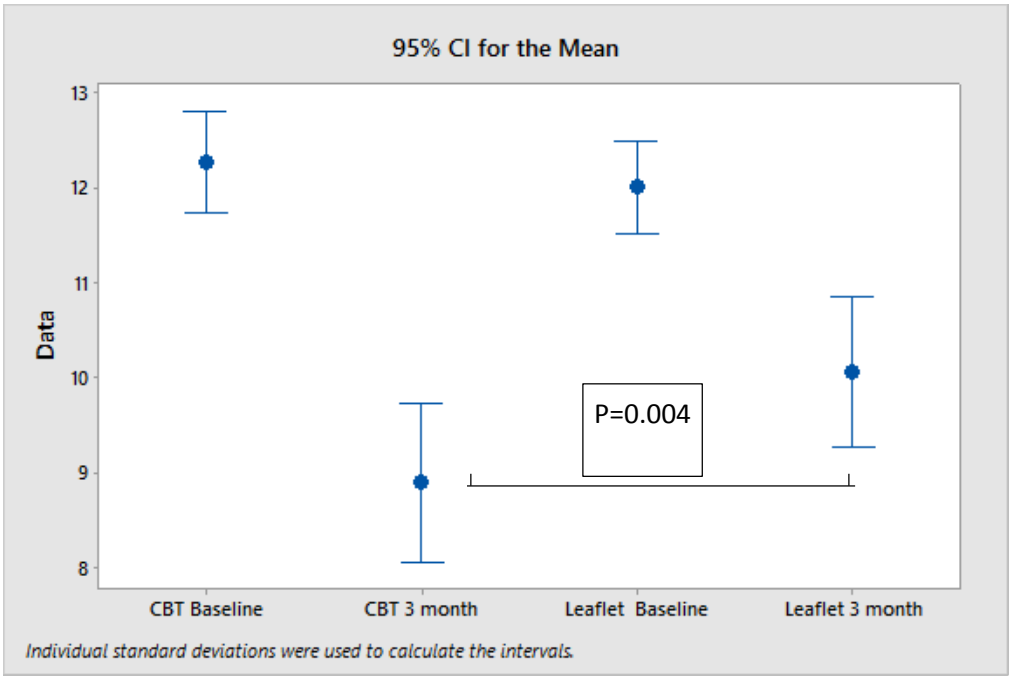
The group mean change in HADS-Anxiety scores was significantly greater in the CBT group compared to the leaflet group (mean difference = 1.52; CI 0.50 – 2.55; p=0.004) (Table 43) and reached the suggested MCID between the groups of ≥1.5.

Table 43 – Mean change in HADS-Anxiety scores in CBT and Leaflet groups at three months (n=236).

	CBT Group (n=115) Mean (SD)	Leaflet Group (n= 121) Mean (SD)	p-value	(95% CI)
HADS-Anxiety Score	3.4 (4.2)	1.9 (3.8)	0.004	0.50 - 2.55

Figure 29 shows an interval plot of the mean in HADS-Anxiety scores for the CBT and Leaflet groups at baseline and three months.

Figure 29– Interval plot of mean HADS-Anxiety scores for CBT and Leaflet groups at baseline and three months.



In total 132 (56%) of patients achieved an improvement in HADS-Anxiety scores at three months reaching the MCID of ≥1.5. In the CBT group 69 (60%) patients improved compared to 63 (52%) in the leaflet group with no significant difference between the groups (Chi-squared statistic 1.50; p=0.22).

6.6.6 Comparison of responders and non-responders for HADS-Anxiety in Leaflet group

Of the 121 patients, 63 (52%) patients achieved a decrease of >1.5 in HADS-Anxiety scores reaching the MCID for their individual scores. There was no difference in any variable between those patients who achieved a fall of HADS-Anxiety scores by ≥1.5 in the Leaflet group compared with those patients who did not respond (Table 44).

Table 44 – Comparison of patients with a HADS-Anxiety score reducing by MCID ≥1.5 in Leaflet group to those who do not.

Variable	Responders (n= 63)	Non-responders (n=58)		
	Mean (SD)	Mean (SD)	p-value	95% CI
Age	68.2 (8.36)	66.2	0.22	-1.25 – 5.32
FEV_1	1.15 (0.5)	1.13 (0.58)	0.85	-0.17 – 0.21
HADS-Anxiety	12.1 (3.13)	11.8 (2.64)	0.63	-0.79 – 1.29
HADS-Depression	8.90 (3.69)	9.16 (3.42)	0.70	- 1.53 – 1.03
CAT	29.1 (6.20)	28.1 (6.26)	0.35	- 1.18 – 3.31
EQ-5D Utility	0.40 (0.30)	0.40 (0.31)	0.75	-0.12 – 0.10

Gender

From the 279 patients recruited 151 patients (54%) were female and 128 (46 %) male. There was no difference between the groups regarding gender at baseline.

Males

In the CBT arm the group mean HADS-Anxiety scores for male patients was 12.0 (SD 2.86), range 8-20 at baseline and this reduced to 8.9 (SD 4.18) range 1-19 at three months. The mean difference change was 3.04 (SD 4.16), 95% CI 1.89 – 4.18 p= <0.001 at three months compared to baseline. The mean change reached the suggested minimal clinical importance difference (MCID) ≥1.5 (122). The mean HADS-Anxiety score for patients in the leaflet group reduced from 12.2 (SD 3.09) range 8-20 at baseline to 9.89 (SD 4.24) range 1-17 at three months. The mean change was 2.13 (SD 3.58), 95% CI 1.17 – 3.08 p= <0.001 at three months compared to baseline. The mean change also reached the suggested MCID of ≥1.5 (122). Unpaired student t-tests were used to compare the group mean change in HADS-Anxiety scores between the two groups at three months. The results can be seen in table 45. There was no significant difference between the CBT and Leaflet groups for males.

Table 45 - Mean change in males HADS-Anxiety scores between CBT and Leaflet groups at three months (n=109).

	CBT Group (n=53) Males Mean (SD) Three months	Leaflet Group (n=56) Mean (SD) Three months	p-value	(95% CI)
HADS-Anxiety	3.04 (4.16)	2.13 (3.58)	0.22	-2.39 – 0.57

Females

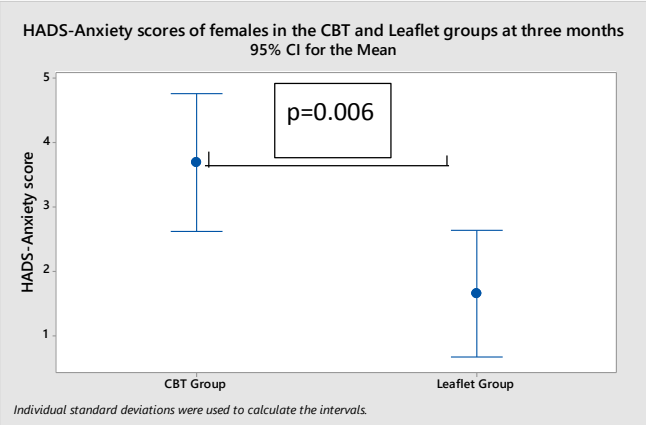
In the CBT arm the group mean HADS-Anxiety scores for female patients was 12.6 (SD 3.40), range 8 to 21 at baseline. The mean HADS-Anxiety scores reduced to 8.8 (SD 4.79) range 0-20 at three months. The mean difference change was 3.69 (SD 4.24) 95% CI 2.62 – 4.77 p= <0.001 at three months compared to baseline, reaching the suggested MCID of ≥1.5 (122). In the leaflet arm the group mean HADS-Anxiety score was 11.7 (SD 2.80), range from 8-20 at baseline. The mean HADS-Anxiety reduced from 11.7 (SD 2.8) to 10.2 (SD 4.63) range 0-19 at three months. The mean difference change was 1.65 (SD 3.97), 95% CI 0.66 – 2.63 p=0.001. Unpaired student t-tests were used to compare the group mean change in HADS-Anxiety scores between the two groups at three months. The results can be seen in table 46.

Table 46 - Mean change in females HADS-Anxiety scores in the CBT and Leaflet groups at three months (n=127)

	CBT Group (n=62) females Mean (SD) at 3 months	Leaflet Group (n=65) Mean (SD) at 3 months	p-value	(95% CI)
HADS-Anxiety	3.69 (4.24)	1.65 (3.97)	0.006	0.60 – 3.49

The interval plot presented in figure 21 shows the mean change in HADS-Anxiety scores for females in the CBT and Leaflet groups at three months.

Figure 21- Interval plot of mean change in HADS-Anxiety scores for females in the CBT and Leaflet groups at three months.

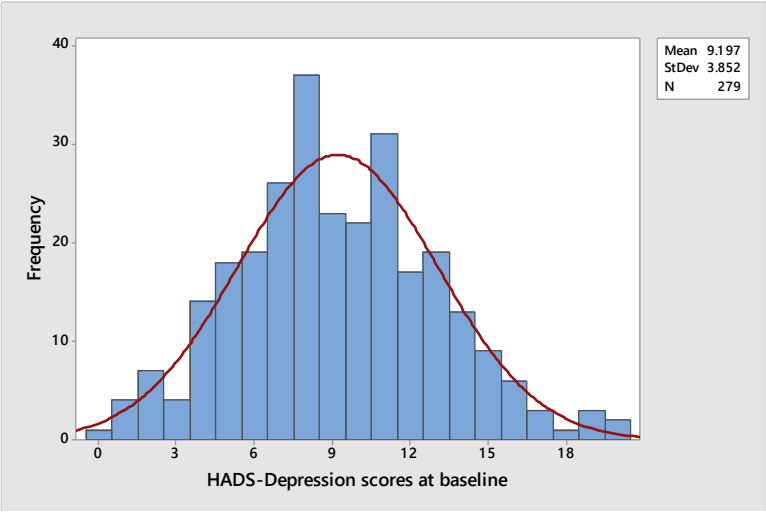


In contrast to the male patients, the mean change in the HADS-Anxiety scores in the CBT group for females was significantly better than the leaflet group as shown in figure 21 above.

6.7 Depression

Baseline HADS-Depression scores ranged from zero to 20 for 279 patients recruited. The HADS-Depression scores were normally distributed (Figure 30). The mean score was 9.2 (SD 3.9), median 9 and IQR 7-20.

Figure 30 – Histogram of the distribution of HADS-Depression scores for patients recruited at baseline (n=279).



There was no difference between the groups for HADS-Depression scores at baseline (Table 47). Two thirds of patients recruited 186 (67%) reported symptoms of depression with a

HADS-Depression score ≥8. A total of 24 (9%) patients reported significant symptoms of depression with HADS-Depressions scores ≥ 15.

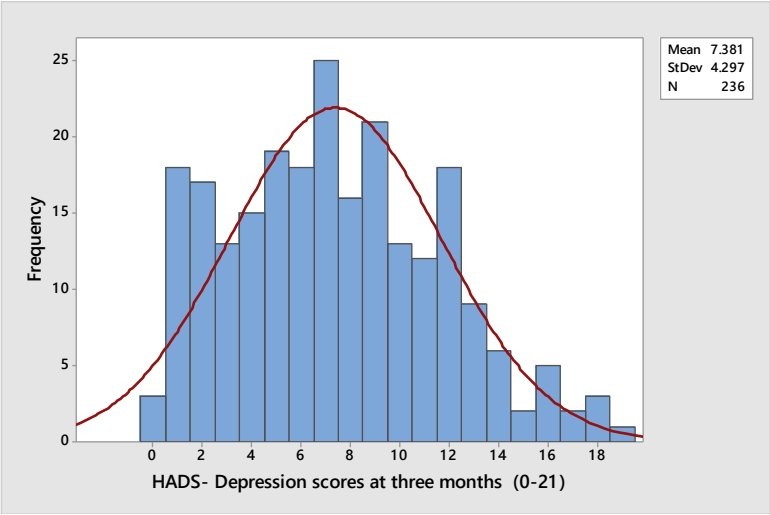
Table 47- HADS-Depression scores at baseline between CBT and Leaflet groups at baseline (n=279).

	CBT Group (n=139) Mean (SD) Baseline	Leaflet Group (n= 140) Mean (SD) Three months	p-value	(95% CI)
HADS-Depression Score	9.42 (4.01)	8.98 (3.68)	0.34	(-0.470 - 1.347)

6.7.1 HADS-Depression Scores for patients at three months.

A secondary outcome measure for this study was a reduction in group mean HADS-Depression scores at three months. This was defined by a clinically meaningful reduction in group mean of ≥1.5 points on the HADS-depression scale at three months. Data collected at three months was normally distributed (Figure 31).

Figure 31– Histogram of the distribution of HADS-Depression scores for patients recruited at three months (n=279).



Logistic regression analysis was performed on all patients (236 patients in total) to assess the impact of a number of factors on the likelihood that they would respond ≥1.5 on the HADS-Depression scale (responders). Baseline continuous variables assessed included baseline age, HADS-Anxiety score, HADS-Depression score, CAT and EQ-5D utility scores. Categorical variables included gender only. Only two variables made a unique contribution to the

model. The strongest predictor was HADS-Depression at baseline with an odds ratio of 1.22 (p= <0.001 95% CI 1.12 – 1.32). The second predictor was age with an odds ratio of 1.06 (p=<0.001 95% CI 1.03 – 1.09). This analysis was repeated in those patients whose HADS-Depression scores were ≥8 at baseline i.e. a significantly raised HADS-Depression at inclusion but had improved ≥1.5 on the HADS-Depression scale. Logistic regression analysis was performed on 108 patients to assess the impact of a number of factors on the likelihood that they would respond ≥1.5 on the HADS-Depression scale (responders). Baseline continuous variables assessed included baseline age, HADS-Anxiety score, HADS-Depression score, CAT and EQ-5D utility scores. Only one variable made a unique contribution to the model. The only predictor was HADS-Depression at baseline with an odds ratio of 1.46 (p= <0.001, 95% CI 1.22 – 1.74).

6.7.2 HADS-Depression Scores for patients in the CBT group at three months.

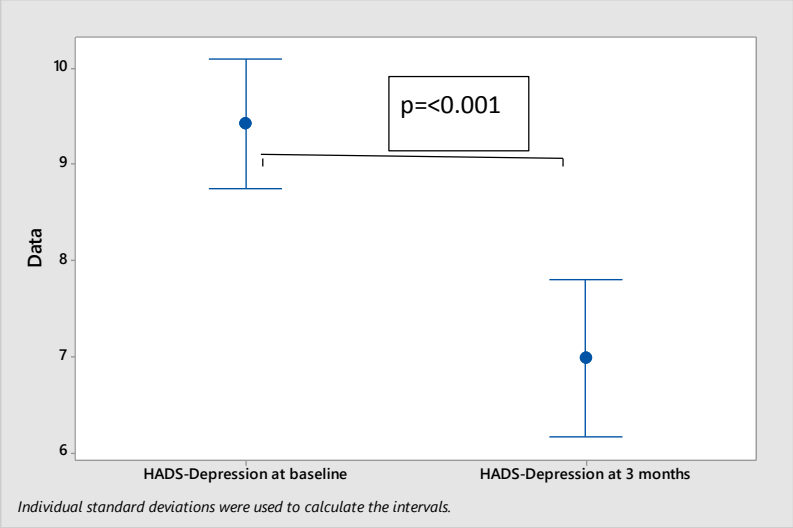
The mean HADS-Depression scores for the CBT group were compared at baseline and three months. The data presented is restricted to those with complete data sets. In the CBT group the mean HADS-Depression score reduced from 9.18 (SD 4.1) at baseline to 6.99 (SD 4.44) at three months (Table 48). The mean difference change was 2.2 (SD 3.62) 95% CI 1.53 – 2.87 p=<0.001 reaching the suggested MCID of ≥1.5 (122).

Table 48 – Mean HADS-Depression scores for patients in CBT group from baseline to three months (n=115).

	CBT Group (n=115) Mean (SD) Baseline	CBT Group (n=115) Mean (SD) Three months	p-value	(95% CI)
HADS-Depression Score	9.18 (4.01)	6.99 (4.44)	<0.001	1.53 - 2.87

Figure 32 shows an interval plot of the mean HADS-Depression scores for the CBT group from baseline to three months.

Figure 32– Mean HADS-Depression scores for CBT group at baseline and three months (n=115).



The results indicate the CBT group achieved a statistically and clinically significant improvement in symptoms of depression from baseline to three months.

6.7.3 Comparison of responders and non-responders in CBT group

From the 115 patients, 60 (52%) patients achieved a decrease of ≥1.5 in HADS-Depression scores (responders) reaching the MCID for their individual scores suggested by Puhan (122) compared to 55 (48 %) who did not (non-responders). Patients who achieved a fall of HADS-Depression scores by ≥1.5 in the CBT group mean change scores were compared with those patients who did not respond (Table 49).

Table 49 – Comparison of patients with HADS-Depression scores reducing by MCID ≥1.5 in CBT group compared to those who did not (n-115).

Variable	Responders (n=60) Mean (SD)	Non-responders (n=55) Mean (SD)	p-value	95% CI
Age	67.1 (8.60)	64.1 (11.1)	0.11	-0.66 – 6.74
FEV_1	1.17 (0.60)	1.24 (0.55)	0.51	-0.28 - 0.14
HADS-Anxiety	12.7 (3.06)	11.8 (3.18)	0.12	-0.24 – 2.07
HADS-Depression	10.2 (3.58)	8.09 (4.20)	0.005	0.64 – 3.54
CAT	28.5 (6.39)	27.1 (6.56)	0.24	-0.95 – 3.84
EQ-5D Utility	0.37 (0.30)	0.49 (0.25)	0.02	-0.23 - -0.02

The results indicate that patients who responded had a higher mean HADS-Depression score at baseline compared to those who did not respond. This finding is interesting as it has been suggested that patients with low scores at baseline generally improve more than those with high scores (216).

6.7.4 HADS-Depression scores for patients in the Leaflet group at three months.

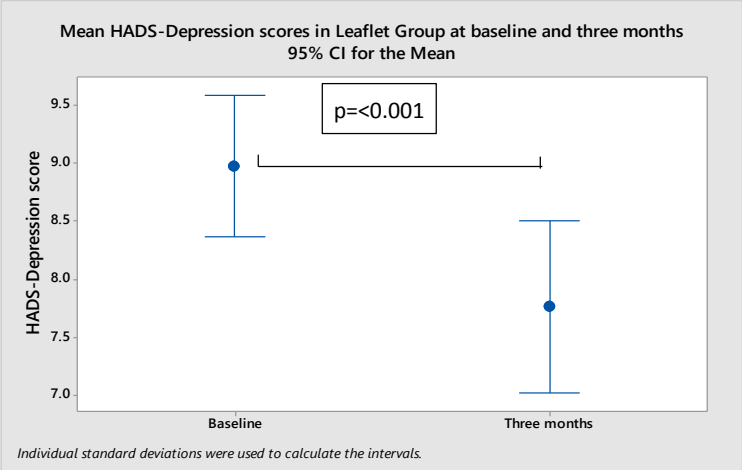
In the Leaflet group the mean HADS-Depression score reduced from 8.84 (SD 3.68) at base-line to 7.76 (SD 4.14) at three months (Table 50). The mean difference change was 1.07 (SD 3.55) 95% CI 0.44 – 1.71 p=<0.001 which did not reach the suggested MCID of ≥1.5 (122). Of the 121 patients with complete data, 50 (41%) patients achieved a decrease of >1.5 in HADS-Anxiety scores.

Table 50– Mean HADS-Depression scores in Leaflet group at baseline and three months (n=121).

	Leaflet Group (n=121) Mean (SD) Baseline	Leaflet Group at three months (n=121) Mean (SD) Three months	p-value	(95% CI)
HADS-Depression Score	8.84 (3.68)	7.76 (4.14)	<0.001	0.44 – 1.71

An interval plot of the HADS-Depression scores for patients in the Leaflet group at baseline and three months is presented in figure 33.

