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## Breathing New Life: Investigating ways to improve the mental health of people living with chronic obstructive pulmonary disease in Western Australia

Tina Phan  
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**Breathing New Life: Investigating ways to improve the mental  
health of people living with chronic obstructive pulmonary disease  
in Western Australia**

**Tina Phan**

BHlthSc (UWA),  
BSc (PubHlth) (Hons) (Curtin)

This thesis is presented for the award of Doctor of Philosophy

Edith Cowan University  
School of Medical and Health Sciences  
Western Australia

2018

**Principal supervisor:** Prof. Mel Ziman

**Associate supervisors:** Dr. Natalie Strobel, Dr. Owen Carter and Prof. Grant Waterer

## DECLARATION

I certify that this thesis does not, to the best of my knowledge and belief:

- (i) incorporate without acknowledgement any material previously submitted for a degree or diploma in any institution of higher education;
- (ii) contain any material previously published or written by another person except where due reference is made in the text; or
- (iii) contain any defamatory material.

.....

**Tina Phan**

20 November 2017

## ACKNOWLEDGEMENTS

Like many students before me, my thesis had its ups and downs and was a rollercoaster full of emotions. Whilst the purpose of the PhD journey was to teach me about the scientific process, it taught me far more valuable lessons about my character and of my limitations and capabilities. Patience, persistence, determination and resilience got me over the finish line. At the time it seemed like an eternity, yet when I reflect back on my candidature, my voyage has passed by in the blink of an eye. I have many people to thank for their support and guidance whilst walking this path with me...

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understand, I cannot thank you enough for your unwavering love and support throughout my PhD. You shared my excitement for the wins and comforted me during hard times. You told me to never give up and were constantly proud of my efforts. I love you so much and cannot wait to see what the future has in store for us.

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Most importantly, to all the Breathing New Life participants—thank you to each and every one of you that gave up your time to contribute to this research. I made close connections with a lot of you and it was a privilege to be involved in your care. Over many a cup of tea, you taught me about the harsh reality of living with the debilitating nature of COPD. This thesis is dedicated to you so that we may one day find a cure.

Finally, all this work could not have been possible without the monetary support from The Government of Western Australia, Department of Health [Grant number G1000794]. Thank you.

## MY CONTRIBUTION TO PUBLICATIONS

### PUBLICATION 1

**Phan T**, Carter O, Waterer G, Chung L, Hawkins M, Rudd C, Ziman M & Strobel N. Determinants of concomitant anxiety and depression in people with chronic obstructive pulmonary disease. Journal of Psychosomatic Research. (Submitted for review on 2 October 2017). (Chapter Three of this thesis).

“I, Tina Phan, contributed to study innovation and design, data collection, analysis and write-up for publication to an extent no less than 50% of the total work conducted to the paper/publication entitled “Determinants of concomitant anxiety and depression in people with chronic obstructive pulmonary disease”.

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Date: 5 September 2017

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Date: 11 September 2017



Maxine Hawkins:

Date: 21 September 2017

Cobie Rudd:

Date: 6 November 2017

Mel Ziman:

Date: 4 September 2017

Natalie Strobel:

Date: 4 September 2017

## **PUBLICATION 2**

**Phan T**, Carter O, Adams C, Waterer G, Chung L, Hawkins M, Rudd C, Ziman M & Strobel N. (2015) Discriminant validity of the Hospital Anxiety and Depression Scale, Beck Depression Inventory (II) and Beck Anxiety Inventory to confirmed clinical diagnosis of depression and anxiety in patients with chronic obstructive pulmonary disease. *Chronic Respiratory Disease*. 2016;13(3):220-228. (Chapter Four of this thesis).

“I, Tina Phan, contributed to study innovation and design, data collection, analysis and write-up for publication to an extent no less than 50% of the total work conducted to the paper/publication entitled “Discriminant validity of the Hospital Anxiety and Depression Scale, Beck Depression Inventory (II) and Beck Anxiety Inventory to confirmed clinical diagnosis of depression and anxiety in patients with chronic obstructive pulmonary disease”.

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Mel Ziman:

Date: 4 September 2017

Natalie Strobel:

Date: 4 September 2017

### **PUBLICATION 3**

**Phan T**, Carter O, Waterer G, Chung L, Hawkins M, Rudd C, Ziman M & Strobel N.

A randomised controlled trial investigating the efficacy of cognitive behavioural therapy on the mental health of people with chronic obstructive pulmonary disease: the 'Breathing New Life' study. *Trials*. (Submitted for review on 21 May 2017). (Chapter Five of this thesis).

"I, Tina Phan, contributed to study innovation and design, data collection and analysis and write-up for publication to an extent no less than 50% of the total work conducted to the paper/publication entitled "A randomised controlled trial investigating the efficacy of cognitive behavioural therapy on the mental health of people with chronic obstructive pulmonary disease: the 'Breathing New Life' study".

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#### **PUBLICATION 4**

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A qualitative investigation of the facilitators and barriers for people with chronic obstructive pulmonary disease to participate in cognitive behavioural therapy. Journal of Health Psychology. (Submitted for review on 13 November 2017). (Chapter Six of this thesis).

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Date: 4 September 2017

## **ABSTRACT**

Anxiety and depression are common comorbidities in people with chronic obstructive pulmonary disease (COPD), contributing to greater morbidity and mortality in an already vulnerable population. Despite the prevalence, few recommendations exist in global management guidelines for the detection and treatment of these comorbidities, reflecting the limited literature available on effective strategies for dealing with mental health issues in COPD populations. There is promising evidence that cognitive behavioural therapy (CBT) improves mental health outcomes in people with COPD. However, investigational studies have commonly reported participants' lack of transport, lack of time and illness as barriers to recruitment and successful completion. This thesis was undertaken in response to a need identified in the literature for an alternative modality of CBT delivery for people with COPD suffering from psychological symptomatology. Thus, a novel home-based self-management CBT learning resource in a DVD format was developed with an accompanying manual. To investigate the primary aim of this thesis, a randomised controlled trial called the 'Breathing New Life' study was conducted to determine the efficacy of CBT to treat anxiety and depression in people living with COPD via two formats: group therapy with a reduced number of sessions or this novel home-based self-management DVD resource, compared to usual care. The secondary aim was to investigate the efficacy of these interventions on improvement in health-related quality of life (HRQoL).

This thesis is presented as a series of papers (i.e. PhD with publication) from data collected from the Breathing New Life study (ACTRN12616001039471). Study One



investigates the risk factors associated with concomitant anxiety and depression and found younger age and having no previous psychological medical history were risk factors for psychological symptomatology compared to those without psychological symptomatology. Study Two investigates the most suitable screening tool for detecting clinically significant anxiety and depression in COPD populations and found simple modifications to the commonly used Hospital Anxiety and Depression Scale (HADS) improved optimal sensitivity and specificity, whilst the Beck Inventories had acceptable sensitivity and specificity without any modifications. Study Three reports the results from the randomised controlled trial investigating the efficacy of CBT delivered in the two different formats. No significant differences over time between those receiving CBT and usual care for anxiety, depression or HRQoL were found in this COPD cohort. However, opinions of benefit expressed in Study Four—a qualitative investigation into the facilitators and barriers COPD participants face when enrolling and completing CBT—provide support that this population find CBT useful, despite being unable to detect any measureable difference.

Globally, this thesis adds new knowledge to the body of literature supporting the importance of early screening and treatment for psychological symptomatology in people living with COPD. Despite the inability of CBT to improve anxiety and depression, findings from this thesis have important implications towards industry discussion surrounding routine screening for concomitant anxiety and depression, the continued use of the HADS and Beck Inventories as appropriate screening tools in COPD populations and how best to engage and retain COPD participants in CBT.

## PUBLICATION LIST

This thesis is submitted as a series of papers.

As a result of the work performed for this thesis, four papers have been

published/submitted for publication:

(in order presented in thesis)

1. **Phan T**, Carter O, Waterer G, Chung L, Hawkins M, Rudd C, Ziman M & Strobel N. Determinants of concomitant anxiety and depression in people with chronic obstructive pulmonary disease. *Journal of Psychosomatic Research*. (Submitted for review on 2 October 2017) (Chapter Three of this thesis).
2. **Phan T**, Carter O, Adams C, Waterer G, Chung L, Hawkins M, Rudd C, Ziman M & Strobel N. Discriminant validity of the Hospital Anxiety and Depression Scale, Beck Depression Inventory (II) and Beck Anxiety Inventory to confirmed clinical diagnosis of depression and anxiety in patients with chronic obstructive pulmonary disease. *Chronic Respiratory Disease*. 2016;13(3):220-228. (Chapter Four of this thesis).
3. **Phan T**, Carter O, Waterer G, Chung L, Hawkins M, Rudd C, Ziman M & Strobel N. A randomised controlled trial investigating the efficacy of cognitive behavioural therapy on the mental health of people with chronic obstructive pulmonary disease: the 'Breathing New Life' study. *Trials*. (Submitted for review on 21 May 2017) (Chapter Five of this thesis).

4. **Phan T**, Carter O, Waterer G, Chung L, Hawkins M, Rudd C & Strobel N. A qualitative investigation of the facilitators and barriers for people with chronic obstructive pulmonary disease to participate in cognitive behavioural therapy. *Journal of Health Psychology*. (Submitted for review on 13 November 2017) (Chapter Six of this thesis).

Please note the formatting and reference style within the following chapters does not coincide with the published (or in review) manuscripts as they have been modified from the journals' preferred styles to provide consistency throughout this thesis. However, the content of the text, tables, figures and references have not been altered in any way.

## OTHER RESEARCH OUTPUTS

### CONFERENCE PRESENTATIONS

1. **Phan T**, Carter O, Waterer G, Chung L, Hawkins M, Rudd C, Ziman M & Strobel N.  
Investigating the efficacy of cognitive behavioural therapy on improving the mental health of chronic obstructive pulmonary disease patients: a randomised control trial – poster presentation. Congress of Asian Pacific Society of Respiriology, Kuala Lumpur, 4 December 2015.
2. **Phan T**, Carter O, Adams C, Waterer G, Chung L, Hawkins M, Rudd C, Ziman M & Strobel N. Discriminant validity of screening measures to confirmed clinical diagnosis of depression and anxiety in patients with chronic obstructive pulmonary disease (COPD) – poster presentation. Congress of Asian Pacific Society of Respiriology, Kuala Lumpur, 4 December 2015.
3. **Phan T**, Carter O, Waterer G, Hawkins M, Chung L, Rudd C, Ziman M & Strobel N.  
Investigating the efficacy of cognitive behavioural therapy on improving the mental health of chronic obstructive pulmonary disease patients: a randomised control trial. The Thoracic Society of Australia and New Zealand Annual Scientific Meeting, Gold Coast, 31 April 2015.
4. **Phan T**, Strobel N, Carter O, Waterer G, Hawkins M, Chung L, Rudd C & Ziman M.  
Anxious and depressive symptomatology in chronic obstructive pulmonary disease patients (COPD). Public Health Association of Australia Annual Conference, Perth, 16 September 2014.

5. **Phan T**, Strobel N, Carter O, Waterer G, Hawkins M, Chung L, Rudd C & Ziman M. Anxiety and Depression in People Living With Chronic Obstructive Pulmonary Disease in Western Australia: Preliminary Results. Australian Society for Medical Research Western Australian Scientific Symposium conference, Perth, 5 June 2013.

#### **SEMINAR PRESENTATIONS**

1. **Phan T**, Ziman M, Strobel N, Carter O & Waterer G. Breathing New Life: Investigating Ways to Improve the Mental Health of People Living with Chronic Obstructive Pulmonary Disease in Western Australia. Lung Information and Friendship for Everyone Support Group Meeting, Perth, 1 November 2017.
2. **Phan T**, Ziman M, Strobel N, Carter O & Waterer G. Breathing New Life: Investigating Ways to Improve the Mental Health of People Living with Chronic Obstructive Pulmonary Disease in Western Australia. Sir Charles Gairdner Hospital, Pulmonary Physiology Department, Perth, 13 October 2014.

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1. 2015 Book Award, Asian Pacific Society of Respiriology—International Association for the Study of Lung Cancer

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1. Thoracic Society of Australia and New Zealand Travel Grant, 2015 (\$520)

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## LIST OF ABBREVIATIONS

Abbreviation	Definition
BAI	Beck Anxiety Inventory
BDI	Beck Depression Inventory
CBT	Cognitive behavioural therapy
CI	Confidence interval
COPD	Chronic obstructive pulmonary disease
GOLD	Global Initiative for Chronic Lung Disease
HADS	Hospital Anxiety and Depression Scale
HRQoL	Health-related quality of life
SGRQ	Saint George's Respiratory Questionnaire
UC	Usual care

## **CHAPTER ONE**

### **1 INTRODUCTION**

#### **1.1 COPD**

Chronic obstructive pulmonary disease (COPD) is typically a progressive lung disease defined by persistent airflow limitation, classically caused by an enhanced chronic inflammatory response of the respiratory system to noxious particles or gases. Prolonged exposure to inhaled irritants is the most common cause of developing COPD, with the primary risk factor being exposure to tobacco smoke. Indoor air pollution (e.g. fuels used for cooking and heating) and having a genetic predisposition (most commonly an alpha-1 antitrypsin deficiency) have also been identified as major risk factors. The characteristic symptoms of COPD include dyspnoea, chronic cough and sputum production (1). Prolonged exposure to inhaled irritants results in an influx of inflammatory cells such as neutrophils, macrophages and CD8+ T-lymphocytes which then initiates an inflammatory cascade that activates the release of cytokines, including tumour necrosis factor alpha, interferon gamma, interleukins (IL-1, IL-6, IL-8), C-reactive protein, matrix-metalloproteinases (MMP-6, MMP-9) and fibrinogen (2). These processes sustain the amplified chronic inflammatory response observed in COPD which results in a combination of parenchymal tissue damage (emphysema), mucociliary dysfunction and numerous structural changes in the lung (obstructive bronchiolitis), propagating airflow limitation (2, 3).

COPD is a leading cause of morbidity and mortality worldwide; it is currently estimated that 65 million people suffer from moderate to severe COPD. Although COPD is a preventable disease, it is predicted to become the third leading cause of death globally by 2030 (4). In Australia, one in five persons over the age of 45 have COPD and the latest data available from 2014 estimated 7,025 deaths eventuated as a result of this comorbidity—making COPD the fifth leading cause of death (5). However, it is often argued the prevalence of COPD is underestimated for a number of reasons, including: the slow nature of COPD development delaying diagnosis until people exhibit moderate symptoms, experience exacerbations or become disabled; misdiagnosis as asthma; and people mistaking their COPD symptoms as signs of ageing or lack of fitness (6).

