OUTCOMES OF PULMONARY REHABILITATION IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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ABSTRACT

Chronic Obstructive Pulmonary Disease (COPD) is a progressive lung disease causing significant impairment and activity limitation. One in 20 Australians over 45 have COPD and in 2004 COPD related diseases were the fifth leading cause of death in Australia (1). COPD remains the second leading cause of avoidable hospital admissions (2). Significant costs are involved to manage persons with COPD including acute hospitalisation, rehabilitation and supportive care (3). COPD affects not only the lungs but has widespread systemic involvement, therefore symptoms extend beyond a productive cough and dyspnoea (4). Up until recently, it was thought that exercise was detrimental for patients with COPD and bedrest was the only appropriate activity (5). Evidence since then has proven that even though physical exercise does not change lung function, it can improve clinically meaningful physical and Quality of Life (QOL) outcomes (6, 7). Despite this, beyond physical exercise, it is unclear which are the best components and intensity in a Pulmonary Rehabilitation (PR) program (8, 9).

The main hypothesis of this thesis is that PR is effective in the management of COPD in relation to improving general wellbeing and QOL as well as reducing healthcare utilisation. The International Classification of Function, Disability and Health (ICF) was utilised to identify impairments, limitations and participation restrictions in persons with COPD. Four linked studies were developed in this thesis to address current gaps in evidence based practice in the management of stable COPD. A standardised framework was utilised to develop protocols for these studies. Firstly, a systematic review was developed to look into existing research into non-pharmacological and non-surgical interventions in the management of COPD and identify areas requiring further research. Two studies were then designed to investigate the performance of PR. One study investigated the acute healthcare utilisation of patients who participate in an Integrated Disease Management (IDM) and a PR program. Another study investigated whether physical and QOL gains following PR were maintained into the longer term. Lastly, a new intervention was added to a pre-existing...
community PR program to further improve its effectiveness. Gaps in evidence in relation to the optimal type of interventions and performance of PR were identified and recommendations were made to enhance current COPD management guidelines and guide future research.

Study 1 presented a systematic review on commonly used non-pharmacological, non-surgical interventions in PR. High quality evidence was available for physical exercise. Interventions such as inspiratory muscle training, self-management and integrated disease management have systematic reviews confirming their effectiveness. Techniques such as breathing exercises and psychological interventions have yet to show consistent improvements between trials. The study highlighted further large trials are required for some of these interventions. The optimal intensity, combination or components of PR remain unknown.

Study 2 was designed to see whether further improvements in patient participation and clinical outcomes could be made to a pre-existing community PR program. A cohort of patients was given additional group based Cognitive Behavioural Therapy (CBT) with themes designed to complement the physical and education components. The CBT group had significant improvements in exercise capacity, fatigue, stress and depression. No significant changes were seen in the control group. This showed CBT should be considered as an add on to current conventional PR programs to enhance its performance.

Studies 3 and 4 looked at the structure and effectiveness of the PR program. Study 3 reassessed patients more than one year after completion of a PR program. The repeat assessment consisted of recording patients’ physical exercise capacity, QOL, anxiety and depression measures. Following PR, many of gains made immediately post PR were lost in the long term. This highlights the need for regular surveillance or monitoring of these patients post-PR to identify those requiring further intervention.

Study 4 investigated changes in acute healthcare utilisation following enrolment in IDM and PR programs. Using 12 years of consecutive patient data, a
comparison was made between hospitalisation and ED presentations before and after participation in IDM. This showed IDM alone was effective in the reduction of healthcare utilisation, however the addition of PR did not reduce healthcare usage further. A survival benefit was seen in those who were PR completers compared to patients who received IDM only. This was the first such study that allowed a comparison of whether the combination of both IDM and PR produced any additional benefit.

In conclusion PR programs are highly effective in improving the QOL and wellbeing of persons with COPD. A multifaceted approach is required for the management of COPD. Rehabilitation strategies act to complement but not replace optimal pharmacological and surgical therapy. The ICF model in which the thesis is based upon allows the accurate documentation and mapping of the disability associated with the disease.
DECLARATION

This is to certify that,

i. the thesis comprises only my original work towards the PhD except where indicated in the preface

ii. due acknowledgement has been made in the text to all other material used

iii. the thesis is less than 100,000 words in length, exclusive of tables, maps, bibliographies and appendices.
I certify that this thesis is my original work. I am indebted to my colleagues who provided valuable assistance in the following areas:

Fary Khan: Advice, and review of all chapters.
Louis Irving: Advice, and review of all chapters.
Alexandra Gorelik: Assistance with statistical analyses.
Bhasker Amatya: Assistance with database setup.

Contribution of co-authors in the following multi-author papers:


A Gorelik: Statistical support and reviewed manuscript.
L Irving: Study design, advice and reviewed manuscript.
F Khan: Study design, advice and reviewed manuscript.


L Irving: Study design, advice and reviewed manuscript.
F Khan: Study design, advice and reviewed manuscript.
3. Luk EK, Kofoed, S, Irving L, Khan F. Rehabilitation interventions for COPD: An overview of systematic reviews. Journal of Rehabilitation Medicine. (Submitted for publication)

S Kofoed: Data analysis.
L Irving: Study design, advice and reviewed manuscript.
F Khan: Study design, advice and reviewed manuscript.


A Hutchinson: Study design, advice and reviewed manuscript.
M Tacey: Statistical support and reviewed manuscript.
L Irving: Study design, advice and reviewed manuscript.
F Khan: Study design, advice and reviewed manuscript.
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Alexandra Gorelik

Sarah Kofoed

Anastasia Hutchinson

Mark Tacey
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LIST OF PUBLICATIONS (peer-reviewed)

Related to this thesis


Luk EK, Khan F, Irving I. Maintaining gains following pulmonary rehabilitation. Lung. 2015;193:709-715

Luk EK. Nose to the grindstone: The hidden dangers of long-term oxygen therapy. International Journal of Therapy and Rehabilitation. 2015;22:544-545

Luk EK, Kofoed, S, Irving L, Khan F. Rehabilitation interventions for COPD: An overview of systematic reviews. Journal of Rehabilitation Medicine. (Submitted for publication)

CONFERENCE PRESENTATIONS

Sep 2013  Invited speaker presenting on evidence of pulmonary rehabilitation at the Australasian Faculty of Rehabilitation Medicine (AFRM) Annual Scientific Meeting, Sydney

Oct 2013  Presenter of COPD workshop of CBT in pulmonary rehabilitation, Royal Melbourne Hospital, Melbourne

Aug 2014  Presented COPD and pulmonary rehab at the National Research and Ageing Institute (NARI), Melbourne

June 2015  Presented “Long Term Outcomes of Pulmonary Rehab” at the 9th World Congress of the International Society of Physical and Rehabilitation Medicine (ISPRM), Berlin Germany

Oct 2015  Poster presented “Outcomes of a Community Rehabilitation Program” at the Australasian Faculty of Rehabilitation Medicine (AFRM) Annual Scientific Meeting, Wellington New Zealand

Oct 2015  Presented “Does Cognitive Behavioural Therapy improve outcomes in pulmonary rehabilitation?” at the AFRM Annual Scientific Meeting, Wellington New Zealand

May 2016  Presented of “Rehabilitation Interventions for COPD: An overview of systematic reviews” at the 10th World Congress of the ISPRM, Kuala Lumpur Malaysia

Oct 2016  Poster presented “Comparing the patterns of acute health care utilisation in patients with chronic obstructive pulmonary disease who received different disease management interventions” at the Rehabilitation Medicine Society of Australia and New Zealand 1st Annual Scientific Meeting, Melbourne
GLOSSARY

Chronic Obstructive Pulmonary Disease (COPD)
COPD is defined by the Lung Foundation Australia has a long-term disease of the lungs which causes shortness of breath. COPD is an umbrella term for conditions including emphysema, chronic bronchitis and chronic asthma which is irreversible.

Integrated Disease Management (IDM)
A system of coordinated healthcare interventions and communications for populations with conditions in which patient self-care is significant.

International classification of functioning, disability and health (ICF)
A classification system developed by the World Health Organisation and is a classification of health and health-related domains. These domains are classified from the body, individual and society perspectives. It uses a standardised common language permitting communication about health and health care across the world in various disciplines and sciences.

Pulmonary Rehabilitation (PR)
An evidence-based, multi-disciplinary, and comprehensive intervention for patients with chronic respiratory diseases who are symptomatic and often have decreased daily life activities. It is based on a thorough patient assessment followed by patient tailored therapies that include exercise training, education, and behaviour change.

Rehabilitation
A process of transforming a person with functional limitations to a person with maximal ability through the use of medical treatment, therapy or adaptive equipment. The aim is to optimise a person’s physical, psychological, social, vocational, avocational and education potential in the presence of physiological or anatomic impairment and environmental limitations.
# GLOSSARY OF ABBREVIATIONS

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>6MWT</td>
<td>6 Minute Walk Test</td>
</tr>
<tr>
<td>CBT</td>
<td>Cognitive Behavioural Therapy</td>
</tr>
<tr>
<td>COPD</td>
<td>Chronic Obstructive Pulmonary Disease</td>
</tr>
<tr>
<td>CRQ</td>
<td>Chronic Respiratory Questionnaire</td>
</tr>
<tr>
<td>DASS</td>
<td>Depression Anxiety Stress Scale</td>
</tr>
<tr>
<td>ED</td>
<td>Emergency Department</td>
</tr>
<tr>
<td>FEV1</td>
<td>Forced Expiratory Volume in one second</td>
</tr>
<tr>
<td>GOLD</td>
<td>Global Initiative for Chronic Obstructive Lung Disease</td>
</tr>
<tr>
<td>HADS</td>
<td>Hospital Anxiety Depression Scale</td>
</tr>
<tr>
<td>IDM</td>
<td>Integrated Disease Management</td>
</tr>
<tr>
<td>ISWT</td>
<td>Incremental Shuttle Walk Test</td>
</tr>
<tr>
<td>MID</td>
<td>Minimal Important Difference</td>
</tr>
<tr>
<td>PAIS</td>
<td>Psychosocial Adjustment to Illness Scale</td>
</tr>
<tr>
<td>PR</td>
<td>Pulmonary Rehabilitation</td>
</tr>
<tr>
<td>QOL</td>
<td>Quality of Life</td>
</tr>
<tr>
<td>SGRQ</td>
<td>St Georges Respiratory Questionnaire</td>
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CHAPTER 1 – THESIS INTRODUCTION

1.1 INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is a chronic respiratory lung disease which causes significant morbidity and mortality worldwide. Approximately 65 million people have COPD worldwide and it is currently the fourth leading cause of death (10, 11). Substantial financial resources are required not only to diagnose and treat COPD, but also for symptomatic and chronic management. The management of COPD is more costly overall per case than cardiovascular disease, osteoporosis or arthritis and in 2008 cost the Australian economy $98 billion (12).

COPD not only causes lung damage, but is also a systemic disorder affecting multiple organ systems (4). Unfortunately, the only intervention that has been shown to slow lung function deterioration is smoking cessation (6). In contrast, other interventions can assist with maintaining Quality of Life (QOL) or physical mobility (6). Optimal management of COPD covers a broad spectrum of services including anticipatory care, acute care, Pulmonary Rehabilitation (PR) and palliative care (13). An effective COPD management plan includes four components: 1) assessing and monitoring disease; 2) reducing risk factors; 3) managing stable COPD; and 4) managing exacerbations (14).

Pulmonary rehabilitation is a comprehensive intervention based on thorough assessment followed by patient-tailored therapies, such as exercise training, education, and behaviour change (15). It is designed to promote the long-term adherence of health-enhancing behaviours (15). Essential elements include patient assessment and correct prescription, physical exercise, education and program evaluation (16). PR has been shown to improve patients’ QOL and physical outcomes (7).

Given that the spectrum and severity of COPD is broad, the treatment of COPD needs to be individualised. However, there needs to be a structure to accurately
document how COPD affects each patient beyond their immediate medical needs. The World Health Organisation has developed standardised terminology and framework for the definition, measurement and description of health and disability (17). The International Classification of Functioning, Disability and Health (ICF) is a classification of health and health-related domains. These domains are classified into the body, individual and society perspectives (17). (See Table 1.1 and Figure 1.1). Figure 1.1 also illustrates how the ICF can be applied for a person with COPD.

Contextual factors are divided into environmental and personal factors. Personal factors describe race, gender, age, education and past and present experiences. They are not coded in ICF because they are independent of the health condition but can influence how a person functions (18). Environmental factors potentially have an impact on all components of functioning and disability, but are not generally within the person's control (18).
Figure 1.1: Interactions between the components of the World Health Organisation International Classification of Functioning, Disability and Health in a person with COPD

At individual level

At institutional level

At social level

Body functions and structures (Impairment)
- Dysepsnoea
- Fatigue
- Muscle weakness
- Impaired gas exchange

Activities (Limitation)
- Reduced mobility
- Difficulty with personal ADLs

Participation (Restriction)
- Work
- Education
- Leisure activities

Environmental factors
- Equipment
- Access to health facilities
- Home access
- Air pollution

CONTEXTUAL FACTORS

Personal factors
- Mood & Anxiety
- Stress
- Social background
- Socio-economic status
- Malnutrition

ADLs = Activities of Daily Living

Adapted from (19)
Table 1.1: Definitions of components of ICF

<table>
<thead>
<tr>
<th>TERM</th>
<th>DEFINITION</th>
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<tbody>
<tr>
<td>Body Functions</td>
<td>Physiological functions of body systems</td>
</tr>
<tr>
<td>Body Structures</td>
<td>Anatomical parts of the body such as organs, limbs and their components</td>
</tr>
<tr>
<td>Impairments</td>
<td>Problems in body function or structure such as a significant deviation or loss</td>
</tr>
<tr>
<td>Activity</td>
<td>Execution of a task or action by an individual</td>
</tr>
<tr>
<td>Participation</td>
<td>Involvement in a life situation</td>
</tr>
<tr>
<td>Activity Limitations</td>
<td>Difficulties an individual may have in executing activities</td>
</tr>
<tr>
<td>Participation Restrictions</td>
<td>Problems an individual may experience in involvement in life situations</td>
</tr>
<tr>
<td>Environmental Factors</td>
<td>The physical, social and attitudinal environment in which people live and conduct their lives</td>
</tr>
</tbody>
</table>

Adapted from (17)

1.2 ISSUES AFFECTING THE DEVELOPMENT AND IMPLEMENTATION OF PULMONARY REHABILITATION

The latest combined American Thoracic Society and European Respiratory Society statement on PR has highlighted pertinent issues facing PR (15). These include:

- Increasing accessibility of PR
- Optimising PR components to produce meaningful and sustainable behaviour change
- Defining the various phenotypes of COPD and consequently personalising PR
The Australian Lung Foundation estimates less than 5% of patients who could benefit with PR are actually referred (20). There have been many barriers to increase patient uptake in PR. This is highlighted in Table 1.2.

**Table 1.2: Factors influencing uptake of pulmonary rehabilitation**

<table>
<thead>
<tr>
<th>FACTORS</th>
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<tbody>
<tr>
<td>Patient</td>
<td>• negative perceptions that PR doesn’t work</td>
</tr>
<tr>
<td></td>
<td>• negative perceptions about exercise and gyms</td>
</tr>
<tr>
<td></td>
<td>• low self-confidence about being seen during exercise</td>
</tr>
<tr>
<td></td>
<td>• lack of transport options</td>
</tr>
<tr>
<td></td>
<td>• distance to PR facility</td>
</tr>
<tr>
<td>Staff</td>
<td>• negative attitude towards efficacy of PR</td>
</tr>
<tr>
<td></td>
<td>• lack of awareness that PR exists</td>
</tr>
<tr>
<td></td>
<td>• some programs require a respiratory physician referral</td>
</tr>
<tr>
<td></td>
<td>• lack of formal training in PR</td>
</tr>
<tr>
<td>Systemic or general</td>
<td>• lack of equipment or venues</td>
</tr>
<tr>
<td></td>
<td>• long waiting lists</td>
</tr>
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</table>

Adapted from (21, 22)

Once patients commence PR, up to 30-50% of patients may not complete the program (23). Similar factors influencing why patients do not start PR are also implicated in its discontinuation. In addition to these factors, the presence of depression, smoking status, living alone and poor social support have been identified as risk factors for non-completion (23).

Future research should be directed at not only the factors impeding the uptake and continuation or completion of PR, but also improving the response to PR. Novel forms of PR such as tele-rehabilitation or home based programs could potentially improve delivery but also yield a cost benefit (22). The optimal duration and intensity of PR has yet to be identified. Lastly, targeting early
stages of COPD, such as in minimally symptomatic individuals could potentially reduce functional and mobility decline further down the course of disease.

1.3 CURRENT GAPS AND ISSUES IN EVIDENCE BASE FOR PULMONARY REHABILITATION

PR is a relatively new intervention when compared to other rehabilitation streams such as orthopaedic or neurological rehabilitation. In recent years, the evidence base and rationale for PR has increased. PR is considered as a “caring” type intervention and obtaining evidence of this can be difficult (24). Furthermore, until recently studies in this area had methodological problems such as small sample size, lack of adequate controls, non-validated outcome measures or the absence of prospective data collection (see Chapter 3 for further details) (24). For instance, dyspnoea is a rather subjective phenomenon and difficult to quantify. Validated outcome measures such as the Modified Medical Research Council (mMRC) scale is now available to allow researchers and clinicians to measure dyspnoea reliably (25).