Figure 33 - Interval plot of mean HADS-Depression scores for patients in Leaflet group at baseline and three months (n=121).



Whilst the results are statistically significant between baseline and three months for Leaflet group, the mean change in HADS-Depression scores failed to reach the MCID of ≥1.5 (122).

6.7.5 HADS-Depression Scores comparison of mean change between the CBT and Leaflet groups at three months.

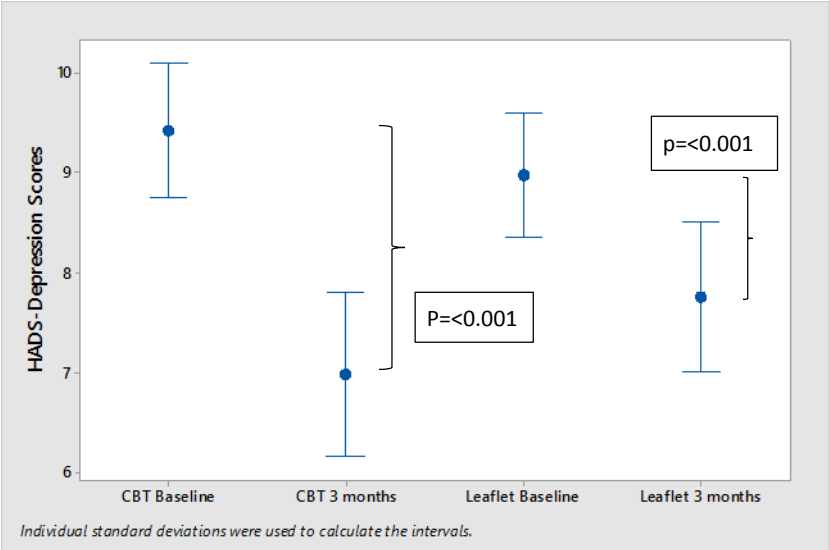
The mean HADS-Depression scores for the two groups were compared at three months. The data presented is restricted to those with complete date sets. The reported MCID of HADS score is an improvement (fall) in scores >1.5. In the CBT group the mean reduction in HADS-Depression scores was 2.20 and the leaflet group was 1.07 (see Table 51). The CBT arm was statistically significantly better than the leaflet arm (p=0.02) this did not reach the MCID when compared across intervention arms (mean difference 1.13).

Table 51 – Mean change in HADS-Depression scores between CBT and Leaflet groups at three months (n=236).

	CBT Group (n=115) Mean (SD) Baseline	**Leaflet Group (n=121) Mean (SD) Three months**	**p-value**	**(95% CI)**
HADS-Depression Score	2.20 (3.62)	1.07 (3.55)	0.02	0.21 - 2.05

The mean change in HADS-Depression scores from baseline and three months for both groups can be seen in figure 34.

Figure 34 – Interval Plot of mean HADS-Depression Scores for CBT and Leaflet groups at baseline and three months.



6.7.6 Comparison of response by MCID of ≥1.5 for HADS-Depression scores in Leaflet group.

From the 121 patients, 50 (41%) patients achieved a decrease of ≥1.5 in HADS-Depression scores (responders) reaching the MCID for their individual scores suggested by Puhan (122) compared to 71 (59 %) who did not (non-responders). Patients who achieved a fall of HADS-Depression scores by ≥1.5 in the Leaflet group were compared with those patients who did not respond (Table 52).

Table 52 – Comparison of patients with HADS-Depression score reducing MCID ≥1.5 in Leaflet group compared to those who did not (n=121).

Variable	Responders (n=50) Mean (SD)	Non-responders (n=71) Mean (SD)	p-value	95% CI
Age	68.8 (9.01)	66.2 (9.02)	0.12	-0.65 – 5.94
FEV_1	1.09 (0.47)	1.15 (0.56))	0.53	-0.246– 0.13
HADS-Anxiety	12.0 (2.96)	11.9 (2.87)	0.86	-0.98 – 1.16
HADS-Depression	9.94 (3.63)	8.06 (3.53)	0.005	0.57 – 3.20
CAT	28.3 (7.54)	29.0 (5.17)	0.60	-3.10 – 1.80
EQ-5D Utility	0.39 (0.36)	0.41 (0.27)	0.68	-0.14 – 0.10

6.8 CAT QOL

A secondary outcome measure for this study was an improvement in HRQOL as measured by the CAT Questionnaire.

6.8.1 CAT QOL Scores for 279 patients recruited at baseline

The baseline CAT scores ranged from 7 to 40. The distribution of the CAT scores were not normally distributed. The CAT scores appears slightly skewed towards higher scores indicating significant impact on HRQOL, reflecting a symptomatic secondary care COPD cohort (Figure 35). The mean score was 28.4 (SD 6.22), the median 30 and IQR 25-40. In total 253 (91%) of patients had a CAT score over 20 suggesting this COPD population had a significant burden of symptoms.

Figure 35 – Histogram of the distribution of CAT Scores for patients recruited at baseline (n=279).

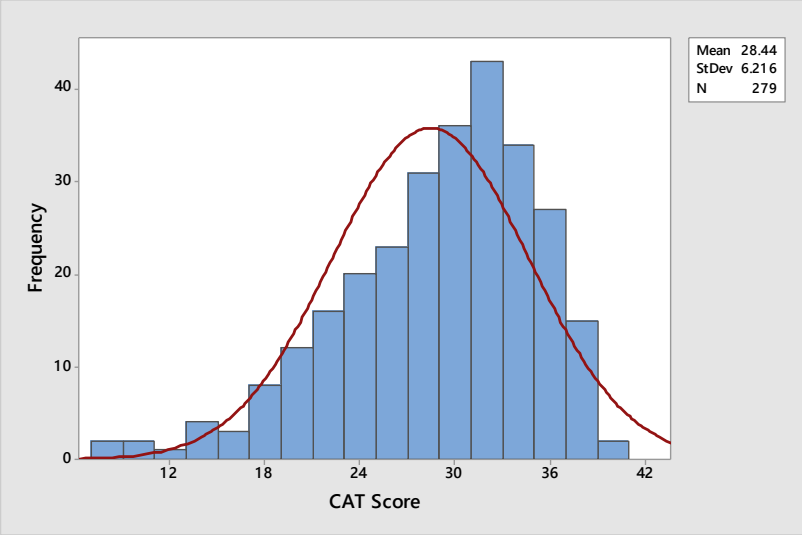


Table 53 shows the CAT scores from all patients recruited at baseline. The high scores observed suggest significant burden of symptoms affecting HRQOL.

Table 53 –Median CAT scores from patients in CBT and Leaflet groups at baseline (n=279).

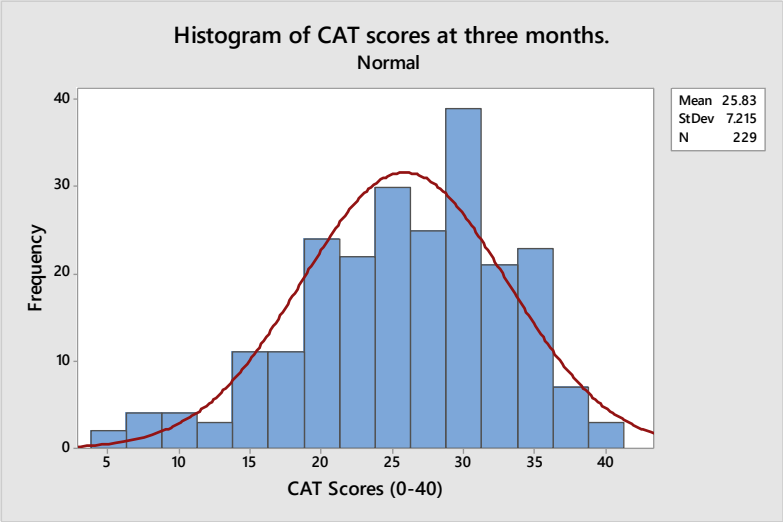
	CBT Group (n=139)	Leaflet Group (n= 140)		
	Median	**Median**	**p-value**	**(95% CI)**
CAT	29	30	0.55	(-2.000-1.000

The results show that there was no difference between the groups for the CAT score at baseline using Mann-Whitney Test.

6.8.2 CAT results at three months.

Complete CAT score data were collected at 3 months for 229 patients (111 from CBT group and 118 from the leaflet group). Data was normally distributed (Figure 36).

Figure 36 – Histogram of the distribution of CAT Scores from patients at three months (n=229).



The mean CAT score was 25.8, range six to 40, median 27, IQR 21-31. From the group, 120 (52%) patients achieved an improvement in CAT scores reaching the previously reported MCID of >2 for their individual scores (214).

6.8.3 CAT results for the CBT group at three months.

In the CBT group the mean CAT score reduced from 27.7 (SD 6.56) at baseline to 25.0 (SD 7.65) at three months (Table 54). The mean difference change was 2.7 (SD 6.36); 95% CI 1.49 - 3.88 p=<0.001. The mean change reached the suggested MCID of 2 points (214). 60 (54%) patients achieved an improvement >2.

Table 54- Mean CAT scores from patients in CBT group at baseline and three months (n=111).

	CBT Group (n=111) Mean (SD) Baseline	CBT Group (111) Mean (SD) Three months	p-value	(95% CI)
CAT (Health Status)	27.7 (SD 6.56)	25.0 (SD 7.65)	<0.001	1.49 - 3.88

6.8.4 CAT Scores for patients in the Leaflet group at three months.

In the Leaflet group the mean CAT score reduced from 28.7 at baseline to 26.6 at three months (see Table 55). The mean difference change was 2.06 (SD 5.30), 95% CI 1.09 - 3.04 p=<0.001. This mean change also reached the suggested MCID of 2 points. Of the 118 patients with complete data, 60 (51%) patients achieved an improvement >2.

Table 55– Mean CAT Scores for patients in the Leaflet group at baseline and three months (n=118).

	Leaflet Group (n=118) Mean (SD) Baseline	Leaflet Group (118) Mean (SD) Three months	p-value	(95% CI)
CAT (Health Status)	28.7 (SD 6.28)	26.6 (6.72)	<0.001	1.09 - 3.04

6.8.5 CAT Scores comparison of mean change between the CBT and Leaflet groups at three months.

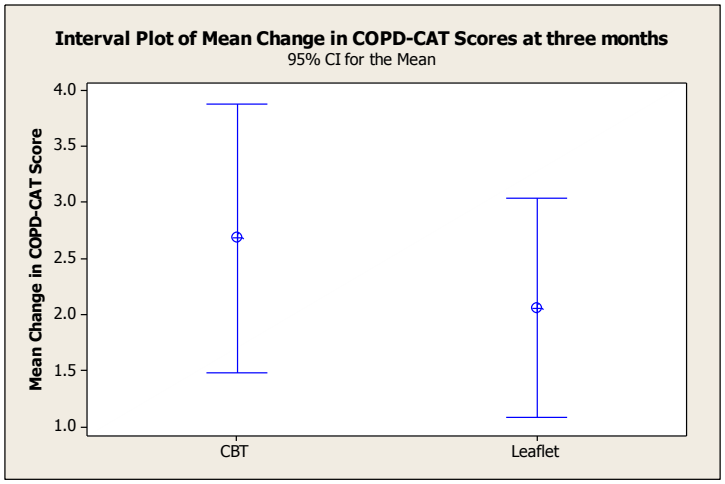
Mean change in CAT scores from baseline were 2.68 (SD 6.36) for the CBT group and 2.06 (SD 5.34) for the Leaflet group. There were no statistical differences between the two groups (Table 56). In total 120 (52%) of patients achieved the recommended minimal improvement of ≥2 or more on the CAT scale (214).

Table 56 – Mean change in CAT Scores between CBT and Leaflet groups at three months (n=229).

	CBT Group (n=111) Mean (SD)	Leaflet Group (n=118) Mean (SD)	p-value	(95% CI)
CAT (Health Status)	2.68 (6.36)	2.06 (5.34)	0.43	-0.91 – 2.16

The mean CAT scores for the two intervention groups were compared at 3 months. The data presented is restricted to those with complete date sets (completer analysis). The reported MCID of the CAT score is an improvement (fall) in scores >2. The fall seen in the CBT group was not significantly different to the leaflet arm (2.68 vs 2.06, p=0.20) (see figure 37).

Figure 37– Interval Plot of mean change in CAT Scores between the CBT and Leaflet groups three months.



However, there was a clinical improvement from baseline CAT scores in both intervention arms as per reported MCID (214).

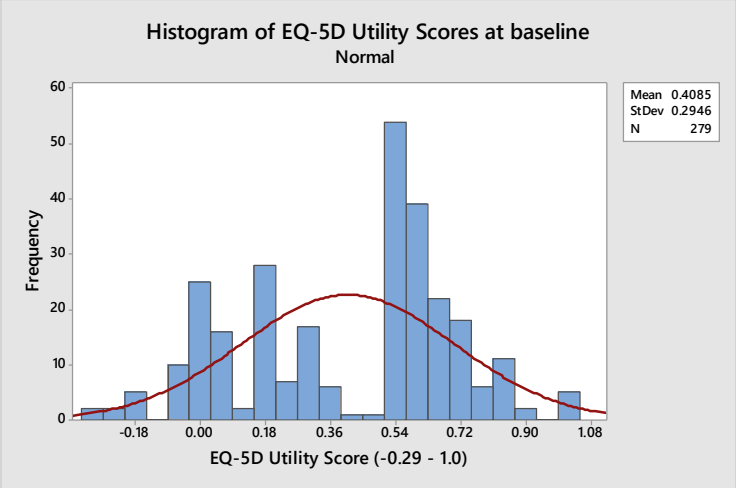
6.9 EQ-5D QOL

A secondary outcome for this study was an improvement in QOL as measured by the EQ-5D Questionnaire.

6.9.1 EQ-5D QOL Scores for 279 patients recruited at baseline

The baseline EQ-5D utility scores for 279 patients ranged from -0.29 (feeling worse than death) to 1.0 (perfect health). The distribution of the EQ-5D utility scores were not normally distributed (Figure 38). At baseline the median score was 0.52 and IQR -0.29 – 1.0.

Figure 38 – Histogram of the distribution of EQ-5D utility scores at baseline (n=279).



There was no difference between the groups for EQ-5D utility scores at baseline using paired student *t*-test (Table 57). At baseline 122 (44%) of patients rated their overall health less than 50%. Furthermore, 37 (13%) patients reported a negative value utility score representing a health state equivalent to 'worse than death' suggesting a significant impact on QOL.

Table 57 – EQ-5D utility Scores for CBT and Leaflet groups at baseline (n=279).

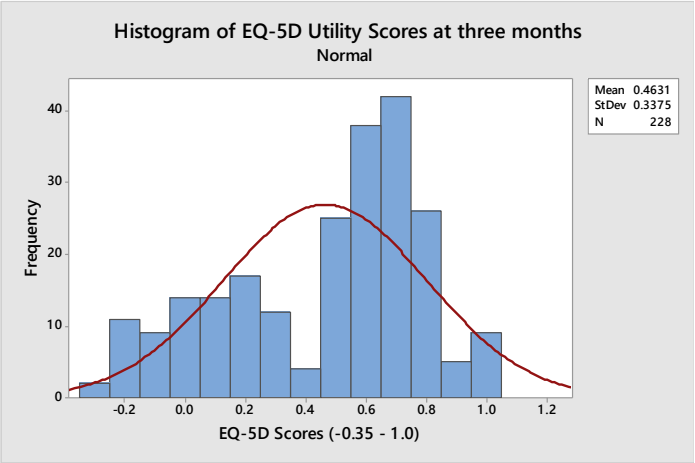
	CBT Group (n=139)	Leaflet Group (n=140)		
	Mean	Mean	p-value	(95% CI)
EQ-5D Utility Score	0.41 (SD 0.29)	0.41 (SD 0.30)	0.95	-0.072—0.067

The reported symptom burden at baseline was high. From the EQ-5D domains, 268 (97%) patients reported problems performing their usual activities. In total, 234 (84%) patients reported problems with mobility, 231 (83%) reported symptoms anxiety and/or depression and 206 (74%) reported pain/discomfort.

6.9.2 EQ-5D utility Scores for all patients at three months.

At three months data was collected on 228 patients (111 from CBT group; 117 leaflet group). The EQ-5D utility scores ranged from -0.35 to 1.0 at three months. The median score was 0.59 and IQR 0.19 -1.0. Data was not normally distributed in this cohort (Figure 39). Due to the sample size, parametric tests were used as advised by the statistician.

Figure 39 – Histogram of distribution of EQ-5D utility scores for all patients at three months (n=228).



6.9.3 EQ-5D utility scores in the CBT group at three months.

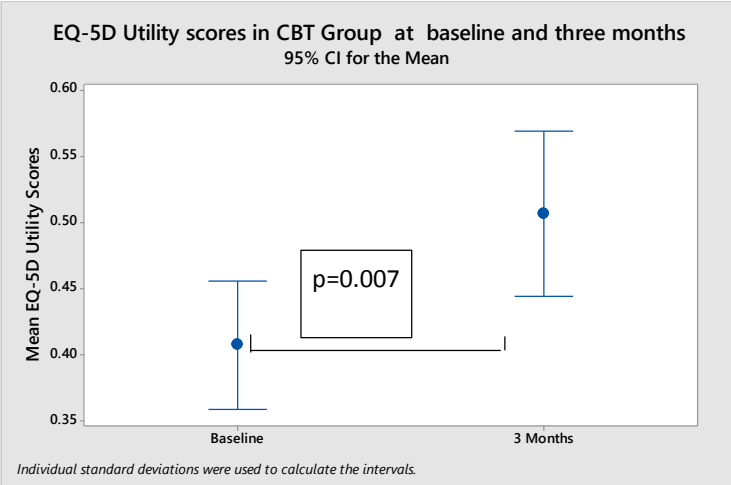
At three months complete data was available for 111 patients in the CBT group. The mean EQ-5D utility score improved from 0.43 (SD 0.28) to 0.51 (SD 0.34) reaching the MCID of ≥0.08 (224). Results are presented in table 58.

Table 58 – EQ-5D utility scores in CBT group at baseline and three months (n=111).

	CBT Group (n=111) Mean Baseline	**CBT Group (n=111) Mean Three months**	**p-value**	**(95% CI)**
EQ-5D Utility Score	0.43 (0.28)	0.51 (0.34)	0.007	-0.11 - -0.02

Figure 40 shows an interval plot of the mean change in EQ-5D utility scores from the CBT group at baseline and three months.

Figure 40 – Interval plot of EQ-5D utility scores for CBT group at baseline and three months.



The QOL measured by EQ-5D utility scores improved significantly from baseline to three months in the CBT group.

6.9.4 EQ-5D utility scores in the Leaflet group at three months.

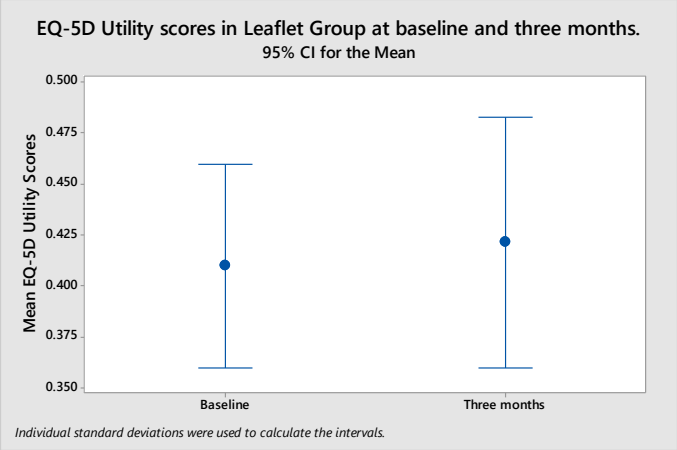
At three months complete data was available for 117 patients in the Leaflet group. The group mean EQ-5D utility scores in the Leaflet group at three months of 0.42 was unchanged at three months. Results are presented in table 59. The Leaflet group did not reach statistical significance or reach the MCID of 0.08 (224).