## **1.2 The problem**

Whilst COPD primarily affects the airways and lungs, it also has significant systemic consequences which affect quality of life and survival (1, 7). People living with COPD may also suffer from co-morbid cardiovascular disease, osteoporosis, lung cancer, sleep-related breathing disorders as well as metabolic syndrome and diabetes (1). These comorbidities may develop independently of a diagnosis of COPD, be related to the disease via similar risk factors or one disease increases the risk of developing another. A major non-systemic comorbidity people with COPD may experience is psychological distress, in particular anxiety disorders and depression—estimated to occur in 36% and 40% of people with COPD, respectively (8-10). Research indicates COPD populations are at a higher risk of developing these psychological comorbidities

than the general population and those with other chronic diseases such as cardiovascular disease and renal disease (9, 11-13). People with COPD suffering from anxiety or depression have poorer outcomes across a number of health domains, including: increased exacerbation rates (14-16); diminished exercise performance and functional mobility (11, 14, 17); poorer health-related quality of life (HRQoL) (16-18); more emergency hospital visits, hospitalisations and lengths of stay as an admitted patient (11, 16, 19) and greater mortality rates (11, 20, 21). Consequently, people with COPD that also suffer from anxiety or depression are a greater economic burden than those that do not have any psychological symptomatology (22-24).

Despite this public health problem, there are few recommendations in the Global Initiative for Chronic Obstructive Lung Disease (GOLD) management guidelines for the treatment of these psychological comorbidities, reflecting the limited literature available on the efficacy of treatment options (1). There is promising evidence to suggest cognitive behavioural therapy (CBT) improves mental health outcomes in COPD populations (25-38). CBT is a psychological intervention generally run over 12 weeks, conducted face-to-face individually or in groups which aims to change the distorted, unrealistic thinking and negative behaviour patterns thought to contribute to psychological symptomatology (39-42). However, an ongoing problem with CBT intervention studies in COPD populations are the low recruitment rates of 13–49% (28, 31, 35, 36, 43) and high attrition rates of 27–47% often reported (28, 32, 44). Possible solutions could be to reduce the number of face-to-face group CBT sessions or to eliminate the necessity for attending face-to-face sessions. However, there is a need to

build upon the limited data currently available to establish the effectiveness of home-based, self-management CBT programs for improving anxiety and depression in people with COPD. Furthermore, as few studies report the reasons why participants drop out of CBT, an exploration of the facilitators and barriers people with COPD face with this type of therapy is warranted to help better explain and improve the rate of uptake and completion of CBT.

The GOLD guidelines also lack clear recommendations on how to identify anxiety and depression in people with COPD. This has important implications for the timely identification and treatment required to reduce the additional morbidity and mortality these comorbidities have on an already vulnerable population. The Hospital Anxiety and Depression Scale (HADS), the Beck Anxiety Inventory (BAI) and the Beck Depression Inventory (BDI-II) are commonly used screening tools to assess the presence of psychological symptomatology in people with COPD. However, the HADS has only been validated for use in this population in two previous studies (45, 46), whereas no previous studies have validated the Beck Inventories, prompting the need for an investigation into the suitability of these measures in COPD populations.

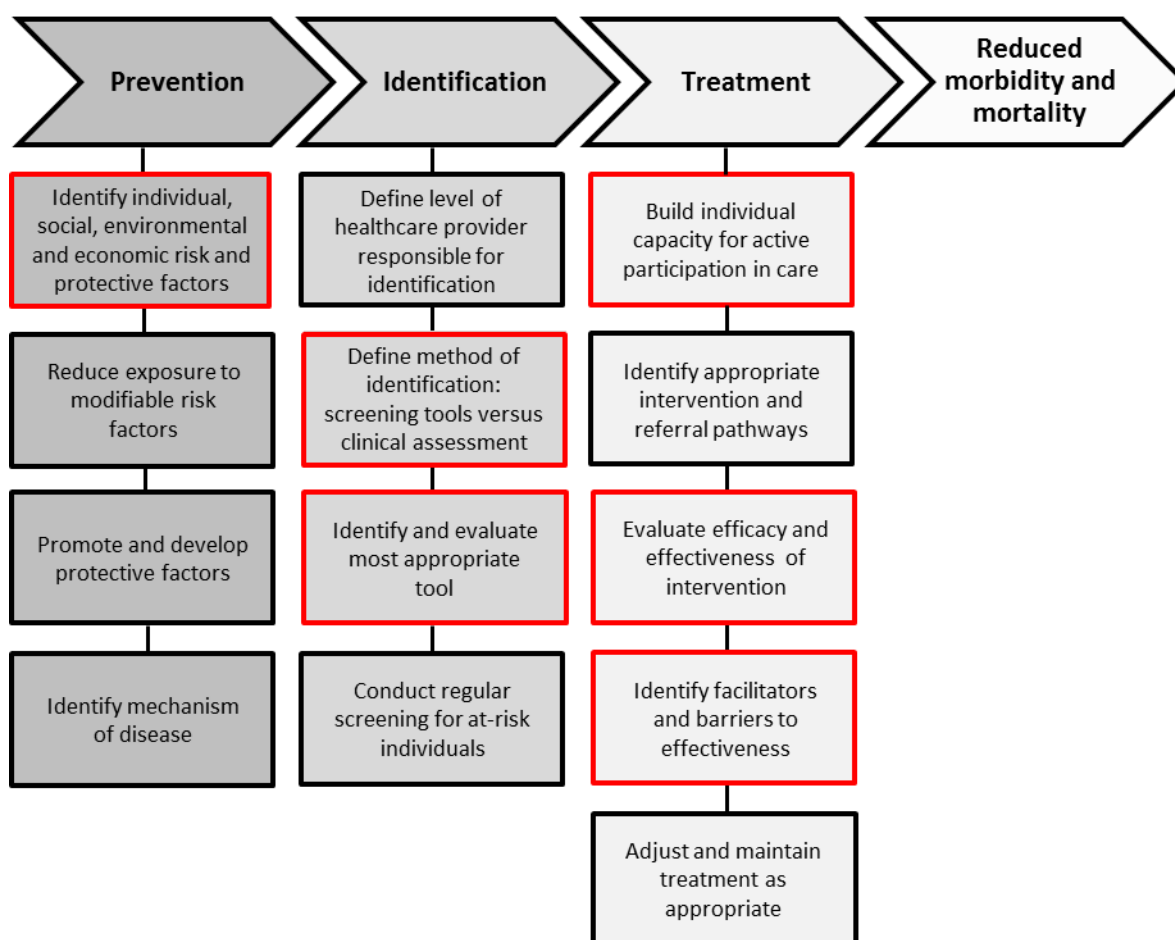
Whilst early detection is vital for early intervention, preventing the onset of anxiety and depression in people with COPD in the first place is a fundamental public health approach to reduce the health services required to ameliorate the morbidity and mortality associated with these comorbidities. This involves reducing exposure to modifiable risk factors for psychological symptomatology as well as enhancing the



protective factors that promote good mental health and wellbeing. Despite the known benefits of prevention, the GOLD guidelines do not specify any strategies to decrease the incidence of anxiety and depression in people with COPD.

### **1.3 Research aims**

The research conducted for this thesis aimed to add evidence to each stage of the conceptual framework (Figure 1.1) used by allied health professionals to improve the morbidity and mortality associated with anxiety and depression in COPD populations. This thesis primarily sought to investigate the efficacy of CBT in addition to usual care for the treatment of anxiety and depression in people living with COPD, compared to usual care alone (UC). CBT was delivered via a traditional group therapy format (CBT) with a reduced number of face-to-face sessions relative to previous programs (25, 27-34, 44, 47, 48), or a home-based self-management DVD format (DVD), with efficacy of both assessed by the level of psychological symptomatology. A randomised controlled trial was conducted (hereafter referred to as the 'Breathing New Life' study) to investigate this primary aim. The secondary aim of this thesis was to investigate the efficacy of these CBT interventions to improve HRQoL relative to usual care. This thesis also sought to investigate the risk factors associated with psychological symptomatology, the most suitable tool(s) for screening anxiety and depression and to explore participants' experiences of CBT to understand the enablers and disablers for people with COPD to successfully enrol and complete a course.



\*Note: investigations conducted in this thesis are outlined in red

**Figure 1.1** A conceptual framework (developed by the candidate) for reducing disease-related morbidity and mortality

## 1.4 Thesis outline

This thesis is presented as a series of papers addressing the research aims utilising data collected from the Breathing New Life study (Clinical Trial Registration Number: ACTRN12616001039471). Edith Cowan University (ECU) supports the submission of PhD theses that comprise a series of papers prepared for publication. ECU's *Requirements of a Thesis with Publication*, 2017 guidelines outline that the submitted

thesis can consist of publications that have already been published, are in the process of being published, or a combination of these (49). These guidelines also state that the number of publications submitted will vary between disciplines and projects, but should be sufficient for the body of work to constitute a substantial and original contribution to knowledge (49).

This structure has been adopted by the candidate in the submission of this thesis. As such, while the theory linking the studies/papers should be clear for the examiner, each study must be stand-alone in content. Consequently, theses submitted as a series of papers sometimes suffer from repetition of literature and methodology from study to study.

#### **1.4.1 Study One**

##### *Determinants of concomitant anxiety and depression in people with chronic obstructive pulmonary disease*

The primary aims of this study were to investigate the prevalence and determinants of concomitant anxiety and depression in people diagnosed with COPD. It was predicted previous risk factors identified separately for anxiety or depression in people with COPD were also shared risk factors for concomitant anxiety and depression. The risk factors found for this COPD cohort adds to the limited data available on potential protective factors to concomitant psychological symptomatology.

#### **1.4.2 Study Two**

*Discriminant validity of the Hospital Anxiety and Depression Scale, Beck Depression Inventory (II) and Beck Anxiety Inventory to confirmed clinical diagnosis of depression and anxiety in patients with chronic obstructive pulmonary disease*

The aims of this study were to investigate the discriminant validity of the Hospital Anxiety and Depression Scale (HADS) with people diagnosed with COPD, and to examine the discriminant validity of the Beck Depression Inventory (BDI-II) and Beck Anxiety Inventory (BAI) as potential alternatives for this population. It was predicted the BDI-II and BAI may be better alternatives for screening people with COPD for psychological symptomology than the HADS. As there are limited data currently available on the validity of commonly used screening tools for psychological symptomatology in people with COPD, the information gathered from this research adds to the body of literature and provides a foundation for recommendations on the most appropriate tool(s).

#### **1.4.3 Study Three**

*A randomised controlled trial investigating the efficacy of cognitive behavioural therapy on the mental health of people with chronic obstructive pulmonary disease: the 'Breathing New Life' study*

The primary aim of this study was to investigate the efficacy of CBT in addition to usual care, to reduce anxiety and depression symptomatology in people living with COPD. CBT was provided via a traditional group therapy format (CBT) with a reduced number of sessions relative to previous programs, or a home-based self-management DVD

format (DVD), compared to usual care alone (UC). The secondary aim was to investigate the subsequent effect of these CBT interventions on HRQoL.

The study hypotheses were:

- People with COPD receiving either format of CBT intervention would demonstrate lower rates of anxiety and depression symptoms after 12 months compared to participants in the usual care group (UC). Moreover, the DVD group would have higher compliance rates during the intervention period than the face-to-face CBT group due to the more convenient nature of the DVD resource
- COPD participants in either CBT interventions would also demonstrate improvements in HRQoL compared to participants in the UC group

There is currently no consensus which is the most effective treatment for anxiety and depression in people with COPD. However, there is emerging data on the effectiveness of home-based self-management programs. This research investigated the efficacy of a novel self-management CBT resource to treat anxiety and depression, in the hopes that the DVD could eventually become a stand-alone resource.

#### **1.4.4 Study Four**

*A qualitative investigation of the facilitators and barriers for people with chronic obstructive pulmonary disease to participate in cognitive behavioural therapy*

The aim of this study was to investigate the facilitators and barriers to successful completion of CBT, delivered either as traditional face-to-face group sessions or a home-based self-management DVD resource. The information gathered from the first-known qualitative investigation of the enablers and disablers for COPD participants towards CBT will help future studies optimise development of their CBT interventions to improve future uptake and retention in order to ultimately improve mental health outcomes in people with COPD.

## **CHAPTER TWO**

### **2 REVIEW OF THE LITERATURE**

#### **2.1 Anxiety and depression**

Anxiety is an emotion characterised by somatic symptoms of tension and behavioural disturbances due to the apprehensive anticipation of future danger or misfortune. The Diagnostic and Statistical Manual of Mental Disorders (5<sup>th</sup> edition, DSM-V) defines the types of anxiety disorders as follows: separation anxiety disorder, selective mutism, specific phobia, social anxiety disorder, panic disorder, panic attack specifier, agoraphobia, generalised anxiety disorder, substance/medication-induced anxiety disorder, anxiety disorder due to another medical condition, other specified anxiety disorder and unspecified anxiety disorder (50). Whilst each specific anxiety disorder has slightly different symptoms, they all share the common themes of excessive, irrational fear and dread (50). In Australia, the latest figures from the 2014–2015 National Health Survey report the 12 month prevalence of anxiety-related conditions to be 11.2% (2.6 million people) (51).

Depression is “the presence of sad, empty or irritable mood, accompanied by somatic and cognitive changes that significantly affect the individual’s capacity to function” (p155) (50). The Diagnostic and Statistical Manual of Mental Disorders (5<sup>th</sup> edition, DSM-V) defines the types of depressive disorders as follows: disruptive mood dysregulation disorder, major depressive disorder, persistent depressive disorder (dysthymia), premenstrual dysphoric disorder, substance/medication-induced

depressive disorder, depressive disorder due to another medical condition, other specified depressive disorder, and unspecified depressive disorder (50). What differs amongst the depressive disorders are specifications of duration, timing or presumed aetiology (50). The Australian 2014–2015 National Health Survey reports the 12 month prevalence of mood disorders (which includes depression) as 9.3% (2.1 million people) (51). It is estimated approximately one in twenty Australians (5.1%) have both an anxiety-related condition and a mood disorder (51).