Multiple studies detailing PR interventions such as exercise training have consistently shown improvements to the point where the Cochrane Collaboration has decreed that further studies are not required (26). However, this does not mean that no further studies or research are required in PR. There still are a number of significant and important areas of PR where good quality evidence is lacking.

Guidelines have suggested the following areas where further research is required (15, 27):

1. The long-term benefits of PR and whether PR leads to meaningful and sustainable behaviour change
2. The efficacy and role of the different components of a PR program
3. Cost effectiveness of PR
4. Use of PR programs with milder forms of COPD
5. Use of PR programs in acute settings, such as following an exacerbation of COPD
6. Understanding the heterogeneity and multisystem complexity of COPD, especially in the context of tailoring PR programs depending on phenotype or stage of COPD

1.4 HYPOTHESIS

The main hypothesis of this thesis is that PR is effective in the management of COPD in relation to improving general wellbeing and QOL as well as reducing healthcare utilisation. Factors affecting PR performance will be identified as well as additional rehabilitation components which improve PR effectiveness.

1.5 OBJECTIVES

Initially, projects were developed to determine what evidence is already available and subsequently, appropriate projects were designed to address areas lacking in good quality evidence. Patients with COPD and enrolled within the Royal Melbourne Hospital (RMH) were analysed in these projects.

The specific aims of the individual studies are:

1. To describe the current evidence base for the non-pharmacological, nonsurgical management of persons with COPD (Study 1).
2. To determine whether the addition of Cognitive Behavioural Therapy (CBT) to a PR program is associated with improved physical and QOL outcomes (Study 2).
3. To describe the long-term outcomes in persons with COPD attending PR in a community setting (Study 3).
4. To identify factors which contribute to increased utilisation of acute health care services (Study 4).
5. To compare the effectiveness between PR and Integrated Disease Management (IDM) in reducing acute healthcare utilisation and mortality (Study 4).

1.6 BRIEF OVERVIEW OF METHODS

A variety of methods and techniques can be utilised in the research of health sciences and specifically, in PR. Once the impairments and disability were identified using the ICF model, and the relevant aims and objectives were set, several study designs were drafted. Further, the advantages and disadvantages of either using a quantitative or qualitative study design were explored (See Table 1.3)

Table 1.3: Comparison between quantitative and qualitative designs

<table>
<thead>
<tr>
<th>GOALS</th>
<th>QUANTITATIVE INQUIRY</th>
<th>QUALITATIVE INQUIRY</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Seeks explanation or causation</td>
<td>• Seeks to build an understanding of phenomena</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Often focused on meaning</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• May be descriptive</td>
</tr>
<tr>
<td>DATA</td>
<td>• Can be manipulated numerically</td>
<td>• May be comprised of words, behaviours or images</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Goal is precise, objective, measurable data that can be analysed with statistical</td>
</tr>
<tr>
<td></td>
<td></td>
<td>procedures</td>
</tr>
<tr>
<td>RESULTS</td>
<td>• To predict, generalise, causality</td>
<td>• Contextually based</td>
</tr>
</tbody>
</table>

Adapted from: (28)

In this thesis, a quantitative research approach was used for the basis of the studies that were designed to address the relevant objectives. Quantitative methods are more frequently used in rehabilitation research and are the gold
standard for establishing the efficacy or applicability of a treatment (29, 30). However, it is recognised that not all problems in medical research can be answered with the quantitative technique and indeed a qualitative approach may allow phenomena to be studied from more perspectives and in greater depth. Potentially, it could allow any research studies be more easily carried out in a normal environment with minimal distraction to clinical duties (29).

Chapter 3 will describe the methodologies used in more detail, however the CBT Study would be considered a phase II, prospective controlled clinical trial, the Long Term Study was a prospective cohort study and the Healthcare Utilisation Study was a retrospective cohort study.

1.6.1 SETTING AND PARTICIPANTS

The projects which involved the use of subjects were conducted between the RMH and Merri Health (previously Merri Community Health Service - MCHS) sites. Ethics approval was obtained from the Melbourne Health Human Research and Ethics Committee (HREC Approvals QA2014002, 2012.174, QA2015130).

In the Cognitive Behavioural Therapy (CBT) Study (Study 2, Chapter 5), patients who were referred to the ambulatory PR program during the 18-month trial were screened and consented for participation into the study. Patients were eligible for this study if they had stable COPD, ability to comprehend English and consent for the study and were able to attend regular PR sessions. Exclusion criteria included prior psychological treatment within the past three months and any significant psychiatric history such as psychosis, bipolar disorder, schizophrenia, mental retardation, borderline personality disorder, chronic suicidal behaviour or major depressive disorder with prior hospitalisation episodes.

In the Long Term Study (Study 3, Chapter 6), eligible patients were identified from a centralised database at MCHS. Inclusion criteria included patients with a confirmed diagnosis of COPD and who have completed PR. This allowed a
minimum period of 12 months follow-up. Patients were excluded if they had severe cognitive impairment or were medically unwell for further assessment and testing.

Lastly, in the Healthcare Utilisation Study (Study 4, Chapter 7), information was obtained from a database containing all patients who were referred to an IDM program at the centre. IDM is a system of coordinated healthcare interventions and communications for populations with conditions in which patient self-care is significant (31). This database also contained information about their pulmonary rehabilitation program participation and was combined with the acute hospital database.

Further description of the methods used in this thesis are listed in more detail in Chapter 3.

1.7 OVERVIEW OF THESIS

Figure 1.2 illustrates the structure and overview of this thesis. A narrative literature search was initially conducted to review current literature in COPD and PR (Chapter 2). Following on from this, four linked studies were developed to address current gaps in evidence based practice in the management of stable COPD. A systematic review was conducted in commonly used non-pharmacological, non-surgical interventions in PR (Study 1, Chapter 4). The information from these two chapters gave the framework into the design of the subsequent chapters (described in Chapter 3). This included the CBT study (Study 2, Chapter 5) which was conducted to determine whether a novel intervention such as CBT could be utilised to improve the effectiveness of a pre-existing PR program. Following on from this, the Long Term Study (Study 3, Chapter 6) and the Healthcare Utilisation Study (Study 4, Chapter 7) describes the outcomes following PR, in particular the physical and QOL outcomes and healthcare utilisation following enrolment into the program.
Lastly, Chapters 8 and 9 contain discussions about the results and findings of this project and conclusions including clinical implications of this project and future research directions.

The next chapter will describe current literature in COPD and in particularly, PR for persons with COPD.
**AIM:** To evaluate the effectiveness of pulmonary rehabilitation for persons with COPD, including the optimal components and intensity of therapy

Study 1 – Systematic review of non-pharmacological, non-surgical rehabilitation interventions for stable COPD (Chapter 4)

Study 2 – Cognitive Behavioural Therapy (CBT) Study
n= 28
Study in the effectiveness of pulmonary rehabilitation with an additional CBT intervention (Chapter 5)

Study 3 – Long Term Study
n=88
Study of long term (>12mths) outcomes following pulmonary rehabilitation (Chapter 6)

Study 4 – Healthcare Utilisation Study
n= 517
Comparison and study of healthcare utilisation in patients enrolled in integrated disease management and pulmonary rehabilitation programs (Chapter 7)

Discussion (Chapter 8)

Conclusion (Chapter 9)
2.1 INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is a respiratory disorder causing a significant burden of disease. Two million people in Australia suffer from COPD. Approximately 12% of sufferers have severe or profound disability and COPD accounted for 3.3% of Disability Adjusted Life Years (DALYs). It is the sixth most common cause of death in men and seventh in women. The burden of COPD is projected to increase in the future because of continued exposure to COPD risk factors and an aging population.

COPD is characterised by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and the lung to noxious particles or gases. COPD is a combination of small airways disease (obstructive bronchiolitis) and parenchymal destruction (emphysema). Both processes may develop and progress independently of each other and therefore each person’s symptoms may vary.

The three most common symptoms in COPD include, cough, sputum production and exertional dyspnoea. Other pertinent medical history may include frequent respiratory infections or increasing fatigue and restriction of activity. People with COPD may have subtle symptoms for many months or years prior to their diagnosis.

The earliest description of COPD was by Laënnec, the inventor of the stethoscope in 1821. He was performing dissections of patients whom he had been following and described the combination of overinflated lungs and bronchi filled with mucous fluid. However, COPD was not recognized as a
disease entity until 1965. Early criteria by the American Thoracic Society (ATS) were based on broad clinical or anatomical terms (34). This included diagnosis based on having symptoms such as chronic bronchitis or having pathologically diagnosed emphysema.

2.2 IMPACT OF COPD

The direct costs to the Australian community amounts to an estimated $8.8 billion annually, increasing to $98 billion if indirect costs such as loss of wellbeing are calculated (35). COPD exacerbations account for the greatest burden on the health system. The costs increase as the disease progresses, with the distribution of costs shifting from medications to hospitalisations and home care. Costs in developing countries may be related to the impact of COPD on the workplace and home productivity(32).

2.3 EPIDEMIOLOGY AND RISK FACTORS

14% of Australians have COPD (3). In comparison, regional specific prevalence varies from 0.2% in Africa to 1.7% in the Western Pacific including China (36). The variability is dependent on the definition of airways obstruction in addition to the presence of risk factors such as smoking (37). Ethnicity may be another factor in COPD, as death rates in indigenous Australians are five times that of non-indigenous Australians(3).

Smoking remains the most important risk factor for COPD. 18% of males and 15% of females in Australia smoke daily(38). Smoking related diseases have
increased substantially in women, and death rates are expected to rise accordingly. The age of starting smoking, total pack-years smoked and current smoking status are all predictive of COPD mortality (37). The occurrence of respiratory symptoms and the decline in respiratory function correlates with the amount of smoking exposure (39). Other types of tobacco and marijuana are also risk factors for COPD (32). Passive exposure to tobacco smoke is known to cause respiratory symptoms, though whether it can be implicated in the development of COPD remains uncertain (39).

Occupational exposures such as dust and fumes have been suggested as risk factors for COPD. This includes coal mining, gold mining and cotton textile dust. It is estimated the population attributable risk from occupational exposure to be at 15% (40).

Air pollution is another important environmental factor. Prevalence rates of COPD as well has cases of respiratory hospitalisation are increased in urban and more polluted areas (11). However it appears the role of outdoor air pollution is small when compared with cigarette smoking (32). Indoor pollution from the use of biomass cooking and heating remains a significant risk factor in developing countries. The reduction of indoor air pollution has been shown to decrease the risk of developing COPD (40).

Lastly, poverty is a risk factor for COPD, with the risk of developing COPD inversely related to socioeconomic status. It remains unclear whether this relates to exposures to air pollutants, overcrowding or poor nutrition which are also associated with low socioeconomic status (32).
2.4 AETIOLOGY AND PATHOGENESIS

2.4.1 PHYSIOLOGY
Early changes in COPD result from an inflammatory response. Noxious particles such as cigarette smoke appear to cause an exaggerated immune response in patients with COPD. This inflammatory process characterised by intense interaction and accumulation of cytokines and enzymes persists after smoking cessation through unknown mechanisms(32, 41). Oxidative stress and an excess of proteinases further modify lung inflammation. These are unique and explain the differences in pathophysiology between COPD and asthma(32). The inflammatory process damages the extracellular matrix of the lung. The adult lung is unable to restore the extracellular matrix and therefore unable to repair damaged alveoli (39).

The relationship between structure and function in COPD is not well understood(41). It is difficult to quantify the amount of emphysematous or bronchitic changes and the degree of airflow obstruction.

2.4.2 AIRFLOW OBSTRUCTION
Airflow obstruction or limitation relates to the ability to force air through the conducting airways. This resistance is dependent upon the physical property of the gas and length and diameter of the airways(41). During exhalation, the amount of airflow is the result of the balance between the elastic recoil promoting flow and the resistance of airways limiting flow (39). In early COPD, these changes are only evident at or below the functional residual capacity, but in more advanced disease this affects the whole expiratory cycle.
The reason why airflow obstruction develops in COPD is unclear. It is likely to be related to the destruction of tissues around the airways in emphysema decreasing the forces to keep airways open. Also, concurrent airways inflammation causes intrinsic narrowing of the airways.

2.4.3 HYPERINFLATION

Whilst airflow obstruction is observed only during exhalation, COPD also affects inspiration as inspiratory resistance is also increased (41). This in conjunction with the inability to expel the inhaled air leads to hyperinflation.

Hyperinflation, or air trapping occurs late in the disease. This compensatory phenomenon preserves maximum expiratory airflow because as lung volume increases, elastic recoil pressure increases with resulting airways enlargement so that airway resistance decreases (39).

Techniques such as pursed lip breathing, which decrease breathing frequency may result in deflation and thereby improve dyspnoea (41).

2.4.4 GAS EXCHANGE

Non-uniform ventilation and ventilation-perfusion mismatching are characteristic of COPD (39). The respiratory centre is located in the upper medulla and is modulated by various inputs including oxygenation, carbon dioxide (CO₂) concentration and acid-base status. Through the nervous system it is able to control respiratory muscles in a manner which usually goes unnoticed and uses little energy (41).
A reduction in the partial pressure of oxygen in arterial blood ($\text{PaO}_2$) is not seen until the Forced Expiratory Volume in one second (FEV1) is decreased to less than 50% of predicted. Further changes such as increase in $\text{PaCO}_2$ does not occur until FEV1 is less than 25% of predicted (39).

### 2.4.5 Dyspnoea

Dyspnoea is defined as a subjective experience of breathing discomfort that consists of qualitatively distinct sensations that vary in intensity(42). Three primary categories of dyspnoea are described 1) – air hunger or the need to breath more 2) – work/effort or the sensation of exerting muscular effort and 3) chest tightness – usually associated with bronchospasm(41).

Multiple factors contribute to the feeling of dyspnoea. Receptors are based in the chest wall, the pulmonary vagus and chemoreceptors detecting oxygen and carbon dioxide levels. Respiratory muscle fatigue is recognized as a cause of dyspnoea in acutely compromised states but its presence in stable respiratory conditions is in doubt. It is likely that in stable disease respiratory muscles are at a level close to the fatigue threshold but are not fatigued(41).

Lastly, psychosocial factors can influence the perception of dyspnoea. Factors such as personality, anxiety, depression and coping strategies can alter the perception of intensity or distress of dyspnoea (39).

### 2.4.6 Airways Response

Beyond the physiological changes other pathological abnormalities are apparent. Pathological changes in COPD are found in the airways, lung parenchyma and pulmonary vasculature (43). In the large airways neutrophils
are found whereas in the small airways lymphocytes and macrophages predominate.

In the large airways, mucous gland enlargement and goblet cell hyperplasia are responsible for symptoms such as cough and mucus production which predominate in chronic bronchitis. Squamous metaplasia occurs which may predispose to carcinogenesis and disrupt mucociliary clearance. Smooth muscle hypertrophy and bronchial hyperactivity leads to airflow limitation (39).

Similar changes also occur in the small airways and alveoli, with goblet cells hyperplasia and smooth muscle hypertrophy also present (39). Luminal narrowing and reduce surfactant leads to alterations in efficiency in gas exchange.

Emphysema is characterised by abnormal enlargement of the airspaces distal to the terminal bronchiole, accompanied by destruction of their walls (44). The four major types of emphysema are defined in terms of anatomic nature and distribution within the lobule. Only centriacinar and panacinar cause clinically significant airflow obstruction (44). Centriacinar emphysema often occurs in the upper lobes and in focal areas. It affects the central or proximal parts of the acini and spares the distal alveoli. This type of emphysema is frequently seen in heavy smokers (39). In contrast, panacinar emphysema affects the whole acinus and is usually more evenly distributed within each lobe of the lung. This type of emphysema is associated with α1-antitrypsin deficiency (44). Whilst each type of emphysema has its own associations and appearance, most patients with COPD have mixed types. How each type of emphysema affects disease progression is unknown (39).


2.5 COMORBIDITIES

Comorbidities are common in COPD. These are defined as the coexistence of other medical conditions alongside COPD. COPD patients self-report higher prevalence of medical comorbidities than those not suffering from COPD (45). 32% have one additional condition, and 39% have two or more concurrent medical conditions (46). A median of nine comorbidities has been reported (47).

Even adjusting for confounding factors, COPD is an independent risk factor for many diseases (3). The reason for their association is unknown, but is believed to be related to systemic inflammation. Markers of systemic inflammation are increased in patients with stable COPD and increases with severity of COPD (48).

The aetiology of this systemic inflammation is unclear. Smoking is capable of triggering this inflammation, as even ex-smokers with COPD still have high levels of inflammation (41). COPD itself produces inflammatory changes within the pulmonary system, but it remains unclear how this causes systemic involvement. One theory includes a “spill over” of lung inflammation into the systemic circulation. Another theory is that hypoxaemia seen in COPD causes tissue hypoxia in other body systems, such as in skeletal muscle (41, 48).

Traditional inflammatory markers such as C-Reactive Protein (CRP), fibrinogen, ferritin and leucocytes are raised in patients with COPD (48). Cytokines such as Tumour Necrosis Factor (TNF-α) and interleukins are also elevated. Higher levels are seen during exacerbations in COPD (41).
The presence of comorbidities can affect Pulmonary Rehabilitation (PR) performance (15). Patients with multiple comorbidities have reduced Quality of Life (QOL) gains. Specific comorbidities such as cardiovascular disease can negatively influence both QOL and physical exercise gains (15).