Table 59 - Mean change in EQ-5D utility scores in Leaflet group at baseline and three months (n=117).

	Leaflet Group (n=1117) Mean Baseline	Leaflet Group (n=117) Mean Three months	p-value	(95% CI)
EQ-5D Utility Score	0.42 (0.30)	0..42 (0.34)	0.09	-0.06 – 0.05

Figure 41 shows an interval plot of the mean change in EQ-5D utility scores from the Leaflet group from baseline and three months.

Figure 41 – Interval plot of EQ-5D utility scores for the Leaflet group at baseline and three months.



The leaflet group did not reach statistical significance or reach the MCID of ≥0.08 (224).

6.9.5 EQ-5D utility scores comparison of mean change between the groups at three months.

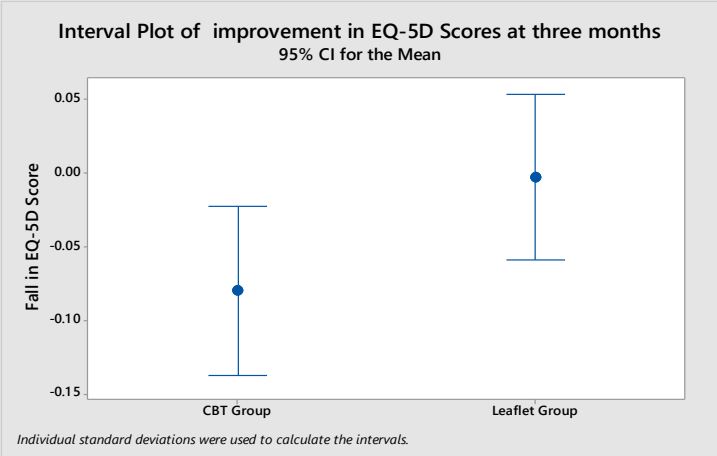
The mean change in the CBT group was -0.08 in CBT group and -0.003 in the leaflet group (Table 60).

Table 60 – Mean change in EQ-5D utility scores between CBT and Leaflet groups at three months (n=228).

	CBT Group (n=111)	Leaflet Group (n= 117)		
	Mean (SD)	Mean (SD)	p-value	(95% CI)
EQ-5D Utility Score	-0.08 (0.31)	-0.003 (0.31)	0.06	-0.16- 0.00

Figure 42 shows an interval plot of the mean change in EQ-5D utility scores from the CBT group compared to the Leaflet group at baseline and three months.

Figure 42 – Interval Plot of mean change in EQ-5D utility scores for CBT and Leaflet groups at three months.



The group mean change in EQ-5D utility scores did not reach statistical or clinical significance between the two groups at three months.

6.10 Correlation between psychological and QOL variables

Pearson product-moment correlation was used to explore the relationship among psychological variables and QOL. A summary of the results is presented in table 61.

Table 61 – Relationship between outcome measures at baseline.

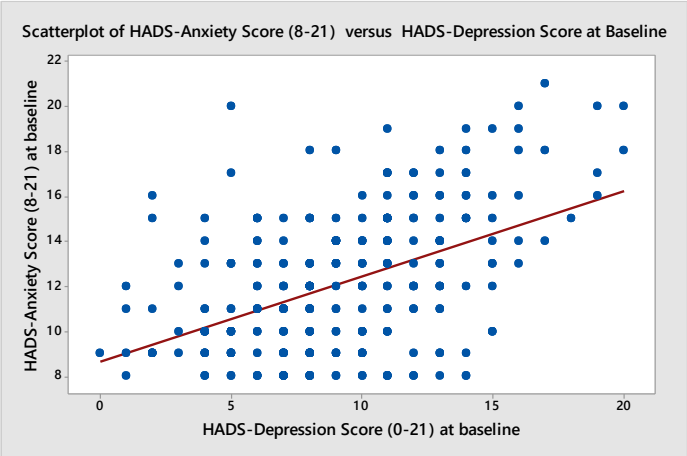
Variables	Pearson Correlation	P Value
HADS-Anxiety and HADS-Depression	0.475	<0.001
HADS-Anxiety and CAT	0.30	<0.001
HADS-Anxiety and EQ-5D utility	-0.28	<0.001
HADS-Depression and CAT	0.427	<0.001
HADS-Depression and EQ-5D utility	-0.40	<0.001
CAT and EQ-5D utility	0.42	<0.001

The results show there was a correlation between the variables tested. These will be now be presented.

6.10.1 Correlation between HADS-Anxiety and HADS-Depression Scores at baseline

There was a positive correlation between symptoms of anxiety and depression at baseline (0.475, p=<0.001) (figure 43).

Figure 43 – Scatterplot of correlation between HADS-Anxiety and HADS-Depression scores at baseline.

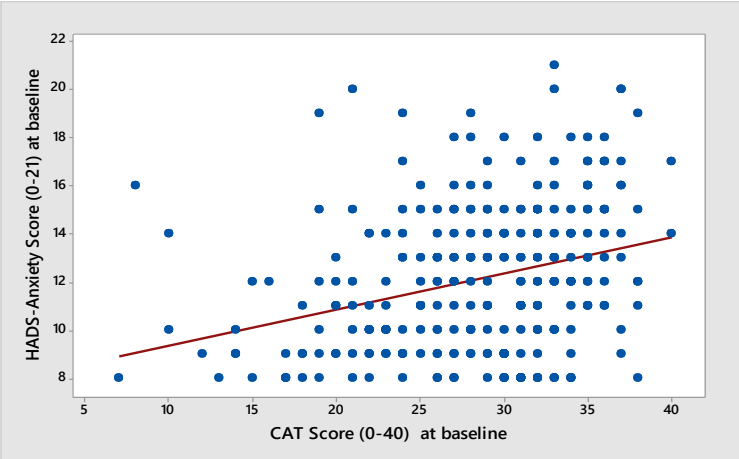


The results indicate that symptoms of depression as measured by the HADS scale increase with symptoms of anxiety.

6.10.2 Correlation between HADS-Anxiety and CAT at baseline.

There was also a positive correlation between HADS-Anxiety and CAT scores at baseline (0.30, p=<0.001) (figure 44).

Figure 44 – Scatterplot of correlation between HADS-Anxiety and CAT scores at baseline.

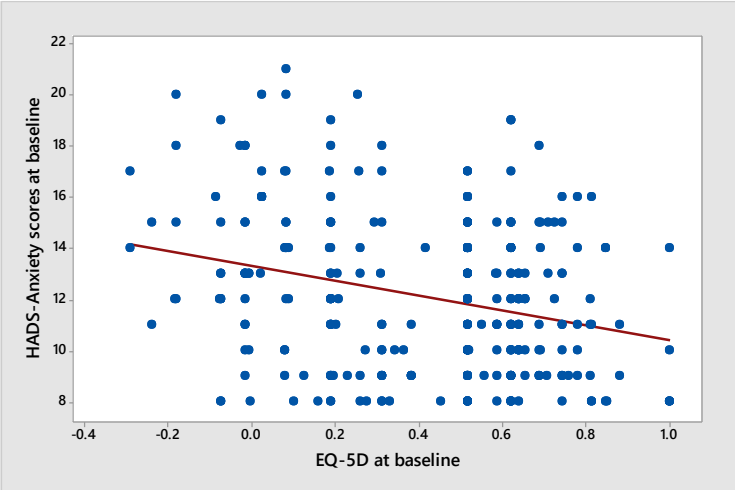


The results indicate that as increased symptoms of anxiety is associated with poorer HRQOL as measured by the CAT.

6.10.3 Correlation between HADS-Anxiety and generic QOL

There was a negative correlation between HADS-Anxiety and generic QOL as measured by the EQ-5D utility scores (-0.28, p= <0.001). This is demonstrated in figure 45.

Figure 45- Scatterplot of correlation between HADS-Anxiety and EQ-5D utility scores at baseline.

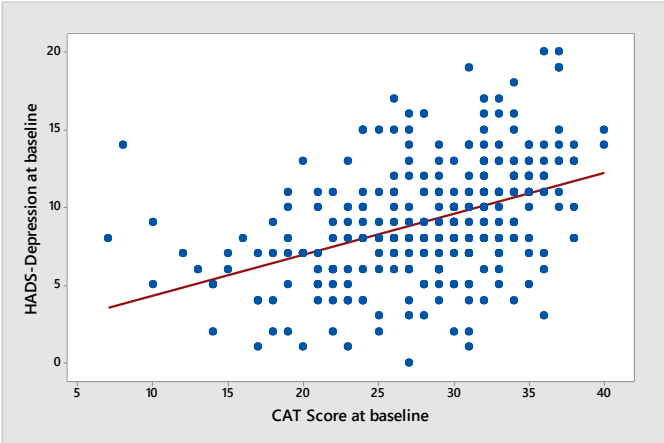


The results indicate that as symptoms of anxiety decrease, QOL as measured by the EQ-5D utility score improves.

6.10.4 Correlation between HADS-Depression and CAT at baseline.

As seen in figure 46, there was a positive correlation between HADS-Depression scores and HRQOL as measured by the CAT at baseline (0.427, p=<0.001).

Figure 46 – Scatterplot of correlation between HADS-Depression and CAT scores at baseline.

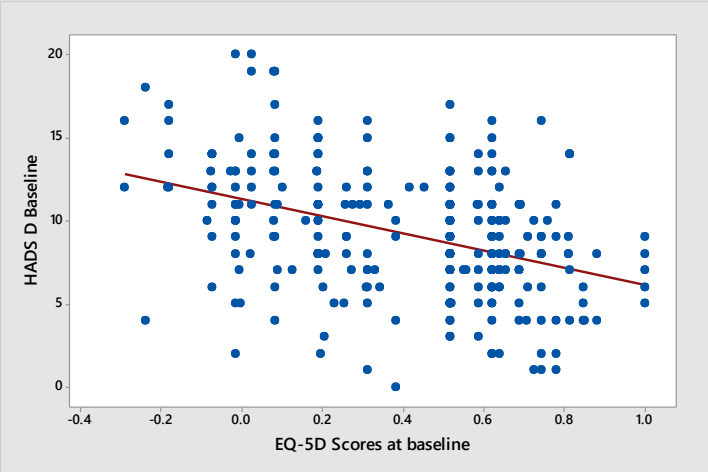


The results indicate that increased symptoms of depression is associated with poorer HRQOL as measured by the CAT.

6.10.5 Correlation between HADS-Depression and EQ-5D utility scores at baseline.

There was a negative correlation between HADS-depression at baseline and generic QOL as measured by the EQ-5D utility scores at baseline (Figure 47).

Figure 47 – Scatterplot of correlation between HADS-Depression and EQ-5D utility scores at baseline.

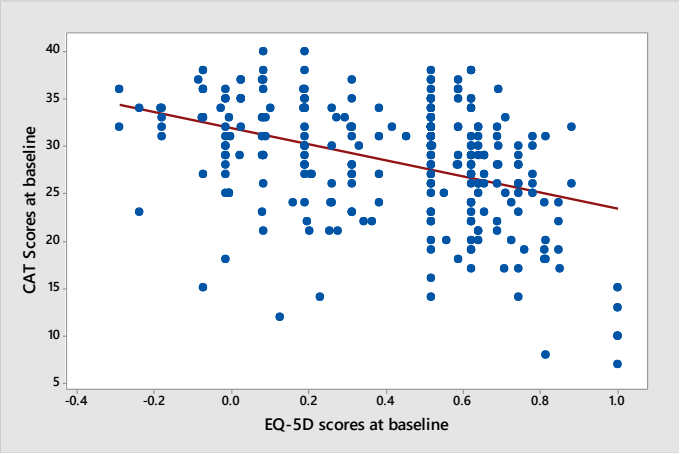


The results suggest that symptoms of depression is associated with poor generic QOL as measured by the EQ-5D utility scores.

6.10.6 Correlation between CAT and EQ-5D utility scores at baseline

There was a negative correlation between HRQOL measured by the CAT and generic QOL measured by the EQ-5D utility scores (0.42, p=<0.001) as seen in figure 48.

Figure 48- Scatterplot of correlation between CAT and EQ-5D utility scores at baseline.



The results indicate that poor HRQOL measured by the CAT scores is associated with poor generic QOL measured by the EQ-5D utility scores.

6.11 Nurse Training

From the 129 patients who received CBT, 93 patients were seen by nurses with Diploma level training. A breakdown of the number of patients seen depending on CBT level of training can be seen in table 62.

Table 62- Breakdown of number of patients seen, mean age and number of sessions delivered depending on level of training.

Training	Number of patients/ (percent)	Mean age	Mean number of sessions
Diploma	93 (72)	65	3.6
Foundation	36 (28)	65	4.0

6.11.1 Results from video validation

Twenty two CBT sessions were video recorded and assessed to evaluate adherence to the Lung Manual and competency delivering the CBT. The modified CFARS rating scale was used. The scoring system for the ten items range from zero (poor skills and competency) to 6 (high level of skill and competency). Nurses with Diploma level training would be expected to achieve high scores to gain their qualification. The average competency scores for the 10 items can be seen in table 63.

Table 63 – Average competency scores for CFARS rating scale.

Competency	Average Score (scale 0-6)
Focus/structure	5
Pacing	4.4
Feedback/summaries	4.5
Integration of CBT	4
Collaborative relationship	4.5
Guided discovery	4.4
Interpersonal effectiveness	4.3
Elicit key components	4.4
Application of appropriate change techniques	4.2
Closure	4.3

The nurses scored highly on focus/structure, therapeutic relationship and feedback/summaries. Scoring four or above is certainly an acceptable level of skills and expertise. A summary of the individual scores can be found in table 64.

Table 64 – Summary of individual scores from video validation.

Focus/ Structure	Pacing	summaries	Integration CBT	relationship	Guided discovery	Interpersonal effect	Elicit key components	Change techniques	Closure
4	4.5	4.5	4.5	5	4.5	5.5	4.5	*4*	4
4	3.5	3.5	4	4	4.5	5	4	*4.5*	4.5
5	5	5.5	5	5.5	5	6	5	*5*	5.5
5.5	5.5	5	5	5.5	5.5	6	5.5	*6*	5
5	5	5	5	5	4.5	5.5	5.5	*4.5*	4
5	5	5	5	5	5	5	5	*4*	4
5	4	6	5	5	5	6	5	*5*	5
5.5	5.5	5.5	6	5.5	5.5	5.5	5.5	*5*	5
5.5	4.5	5.5	5	4.5	5.5	5.5	5.5	*5.5*	5.5
5	4	6	5	5	5	6	5	*5*	5
5	4.5	5.5	5.5	5.5	5	5.5	5	*5.5*	5.5
4.5	4	4	4.5	4	4.5	4.5	3.5	*4.5*	4.5
5	5	5.5	5.5	5	5	5	5	*4.5*	5
4.5	4	4	4	4.5	3.5	5	4	*3.5*	3.5
4	5	5	4.5	5	4.5	5.5	4	*5*	4.5
4	4.5	5	4.5	4.5	5	5	5	*4.5*	4
3.5	3.5	4	4	4	3	4	3.5	*3*	3.5
2	2.5	3	3	2.5	2.5	3.5	2.5	*3*	3
4	3	3.5	3.5	3.5	3.5	3.5	3.5	**3**	4
2.5	2	2.5	3	2.5	2.5	3.5	3.5	**2.5**	3.5
2	2	2	3	2.5	2	3.5	2	**1.5**	2
3.5	3.5	3.5	4.5	4	3.5	5	5	**2.5**	4

6.11.2 Effectiveness of the CBT intervention for Diploma and Foundation Level Training

A secondary outcome for this study was to explore the effectiveness of the CBT intervention when delivered by nurses with post-graduate diploma and foundation level training (consisting of 3.5 days training) plus clinical supervision. Descriptive results are presented here as the study was not powered to conduct a comparative analysis (Table 65).

Table 65- Summary of outcome from nurses delivering the CBT intervention.

Level of Training	Number of patients/(percent)	Mean HADS-Anxiety/SD at baseline	Mean HADS-Anxiety at Three months	Mean Difference at three months	p-value	(95% CI)
Diploma level	83 (72)	12.3 (3.11)	8.93 (4.36)	3.37	<0.001	2.43 - 4.34
Foundation level	32 (28)	12.2 (3.26)	8.8 (4.92)	3.41	<0.001	2.05 - 4.76

The mean number of CBT sessions was similar between the nurses in the diploma level training group (3.62, median 3 and IQR 2-5 for diploma level training) compared to foundation level training (3.98, median 3, IQR 5). The mean severity of COPD, HADS-Anxiety scores and number of CBT sessions was not discernably different between the diploma and foundation level. Given the prior definition of a MCID in HADS-Anxiety score a definition of a responder can be made. If a responder to an intervention was defined as a change in HADS domain of ≥1.5 then an analysis of characteristics or responders to CBT treatment compared to those who did not respond to CBT delivered by nurses with Diploma level training. Table 66 shows a comparison of responders to non responders in the CBT group for diploma level nurses.

Table 66 – Comparison of responders (HADS-Anxiety scores falling by ≥1.5) and non-responders from Diploma Level Nurses.

Variable	Responders (n=45) Mean (SD)	Non-responders (n=38) Mean (SD)	p-value	95% CI
Age	68.1 (8.28)	63(11.0)	0.02	0.84 – 9.50
FEV_1	1.16 (0.68)	1.30 (0.54)	0.32	-0.40 – 0.13
HADS-Anxiety	12.9 (2.91)	11.6 (3.22)	0.05	0.002 – 2.71
HADS-Depression	9.29 (3.47)	10.0 (4.28)	0.88	-1.63 – 1.89
CAT	27.4 (6.32)	29.2 (5.95)	0.20	-4.45 – 0.92
EQ-5D Utility	0.47 (0.27)	0.39 (0.28)	0.15	-0.03 – 0.21

Table 67 presents a comparison of responders to CBT treatment compared to those who did not for nurses with Foundation level training.

Table 67 – Comparison of responders (HADS-Anxiety scores falling by HADS ≥1.5) and non-responders for foundation level nurses.

Variable	Responders (n=22) Mean (SD)	Non-responders (n10) Mean (SD)	p-value	95% CI
Age	68.1 (9.60)	60.1(10.0)	0.05	0.05 – 16.03
FEV_1	1.13 (0.46)	1.17 (0.46)	0.79	-0.42 – 0.32
HADS-Anxiety	11.8 (2.94))	13.1.(3.87)	0.35	-4.30 – 1.64
HADS-Depression	8.0 (3.66)	11.4 (5.02)	0.08	-7.22 – 0.42
CAT	26.1 (7.19)	8.4 (7.44)	0.43	-8.22 – 3.69
EQ-5D Utility	0.47 (0.29)	0.24 (0.30)	0.06	-0.12 – 0.46

6.12 Patient Feedback

When data was collected at three months, patients were asked if they had read the written information leaflets provided. In total 30 (22%) of patients reported that they did not read the information provided. Table 68 below shows patient responses regarding reading written information provided.

Table 68 – Patient responses on reading written information.

	No of patients/(percent)	**Number of patients/(percent)**	**Number of patients/(percent)**
	Not read	**Part-read**	**Answer not provided**
CBT Group	18 (14)	56 (44%)	17 (13)
Leaflet Group	12 (9)	49 (35)	19 (14)

Patients were asked if they would like to provide feedback about their experience participating in the study. The comments provided have been formulated into positive comments and negative comments.