## **2.2 Negative impact of anxiety and depression**

People with chronic obstructive pulmonary disease (COPD) suffering from anxiety and depression have poorer health outcomes compared to those without these psychological comorbidities. Further adding to the debilitating nature of COPD, people with anxiety and depression symptomatology experience more frequent exacerbations (14-16); reduced functional mobility and exercise performance (e.g. less laps achieved during the six-minute walk distance test) (11, 14, 17); poorer health-related quality of life (HRQoL) (16-18); increased hospital emergency department visits, increased hospital admissions and increased lengths of hospital stays (11, 16, 19); and greater mortality rates (11, 20, 21). In addition, people with COPD that suffer from psychological symptomatology are also a greater economic burden through increased expenditure to health and welfare systems, and lost productivity due to lower employment, absenteeism and premature death (22-24). Early detection of anxiety and depression in people with COPD is essential in order to appropriately manage the



comorbidities at the earliest possible stages to reduce the already high rates of morbidity and mortality in people with COPD.

### **2.3 Risk factors**

Several risk factors have been identified to increase the likelihood of developing anxiety or depression symptomatology in people with COPD. Shared risk factors for either anxiety or depression commonly reported in the literature include severe dyspnoea, poor HRQoL, smoking, lower education levels, lower socioeconomic status and having other non-psychological comorbidities (52-55). Other determinants commonly but inconsistently reported include age (some studies suggesting younger COPD populations, whilst others suggest older COPD populations are at greater risk), being female, having lower values for forced expiratory volume (FEV<sub>1</sub>) and greater severity of COPD (52-54, 56-59). Unique determinants associated with depression include living alone and not being married (53, 54). There appear to be no unique risk factors that contribute to people with COPD having anxiety symptomatology alone. However, there are limited data available on risk factors associated with concomitant anxiety and depression in people with COPD. It would be reasonable to assume that the majority of the risk factors identified in the literature for anxiety or depression are also shared risk factors for concomitant anxiety and depression but this remains to be determined.

## 2.4 Prevalence

The estimated prevalence of anxiety and depression in people with COPD varies greatly, with estimates for anxiety ranging anywhere from 2–96% and from 8–88% for depression (9, 60-63). A meta-analysis of reported prevalence of anxiety disorders and depression in COPD patients, conducted by Yohannes *et al.* (2010) calculated a standard measure of effect size for n=13 previous studies and used weighted pooled estimates to suggest a mean prevalence of 36% for anxiety and 40% for depression can be used as a clinical benchmark of prevalence estimates in people with COPD (10). The majority of studies included in the meta-analysis used self-report screening tools rather than diagnostic clinical interviews.

Another systematic review (n=10 included studies) reported the prevalence of clinical anxiety to be 10–55% amongst COPD in-patients and 13–46% amongst out-patients (62). The greatest strength of this review is that all the included studies diagnosed anxiety disorders via a clinical interview using a recognised, industry standard format (DSM-IV or previous versions or International Classification of Disease and Related Health Problems, 10<sup>th</sup> edition (ICD-10)). For depression, a systematic review found that those with COPD had a higher prevalence of depressive symptoms than healthy controls; 24.6% (95% CI: 20.0–28.6%) in COPD patients compared to 11.7% (95% CI: 9.0–15.1%) in controls (63). The strength of this review was that a comprehensive meta-regression analysis and subgroup effect size analysis was performed to determine the prevalence of depression. However, limitations of this review include

the fact that depression was assessed by a variety of measures rather than via diagnostic clinical interviews, and the number of studies included was small (n=8).

The large variation in data may be attributed to a number of methodological discrepancies. Method of psychiatric diagnoses vary greatly, with the majority of studies utilising self-report questionnaires as opposed to diagnostic clinical interviews. An overlap between somatic symptoms of anxiety and depression with those of COPD also complicates diagnoses. Screening measures used to detect depression in the elderly may be less precise due to the overlap of somatic symptoms and those that occur due to the ageing process. Furthermore, differing degrees of COPD severity, differing study settings (e.g. clinical populations vs. community based patients) and sample sizes all contribute to the variations in prevalence figures.

In Australia, there is a paucity of data available on the prevalence of anxiety and depression in people with COPD. To date, only three published studies have investigated the prevalence of these comorbidities. The first, by Livermore *et al.* (2010) reports that 19% of participants (n=10 out of 52) were clinically diagnosed with panic attacks, 17% of participants (n=9 out of 52) with panic disorder and 4% with major depression using the Anxiety Disorders Interview Schedule of the DSM-IV (ADIS-IV) (33). Panic attacks and panic disorder fall under the larger umbrella of anxiety disorders, but do not represent all other types of anxiety disorders in Australia. The second study by Doyle *et al.* (2013) screened for anxiety and depression using the self-report Hospital Anxiety and Depression Scale (HADS) and found 27.2% of participants

reported symptoms for anxiety and 20.4% reported symptoms for depression (64). The last study by Walters *et al.* (2013) also utilised the HADS and found 40% of participants reported symptoms of anxiety and 20% reported symptoms of depression (36). Although there are large variations in the prevalence of anxiety and depression in all three studies, these Australian rates fall within the scope of other international estimates (9, 60-63).

## **2.5 Screening for anxiety and depression**

A wide range of measures have been reported in the literature for detecting the presence of anxiety or depression in people with COPD (Table 2.1). The majority of these measures are self-report screening tools which identify the presence of clinically significant levels of anxiety or depression symptomatology. A clinical diagnosis of anxiety or depression is determined via a structured clinical interview which meets The Diagnostic and Statistical Manual of Mental Disorders or the International Classification of Diseases and Related Health Problems criteria. The distinction between the types of measures used in the literature is important, as the majority of studies examining the prevalence of anxiety and depression in people with COPD have utilised self-report measures which indicate rates of clinically significant distress levels rather than provide an actual clinical diagnosis through a psychologist or psychiatrist. Benefits of using self-report questionnaires include the low costs involved, the relatively short time it takes to complete, either patients or health service providers can complete the questionnaires, the questionnaires are extremely easy to administer, and they can be adapted and validated for specific populations. However, a

disadvantage of using self-report measures is the potential for inflated misdiagnosis due to the overlap of somatic symptoms typical of COPD with those of anxiety or depression. Narrow time-frames for reporting of symptoms (e.g. over the past week or two weeks) are also a limitation of these types of measures as psychological conditions can be missed.

The current Global Initiative for Chronic Obstructive Lung Disease (GOLD) management guidelines lack recommendations for the screening and treatment of psychological comorbidities in people with COPD (1). Consequently, screening for mental health symptomatology in COPD populations has not become standard practice and there is a lack of consensus with respect to the most appropriate tool/s for measurement of these symptoms. This is likely to result in a lack of timely and effective treatment for those suffering from these comorbidities. The GOLD guidelines do acknowledge the “Hospital Anxiety and Depression Scale (HADS) and the Primary Care Evaluation of Mental Disorders (PRIME-MD) Patient Questionnaire [screening tools] have been used to improve identification and treatment of anxious and depressed patients” (p90) (1). Indeed the HADS is one of the most commonly cited screening tools used in COPD studies (11, 16, 19, 41, 45-47, 56, 65-74) but only two published papers have established its validity for use in this population (45, 46). The Beck Anxiety Inventory (BAI) and Beck Depression Inventory (BDI-II) are also popular screening tools commonly used in the literature to measure anxiety or depression respectively (26-28, 31, 32, 37, 48).

**Table 2.1** Diagnostic and screening measures used to detect anxiety and depression in people with COPD

Structured Clinical Interviews
Anxiety Disorders Interview Schedule (ADIS)
Composite International Diagnostic Interview (CIDI)
Diagnostic Interview for Psychiatric Disorders (DIPS)
Geriatric Mental State Schedule (GMS)
International Statistical Classification of Diseases and Health Related Problems (ICD)
Mini International Neuropsychiatric Interview (MINI)
Structured Clinical Interview for DSM Disorders (SCID)
World Mental Health Composite International Diagnostic Interview (WMH-CIDI)
Screening Measures
<b><i>Anxiety and Depression</i></b>
Edmonton Symptom Assessment Scale (ESAS)
Geriatric Mental State Schedule
Hospital Anxiety and Depression Scale (HADS)
Kellner's Symptom Questionnaire (SQ)
Primary Care Evaluation of Mental Disorders (PRIME-MD)
Profile of Mood States (POMS)
Symptom Checklist-90-R (SCL-90-R)
<b><i>Anxiety</i></b>
Beck Anxiety Inventory (BAI)
Geriatric Anxiety Inventory (GAI)
Manifest Anxiety Scale (MAS)
Spielberger State Trait Anxiety Inventory (STAI)
<b><i>Depression</i></b>
Beck Depression Inventory (BDI-II)
Brief Assessment Schedule for Depression Cards (BASDEC)
Centre for Epidemiologic Studies Depression Scale (CES-D)
Geriatric Depression Scale (GDS)
Montgomery-Åsberg Depression Rating Scale (MADRS)
Zung Self-Rating Depression Scale (ZDS)

## **2.6 Mechanisms**

The mechanism(s) that lead to anxiety and depression in people with COPD are still largely unknown and poorly understood. It is unclear whether the onset of psychological symptomatology is a result of the disease itself or due to pre-existing mental health conditions prior to developing COPD. Several theoretical models have been proposed for the development of anxiety and depression disorders in the general population and these have also been applied in COPD populations which are summarised below.

### **2.6.1 Mechanisms for anxiety**

As dyspnoea and hyperventilation are recurrent symptoms commonly suffered by both people with COPD and panic anxiety, a number of models have been suggested to explain the possible shared pathophysiology. These models arise from the literature surrounding mechanisms for anxiety in people with COPD which mainly describes panic anxiety; the literature surrounding mechanisms for other anxiety conditions is presently lacking.

#### **2.6.1.1 The hyperventilation model**

The hyperventilation model assumes that panic, anxiety and dyspnoea arise from the same clinical presentation, i.e. the hyperventilation syndrome whereby symptoms such as dyspnoea, heart palpitations and chest pain exist but there are no other causes. People with COPD and anxiety generally have dysfunctional ventilator patterns which may be connected with hyperventilation. The resultant hypocapnic alkalosis

may then be responsible for certain symptoms of anxiety and dyspnoea, thereby producing an exacerbated response (75).

#### **2.6.1.2 The carbon dioxide hypersensitivity model**

The carbon dioxide hypersensitivity model is based on the idea that people with COPD suffering from panic disorder have an abnormally sensitive brainstem respiratory control mechanism. The pathophysiological mechanism is unclear but it is theorised that in response to increased carbon dioxide or lactate, abnormally sensitive brainstem chemoreceptors elicit a 'suffocation false alarm' when impending challenges to suffocation occurs, provoking hyperventilation and a fear of dyspnoea leading to a panic attack (76). It is proposed that both carbon dioxide and lactate share mechanisms of action, suggesting a physiological and neuroanatomical overlap.

#### **2.6.1.3 The cognitive behavioural model**

The cognitive behavioural model (also known as 'Clark's cognitive model' or the 'dyspnoea-fear theory') is the most widely accepted theory for the occurrence of panic attacks and panic disorder in physically healthy adults. The model is based on the idea that fear and misinterpretation of physical experiences induced by dyspnoea and hyperventilation catalyses a panic reaction (77). The cognitive behavioural model has also emerged as the most widely accepted theory for the onset of anxiety in people with COPD, as somatic symptoms of anxiety are similar to those associated with the lung disease. It is hypothesised that people with COPD misconstrue the severity of their dyspnoea through catastrophic cognitions. This fear of severe breathlessness



leads to a heightened state of psychological arousal, resulting in further misinterpretation of increased dyspnoea and worsening of breathlessness due to hyperventilatory panic attacks, i.e. a positive feedback loop is created (78). It has been hypothesised that people with COPD with regular catastrophic thoughts about symptoms have an increased risk of anxiety compared to those who do not have these regular invasive thoughts (41, 42, 79, 80).

#### **2.6.1.4 The stress model**

The most recent theory which has emerged explores the relationship between stress and anxiety. Pate and Davenport (2013) propose the notion of constant tracheal occlusion stimulating the persistent release of the stress hormone cortisone which promotes anxiety (81). Supporting evidence for this proposal comes from the measure of cortisone in mice where the trachea was occluded. This study found that when mice were tracheal occluded to mimic the recurrent airway obstruction experienced by people with COPD, they had a higher release of cortisone. Therefore, it is hypothesised that people with COPD experience both a psychological and a systemic stress.

#### **2.6.1.5 Smoking**

The relationship between smoking and nicotine use in people with COPD and anxiety is complex, with both anxiogenic and anxiolytic effects being found (60, 82). Support for this complex pathogenesis comes from studies of general population smokers who have higher lifetime prevalence rates of anxiety disorders and those with a history of anxiety disorders reporting more severe nicotine withdrawal symptoms (83, 84). These

results suggest nicotine may induce anxiety or people with COPD susceptible to anxiety use nicotine for its sedative effect during heightened states of psychological arousal. Furthermore, nicotine withdrawal may mimic anxiety symptomatology and people with COPD smoke to help alleviate these feelings.

### **2.6.2 Mechanisms for depression**

The pathogenetic mechanisms of comorbid depression in COPD are also poorly understood. Three prevailing biological factors have been put forward as the causes of depression in people with COPD: smoking, hypoxia and exacerbation of COPD (59, 60, 85, 86). The impact of illness on patients' lives has also been theorised as a contributing factor to the onset of depression. These theories are briefly described below.

#### **2.6.2.1 Biological mechanisms**

Smoking is a risk factor for depression in people with COPD, with depression playing a role in the initiation and maintenance of smoking, smoking being the primary risk factor for developing COPD, and COPD in turn contributing to the aetiology of depression (86). However, smoking also appears to play a complex pathogenic role via the hypoxia generated as a result of smoking. Hypoxia is a consequence of both smoking and COPD and known to induce neuropsychiatric disturbances such as psychomotor slowing, memory impairment and depressed mood (56). Various pathogenetic mechanisms have been suggested, including vascular endothelial damage, direct damage of white matter in the brain and oxidative stress (56).

Inflammatory biomarkers have also been postulated to contribute to the onset of depressive symptomatology in people with COPD due to the link between the characteristic chronic inflammation of the respiratory system and exacerbations seen in this disease. People with COPD and depression suffer from increased exacerbation rates (14-16) and support for the shared inflammation pathway theory comes from findings of depression being associated with impaired immune function (87-89), increasing susceptibility to infections (90) and thus infective exacerbations in COPD populations (91, 92).

#### **2.6.2.2 Impact of COPD**

The impact of a chronic illness on peoples' lives has been theorised as a complex contributing factor to the onset of depression. Norwood (2007) summarises this complex relationship into three domains: loss of functionality, increased burden on internal coping mechanisms and perceived social support (86). People with COPD may experience a lack of mobility, an inability to physically perform previous occupational activities or participate in recreational activities, and may require the use of oxygen therapy. Norwood states "the psychological losses attached to each of these insults are first the loss of the phenomenon itself and secondly of the emotion or material benefits derived from it" (p486) (86). Poor coping and low self-efficacy skills that accompany the grief and functional loss with COPD have been proposed to decrease the sense of self-mastery a person requires to optimally adjust to living with the disease and thus increases the likelihood of depressive symptomatology. Finally, Norwood proposes the level of social support that a person with COPD perceives (e.g.

social inclusion, marital status, having a carer) contributes to their resilience to depression (86).