2.5.1 SKELETAL MUSCLE DYSFUNCTION

Skeletal muscle dysfunction is defined by the net loss of muscle mass and malfunction of the remaining muscle mass (41). Patients with COPD have greater weakness (quadriceps strength) than those without COPD (4). The prevalence has been quoted to be approximately 15%, with increased prevalence with increased age, GOLD stage and Body-mass index, airflow Obstruction, Dyspnoea, and Exercise (BODE score) (49). Skeletal muscle dysfunction affects exercise capacity in PR (41). Systemic inflammation remains a major cause, however other factors may also be involved (see table 2.1). There is evidence that oxidative stress is consistently found in limb muscles, however, there is no strong relationship between muscle oxidative stress and local inflammation in patients with COPD (4).

Many COPD patients with skeletal muscle dysfunction also have overlapping muscle disuse/deconditioning. It is difficult to ascertain the degree of disuse and skeletal muscle dysfunction or myopathy in each patient (4). Similar clinical features are seen in both. Rehabilitation strategies must be targeted at both causes in order to be effective.
Table 2.1: Aetiologies of Skeletal Muscle Dysfunction

<table>
<thead>
<tr>
<th>Disuse</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inflammation</td>
</tr>
<tr>
<td>Oxidative stress</td>
</tr>
<tr>
<td>Hypoxaemia</td>
</tr>
<tr>
<td>Hypercapnia</td>
</tr>
<tr>
<td>Low levels of anabolic hormones and growth factors</td>
</tr>
<tr>
<td>Impaired energy balance</td>
</tr>
<tr>
<td>Vitamin D deficiency</td>
</tr>
</tbody>
</table>

Adapted from (4)

2.5.2 OBESITY

Both weight loss and weight gain are issues in COPD. Up to 30% of in patients with Global Initiative for Chronic Obstructive Lung Disease (GOLD) class 4 disease are underweight (4). In contrast, obesity rates vary between 24 to 54% in the COPD population (4). Those with predominantly chronic bronchitis (blue bloaters) are more likely to be overweight, whereas those with predominantly emphysema (pink puffers) are more likely to be underweight (4).

Using Body Mass Index (BMI) does not accurately measure changes in body composition such as muscle atrophy. COPD causes accelerated loss of lean tissue, leading to sarcopenia and cachexia (50). In addition, energy demands may be increased due to the work of breathing and respiratory tract infections (51). Fat Free Muscle Index (FFMI), provides a better measure of muscle mass in COPD. An FFMI less than 16 kg/m2 in men and less than 15 kg/m2 in women is associated with a 1.9-fold increase in mortality after adjusting for age, sex, and FEV1(52).
Many risk factors for COPD are shared with cardiovascular diseases (3). Even adjusting for smoking as a risk factor, patients with COPD are at nearly five times more likely to develop cardiovascular disease and three times more likely to suffer from stroke(3). Patients with COPD have more deaths and hospitalisations for cardiovascular causes than from COPD itself (48). Several mechanisms have been proposed. This includes endothelial dysfunction and systemic inflammation causing arterial thickness (53). COPD also produces a pro-coagulant state with higher levels of tissue factor and factor VIIa (53).

2.5.3 OSTEOPOROSIS

An increased prevalence of osteoporosis (35.1%) has been noted in patients with COPD (3). Postulated mechanisms included inhaled and oral corticosteroid use, reduced muscle mass (skeletal muscle dysfunction) and systemic inflammation (3, 48). Reduced FEV1, BMI and FFMI have been identified as risk factors for osteoporosis (3). Given that cigarette smoking has been identified as a risk factor for osteoporosis, it is difficult to discern at this stage whether the additional presence of COPD is an independent factor (54).

2.5.4 DEPRESSION AND ANXIETY

People with COPD are vulnerable to developing symptoms of anxiety and depression (3). There is an increased prevalence of depression (36%) and anxiety (40%) (55). The symptoms of COPD and depression often overlap (56). The presence of anxiety and depression leads to an earlier time to first admission with an exacerbation of COPD (53). Anxiety might be provoked by an altered autonomic nervous system (48).

It is difficult to establish the exact mechanism between COPD and anxiety or depression (57). The relationship between the conditions may be bidirectional
There may be a common pathophysiological process such as an increased inflammatory response leading to both COPD and anxiety or depression (56). Smoking and nicotine dependence itself can contribute to depression and anxiety.

**Figure 2.1: The theoretical relationship between anxiety and depression and COPD Exacerbations**

![Diagram showing the relationship between increased anxiety and depression, decreased ability to cope, increased hospital admissions, and increased exacerbations.](image)

Adapted from (58)

Other comorbidities more frequently associated with COPD include (3, 53):

- Cognitive impairment
- Gastro-oesophageal reflux disease
- Other lung disorders such as lung cancer and obstructive sleep apnoea
2.6 DIAGNOSIS

Most patients are diagnosed at a later GOLD stage of disease (59). Half of patients in the United States remain undiagnosed (60).

Symptoms such as dyspnoea, cough, sputum production and activity limitation are suggestive of COPD. Physical examination alone has been shown to have high specificity but low sensitivity for airflow obstruction (61). A combination of history and physical findings can improve the prediction of COPD but spirometry is required to make a formal diagnosis (39). The diagnosis can be confirmed by the following (61):

- Spirometry showing airflow limitation (Forced Expiratory Volume in 1 second/Forced Vital Capacity (FEV1/FVC) ratio less than 0.70 and FEV1 less than 80% of predicted)
- Absence of an alternative explanation for the symptoms and airflow limitation

At this point, there is no recommendation to screen asymptomatic individuals with spirometry (61).

Similarly, chest imaging has poor sensitivity and specificity for diagnosing COPD (62). Whilst patient with COPD have characteristic radiological changes suggestive of COPD, imaging such as X-Ray and Computed Tomography are commonly used to exclude differential diagnoses or complications of COPD.
2.7 NATURAL HISTORY

Fletcher et al has shown that lung function declines in normal individuals over time (63). Whilst cigarette smoking has been implicated as a risk factor for COPD, it is also responsible for a greater decline in lung function. Smokers can experience a decrease in FEV1 of 25–100mL/year (3). Stopping smoking will slow the rate of decline and eventually return to the same rate as that for non-smokers (63).

The reductions in lung function are not linear however. Greater reductions were seen in GOLD stage 2 and 3 disease (64). Mortality was higher in higher stages of GOLD classification disease (65).

2.8 CLASSIFICATION

The most common classification of severity of COPD is using spirometry or FEV1. The GOLD classification has four categories, ranging from one to four (32) (See Table 2.2). The GOLD classification cannot reliably predict symptomatology and QOL. Also, evidence is variable about the reliability of predicting morbidity and burden based on the GOLD classification (3, 11).
Table 2.2: GOLD Classification in relation to symptoms

<table>
<thead>
<tr>
<th>SYMPTOMS</th>
<th>MILD GOLD 1</th>
<th>MODERATE GOLD 2</th>
<th>SEVERE GOLD 3-4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Few symptoms</td>
<td>Increasing dyspnoea</td>
<td>Dyspnoea on minimal exertion</td>
<td></td>
</tr>
<tr>
<td>Breathlessness on moderate exertion</td>
<td>Breathlessness walking on level ground</td>
<td>Daily activities severely curtailed</td>
<td></td>
</tr>
<tr>
<td>Little or no effect on daily activities</td>
<td>Cough and sputum production</td>
<td>Chronic cough</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>LUNG FUNCTION</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV1≥80% predicted</td>
<td>FEV1 between 50-80% predicted</td>
<td>FEV1≤80% predicted</td>
<td></td>
</tr>
</tbody>
</table>

Adapted from (3, 11)

Other outcome measures apart from GOLD classification have been devised to add further information (32). Scales such as the COPD Assessment Test (CAT) provides added QOL details. The modified British Medical Research Council Questionnaire (mMRC) and the BODE index are able to predict future morbidity risk (25, 66, 67). Each of these indexes requires additional information such as subjective information from the patient in the mMRC index or functional exercise capacity and body mass index in the BODE index (See Tables 2.3 & 2.4).
### Table 2.3: The modified British Medical Research Council Questionnaire (mMRC)

<table>
<thead>
<tr>
<th>GRADING</th>
<th>SYMPTOMATOLOGY</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>I only get breathless with strenuous exercise</td>
</tr>
<tr>
<td>1</td>
<td>I get short of breath when hurrying on level ground or walking up a slight hill</td>
</tr>
<tr>
<td>2</td>
<td>On level ground, I walk slower than people of the same age because of breathlessness, or I have to stop for breath when walking at my own pace on the level</td>
</tr>
<tr>
<td>3</td>
<td>I stop for breath after walking about 100 metres or after a few minutes on level ground</td>
</tr>
<tr>
<td>4</td>
<td>I am too breathless to leave the house or I am breathless when dressing or undressing</td>
</tr>
</tbody>
</table>

Adapted from (66)

### Table 2.4: The Body-mass index, airflow Obstruction, Dyspnoea, and Exercise (BODE) index

<table>
<thead>
<tr>
<th>VARIABLE</th>
<th>POINTS ON BODE INDEX</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
</tr>
<tr>
<td>FEV₁ (% of predicted)</td>
<td>≥65</td>
</tr>
<tr>
<td>6 Minute Walk Test (6MWT)</td>
<td>≥350</td>
</tr>
<tr>
<td>Body mass index</td>
<td>&gt;21</td>
</tr>
</tbody>
</table>

Adapted from (25)
### 2.9 MEASUREMENT TOOLS

Given the broad spectrum of symptoms encountered by persons with COPD, a number of outcome measures are used in COPD research. Outcome measures are grouped according to the International Classification of Functioning (ICF) framework (68). Impairments that are measured include activity limitation (‘‘disability’’), participation limitation (‘‘handicap’’) and QOL. There is often overlap between all three elements. Commonly used outcome measures are listed in table 2.5.

#### Table 2.5: Commonly used objective measures in COPD

<table>
<thead>
<tr>
<th>Name of scale</th>
<th>Author, year</th>
<th>Subscales</th>
<th>No. of items</th>
<th>Scoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 Minute Walk Test (6MWT)</td>
<td>Butland et al, 1982 (69)</td>
<td>N/A</td>
<td>N/A</td>
<td>Ordinal scale</td>
</tr>
<tr>
<td>Borg Scale</td>
<td>Borg, 1982 (70)</td>
<td>N/A</td>
<td>N/A</td>
<td>0-10 (Modified version)</td>
</tr>
<tr>
<td>Chronic Respiratory Questionnaire (CRQ)</td>
<td>Guyatt et al, 1987 (71)</td>
<td>Dyspnoea, Fatigue, Emotion, Mastery</td>
<td>20</td>
<td>1-7 (Likert Scale)</td>
</tr>
<tr>
<td>Hospital Anxiety and Depression Scale (HADS)</td>
<td>Zigmond et al, 1983 (72)</td>
<td>Anxiety, Depression</td>
<td>14</td>
<td>0-3 (Likert Scale)</td>
</tr>
<tr>
<td>Incremental Shuttle Walk Test (ISWT)</td>
<td>Singh et al, 1992 (73)</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Modified Medical Research Scale (MMRC)</td>
<td>Fletcher et al, 1959 (74)</td>
<td>N/A</td>
<td></td>
<td>0-4 (Likert Scale)</td>
</tr>
<tr>
<td>St Georges Respiratory Questionnaire (SGRQ)</td>
<td>Jones et al, 1991 (75)</td>
<td>Symptoms, Activity, Impact</td>
<td>50</td>
<td>Dichotomous (true/false) except last question (4-point Likert scale)</td>
</tr>
</tbody>
</table>
The 6 Minute Walk Test (6MWT) or the Incremental Shuttle Walk Test (ISWT) are used to assess exercise capacity and therefore accurate exercise prescription. The walk test can provide the following information (16):

- Level of functional impairment and activity limitation
- Factors that limit exercise capacity
- Identify oxygen desaturation during exercise and prescription of supplemental oxygen
- Determine the extent of dyspnoea both at rest and on exertion
- Starting exercise prescription

The 6MWT is commonly utilised in PR and measures the distance patients can walk in 6 minutes (76). The ISWT differs from the 6MWT in that it is externally paced and incremental requiring the participant to gradually increase gait speed. The test is terminated when the participant is breathless or can no longer can keep up with the beeps (73).

Improving QOL remains an important goal in PR. Both general and respiratory specific QOL questionnaires are available. Respiratory specific questionnaires are more likely to be responsive to changes after PR and to specific respiratory issues (16). Two respiratory specific QOL scales are in use in PR. Both the Chronic Respiratory Questionnaire (CRQ) and St George’s Respiratory Questionnaire (SGRQ) have been shown to be efficacious.

The CRQ is a consists of a 20 item questionnaire which can either be self-administered or assisted by a clinician(71). The 20 items assess across four domains, dyspnoea, fatigue, emotional function, and mastery. Similarly, the
SGRQ can also be self-administered or clinician assisted (75). It contains 50 items assessing domains including symptoms, activity and impact.

Despite the increased prevalence of anxiety and depression, the current guidelines have not recommended routine screening (55). A variety of outcome measures are used to assess for the presence of anxiety and depression, though none were specifically designed to assess persons with COPD. Commonly used tools include the Hospital Anxiety and Depression Scale (HADS) and the Depression Anxiety and Stress Scale (DASS).

The HADS is a fourteen item scale that measures levels of anxiety and depression(72). Both anxiety and depression subscales have seven items each. Each item is rated on a scale of 0-3. Subscale scores greater than 8 has been used to indicate anxiety or depression (15). Alternatively, the total HADS score may be regarded as a global measure of psychological distress (77).

DASS similarly measures depression and anxiety but also has a third stress subscale. This is a 21 item self-reported questionnaire that measures the three related negative emotional states of depression, anxiety and tension/stress (78). Participants rated the extent to which they experienced each state over the past week on a 4-point Likert rating scale. When totalled, three domain scores are given. Scores of greater than 9, 7 and 14 are suggestive of depression, anxiety and stress respectively (78).
2.10 PHARMACOLOGICAL TREATMENT

Pharmacological agents are typically used to reduce symptoms, exacerbations and improve health status and exercise tolerance (11). However, no treatment can modify the long term decline in lung function (79). Common types of agents include:

- Bronchodilators
- Corticosteroids
- Antibiotics
- Mucolytics

2.10.1 BRONCHODILATORS

Bronchodilators affect smooth muscle relaxation causing improved lung emptying, reduce dynamic hyperinflation and improve exercise tolerance (11). FEV1 improvements are seen in spirometry. Bronchodilators can be given on an as-needed or a regular basis to reduce symptoms. Common bronchodilators include beta agonists, anti-cholinergics and theophylline.

Beta agonists act on the beta2 adrenoceptors (80). Short acting beta agonists such as salbutamol have rapid onset of action and lasts for 4-6 hours (11). Long acting beta agonists such as salmeterol and formoterol are used for long term maintenance therapy with its duration of action greater than 12 hours (80).

Anticholinergics target muscarinic receptors and inhibits cholinergic bronchomotor tone (80). Similar to beta agonists, both short and long acting forms are available. Ipratropium is a short acting inhaled anticholinergic with a
Longer duration of action than beta agonists (11). Longer acting anticholinergics such as tiotropium have duration of onset greater than 24 hours. Long acting anticholinergics are preferred in COPD management (80). Tiotropium has been shown to reduce exacerbations and improve health status (11). Newer long acting agents such as glycopyrronium, aclidinium and umeclidinium have been released to the Australian market. Few good quality trials exists comparing anticholinergics (81).

Theophylline is currently not recommended for the treatment of COPD due to its low patient tolerance and risk of overdose (80).

### 2.10.2 CORTICOSTEROIDS

Corticosteroids in both oral and inhaled forms have been used in COPD. Inhaled forms have been shown to decrease exacerbations and improve symptoms in some trials but the evidence has not been consistent (82). It has been suggested that inhaled corticosteroids should not be used as sole therapy and offers greater benefit in a certain subset of COPD patients such as those with frequent exacerbations (79).

Oral or systemic corticosteroids are commonly used for COPD exacerbations. However, its use in stable COPD is not recommended due to its multi-organ system side effects (82).

### 2.10.3 ANTIBIOTICS

Bacterial infection is one cause of COPD exacerbations, so the use of prophylactic antibiotics may be able to prevent exacerbations (83). Macrolides have been proposed to have anti-inflammatory and anti-secretory in addition to
its anti-microbial properties (84). The latest Cochrane systematic review has shown that continuous antibiotics reduces exacerbation rates (Odds Ratio (OR) 0.55; 95% confidence interval (CI) 0.39 to 0.77), however there was no change to secondary outcomes such as hospitalisation, mortality or lung function (83). Given the concerns about antibiotic resistance, guidelines do not recommend the general use of prophylactic antibiotics at this point (82).

2.10.4 MUCOLYTICS

Mucolytic agents such as N-acetylcysteine have a limited role in COPD and only patients with viscous sputum may benefit (11). The 2014 Cochrane systematic review showed that mucolytics produces a small reduction in acute exacerbations and quality of life (85). Despite this current treatment guidelines do not recommend its use (3).

2.11 NON-PHARMACOLOGICAL MANAGEMENT

The management of COPD requires both pharmacological and nonpharmacological therapies (86). Elements include encouragement and education in relation to exercise and smoking cessation. Many of these elements are included in PR programs. Surgical interventions are also available and of benefit to a subgroup of carefully selected COPD patients.

2.11.1 SMOKING CESSATION

Cigarette smoking is a major risk factor to COPD, hence smoking cessation should be a significant focus in COPD management (11). Stopping smoking
prevents the rate of FEV1 deterioration and has the greatest capacity to influence the natural history of COPD (3). Smoking cessation strategies should be made readily available.