Positive Comments

Leaflet helped with cutting back on smoking and changing my lifestyle to lose weight.
Help with breathing techniques was particularly useful.
Breathing sections helpful. Exercise part not helpful.
Very helpful - some exercises were challenging.
Learning about breathing control using the elephant exercise to control my breathing very helpful.
Information was good but I find it hard to concentrate. I feel very forgetful and tired all the time.
Found the leaflet very good - helped to deal with anxiety.
I think the information is OK. Will read again.
The information was thorough, adequate good information. Incorporating lots of information.
Straight forward. Use questions, take time. Excellent. Distraction very good. I read it weekly.
Extremely helpful - nurse was excellent, informative.
Read all of the leaflet - found it very helpful. Support was very good.
Mostly helpful, recognised I had a problem.
Information was useful - you don't realise that many people feel like you.
Leaflet has given me a better understanding of my condition and a different way of dealing

with anxious situation, which I found helpful.

One to one sessions were more helpful.

Information very good. Answered all my questions. I regularly look at the leaflets - marvelous.

Handy - explains thing you don't know anything about.

Improved my knowledge and increase my understanding of how I felt.

Enlightening.

Helpful.

Ideas about coping were helpful.

Information gives you an insight into your condition.

A little bit helpful.

Really good.

Quite good - found that questions were answered in a simplistic way.

Reading booklets took me back when I had stress and anxiety when I was younger.

Throws light on things to do. Pretty informative - how to overcome little things and calm down.

Helped cope better with panic attacks and manage with breathing exercises.

Very helpful- easy to read and take in.

Best to be worked through with someone else - without guidance I think it might be potentially dangerous.

Most of it was concerned with what I am already doing. I found a positive benefit from talking to the nurse.

Relaxation helps a lot.

Absolutely brilliant - makes a big difference to life.

Leaflet was good for anxiety.

Very very helpful and good. Makes you think twice.

Please with information. Lots of explanation of things I didn't understand. Very helpful indeed. My son also found it helpful.

Helpful with panic attacks. Made them better. Not as bad now.

I have tried to do what it says in the book. Sometimes it seems to work, sometimes it takes longer.

I found the information helpful- explained everything I needed to know.

I feel benefit from talking in the Chest Clinic.

Good idea to have the study - really appreciate the opportunity. Very good to look at the whole person.

Found techniques helpful.

Panic leaflet most helpful.

Good made me think about pacing my activities prior to carrying them out.

Really helpful - I've have the booklets to look at again if needed.

Supports lots of strategies which work well.

Quite helpful- common sense.

Helpful - showed how to control breathing.

Good reading about using distraction.

Brilliant study- helpful to my care. Using booklets during a current exacerbation.

Feel like I have improved 100%. I'm getting out and about due to the information and support.

A lot didn't apply to me but I found the list making very helpful – even if it is a simple task.

It's a good thing - good to know I'm not by myself.

Felt it was really helpful especially when experiencing night time panic attacks.

Definitely helpful - good to talk. Everything was excellent. Put me at ease.

Some information was given in the rehab class such as using distraction.

Found information from the study extremely helpful. I have been able to use certain strategies to help manage breathlessness.

I learnt how to cope with panic attacks - very helpful. Big help- helped a lot.

Information was quite useful. I was made aware of things I wasn't told about to manage and what symptoms to look for.

Certainly beneficial, positive thoughts and coping strategies, able to more readily accept my condition and prognosis.

Very improved with the written information.

Yes - I knew a lot about panic attacks and anxiety as I have had depression and have agoraphobia.

Helps with breathing by using distraction.

Useful- I keep going back to the information. I'm getting the hang of it. It's helpful thinking more of why problems occur and questioning yourself.

Negative Comments

Couldn't see how leaflet would help.

Panic leaflet wasn't helpful. I thought it apply to those who have had a stroke.

Learning about pacing myself was more helpful than the leaflet.

Helped at first but lost interest in it - lost interest in everything.

I was unable to read information and someone had to go through it with me.

Cannot see very well so had difficulties reading information.

Made me feel depressed.

Fine - helpful in some ways. Difficult getting time to read them.

I was hoping to have CBT in the study.

No - not useful.

Can't remember if useful. Feels more accepting of condition now that there is nothing he can do to get better and that COPD is a chronic condition. I would prefer more effective treatment for my physical symptoms rather than CBT.

It's not made any difference.

Same as I already knew.

Haven't had time to read them.

I need help with reading and writing – haven't been through it with anyone yet.

Didn't feel I could use the strategies - feel very anxious all of the time.

Not helpful at all- didn't apply to me.

A little bit helpful. Kept forgetting after I read things.

It was complicated.

6.13 Summary

The findings from this study result from an exploration of data from the population screened and recruited for this RCT. From 1518 patients screened, 898 (59%) reported symptoms of anxiety and 667 (44%) reported symptoms of depression. A total of 279 patients were recruited. The groups were well matched at baseline. The mean age was 66.5 so the cohort were relatively young (range 41 – 88). In total 57 % of patients had severe or very severe COPD indicating significant lung disease. The population as a whole had few formal educational qualifications and nearly 50% of patients had to retire early due to ill health. The baseline HADS-Anxiety scores was from patients recruited was 12.1 suggesting significant symptoms. From the cohort a large number of patients recruited also reported symptoms of depression with 186 (67%) compounding their psychological difficulties. At baseline the mean HADS-Depression scores were 9.2 (SD 3.9). Whilst the baseline scores for depression were lower than anxiety scores, they were still in the abnormal range.

The primary outcome for this study was a change in group mean HADS-Anxiety scores at three months. As recommended in the literature, the clinically meaningful reduction is defined as of ≥1.5 points on the HADS-Anxiety scale. There was a significant reduction in HADS-anxiety scores in both groups from baseline at three months: CBT group mean change 3.4 (SD 4.20) p=<0.001 CI 2.62- 4.17 and leaflet group mean change 1.9 (SD 3.80) p= <0.001 CI 1.19 - 2.55. The reduction was more marked in the CBT group with a mean change of 1.52 p =0.004 CI 0.50 – 2.55. There was a significant reduction in HADS-depression scores in both groups at three months: CBT group mean change 2.20 (SD 3.62) p=<001 CI 1.53 – 2.87 and leaflet group mean change 1.07 (SD 3.55) p=0.001 CI 0.44 – 1.71. The CBT group reached the MCID reduction of 1.5 at three months but the leaflet group did not.

There was a significant reduction in the group mean change in the CAT scores from baseline in both groups : CBT group mean change 2.68 (SD 6.36) p=< 0.001 CI 1.49 – 3.88 and leaflets group mean change 2.06 (SD 5.34 p=<0.001 CI 1.09 – 3.04 but no difference between the groups at three months (p =0.43 CI -0.161 – 0.00). There was a significant reduction in the group mean change in the EQ-5D utility scores from baseline in the CBT group: mean change improvement 0.08 (0.31) p=0.007 CI -0.14 - -0.02 and leaflet group mean change -0.003 (SD 0.31) p= 0.09 CI -0.06 – 0.05) but no difference between the groups at three months (p =0.06 CI -0.161 – 0.00). The CBT reached the MCID of 0.08 but the Leaflet group did not. There was no correlation between FEV_1 for symptoms of anxiety or depression but positive correlations were found between HADS-anxiety and HADS-Depression, HADS-Anxiety and the CAT, HADS-Depression and CAT and the CAT and EQ-5D utility scores. Negative correlations were found between HADS-Anxiety and EQ-5D utility scores and HADS-Depression and EQ-5D utility scores.

This was a pragmatic trial which included patients with all severities of COPD and ages. This study has identified that symptoms of anxiety are highly prevalent in COPD patients in this cohort from the North East of England. Both self-help leaflets and Respiratory nurses delivered CBT based intervention significantly reduced symptoms of anxiety and depression. The CBT intervention achieved clinically and significantly better reductions in HADS-Anxiety, HADS-Depression, CAT and EQ-5D utility scores at 3 months. The Leaflet group achieved a significantly significant reduction in HADS-Anxiety and CAT scores at three months but did

reach the clinical or statistically important improvements in the HADS-Depression and EQ-5D utility scores. Overall the CBT intervention was superior to the Leaflet intervention.

Chapter 7 – Discussion

7.1 Introduction

This thesis began with an introduction to COPD and the psychological impact of the disease. There seems to be an overwhelming consensus that the prevalence of anxiety and depression is a significant problem for patients with COPD but given the scale of the problem, limited attempts have been made to address symptoms of anxiety and depression in the COPD population. Breathlessness has physical and psychological causes and patients have entirely appropriate fears about their breathing difficulties. There is no doubt that patients may have a life threatening illness and may have realistic negative thoughts about dying from their COPD. However, anxiety can play a massive role in fueling fears of dying when perhaps this is not imminent. Patients often do not see the link between anxiety and breathlessness. Psychological therapies such as CBT are effective interventions for the treatment of anxiety and depression in the general population but there was limited evidence for the use in patients with COPD.

Several researchers have tried to evaluate the effectiveness of treatments to manage anxiety and depression in the COPD population. A criticism of previous research is that a number of methodological problems have been identified. Firstly, a significant problem with studies on CBT in COPD is the low sample sizes, lack of power calculation or failing to recruit enough patients required. Secondly, most studies have a serious weakness of investigating the use of CBT in patients who were not anxious at baseline. Patients without symptoms of anxiety are unlikely to need any psychological intervention unless the study is to prevent symptoms developing.

Thirdly, the possibility of bias was also highlighted. The quality and methods of randomisation were poorly reported raising the possibility of selection bias. As with all complex interventions it is difficult to blind participants. However, steps can be taken to minimise bias by ensuring outcome measures are collected by individuals blinded to the allocated treatment. Previous studies appear to have a high risk of bias as many of the studies did not report blinding for outcome measurements.

Another significant problem identified in the literature was the number of outcome measures used. One study acknowledged the measures were defective and yielded variable results making it difficult to draw conclusion from the small sample (154). Existing research fails to answer the important question as to the effectiveness of CBT in the COPD population. The conclusion of all of the studies and systematic reviews published so far recommend a high quality and significantly powered randomised controlled trial.

This research was developed to build upon the current evidence for CBT in COPD and a RCT was considered the most appropriate method to test the research hypothesis. The objective of this study was to develop an appropriately designed high quality RCT and address the impact, feasibility and efficacy of teaching CBT skills to non-mental health professionals (such as respiratory nurses), to treat anxiety and depression in a clinical population of COPD patients. This study is the first to use respiratory nurses who have skills in respiratory disease and training in psychological skills such as CBT. Respiratory nurses are at the front line caring for patients with COPD and are well placed to provide holistic care for COPD patients. The Newcastle COPD CBT CARE Study presented in this thesis was an ambitious trial as it is the biggest study ever to be undertaken in COPD patients with symptoms of anxiety. The intervention used in this study has developed over many years and had been evaluated before embarking on this RCT.

A large number of patients attending secondary care clinics were screened for suitability for the study and a considerable number reported symptoms of anxiety. The prevalence of anxiety in this cohort was 59%, which is significantly higher than the prevalence of 36% quoted in the systematic review by Yohannes et al (225). It had been suggested that there may be a dose-response relationship between illness severity and symptoms of anxiety and depression but this was not found to be the case in this study. No relationship was found between lung function and psychological symptoms. It is clear that the impact on patients' lives from COPD is extensive. From 279 patients recruited a total of 268 (96%) patients reported problems performing usual activities. Importantly 231 (83%) reported comorbid symptoms of anxiety and depression and 206 (74%) reported pain or discomfort on the EQ-5D Questionnaire. Neither of these symptoms are commonly addressed in clinical practice.

The results of this study have demonstrated that CBT is effective for patients with COPD. Clinical and statistically significant results were found for:

- Symptoms of anxiety (HADS-Anxiety) (p=<0.001)
- Symptoms of depression (HADS-Depression) (p=0.001)
- Health related QOL (CAT) (p=0.001)
- Generic QOL (EQ-5D utility scores) (p=0.007)

Whilst this is an important result, it is also prudent to consider that 60% of patients in the CBT group improved >1.5 on the HADS-Anxiety Scale reaching the MCID. Patients who responded were older (p= 0.002) and had a significantly higher score on the EQ-5D utility scores suggesting better QOL (p= 0.02). The mean number of sessions of CBT required in this study was four confirming that this brief intervention is not only clinically effective but potentially is cost effective. Further analysis of the 12 month data is required to establish the cost effectiveness of the intervention. An important finding was that no difference was identified between CBT delivered by nurses with diploma or foundation level training.

Whilst the CBT intervention was superior to the self- help leaflets, the results of the study have shown that the self-help leaflets were also effective. Clinical and statistical significance was achieved for:

- Symptoms of anxiety (HADS-Anxiety) (p=0.004)
- Health related QOL (CAT) (p=0.001)

In the leaflet group 53% of patients improved >1.5 on the HADS-Anxiety scale achieving the MCID quoted by Puhan (122).

It is interesting that there was no correlation between HADS-Anxiety or Depression scores and lung function in this study. Females in the CBT group improved significantly from baseline and the results were significantly better than the Leaflet group. One possible explanation for this is that females are happy to talk about their difficulties and responded well to the one to one intervention.

7.2 Trial Design

The study design was very important to ensure this research was credible and would be useful and acceptable to be used in clinical practice. One of the key issues in the design of RCTs

is the choice of intervention. As a criticism of many trials is that the design is inappropriate, it was important to consider the options carefully. In addition to recommendations from previous researchers, patients, carers, the NIHR RDS and experienced researchers were all consulted in the planning phase and this was time well spent. A critical area considered in the design of this study was an appropriate control group. Many studies use 'standard or usual care' as the control group. Generally, psychological screening for symptoms of anxiety and depression is not conducted as routine practice in respiratory clinics. The team did not feel it was appropriate to offer 'less' than our 'usual care'.

For pragmatic reasons two active arms were agreed (CBT with self-help leaflets and self-help leaflets alone) to take into account current 'standard care' with the Trust. The rationale behind these two arms was complex. Firstly, it would be unethical to withhold 'standard practice' from patients attending Newcastle upon Tyne Hospital Trust Respiratory Clinics. Secondly, patients are likely to deteriorate physically during the study and self-help leaflets may well be effective in reducing symptoms of anxiety and depression. Another important consideration was if CBT would be delivered individually or in groups. Previous research into psychological interventions into CBT in COPD have used either group or individual CBT. Like many interventions it would be more cost effective to provide group CBT. Local experience within Newcastle Hospitals and patient feedback suggested patients would prefer individual CBT sessions. Discussing intimate feelings about the impact of COPD can be embarrassing for patients. More recently studies have used self-help manuals for patients which may also be a useful method of providing CBT in the future.

It was noted that some patients dropped out of the study once they had been randomised to the Leaflet arm and preceded to request CBT. In this study it is feasible that self-help leaflets could be seen as inferior to patients and indeed clinicians. One clinician requested that a patient in the Leaflet arm was withdrawn as the patient's health was deteriorating and he requested CBT.

7.3 Setting

In non-pharmacological studies it is important that the description of the setting in which participants treatment is provided to help readers appraise the risk for bias and the applicability of the results (173). Evidence suggests that patient outcome can be associated with

hospital and care providers' volume (226). For this study there were high volumes of patients with COPD who had symptoms of anxiety. Non-pharmacological treatment such as CBT might be found to be safe and effective in an RCT performed in high-volume center's by high volume care providers and this could mean that different results could be obtained in low volume center's (173).

Many patients with a diagnosis of COPD are managed within primary care rather than attending secondary care clinics. A major limitation of the recruitment strategy for this study is the exclusion of patients with COPD from primary care. Including patients from primary care would have increased access to patients who may have less physical disability but as the results of this study suggest, may have significant comorbid anxiety and/or depression. Such patients may be more willing to participate in a study of this kind.

7.4 Attempts to reduce bias

In this study every effort was made to reduce bias. A computer generated program randomised the intervention and allocation concealment was maintained. It was not possible to blind participants and this may introduce bias and influence the research. However, to minimise the risk of further bias the staff collecting outcome data were blinded to the treatment allocation. Analysis was undertaken using data from all patients who completed follow up at the primary outcome for this PhD but an intention to treat analysis for the longitudinal follow up data once all of the data is collected is planned.

7.5 Primary outcome measures for anxiety and depression.

Choosing a primary endpoint is an important decision to make and should be based on the main objective of the study (227). In an excellent article on the art of choosing sound study endpoints, Hanson suggests that it is of particular importance that the primary endpoint can be measured with a valid, reliable, and responsive instrument (227). The study team agreed that anxiety was a significant and frightening problem for breathless patients with COPD and this was chosen as the primary outcome for the study. Careful consideration was given to the most appropriate outcome measure for this study. The advantages and disadvantages of using each measure was discussed with the research team. For the measurement of anxiety and depression Dr. Chris Baker, Consultant Clinical Psychologist was consulted.

The HADS questionnaire was chosen for several reasons. Firstly, the HADS questionnaire had been used extensively with the Respiratory Clinics and staff were familiar with their use. Secondly, the HADS questionnaire had been used most in previous studies and was recommended for future research. Thirdly, the HADS questionnaire had been validated in the COPD populations and therefore was considered the most appropriate questionnaire to collect outcome data {Dowson, 2001 #1929}. Finally, the HADS questionnaire only has 14 items and only takes a few minutes to complete. This was an important consideration for elderly COPD patients. However, classifying patients as being 'anxious or depressed' with the HADS questionnaire is controversial and users should be mindful that the HADS questionnaire is a screening tool and should not be used to imply a clinical diagnosis of anxiety or depression. The use of self-report outcome measures has also been debated.

7.6 Severity of Lung Function

Most COPD studies do classify COPD entry on FEV_1/FVC ratio of ≤70 but this excludes potentially eligible people who may fulfil all other entry criteria. Several patients in this study were identified with a diagnosis of COPD but the FEV_1/FVC ratio was above 70% so were excluded. It could be argued that the diagnosis of COPD is questionable in such patients, however, there are a minority of patients who have a well preserved FEV_1/FVC ratio but have severe emphysema on lung function testing. Melek and Norris suggested that it is likely that some patients with more severe chronic medical disease will become depressed or anxious (79). It does seem intuitive to think that anxiety would be more prevalent in patients with severe lung disease. Interestingly, in this study there was no correlation between anxiety and depression and lung function. This suggests that patients may have mild airway obstruction and severe symptoms of anxiety and/or depression. Conversely, there are some patients with severe airway obstruction who experience low symptoms of anxiety and/or depression.

7.7 Ethnic Group

All of the patients recruited were white British. From the patients screened there was only one patient from an ethnic minority group and they declined to participate in the study. This may be unusual to other areas in the country. As a result it might be argued that CBT works in a particular cultural group.

7.8 CBT Intervention

CBT continues to evolve and is full of controversies (127). CBT is one of the most extensively researched forms of psychotherapy extending to a wide range of psychological problems. Indeed, a simple search in Medline in August 2015 found 886 randomised controlled trials of CBT. A comprehensive review of 16 meta-analysis of CBT was undertaken in 2006 (228). The review concluded that CBT is effective for anxiety and depression and there appears to be robust evidence that the benefits are maintained beyond the cessation of treatments and indeed relapse rates are half those of pharmacotherapy (228). On the whole it is generally agreed that the evidence does support CBT for a number of psychological problems.

CBT is recommended by NICE for the treatment of many psychological problems including anxiety, panic and depression (125). There have been several criticisms of the NICE Guidelines. Firstly, it has been suggested that NICE supports 'the medical model' of mental health which promotes diagnoses or specific disease entities (184). As a result it is suggested that the guidelines ignore the 'biopsychosocial model of mental health' (which is well established in psychiatric training) (184). Instead, it is argued that repeated comparisons with drugs imply a notion of a disease entity that can be corrected by the right combination of pharmacological or psychological ingredients (184). Another pertinent point raised is the notion that patients studied in formal trials that inform guidelines are quite different from those seen in real life settings (184). The research undertaken for this PhD was a pragmatic trial and in contrary to Mollon's conclusions, patients included in this study were 'real-life' patients, many from socially deprived areas in the North East of England.