## **2.7 Treatment of anxiety and depression in people with COPD**

Despite anxiety and depression being major comorbidities in people with COPD, there are no standardised guidelines—either internationally or in Australia—for their treatment. The lack of research on the effectiveness of pharmacological and non-pharmacological therapies used to treat anxiety and depression in COPD has contributed to the absence of clear recommendations for treatment in global guidelines. The only advice given in the recently updated GOLD guidelines published in 2017 is that: “there is no evidence that anxiety and depression should be treated differently in the presence of COPD” (p117) (1). The current Australian and New Zealand COPD management guidelines merely state that there is “promising evidence” for the use of cognitive behavioural therapy (CBT) and medication prescribed by psychiatrists and psychologists for treating anxiety and depression symptomatology (93). With no standard procedures in place for the treatment of anxiety or depression in this population, the current management of these comorbidities is largely dependent on the discretion of the treating physician (Prof. Grant Waterer, personal communication with Dr. Natalie Strobel, 17 Feb 2012). In the general population, these psychological comorbidities are treated with either pharmacotherapy, psychotherapy or a combination of these two—with treatment being dependent on the severity of the psychological disorder and personal preference. These treatment options have also been applied in people with COPD, as well as the use of pulmonary rehabilitation and

relaxation therapy to manage anxiety disorders and depression, with mixed effects. The following section aims to summarise the treatment methods and the evidence surrounding their application in people with COPD.

### **2.7.1 Pharmacotherapy**

Pharmacological interventions have long been used in standard clinical practice to treat anxiety and depression in the general population. The principal medications used to control symptoms include antidepressants (selective serotonin re-uptake inhibitors, tricyclic antidepressants and monoamine oxidase inhibitors), benzodiazepines, azapirones and less commonly, antipsychotic agents and anticonvulsants (94). Some of these medications have also been commonly applied in people with COPD, despite the lack of quality studies to assess their efficacy in this population. Of the few studies which have been conducted to determine the effects of pharmacological treatment of anxiety and depression in people with COPD, evidence remains equivocal. These studies have typically been fraught with differing sample sizes, large dropout rates and/or short follow-up periods. A Cochrane review conducted by Usmani *et al.* (2006) on the various pharmacological interventions used was unable to conclude on effective treatment options due to the sub-optimal quality of the research, noting the included studies (n=4) had small sample sizes, short follow-up periods and non-statistically significant results (95). Their review highlights the paucity of data with respect to quality randomised controlled trials. Previous researchers have identified numerous problems with the use of pharmacotherapy for the treatment of anxiety and depression in people with COPD, including: adverse side effects, misapprehension

about being stigmatised, non-compliant use of medication, negative previous experiences with pharmacotherapy, mistrusting the psychiatrist and side effects aggravating other comorbidities (96). Despite the lack of published evidence on the effectiveness of pharmacotherapy to treat anxiety disorders and depression in this population, it remains a common treatment option selected by treating physicians (Prof. Grant Waterer, personal communication with Dr. Natalie Strobel, 17 Feb 2012).

### **2.7.2 Pulmonary rehabilitation**

Pulmonary rehabilitation is an “evidence-based, multidisciplinary, and comprehensive intervention for patients with chronic respiratory diseases who are symptomatic and often have decreased daily life activities” (p2) (97). The objective of pulmonary rehabilitation is to “reduce symptoms, optimize functional status, increase participation, and reduce health care costs” through exercise training, education, nutritional intervention and psychosocial support (p2) (97). There is an emerging body of literature on the effect of pulmonary rehabilitation to reduce symptoms of anxiety and depression in people with COPD (1, 98). In the most recent meta-analysis available (n=6 studies), comprehensive pulmonary rehabilitation programs that incorporated exercise, education and social support reported significantly reduced anxiety and depression in people with COPD compared to standard care (98). However, there was large heterogeneity in the pulmonary rehabilitation programs, making it difficult to determine which aspects of the pulmonary rehabilitation program had the greatest impact on psychological symptomatology (98).

### **2.7.3 Self-management programs**

Self-management programs in people with COPD are defined as “structured but personalised and often multi-component, with goals of motivating, engaging and supporting the patients to positively adapt their health behaviour(s) and develop better skills to manage their disease” (p4) (99). Self-management programs have historically been developed for a variety of medical populations, employed in a variety of settings (e.g. clinical and primary care settings) using an array of mediums (e.g. video-based programs, Internet-based programs) and may or may not include support from a healthcare provider/team. To date, there are limited data available on the efficacy of self-management programs to treat anxiety and depression in people with COPD, as most self-management programs mainly focus on physiological outcomes and health-care use (100). However, results from a recent Cochrane review (n=29 included studies) found self-management improved HRQoL in people with COPD compared to usual care, providing support for the use of this treatment to alleviate mental health disorders in this population (101). Growing support is also provided by two recent studies which specifically examined the benefits of a self-management program designed to treat anxiety and depression in people with COPD. The first, by Howard and Dupont (n=222) investigated a self-management ‘COPD breathlessness manual’ based on the principles of cognitive behavioural therapy, relative to usual care. Results indicated those who participated in the five week home-based self-management intervention significantly decreased their anxiety and depression symptomatology at six months compared to usual care (38). The second, a study by Jiang and He (n=96) investigated an uncertainty management intervention in the form of an audio CD and self-help manual, complimented by telephone guidance provided

by a nurse against usual care. They found a significant reduction in anxiety and depression at 10 month follow-up in the intervention group compared to usual care (35). These promising studies highlight the need for continued research into the efficacy of self-management programs on psychological symptomatology in people with COPD.

#### **2.7.4 Self-help groups**

Self-help groups are typically small voluntary groups, structured for the mutual help of its members and are widely used by people with a chronic disease. Face-to-face social interaction in these groups is highly encouraged to facilitate the feeling of a helpful support network (94). The numerous benefits of self-help groups include enhanced perceived social support and associated psychological benefits which may stem from a general increase of positive emotions, a boost in self-esteem and feelings of control and stability of one's environment (102, 103). Whilst self-help group sessions are often incorporated in pulmonary rehabilitation programs or self-management programs, there is a paucity of data on the effectiveness of the use of these groups in the literature. To date, there are no studies reporting the efficacy of an intervention that only consists of a self-help support group to treat anxiety and depression in people with COPD.



## **2.7.5 Psychotherapy**

### **2.7.5.1 Relaxation therapy**

The aim of relaxation therapy is to facilitate the relaxation response by effectively dealing with some of the physiological responses which may accompany feelings of anxiety, as well as increasing a person's perception of self-control, and thus ultimately wellbeing (86). Regulation of the sympathetic nervous system and stimulation of certain regions of the hypothalamus which control the 'flight or fight' response is central to this relaxation response (104). Relaxation therapy encompasses an assortment of techniques including: breathing exercises, progressive muscle relaxation, isometric muscle relaxation, biofeedback, meditation and hypnosis. (94). Relaxation therapy has been found to be effective in reducing a range of symptoms (e.g. hypertension, pain and insomnia) in other chronic diseases such as cardiovascular disease and cancer (105). However, despite relaxation therapy often forming a component of pulmonary rehabilitation, cognitive behavioural therapy and self-management programs in people with COPD, there is limited literature about the immediate and long-term effects of these techniques on reducing anxiety and depression in people with COPD. A recent meta-analysis of relaxation therapy in a COPD population conducted by Volpato *et al.* (2015) found a slight effect on improving psychological wellbeing but acknowledged "higher quality research is required" (p1) (106).

### **2.7.5.2 Cognitive Behavioural Therapy (CBT)**

CBT is a structured, psychological intervention whereby the participant works collaboratively with the therapist to identify the types and effects of thoughts, beliefs and interpretations of current symptoms, feeling states and/or problem areas (40). CBT combines both cognitive interventions (cognitive restructuring i.e. attempts to alter individual appraisals and thinking patterns) and behavioural interventions to reduce dysfunctional emotions and behaviours. Such therapies are used to change the way people think and act and to give them a sense of control and encourage engagement in coping (40). The use of CBT is effective in treating many mental health problems, and international guidelines recommend CBT as the treatment of choice for a range of anxiety and mood disorders in the general healthy population. CBT treatment of these psychological disorders assists participants to recognise and challenge the negative thinking patterns and irrational beliefs that typically fuel their psychological symptomatology. CBT generally runs over 12 weeks and can be conducted either individually or in groups of people who are experiencing the same problems (107).

CBT has shown potential as a treatment to improve anxiety and depression in a variety of chronic illnesses including cancer (particularly lung and breast), diabetes mellitus and Parkinson's disease (107-112). There is also promising evidence from a growing body of studies that suggests CBT can also help reduce symptoms of anxiety and depression in people with COPD. In a recent Cochrane review of psychological therapies for the treatment of anxiety disorders in people with COPD, the authors

reported there was some evidence CBT was effective in reducing anxiety symptomatology (113). However the substantial heterogeneity between the studies included in the analysis limited the ability to draw reliable conclusions. Support for the ability of CBT to reduce depression in COPD populations comes from another meta-analysis which reported a small but significant improvement in depression but not anxiety for this type of intervention (114). Appendix 2.1 presents a summary of 18 published studies that have examined the effect of CBT on COPD populations. The CBT sessions were highly variable, with some being conducted individually either by face-to-face interview or by telephone, while others were conducted in a group, some as part of a comprehensive program and others conducted utilising the principles of self-management. Duration of treatment varied from one CBT session to 16, and the majority of these studies utilised the HADS, BAI and/or BDI-II to screen for anxiety and depression in their COPD population. The majority of studies found a CBT intervention significantly reduced symptomatology for anxiety and/or depression relative to the control group, whether that was treatment as usual, enhanced standard care, education interventions and/or exercise. In one study by Kunik *et al.* (2001), as little as a single intensive two hour session of group CBT was associated with a reduction in anxiety and depression symptomatology relative to an education-only intervention, suggesting minimal exposure to CBT is enough to elicit at least some improvement in psychological outcomes (26). CBT has also been demonstrated to maintain improvements long-term, with another study by Kunik *et al.* (2008) reporting a significant reduction in anxiety and depression at 12 months post-intervention (28), and a study by Livermore *et al.* (2010) reporting a significant reduction in anxiety at 18 months post-intervention (33). However, the COPD participants recruited for the

studies conducted by Kunik *et al.* were predominately male and from a veterans hospital, thus limiting the generalisability of these results (26, 28). Broad applicability of such studies to COPD populations is also difficult due to differences in population groups between each study, including differences in the proportion of males to females, the mean age, COPD severity of participants and where they were sourced (e.g. primary vs secondary care patients). Of the three studies that found CBT had no effect on anxiety and depression, two studies had extremely small sample sizes (n=8 and n=18) and therefore underpowered to detect a statistically significant difference, the CBT treatment was quite demanding for all three studies (8 x 90 minute sessions, 6 x 90 minute sessions and 10 x 60 minute sessions) and there was a very short follow-up period (nil, 12 weeks and nil) (25, 44, 47). These reasons may partly explain why no effect was found.

To date, there have been two studies conducted in Australia exploring the effectiveness of CBT in people with COPD. The first, by Livermore *et al.* (2010) recruited people with COPD who had undergone pulmonary rehabilitation (n=41) and randomised them into a CBT intervention whereby participants were individually administered weekly hour long sessions over four weeks (n=21) or a routine care group (n=20). Assessments were made at baseline, post-intervention and at six, 12 and 18 month intervals. The study found significant reductions in anxiety and catastrophic cognitions in the CBT group at follow-up compared to usual care. Livermore also found the CBT group did not experience any panic attacks during follow-up whereas patients in the routine care group did (60%) (33). The second study by Walters *et al.* (2013)

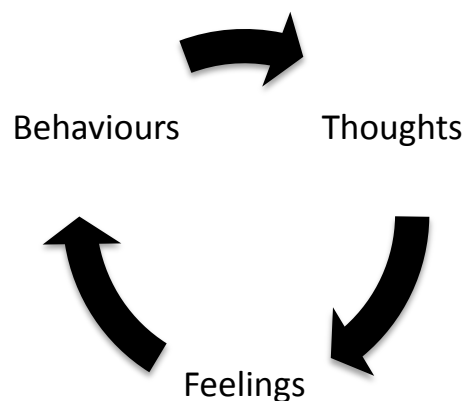
recruited people with COPD from general practises (n=182) and investigated CBT in a self-management format where it was delivered via nurses over the telephone. Participants were randomised into a 'telephone health monitoring' group where they received CBT via 16 x 30 minute phone calls over a year or in to a control group which received usual care as provided by a GP and a regular monthly phone call. Assessments were made at baseline, 6 months and post-intervention. Those in the telephone health monitoring group had significantly reduced anxiety but not depression (36).

Despite the promising efficacy of CBT in people with COPD, a common problem encountered by investigational studies are the relatively high attrition rates of up to 27–47% reported (28, 32, 44). This is a problem as it may demonstrate the impracticality of conducting CBT sessions in COPD populations. Whilst not every study reported reasons for the attrition from CBT programs, of the few that did, competing illness and logistical problems with time and transportation were barriers reported (25, 27, 28, 31, 44). There is a clear need to investigate the facilitators and barriers to people with COPD attending CBT in order to address these issues to develop a feasible treatment for this population. Furthermore, research into the benefits of self-management CBT is warranted due to the limited literature currently available of its effectiveness.

## **2.8 Theoretical Framework**

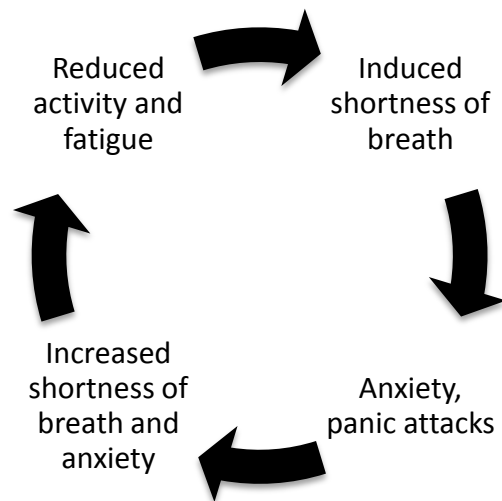
The cognitive behavioural model was adopted for this thesis. The cognitive behavioural model of panic has emerged as a widely accepted theory for onset of anxiety in people

with COPD. As the fundamental basis for this model stems from the idea that catastrophic cognitions (thoughts) are the cause of anxiety, and that these cognitions are misinterpretations which can be reversed, this model provides a compelling rationale for the use of CBT to treat this comorbidity. CBT is based upon the theory that thoughts affect feelings, which in turn has a flow-on effect on behaviours, which then consequently affects thoughts again in a constant cycle (Figure 2.1).