Both psychotherapy and pharmacological therapy are available. The combination of the two provides the greatest benefit and both are considered equal contributors to success rates (3, 87).

Psychotherapy can include many forms. Brief counselling is effective and takes less than five minutes (88). Interventions which take little time are especially useful given not all patients are ready to quit smoking. According to the stages of change model, smokers can vary between pre-contemplation (not ready to quit) to maintenance (achieved smoking cessation) (88).

Other behavioural interventions are group based and include coping and social skills training, contingency management, self-control, and cognitive-behavioural interventions (89). Group sessions allow participants to share their experiences with quitting smoking and may lead to increase quit rates (89).

Current pharmacological interventions include Nicotine Replacement Therapy (NRT), bupropion and varenicline. NRT in particular, when combined with psychosocial interventions, has been shown to be effective (90). Varenicline appears to give more superior results than bupropion (91). All pharmacological treatments should be combined with a supportive intervention program (11).
2.11.2 LUNG VOLUME REDUCTION SURGERY

Lung Volume Reduction Surgery (LVRS) is a surgical technique in advanced emphysema with poor control despite maximal medical therapy (92). LVRS is a surgical procedure in which parts of the emphysematous lung are resected and consequently lung volume is reduced. The exact mechanism why LVRS works remains unknown, but is believed to be related to improving mechanical efficiency, reduced dynamic hyperinflation and improved left ventricular filling (11, 92). Patients with predominant upper-lobe emphysema and a low post-rehabilitation exercise capacity are most likely to benefit from LVRS (39). However, current guidelines maintain that LVRS is currently an experimental procedure (11).

Bronchoscopic LVRS is an emerging minimally evasive procedure whereby a valve, plug or coil is used to collapse emphysematous areas. It may provide benefit to highly selective patients in specialised centres (11). Further studies are required to confirm that bronchoscopic LVRS reduces morbidity and mortality compared to the open technique.

2.12 PULMONARY REHABILITATION

2.12.1 INTRODUCTION

Medical rehabilitation is defined as the process of transforming a person with functional limitations to a person with maximal ability through the use of medical treatment, therapy or adaptive equipment (93). PR, being a specialist branch of rehabilitation, is an evidence-based, multi-disciplinary, and comprehensive intervention for patients with chronic respiratory diseases who are symptomatic.
and often have decreased daily life activities (9, 16). It is based on a thorough patient assessment followed by patient tailored therapies that include exercise training, education, and behaviour change (15). PR is designed to reduce symptoms, optimise functional status, increase participation, and reduce health care costs through stabilising or reversing systemic manifestations of the disease (16).

The essential phases and components in a comprehensive PR program include (16, 94-97):

Assessment and evaluation phase

- Identification and quantifying effects of disablement (limitation in activity and participation)
- History and examination to determine patient’s ability to safely participate in an exercise program
- Prioritised goal setting through an interdisciplinary process and goals should result in improvement in patients’ potential
- Active patient participation to achieve set goals
- Measure outcomes (such as exercise capacity and QOL) to determine effectiveness of PR

Intervention phase

- Aim to arrest the pathophysiological processes causing tissue injury
- Therapeutic exercises which focuses on enhancement of organ performance
- Task reacquisition that emphasises total body adaptive techniques
• Environmental modification that directs effort towards environmental enhancement to improve participation

Evaluation phase

• Re-evaluate goals that were set at the beginning of the PR program
• Re-assess outcome measures (should be able to demonstrate reduction in impairments and improvements in activity and participation)
• Feedback to patient/client as well as their treating clinicians (such as the general practitioner and respiratory physician)
• Provide ongoing monitoring follow-up
• Offer appropriate maintenance exercise programs (dependent on local availability)

Similarly, the essential components of a comprehensive PR program are:

• Exercise training
• Breathing retraining
• Education
• Nutritional intervention
• Psychological support
• Program evaluation and outcomes
• Maintenance

The benefits of PR are wide-ranging, and are listed in the below table:
Table 2.6: Benefits of Pulmonary Rehabilitation

<table>
<thead>
<tr>
<th>Benefits</th>
<th>Level of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Improves exercise capacity</td>
<td>A</td>
</tr>
<tr>
<td>Reduces the perceived intensity of breathlessness</td>
<td>A</td>
</tr>
<tr>
<td>Improves health-related QO</td>
<td>A</td>
</tr>
<tr>
<td>Reduces the number of hospitalizations and days in the hospital</td>
<td>A</td>
</tr>
<tr>
<td>Reduces anxiety and depression</td>
<td>A</td>
</tr>
<tr>
<td>Improves arm function</td>
<td>B</td>
</tr>
<tr>
<td>Improves survival</td>
<td>B</td>
</tr>
<tr>
<td>Improves recovery after hospitalization for an exacerbiation</td>
<td>A</td>
</tr>
<tr>
<td>Enhances the effect of long-acting bronchodilators</td>
<td>A</td>
</tr>
</tbody>
</table>

Evidence derived from Global Initiative for Chronic Obstructive Lung Disease (GOLD), A = rich body of data, B = limited body of data

Adapted from (98)

Careful patient selection will optimise results in PR. Current guidelines recommend patients be referred when their FEV1 is less than 50% predicted or in those patients with symptoms (see Table 2.7) (15). Referral of patients with milder disease will allow for more emphasis on preventive strategies and maintenance of physical activity (15).
Table 2.7: Indications for pulmonary rehabilitation

- Dyspnoea/fatigue and chronic respiratory symptoms
- Gas exchange abnormalities including hypoxemia
- Decreased functional status
- Decreased occupational performance
- Difficulty performing activities of daily living
- Psychosocial problems
- Nutritional depletion
- Increased use of medical resources
- Impaired health-related quality of life

(Adapted from (15))

A thorough assessment includes taking a comprehensive medical history of both COPD and other medical problems including smoking history and investigation results, such as spirometry. Comorbid hearing, literacy and visual difficulties will affect the ability of patients to complete self-report questionnaires and exercise diaries (95). Those who are not motivated or have severe cognitive impairment are unlikely to benefit and should not be referred (95). Other contraindications to rehabilitation are listed in table 2.8:
Table 2.8: Relative contraindications to pulmonary rehabilitation

<table>
<thead>
<tr>
<th>Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe cognitive impairment</td>
</tr>
<tr>
<td>Severe psychotic disturbance</td>
</tr>
<tr>
<td>Infectious disease (that cannot be contained)</td>
</tr>
<tr>
<td>Musculoskeletal or neurological disorders that prevent exercise</td>
</tr>
<tr>
<td>Unstable cardiovascular disease (unstable angina, aortic valve disease,</td>
</tr>
<tr>
<td>unstable pulmonary hypertension)</td>
</tr>
</tbody>
</table>

(Adapted from (16))

Despite this even those with advancing age or severe COPD (either by low FEV1 or high MMRC) can benefit with PR (15, 95, 99). Comorbidities such as arthritis may impede PR but modifications to the exercise program can be made to accommodate their special needs and requirements (16).

Goal setting is another important element in the assessment. Functional orientated goal setting is an integral part of rehabilitation intervention as it encourages participants to set their goals and priorities, and supports team communication and coordination (100). Accurate identification of activities that a patient is no longer able to do due to dyspnoea, will assist with goal setting, motivation and adherence (95).

A baseline evaluation should be performed prior to commencement. This not only allows a comparison between participants but also enables the accurate prescription of an individualised exercise program and the emphasis of patient centred outcomes. Given that COPD is a complex disorder clinicians have recognised the need for both clinical and patient reported outcome measures (101). Commonly assessments are made in exercise capacity, dyspnoea, QOL and psychological status. The evidence base in PR is based on improvements seen in outcome measures. These include reducing symptomatology, improving exercise performance and QOL (15).
2.12.2 PULMONARY REHABILITATION PROGRAM DELIVERY

PR can be given in a number of settings, the most common in Australia being in an outpatient hospital or community based setting (97). Other options available include home based or inpatient based settings. The effectiveness of non-hospital based settings is comparable to hospital based settings (15). Factors that influence this decision include a patient’s disease status and severity. This consequently dictates the level of supervision required during exercise or the need for individualised interventions (15).

Most programs are directed at patients who have stable COPD or those who are currently not suffering from an exacerbation. A recent study comparing the commencement of PR as an inpatient showed no advantage when compared to usual care or receiving PR at a later point (102).

In relation to staffing requirements, the current Australian PR guidelines suggest a staff-to-patient ratio of 1:4 (16). Education sessions should have 1:8 and for complex patients 1:1 staffing might be necessary (103). The European Respiratory Society guidelines state PR should be delivered by a multidisciplinary team that includes at least a physiotherapist, an occupational therapist, a psychologist and a dietician (104). The current guidelines do not make any recommendations in relation to medical (respiratory or rehabilitation physician) staffing. This includes whether there should be direct supervision of the program, exercise prescription or medical clearance. In Australia, most programs are coordinated by either physiotherapists or nurses (97).

In relation to the optimum duration, it has been suggested that the optimal length should be six weeks or 12 sessions (105). Each week should have 2 to 3 sessions and each session should last between 1 to 4 hours (15). Most
programs in Australia run over eight weeks. Longer total duration of programs and where patients attend the most sessions are likely to produce the maximal effect (15).

2.12.3 REHABILITATION INTERVENTIONS

Local programs often incorporate physical exercise and education but not additional or other interventions (16). Major respiratory society guidelines do not mandate or recommend inclusion of interventions such as psychological, inspiratory muscle training or self-management (15, 105).

Figure 2.2 shows a typical PR process starting from patient referral to the actual program and the assessment process.
Physical training, particularly of the lower extremities, is considered mandatory in a PR program (104). Education is considered an important component (106). Different centres may offer additional interventions specific to their cohort. For example, psychological interventions may be offered specifically targeting anxiety related to COPD symptoms or breathing exercises targeting dyspnoea management.

Brief descriptions of common interventions in PR are listed below:
Exercise Training

Exercise training is specifically directed at skeletal muscle dysfunction commonly seen in patients with COPD (4). Exercise usually encompasses either upper or lower limb exercises with the purpose of increasing cardiorespiratory endurance, strength and flexibility (15).

Inspiratory muscle training

In COPD, the effects of pulmonary hyperinflation results in flattening and shortening the diaphragm and places it at a mechanical disadvantage (15). Inspiratory Muscle Training (IMT) incorporates a mechanical device to impose a resistive load. This improves inspiratory muscle strength and endurance but it is uncertain whether the results extend to overall wellbeing such as QOL.

Breathing exercises

Another method to target hyperinflation in COPD is the use of breathing exercises. Breathing exercises are techniques to time breathing especially in the expiratory phase. These results in the reduction of the amount of air trapped in the lungs and reduce exercise induced hyperinflation (5). Techniques include Pursed Lip Breathing (PLB), Diaphragmatic Breathing (DB) and yoga. PLB works by placing the lips closer than usual and creating a smaller opening for air to go through (21). DB educates patients to move the abdominal wall predominantly during inspiration to reduce upper rib cage motion (22). This improves chest wall motion and makes breathing more efficient. Pranayama yoga uses timed breathing techniques with a focus on expiration (23).

Self-management

Self-management refers to an individual’s ability to manage symptoms, treatment, physical and psychosocial consequences and lifestyle changes.
inherent in living with a chronic condition (107). Interventions can include education sessions delivered in a centre or by phone.

Integrated disease management

In comparison to self-education, Integrated Disease Management (IDM) relies on multiple components or interventions to manage chronic disease. It is a system of coordinated healthcare interventions and communications for populations with conditions in which patient self-care is significant (31). IDM was created with the aim of streamlining care as well as increasing cost-effectiveness.

Many of the IDM interventions are in common use in PR, such as education or exercise, but the Cochrane review has suggested the following criteria needs to be met (108):

- Two or more components or interventions
- Two or more allied health disciplines providing the interventions
- Minimum IDM duration of three months

Some health services would consider IDM to be distinctively different to PR and offer them in separate streams. Conversely, IDM and PR could be offered together and delivered simultaneously.

Nutrition

Nutritional interventions aim to reverse the presence of malnutrition and reduced FFMI in COPD patients. These interventions can include dietary advice to oral and enteral nutritional supplements (50).
Psychological Interventions

Psychological interventions can include cognitive and/or behavioural therapies, psychodynamic psychotherapy, interpersonal psychotherapy, non-directive therapy, support therapy and counselling (109). It can be delivered in a group or individual setting. Specific COPD elements include addressing activity avoidance, increasing activity level and coping skills for symptoms such as dyspnoea.

2.12.4 CHALLENGES IN EVALUATING PULMONARY REHABILITATION PROGRAMS

Following referral to a PR program, clinicians often notice that patients do not attend the initial PR session. Up to half of patients referred to PR never attend (110). Factors that are raised by patients include transportation issues, lack of family supports, depression and comorbid illness (110).

Once patients commence in a PR program, some still experience difficulties in attending every session that is offered. Reasons for drop-out include medical reasons such as COPD related exacerbations or hospitalisations (111). Non-medical related reasons can include the lack of perceived benefit or lack of support (15).

Evaluation of the PR program is an important element following the completion of PR (16). Patient outcome measures should be retested or reevaluated. In addition, opportunities should be given to the patient and/or carer for feedback in relation to participation in the PR program (16). As a minimum, measurements should be taken immediately following the program, but ideally revaluations should take place at regular intervals for up to one year post completion (15). Long term assessments are useful to monitor for any patient decline and identify patients who may benefit with a repeat stint of PR or
another intervention. Some studies have shown that benefits such as QOL persist beyond 12 months (15, 112). Others studies have shown that patients often return to baseline or even deteriorate further (113-115). Up to one in five patients repeat PR (116).

Correct interpretation of any changes in outcome measures remains crucial. The extent and amount of improvement needs to be interpreted with the Minimal Important Difference (MID) in mind. MID attempts to define the smallest difference in score that patients would perceive as important (117). This is usually greater than statistical significance.

Information needs to be conveyed back to the patient but in a format which they can understand. Similarly the patient’s referring clinician and/or their general practitioner should be informed of their patient’s progress and follow up plans (16).

Given some patients lose their gains in physical fitness and QOL, a repeat stint of PR may be helpful. The results following the second period of PR were mixed. The improvements in exercise capacity (6MWT) were less than the repeat PR program however improvements in all domains of the CRQ were similar (116).

2.12.5 MAINTENANCE PROGRAMS

Following the completion of the PR program many centres offer maintenance or step down programs. This consists of phone, exercise or education sessions ranging from weekly to monthly sessions. Maintenance programs can be either centre or home based. This allows PR participants to put into practice skills learned in a PR program environment whilst having some supervision or
guidance and ultimately encourage long term adherence (3). It also allows a transition between a high intensity PR program to a self-directed home exercise program.

The evidence for the benefit of maintenance programs remains equivocal. Studies vary in terms of the intensity or the type of supervision. In addition, it can be difficult to distinguish between a ‘maintenance’ program and extension of the initial PR program (105).

The American Thoracic Society guidelines do not recommend a maintenance program at this stage (15). In contrast, the European Respiratory Society suggests that all patients graduating from a PR program should be provided with opportunities for physical exercise (105). This includes maintenance programs. The Australian Lung Foundation lists the optimal intensity and duration of a maintenance program which is 3 to 5 days per week of which one session is supervised (16).

The next chapter describes the methodology of this thesis.
CHAPTER 3 METHODOLOGY

This chapter describes the general methodology used in all studies contained in this thesis. The study model selection and analysis methods are also discussed. The subsequent chapters describing each of the studies will explain each study methodology in more detail.

3.1 GENERAL OVERVIEW

Study 1, Chapter 4 is a systematic review of common rehabilitation interventions in COPD, with its methods being different to the remaining three studies. Section 3.2 will describe the methods for the systematic review and sections 3.3 to 3.5 will cover the methods, ethics, subjects and assessments conducted for the experimental studies. Lastly, section 3.6 will describe both general and rehabilitation specific research and methodological models.

3.2 METHODS FOR SYSTEMATIC REVIEW (STUDY 1, CHAPTER 4)

Methods for systematic review
A comprehensive literature search was undertaken with the aim of retrieving any Randomised Controlled Trials (RCTs) comparing any non-pharmacological or non-surgical intervention against conventional care in stable COPD patients.

Interventions included, but were not limited to, physical therapy, psychotherapy, education, dietetics or case management.

The following databases were searched:
- MEDLINE/Ovid
- EMBASE
Each article extract included a number of outcome measures, some were generalised and some were Pulmonary Rehabilitation (PR) specific. Common outcome measures of interest have been presented and are listed in Table 2.5.
The following sections relate to Chapters 5-7 (Studies 2-4).

3.3 ETHICS

All three research projects were approved by the Melbourne Health (MH) Human Research and Ethics Committee (HREC) and were responsible for the general oversight of the studies (HREC Approvals QA2014002, 2012.174, QA2015130). The role of the MH HREC is to ensure compliance with the National Statement on Ethical Content in Human Research and compliance with relevant Victorian and Australian laws (118). Participants in study 2 (Chapter 5, Cognitive Behavioural Therapy, CBT Study) received a participant information and consent form in plain language. This was signed following explanation of the project and an opportunity to address any concerns from the primary investigator (EL). Information from all projects (Studies 2-4) such as data sheets were de-identified with a participant ID and kept in a locked office at the Royal Melbourne Hospital (RMH). Electronic data was equally de-identified and secured in a password protected database.