On a positive note it has been suggested that CBT is an efficient therapy that is relatively easy to learn and deliver and produces good results in many instances (229). In addition, CBT researchers have set standards in detailed description of their methods ("manualisation"), monitoring of adherence (e.g. video recording sessions), and tailoring treatments to specific disorders (229). However, despite this, CBT has been criticised for its simplistic 'cookbook' approach to therapy (127). Whilst CBT can appear to be mechanistic, it is similar to the medical model of patient care. A diagnosis is sought and treatment is given. The medical model has been beneficial in one sense, it has forced psychotherapies to strive for scientific credibility and conduct RCTs to establish the worth of their therapies. In contrast, it

could be argued that psychotherapy is essentially concerned with people, not conditions or disorder, and its methods arise out of an intimate relationship between two people that cannot easily be reduced to a set of prescribed techniques (229).

Another key component of CBT is the role of 'unhelpful cognitions'. It has also been questioned that CBT techniques aimed at tackling 'negative cognitions', such as those found in depression, require mindful techniques such as meditation to help patients divorce themselves from their emotional pain (230). The theory behind this is that it may be helpful for patients to learn to tolerate and accept thoughts rather than challenging or changing negative thoughts. As a result of this criticism, mindfulness based CBT has evolved. These claims could be contested as a key intervention for depression is behavioural activation rather than addressing cognitions. There is also uncertainty about the long term course of psychiatric illness and whether CBT is effective in this area. Problems such as depression are increasingly seen as a relapsing chronic illness and without long term comparative follow up studies it is argued that further research into the effectiveness of all therapies is needed (229). An interesting point highlighted in the literature is that unlike psychoanalytic psychotherapy which is a compliance neutral therapy, CBT is particularly dependent on compliance (231). However, many interventions rely on compliance, particularly pharmacological interventions. Indeed, an inhaler will not be effective is it is not taken.

It is of course right and proper that patients have the best treatment. To achieve this, It is vital that CBT proponents and critics work together to establish the most effective treatment for patients emotional distress. As suggested by the MRC it is paramount that an emphasis is placed on active ingredients which help address the patient's needs, and identify the skills needed to deliver them (229). From the literature identified in this review it is apparent that interventions such as CBT are complex. Previous research has stressed the importance of developing a clearly defined intervention's from existing models (e.g. panic) and report in a way that encourages replication studies (129). Whilst it could be argued that few interventions are 'simple' some interventions are obviously more complex than others.

A number of dimensions add to the complexity of CBT interventions including the number and difficulty of behaviours required by those delivering the intervention or receiving the intervention, number and variability of outcomes, number of groups or organisational levels

targeted by the intervention and the degree of flexibility or tailoring the intervention to the patient's individual needs (172). In addition, extra problems relate to the difficulty of standardising the design and delivery of the interventions, their sensitivity to features of the local context and culture. The development, evaluation and implementation of complex interventions are important areas to consider and all stages are important. Without adequate development and piloting work, or proper consideration of the practical issues of implementation, weaker interventions will be developed that are harder to evaluate and less likely to be implemented (172).

The complex intervention used in this study was based on the theoretical underpinnings of CBT and guided self-help. CBT techniques were used to specifically target breathlessness which may result from COPD, anxiety or panic. The CBT treatment programme for COPD patients was developed and refined over several years. The refinement of the treatment enabled teething problems to be addressed along the way and this may have contributed to the positive impact of the intervention in this study. Lack of impact of other studies may merely reflect teething problems rather than genuine ineffectiveness of the intervention (172). A key question in evaluating complex interventions such as CBT is about practical effectiveness (172). Practical assessment of non-pharmacological treatments in RCTs presents special difficulties because of the complexity of the treatment (172). It is important to provide a detailed description of non-pharmacological treatments used in a study.

This trial is one of the few trials that have provided sufficient detail of the CBT intervention provided. Future studies could incorporate the Behavioural Change Taxonomy to standardise the reporting of interventions in trials (174). The CBT intervention used in this study has been shown to be effective. However, what is not known is which interventions are the most effective.

A question that has not been addressed in this study is if patients will require further treatment. It is conceivable that some patients will benefit from booster or repeat sessions of CBT, similar to pulmonary rehabilitation. This question should be addressed in future research. Finally, maintaining the efficacy of an evidence based CBT intervention as it transfers from the research context into 'routine care' is not an easy process (186). RCTs dedicate

time and resources ensuring that nurses demonstrate competence and adhere to the treatment manual for which they have been trained to use (186). This research has demonstrated that CBT delivered by respiratory nurses is an effective and acceptable treatment. Due to the constraints on the NHS it may be difficult to implement in practice. Ideally, patients should have a choice of treatments. Some patients may prefer self-help leaflets, others a one to one session with the nurse. However, there may well be alternative ways of delivering the intervention which may be a novel way of delivering this CBT intervention and less resource intensive.

Towards the end of this research £60,000 was obtained from the Academic Health Science Network to develop the COPD intervention used in this study as an interactive on-line version of the CBT treatment. A focus group has been held to gain views of patients and their families. The program has been built and is in the pilot phase. It is hoped this research may address problems of health literacy especially for patients who are unable to read as videos will be presented in conjunction with written material.

7.9 Feasibility and Acceptability.

When this study was planned it was anticipated that 70% of patients approached who were eligible would be happy to participate. This was optimistic as only 43% of patients eligible declined to participate in the study. However, the percentage of patients declining compares favourably with studies on pulmonary rehabilitation where approximately two thirds of patients declined to get involved in the research (232) and other studies of CBT (148). Recruitment took a year longer than planned to ensure the number stipulated in the power calculation was met. The reasons for non-participation in this study is similar to other non-pharmacological studies. Mood will clearly have a role to play. As expected, feeling anxious or depressed may well reduce engagement in treatment, similar to engaging in pulmonary rehabilitation.

Alternatively, it may well be that the intervention was not acceptable to patients and drug therapy may be preferred. This would contradict previous suggestions that patients prefer non-drug interventions (137). It is also possible the stigma of mental health issues may also lead to non-participation. The stigma associated with mental illness has been widely researched and seen as a factor effecting engagement (233). In a study involving pulmonary

rehabilitation, reasons for non-participation included travelling, perception of benefit, competing commitments or demands, past negative experiences and perception of health status (232).

Identifying barriers and potential facilitators to recruitment should be a fundamental step when planning research (233). It was apparent that for some patients in this study the motivation for participating was their perception that it would help other patients. This has been identified as a major motivating factor in participation of many studies. Furthermore, receiving feedback from a study can reinforce the perception that research can help others and show participants how they are contributing to the development of knowledge in the area of interest (233) which is relevant or important to them. Significant steps were taken to enhance recruitment for this study including:

- Developing an acceptable experimental design involving self-help leaflets or brief intervention involving between two and six sessions of CBT.
- Provision of transport to hospital or conducting home visits to limit costs to patients depending on patients' wishes.
- Avoiding lengthy, tedious questionnaires.
- Avoiding lengthy consultations and working at patient's own pace depending on their physical health.
- Hopefully providing enjoyable, therapeutic contact with staff.
- Demonstrating good interpersonal skills with patients during interactions such as being respectful, approachable, caring and compassionate. Steps were taken to assess interpersonal skills with video recordings of therapy.
- Being flexible and accommodating with participants when arranging therapy sessions.
- Ethical approval was obtained to increase study awareness with the development of a poster which was displayed in key locations including the Chest Clinic at the RVI and Freeman Hospital.

What was noticeable was how patients were approached. When patients were asked if they would like to participate in a study of CBT for anxiety they were more inclined to decline. If

patients were asked if they would like to participate in a study that would help manage symptoms of breathlessness which may be exacerbated by symptoms of anxiety they were more likely to engage in the study. Patients with COPD do not seem to see the link between anxiety and their COPD so focusing on a difficult symptom such as breathlessness may well improve engagement.

A number of health care professionals could potential delivery CBT. Prior studies show non-psychotherapists with supervision can successfully administer interventions like CBT to emotionally distressed patients; (187). In a non-RCT case series I reported clinically and statistically significant improvements in anxiety and depression scores. A statistically significant reduction in hospital admissions after nurse delivered CBT was also seen and the mean HADS-Anxiety score fell from 10.6 (range 6-15) to 3.8 after CBT (1-7; $p < 0.001$) (187). In an audit of 42 patients (21 patients received nurse led CBT matched to 21 historical controls) we demonstrated that CBT significantly reduced anxiety ($p<0.01$), depression ($p<0.001$) and hospital admissions ($p <0.01$) (183).

A key benefit of using respiratory nurses is their widespread availability within NHS and the skills of this group of healthcare providers in providing holistic care in COPD. Notably their unique skill set allows them to distinguish physical and psychological aspects of symptoms. Respiratory nurses have knowledge, skills and expertise in caring for patients' physical well-being. This model may be more acceptable to patients rather than being referred to yet another healthcare professional who may have little knowledge of the complexity of COPD. It is reassuring that feedback from patients suggested the intervention was acceptable to them and indeed they would prefer to speak to the respiratory nurse involved in their care rather than see a mental healthcare professional who may not understand the complexities of COPD. This study has demonstrated that it is possible for respiratory nurses to have additional training in addressing psychological skills.

However, it should not be under estimated that one of the key components of successful treatment is attributed to the nurse's capacity to engage and retain the patient in treatment. The process of engagement requires the patient and nurse to construct a therapeutic relationship or alliance (234). Importantly, one of the most robust findings in psychological research is that a good therapeutic relationship (or alliance) is the best predictor of outcome

(229). Therapeutic alliance broadly means the collaborative and effective relationship between a therapist and a patient (235). It is suggested that the patient's perception of the quality of the relationship is related to outcome (235). However, there are conflicting views on the notion of therapeutic alliance and it has been proposed that better outcomes lead to the perception of better therapeutic alliance. A further factor is that the 'alliance' may therapeutic itself regardless of the psychological intervention (235).

Nurses with the appropriate knowledge, skills and attitude will be an important consideration when thinking about addressing patient engagement and the acceptability of the CBT intervention for COPD patients. Not every nurse or indeed any other healthcare professional may have the therapeutic skills required to undertake CBT. It is quite easy to learn the techniques but putting them into practice is another matter. If the relationship is not formed patients are unlikely to discuss private intimate matters with someone they do not have a rapport with and will vote with their feet. In this study, once patients were recruited, retention was excellent and patient feedback was very positive.

As this study involved written patient materials the issue of health literacy should be considered. Health literacy has been defined as the cognitive and social skills which determine the motivation and ability of individuals to gain access to, understand and use information in ways which promote and maintain good health (236). Whilst this definition may be complex, in the context of this study health literacy would include a patient's motivation, their ability to read the information provided and using the information to help reduce symptoms of anxiety and depression. It is interesting that three patients provided valuable feedback that they were unable to read the leaflets but did not disclose this when they were enrolled into the study. Only one patient admitted he could not read and I arranged for a health care assistant to read the information leaflet to him. It has been estimated that 46% of people in the North East do not have the literacy skills to read standard health information materials (236). Poor understanding may lead to poor participation, lack of compliance with treatment, low self-management and will not gain benefit from the information (236).

It was also interesting that a few patients did not feel that the information referred to them, for example one patient stated:

"The panic leaflet wasn't helpful. I thought it applied to those who have had a stroke"

It may be more appropriate to develop specific information for patients with COPD in a number of different formats such as written information or digital format such as an internet based program.

7.10 Patient and Public Involvement

Members of the public have been involved in research for many years in a number of ways (193). Patient and public involvement in research means more than merely being 'subjects' of the research. Common areas of public involvement include setting the research agenda, research design, assisting with the management of research, interpreting and disseminating research. PPI involvement can start at any stage but there are certainly advantages of early PPI involvement. A very important benefit of involving patients early in particular is that they can provide a different view of the research project from the patients' perspective and can identify issues that are important to them. I was very aware of the importance of PPI when developing the research proposal for this study and incorporated PPI at an early stage.

It is understandable that it can be daunting for patients and carers to contribute to discussions with health care professionals and express their views and concerns. In addition, patients with long term physical health problems such as COPD can find it hard to commit to attending meetings for long periods of time, may be physically unwell or may even die during the process due to their life threatening condition. This can be very upsetting for the whole TSC. Indeed during this study the carer representative was replaced with another as the initial representative died unexpectedly. PPI and third sector representatives played an active role in the study. I met with patient and carer representatives prior to TSC meetings to go through any questions they may have and brief them on the forth coming agenda. In future studies I would organise specific training to ensure participants understand what is expected of them such as attending formal meetings. I am aware the European Lung Foundation is developing such a training package.

During the study two events were held to inform patients and relatives about the progress of the study. These were held at Freeman Hospital and in a community setting (Marie Curie Hospice). Attendance was in the order of 50-60 at each event and mostly attendees were from secondary care clinics. The trial design, aims, objectives recruitment progress was pre-

sented and discussed with patients with COPD. It is extremely important to present the results to patients before publishing information about the research in the media (193). The British Lung Foundation have published small articles about the study in their national newsletter and a further publication of the results is planned for January 2016.

At recruitment patients participating in the trial were informed that the results would be sent in a trial newsletter as soon as the results were available. A conference has also been organised to present the results of the research and will be open to all patients who have participated in the trial. The aim of the meeting is to thank the participants, present the results personally and gain comments that might aid the interpretation of the results from a patients' perspective. Other PPI events will also be organised for local Breathe Easy Groups who are aware of the research and are interested in the outcome of the trial. Feedback from the participants and future recipients of CBT will help in disseminating to healthcare professionals. Patients who use services are most likely to want to see research being implemented to change practice for the better (193). Involving organisations such as the BLF can be instrumental in disseminating research results and campaigning to implement results.

It is important to evaluate the research process from a patient perspective and identifying what went well and what could be carried out differently if this research is expanded in the future. This research was very ambitious and thus the ability to carry out in-depth qualitative interviews was not considered feasible for this PhD fellowship. In an attempt to gain some feedback patients were asked for their comments at three, six and twelve months when approached to complete the follow up questionnaires. The feedback was positive and will be useful when implementing future research. Research should be conducted 'with' patients not just 'to' them (237). PPI is an important and integral part of the research process. This study incorporated PPI in a number of different levels including research design and management.

7.11 Limitations of this study

A number of limitations of this study must be acknowledged. Possible primary outcomes of interest for this study were a reduction in patient reported anxiety symptoms or a reduction in hospital admissions. Any intervention that can reduce hospital admissions could be very attractive to commissioners. Assuming an exacerbation rates of 2 per year it was estimated

that a sample size of 378 patients (189 per group) would allow an 80% power to detect 27% reduction in exacerbations. Assuming withdrawal rates as above >474 patients randomised (237 per arm) would be required. With a limited budget and time frame it was felt beyond the scope of a PhD study. The numbers required for admission prevention and applicability of study findings may well inform and lead to a multicenter RCT.

We did not undertake formal screening for memory problems or mental health problems as compared to some (238). Three patients in the CBT arm were found to have mental health problems which were long standing but their clinical teams were not aware of this. There may well be patients in leaflet group who had issues but were not identified. Patients with COPD were screened for symptoms of anxiety and depression from a case finding questionnaire rather than given a diagnosis using formal assessments. Patients did not undergo formal psychiatric assessments for this study.

As with most behavioural interventions this was an un-blinded study. Obviously patients and the nurses were aware of the patient's allocated intervention. There was no placebo limb and so the improvements might in part have reflected spontaneous improvements, changes in medication, the effects of pulmonary rehabilitation or improvements associated with increased familiarity with the clinical setting and staff. Previous researchers have tried to address the issue of blinding participants. In De Godoy's paper it is suggested that 'both groups were blinded in relation to activities of the other group' (page 1155). The paper is confusing as it states that both groups received education including several techniques that are classified as CBT techniques such as coping with illness, stress management, relaxation, energy saving techniques and the benefits of exercise. There is minimal information about the 'cognitive therapy' and 'logotherapy' which the intervention group received. With this in mind, it is difficult to comprehend how patients could give informed consent if they were not aware of the activities entailed in each group.

During the study three of the nurses involved in delivering the CBT treatment gained employment elsewhere subsequently one nurse delivered 71 (55%) of the CBT intervention. The use of a standardised manual-based approach and video validation should have minimised the influence of individual therapists' approaches. As CBT is a complex individualised

intervention it is not possible to state which particular aspect of the Lung Manual protocol was most effective.

Some patients were taking medication for anxiety (7%) and depression (35%) which may impact on the results. However, this will be similar for both groups. Another confounding factor is the increased availability of IAPT which was introduced shortly after the launch of this study. However, as psychological well-being tends to be ignored for patients with COPD it is unlikely this will have a significant impact on the outcome.

A further limitation of this study is the use of multiple significance testing. Whilst the primary and secondary outcomes were stated in a pre-analysis plan a priori, multiple testing was undertaken for sub-group analysis. As the number of comparisions increases, the risk of Type I error increases and incorrect inferences can be made. As the significance level of the test was 0.05, the test had a 5% chance of incorrectly rejecting the null hypothesis. Consideration was given to reducing the significance level to 0.01 or using the conservative Bonferroni's correction test which adjusts the critical level of significance for each test by dividing the critical level of significance by the number of tests performed. However, the Bonferroni's test errs on the side of non-significance and its use can inflate the type II error rate which will lead to a non-significant result when a difference does exist. The aim of the subgroup analysis was for evaluation of the CBT and leaflet groups in terms of clinical significance and application rather than hypothesis testing.

Finally, ideally research needs to have external validity in that the results can be generalised beyond the very specific conditions which pertained to the study (239). However, the entry criteria were broad but as the study was undertaken in secondary care it is not clear whether the findings can be generalised to primary care. Further research is needed to test the validity of the intervention and findings in other settings

7.12 Strengths

This study is the largest to date of CBT in COPD. The study was carried out within a normal clinical setting and demonstrated that respiratory nurses can incorporate CBT into usual clinical care. One of the strengths of this study is that it was adequately powered. The selection of suitable endpoints depends on the purpose and scope of the study, available evidence

from previous trials, the clinical setting, the intervention of interest and anticipated treatment effects (227). This study has addressed weaknesses of previous studies in that a power calculation was undertaken and the appropriate number of patients were recruited. In contrast to many other studies, a considerable strength of this research is the fact that patients all have anxiety at baseline.

In addition, patients with all levels of COPD severity were included and so the study is likely to be representative of patients in the UK attending secondary care clinics. Importantly, all patients had quality assured spirometry to ensure they fulfilled the entry criteria. Spirometry was repeated in the hospital clinical physiology department if needed. Previous studies have accepted a diagnosis of COPD based on spirometry which may not be quality assured and therefore the diagnosis of COPD may be in question. For this study only quality assured spirometry was accepted. Attempts were made to minimise bias from randomisation, data collection and data analysis. The outcome measures used were all standardised and previously validated.

Treatment integrity has important considerations for drawing inferences about the efficacy of treatments (240). In the past psychotherapy studies have been criticised for inadequately assessing treatment integrity procedures (241). A strength of this study is that adherence to the CBT intervention manual was assessed as 22 session's video recorded and assessed by an independent cognitive behavioural therapist using a validated rating scale. However, ensuring strict fidelity to a protocol may be inappropriate. The intervention may work better if adaption to local settings is allowed (172).

This study demonstrated that CBT approaches can be developed for COPD patients with a progressive illness and help manage difficult symptoms of anxiety which are intrinsically linked with breathlessness. The CBT intervention used in this study was well described to facilitate replication. The intervention used in this research has been specified in this thesis and a detailed manual and training program has been developed to replicate its use.