**Figure 2.1** Cognitive behavioural theory

The cognitive behavioural theory suggests when CBT is applied in people with COPD, the negative feedback loop (Figure 2.2) of the dyspnoea-anxiety-dyspnoea cycle experienced by people with COPD, is interrupted.



**Figure 2.2** The dyspnoea-anxiety-dyspnoea cycle

CBT also has the potential to alleviate symptoms of depression commonly experienced by people living with COPD by restructuring pessimistic thought patterns and negative behaviours. The use of CBT in people with COPD aims to help participants recognise their dysfunctional thinking patterns and factors contributing to their anxiety and depression, and re-interpret their physiological and cognitive symptoms in a more positive manner.

## **2.9 Summary**

Anxiety and depression are common comorbidities in people with COPD which contribute to greater morbidity and mortality. The cognitive behavioural model has emerged as a widely accepted theory for onset of psychological symptomatology in this population, and there is promising evidence to suggest CBT improves mental health outcomes by disrupting this cycle. However, there is a need for an alternative modality of CBT delivery for people with COPD suffering from anxiety and depression

to overcome the logistical barriers reported by previous investigational studies. Thus, a novel home-based self-management CBT learning resource in a DVD format was developed with an accompanying manual. The primary aim of this thesis was to investigate the efficacy of CBT delivered as traditional group therapy with a reduced number of sessions, and this novel home-based self-management DVD resource compared to usual care, to improve anxiety and depression symptomatology. The secondary aim was to investigate the efficacy of these interventions on improvement in HRQoL. This thesis also sought to investigate the risk factors associated with psychological symptomatology, the most suitable tool(s) for screening anxiety and depression and to explore participants' experiences of CBT to understand the enablers and disablers for people with COPD to successfully enrol and complete a course.



## 2.10 Appendix

### Appendix 2.1 Cognitive behavioural therapy in people with COPD

Author	Population and country	Design	Sample	Treatment	Delivery of CBT	Psychological outcome measures	Time-points	Attrition rate	Outcome*
Lisansky & Clough 1996 (44)	Self-selected convenience sample, USA	One-group pre- and post-test	n=8; mean age=70 (SD not specified); m=38%; f=63%	1. CBT: 8 x 90 minute weekly sessions, (one group of 8) (n=8)	Researchers and nurse	Kellner's Symptom Questionnaire (SQ)	Pre- and post-intervention	31%	No change in symptoms of anxiety disorders or depression post-treatment
Eiser et al. 1997 (47)	Outpatients, England	Repeated measures pre-post	n=18; intervention group: mean age=73 (SD not specified), m=40%, f=60%; control group: mean age=71, m=50%; f=50%	1. CBT: 6 x 90 minute weekly sessions (groups of 5–6) (n=10) 2. Control: 6 x 6 minute walking tests & lung function tests per week, no psychotherapy (groups of 5–6) (n=8)	Psychiatrist	HADS	1. CBT: Pre-intervention, post intervention and follow-up at 12 weeks 2. Control: Baseline, week 2 and week 7	10%	No change in symptoms of anxiety or depression post-treatment
Emery et al. 1998 (25)	Community participants via advertising and physician referral, USA	RCT	n=79; mean age=67±6.5; m=47%; f=53%	1. Exercise, education and stress management: 10 weeks of exercise, 16 education and 10 x 1 hour stress management sessions based on CBT (n=29) 2. Education and stress management: 16 education and 10 x 1 hour stress management sessions based on CBT (n=25) 3. Control: Waiting List (n=25)	Clinical psychologist	CES-D, The Bradburn-Affect-Balance Scale, STAI, SCL-90-R	Pre- and post-intervention	11%	Exercise, education and stress management group significantly decreased symptoms of anxiety and depression . Waiting List group also significantly decreased symptoms of depression.

Author	Population and country	Design	Sample	Treatment	Delivery of CBT	Psychological outcome measures	Time-points	Attrition rate	Outcome*
Kunik et al. 2001 (26)	Patients from a veteran hospital & advertising, USA	Single blind RCT	n=53; mean age =71±5.9; m=83%; f=17%	1. CBT: 1 x 2 hour group session (6–10 participants) and weekly phone calls for 6 weeks (n=21) 2. Control: 1 x 2 hour education session (groups of 6–10) and weekly phone call for 6 weeks (n=27)	Gero - psychiatrist and internist	BAI, GDS, SF-36	Pre- and post-intervention	9%	CBT significantly decreased symptoms of anxiety and depression
de Godoy & de Godoy 2003 (27)	Outpatients attending PR, Brazil	Single blind RCT	n=30; intervention group: mean age=62±14.9; m=86%, f=14%; control group: mean age=59±11.8, m=63%, f=37%	1. PR: 12 week program, each week: 2 x physiotherapy sessions, 2 x physical exercise sessions, 1 x CBT session (groups or individual not specified) and 1 x educational session p/month (n=14) 2. Control: same as PR group with no CBT (n=16)	Not specified	BAI, BDI	Pre- and post-intervention	Not reported	PR group with CBT significantly reduced symptoms of anxiety and depression
de Godoy et al. 2005 (48)	Outpatients, Brazil	Single blind RCT	n=49, mean age not specified (all >50 years), m=73%, f=27%	12 week PR program: G1: 2 x weekly physical exercise sessions, weekly individual psychotherapy sessions, monthly group education sessions, 2 x weekly physical therapy (n=19) G2: Same as G1 without physical therapy (n=16) G3: Same as G1 without individual psychotherapy (n=14)	Psychologist	BAI, BDI	Pre- and post-intervention	Not reported	Groups 1 and 2 significantly reduced symptoms of anxiety and depression. Group 3 significantly reduced symptoms of anxiety but not depression

Author	Population and country	Design	Sample	Treatment	Delivery of CBT	Psychological outcome measures	Time-points	Attrition rate	Outcome*
Kunik et al. 2008 (28)	Patients from a veteran hospital & advertising, USA	Single blind RCT	n=238; intervention group: mean age=66±10.1, m=97%, f=3%; control group: mean age=67±10.4, m=96%, f=4%	1. CBT: 8 x weekly 1 hour group sessions (up to 10 participants) (n=118) 2. Control: 8 x 1 hour sessions of COPD education (n=120)	Psychology interns and post-doctoral fellow	SF-36, BAI, BDI-II	Pre-intervention, 4 weeks, post-intervention and follow-up at 4, 8 and 12 months	27%	Both groups significantly reduced symptoms of anxiety disorders and depression post-treatment. Improvements were maintained with no significant change during follow-up
Heslop et al. 2009 (29)	Outpatients, England	Repeated measures pre-post	n=10; mean age=68 (SD not specified); m=50%; f=50%	1. CBT: Individual fortnightly sessions (length not specified), (average 4 sessions, range 2–13 sessions) (n=10)	Respiratory nurse	HADS	Pre-intervention and post-intervention (varying 2-4 weeks after intervention)	Nil	Significantly reduced symptoms of anxiety and depression
Howard et al. 2010 (30)	Outpatients, England	Repeated measures pre-post	n=48; intervention group: mean age=70.9±9.6, m=60%, f=40%; control group: mean age=72.9±10.0, m=60%, f=40%	1. Cognitive-behavioural breathlessness intervention: 4 x weekly 2 hour sessions (groups of up to 10)	Team consisting of a psychologist, respiratory clinical nurse specialist, health psychologist, physio-therapist and occupational therapist	HADS	Pre- and post-intervention and follow-up at 6 weeks	Not specified	Significantly reduced symptoms of depression but not anxiety at post-intervention and follow-up

Author	Population and country	Design	Sample	Treatment	Delivery of CBT	Psychological outcome measures	Time-points	Attrition rate	Outcome*
Hynninen et al. 2010 (31)	Outpatient pulmonary clinic and newspaper advertising, Norway	RCT using matched pairs	N=51; intervention group mean age=59±7.6; control group mean age=63±9.9; total m=50%, f=50%	1. CBT: 7 x weekly 2 hour group sessions (4–6 participants) and phone call at 1 and 3 months post-treatment (n=25) 2. Control: enhanced standard care for COPD (groups of 4–6) and phone call every two weeks during intervention period to monitor psychological status (n=26)	Post-graduate psychology student	BAI, BDI-II	Pre-and post-intervention and follow-up at 6 months	17%	CBT significantly reduced symptoms of anxiety and depression post-treatment compared to control group. Decrease in anxiety (but not depression) also maintained at follow-up for CBT group compared to control group
Lamers et al. 2010 (32)	Patients from general practises, Netherlands	RCT	n=187; intervention group: mean age=71±6.3; m=62%, f=38%; control group: mean age=72±7.1, m=58%, f=42%	1. Minimal Psychological Intervention with elements of CBT and self-management: 2–10 visits depending on patient progress over a period of at most 3 months (n=96) 2. Control group: Care as usual (n=91)	Nurse	SCL-90-R, BDI	Pre- and post-intervention (1 week) and follow-up at 3 and 9 months	47%	Minimal Psychological Intervention group significantly reduced symptoms of anxiety and depression at 9 months compared to usual care
Livermore et al. 2010 (33)	Hospital outpatients and in-patients, Australia	RCT	n=41; intervention group mean age=73±6.4; control group mean age=74±8.1; total m=24%; f=76%	1. CBT: 4 x 1 hour weekly individual sessions (n=21) 2. Control: routine care (n=20)	Researcher	ADIS-IV, HADS	Pre- and post-intervention and follow-up at 6, 12 and 18 months	15%	Significantly reduced symptoms of anxiety and no experiences of panic attacks in CBT group compared to control at post-treatment and follow up.

Author	Population and country	Design	Sample	Treatment	Delivery of CBT	Psychological outcome measures	Time-points	Attrition rate	Outcome*
Kapella et al. 2011 (34)	Community participants via advertising, USA	Mixed method	n=23; phase 1 group: mean age=60±10.0, m=78%, f=22%; phase 2 group: mean age=65±9.0; m=78%, f=22%	1. Phase 1: 6 x 1 hour weekly CBT sessions (n=5) 2. Phase 2: CBT: 6 x 1 hour weekly sessions (n=9) or 6 x wellness education sessions (9)	Specialised nurse	POMS	Pre- and post-intervention	One person dropped out	Wellness education sessions significantly reduced symptoms of depression but not anxiety post- treatment compared to CBT
Jiang and He 2012 (35)	Outpatients, China	RCT	n=96; intervention group: mean age=65±9.0, m=71%, f=29%; control group: mean age:65±8.1, m=68%, f=32%	1. Uncertainty Management: 4 x 35 minute telephone calls weekly based on CBT, last 2 calls used to guide participants through audio CD and self-help manual (n=50) 2. Control group: standard care (n=50)	Research nurse	STAI, HADS Depression Subscale	Pre-intervention and 10 month follow-up	3%	Uncertainty Management significantly reduced symptoms of anxiety and depression
Walters et al. 2013 (36)	Patients from general practises, Australia	Cluster RCT	n=182; intervention group: mean age=68.2±7.9; m=54%, f=46%; control group: mean age= 67.3±7.6, m=51%, f=49%	1. Telephone Cognitive Behavioural Health Monitoring: 16 x 30 minute phone calls over 12 months (n=90) 2. Control group: Usual care as provided by a GP plus regular monthly phone call from research nurse (n=92)	Community health nurses	HADS, CES-D, Post-Traumatic Stress Disorder Checklist-Civilian Version, SF-36	Pre-intervention, 6 months and post-intervention	18%	Telephone Health Monitoring significantly reduced symptoms of anxiety but not depression

Author	Population and country	Design	Sample	Treatment	Delivery of CBT	Psychological outcome measures	Time-points	Attrition rate	Outcome*
Blumenthal et al. 2014 (37)	Outpatients recruited from university hospitals, USA	RCT	n=326; intervention group: mean age=66±7.9, m=62%, f=38%; control group: mean age=66±8.7, m=60%, f=40%	1. Telehealth Cognitive Behavioural Coping Skills Training: 12 x weekly telephone sessions followed by 2 x bi-weekly sessions for 1 month (total 14 sessions roughly 30 minutes in duration over 16 weeks) (n=162) 2. Control Group: COPD education. Same as above (n=164)	Clinical psychologists and health educators	STAI, BDI-II, SF-36?	Pre-and post-intervention	7%	Telehealth Coping Skills Training significantly reduced symptoms of anxiety and depression compared to COPD education
Howard & Dupont, 2014 (38)	Patients from GP practises, England	Single blind RCT	n=222; intervention group: mean age=71±10.4, m=56%, f=44%; control group: mean age=73±11.4, m=41%, f=59%	1. Cognitive Behavioural Manual (n=112) 2. Control: British Lung Foundation Information Booklets (n=110) Both groups encouraged to follow their program for 1 hour per day over 5 weeks. 2 x telephone booster call sessions provided at weeks 3 and 6.	Psychologists	HADS	Pre- and post-intervention, and follow-up at 6 months	2%	Cognitive Behavioural Manual significantly reduced symptoms of anxiety and depression at 6 months follow-up
Bove et al., 2016 (43)	Outpatients, Denmark	RCT	n=66; intervention group: mean age=71±8.39; m=33%, f=67%; control group: mean age=70±8.73, m=33%, f=67%	1. 1 x home-based CBT and psychoeducation session (mean duration of 1 hour) and 1 x 20 minute telephone booster session 2 weeks after 2. Control: standard care (n=33)	Nurse	HADS	Pre- and post-intervention and follow-up at 1 and 3 months	10%	Home-based CBT and pschoeducation significantly reduced Symptoms of anxiety at post-treatment and follow-up

BAI: Beck Anxiety Inventory; BDI: Beck Depression Inventory; CES-D: The Centre for Epidemiological Studies—Depression Inventory; GDS: Geriatric Depression Scale; HADS: Hospital Anxiety and Depression Scale; POMS: Profile of Mood States PR: Pulmonary Rehabilitation; SCL-90-R: The Hopkins Symptom Checklist; STAI: The State-Trait Anxiety Inventory; RCT: Randomised Control Trial

\*Effect sizes not summarised due to unreported data and inconsistent coefficients used within the literature

## CHAPTER THREE

### **Determinants of concomitant anxiety and depression in people with chronic obstructive pulmonary disease**

This manuscript was submitted for publication in the Journal of Psychosomatic Research on the 2<sup>nd</sup> of October 2017 and is currently under review.