3.4 SUBJECTS

All three clinical studies were based at the RMH and a local community health service (Merri Health - MCHS). Patients who were diagnosed with COPD and treated by the RMH respiratory service were referred to MCHS for ongoing pulmonary management and rehabilitation. The diagnosis and severity grading of COPD was based on the Global Initiative for COPD (GOLD) criteria, as assessed by the respiratory and rehabilitation physicians at RMH (10). The eight-week PR program consists of multidisciplinary management including medical, nursing and allied health using standardised therapy protocols.

In the CBT Study (Study 2, Chapter 5), all patients who were referred to the ambulatory PR program during the 18-month trial were screened and consented
for participation into the study. Patients were eligible for this study if they had stable COPD, ability to comprehend English and able to consent for the study and were able to attend regular PR sessions. Exclusion criteria included prior psychological treatment within the past three months and any significant psychiatric history such as psychosis, bipolar disorder, schizophrenia, mental retardation, borderline personality disorder, chronic suicidal behaviour or major depressive disorder with prior hospitalisation episodes.

A total of 70 patients were screened for the study, 34 patients were consented. 28 patients finished PR and completed all their assessments. There were 14 patients in the CBT (treatment) group and 14 patients in the control group.

In the Long Term Study (Study 3, Chapter 6), eligible patients were identified from a centralised database at MCHS. Inclusion criteria included patients with a confirmed diagnosis of COPD and have completed PR between 2003 and 2012 were targeted. Patients were excluded if they had severe cognitive impairment or were medically unwell for further assessment and testing. Following consent, eligible patients were invited to attend the community centre for assessment (long term assessment).

The Health Care Utilisation Study (Study 4, Chapter 7), was a retrospective cohort study of people who were referred to the health service Integrated Disease Management (IDM) over a 10 year period. Patients who were diagnosed with COPD and treated by the ambulatory respiratory service were offered IDM and an 8 week PR program. Patients were referred if they lived within the health service catchment area and the treating clinician assessed that they had COPD that was having an impact on their functional status. The IDM program consisted of respiratory and rehabilitation physicians, respiratory trained nurses and allied health professionals who provided a variety of interventions in both home and centre based settings. Between 2002 and 2012, there were 670 acute care discharges that were referred to IDM. Of this number, 315 patients (61%) were assessed for PR and of those, 220 patients (70%) completed PR.
3.5 ASSESSMENTS AND DATA COLLECTION

In the CBT Study (Study 2), assessments were conducted at three time points; pre PR, immediately post PR and 3 months post PR. All baseline participant interviews and clinical assessments were completed using a structured format. Demographic, functional and Quality of Life (QOL) assessments were completed using standardised instruments. Assessors did not prompt patients, but provided assistance for those who had difficulty with completing the questionnaires.

A similar baseline interview and assessment was conducted in the Long Term Study (Study 3). This same assessment was repeated at the long term assessment (which was longer than one year post completion of PR).

Information and data for the Health Care Utilisation Study (Study 4) were obtained from an already established database. This contained data such as basic demographic information, severity of COPD and number of PR episodes. This dataset was linked to the acute health service administrative dataset, to obtain data on all ED and outpatient attendances and acute inpatient admissions.

3.5.1 OUTCOME MEASURES

A variety of outcome measures were utilised in all three clinical studies. Not all outcome measures listed below were used in every single study. There was a mixture of respiratory specific and generalised measures. Time points used in each study varied, from pre PR, immediately following PR and 3 months post PR for the CBT Study (Study 2) to a repeat long term outcome measure which was greater than 12 months post PR completion in the Long Term Study (Study 3).

Exercise Capacity
6 Minute Walk Test (6MWT) - This test measures the distance patients can walk in 6 minutes and is a measure of functional exercise capacity (76). The best score out of two attempts is recorded.

Incremental Shuttle Walk Test (ISWT) - This is a field based test that progressively increases walking speed and measures the functional capacity of COPD patients (73). ISWT is a true symptom-limited maximal exercise capacity test, and distance walked relates strongly to peak aerobic capacity (15). Normal healthy subjects are able to complete 810m (119).

Comorbidities
Elixhauser Comorbidity Score. The Elixhauser score is a comorbidity measure used to take into account whenever chronic disease burden is associated with a particular outcome (120). The summary score is a weighted combination of the 30 Elixhauser comorbidities, where a larger comorbidity weight indicates a stronger association between the comorbidity and in-hospital mortality (121).

Anxiety and Depression
Hospital Anxiety and Depression Scale (HADS) - The HADS is a fourteen item scale that measures levels of anxiety and depression. Each item is rated on a scale of 0-3. Total scores greater than 8 has been used to indicate anxiety or depression (122).

Depression, Anxiety Stress Scale (DASS) - This is a 21 item self-reported questionnaire that measures the three related negative emotional states of depression, anxiety and tension/stress (78). Participants rated the extent to which they experienced each state over the past week on a 4-point Likert rating scale. When totalled, three domain scores are given. Scores of greater than 9, 7 and 14 are suggestive of depression, anxiety and stress respectively (78).

Adjustment to Illness
Psychosocial Adjustment to Illness Scale (PAIS) - This is a 46 item self-report questionnaire that assesses psychosocial adjustment to chronic illness (123). It measures psychosocial adjustment to illness in terms of 7 primary domains of
adjustment: health care orientation, vocational environment, domestic environment, sexual relationships, extended family relationships, social environment and psychological distress. Each PAIS item is rated on a 4-point (0 to 3) scale of adjustment, with higher ratings indicating poorer adjustment status.

**Quality of Life**

Chronic Respiratory Questionnaire (CRQ) - The CRQ consists of a 20 item questionnaire with four major domains (Dyspnoea, Fatigue, Emotion, Mastery) which patients self-administer. This measures the health-related QOL in respiratory patients (15).

### 3.5.2 INTERVENTION

In the CBT Study (Study 2), patients were allocated to either the treatment group consisting of group based CBT in additional to the usual PR or the control group consisting of PR alone. Patients in both groups received the usual PR program. The CBT program in the treatment group consisted of six sessions of group based CBT delivered by a psychologist. The content was designed in conjunction with the treating team to complement the pre-existing exercise and education programs. The program was not specifically directed at anxiety and depression, but incorporated common issues facing a PR participant.

### 3.5.3 STATISTICAL ANALYSIS

Data was keyed into Microsoft Excel (Microsoft, WA USA) and exported into Stata12 (StataCorp, TX USA) for data analysis and reporting. Descriptive analysis of study cohort was undertaken and results reported as n(%) for categorical data (e.g. gender) and median (Interquartile Range) for continuous data (FEV1, FVC, BMI, etc). Please refer to the individual chapters for more detailed descriptions especially in the analysis of outcome measures where different tests were used for each study.
3.6 CHOOSING A METHODOLOGICAL MODEL AND STUDY DESIGN

The structure and the studies of this thesis was based upon several pre-existing concepts and methodological models used in biomedical and more specifically, rehabilitation research. These models and methods were used to a) understand the current issues or impairments facing people with COPD, b) accurately map out current treatments and programs available and c) design studies to address the aims of this thesis.

The following models and concepts were used in this thesis:

1. The International Classification of Functioning, Disability and Health (ICF)
2. The Medical Research Council (MRC) model
3. A taxonomy for disease management from the American Heart Association Disease Management Taxonomy Writing Group
4. The RE-AIM Framework

3.6.1 THE ICF MODEL

Firstly, the link between impairments and disability were mapped out using the International Classification of Functioning, Disability and Health (ICF) model. The ICF model was designed by the World Health Organisation and was initially discussed in chapter 1. In brief, the ICF aims to classify health and health-related domains to from the body, individual and society perspectives (17). Impairments in a person with COPD may vary from gas trapping, reduced gas exchange and sarcopenia. Activity limitations such as difficulties in showering or making a bed may result. Participation restrictions can include difficulties in attending work or studies. The next step of using the ICF is attempting to link the three components together. For instance, analyses were performed in the Healthcare Utilisation study to see whether there was a correlation between severity of COPD and completion of pulmonary rehabilitation.
The main limitation of the ICF model is that it only identifies links between the three domains but it cannot determine how strong these links are. In addition, it cannot assist clinicians or researchers what studies or analyses are necessary to confirm these associations.

3.6.2 APPLYING METHODOLOGICAL MODELS IN REHABILITATION RESEARCH

Techniques and methodology commonly used in acute healthcare cannot simply be applied to rehabilitation research. Firstly, as per the ICF some diseases produce multiple impairments, so there may not be a correlation between pathology and impairments (124). Rehabilitation, such as PR would base their success on improvements in QOL, reducing dyspnoea, increasing physical, mental and emotional suffering (24). In contrast, traditional biomedical treatments are aimed at pathology and so may not lead to functional improvements. Conversely, reversing impairments may not improve pathology (124). Secondly, rehabilitation is a complex intervention, where the active ingredient of the intervention cannot be easily identified. Rehabilitation interventions often contain multiple components that are interdependent and cannot be separated for research. Sometimes rehabilitation interventions are given concurrently with medical interventions, so it would be difficult to attribute gains to rehabilitation alone (125). Timeframes for rehabilitation interventions can be long, so any functional gains that are observed maybe partly or wholly due to spontaneous recovery (125).

3.6.3 THE MEDICAL RESEARCH COUNCIL (MRC) MODEL FOR COMPLEX INTERVENTIONS

In contrast, the Medical Research Council (MRC) in the United Kingdom published a framework to guide clinicians about the evaluation of a complex intervention (See figure 3.1). This MRC model clearly displays a framework whereby a sequential series of phases of interventions in the evaluation of a complex intervention (126). The framework helps investigators determine what the state of knowledge and uncertainty is regarding a complex package at a
given time (126). This allows a clear identification of where the current level of evidence is available for an intervention and where future research should be targeted. The MRC document does emphasise that not all phases requires the same amount of research and in some instances, multiple stages can be addressed simultaneously. Multiple trials in each phase may be required to identify statistical and clinically meaningful differences.

**Figure 3.1: Framework for Trials of Complex Interventions**

![Framework for Trials of Complex Interventions](image)

Adapted from (126)

Whilst the RCT is highest band of evidence, it is not always feasible in the rehabilitation setting. Small sample sizes commonly encountered in rehabilitation studies produce underpowered results (125). Blinding of subjects and clinicians may not be possible with the delivery of truly “sham” therapies (127). Many outcome measures have been borrowed from the acute medicine setting which only measures impairments, not activity or participation restrictions (127). In addition, many outcome measures already in use in the rehabilitation settings have either not been validated for a particular condition or population that is being studied (125). Some, but not all outcome measures now have established Minimal Important Differences (MID) which is defined as the smallest difference in score in the outcome of interest that patients perceive as important (117). This is different to the statistical difference often quoted in acute medicine studies.
Applying this information to the planned studies, the CBT Study (Study 2) would be considered a Phase II, prospective controlled clinical trial. The Long Term Study (Study 3) was a prospective cohort study and the Healthcare Utilisation Study (Study 4) was a retrospective cohort study.

### 3.6.4 A TAXONOMY FOR DISEASE MANAGEMENT FROM THE AMERICAN HEART ASSOCIATION DISEASE MANAGEMENT TAXONOMY WRITING GROUP

The American Heart Foundation devised a system of classification to categorise and compare disease management programs and to identify specific factors associated with effectiveness (128). Cardiac diseases have similarities to respiratory diseases such as COPD as both chronic diseases are becoming more prevalent and disease management programs such as Integrated Disease Management (See chapter 2 for definition) are being utilised to improve quality of life and health outcomes. In addition to allowing comparison between programs, this schema also allows researchers and clinicians to successfully replicate and generalised programs to larger populations. This is because clinical trials have typically small sample sizes and only utilise single sites.

The taxonomy that was created incorporates eight domains (128). These included:

1) Patient Population: The identity of the target population, taking into account risk factors, comorbidities and other non clinical characteristics (such as ethnicity and education level).

2) Recipient: The patient population that is expected to benefit from disease management. This may differ from the patient population, for instance a program might be targeted for patients with COPD but the recipient might be for health care workers who may deliver the program.
3) Intervention Content: This describes the interventions offered in the disease management program.

4) Delivery Personnel: This refers to the number and type of staff members or clinicians involved in the delivery of a disease management program. Commonly, programs would be of a multi-disciplinary nature and involve both nursing, medical and allied health disciplines.

5) Method of Communication: Traditional management programs were face-to-face, but now newer, more novel delivery methods are being utilised. Phone, web based or other types of telemonitoring can be utilised.

6) Intensity and Complexity: This refers to both the frequency and duration of a program as well as the type of content. Interventions which contain simpler, easier to understand content may provide better benefits than more complex ones.

7) Environment: This is similar to the method of communication. Environment refers to the physical location where the program is delivered. Examples commonly include inpatient and outpatient settings, but programs can be delivered in the local community centre or at home as well.

8) Outcome Measures (Clinical Outcomes): Any program will need to be evaluated based clinical outcomes. Multiple outcome measures are available and clinicians, patients and hospital administrators may judge the usefulness of each outcome differently. For instance, clinicians may value a reduction in admission rate highly, whereas patients would rather see improvements in their exercise capacity or quality of life.

The use of this model to compare pulmonary rehabilitation programs is shown on Table 3.1. The example is provided of the pulmonary rehabilitation program at Merri Health and described in both the Long Term and CBT studies.
Table 3.1: Use of a disease management taxonomy for classifying pulmonary rehabilitation programs

<table>
<thead>
<tr>
<th>Taxonomic Domain</th>
<th>Pulmonary Rehabilitation Program</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention recipient</td>
<td>Primarily patients, sometimes carers, families of patients</td>
</tr>
<tr>
<td>Patient population</td>
<td>Patients with diagnosed chronic respiratory disease (in this study, patients with stable COPD stabilised on pharmacotherapy and no recent exacerbations)</td>
</tr>
<tr>
<td>Intervention content</td>
<td>Baseline and end of treatment evaluation</td>
</tr>
<tr>
<td></td>
<td>Functional goal setting with patient</td>
</tr>
<tr>
<td></td>
<td>Optimisation of medications</td>
</tr>
<tr>
<td></td>
<td>Cardiovascular and strength training</td>
</tr>
<tr>
<td></td>
<td>Education on diet, medication use, future planning, recognising dyspnoea triggers</td>
</tr>
<tr>
<td>Delivery personnel</td>
<td>Respiratory trained nurses and allied health staff</td>
</tr>
<tr>
<td>Method of communication</td>
<td>Face to face group based</td>
</tr>
<tr>
<td>Intensity and complexity</td>
<td>Eight week program, two 1.5hr sessions per week</td>
</tr>
<tr>
<td>Environment</td>
<td>Delivered in a community centre</td>
</tr>
<tr>
<td>Clinical outcomes</td>
<td>Exercise capacity</td>
</tr>
<tr>
<td></td>
<td>Depression and Anxiety</td>
</tr>
<tr>
<td></td>
<td>Quality of Life</td>
</tr>
</tbody>
</table>

Based on (128)

In this thesis, this classification model was used initially to identify the typical components of a PR program (Chapter 2) and the components that were in the PR program at Merri Health (Studies 3-4, Chapters 6-7). Adding the intervention (Cognitive Behavioural Therapy, CBT) in the CBT Study (Chapter 5) was based on classifying the pre-existing PR program.
It is important to consider that this taxonomy is a framework only. Whilst it allows simplicity of comparing programs it does not actually define what is disease management or indeed it does not imply which programs are most effective.

3.6.5 THE RE-AIM FRAMEWORK

There are many programs and interventions that are offered to COPD patients. The RE-AIM framework devised by Glasgow et al (1999) aims to provide a method of comprehensively evaluating these programs beyond just whether the intervention is effective on a single measure (129). Analysing programs only based on outcome measures could be potentially biased towards only the clinician without taking into other stakeholders such as the patient or hospital administrators. RE-AIM also allows evaluation of the potential to translate and adapt research into real life settings and gauge the public health impact (130).

The RE-AIM framework has five factors: reach, efficacy, adoption, implementation and maintenance (See table 3.2). Each factor was chosen to assess the impact of a program on both the individual and organisational levels.
Table 3.2: Factors in the RE-AIM framework

<table>
<thead>
<tr>
<th>FACTOR</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reach</td>
<td>This refers to how number of people willing to participate in a given program. It also refers to what type of demographic is the program likely to target and attract.</td>
</tr>
<tr>
<td>Efficacy</td>
<td>The impact of an intervention towards outcome measures of interest. RE-AIM emphasises the need to consider not only positive outcomes, but negative or unwanted outcomes as well. It also discusses the need for behaviour and quality of life outcomes for interventions.</td>
</tr>
<tr>
<td>Adoption</td>
<td>Adoption refers to the proportion and representativeness of settings or health services that will adopt the program. This allows potential barriers to starting a program to be identified and rectified.</td>
</tr>
<tr>
<td>Implementation</td>
<td>The extent to which a program is delivered as intended in real world settings rather than in clinically controlled research settings.</td>
</tr>
<tr>
<td>Maintenance</td>
<td>In the institutional sense this refers to the extent to which the new program becomes routine and embedded into everyday practice. In the individual sense, this means the ability for patients to sustain any improvements in outcomes not just immediately post treatment but six months or beyond.</td>
</tr>
</tbody>
</table>

Based on (129)

As with all models that have been described, the RE-AIM framework has some limitations. Importantly the framework places an equal weighting and thereby equal importance for each domain. Additionally, the original RE-AIM concept was to provide a score as a numeric total of all the elements, but this has not been put into practice and has not been validated. Once this research has been completed then it may be possible to directly compare one program versus another. Lastly, the period required to follow-up and monitor patients after their
participation in the program has yet to be determined. It would be important to know whether patients maintain their gains following completion of a program.