7.13 Interpretation

This is the first study to demonstrate that respiratory nurses without a clinical psychology background can be trained to undertake CBT based intervention. The results suggest that older patients treated with CBT seem to respond better than younger patients and patients

with a better QOL are more likely to respond. The intervention is more effective than leaflet support. Respiratory services should screen patients for symptoms of anxiety and consider providing CBT or at the very least the self-help leaflets used in this study. The cost-effectiveness of the intervention is uncertain until further analysis of the data is complete. Further refinement of CBT techniques should also be considered to establish the most effective elements of the intervention. There is scope to develop alternative methods of delivering the intervention such as an interactive CBT digital program.

7.14 Generalisability

Given the wide range of COPD severity studied the findings are likely to be generalisable to the wider COPD population of similar ethnic origin and background.

7.15 Dissemination of results

The results of the study will be disseminated via publications once the 12 month data have been analysed. In addition, the results will be disseminated to patients and their families involved in the study and beyond. The major benefit of PPI is the ability to focus on issues important to service users. In addition new evidence is not always implemented. Involving patients in research dissemination not only feeds back the findings but allows patients to use pressure groups and other advocates to promote wider uptake of new treatments or management strategies. PPI involvement in research dissemination not only feeds the findings but allows patients to use pressure groups such as the BLF and other advocates to promote wider uptake of new treatment or management strategies. Importantly, another advantage of using national charities such as the BLF is that this may help reduce the stigma of anxiety in COPD and potential for treatment to help with the distressing symptoms. It may also lead to higher participation in future studies e.g. Health Technology Assessment.

7.16 Contributions to knowledge

This study has demonstrated that CBT is effective for COPD patients with symptoms of anxiety and depression. With adequate training and supervision, respiratory nurses can be trained to use CBT skills and can provide effective treatment with a brief intervention following the Lung Manual. The results have also shown that providing self-help leaflets is also effective in reducing symptoms of anxiety and depression but are not as effective as one to one CBT delivered by a respiratory nurse.

7.17 Policy implications

This study suggests that simple treatment in the form of self-help leaflets and CBT delivered by a respiratory nurse can improve psychological well-being. Routine screening for symptoms of anxiety in patients with COPD should be incorporated into standard practice.

7.18 Summary

It is argued that people with long term health conditions and mental health receive fragmented care and also may be more expensive to treat (79). Anxiety and depression are common comorbidities experienced by COPD patients. In this study of secondary care patients, symptoms of anxiety were high with 59% of patients screened reporting symptoms. These findings are higher than those of an earlier systematic review and meta-analysis that identified anxiety symptoms in 36% of patients (225). Many patients with mild COPD as judged by spirometry were anxious. This raises the possibility that a significant proportion of primary care patients with COPD will also have un-recognised comorbid anxiety if screened for these symptoms. Given this high prevalence we now show potential effective therapies to tackle this co-morbidity.

Previous studies have tried to investigate the effectiveness of CBT in COPD but have failed to demonstrate a significant benefit. This study is unique as it is the first to investigate the effectiveness of a brief CBT delivered by respiratory nurses who are well placed to provide physical and psychological support for patients. Both CBT and self-help leaflets interventions were associated with a reduction in anxiety symptoms at three months that for most patients reached the MCID suggested by Puhan (122). There was a greater improvement in those receiving CBT delivered by respiratory nurses. The health status of both groups also improved as judged by the COPD-CAT and EQ-5D utility scores but again there were greater improvements in the CBT intervention group. Collectively these data indicate that comorbid anxiety in COPD is both common and treatable.

It is recognised that depression is two to three times more common in patients with chronic physical health conditions (111) and is associated with poorer survival, longer hospitalisation stay, persistent smoking, increased symptom burden, and poorer physical functioning (66). Two-thirds of patients in our study had symptoms of depression. CBT is an effective treatment for depression but the programme we used was not specifically designed to address

this. We found improvements in depression symptoms following both CBT and leaflet intervention but these were less marked than the improvements in anxiety and for most patients the improvement was not of a clinically significant magnitude. CBT targeting at depression as well as anxiety might be worthwhile.

Patients and clinicians often fail to recognise the psychological complications of the illness leading to under diagnosis. There are also significant challenges to implementing CBT for physical illness including cost, the availability of trained therapists and patient reluctance to engage in psychological treatments The potential benefits of actively screening for comorbid anxiety in clinic and having a dual skilled nurse in medical outpatient setting is that stigma or other barriers to accessing care may be more easily overcome thus providing more holistic care.

RCT's are the most rigorous way to evaluate the effectiveness of interventions, regardless of complexity. RCT's of complex interventions pose methodological challenges to researchers. There is surprisingly little consensus as to develop and evaluate complex interventions, guidance is increasing with the publication of the MRC Framework (172, 178). Studies continue to emerge that suggest that over 40% of patients who are high users of healthcare resources have comorbid anxiety, depression or dysthymia (79). It has been suggested that patients with more severe chronic medical conditions will become depressed or anxious but this has not been found to be the case in this study.

As this research was funded for five years it was appropriate to conduct a RCT with 12 month follow up. This long term follow up will be beneficial in identifying if CBT was effective for patients with COPD and identify how long the effect was maintained. However, the longitudinal results of the study will be analysed and published when available. The cost effectiveness of this intervention will be important and 12 month data will allow a cost effectiveness evaluation to be undertaken. If hospital admissions are improved with both interventions it would be more cost-effective to provide self-help leaflets in the first instance and offer one to one CBT therapy for those patients who do not respond to the bibliotherapy or who prefer face to face treatment.

Chapter 8 - Recommendations for practice and future research

Several recommendations for practice are suggested.

1. Health care professionals working with patients with COPD should increase their awareness and understanding of the psychological impact of COPD. Staff working with COPD patients should be able to recognise psychological needs, provide effective and compassionate general psychological support.
2. Screening for symptoms of anxiety and depression is essential if appropriate treatment is to be offered. Brief screening questions could be used and if symptoms are identified then a HADS Questionnaire should be completed.
3. A step-wise approach to manage symptoms of anxiety and depression should be adopted. Patients should be offered a range of options including:

a) Self-help written information (Bibliotherapy).

b) Guided self-help with a professional trained in the use of written materials used.

c) One to one CBT with an appropriately training professional. Respiratory nurses are well placed to undertake this role with training and supervision. Without these important elements the intervention may not be as effective. Implementing evidence – based therapy could be undermined if the training and supervision associated with this intervention are neglected. Therapeutic alliance and empathy can influence the effectiveness of treatment. Effective therapists need a sophisticated set of interpersonal skills to help the patients feel understood, gain their trust and react to verbal and non-verbal cues especially in the initial interaction with the patient to ensure engagement in the process (242).

4. Basic CBT training should be provided to student nurses working in the physical health setting to develop their awareness, knowledge and skills to improve patients' psychological well-being.
5. Clinical Commissioning Groups should identify ways of integrating physical and psychological well-being into care of patients with COPD.

8.1 Recommendations for future research

Over the last ten to fifteen years psychological research for anxiety and depression in COPD has slowly developed. This study is the largest study to date but there remain several unanswered questions:

1. A key question in evaluating complex interventions is how the intervention works and what are the active ingredients within the intervention that are exerting their effect (172) in the COPD population. By addressing this question we can build on our understanding of causal mechanisms, design more effective interventions and apply them more appropriately across group and setting (172).
2. Future research should be undertaken to identify if the face to face brief therapy could be delivered to patients with COPD in novel ways such as a digital interactive internet program.
3. To maximise recruitment future studies should carefully consider the barriers and facilitators to participation in research on anxiety and depression. Focusing on breathlessness rather than a psychological issue may be more acceptable to patients than a 'psychological therapy' and increase engagement in future research. Ensuring treatment is accessible and understandable to patients is key to successful therapy. This will require future studies avoiding unnecessary terminology and keeping the treatment simple and easy to understand.
4. Future studies may also find it helpful to screen for cognitive impairment and exclude patients who score less than 24 using an appropriate screening tool e.g. Mini Mental State Examination (MMSE).
5. The EQ-5D utility has been updated and the new version with five domains should be used. Using the EQ-5D utility scores will allow a cost-benefit analysis to be undertaken.
6. Booster sessions of CBT may be required. Future research could be developed to answer this question.
7. Future researchers should consider including an-depth process evaluation.

8.2 Conclusion

Anxiety and depression are significant problems for patients with COPD. There is clearly an opportunity to improve clinical care for patients with COPD. Screening should be implemented and patients provided with self-help leaflets or offered CBT. The results from this study demonstrate feasibility, acceptability and effectiveness of CBT delivered by respiratory nurses for anxiety and depression in COPD.

Appendices

Appendix 1 HADS Questionnaire

Hospital Anxiety and Depression Scale (HADS)

QL assessment
the measure of potential

Name: _____ Date: _____

Clinicians are aware that emotions play an important part in most illnesses. If your clinician knows about these feelings he or she will be able to help you more.

This questionnaire is designed to help your clinician to know how you feel. Read each item below and **underline the reply** which comes closest to how you have been feeling in the past week. Ignore the numbers printed at the edge of the questionnaire.

Don't take too long over your replies, your immediate reaction to each item will probably be more accurate than a long, thought-out response.

FOLD HERE

FOLD HERE

A	D		A	D
		I feel tense or 'wound up'		
3		Most of the time		3
2		A lot of the time		2
1		From time to time, occasionally		1
0		Not at all		0
		I still enjoy the things I used to enjoy		
	0	Definitely as much		
	1	Not quite so much	0	
	2	Only a little	1	
	3	Hardly at all	2	
			3	
		I get a sort of frightened feeling as if something awful is about to happen		
3		Very definitely and quite badly		3
2		Yes, but not too badly		2
1		A little, but it doesn't worry me		1
0		Not at all		0
		I can laugh and see the funny side of things		
	0	As much as I always could		
	1	Not quite so much now		
	2	Definitely not so much now		
	3	Not at all		
		Worrying thoughts go through my mind		
3		A great deal of the time		
2		A lot of the time		0
1		Not too often		1
0		Very little		2
				3
		I feel cheerful		
	3	Never		
	2	Not often		
	1	Sometimes		
	0	Most of the time		
		I can sit at ease and feel relaxed		
0		Definitely		
1		Usually		
2		Not often		
3		Not at all		
		I feel as if I am slowed down		
		Nearly all the time		
		Very often		
		Sometimes		
		Not at all		
		I get a sort of frightened feeling like 'butterflies' in the stomach		
		Not at all		
		Occasionally		
		Quite often		
		Very often		
		I have lost interest in my appearance		
		Definitely		
		I don't take as much care as I should		
		I may not take quite as much care		
		I take just as much care as ever		
		I feel restless as if I have to be on the move		
		Very much indeed		
		Quite a lot		
		Not very much		
		Not at all		
		I look forward with enjoyment to things		
		As much as I ever did		
		Rather less than I used to		
		Definitely less than I used to		
		Hardly at all		
		I get sudden feelings of panic		
		Very often indeed		
		Quite often		
		Not very often		
		Not at all		
		I can enjoy a good book or radio or television programme		
		Often		
		Sometimes		
		Not often		
		Very seldom		

Now check that you have answered all the questions

A D

Appendix 2 – Modified CBT Rating Scale

CBT Techniques for Palliative Care Practitioners:

Rating Scale

Devised by:

I-M. Blackburn, J. Scott, S. Moorey, A. Garland, K. Mannix, C. Baker, S. H. Standart, M. Ley-land

Scoring System: Scoring is on a 7 point scale extending from 0 where the practitioner did not adhere to that aspect of therapy, to 6 where there is adherence and high skills, or proficient skill in the face of difficulties.

Item 1 – Focus / Structure

Key features: to address adequately topics that have been agreed and set in an appropriate way. In this study, practitioners are unlikely to be using cognitive therapy as a stand-alone approach, but are likely to be using techniques appropriately during their day to day clinical work. Thus, the setting of a discreet agenda in a collaborative manner is only one example of structuring a session.

Features that need to be considered when scoring this item are:

- The presence of a focus to the intervention, which may be implicit (e.g. patient attending for a pain assessment; patient discussing breathlessness in the context of a chest clinic) or explicit and arrived at unilaterally, by practitioner or patient, or bilaterally and collaboratively.
- Structure of approach, which maintains the implicit or explicit focus of the session, or agrees a change of focus where this becomes appropriate.
- Collaborative agenda setting may not be an appropriate part of palliative care intervention, and the practitioner should not necessarily lose marks if this is absent.

Competence Level	**Examples** **NB: Score according to features not examples!**
0	No focus or structure.
1	Inappropriate focus.
2	An attempt to focus made, but strays from this.
3	Appropriate at focus but not enough structure (poor adherence).
4	Appropriate focus, minor difficulties evident, but structures appropriate (moderate adherence).
5	Appropriate focus, structure maintained and progress reviewed at the end. Minimal problems.
6	Highly focused and structured, or well-maintained focus and structure in the face of difficulties.

Item 2 – Pacing

Notes To raters: Raters will need to consider that palliative care patients are often physically frail, and may tire suddenly and without much warning. It may therefore be difficult to pace a structure with equal start, middle and concluding phases, and indeed a concluding phase may be very short (and should then be rated under item 10 appropriate closure). The work must be paced well in relation to the patient's needs.

Competence Level	Examples NB: Score according to features, not examples!
0	Good pacing evident some of the time, but diffuse at times. Some problems evident.
1	Poor time management leads to either aimless or overly rigid session.
2	The session is too slow or too fast for the current needs or capacity of the patient.
3	Reasonable pacing but digression or repetitions from the practitioner and/or patient leads to inefficient use of time.
4	Balanced allocation of time with discrete start and middle. Concluding phase evident where clinical circumstances permit. Minor problems evident.
5	Good time management skills evident. Session running smoothly. Practitioner working effectively in controlling the flow within the session. Minimum problems.
6	Excellent time management or highly effective time management evident in the

Item 3 – Chunking/Feedback/Capsule Summarising

Notes to raters: The patient and practitioner's understanding of key issues should be helped with the use of 2-way feedback. This includes feeding back information as general summaries, and chunking of important units of information.

Competence Level	Examples NB: Score according to features, not examples!
0	Absence of feedback or highly inappropriate feedback.
1	Minimal appropriate feedback.
2	Appropriate feedback, but not given frequently enough by practitioner, with insufficient attempts to elicit and offer feedback.
3	Appropriate feedback given by the practitioner and elicited from patient frequently, although some difficulties evident in terms of content or method of delivery.
4	Appropriate feedback given by the practitioner and elicited from patient frequently, facilitating moderate therapeutic gains. Minor problems evident (e.g. inconsistent).
5	Highly appropriate feedback given and elicited regularly, facilitating shared understanding and enabling significant progress. Minimal problems.
6	Excellent use of feedback or highly effective feedback given and elicited regularly in the face of difficulties.

Item 4 – Integrating Professional Model of Care with CBT

Note to raters: This item is looking at skills in incorporating concepts and skills from a CBT model into the professional model of everyday use by the practitioner, e.g. nursing model, social work etc.

Competence Level	**Examples NB: Score according to features, not examples!**
0	The absence of an appropriate integration: no bridge between the models.
1	Inappropriate or misapplication of integration between the models leads to neutral impact (e.g. interferes with progress or leads to aimless application of techniques.
2	Some rudimentary integration arrived at but not well linked with the goals of therapy.
3	Attempts to link cognitive conceptualisation with professional model but with some difficulties evident. Leads to appropriate interventions.
4	Coherent integration with the beginnings of a cognitive conceptualisation.
5	Coherent integration with an appropriate conceptualisation leads to therapeutic shifts. Minimal problems.
6	Excellent integration of models with a coherent cognitive conceptualisation, which leads to therapeutic shifts (I.e. evidence of elegance, style or high effectiveness in the face of difficulties).

Item 5 – Collaborative Relationship

Notes to raters: The patient should be encouraged to be active in the session. There must be clear evidence of productive team work, with the practitioner skilfully encouraging the patient to participate fully through questioning techniques, shared problem solving and decision making, etc. The patient should be guided by the practitioner rather than allowed to ramble in an unstructured way. Features which need to be considered include verbal skills, non-verbal skills and, occasionally in palliative care, sharing of written summaries.

NB: although questioning is a central feature for this item, questions designed to facilitate reflections and self-discovery should be scored under item 6: Guided Discovery.

Competence	Examples
Level	**NB: Score according to features, not examples!**

0 The practitioner does not attempt to establish collaboration, or discourages the patient from being collaborative.

1 The practitioner is too controlling, dominating or passive, discouraging collaboration.

2 Some occasional attempt at collaboration but didactic style or passivity of practitioner encourages passivity or other problems in the therapeutic relationship.

3 Teamwork evident, but some problems with collaboration e.g. not enough time allowed for the patient to reflect and participate actively.

4 Effective teamwork is evident but inconsistent. Minor problems evident.

5 Effective teamwork is evident throughout most of the session. Minimal problems.

6 Excellent teamwork or highly effective teamwork in the face of difficulties.

Item 6 – Guided Discovery

Notes to raters: In a palliative care setting, the practitioner may be helping a patient to develop a hypothesis regarding their situation including attributions and meanings of physical symptoms. Effective guided discovery will create doubt where previously there was certainty, thus providing the opportunity for re-evaluation and new learning to occur.

In this context, two elements need to be considered:

1. The style of the practitioner, which should be open and inquisitive
2. The effective use of questioning techniques should encourage the patient to discover useful information that can be used to help the patient to gain a better level of understanding.

Competence	Examples
Level	**NB: Score according to features, not examples!**

0 No attempt at guided discovery, for example hectoring and lecturing.

1 Little opportunity for discovery by patient. Persuasion and debate used excessively.

2 Minimal opportunity for discovery. Some use of questioning but unhelpful in assisting the patient to gain access to their thoughts or emotions or to make connections between themes. Over use of reassurance.

3 Some reflection evident. Practitioner uses primary a questioning style, which is following a productive line of discovery. Minimal reliance on reassurance.

4 Moderate degree of discovery evident. Practitioner uses a questioning style with skills, and this leads to some synthesis. Minor problems evident.

5 Effective reflection evident. Practitioner uses skillful questioning style, leading to reflection, discovery and synthesis. Minimal problems.

6 Excellent guided discovery leading to a deep understanding by the patient. Highly effective discovery produced in the face of difficulties.

Item 7 – Interpersonal Effectiveness

Note to raters: The assessment is how the patient is put at ease by the practitioner's verbal and non-verbal behaviour. Empathy, genuineness and warmth are components of this construct.

Competence Level	Examples NB: Score according to features, not examples!
	0 Practitioner's manner and interventions make the patient disengage and become distrustful.
	1 Difficulty in showing empathy, genuineness and warmth.
	2 Practitioner's style at times impedes their empathetic understanding of the patient's communications.
	3 The practitioner is able to understand explicit meanings of patient's communications resulting in some trust developing.
	4 The practitioner is able to understand the implicit as well as the explicit meanings of the patient's communications, and demonstrates this in their manner. Minor problems evident.
	5 The practitioner demonstrates very good interpersonal effectiveness. Patient appears confident about being understood, which facilitates self-disclosure. Minimal problems.
	6 Highly interpersonally effective, and even in the face of difficulties.

Item 8 – Eliciting Key Components of the Model

Note to raters: This is a measure of the practitioner's ability to differentiate thoughts, moods, behaviours and physiology. With increasing demonstration of understanding, practitioners will be able to elicit these components, link them to each other and demonstrate the link clearly to the patient. With increasing demonstration of skill, the practitioner will lead the patient to a new understanding of the role of these components in their experience of their problems, selecting key components for further guided discovery in order to make therapeutic gains.

Feature which need to be considered are:

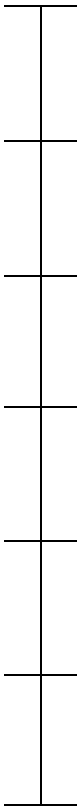
1. Eliciting components which are associated with distressing emotions
2. Demonstrating an understanding of the link between the components
3. Demonstrating skilfulness and breadth in the method used to elicit and link the components.