Tina Phan, Owen Carter, Grant Waterer, Li Ping Chung, Maxine Hawkins, Cobie Rudd, Mel Ziman & Natalie Strobel. Determinants of concomitant anxiety and depression in people with chronic obstructive pulmonary disease. Journal of Psychosomatic Research. (Submitted for review on 2 October 2017).

### **3 Study rationale**

People with chronic obstructive pulmonary disease (COPD) frequently suffer from both anxiety and depression. However, the literature surrounding determinants for having both these psychological comorbidities is limited. Furthermore, generalisability of results are constrained due to the populations sampled. The following chapter (Study One) seeks to investigate the determinants of concomitant anxiety and depression in a more representative sample of people with COPD than previously used. It was hypothesised previous risk factors identified separately for anxiety or depression in people with COPD were also shared risk factors for concomitant anxiety and depression.

This study was cross-sectional in design, and utilised baseline data collected from the Breathing New Life study to provide a picture of prevalence in an Australian COPD population. In addition, we also assessed the association between demographic predictor variables and psychological symptomatology score using logistic regression. Three factors were found to increase the risk of having both anxiety and depression in our COPD cohort: younger age, previous history of psychological illness and greater number of non-psychological comorbidities.



## CHAPTER FOUR

### **Discriminant validity of the Hospital Anxiety and Depression Scale, Beck Depression Inventory (II) and Beck Anxiety Inventory to confirmed clinical diagnosis of depression and anxiety in patients with chronic obstructive pulmonary disease**

This manuscript was submitted for publication in the journal Chronic Respiratory Disease on the 6<sup>th</sup> of May 2015, was invited for second review on the 11<sup>th</sup> of November 2015 and resubmitted on the 1<sup>st</sup> of December 2015. It was accepted for publication on the 17<sup>th</sup> of December 2015 and available online ahead of print on the 3<sup>rd</sup> of March 2016.

Tina Phan, Owen Carter, Claire Adams, Grant Waterer, Li Ping Chung, Maxine Hawkins, Cobie Rudd, Mel Ziman & Natalie Strobel. Discriminant validity of the Hospital Anxiety and Depression Scale, Beck Depression Inventory (II) and Beck Anxiety Inventory to confirmed clinical diagnosis of depression and anxiety in patients with chronic obstructive pulmonary disease. Chron Respir Dis. 2016;13(3):220-228.

## 4 Study rationale

There is a lack of recommendations for psychological comorbidity screening measures in the Global Initiative for Chronic Obstructive Lung Disease management guidelines, and despite being commonly used in people with chronic obstructive pulmonary disease (COPD), the Hospital Anxiety and Depression Scale (HADS) has only been validated for use in this population twice beforehand and not at all for the Beck Depression Inventory (BDI-II) and Beck Anxiety Inventory (BAI). The following chapter (Study Two) seeks to add to the limited body of literature by investigating the discriminant validity of the HADS with people diagnosed with COPD, and to examine the discriminant validity of the BDI-II and BAI as potential alternatives for this population. It was hypothesised the BDI-II and BAI may be better alternatives to screening people with COPD for psychological symptomology than the HADS.

This study used a subset of people from the wider Breathing New Life study cohort who were randomised to additionally self-complete the HADS, followed by a structured clinical interview with a provisional psychologist conducting the Mini Neuropsychiatric Interview (MINI) at baseline. Results of this study did not replicate previously reported low sensitivity and specificity of the HADS depression subscale (HADS-D) in people with COPD. However, the HADS anxiety subscale (HADS-A) as well as the BDI-II and BAI produced acceptable sensitivity and specificity. Recommendations for simple modifications of the HADS-D to improve its sensitivity and specificity for depression are given.

## **4.1 Abstract**

### **Objectives**

To investigate the discriminant validity of commonly used depression and anxiety screening tools in order to determine the most suitable for patients with chronic obstructive pulmonary disease (COPD).

### **Methods**

COPD patients (n=56) completed the Hospital Anxiety and Depression Scale (HADS), Beck Depression Inventory (BDI-II) and Beck Anxiety Inventory (BAI). These scores were compared to confirmed clinical diagnoses of depression and anxiety using the Mini Neuropsychiatric Interview (MINI).

### **Results**

HADS-D sensitivity/specificity was 78/81%; BDI-II 89/77%; HADS-A 71/81%; and BAI 89/62%. HADS-D sensitivity/specificity was improved (100/83%) with removal of Q4 'I feel as if I am slowed down' and adjusted cut-off ( $\geq 5$ ). Removal of BDI-II Q21 'Loss of interest in sex' with adjusted cut-off  $\geq 12$  resulted in similar improvement (100/79%). No problematic items were identified for HADS-A or BAI.

## Conclusions

Previously reported low sensitivity/specificity of the HADS for COPD patients was not replicated. Furthermore, simple modifications of the HADS-D markedly improved sensitivity/specificity for depression. BDI-II, HADS-A and BAI produced acceptable sensitivity/specificity unmodified. Pending further research, for COPD patients we recommend continued use of the HADS-A with standard cut-off ( $\geq 8$ ) and removal of Q4 of the HADS-D with lower cut-off  $\geq 5$ .

## 4.2 Introduction

Depression and anxiety are common comorbidities in patients diagnosed with chronic obstructive pulmonary disease (COPD), with benchmark prevalence estimates of 40% for depression and 36% for anxiety (10). Screening COPD patients for concomitant psychological distress is important as it has been found to contribute to poorer health outcomes across a number of domains, including: increased exacerbation rates, diminished exercise performance and functional mobility, reduced health-related quality of life, increased number of emergency hospital visits, increased hospitalisations, increased length of stay as an admitted patient, increased mortality rates and in general greater economic burden (14-17, 19, 20, 22). Consequently, European and Australasian COPD management guidelines recommend routine screening for depression and anxiety in COPD patients using the Hospital Anxiety and Depression Scale (HADS) (115, 116). Use of the HADS with COPD patients is widespread; being reported in at least 17 published studies (11, 16, 19, 41, 45, 47, 56, 65-74). However, only two previous studies have investigated the discriminant validity

of the HADS with COPD populations and both cast doubt about its usefulness. Cheung *et al.* confirmed clinical diagnoses of anxiety disorders with 55 elderly New Zealand COPD patients using the Mini Neuropsychiatric Interview (MINI) and reported at the standard cut-off  $\geq 8$  the HADS anxiety subscale (HADS-A) provided sensitivity/specificity of 36/90% and Area Under Curve (AUC) of 79% (45). They recommended a lower cut-off  $\geq 4$  that yielded an improved sensitivity/specificity of 79/71%. Nowak *et al.* used the German version of the HADS depression subscale (HADS-D) to assess 259 Swiss COPD patients for depression, cross-referenced with diagnoses of depression co-morbidity noted in patients' clinical records, and also reported low discriminant validity at the standard cut-off  $\geq 8$  (sensitivity/specificity 25/84%; AUC 66%) (46). They recommended a lower optimal cut-off score of  $\geq 5$  but this still yielded fairly low sensitivity/specificity 62/63%. These results cast doubt over the appropriateness of using the HADS for patients with COPD. However, these results demand replication before any firm conclusions can be drawn.

Potential alternatives to the HADS for COPD patients include the Beck Depression Inventory (II), also a popular research measure to screen COPD patients for depression, and the counterpart for anxiety, the Beck Anxiety Inventory (BAI). These tests are longer than the HADS, with 21 items each, compared to the 14 items in total for the HADS, but are well established and popular for screening COPD patients for studies involving cognitive behavioural therapy (26-28, 31). However, we are unaware of any studies that have established the discriminant validity of either the BDI-II or BAI in COPD patients. Therefore, the aims of the present study were to investigate the

discriminant validity of the HADS with patients diagnosed with COPD, and to examine the discriminant validity of the BDI-II and BAI as potential alternatives for this population.

## **4.3 Method**

### **4.3.1 Sample**

Participants were outpatients attending community-based COPD clinics in Perth, Western Australia. Participants were excluded if they had a life expectancy of less than six months, were currently involved in another research study, had an illness exacerbation resulting in hospitalisation within the previous month, were not fluent in English, or were blind, deaf or diagnosed with dementia or Alzheimer's disease. Ethics approval for the study was granted by Royal Perth Hospital, Edith Cowan University and the South Metropolitan Health Service Human Research ethics committees. We attempted to contact a list of 164 outpatients. Thirty-five individuals were uncontactable because they were either deceased, discharged from the clinics, had disconnected telephones or we were unable to contact them after five separate attempts. Of the 129 successfully contacted, 27 did not meet our inclusion criteria and 46 declined to participate, citing ill-health or 'lack of time'. The final sample consisted of 56 patients with confirmed diagnosis of COPD by respiratory physicians who gave their informed consent to participate in the study, representing 34% of our original sampling pool, and a consent rate of 55% of contactable and eligible participants. The mean age of participants was 73.3 years (SD 8.9; range 50–91). There were more

females (58.9%) than males (41.1%) and the majority of participants were retired (73.2%) and married or in a de-facto relationship (69.7%) (Table 4.1).

**Table 4.1** Participant characteristics

<b>Characteristic</b>	<b>N</b>	<b>%</b>
Males	23	41.1
Female	33	58.9
Aboriginal or Torres Strait Islander	1	1.8
Education		
Up to 10 years of school	26	46.4
11 years and above	27	48.2
Other	3	5.4
Marital status		
Married/De-facto	39	69.7
Not in a current relationship	17	30.3
Has a carer	41	73.2
Occupation		
Employed	4	7.2
Retired	41	73.2
Other	11	19.6
GOLD stage		
Mild	2	3.6
Moderate	18	32.1
Severe	25	44.6
Very severe	3	5.4
Missing	8	14.3

#### **4.3.2 Instruments**

Participants were asked to self-complete the HADS, BDI-II and BAI, followed immediately by a structured clinical interview with a provisional psychologist conducting the MINI. The MINI (v6.0.0) is considered a 'gold standard' in determining incidence of Axis I psychiatric disorders as per DSM-IV and ICD-10 criteria (117). The

provisional psychologist was blinded to the results of the other questionnaires before conducting the MINI.

#### **4.4 Statistical analyses**

Aggregated and item-by-item scores were examined for the HADS, BDI-II and BAI and compared to clinically-confirmed current major depression and any anxiety disorders (panic disorder, agoraphobia and generalised anxiety disorder) based upon MINI diagnostic criteria. The sensitivity, specificity, Youden's index  $J$ , positive predictive value, negative predictive value, kappa coefficient and AUC values were calculated using the MINI as the clinical standard for the presence or absence of psychological comorbidity. Independent samples  $t$ -tests were also used to compare the mean HADS, BDI-II and BAI scores of participants in various groups. IBM SPSS (v22) was used for all statistical analyses.

#### **4.5 Results**

##### **4.5.1 Depression**

Nine of 56 patients (16.1%) met the clinical diagnosis for major depression according to the MINI. The mean HADS-D and BDI-II scores for these patients are compared to others in Table 4.2.



**Table 4.2** Proportions and averages of depression and anxiety scores for the MINI, HADS-D, HADS-A, BDI and BAI

<b>Depression Measure</b>	<b>MINI</b>	<b>HADS-D ≥8</b>	<b>BDI-II ≥14</b>
Prevalence	16% (95% CI ±10)	29% (95% CI: 11.8)	34% (95% CI: ±12.4)
Average scores with depression	-	12.33 (SD = 4.15)	32.44 (SD = 12.04)
Average scores without depression	-	4.34 (SD = 2.83)*	9.40 (SD = 8.21)*
<b>Anxiety Measure</b>	<b>MINI</b>	<b>HADS-A ≥8</b>	<b>BAI ≥8</b>
Prevalence	25% (95% CI 14–36%)	32% (95% CI: ±12.2)	48% (95% CI: ±13.1)
Average scores with anxiety	-	9.14 (SD = 4.07)	20.79 (SD = 12.63)
Average scores without anxiety	-	4.36 (SD = 4.03)*	8.60 (SD = 10.39)*

\*denotes statistically significant difference to participants with depression at  $p < 0.001$

Both HADS-D and BDI-II scores were significantly different between participants with clinically confirmed depression compared to those without. AUC statistics for the HADS-D and BDI-II were both close to perfect (94.8%,  $p < 0.001$ ; 94.9%,  $p < 0.001$  respectively). As can be seen in Table 4.3, the recommended HADS-D cut-off of  $\geq 8$  identified 7 out of 9 (77.8%) true positive cases and 38 out of 47 (80.9%) true negative cases. Youden's index  $J$  suggested a similar optimal cut-off of  $\geq 7$ . The mean score of false positive cases was significantly lower ( $M = 9.38$ ,  $SD = 1.30$ ) than true positives ( $M = 13.86$ ,  $SD = 3.29$ ) ( $t(8.36) = -3.571$ ,  $p = 0.003$ ). The recommended BDI-II cut-off  $\geq 14$  identified 8 out of 9 (88.9%) true positive cases and 36 of 47 (76.6%) true negative cases. Youden's index  $J$  suggested a similar optimal cut-off of  $\geq 13$ . BDI-II true positives cases had a significantly higher mean score ( $M = 32.4$ ,  $SD = 12.0$ ) than the false negative cases ( $M = 22.5$ ,  $SD = 5.6$ ) ( $t(18) = -2.454$ ,  $p = 0.025$ ).

An examination of each item of the HADS-D using independent samples *t*-tests identified the mean score for Question 4 'I feel as if I am slowed down' as substantially higher than all other items. This was the only item of the HADS-D for which no participant scored zero, and the only item for which there was no statistically significant difference in mean scores between those with clinically diagnosed depression ( $M = 2.56, SD = 0.73$ ) and those without ( $M = 2.09, SD = 0.86$ ) ( $t(54)=-1.544, p=0.128$ ). The sensitivity and specificity of the HADS-D was therefore recalculated when excluding this item. With Question 4 excluded, Youden's index *J* suggested an optimal cut-off of  $\geq 5$  which detected all true positive cases (100.0%) and 39 out of 47 true negative cases (83.0%) within our sample (Table 4.3). True positive cases still had a significantly higher mean HADS-D score ( $M = 11.0, SD = 3.22$ ) than false positive cases ( $M = 6.33, SD = 1.80$ ) ( $t(14)=-3.694, p=0.002$ ).