For this thesis, the RE-AIM framework was used to evaluate PR programs (Chapter 2). The particular elements that was considered and used for analysis is shown in Table 3.3.

Table 3.3: Use of the RE-AIM framework for analysis of studies

<table>
<thead>
<tr>
<th>FACTOR</th>
<th>STUDIES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reach</td>
<td>Healthcare Utilisation Study</td>
</tr>
<tr>
<td>Efficacy</td>
<td>All studies</td>
</tr>
<tr>
<td>Adoption</td>
<td>Healthcare Utilisation Study</td>
</tr>
<tr>
<td>Implementation</td>
<td>Healthcare Utilisation Study, Long Term Study</td>
</tr>
<tr>
<td>Maintenance</td>
<td>All studies</td>
</tr>
</tbody>
</table>

3.7 CONCLUSION

The research in this thesis aims to address gaps in evidence in COPD and PR that were identified in the literature review (Chapter 2). Information obtained from the studies will guide changes in current rehabilitation practice and further research.

The next step is a comprehensive systematic review of common rehabilitation interventions in COPD. Chapter 4 presents the types of studies, participants, interventions and effectiveness of each intervention.
CHAPTER 4 SYSTEMATIC REVIEW OF NON-PHARMACOLOGICAL, NON-SURGICAL REHABILITATION INTERVENTIONS FOR STABLE CHRONIC OBSTRUCTIVE PULMONARY DISEASE

There is no current review of commonly available for non-pharmacological and non-surgical interventions for persons with Chronic Obstructive Pulmonary Disease (COPD). This chapter presents the evidence base for interventions that are typically utilised in the pulmonary rehabilitation setting.

4.1 INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is a broad term encompassing symptoms resulting from chronic bronchitis and emphysema (131). It is a major cause of mortality, morbidity and health service use in Australia. COPD is the fourth and sixth leading cause of death for men and women respectively, and is expected to rise further into the future (132).

Whilst characteristic COPD symptoms include dyspnoea, cough and sputum production, other impairments are present which affects the ability of sufferers to perform their activities of daily living which in turn affect their quality of life (32). These impairments include fatigue, muscle dysfunction, cachexia and anxiety and mood issues.

The severity of COPD is commonly measured by respiratory function testing and based on the Forced Expiratory Volume in 1 second (FEV1). It has been increasing recognised that COPD is a systemic disease and both generic and COPD specific measures have been devised and used in the clinical setting (32). In the previous section, table 2.5 lists common outcome measures in COPD. Unfortunately, not one available measure can assess all impairments and limitations in persons with COPD.
Pulmonary Rehabilitation (PR) has been shown to be effective in the management of COPD. It consists of a multidisciplinary program of care for patients with chronic respiratory impairment that is individually tailored and designed to optimise physical and social performance and autonomy (133). PR has been recognized as a core component of the management of individuals with chronic respiratory disease (15).

Elements of PR include: (95)

- Patient assessment
- Exercise training
- Education
- Nutritional intervention
- Psychological support

Most studies have been centred on the effects of physical therapy in COPD (133). Local programs often incorporate physical exercise and education but not additional or other interventions (16). In a multidisciplinary PR setting, there has been minimal evidence to show which components offer the most benefit or the ideal duration or intensity (133). Major respiratory society guidelines do not mandate or recommend inclusion of interventions such as psychological, inspiratory muscle training or self-management (15, 105).

Systematic reviews of individual interventions used in COPD have been widely published. This review however aims to present, investigate and compare the different types of interventions available in the PR setting.

4.2 DESCRIPTION OF THE INTERVENTIONS
4.2.1 EXERCISE TRAINING

Most PR programs include exercise training or physical therapy. Exercise training is considered the cornerstone of pulmonary rehabilitation. It is specifically directed at skeletal muscle dysfunction commonly seen in patients with COPD (4). Exercise usually encompasses either upper or lower limb exercises with the purpose of increasing cardiorespiratory endurance, strength and flexibility (15). Longer exercise programs produce greater physiological effects, with substantial effect at 8 weeks (134). Cardiovascular training such as cycling and walking (ground or treadmill) are commonly utilised.

4.2.2 INSPIRATORY MUSCLE TRAINING

Whilst exercise training improves physical status and QOL in patients with COPD, it does not improve lung function (135). The effects of pulmonary hyperinflation in COPD results in flattening and shortening the diaphragm and places it at a mechanical disadvantage (15). Inspiratory Muscle Training (IMT) incorporates a mechanical device to impose a resistive load. This load progressively increases in order to improve inspiratory muscle strength (136). This reduces dyspnoea by improving the capacity of patients to sustain high levels of ventilation and decreases hyperinflation but it is uncertain whether it extends to overall wellbeing such as QOL (137).

4.2.3 BREATHING EXERCISES

Another method to target hyperinflation in COPD is the use of breathing exercises. Breathing exercises are techniques to time breathing especially in the expiratory phase. These result in the reduction of the amount of air trapped in the lungs and reduce exercise induced hyperinflation (5). Techniques include Pursed Lip Breathing (PLB), Diaphragmatic Breathing (DB) and yoga. PLB works by placing the lips closer than usual and creating a smaller opening for
air to go through (21). DB educates patients to move the abdominal wall predominantly during inspiration to reduce upper rib cage motion (22). This improves chest wall motion and makes breathing more efficient. Pranayama yoga uses timed breathing techniques with a focus on expiration (23).

4.2.4 SELF MANAGEMENT

Self-management is an essential component of PR. Self-management refers to an individual’s ability to manage symptoms, treatment, physical and psychosocial consequences and lifestyle changes inherent in living with a chronic condition (107). Self-management is only one component of chronic disease management and is designed to complement pharmacological care. The aims of self-management in COPD should include not only reduced exacerbations or hospitalisations but sustained behavioural change in how patients deal with the disease.

4.2.5 INTEGRATED DISEASE MANAGEMENT

As there is a great variation in symptoms in COPD, a multi-faceted response including different elements is required (108). IDM is a system of coordinated healthcare interventions and communications for populations with conditions in which patient self-care is significant (31). IDM was created with the aim of streamlining care as well as increasing cost-effectiveness. Essential components of IDM include (138):

- planned and proactive care intended to keep people as well as possible
- coordinated care using team based approaches
- evidence based care
- support for self-management
- regular review and follow up

The goals of IDM are to promote self-management by patients and to address the illness or conditions according to disease severity and patient needs. It
utilises the best available evidence to maximizing clinical effectiveness and efficiency regardless of treatment setting (139).

Many of the IDM interventions are in common use in PR, such as education or exercise, but the Cochrane review has suggested the following criteria needs to be met (108):

- Two or more components or interventions
- Two or more allied health disciplines providing the interventions
- Minimum IDM duration of three months

4.2.6 NUTRITION

Malnutrition is seen in patients with COPD. Prevalence rates increase with disease severity, with rates up to 30% in Global Initiative for Chronic Obstructive Lung Disease (GOLD) class 4 disease (140). Low weight COPD patients have greater gas trapping, lower diffusing capacity and lower exercise capacity than patients with the same degree of airflow obstruction but normal weight (141).

Using Body Mass Index does not accurately measure changes in body composition such as muscle atrophy. COPD causes accelerated loss of lean tissue, leading to sarcopenia and cachexia (50). In addition, energy demands may be increased due to the work of breathing and respiratory tract infections (51).

Fat Free Muscle Index (FFMI), provides a better measure of muscle mass in COPD. An FFMI less than 16 kg/m2 in men and less than 15 kg/m2 in women is associated with a 1.9-fold increase in mortality after adjusting for age, sex, and FEV1(52).

4.2.7 PSYCHOLOGICAL INTERVENTIONS

People with COPD are vulnerable to developing symptoms of anxiety and depression (13). There is an increased prevalence of depression (36%) and anxiety (40%) (55). Patients with psychological co-morbidities are more likely to
have reduced engagement and participation and subsequently reduced quality of life (13).

Examples of psychological interventions include cognitive and/or behavioural therapies, psychodynamic psychotherapy, interpersonal psychotherapy, non-directive therapy, support therapy and counselling (109). It can be delivered in a group or an individual setting. Specific COPD elements include addressing activity avoidance, increasing activity level and coping skills for symptoms such as dyspnoea.

4.3 METHODS

4.3.1 DATA SOURCES

A comprehensive literature search was undertaken with the aim of retrieving any Randomised Controlled Trials (RCTs) and systematic reviews comparing any non-pharmacological or surgical intervention against conventional care in stable COPD patients. This search included all articles available from 1980 until February 2017.

A search strategy was developed to include any COPD intervention studies using (MeSH) search terms for all databases and a keyword search was used if the MeSH term was not available (See Table 4.1). The bibliographies of identified articles were scrutinised for additional references and a manual search of relevant journals was undertaken.

Table 4.1: Search strategy (Medline)

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>S1</td>
<td>(MH &quot;Lung Diseases, Obstructive&quot;)</td>
</tr>
<tr>
<td>S2</td>
<td>(MH &quot;Pulmonary Disease, Chronic Obstructive+&quot;)</td>
</tr>
<tr>
<td>S3</td>
<td>TX emphysema*</td>
</tr>
<tr>
<td>S4</td>
<td>TX chronic* N3 bronchiti*</td>
</tr>
</tbody>
</table>
S5  TX obstruct* N3 (pulmonary or lung* or airway* or airflow* or bronch* or respirat*)
S6  TX COPD
S7  TX COAD
S8  TX COBD
S9  TX AECB
S10 S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9
S11 (MH "Rehabilitation")
S12 (MH "Physical Therapy Modalities")
S13 (MH "Exercise Therapy")
S14 (MH "Orthotic Devices")
S15 (MH "Acupuncture Therapy+")
S16 (MH "Behavior Therapy+")
S17 (MH "Social Work")
S18 (MH "Occupational Therapy")
S19 (MH "Massage")
S20 (MH "Dietetics")
S21 (MH "Breathing Exercises")
S22 (MH "Electric Stimulation Therapy")
S23 (MH "Relaxation")
S24 (MH "Counseling")
S25 (MH "Health Education")
S26 (MH "Patient Education as Topic")
S27 (MH "Self Care")
S28 (MH "Ambulatory Care")
S29 (MH "Hospitalization")
S30 (MH "Outpatients")
S31 (MH "Inpatients")
S32 (MH "Patient Care Team")
S33 TX multidisciplin* OR interdisciplin* OR integrated OR unidisciplin* OR multimodal*
S34 TX rehabilitat* OR physiotherap* OR physical therap* OR occupation* OR acupuncture OR social work OR orthotic*
S35  TX cognitive therap* OR behavio#r therap* OR counsel* OR massag* OR electrical stimulation OR relaxation therap*
S36  TX nutrition* OR diet* OR food*
S37  TX outpatient* OR inpatient* OR hospital* OR home
S38  TX pac* OR purse* lip breath* OR self-manage*
S39  TX manage* OR educat* OR train*
S40  PT randomized controlled trial
S41  PT controlled clinical trial
S42  AB randomi#ed OR TI randomi#ed
S43  AB placebo OR TI placebo
S44  (MH "Clinical Trials as Topic")
S45  AB randomly OR TI randomly
S46  TI trial
S47  (MH "Qualitative Research")
S48  (MH "Evaluation Studies") OR (MH "Evaluation Studies as Topic+")
S49  TX interview*
S50  TX qualitative
S51  TX experience*
S52  S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S26 OR S27 OR S28 OR S29 OR S30 OR S33 OR S34 OR S35 OR S36 OR S37 OR S38 OR S39
S53  S40 OR S41 OR S42 OR S43 OR S44 OR S45 OR S46 OR S47 OR S48 OR S49 OR S50 OR S51
S54  S10 AND S52
S55  S53 AND S54
S56  (MH "Thoracic Surgery") OR TX surger*
S57  MW su
S58  MW dt
S59  S56 OR S57 OR S58
S60  MH animals NOT MH humans
S61  S55 NOT S59
S62  S61 NOT S60
Interventions included, but were not limited to, physical therapy, psychotherapy, education, dietetics or case management.

The following databases were searched:

- MEDLINE/Ovid
- EMBASE
- PsycINFO
- Web of Knowledge
- CINAHL
- PEDro
- WHO International Clinical Trials Registry Platform (ICTRP)
- Allied and Complementary Medicine Database (AMED)
- Social Work Abstracts
- LILACS (South American journals)
- Cochrane Databases (Cochrane, DARE, HTA, NHS-EED, CENTRAL)

4.3.2 INCLUSION CRITERIA

Limits placed included English-language publication and inclusion of adults aged 18 years and above.

Studies that compared an intervention in the management of stable COPD with routinely available local services, lower levels of intervention or placebo, or studies that compared such interventions in different settings or at different levels of intensity, were included. All systematic reviews, meta-analyses and RCTs were included. Where high quality systematic reviews or meta-analyses were identified, articles published prior to the date of that review's search strategy were excluded.

Studies were included if the study population had the diagnosis of stable COPD and participants were living in the community. Studies could include single or multiple disciplines. The disciplines included physiotherapy, occupational therapy, speech pathology, dietetics, social work, psychology and
neuropsychology. Settings were either inpatient (hospital ward or specialist rehabilitation unit), outpatient (hospital or community), or home-based settings.

All studies that involved an intervention or multiple interventions were included, provided they compared the named intervention with some form of control condition (such as usual care or monitoring).

4.3.3 EXCLUSION CRITERIA

As seen in other systematic reviews, this review of systematic reviews will exclude theses, narrative reviews, editorials, case reports, economic evaluation, conference proceedings and studies evaluating surgical intervention or diagnostic procedures were excluded. Nursing care alone was specifically excluded as this is usually provided on a long term basis to provide ongoing support and not delivered on a fixed or short term basis.

4.3.4 STUDY SELECTION

Two review authors (EL, SK) independently screened and short-listed all abstracts and titles of studies identified by the search strategy for appropriateness based on the selection criteria. Each study was independently evaluated from the short-list of potentially appropriate studies for inclusion or exclusion. If necessary, the full text of the article was obtained for further assessment to determine if the study met the inclusion/exclusion criteria. If no consensus was met about the possible inclusion/exclusion of any individual study, a final consensus decision was made by discussion amongst all the authors. Review authors were not masked to the name(s) of the author(s), institution(s) or publication source at any level of the review. Further information was sought about the method of randomisation.

Studies with fatal flaws (for instance, withdrawals by more than 40% of the participants or nearly total non-adherence to the protocol or very poor or non-adjusted comparability in the baseline criteria) were excluded.
4.3.5 DATA EXTRACTION

One review author (EL) extracted data from included systematic reviews and trials by using a standardised data extraction form including the following information:

- Year of publication
- Number of participants included, their age and gender
- Severity of COPD
- Type of study intervention and treatment duration
- Information about the control intervention(s)
- Duration of the study recruitment and follow-up time
- Information about adverse events
- Information about withdrawals
- Information about study quality
- Measures of treatment effect (outcome measures)

In the case of systematic reviews further information extracted included:

- Assessment of methodological quality of the review (using AMSTAR)
- Comparisons performed and meta-analysis details
- Any assessment of methodological quality and risk of bias (using GRADE)

4.3.6 QUALITY OF INCLUDED STUDIES

Evidence for all included studies was categorised according to study design using a hierarchy of evidence in descending order. Priority was given to the most recently published high quality systematic reviews or meta-analysis and RCT.

For systematic reviews, two authors (EL & SK) independently assessed the methodological quality of each review. The AMSTAR tool was used (142). AMSTAR comprises of 11 items, with scores given if the specific criterion is met (see table 4.2). A total score is then calculated. Scores between 8 to 11 is considered high quality, 4 to 7 is medium quality and 0 to 3 is low quality (143).
Disagreements were resolved by discussion between EL and SK, and if necessary with all authors.

In individual trials, the GRADE tool was used to access the quality of evidence (144). This was reported by the authors of the original review.