Competence	Examples
Level	**NB: Score according to features, not examples!**
0	Practitioner fails to elicit components of the model.
1	Inappropriate components focused on.
2	Some components elicited but links between behaviours, cognitions, physiology and emotions not evident.
3	Some components elicited in a component way, although some problems evident.
4	A number of components elicited in verbal or written form leading to a new understanding of components. Minimal problems.
5	Effective eliciting of a number of appropriate components leading to a new understanding of links between components. Minimal problems.
6	Excellent work on eliciting and demonstrating components of the model of the patient, even in the face of difficulties.

Item 9 – Application of appropriate change techniques

Note for raters: Practitioners have been trained in a number of CBT techniques. They have been encouraged to take a "top down" approach, working to reduce distress and promote coping. This section is evaluating their skill in selecting and applying appropriate CBT techniques. It is unlikely, even in later sessions that they will be working at schema level, although some opportunity to work with dysfunctional assumptions may present itself in some tapes.

Competence	Examples
Level	**NB: Score according to features, not examples!**



0 Practitioner fails to use or misuses appropriate cognitive and behavioural methods.

1 Practitioner applies either insufficient or inappropriate methods, and/or with limited skill or flexibility.

2 Practitioner applies appropriate methods, but major difficulties evident.

3 Practitioner applies appropriate intervention in a competent way although some problems evident.

4 Practitioner applies an appropriate intervention with skills and flexibility, enabling the patient to develop new perspectives. Minor problems evident.

5 Practitioner systematically applies an appropriate range of interventions in a creative, resourceful and effective manner. Minimal problems evident.

6 Excellent range of application or successful application of methods in the face of difficulties.

Item 10 – Appropriate Closure

Note to raters: The opportunity for closure may be brief if a palliative care patient tires suddenly during an interview. However, palliative care practitioners ought to be familiar with this situation and be capable of managing a smooth if swift closure.

The skill being assessed is the practitioner's ability to allow the patient to leave a session with the feeling that the problems addressed have been dealt with in such a way that they feel contained (i.e. able to tolerate the distress), and/or able to deal effectively with distress in the future.

Features of success would include obvious reduction in distress by the end of the session; new learning/understanding about their problem, or a coherent action plan.

Competence	Examples
Level	**NB: Score according to features, not examples!**

0 No attempt to use closure strategies.

1. Abrupt termination; inappropriate closure strategies. Patient emotionally unsafe and unprepared for the end of the session. No action plan.

2. Minimal use of closure strategies. Patient poorly prepared; still emotionally distressed without new understanding, or no action plan. Practitioner partially aware or unappreciative of patient's distress.

3. Some preparation for closure: patient is warned of imminent closure by practitioner. Some use of appropriate closure strategy but problems evident.

4. Coherent use of closure strategies; attempts by practitioner to leave patient with reduced distress.

5. Good use of closure strategies smoothly executed. Practitioner demonstrates procedures to reduce patient's distress and/or give new understanding and/or a plan of action.

6. Excellent closure strategies used with skill, or highly effective in the fact of difficulties.

Appendix 3 – Lung Manual (CD provided)

Appendix 4– CBT Foundation Workbook

This workbook is designed to help you develop your skills using CBT techniques by trying them yourself. It contains exercises to help you practice the tasks which help patients enormously and reinforces what you have learnt on the CBT course. In CBT we use homework as a way of helping us learn and improve our situation. Try to work through the exercises in this workbook over the next four weeks to help develop your own understanding of them. It may be helpful to keep a reflective diary of your progress. Remember practice makes perfect. I recommend the following textbook:

Sage N, Sowden M, Chorlton E and Edeleanu A. (2008) CBT for Chronic Illness. A workbook and Toolkit Wiley Publications.

You will be guided to read certain chapters prior to undertaking some of the exercises in this workbook.

Exercise 1 – Recognising our own thinking errors.

We know that 'what we think affects how we feel and what we do'. We all have unhelpful thinking errors at some point in our lives. We may jump to conclusions, make a crisis out of nothing, take things personally or discount the positive of a situation. Unhelpful thinking can lead to unhealthy negative emotions such as anxiety, depression or guilt. Understanding our thinking errors may help us change them. If you can recognise unhelpful thinking you are more likely to correct it.

Activity - Think about a personal or situation in your area of practice and consider if you have any thinking errors. (See handout to refresh your memory). Being aware of our thinking style can help us challenge unhelpful thinking.

Exercise 2 – Noticing Negative Thoughts

Negative automatic thoughts (NATS) pop into your head without warning. They may be unhelpful and upsetting and are often not challenged. NATS can also be examples of thinking errors. Most people don't notice their NATS so a thought record can be useful in making sense of situations. A critical step in CBT is to recognise how our thoughts affect how we feel.

Activity - Try to think about a situation where you experienced NATS and complete the thought diary overleaf.

Thought Diary	Answer
What was the trigger?	
What were your negative automatic thoughts?	
What emotion did you experience?	

Exercise 3 – Challenging Negative Automatic Thoughts

Having identified NATS we need to think about how we can change them to more balanced thoughts. This can be undertaken in a number of ways e.g. thinking carefully about how you can challenge these thoughts – asking yourself what evidence there is for thinking this way. Does your thought fairly and accurately sum up the situation? Are you taking personal responsibility for things that are outside your control? Are you ignoring any relevant facts? How might you benefit from thinking differently?

Activity - Read chapter 15 in Sages et al text book. Alternatively you could try to complete the chart overleaf.

Activity - Fill in as much information as possible to make sense of the situation. Remember it is not the event that is important but what we think about it.

Situation	
What is your automatic thought:	
Is the thought realistic or fact?	
Is your thought extreme/rigid or balanced/flexible?	
Is your thought leading to healthy feelings and behaviours?	
How are you likely to feel and act if you continue thinking this way?	
Would you encourage a friend to think in this way?	
What evidence can you find against my thought?	
What thought would be more helpful in order to feel better or do things differently?	
How would thinking in a more balanced/flexible way help you?	

Exercise 4 – Positive Thinking

It is easy to focus on negatives and discount information that is positive.

Activity - Keep a log of everything positive for the at least 1 week and reflect on what you have learnt at the end of the exercise. Use a chart like the one overleaf.

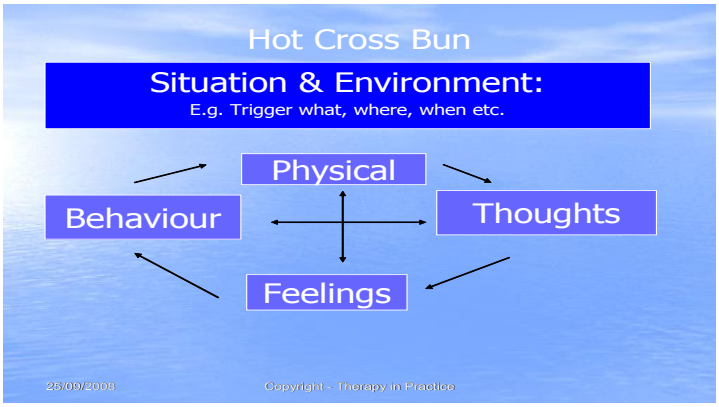
Date	Description

Activity - What was helpful about this activity? What made it difficult? Did it help? What did you notice about this exercise?

Exercise 5 – The Hot Cross Bun

Formulations are the basis of understanding patient's difficulties and identifying interventions that might help improve the patient's difficulties.

Activity - Complete as many 'Hot Cross Buns' as you can to gain develop your skills with this critical CBT technique.



Exercise 5 – Problem solving

Problems are part of everyday life. We all have problems at some time or another. This may be the way you think about something (cognitive) or what you do (behaviour). The first step in problem solving is defining what your problem or problems are. From here you can prioritise where to start. Next think about as many different solutions to each problem. The next step is to work out which is the best solution. Thinking about the positive and negative consequences of each idea then chooses the one you think is the one that will work best.

Activity - Read page 275 in Sages textbook.

Activity - Think about a problem you have been facing and complete the following table.

My Problem is:		
Possible Solution	**Positive Consequences**	**Negative Consequences**
On balance, the best way to tackle this problem is:		

Exercise 7 – Tackling Avoidance

We all use avoidance strategies at times. These can actually maintain our problems or even make them worse e.g. avoid situations that make us anxious or put off dealing with practical problems and tasks that we find unpleasant, withdrawing for our usual routine or worrying a lot. This exercise helps us deal with the self-defeating strategy of avoidance. Facing your fears and doing things you don't want to do can be very worthwhile.

Activity - Read page 201 in of Sages textbook.

Activity - Think about situations or tasks you are avoiding and complete a chart like the one overleaf.

Things I am avoiding	Reason for Avoidance	Effects of Avoidance

Exercise 8 – Goal setting

Setting goals for therapy is often undertaken early. As stated in this book, the purpose of therapy is to help you move from your problems to achieve your goals. When thinking about a goal you should think about developing goals which are:-

- Specific
- Positive
- Observable
- Realistic
- Time frame

Activity - Read chapter 10 in Sages textbook or CBT with Older People Chapter 3.

Activity - Think about a goal you would like to achieve using the 5 areas above.

Activity - Consider how you help patients/clients to identify their goals? What kind of goals would your patients set and how could they be defined?

Exercise 9 – Activity Scheduling

One of the best ways to overcome depression is to become more active and take control. A useful way to do this is to increase activities you enjoy or want to achieve. If tasks are too difficult it is helpful to break them down into small manageable steps. This increases the chances of success. Activity scheduling helps us get engaged in valuable activities, notice how they make us feel, levels of satisfaction/achievement or pleasure after completing the activity.

Activity - Read page 249 from Sages textbook or CBT with Older People Chapter 5 Behavioural techniques pages 55-62.

Activity - Try activity scheduling for 1 day. Record your activities on a simple chart such as the one below.

Date and Time	Activity	Rating out of 10

Exercise 10 - Mental Distraction

Try this technique if a patient has persistent emotional or physical distress that seems overwhelming. Some patients find counting backwards in 7's from 100 helpful, looking for red objects in the room etc.

Activity - Read page 272 from Sages textbook or CBT with Older People page 104 – thought stopping.

Activity - Record how effective this strategy was. Did it show the patient how their attention and thinking influenced their feelings? Did it help the patient take control of the situation? Did it challenge catastrophic thoughts?

Situation	Distraction Used	Outcome

Exercise 11 - Behavioural Experiments

Behavioural experiments are used to challenge and change unhelpful thoughts and behaviour.

Activity - Read chapter 13 from Sages textbook or CBT with Older People page 79 behavioural experiments in cognitive restructuring.

Activity - Devise a behavioural experiment:-

- Outline an unhelpful thought or belief you wish to test out.
- Predict what the outcome might be.

- Decide on your experiment – be as clear as you can about the task and how you will measure your results.
- Carry out the experiment.
- Evaluate the result (how accurate were your predictions?).

Prediction	Experiment	Results	Conclusion

Other useful resources

Cognitive Behavioural Therapy with Older People: Interventions for Those with and Without Dementia [Paperback]

Ian Andrew James

Publisher: Jessica Kingsley Publishers (6 Jan 2010)

ISBN-10: 1849051003

ISBN-13: 978-1849051002

General CBT books:

An Introduction to Cognitive Behaviour Therapy: Skills and Applications [Paperback]

David Westbrook Publisher: SAGE Publications Ltd; Second Edition (17 Mar 2011)

ISBN-10: 1848606877

ISBN-13: 978-1848606876

Cognitive Behavior Therapy: Basics and Beyond [Hardcover]

Aaron T. Beck (Foreword), Judith S. Beck

Publisher: Guilford Press; 2 edition (17 Aug 2011)

ISBN-10: 1609185048

ISBN-13: 978-1609185046

General CBT internet resources:

www.getselfhelp.co.uk

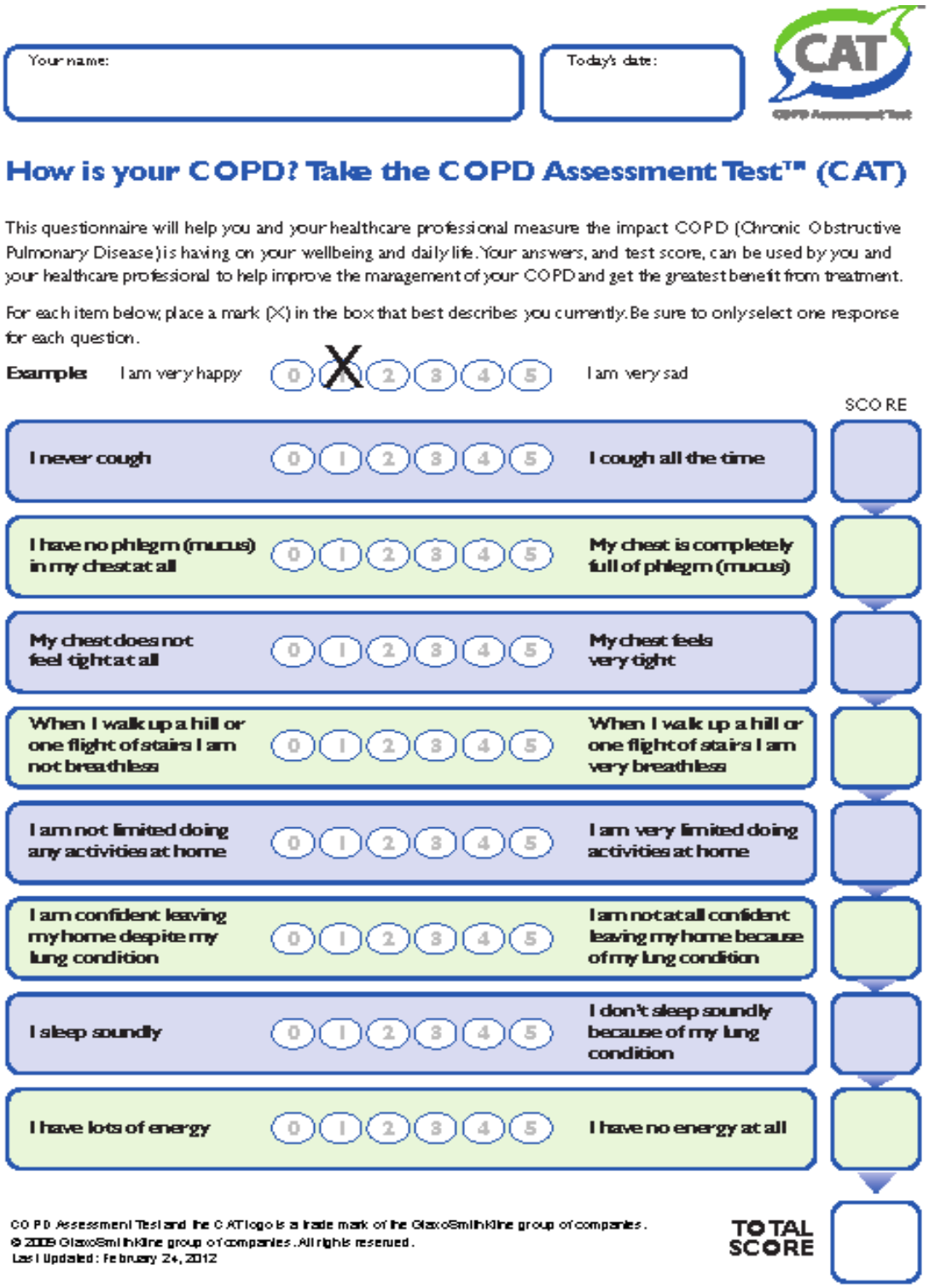
www.psychologytools.org

www.sleepstation.com

Summary

- This workbook will help you develop a cognitive behavioural approach to your work.
- In order to become more competent using CBT skills you will need to practice and read extensively around the subject.
- It may be helpful to work with another colleague at a similar stage of learning if this is possible to support and encourage each other.
- Find a skilled CBT practitioner (preferably in your field of work) who will act as a supervisor or guide to some of your work. (This is compulsory for all CBT therapists).
- You can email therapy-in-practice for online advice if you would like further support or information regarding further training.[1]

Appendix 5 – CAT Questionnaire



Your name:

Today's date:

CAT
COPD Assessment Test

How is your COPD? Take the COPD Assessment Test™ (CAT)

This questionnaire will help you and your healthcare professional measure the impact COPD (Chronic Obstructive Pulmonary Disease) is having on your wellbeing and daily life. Your answers, and test score, can be used by you and your healthcare professional to help improve the management of your COPD and get the greatest benefit from treatment.

For each item below, place a mark (X) in the box that best describes you currently. Be sure to only select one response for each question.

Example	I am very happy	0 X 2 3 4 5	I am very sad

			SCORE
I never cough	0 1 2 3 4 5	I cough all the time	
I have no phlegm (mucus) in my chest at all	0 1 2 3 4 5	My chest is completely full of phlegm (mucus)	
My chest does not feel tight at all	0 1 2 3 4 5	My chest feels very tight	
When I walk up a hill or one flight of stairs I am not breathless	0 1 2 3 4 5	When I walk up a hill or one flight of stairs I am very breathless	
I am not limited doing any activities at home	0 1 2 3 4 5	I am very limited doing activities at home	
I am confident leaving my home despite my lung condition	0 1 2 3 4 5	I am not at all confident leaving my home because of my lung condition	
I sleep soundly	0 1 2 3 4 5	I don't sleep soundly because of my lung condition	
I have lots of energy	0 1 2 3 4 5	I have no energy at all	
		TOTAL SCORE	

Last Updated: February 24, 2012

Appendix 6- EQ-5D Questionnaire

Health Questionnaire

English version for the UK

(Validated for Ireland)

By placing a tick in one box in each group below, please indicate which statements best describe your own health state today.

Mobility

I have no problems in walking about ❑

I have some problems in walking about ❑

I am confined to bed ❑

Self-Care

I have no problems with self-care ❑

I have some problems washing or dressing myself ❑

I am unable to wash or dress myself ❑

Usual Activities (*e.g. work, study, housework, family or leisure activities)*

I have no problems with performing my usual activities ❑

I have some problems with performing my usual activities ❑

I am unable to perform my usual activities ❑

Pain/Discomfort

I have no pain or discomfort ❑

I have moderate pain or discomfort ❑

I have extreme pain or discomfort ❑

Anxiety/Depression

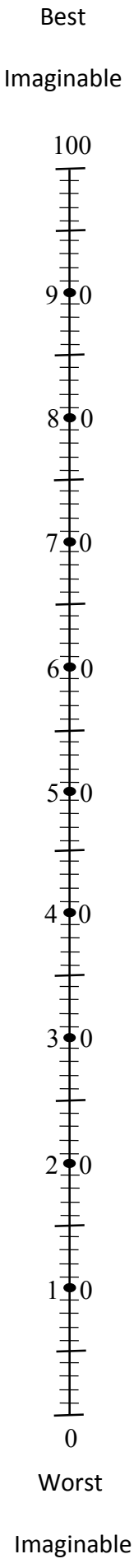
I am not anxious or depressed ❑

I am moderately anxious or depressed ❑

I am extremely anxious or depressed ❑

To help people say how good or bad a health state is, we have drawn a scale (rather like a thermometer) on which the best state you can imagine is marked 100 and the worst state you can imagine is marked 0.

We would like you to indicate on this scale how good or bad your own health is today, in your opinion. Please do this by drawing a line from the box below to whichever point on the scale indicates how good or bad your health state is today



Appendix 7 - Patient Information Booklet

The Newcastle upon Tyne Hospitals NHS
NHS Foundation Trust

The Newcastle COPD CBT CARE Study

Name of researchers: Karen Heslop, Dr A De Soyza, Dr D Carrick-Sen, Dr C Baker and Dr G Burns

Introduction

You are being invited to take part in a research study. This leaflet tells you what this study is about and what it will involve. If anything is unclear, or if you have further questions, please feel free to ask the person who gave you this leaflet, or speak to a member of the research team directly on 0191 – 2829095.