Independent samples *t*-tests for each item of the BDI-II also highlighted Question 21. The mean score for Question 21 'Loss of interest in sex' did not differ significantly between those with a clinical diagnosis of depression ( $M = 1.30, SD = 0.43$ ) and those without ( $M = 1.32, SD = 1.92$ ) ( $t(54)= -1.181, p=0.243$ ). Therefore, the sensitivity and specificity of the BDI-II was recalculated to exclude Question 21. Upon removal of Question 21, Youden's index *J* suggested an optimal cut-off of  $\geq 12$  that detected all true positive cases (100.0%) and 37 out of 47 true negative cases (78.7%) within our sample (Table 4.3).

**Table 4.3** The sensitivity and specificity of the HADS-D, HADS-D excluding Question 4, BDI-II and BDI-II excluding Question 21 for detecting major depression in COPD patients (%)

Cut-off points	Sensitivity	Specificity	Youden's index <i>J</i>	PPV*	NPV*
<b>HADS-D</b>					
3	100.0	31.9	0.32	22.0	100
4	100.0	46.8	0.47	26.5	100
5	100.0	57.4	0.57	31.0	100
6	100.0	74.5	0.75	42.9	100
<b>7**</b>	<b>100.0</b>	<b>78.7</b>	<b>0.79</b>	<b>47.4</b>	<b>100</b>
8	77.8	80.9	0.59	43.8	95.0
9	77.8	85.1	0.63	50.0	95.2
10	77.8	91.5	0.69	63.6	95.5
11	55.6	95.7	0.51	71.4	91.8
<b>HADS-D ex Qu 4</b>					
1	100.0	28.3	0.28	21.4	100
2	100.0	47.8	0.48	27.3	100
3	100.0	69.6	0.70	39.1	100
4	100.0	78.3	0.78	47.4	100
<b>5**</b>	<b>100.0</b>	82.6	0.83	52.9	<b>100</b>
6	88.9	87.0	0.76	57.1	97.6
7	77.8	93.5	0.71	70.0	95.7
8	55.6	95.7	0.51	71.4	91.8
9	55.6	97.8	0.54	83.3	92.0
<b>BDI-II</b>					
9	100.0	63.8	0.64	34.6	100
10	100.0	70.2	0.70	39.1	100
11	100.0	70.2	0.70	39.1	100
12	100.0	76.6	0.77	45.0	100
<b>13**</b>	<b>100.0</b>	<b>76.6</b>	<b>0.77</b>	<b>45.0</b>	<b>100</b>
14	88.9	76.6	0.66	42.1	97.3
15	88.9	78.7	0.68	44.4	97.4
16	88.9	78.7	0.68	44.4	97.4
17	88.9	78.7	0.68	44.4	97.4
<b>BDI-II ex Qu 21</b>					
8	100.0	61.7	0.62	33.3	100.0
9	100.0	70.2	0.70	39.1	100.0
10	100.0	74.5	0.75	42.9	100.0
11	100.0	74.5	0.75	42.9	100.0
<b>12**</b>	<b>100.0</b>	<b>78.7</b>	<b>0.79</b>	<b>47.4</b>	<b>100.0</b>
13	88.9	78.7	0.68	44.4	97.4
14	88.9	78.7	0.68	44.4	97.4
15	88.9	80.9	0.70	47.1	97.4
16	88.9	80.9	0.70	47.1	97.4

\*Note: PPV: positive predictive value, NPV: negative predictive value

\*\*Optimal cut-off

#### 4.5.2 Anxiety

Fourteen of 56 patients (25.0%) met the MINI criteria for an anxiety disorder. This included 6 patients diagnosed with panic disorder, 5 with agoraphobia and 3 with generalised anxiety disorder. Table 4.2 shows the proportion and average scores of patients identified as meeting the diagnostic criteria for any anxiety disorder via the MINI and those meeting clinically relevant anxiety symptomatology via the HADS-A and BAI.

Independent samples *t*-tests suggested both HADS-A and BAI scores were significantly different between participants with clinically confirmed anxiety disorders compared to those without. AUC statistics for the HADS-A and BAI were both in the 'fair' range (78.4%,  $p < 0.01$ ; and 78.5%,  $p < 0.01$  respectively). At the recommended cut-off  $\geq 8$  the HADS-A identified 10 out of 14 true positive cases (71.4%) and 34 out of 42 true negative cases (81.0%). With our sample Youden's index *J* suggested an optimal cut-off of  $\geq 9$ . There were no significant differences between the mean scores of true positives ( $M = 11.20$ ,  $SD = 2.44$ ) versus false positives ( $M = 11.38$ ,  $SD = 2.62$ ) ( $t(16) = 0.146$ ,  $p = 0.885$ ). With the recommended cut-off  $\geq 8$  the BAI identified 11 out of 14 true positive cases (78.6%) and 26 out of 42 true negative cases (61.9%). For our sample, the optimal cut-off was  $\geq 12$ , which maintained true positives at 78.6% but improved false negatives to 76.2% (Table 4.4). No significant differences in BAI score were found between true positive cases ( $M = 25.10$ ,  $SD = 10.23$ ) and false positive cases either ( $M = 18.44$ ,  $SD = 11.01$ ) ( $t(16) = -1.542$ ,  $p = 0.136$ ).

**Table 4.4** The sensitivity and specificity of the HADS-A and BAI for detecting anxiety in COPD participants

Cut-off points	Sensitivity	Specificity	Youden's index <i>J</i>	PPV	NPV
<b>HADS-A</b>					
5	85.7	64.3	0.50	44.4	93.1
6	78.6	71.4	0.50	47.8	90.9
7	71.4	78.6	0.50	52.6	89.2
8	71.4	81.0	0.52	55.6	89.5
<b>9**</b>	<b>71.4</b>	<b>85.7</b>	<b>0.57</b>	<b>62.5</b>	<b>90.0</b>
10	64.3	85.7	0.50	60.0	87.8
11	28.6	88.1	0.17	44.4	78.7
12	14.3	90.5	0.05	33.3	76.0
13	14.3	92.9	0.07	40.0	76.5
<b>BAI</b>					
8	78.6	61.9	0.41	40.7	89.7
9	78.6	71.4	0.50	47.8	90.9
10	78.6	76.2	0.55	52.4	91.4
11	78.6	76.2	0.55	52.4	91.4
<b>12**</b>	<b>78.6</b>	<b>76.2</b>	<b>0.55</b>	<b>52.4</b>	<b>91.4</b>
13	71.4	78.6	0.50	52.6	89.2
14	71.4	81.0	0.52	55.6	89.5
15	71.4	81.0	0.52	55.6	89.5
16	71.4	81.0	0.52	55.6	89.5

\*Note: PPV: positive predictive value, NPV: negative predictive value

\*\*Optimal cut-off

An examination of the mean response to each question within the HADS-A revealed no conspicuously inflated items for COPD patients.

Examining the mean response to each question within the BAI revealed Question 15 'Difficulty breathing' was substantially higher than other items. However, the mean score for this question remained statistically different between those with clinically diagnosed anxiety ( $M = 1.71$ ,  $SD = 1.07$ ) and those without ( $M = 1.0$ ,  $SD = 1.12$ ) ( $t(54) = -2.05$ ,  $p=0.045$ ), suggesting discriminant validity still existed and removal of this item was therefore not warranted.

## 4.6 Discussion

The first aim of this study was to investigate the discriminant validity of the HADS with patients diagnosed with COPD. We were unable to replicate the findings of Cheung *et al.* and Nowak *et al.* (45, 46). In contrast to Cheung *et al.*, who found a much lower optimal cut-off for the HADS-A of  $\geq 4$ , our optimal cut-off ( $\geq 9$ ) was a very close approximation to the standard recommendation of  $\geq 8$ . The reason for the different results is far from clear. The proportion of our sample diagnosed with anxiety disorders (25.0%) corresponded very closely with the sample of Cheung *et al.* (25.5%) using the same diagnostic test (MINI) and extremely similar patient profiles (Anglo-Saxon dominant cultures i.e., New Zealand v. Australia). So too, both studies had similar sample sizes ( $n=55$  v.  $56$ ), demonstrated similar levels of discriminant validity (AUC 79% v. 78.4%), and shared fair sensitivity (79% v. 71%) and specificity (71% v. 86%) at their optimal cut-offs. However, the COPD severity in the population studied by Cheung *et al.* was not reported, raising the question as to whether this may have affected prevalence rates which would ultimately impact on sensitivity and specificity scores. Cheung *et al.* acknowledged their optimal cut-off was 'unusually low' and further replication of their results was therefore warranted. The fact that we were unable to replicate their results now casts doubt over their suggestion of a HADS-A cut-off of  $\geq 4$  for COPD patients. Further attempts to replicate the results of Cheung *et al.* are needed to clarify this matter.

Contrary to Nowak *et al.* who suggested the HADS-D provided poor discriminant validity for COPD patients (AUC 66.2%), our results suggested its discrimination was

excellent (AUC 94.8%). Even with their optimal cut-off  $\geq 6$ , Nowak *et al.* observed a borderline sensitivity/specificity of 62.1/62.6% contrasting with our optimal cut-off  $\geq 7$  achieving 100.0/78.7%, and improving even further with removal of Question 4 and lowering the cut-off to  $\geq 5$  yielding 100.0/83.0%. There are many possibilities why we were unable to replicate the results of Nowak *et al.*, including vastly differing sample sizes ( $n=259$  v. 56), differing prevalence of major depression (16.1% vs 11.2%), use of the German v. English version of the HADS, differing cultures and use of pre-diagnosed depression based on medical records subsequently confirmed by the patient's physician v. current diagnosis confirmed by a psychologist using a structured clinical interview.

Despite the HADS being created to avoid somatic symptom overlap with anxiety and depression in medical patients, the continued use of HADS with chronic diseases remains contentious as a variety of cut-offs have been suggested differing from optimal cut-off scores suggested for the general patient population e.g. HADS-D  $\geq 4$  in coronary heart disease (118) and HADS-D  $\geq 11$  in end-stage renal disease (119). Given that the discriminant validity of the HADS has only been tested in COPD populations three times with divergent results, the recommendation of using this screening tool in international management guidelines remains contentious. More population-specific tools, such as the Geriatric Anxiety Inventory and COPD Anxiety Questionnaire (German: CAF), may be preferable (120, 121). However, Cheung *et al.* investigated the Geriatric Anxiety Inventory as another alternative measure for use with COPD patients but found it no more useful than the HADS, and to the best of our knowledge the CAF

has yet to be translated and validated for use in English and we are unaware of any others for COPD.

The second aim of our study was to examine the discriminant validity of the BDI-II and BAI as viable alternatives to the HADS for use with patients diagnosed with COPD. The BDI-II demonstrated excellent discriminant validity and very similar sensitivity/specificity to the HADS-D. Question 21 did not discriminate between those with and without clinical depression. However, its removal only marginally improved the validity of optimal cut-offs ( $J = 0.77$  vs  $0.79$ ). Therefore we see little value in unnecessarily modifying the BDI-II for use with COPD patients. Likewise, the BAI demonstrated similar discriminant validity to the HADS-A. However, given the shorter length of the HADS (14 items combined) compared to the BDI-II and BAI (42 items combined) and the free use of the former, versus cost per test of the latter, there may be limited advantage of using the Beck inventories over the HADS.

The relatively modest sample size of stable COPD patients in our study increases the probable error of our prevalence estimates. However, they were highly consistent with previous estimates, giving us some reassurance that they are reasonably representative. It is possible our study suffered selection bias; patients suffering poorer mental health may have been more motivated to participate, thus inflating our prevalence estimates. Fortunately, we achieved a consent rate of 55% implying our data represent the majority of our sample, thereby reducing this potential for sampling error. Another potential limitation is that we did not exclude participation in



pulmonary rehabilitation as a possible confounder, which previous evidence suggests can be effective for reducing anxiety and depression in COPD patients (25, 122). Cheung *et al.* and Nowak *et al.* also failed to control for this, as such future studies should ensure that pulmonary rehabilitation is treated as a covariate.

#### **4.7 Clinical implications**

Since Question 4 from the HADS-D appears to be a universal symptom of COPD patients and our data suggests the removal of this question and lowering the cut-off to  $\geq 5$  provides superior sensitivity and specificity, we recommend this course of action when using the HADS-D specifically with people diagnosed with COPD. As the HADS-A provided fair sensitivity and specificity and no items appeared to overlap with the symptomatology of COPD we recommend retaining the standard cut-off point of  $\geq 8$  for the HADS-A until such time as future studies suggest otherwise. Our results therefore support current guidelines of routine use of the HADS as a screening instrument for COPD patients, retaining the traditional HADS-A cut-off score of  $\geq 8$  whilst removing Question 4 for the HADS-D and using a lower cut-off score of  $\geq 5$ .

Our investigation into the validity of screening tools for use in a clinical setting further highlights the importance of appropriate follow-up measures for those that screen positive. However, due to the restrictive time-frame of these measures, it is possible that patients may feel depressed without being flagged as suffering from clinical levels and should therefore also be considered for follow-up. Our study found that those clinically diagnosed with depression via the MINI and also screened as having

depression symptomatology in both the HADS-D and BDI-II had significantly higher mean scores than those that did not screen positive. Whilst the proportion of true positive to false positive cases was too small to be able to draw any definitive conclusions, another avenue for future research which has very important implications for targeted screening and treatment may be to investigate the demographic and physiological differences (e.g. FEV1, 6MWT, number of exacerbations) in COPD patients which may help to distinguish between these two subgroups.

## CHAPTER FIVE

**A randomised controlled trial investigating the efficacy of cognitive behavioural therapy on the mental health of people with chronic obstructive pulmonary disease: the 'Breathing New Life' study**

This manuscript was submitted for publication in the journal *Trials* on the 21<sup>st</sup> of May 2017 and is still currently under review.

Tina Phan, Owen Carter, Grant Waterer, Li Ping Chung, Maxine Hawkins, Cobie Rudd, Mel Ziman, Johnny Lo & Natalie Strobel. A randomised controlled trial investigating the efficacy of cognitive behavioural therapy on the mental health of people with chronic obstructive pulmonary disease: the 'Breathing New Life' study. *Trials*. (Submitted for review on 21 May 2017)

## 5 Study rationale

The following chapter (Study Three) seeks to investigate the efficacy of cognitive behavioural therapy (CBT) in addition to usual care for the treatment of anxiety and depression in people living with chronic obstructive pulmonary disease (COPD), compared to usual care alone. As investigational studies have commonly reported participants' lack of transport, lack of time and illness as barriers to recruitment and successful completion, a novel self-management resource was developed in the format of a DVD with accompanying manual to overcome these issues. A randomised controlled trial was conducted to investigate the efficacy of CBT delivered via a traditional group therapy format with a reduced number of sessions (CBT) or a home-based self-management DVD format (DVD) in reducing psychological symptomatology. The secondary aim was to investigate the efficacy of these CBT interventions to improve health-related quality of life (HRQoL) relative to usual care. It was hypothesised the CBT and DVD groups would have better mental health and HRQoL outcomes after 12 months compared to the usual care alone group, with the DVD group likely to have higher treatment compliance due to the nature of the resource.