**Table 4.2: AMSTAR tool: Quality assessment criteria**

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Score (Yes =1, No = 0)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1  Was an 'a priori' design provided?</td>
<td></td>
</tr>
<tr>
<td>2  Was there duplicate study selection and data extraction?</td>
<td></td>
</tr>
<tr>
<td>3  Was a comprehensive literature search performed?</td>
<td></td>
</tr>
<tr>
<td>4  Was the status of publication (i.e. grey literature) used as an inclusion criterion?</td>
<td></td>
</tr>
<tr>
<td>5  Was a list of studies (included and excluded) provided?</td>
<td></td>
</tr>
<tr>
<td>6  Were the characteristics of the included studies provided?</td>
<td></td>
</tr>
<tr>
<td>7  Was the scientific quality of the included studies assessed and documented?</td>
<td></td>
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<tr>
<td>8  Was the scientific quality of the included studies used appropriately in formulating conclusions?</td>
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<td>9  Were the methods used to combine the findings of studies appropriate?</td>
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<td>10 Was the likelihood of publication bias assessed?</td>
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<td>11 Was the conflict of interest included?</td>
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</table>

**TOTAL SCORE**

4.4 RESULTS

The electronic database search retrieved 15980 published articles on rehabilitation interventions in COPD (See figure 4.1). Following abstract screening this was reduced to 707 articles. A total of 180 articles were included in this review. This consisted of 8 systematic reviews and individual 13 RCTs (See table 4.3).
Figure 4.1: PRISMA flow diagram showing selection of article review

Identification

Articles identified by electronic searching (n = 15980)

Screening

Articles screened after duplicates removed (n = 15679)

Duplicates removed (n = 301)

Eligibility

Articles assessed for abstract eligibility (n = 707)

Articles excluded after abstract review (n = 14972)

Full-text articles assessed for eligibility (n = 476)

Full-text articles excluded (n = 231)

Included

Studies included in the review (n = 180)
Systematic reviews = 8
RCT = 13
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<th>Study, year</th>
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<td>Study country</td>
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<td>Outcome measures for COPD</td>
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<tr>
<td>Main findings</td>
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<td>AMSTAR Rating*</td>
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**Physical Therapy**

| McCarthy et al, 2015, Ireland | Systematic review N = 65 RCTs | Exercise therapy (either as sole therapy or in conjunction with other therapies) (lower or upper limb exercises) | 6MWT, CRQ, SGRQ | • Statistically improved exercise capacity exceeding MCID  
• Significant improvements in 4/4 CRQ and 3/3 SGRQ domains | 9 |

**Inspiratory Muscle Training**

| Gosselink et al, 2010, Belgium | Systematic review N = 32 RCTs | Inspiratory Muscle Training | 6MWT, 6MWD, 12MWD, CRQ, Inspiratory muscle strength, Incremental Threshold Loading, Borg score | • Improvements in inspiratory muscle strength, Borg score  
• Improvements in 2/3 CRQ domains  
• Improvements in 6MWT, 6MWD and 12MWD | 5 |

**Breathing Exercises**

| Holland et al, 2012, Australia | Systematic review N = 16 RCTs | PLB, DB, Pranayama Yoga | 6MWT, CRQ, Borg scale | • Pooled analyses not performed  
• Inconclusive results with both PLB and DB | 9 |

| Roberts et al, 2011, UK | RCT, N = 41 | PLB | CRQ, ESWT | • Nil differences between the 2 groups | N/A |

<p>| Liu et al, 2014, China | Systematic review N = 5 RCTs | Yoga | FEV1, 6MWT, PaO2, PaCO2 | • Significant improvement in FEV1 and 6MWT | 6 |</p>
<table>
<thead>
<tr>
<th>Study, year country</th>
<th>Study design</th>
<th>Potential intervention</th>
<th>Outcome measures for COPD</th>
<th>Main findings</th>
<th>AMSTAR Rating*</th>
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</table>
| Bhatt et al, 2013, USA | RCT, N = 14 | PLB | 6MWT, VAS of dyspnoea, RR | • Significant improvement in walk test and RR  
• No difference with VAS of dyspnoea | N/A |
| Yamaguti et al, 2012, Brazil | RCT, N = 30 | DB | rib cage to abdominal motion ratio, diaphragmatic mobility, 6MWT, SGRQ | • Significant improvement in breathing mobility  
• Significant improvement in walk test  
• Significant improvement in SGRQ | N/A |
| Mathew et al, 2011, India | RCT, N = 40 | DB | FEV1, FVC | • Improvement in FEV1 and FVC | N/A |
| Borge et al, 2015, Norway | RCT, N = 150 | DB | GRC scale | • Significant improvements in GRC and SGRQ | N/A |

**Education / Self-Management**

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<tr>
<th>Study, year country</th>
<th>Study design</th>
<th>Potential intervention</th>
<th>Outcome measures for COPD</th>
<th>Main findings</th>
<th>AMSTAR Rating*</th>
</tr>
</thead>
</table>
| Zwerink et al, 2014, Australia | Systematic review N = 23 RCTs & CCTs | Self-management | SGRQ, mMRC Scale, 6MWT, hospitalisations, mortality | • Statistical improvement in SGRQ  
• Reduced hospitalisation (all cause & respiratory related)  
• Improved dyspnoea  
• No changes with mortality or 6MWT | 9 |

**Integrated Disease Management**

<table>
<thead>
<tr>
<th>Study, year country</th>
<th>Study design</th>
<th>Potential intervention</th>
<th>Outcome measures for COPD</th>
<th>Main findings</th>
<th>AMSTAR Rating*</th>
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</table>
| Kruis et al, 2013, Netherlands | Systematic Review, N = 26 RCTs | Integrated Disease Management | CRQ, SGRQ, 6MWT, hospitalisation, mortality, | • Improvement in all 4 domains of CRQ but only single domain of SGRQ  
• Improvement in 6MWT  
• Reductions in time to hospitalisation and hospitalisation days | 9 |
<table>
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<tr>
<th>Study, year country</th>
<th>Study design</th>
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<td>• No changes in mortality</td>
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<td><strong>Nutrition</strong></td>
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<tr>
<td>Ferreira et al, 2012, Canada</td>
<td>Systematic Review, N = 14 RCTs</td>
<td>Oral, enteral or parental nutritional support</td>
<td>Weight, FFMI, 6MWT, muscle circumference, inspiratory/expiratory pressure, SGRQ, CRQ</td>
<td>• No significant difference in weight for all subjects, difference shown of only malnourished subjects were analysed • Low quality evidence of change in FFMI and muscle circumference • Malnourished pts have improved inspiratory and expiratory pressures • No differences in QOL or 6MWT</td>
<td>9</td>
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<tr>
<td>Gurgun et al, 2013, Turkey</td>
<td>RCT, N = 46</td>
<td>Oral nutritional support</td>
<td>ISWT, 6MWT, SGRQ, weight, FFMI, BMI, HADS, mid-thigh CSA</td>
<td>• Increases in body weight and FFMI • Increased mid-thigh CSA • No difference with 6MWT, SGRQ or HADS</td>
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<tr>
<td>Collins et al, 2014, Australia</td>
<td>RCT, N = 84</td>
<td>Oral nutritional support</td>
<td>Protein intake, QOL</td>
<td>• No difference with QOL</td>
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<td><strong>Psychological Interventions</strong></td>
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<tr>
<td>Farver-Vestergaard et al, 2015, Denmark</td>
<td>Systematic Review, N = 20 RCTs, 1 NRCT</td>
<td>CBT, mind-body interventions, behavioural therapy</td>
<td>BAI, SAI, GDS, BDI, HADS</td>
<td>• Statistically significant effect for psychological outcomes overall • CBT more effective for psychological outcomes, mind-body interventions more effective for physical outcomes</td>
<td>5</td>
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</tbody>
</table>

* Assessment of Multiple Systematic Reviews tool
6MWD, 12MWD 6MWT = 6 Minute Walk Test, BAI = Beck Anxiety Inventory, BDI = Beck Depression Inventory, CRQ = Chronic Respiratory Questionnaire, CBT = Cognitive Behavioural Therapy, CSA = Cross Sectional Area, DB = Diaphragmatic Breathing, ESWT = Endurance Shuttle Walk Test, FFMI = Fat Free Muscle Index, GDI = Geriatric Depression Scale, GRC = Global Rating Change, HADS = Hospital Anxiety and Depression Scale, PLB = Pursed Lip Breathing, RR = Respiratory Rate, SAI = Spielberger Anxiety Inventory, SF-36 = Short Form 36, SGRQ = St George Respiratory Questionnaire, VAS = Visual Analogue Scale
Data from available studies were presented in a narrative format. Studies were grouped to the most popular interventions available in pulmonary rehabilitation. The mean difference between groups was presented in most studies. Effect sizes were presented if the data was available.

The major categories of interest were:

- Exercise training
- Inspiratory muscle training
- Breathing exercises
- Self-management
- Integrated disease management
- Nutrition
- Psychological interventions

Note that most of the systematic reviews analysed in this overview included trials that either compared the intervention in question with another intervention or included combinations of interventions together. Not all trials that were analysed were placebo controlled. This could potentially under or overstate the effects of the intervention.

4.4.1 QUALITY OF INCLUDED REVIEWS

Table 4.44 lists the results of the AMSTAR quality agreement. Scores ranged between 5 and 9 (median 9) and is considered high quality (143). No systematic review met item 11 “conflict” and all except one met item 10 “bias”.
Table 4.4: Results of AMSTAR* quality assessment

<table>
<thead>
<tr>
<th>Review ID</th>
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* Assessment of Multiple Systematic Reviews tool

Y = Yes - criteria met (score 1 point), N = No - criteria not met (score 0 points),
CA = Can't answer (score 0 points), NA = not applicable (score 1 point)

4.4.2 EXERCISE TRAINING

In the most recent Cochrane review, McCarthy et al analysed 65 articles which showed statistical significance in all outcome measures in both exercise capacity and QOL (7).

In relation to QOL, all four domains of the Chronic Respiratory Questionnaire (CRQ) had significant improvements (Fatigue: Mean Difference (MD) 0.68, 95% CI 0.45 to 0.92; Emotion: MD 0.56, 95% CI 0.34 to 0.78; Mastery: MD 0.71, 95% CI 0.47 to 0.95; Dyspnoea: MD 0.79, 95% CI 0.56 to 1.03), moderate level evidence. All improvements exceeded the Minimally Clinical Important Difference (MCID) of a change in score of 0.5 on a 7 point scale (117). Another
respiratory QOL scale, the St George Respiratory Questionnaire (SGRQ) was analysed and showed the total score and its individual domains had significant improvements (total: MD -6.89, 95%CI -9.26 to -4.52; symptoms: MD -5.09, 95% CI -7.69 to -2.49; impact: MD -7.23, 95% CI -9.91 to -4.55; activity: MD -6.08, 95%CI -9.28 to -2.88), moderate evidence. All exceeded MCID of four (145).

The improvement in 6MWT of 43.93m (95% CI 32.64 to 55.21) was of very low evidence and exceeding the MCID of 30m (146).

Another walk test commonly used in pulmonary rehabilitation is the Incremental Shuttle Walk Test (ISWT). A statistical improvement of 39.77m (95% CI 22.38 to 57) was seen and of moderate evidence. This improvement did not reach the MCID of 47.5m (147).

Trials in this systematic review were heterogeneous, as it included trials with interventions such as psychology or education in conjunction with exercise.

**Conclusion:**
On the basis of this review, it has been concluded that large & clinical significant changes were obtained and further RCTs would be unnecessary.

### 4.4.3 INSPIRATORY MUSCLE TRAINING

In the most recent review (2011), Gosselink et al analysed 32 articles (148). Respiratory muscle strength increased by 13 cmH₂O (summary effect size (SES) 0.68, 95% CI 0.54–0.82; p<0.001) and a significant change was observed in the Borg score (SES -0.45, 95% CI -0.66– -0.24; -0.9 point; p<0.0001).

The CRQ total score also had a significant increase of 3.8 points (SES 0.34, 95% CI 0.09–0.60; p<0.01). The dyspnoea and fatigue domains showed a significant increase. The improvements in emotion were not statistically
significant. The mastery domain showed no improvement. The change in CRQ total score also exceeded MCID.

The 6MWT increased by 32m (SES 0.28, 95% CI 0.12–0.44; p<0.001), which exceeded the MCID.

Quality of evidence was not analysed or reported in this review.

**Conclusion:**
The latest systematic review showed IMT can improve respiratory muscle function and provide systemic effects as shown in improvements in QOL and exercise capacity.

### 4.4.4 Breathing Exercises

16 RCTs were identified in the Cochrane analysis of this topic (149). Interventions analysed include PLB, DB and Pranayama Yoga. Pooled analyses were unable to be performed. PLB in two studies showed inconsistent changes in severity of dyspnoea. Only one study showed an improvement in 6MWT (150). Improvements in QOL were inconsistent between studies. The GRADE quality of evidence was low for these outcomes.

Two studies involving DB were identified. Each study showed contrasting results in changes to ratings of dyspnoea. One study reported a 6MWT change (34.7m (95% CI 4.1 to 65.3m) and improvements in SGRQ (QOL) (MD -10.5 points; 95% CI -17.7 to -3.3 points) (151). The GRADE quality of evidence was moderate for these outcomes.

Two studies using Pranayama yoga revealed significant improvements in 6MWT - 45m (95% CI 28 – 61m), but only one study measured dyspnoea which remained unchanged. The GRADE quality of evidence was low for the dyspnoea scales and moderate for the walking and QOL measures.
Another systematic review into the effects of yoga (Pranayama and other techniques) showed significant results in relation to exercise and lung capacity (152). Five RCTs were analysed showing a significantly improved FEV1 (WMD: 123.57 mL, 95% CI: 4.12-243, P=0.04) and 6MWT (WMD: 38.84 m, 95% CI: 15.52-62.16, p=0.001). The change in 6MWT exceeded MCID. No QOL data was analysed.

Following the publication of the Cochrane analysis, two further RCTs of PLB were published (153, 154). Only one of the two studies showed improvement in the walk test (34.9m, SD 26.4m) (154). Roberts did measure QOL using CRQ but only the dyspnoea subscale showed significant improvement (153).

Two additional studies of DB were undertaken. One study did not measure QOL or exercise capacity (155). In another study, a novel device was used to guide DB training (156). This RCT with 150 patients showed significant improvements in the Global Rating Change scale when compared to the control group (p=0.03), however there were no significant differences in improvements in SGRQ scores between all three groups.

Three further studies using various breathing exercises showed inconsistent changes in QOL and walk test scores (157-159).

Conclusion:
Studies involving PLB showed inconsistent results. Other types of breathing exercises again lack conclusive evidence about their benefits. Larger RCTs will need to be conducted. Given the heterogeneity of breathing exercises used, it may be beneficial to analyse each method separately.

### 4.4.5 SELF-MANAGEMENT

The latest Cochrane review published in 2014 included 23 studies (160). Both RCTs and CCTs were analysed. This review showed a statistical improvement in QOL through the SGRQ total score (-3.51, 95% CI -5.37 to -1.65). Only the impact domain of the SGRQ reached MCID (-5.71, 95% CI -9.17 to -2.25).
Patients who received the intervention were less likely to require hospitalisation (either all cause or respiratory related) (OR 0.57, 95% CI 0.43 to 0.75 and OR 0.60; 95% CI 0.40 to 0.89 respectively). Dyspnoea improved as measured by the modified Medical Research Council Scale (mMRC) (-0.83, 95% CI -1.36 to -0.30).

No changes were seen with mortality or exercise capacity on the 6MWT. The quality of evidence ranged from moderate to very low.

**Conclusion:**
Whilst the improvements seen were significant, further high quality RCTs may assist with the low to moderate level of evidence. With the definition of self-education being quite broad, further studies on each specific intervention would offer useful information. Similarly, studies are also to assess whether combining self-management with exercise therapy would provide additional benefits.

### 4.4.6 INTEGRATED DISEASE MANAGEMENT

In 2013, the most recent Cochrane review on IDM (as defined from above) was published (108). 26 RCTs were analysed. This showed statistically significant improvements in all four domains of CRQ; dyspnoea (1.02; 95% (CI) 0.67 to 1.36); fatigue (0.82; 95% CI 0.46 to 1.17); emotional (0.61; 95% CI 0.26 to 0.95) and mastery (0.75; 95% CI 0.38 to 1.12). All increases exceeded MCID. Only the impact domain of SGRQ reached both statistical significance and MCID (-4.04; 95% CI -5.96 to -2.11).

Improvements (both statistical significant and exceeding MCID) were shown in the 6MWT (43.86; 95%CI 21.83 to 65.89). There was a reduction in hospitalisations in the IDM group (OR 0.68; 95% CI 0.47 to 0.99; number needed to treat = 15). No change was seen in mortality. The quality of evidence ranged from moderate to high.
Conclusion:
Given the number of trials in the Cochrane review and the evidence rated as being of moderate to high quality, additional RCTs would be unnecessary. Further studies however would assist in determine which exact components of IDM is most effective.

4.4.7 NUTRITION

In the Cochrane systematic review, 14 studies were analysed (161). This showed no significant difference in final weight in those who received supplementation compared to the control group (0.69 kg; 95% CI -0.86 to 2.24). If only malnourished subjects were analysed, this showed a statistically significant weight gain (1.65 kg; 95% CI 0.14 to 3.16) in favour of supplementation. There was low quality evidence of change in FFMI (MD 0.57; 95% CI 0.04 to 1.09). No significant difference was found in changes to either QOL measures or 6MWT (low level evidence). Further attempts were made to stratify the data which yielded low level evidence of change. A sub-analysis of five studies that included exercise in the review showed a statistically significant change in weight of 1.80kg (95%CI 1.28 to 2.33) (161). The quality of evidence varied from moderate to low.

Two RCTs have been published following the publication of the Cochrane review. One showed that nutritional supplementation in conjunction with exercise offered statistical significant increases to body weight and FFMI then with exercise alone (P<0.05) (162). However, there were no additional benefits seen in 6MWT, QOL and HADS. In another study with 84 subjects, the use of oral nutritional supplements showed a substantial increase in protein intake but no differences with QOL (163). Exercise capacity was not tested.

Conclusion:
Given the Cochrane review only contained 14 studies, it could only find supplementation being of benefit to those already malnourished. Until further studies are pooled and analysed, it is difficult to determine whether nutritional supplementation would offer other improvements with other measures such as
anthropometry, lung function, QOL or exercise. Given the unequivocal benefit of exercise further nutrition studies should also be designed around a physical exercise program.

4.4.8 PSYCHOLOGICAL INTERVENTIONS

Several systematic reviews have been conducted in this area. The latest systematic review conducted in 2014 analysed 20 articles (8). Overall, a statistically significant effect was found for psychological outcomes (Hedges’ g = 0.38, 95% CI 0.19 – 0.58, p<0.001). CBT interventions were more effective at improving psychological outcomes (g = 0.39; CI = 0.15-0.62; p = 0.001). In contrast, mind-body interventions (e.g. mindfulness-based therapy, yoga and relaxation) were more effective for physical outcomes (g = 0.40; CI = 0.01 - 0.79; p = 0.042). A quality rating was not used.