What is the purpose of the study?

Chronic obstructive pulmonary disease (COPD) is a common chest problem and includes chronic bronchitis and emphysema. Approximately 40% of patients with COPD have symptoms of anxiety. A large number of patients also have depression. Cognitive Behavioural Therapy (CBT) is a talking therapy. It has been shown to be one of the most effective treatments for anxiety and depression and is recommended by the National Institute of Clinical Excellence (NICE).

Cognitive Behavioural Therapy (CBT) is a method used to explore how we think, feel and act when we have a physical health problem. The benefit of CBT is that it can hopefully change the way you think and manage situations in a practical, problem solving way.

In Newcastle, we did a small study in 2009 which showed that CBT helped physical symptoms such as breathlessness as well as psychological symptoms such as anxiety, depression and panic attacks. However, the number of patients involved in the study was too small to say for sure if there was a real difference. This study plans to recruit 312 patients with COPD to see if CBT makes a difference. This study is being conducted in part towards an educational- qualification at Newcastle University.

Why have I been chosen?

You will have been chosen because you have COPD and were found to have symptoms of anxiety.

Do I have to take part?

Absolutely not. It is entirely up to you if you wish to join the study. Please take the leaflet home and talk it over with others. If you want to know more before you make your decision, either talk to the health care professional who gave you this leaflet, or contact a member of the research team at the address, e-mail or phone numbers below. The Patient Advice and Liaison Service (PALS) can be contacted and aims to advise and support patients, their families and carers. This service is confidential and can be contacted on 0800 032 02 02. Alternatively advice could be sought from the British Lung Foundation on 0191 – 2630276.

If you do decide to take part, you will be asked to sign a consent form. You will be given a copy of this leaflet and the consent form to keep. You are free to withdraw at any time, and you do not have to explain why. If you decide not to take part, your decision will have no effect on any aspect of your care.

What will happen if I do take part?

As we do not know the best way of treating COPD patients with anxiety and depression we need to compare cognitive behavioural therapy (CBT) given by respiratory nurses who have been trained in this technique with standard care and advice you would normally have received if the study was not taking place. The results will help us decide which treatment is best. This leaflet will take you through what will happen step by step, including what each treatment would involve.

Step One: Randomisation

We need to make sure that the patients in each group are similar. The fairest way to do this, is to select which treatment a person gets randomly (by chance). This means neither you nor we get to choose which treatment you will receive. You will have a 50-50 chance of getting either treatment. Once you have agreed to enter the study, and have signed the consent form, a member of the research team will enter your details into a computer. The computer programme will allocate you to one of the two groups.

Step Two: Questionnaires

At the start of the study, we will ask you to fill in a questionnaire which contains three sub questionnaires about your health. The questionnaire will take you about 30 minutes to complete. This allows us to take a snapshot of how you are before treatment. We will also ask you to fill in the same questionnaire at 3, 6 and 12 months after you were randomised.

Step Three: Treatment and follow-up

Treatment One - CBT Group

The CBT treatment for this study has been specially designed for nurses working with respiratory patients. All of the nurses will be under the supervision of Dr Christine Baker who is a very experienced Cognitive Behavioural Therapist. Treatment involves:-

Attending an appointment in the outpatient clinic or at home every two weeks for a minimum of 2 visits and maximum of 6 visits.

These will be at the hospital or within the home if needed.

The first appointment will last up to 1 hour. The respiratory nurses will ensure you do not become overtired whilst having the CBT treatment.

Follow up visits will last for approximately 30 minutes.

The respiratory nurse will work with you to understand your current difficulties and develop strategies to help. These will be simple techniques, easy to learn and easy to carry out. For instance, making small changes to your routine or daily activities can help improve your mood and respiratory symptoms.

Written information on anxiety and depression will be provided to read.

If you consent we plan to video-tape 60 sessions. This part of the study is optional. If you do not wish to take part in the video you can still take part in the main study. The videos will be reviewed by an expert CBT professional to see how the therapist delivers the CBT. The video will film the therapist's face, your face will not be videoed. However it will record all that is spoken including your voice. The videos will be destroyed after 5 years of the end of the study.

We welcome any written or verbal feedback you have about your experience.

Finally at the end of the study we will access your records to see how often you have been admitted to hospital and what medication you are taking.

In summary, if you take part in this study and are allocated to this group you will need to attend the out-patient clinic (or have a home visit) between 2 – 6 sessions. The first session will last up to 60 minutes and the remaining sessions will last up to 30 minutes.

Treatment Two – Standard Care.

If you are allocated this group you will receive standard care which involves:-

Written information will be provided on anxiety and depression identical to that in the CBT group.

Your GP will be informed of the results from the anxiety and depression questionnaire, your participation in the study and the group you have been allocated to.

We welcome any written or verbal feedback you have about your experience.

Finally at the end of the study we will access your records to see how often you have been admitted to hospital and what medication you are taking.

In summary, if you take part in this study and are allocated to this group you will be required to complete four questionnaires, before allocation of the group and 3, 6 and 12 months later. We will provide a self -addressed envelope for you to ensure you are not out of pocket.

Expenses and Payments

Expenses will be reimbursed including car parking charges and taxi fares. A receipt may be required.

What do I have to do?

If you are willing to take part in the study, then what you have to do will depend on the group you are allocated to (as above). All patients involved in the study will be asked to complete a questionnaire at four time points. Both groups will receive written information on anxiety and depression. This information is important so filling in the questionnaires is an important part of you taking part in the study.

What are the possible disadvantages of taking part in the trial?

1. The main possible disadvantage from CBT is that it may hit on "sore spots" in your life which can be upsetting. Be assured:-

a. You will not be forced to talk about anything that you do not want to talk about. We will stop the session and give you time to consider if you would like to continue.

b. The respiratory nurses are very experienced in dealing with distress and difficulty. They will guide you through dealing with this issue, under the supervision of an experienced cognitive behavioural therapist.

c. If either of you feel that any area you have touched on is too much to deal with in CBT, then you will, as a first step, be able to talk it over with Karen Heslop, the cognitive behavioural therapist supervising the study or another member of the study team. You, your respiratory nurse and study team can then decide what the best course of action is.

No-one in our previous small study found the treatment distressing or difficult. But there are measures in place if you do.

2. The other disadvantage is that you may not get the treatment you want. Being randomised means not getting to choose. If it turns out, at the end of the study, that one treatment is better, we will let you know. If we find that CBT is the better treatment, we will offer it to you then.

3. We would need to inform your GP if you disclose information that may put you at risk e.g. if you feel so low that you feel suicidal. Obviously we would discuss this carefully with you.

Are there any side effects?

Cognitive behavioural therapy is a very practical therapy, one that works on how you manage problems in the here and now – what you do about them, or what you think about them. As it is about making practical changes in how you manage, some people can feel a very slight and temporary worsening of symptoms. For instance, if you were working on dealing with a particular worry, because you are focusing on it, you might feel a little more worried about it at first. Or if you work on managing your breathlessness or activities differently, you might feel a little more tired at first. This is a normal part of changing how we deal with things, and is only a temporary stage in feeling better.

What are the possible benefits of taking part?

In either treatment, your anxiety (and depression if you also suffer from this) is likely to improve. The main evidence we have for how people feel about CBT is from our small study, and the patients who took part in that were very positive about it. They liked the fact that they got practical help with other aspects of their life besides their breathing problem. You might find this useful too. However the main benefit could be for future patients suffering from this condition. Should one treatment emerge as superior to another, this study will help us to improve treatment options.

What happens if there is a problem?

If you have any concerns, you should first talk to your respiratory nurse. If this is not satisfactory, or you do not wish to do so, you can talk to a member of the research team on the number at the end of this leaflet. You may also raise your concerns with someone who is not involved in your care, the Patient Advice and Liaison Service (PALS) aims to advise and support patients, their families and carers and provide information on NHS services. This service is confidential and can be contacted on 0800 032 02 02. If you wish to complain formally in writing. You can do so by writing to Sir L R Fenwick CBT, Chief Executive, Newcastle Upon Tyne Hospitals NHS Trust, Freeman Hospital, High Hea-

ton, Newcastle upon Tyne NE7 7DN. To ensure patient safety and continual improvements any possible unsatisfactory standards noted during the conduct of the study will be investigated and where required reported to the relevant regulatory authorities.

What happens when the research study stops?

At the end of the study we will be in a position to say if one treatment is better than another. Should CBT be the best treatment, we will offer it to those in the standard care group. Data obtained during the study will be retained for 5 years.

Will my taking part in the trial be confidential?

Yes, all information will be confidential. Your notes for this study will be stored in a locked filing cabinet at the Royal Victoria Infirmary which only your respiratory nurse and the research team will have access to, all of whom are legally bound by codes of patient confidentiality. Any data relating to this trial which ends up being published will be anonymised, so no-one could identify you from it.

Involvement of my GP and/or referring doctor

It is standard practice for us to write to your GP and whoever referred you to the chest clinic, briefly describing your condition and intended care. Should you agree to enter the study, we will inform them of this, along with a brief description of the treatment you will be receiving.

What if new information becomes available about the treatment?

CBT has a very good track record of success. In the unlikely event that information arises from either this study or another source, to indicate a severe problem you will be informed immediately and we will stop the treatment.

What will happen if I do not want to carry on with the study?

You are free at any point to decide not to carry on with the study, and you do not need to tell us why. We would still like to know how you get on, and we will ask if you would still be prepared to still complete the questionnaire. You are, of course, free to refuse. Existing data already collected will be retained and used in the study.

What if I were harmed during the study?

It is highly unlikely that any harm could come to you in this study. It is possible that during the CBT treatment you may become upset. The respiratory nurses have all received training and have extensive experience caring for patients with COPD. We would discontinue the treatment and refer you to your GP if needed.

What will happen to the results of the study?

We will use the findings from this study to improve future treatment for your kind of condition. We will present our findings in academic journals and at conferences. We will also send you, at the end of the trial, a brief summary of our main findings. If the CBT treatment is proven to be beneficial you will be offered this if you received standard care. A thesis will be written at the end of the study and will be retained by Newcastle University but this will not contain any personal information about you.

Who is organising and funding the research?

This study is funded by the National Institute of Health Research. The research team combines researchers based at University of Newcastle and in the respiratory clinical teams at the Royal Victoria Infirmary and Freeman Hospital.

Who has reviewed the study?

Sunderland Local Research Ethics Committee has reviewed and approved this study.

What do I do now?

A member of the research team will contact you within 2 weeks to find out if you would like to participate in the study. Should you agree to continue, we will make an appointment for you to sign the consent form. After this you will be randomised and allocated to your treatment group.

Where can I get further information?

You contact a member of the research team on telephone 0191 2829095 or leave a message on the research team mobile/ answerphone 07920547420 and we will get back to you as soon as we are able. You may also email the lead researcher Karen Heslop on karen.heslop@nuth.nhs.uk.

Thank you for taking the time to read this leaflet.

Appendix 8 –Patient Consent

The Newcastle COPD CBT CARE Study

CONSENT FORM

Research Team: K. Heslop, Dr A De Soyza, Dr D Carrick-Sen, Dr C Baker & Dr G Burns

Please initial box

1. I confirm that I have read and understand the information sheet dated 21/02/2012 (version 1.3) 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 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.	
3. I understand that relevant sections of my medical notes and data collected during the study may be looked at by individuals from Newcastle Hospitals NHS Foundation Trust where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records/data.	
4. I agree to my GP being informed of my involvement in the study.	
5. I agree/do not agree (delete as appropriate) to the optional video recording aspect of the study.	
6. I agree to take part in this study.	
7. I would/ would not (delete as appropriate) like to receive a summary of the study findings.	

Name of participant Date Signature

Name of person taking consent Date Signature

Appendix 9- GP Letter

[Doctor]

[Address]

[Date]

Dear [Doctor]

Re [Patient, DOB, and Address]

The above patient currently attends Clinic under the care of

[Consultant]. [Patient] has agreed to participate in The Newcastle COPD CBT CARE Study. The purpose of the study is to identify if CBT delivered by respiratory nurses reduces symptoms of anxiety in patients with COPD. We are following patients up to 12 months after randomisation.

[Patient] has been screened for anxiety and depression using the Hospital Anxiety and Depression Scale and scored as probable anxiety. This patient has been randomised and allocated to the [intervention or control] group. The intervention group will undertake 2- 6 sessions of CBT either in the Chest Clinic, RVI or home setting. The control group will receive standard care which includes screening and written information on anxiety and depression. This patient is in active follow up for this study for 1 year and should not enter another interventional clinical trial during this time. If you require further information please do not hesitate to contact me on the number below.

Yours sincerely

Karen Heslop MSc
Nurse Consultant Respiratory Medicine
Tel 0191 – 2829095

Appendix 10 – Baseline data Collection Sheet

Study ID Number:			Telephone No:	
PIS / Consent: Y / N Postcode:				
Date of Baseline Assessment:				
First name			Surname	
Hospital Number			Consultant	
Gender M / F			DOB	
Marital Status (1 married, 2 Single, 3 divorced, 4 separated)				
Education Level 0 NVQ, 1 <GCSE, 2 GCSE, 3 A Level, 4 HNC/HND, 5 Diploma, 6 Degree:				
Occupation:				
HADS A:			HADS D:	
CAT Score:			EQ5D:	
MRC Dyspnoea Score 1-5:				
FEV1:	% Pred:	Ratio:	TLCO %:	O2 Sats:
Weight	Height	BMI		
Ethnic Group				
Pulmonary rehabilitation Y/N		SCA	Pack Years	
COPD Meds: SABA Y/N SAMA Y/N LABA Y/N LAMA Y/N ICS/LABA Y/N Muco Y/N PD4 Y/N Nebs Y/N Pre-pack Y/N Other Mediction				
Oxygen: 1 Short burst, 2 LTOT, 3 Ambulatory 4 None			Inhaler Technique Checked:	
Antidepressants: Y / N Anxiolytic: Y/N Diuretic: Y/N				
GP Letter sent: Y Consultant Letter: Y Entered onto database: Y Signature:				

Appendix 11 – CBT Supervision Record

Date: Attendee(s):

Duration: Venue:

Format: Individual ☐ Facilitated Group ☐ Peer Group ☐

Supervision Question(s)

Is there anything you want to recap/discuss from last session? What would you like to discuss to develop your skills? What has been difficult? What have you researched or observed?

Summary of key learning points (shared feedback)

What were the main things you learned today?

Individual reflection/action points (implications for practice development)

For example: How will you maximise today's learning? What will you put into practice, research observe or set out before the next supervision session?

Appendix 12 - Publications and Presentations

Publications and presentations completed since 2011 are presented below in table 69.

Table 69 - List of publications since commencement of PhD.

Title	Authors	Reference
Effectiveness of cognitive behavioural therapy (CBT) interventions for anxiety in patients with chronic obstructive pulmonary disease (COPD) undertaken by respiratory nurses: the COPD CBT CARE study: (ISRCTN5520695).	K. Heslop J. Newton C. Baker G. Burns D. Carrick-Sen A. De Soyza	BMC Pulmonary Medicine. 04/11/2013 Article URL http:www.biomedcentral.com/1471-2466/13/62
BTS Guideline on Pulmonary Rehabilitation in Adults.	CE Bolton EF Bevan-Smith J Blakey P Crowe S Elkin R Garrod NJ Greening K Heslop JH Hull WDC Mann MD Morgan D Proud CM Roberts L Sewell SJ Singh PP Walker S Walmsley	Thorax 2013 Volume 68 Supplement 2.
Psychological therapies for the treatment of anxiety disorders in chronic obstructive pulmonary disease (Protocol).	ZA Usmani KV Carson K Heslop AJ Esterman A De Soyza BJ Smith	The Cochrane Library Article URL http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD010673/pdf
Non-pharmacological treatment of anxiety and depression in COPD.	K Heslop	Nurse Prescribing 2014 Volume 12 No 1

Are We Missing Anxiety in People with Chronic Obstructive Pulmonary Disease (COPD)?	K Heslop-Marshall A De Soyza	Annals of Depression and Anxiety 2014; 1 (5):1023.
Cost savings in the provision of home oxygen for COPD.	C. Irving M Scott K Heslop	Nurse Prescribing 2015 Volume 13 No 6 p 278-281.
Effectiveness of self-management interventions on QOL and healthcare utilisation in people with COPD: meta- analysis with meta-regression.	JJ Newham K Heslop-Marshall B Hanratty E Kaner J Presseau	(In press – 2015)
Validation of the DECAF score to predict hospital mortality in acute exacerbations of COPD.	C Echevarria J Steer K Heslop-Marshall SC Stenton P Hickey R Hughes M Wijesinghe R Harrison N Steen A Simpson G Gibson	(In press – 2015)

Presentations

I have been invited to present at the following conferences. Conference presentations are listed in table 70.

Table 70– Conference presentations.

Title	Organisation	Date
The Newcastle COPD CBT Study.	North East Thoracic Society, Newcastle.	2012
CBT for patients with COPD.	National Respiratory Nurse Conference, Warwick.	2012
CBT for patients with COPD.	Department of Health- National NHS Innovations Conference, London.	2013
CBT for patients with COPD.	National Association of Respiratory Physiotherapists Conference, Leicester.	2013
Live National webinar on anxiety and depression	British Lung Foundation, London.	2013
CBT What it is and how it can help respiratory patients.	Nottingham Respiratory Conference, Nottingham.	2013
From CBT first aider to diploma, trainer and researcher. London	British Association of Cognitive Behavioural Therapists 41st Annual Conference, London.	2013
Innovations in the treatment of COPD.	Northern Association for Persistent Physical Symptoms (NAPPS), Newcastle.	2013
CBT- how can it help COPD Patients	Improving Access to Psychological Therapies (Insight) Northumberland Regional Service.	2014
CBT in COPD	Yorkshire Respiratory Nurse Conference, York.	2015
CBT in COPD	Yorkshire Thoracic Society, Leeds.	2015
Making progress in your clinical academic career.	NIHR conference Great North Museum, Newcastle. (Joint presentation)	2015
CBT made easy – changing lifestyle	Primary Care Respiratory Society-UK, Northampton.	2015

Poster Presentations.

A summary of moderated poster presentation can be found in table 71.

Table 71– Moderated Poster presentations since commencement of PhD

Title	Organisation	Year
Prevalence of anxiety and depression in 196 patients with chronic obstructive pulmonary disease (COPD).	European Respiratory Society Annual Congress. Vienna.	2012
Recruitment for psychological therapy in chronic obstructive pulmonary disease (COPD) Might we miss those who need us most.	European Respiratory Society Annual Congress. Barcelona.	2013
Prevalence of anxiety and patient characteristics from a randomised controlled trial (RCT) to identify if cognitive behavioural therapy (CBT) by respiratory nurses reduces anxiety in COPD.	British Thoracic Society Winter Conference. London. (Accepted for 2015).	2015

Webinar Presentation

I was invited to present a live webinar for the British Lung Foundation to increase awareness of psychological issues in COPD. This is listed in table 72.

Table 72 – Webinar presentations.

Title	Organisation	Year
National webinar on anxiety and depression in COPD.	British Lung Foundation, London.	2013

Awards

The CBT service has been nominated for several awards which are listed in table 73.

Table 73 –Award Nominations.

Title	Outcome	Year
Nursing Times Respiratory Award for CBT service.	Highly commended service.	2012
Nursing Times Respiratory Award for CBT service.	Shortlisted.	2013
Royal College of Nursing –Nursing Standard Awards. Respiratory Award for CBT service.	Shortlisted.	2014
Royal College of Nursing –Nursing Standard Awards. Nurse of the Year category.	Nominated.	2014
British Journal of Nursing –Innovation Award.	2nd Place.	2015

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