The study was a randomised controlled trial comparing two half-day group face-to-face CBT sessions with a one-hour telephone booster session and the six week 'Breathing New Life' home-based self-management CBT learning resource (DVD) and accompanying manual, relative to usual care alone. Results of the study indicate there were no significant changes over time in anxiety, depression or HRQoL between any for our COPD study groups.

## CHAPTER SIX

### **A qualitative investigation of the facilitators and barriers for people with chronic obstructive pulmonary disease to participate in cognitive behavioural therapy**

This manuscript was submitted for publication into Journal of Health Psychology on the 13<sup>th</sup> of November 2017 and is currently under review.

Tina Phan, Owen Carter, Grant Waterer, Li Ping Chung, Maxine Hawkins, Cobie Rudd & Natalie Strobel. A qualitative investigation of the facilitators and barriers for people with chronic obstructive pulmonary disease to participate in cognitive behavioural therapy. Journal of Health Psychology. (Submitted for review on 13 November 2017).

## **6 Study rationale**

Cognitive Behavioural Therapy (CBT) is a promising treatment option for people with COPD suffering from anxiety and depression, but many investigative studies report low recruitment and high attrition rates. The following chapter (Study Four) seeks to investigate the facilitators and barriers to successful completion of CBT delivered via face-to-face groups (CBT) or DVD (DVD) as reported in the previous chapter (Study Three), with the aim to improve future recruitment and retention.

This is the first known qualitative study undertaken to specifically investigate the facilitators and barriers to uptake and completion of CBT in people with COPD. In-depth interviews were conducted with a subset sample of people from the wider Breathing New Life study cohort. Transcriptions were analysed using a phenomenological approach. Key facilitators for traditional face-to-face group CBT included the social interaction, whilst for both modalities the ability to identify with other people suffering from COPD was important. Some DVD participants lacked the technical skills required to actively engage with technology and the accompanying manual.

## CHAPTER SEVEN

### 7 GENERAL DISCUSSION

#### 7.1 Discussion

This thesis was originally undertaken in response to a need suggested in the literature for greater accessibility to psychological treatment options for anxiety and depression for people living with chronic obstructive pulmonary disease (COPD). Building upon a promising body of literature demonstrating the efficacy of traditional face-to-face group cognitive behavioural therapy (CBT) for people with COPD, a novel, home-based self-management CBT resource in the form of a DVD with accompanying manual, was specifically developed for people with COPD. This resource was developed using considerable expertise from a multi-disciplinary team, including respiratory physicians, psychologists, physiotherapists, nurses, health consumer representatives and COPD patients themselves. A randomised controlled trial methodology was devised and undertaken to test the efficacy of this novel intervention compared to CBT delivered as shortened group sessions and care as usual defined as treatment prescribed by participants' GPs. However, the study failed to establish the efficacy of either format of CBT to improve anxiety, depression or health-related quality of life (HRQoL). A number of possible explanations exist for why this thesis failed to replicate previous findings that demonstrated the efficacy of CBT for this cohort. Some explanations have already been discussed in Chapter Five but there are others that also need to be acknowledged in the context of this thesis. Given that the cognitive behavioural paradigm is well established in psychological science as an effective theoretical framework for the

treatment of anxiety and depression (123), it seems more likely that failure lay in the treatment modalities. In previous studies that conducted face-to-face CBT sessions with COPD populations, the number and length of sessions is highly variable, with the number of sessions ranging from 1–12 with an average of six sessions conducted between 90–120 minutes' duration, with 120–720 minutes total time spent in sessions and 0–6 follow-up phone calls provided (Appendix 2.1). However, the number of face-to-face CBT sessions in the present research was reduced to two 4.5 hour sessions, plus a single follow-up 1 hour telephone call, to reduce the demand on participants. Thus, the failure of the group CBT intervention to affect measurable improvements may be due to an insufficient number of sessions; two sessions plus a telephone call may not be enough for participants with COPD to establish measurable behavioural changes that reduce anxious and depressive thoughts and feelings. More sessions may be required but it is unclear exactly how many sessions would be optimal for a benefit to be seen whilst simultaneously reducing the burden of attending face-to-face sessions to prevent high drop-out rates in COPD participants. Furthermore, for those with concomitant anxiety and depression, the question of how many sessions are optimally required to treat both psychological conditions must also be considered, as the brief CBT intervention used in this thesis may not simply have been enough.

The home-based self-management CBT intervention on DVD with accompanying manual was also developed to reduce the need to travel and was based upon two previous studies in people with COPD demonstrating positive mental health outcomes from CBT delivered via an audio CD and self-help manual, and via a manual alone (35, 38). However, the present research was unable to demonstrate the efficacy of this six



week, self-paced, CBT intervention on DVD with accompanying manual. One possible reason why the home-based self-management intervention did not work may have been due to the lack of interactive support. Both studies which found a significant improvement on anxiety and depression had telephone support in addition to the self-management resources. However, the DVD resource investigated in this thesis had no additional telephone coaching supplied—follow-up phone calls were only undertaken to monitor compliance. Self-management CBT may require additional personal support when delivered to people with COPD. Further investigation of self-management CBT resources in people with COPD are clearly required and should aim to compare the delivery of home-based self-management CBT resources whilst systematically varying telephone support to investigate whether this is the case.

It is possible that the study was statistically underpowered due to its sample size. Increasing the sample size would undoubtedly have improved the chance of producing a statistically significant result but as previously discussed in Chapter Five, this difference would have been small (one point mean difference between groups on the BAI and BDI-II) raising the question whether the difference would translate into any practical, clinical meaningfulness. This highlights the importance of developing an intervention to achieve clinically meaningful outcomes so that the patient population directly benefits from noticeable improved symptomatology. It is also entirely possible that only two published manuscripts describing successful self-management CBT interventions for people with COPD exist so far due to publication bias, evident where scientific journals are more likely to report statistically significant results and less likely

to publish results of studies with null hypotheses (124). Consequently, publication bias may also deter researchers from submitting their manuscripts with null hypotheses. Thus it is conceivable that other studies also found a lack of significant clinical improvements to psychological symptomatology using self-management CBT resources and this thesis was not alone in that conclusion, potentially explaining why a positive effect was not detected because this method of delivering CBT is not efficacious.

Although no measurable benefit was detected for either of the CBT interventions used in the randomised controlled trial, the qualitative results from Study Four (Chapter Six) suggest participants perceived some value. This dissonance raises the question as to why their perceived value did not translate to quantifiable improvements in symptomatology scores. One possible explanation is that despite the interviewer's best efforts to establish rapport and pursue in-depth lines of enquiry, the interviewed participants potentially remained too polite to complain about the interventions and the interviews suffered from a degree of socially desirable response bias. A second explanation is that the interviews suffered from response bias with participants who found the intervention helpful more likely to consent to participate in the interviews than those who found it unhelpful. Fortunately, a comparison of interviewed versus non-interviewed participants' quantitative anxiety and depression measures is possible. If the former explanation was the case, then it would be expected that interviewed participants' scores would differ little from non-interviewed participants' scores. If the latter explanation is true then it would be expected that interviewed

participants' scores would differ significantly from those not interviewed. As it turns out, interview participants had slightly, but significantly, lower anxiety scores and significant and substantially lower depression scores than their non-interviewed counterparts six months after the interventions—the time when the interviews took place (Table 7.1). These data support the theory that there was selection bias for the interviews, thereby providing a compelling explanation for the discord between the quantitative and qualitative results of the present dissertation. To overcome this limitation, future research would benefit from further stratifying the interview sample into groups of participants who objectively improved their psychological symptomatology.

**Table 7.1** Independent *t*-tests comparing 6-month post-intervention Beck Anxiety Inventory (BAI) and Beck Depression Inventory (BDI-II) mean scores of participants interviewed vs. not-interviewed

Measure	Group	Mean $\pm$ SD	Mean difference	p-value
BAI	Interviewed	15.56 $\pm$ 8.88	0.752	0.858
	Not-interviewed	16.31 $\pm$ 12.00		
BDI-II	Interviewed	13.44 $\pm$ 8.16	8.152	0.046
	Not-interviewed	21.60 $\pm$ 11.49		

Another possible cause of selection bias which future research would benefit from addressing is the differing stages of behaviour change in participants. The benefits reported by the subset of participants interviewed may not accurately reflect the opinions of all involved in the Breathing New Life study as those interviewed may have entered the study at a stage receptive to long-term behaviour change. Thus, as

outlined in the Transtheoretical model of behaviour change (125), these participants believed the CBT interventions helped them because they were open to the possibility. However, those not interviewed and the vast majority of participants may have inversely been in the 'pre-contemplation' stage with either no-to-little intention to change before entering the study or the 'action' stage where active efforts to change occurred but participants were unable to maintain these new positive behaviours and instead relapsed into a previous stage (125). Future research would benefit from building individual capacity for COPD participants to engage in their care by actually asking whether they are ready for change before involvement in CBT and investigating how best to support participants once enrolled, to maximise mental health outcomes.

Due to the convenient nature of the DVD resource, it was hypothesised that compliance rates in the DVD group would be higher than those in the CBT group. However, comparable compliance rates were found that reinforced the opinions reported by participants in Study Four (Chapter Six) that the CBT treatments were sufficient in terms of setting, delivery, content, duration and number of sessions which were hypothesised as potential barriers. People with COPD appear to enjoy CBT and find it is a useful treatment approach once engaged. Recruiting participants in the first place remains a great hurdle. Findings from Study Four (Chapter Six) suggest that the best way to target this type of therapy to COPD populations is to describe the benefits of better breathing control skills gained and the importance of learning and benefitting from shared experiences with their peers.

The present research also specifically investigated the determinants for concomitant anxiety and depression in people with COPD in order to build a holistic picture of risk factors for this population which are currently lacking. As mentioned previously, it is somewhat surprising that the literature investigating risk factors has primarily treated the morbidity and mortality attributed to anxiety and depression independently, given that 22–48% of people with COPD are estimated to suffer from concomitant psychological symptomatology (61). The finding that people with COPD at a younger age are at greater risk of both anxiety and depression makes implicit sense. Receiving a diagnosis of an irreversible, progressive lung disease at a younger age would be more distressing than receiving the same diagnosis at an older age due to the life-long implications and greater loss potentially perceived by people of younger age. It would be advantageous for clinicians to be particularly mindful of their patient's mental health when dealing with those diagnosed with COPD at a relatively younger age compared to most other patients.

Lastly, findings of this thesis support the use of screening tools for psychological symptomatology in people with COPD. The commonly used screening measures in people with COPD tested for this thesis all demonstrated good discriminant validity with a structured clinical interview, with minor adjustments to the BDI-II and the Hospital Anxiety and Depression Scale (HADS) depression subscale further improving sensitivity and specificity. However, our results for the HADS remain equivocal as they contrasted with the two previous studies investigating this tool in people with COPD. Furthermore, the Beck inventories have yet to be validated for use in people with COPD despite their popularity as screening tools in COPD literature. Replication is the

cornerstone of the scientific method and future validation studies are clearly required to provide more clarity to this area.

## **7.2 Thesis limitations**

The strengths and limitations of individual studies presented in this thesis have been discussed in each corresponding chapter. Thus, this section will focus on research limitations applicable to the greater research findings. As previously mentioned, some of the key strengths of this thesis are the use of a representative sample of people with COPD, validated and popular outcome measures to screen for clinically significant levels of anxiety and depression, and a randomised controlled design. Thus, readers can be assured the study findings are based on sound methodology. However, due to the nature of the study topic, it is possible this sample of people with COPD suffered from selection bias with those who were not anxious or depressed less likely to volunteer to participate or relate to the treatment options, or see the need for continued follow-up. There are limited solutions to control for this problem, thus readers should bear this in mind when interpreting the results of this thesis.

Some may also argue the use of screening tools to examine the prevalence of clinically significant levels of anxiety and depression distress levels in our COPD cohort limits conclusions drawn due to their inability to provide a psychiatric diagnosis that comes from a structured clinical interview. However, whilst a diagnosis from a structured clinical interview that meets The Diagnostic and Statistical Manual of Mental Disorders or the International Classification of Diseases and Related Health Problems criteria is

considered gold standard, the use of these measures can be a costly and time-intensive endeavour, hindering recruitment timelines. Study Two (Chapter Four) established the discriminant validity of the Beck inventories to the Mini Neuropsychiatric Interview and found they produced adequate sensitivity and specificity, thus providing confidence that the use of these screening tools was appropriate for our cohort. Furthermore, the Beck inventories are commonly used in previous studies and our use of these tools facilitates easy comparisons. Future studies may prefer to use structured clinical interviews to address these concerns.

The randomised controlled trial (RCT) conducted for this thesis was based upon literature that seemed clear and consistent on the efficacy of brief interventions. As such, the study was based upon the best available evidence. The fact that this thesis was unable to replicate previous findings is useful science as it suggests the extant literature is less robust than previously thought. It may be seen as a limitation that no pilot study was conducted to collect preliminary data and information to adapt the CBT interventions for optimal success in the RCT. Conducting the qualitative investigation into the barriers and facilitators to CBT faced by people with COPD after the interventions were carried out also limited the range of data collected and subsequent opportunity to shape and inform the RCT for this dissertation. It would be of great benefit to ensure these factors are investigated prior to conduction of future CBT intervention studies to maximise study design for optimal success.

### **7.3 Concluding comments**

There is little doubt that anxiety and depression are common comorbidities in people with COPD which contribute to greater morbidity and mortality in an already vulnerable population. Globally, findings from this thesis confirm the importance of routine screening and treatment for anxiety and depression in people living with COPD, especially those diagnosed at a younger age and without prior psychological medical history. The HADS is recommended as a short, free and validated tool for such screening but clinicians might consider a simple adjustment to the HADS depression subscale, as outlined in Chapter Four. People with COPD tend to be sceptical about the potential benefit for CBT to improve their lives. However, CBT can be promoted to this cohort by emphasising that it is a non-pharmacological approach to symptom reduction, techniques are taught to control breathing and support can be gained from sharing experiences with other people suffering from COPD. It is the author's hope that the research conducted as part of this thesis will eventually contribute to clear mental health recommendations in global guidelines for clinicians to refer to in order to improve the quality of life of people living with COPD.



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