Conclusion:
The importance of addressing psychological burden in COPD patients has been identified, with the latest and biggest systematic review to date showing psychological interventions does produce significant psychological results. Further large sample and high quality trials of each individual intervention are required to determine which intervention is most efficacious.

4.5 SUMMARY

Symptoms and activity limitations experienced by people with COPD are wide ranging and extend beyond dyspnoea and chronic cough. Non-pharmacological, non-surgical interventions are multi-faceted and span across multiple disciplines. Physical exercise such as cardiovascular training has high levels of evidence. It is extensively incorporated in PR and is considered an essential component in both Australian and international guidelines (15, 16). Other interventions such as inspiratory muscle training, self-management and integrated disease management have systematic reviews confirming their
effectiveness, but not yet commonly utilised in practice or recommended in guidelines. Due to the limited number of RCTs, techniques such as breathing exercises and psychological interventions have yet to show consistent improvements between trials. Further large trials are required for these interventions. The quality of evidence shown in the included systematic reviews using AMSTAR is novel and were of high quality, however not one review was able to satisfy all 11 AMSTAR criteria. The criteria in relation to conflict was not met by any systematic review as none reported sources of financial support. The optimal intensity, combination or components of PR remain unknown.

The next chapter (Chapter 5) looks whether the use of an additional intervention (Cognitive Behavioural Therapy) to a pre-existing PR program improves outcomes.
CHAPTER 5: Cognitive Behavioural Therapy Study

This chapter describes a prospective clinical cohort study to determine whether the effectiveness of a pre-existing community Pulmonary Rehabilitation (PR) program could be further improved with the addition of group based Cognitive Behavioural Therapy (CBT) sessions.

5.1 INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is a major cause of mortality, morbidity and health service use worldwide. COPD affects the ability of sufferers to perform their activities of daily living and their quality of life. It is projected that COPD will be the seventh leading cause in Disability Adjusted Life Years (DALYs) lost worldwide by 2030 (32).

It has now been established that COPD affects not only the lungs, but is a systemic disease causing other body system pathology such as skeletal muscle dysfunction (4). Patients with COPD often experience limitations in physical and functional activity but it is difficult to determine whether these changes relate to the disease itself or reduced activity levels as a consequence of progressive lung disease (164).

PR involves patient assessment, exercise training, education, behaviour change, nutritional intervention and psychosocial support (15). Benefits of PR include improved exercise tolerance, improved quality of life and lowered perception of dyspnoea (165). Exercise programs alone have clear benefits, while the benefits of education or psychosocial support without exercise training are less well documented (13). Comprehensive programs incorporating all three interventions (exercise, education and psychosocial support) have the greatest benefits.

Comorbid psychological disorders are a significant burden for patients with COPD, in whom there is an increased prevalence of depression (36%) and
anxiety (40%) (55). Patients with psychological co-morbidities are more likely to have reduced engagement and participation and subsequently reduced quality of life (13). The presence of anxiety or depression worsens the degree of dyspnoea and consequently patients are more likely to be sedentary at home (166).

Despite this, the treatment and rehabilitation of these patients focuses only on the physical characteristics of the disease. A systematic review of various psychological interventions showed some improvements in psychological outcomes when these were analysed together. However, when CBT was analysed as an intervention alone, there were significant improvements in psychological but not for physical outcomes (8). Alternately, in some trials CBT was offered only to participants who were identified as having either depression or anxiety (167). Ultimately, the optimal type or intensity of psychological interventions remains unknown (8).

The objectives of this study were to: 1) conduct a Clinical Controlled Trial (CCT) comparing the current PR regime with a program adding Cognitive Behavioural Therapy (CBT) to the existing schedule and 2) confirm that a directed psychological intervention consisting of CBT improves patient participation and clinical outcomes in PR.

5.2 MATERIAL AND METHODS

5.2.1 PARTICIPANTS AND SETTING

This was a prospective CCT conducted at Royal Melbourne Hospital (RMH) and Merri Community Health Service (MCHS). Approximately 100 patients with stable COPD undertake outpatient PR each year at MCHS. Patients who were diagnosed with COPD and treated by the RMH respiratory service were referred to MCHS for ongoing pulmonary management and rehabilitation. The diagnosis and severity grading of COPD was based on the Global Initiative for COPD
(GOLD) criteria, as assessed by the respiratory and rehabilitation physicians at RMH(11). This study was approved by the Human Research Ethics Committee at Melbourne Health (HREC Approval 2012.174).

5.2.2 PROCEDURE

All patients who were referred to the ambulatory PR program during the 18-month trial were screened and consented for participation into the study. The multidisciplinary team consisting of respiratory and rehabilitation specialists, physiotherapists and nurses screened each patient according to the criteria. Patients were eligible for this study if they had stable COPD, ability to comprehend English and consent for the study and were able to attend regular PR sessions. Stable COPD was defined as no exacerbations within the previous six weeks and on optimal pharmacological therapy. Exclusion criteria included prior psychological treatment within the past three months and any significant psychiatric history such as psychosis, bipolar disorder, schizophrenia, mental retardation, borderline personality disorder, chronic suicidal behaviour or major depressive disorder with prior hospitalisation episodes. The patient’s general practitioner was contacted if the psychiatric diagnosis was unclear.

Patients were allocated to either the treatment group consisting of additional group based CBT and the usual PR or the control group consisting of PR alone. Allocation was not randomised. Once patients were referred and assessed to be eligible for PR, they were enrolled into the next PR group. Due to resources, the CBT program was delivered to consecutive patients in two PR cohorts during the 18-month period. Patients who were recruited outside of these times did not receive CBT and were allocated to the control group.

5.2.3 TREATMENT SCHEDULES

Patients in both groups received the usual PR programme. This eight-week program consisted of multidisciplinary management including medical, nursing and allied health using standardised therapy protocols. Each week contained
two 2-hourly sessions consisting of group physical therapy and general education sessions. The 45-minute exercise session consisted of 15 minutes treadmill/walking, 15 minutes cycling and 15 minutes’ circuit exercises. Patients were educated and monitored to ensure they spent most of their time on the treadmill or bike at a high level of intensity as per current American Thoracic Society guidelines(15). Group education was provided on issues such as how the lungs work, nutrition, advanced care planning and medication management. Whilst patients were educated on the link between dyspnoea and COPD, no specific information was provided in relation to recognising triggers of dyspnoea or the use specific breathing strategies. An a priori compliance with outpatient treatment was participant attendance in >80% of treatment sessions.

The CBT program in the treatment group consisted of an additional 6 sessions of group based CBT delivered by a psychologist. The psychologist did not take part in patient assessment. The content was designed in conjunction with the treating team to complement the pre-existing exercise and education programs. The program was not specifically directed at anxiety and depression, but incorporated common issues facing a PR participant. Table 7.1 lists the themes in the CBT group included:

**Table 5.1: Themes in the CBT program**

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Breathing and relaxation</td>
</tr>
<tr>
<td>2.</td>
<td>Anxiety management</td>
</tr>
<tr>
<td>3.</td>
<td>Monitoring and responding to thoughts/self-talk</td>
</tr>
<tr>
<td>4.</td>
<td>Barriers to changing behaviour</td>
</tr>
<tr>
<td>5.</td>
<td>Goals, objectives and problem –solving</td>
</tr>
<tr>
<td>6.</td>
<td>Understanding and responding to the risk of depression</td>
</tr>
</tbody>
</table>
Participant progress was assessed in weekly meetings. Exercise schedules were altered dependent on patient’s dyspnoea symptoms and vital signs during exercise. Adverse effects of rehabilitation were noted (e.g. falls, injury during treatment).

5.2.4 OUTCOME MEASURES

ASSESSMENT INTERVIEWS
All baseline participant interviews and clinical assessments were completed using a structured format. Demographic, functional and Quality of Life (QOL) assessments were completed using standardised instruments (see measures). Assessors did not prompt patients, but provided assistance for those who had difficulty with completing the questionnaires. COPD related measures such as socio-demographic, clinical and treatment data were obtained from the medical record.

The primary outcome measure in this study was the Depression Anxiety Stress Scale (DASS) (short form). This is a 21 item self-reported questionnaire that measures the three related negative emotional states of depression, anxiety and tension/stress (78). Participants rated the extent to which they experienced each state over the past week on a 4-point Likert rating scale. When totalled, three domain scores are given. Scores of greater than 9, 7 and 14 are suggestive of depression, anxiety and stress respectively (78).

Secondary outcome measures included:

- 6-minute walk test (6MWT). This test measures the distance patients can walk in 6 minutes and is a measure of functional exercise capacity (76). The best score out of two attempts is recorded. The Minimal Important Difference (MID) is 25m (168).

- Chronic Respiratory Questionnaire (CRQ). The CRQ consists of a 20-item questionnaire with four major domains (Dyspnoea, Fatigue,
Emotion, Mastery) which patients self-administer. This measures the
health-related QOL in respiratory patients. The MID is reflected by a
change in score of 0.5 on a 7 point scale (117).

- Hospital Anxiety and Depression Scale (HADS). The HADS is a fourteen-
  item scale that measures levels of anxiety and depression. Each item is
  rated on a scale of 0-3. Total scores greater than 8 has been used to
  indicate anxiety or depression (122). The MID is 1.5 (169).

- Psychosocial Adjustment to Illness Scale (PAIS). This is a 46 item self-
  report questionnaire that assesses psychosocial adjustment to chronic
  illness (123). It measures psychosocial adjustment to illness in terms of 7
  primary domains of adjustment: Health Care Orientation, Vocational
  Environment, Domestic Environment, Sexual Relationships, Extended
  Family Relationships, Social Environment and Psychological Distress.
  Each PAIS item is rated on a 4-point (0 to 3) scale of adjustment, with
  higher ratings indicating poorer adjustment status.

5.2.5 STATISTICAL ANALYSIS

Data was keyed into Microsoft Excel (Microsoft, WA USA) and exported into
Stata12 (StataCorp, TX USA) for data analysis and reporting. Descriptive
analysis of study cohort was undertaken and results reported as n(%) for
categorical data (e.g. gender) and median (IQR) for continuous data (FEV1,
FVC, BMI, etc.).

The change in outcomes of interest between pre and post PR was calculated
based on the score at end of PR minus the score at baseline. The three-month
post PR change was calculated based on the score at the three-month post PR
visit minus either the score at baseline or end of rehabilitation. Cohen’s d test
was used to measure effect size. The differences were assessed for normality
using Shapiro-Wilks test. Scores that were normally distributed, an one-sample
t-test was utilized to determine the significance of the change and its magnitude. Level of significance for the study was set at p<0.05.

5.3 RESULTS

A total of 70 patients were screened for the study, 34 patients were consented (See figure 5.1). 28 patients completed PR and completed all their assessments. There were 14 patients in the CBT (treatment) group and 14 patients in the control group. Of the six non-completers, five were male, otherwise there were no statistical differences between the completers and non-completers.
Figure 5.1: Flow chart of recruitment process

Patients Screened  
\textit{n} = 70

Patient \textbf{eligible} for inclusion in the study and invited to participate  
\textit{n} = 55

Excluded (\textit{n} = 21)  
- Refused to participate = 7  
- Patient not starting PR = 5  
- Admitted to hospital = 1  
- Other reason = 8

Patient consented to participate  
\textit{n} = 34

Intervention (CBT) group  
\textit{n} = 16

Completed PR  
\textit{n} = 14

Control group  
\textit{n} = 18

Completed PR  
\textit{n} = 14

Patients Screened  
\textit{n} = 70
Table 5.2 shows the baseline characteristics between the two groups. The mean age of study participants was 72.4±7.4 years, with 100% being smokers (past or present), mean FEV1 was 57.4±23.4% and 21% were on long term oxygen therapy. 43% of participants lived alone and 7% of participants had only a primary education. There were no statistical differences between the two groups.
Table 5.2: Baseline demographics

<table>
<thead>
<tr>
<th>Demographic</th>
<th>CONTROL GROUP (n=14)</th>
<th>TREATMENT (CBT) GROUP (n=14)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male, n(%)</td>
<td>6 (42.9)</td>
<td>7 (50.0)</td>
</tr>
<tr>
<td>Age, Mean(SD)</td>
<td>70.5 (7.5)</td>
<td>74.2 (7.2)</td>
</tr>
<tr>
<td>Body Mass Index (BMI – kg/m²)</td>
<td>24.1 (12.3)</td>
<td>22.3 (8.0)</td>
</tr>
<tr>
<td>Lung Function</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FEV1 (%), Median (IQR)</td>
<td>61.5 (39-67)</td>
<td>49 (37-77)</td>
</tr>
<tr>
<td>Current smoker/Past smoker</td>
<td>4/10</td>
<td>3/11</td>
</tr>
<tr>
<td>Smoking (pack years), median(IQR)</td>
<td>48 (30-55)</td>
<td>38 (30-56)</td>
</tr>
<tr>
<td>Long Term Oxygen Therapy (LTOT)</td>
<td>2 (14%)</td>
<td>4 (29%)</td>
</tr>
<tr>
<td>Ischaemic Heart Disease (IHD)</td>
<td>4 (29%)</td>
<td>4 (29%)</td>
</tr>
<tr>
<td>Congestive Cardiac Failure (CCF)</td>
<td>1 (7.1%)</td>
<td>2 (14%)</td>
</tr>
<tr>
<td>Diabetes Mellitus (DM)</td>
<td>4 (29%)</td>
<td>1 (7%)</td>
</tr>
<tr>
<td>Previously Diagnosed Anxiety</td>
<td>3 (14%)</td>
<td>1 (7%)</td>
</tr>
<tr>
<td>Previously Diagnosed Depression</td>
<td>4 (29%)</td>
<td>5 (36%)</td>
</tr>
</tbody>
</table>

IQR = Interquartile Range
Table 5.3 describes participant’s outcome measures at baseline. There were no statistical differences between the two groups. DASS scores showed approximately half of the participants had probable depression and anxiety in both groups. These rates are higher when compared with the HADS scores or self-reporting.
<table>
<thead>
<tr>
<th>OUTCOME MEASURE (IQR)</th>
<th>CONTROL GROUP (n=14)</th>
<th>TREATMENT (CBT) GROUP (n=14)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 Min Walk Test (6MWT)</td>
<td>346.9 (105.7)</td>
<td>329.4 (111.1)</td>
</tr>
<tr>
<td><strong>CRQ</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total (range 20 – 140)</td>
<td>87.5 (80-104)</td>
<td>93.5 (79-111)</td>
</tr>
<tr>
<td>Dyspnoea (range 5–35)</td>
<td>16 (14-20)</td>
<td>21 (14-25)</td>
</tr>
<tr>
<td>Fatigue (range 4–28)</td>
<td>16.5 (15-22)</td>
<td>15.5 (13-21)</td>
</tr>
<tr>
<td>Emotion (range 7–49)</td>
<td>36.5 (30-44)</td>
<td>36.5 (28-41)</td>
</tr>
<tr>
<td>Mastery (range 4–28)</td>
<td>22 (18-23)</td>
<td>23 (19-25)</td>
</tr>
<tr>
<td><strong>HADS</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anxiety Score</td>
<td>4.5 (1-6)</td>
<td>5.5 (2-7)</td>
</tr>
<tr>
<td>Depression Score</td>
<td>3.5 (3-6)</td>
<td>4 (1-8)</td>
</tr>
<tr>
<td>Prob Anxiety (score 8-21)</td>
<td>3 (21.4)</td>
<td>3 (21.4)</td>
</tr>
<tr>
<td>Prob Depression (score 8-21)</td>
<td>1 (7.1)</td>
<td>4 (28.6)</td>
</tr>
<tr>
<td><strong>DASS</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depression</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median Score (IQR)</td>
<td>7 (0-14)</td>
<td>9 (4-12)</td>
</tr>
<tr>
<td>Normal (0-9)</td>
<td>8 (57.1)</td>
<td>7 (50.0)</td>
</tr>
<tr>
<td>Mild/Mod/Severe/Ext (&gt;9)</td>
<td>6 (42.9)</td>
<td>7 (50.0)</td>
</tr>
<tr>
<td>Anxiety</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median Score (IQR)</td>
<td>7 (2-10)</td>
<td>8 (6-10)</td>
</tr>
<tr>
<td>Normal (0-7)</td>
<td>7(50.0)</td>
<td>5 (35.7)</td>
</tr>
<tr>
<td>Mild/Mod/Severe/Ext (&gt;7)</td>
<td>7(50.0)</td>
<td>9 (64.3)</td>
</tr>
<tr>
<td>Stress</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median Score (IQR)</td>
<td>6 (0-12)</td>
<td>10 (6-14)</td>
</tr>
<tr>
<td>Normal (0-14)</td>
<td>12 (85.7)</td>
<td>12 (85.7)</td>
</tr>
<tr>
<td>Mild/Mod/Severe/Ext (&gt;14)</td>
<td>2 (14.3)</td>
<td>2 (14.3)</td>
</tr>
<tr>
<td><strong>PAIS</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean Score (SD)</td>
<td>31 (17)</td>
<td>37 (22)</td>
</tr>
</tbody>
</table>

IQR = Interquartile Range
SD = Standard Deviation
5.3.1 PRIMARY OUTCOME

In the CBT group, statistical reductions were seen in depression and stress scores of the DASS (p<0.05, p<=0.02 respectively, see Table 5.4). These improvements were not sustained at 3 months post PR. In the anxiety sub scale, a reduction was seen immediately post PR but was not statically significant. By 3 months post PR, a bigger reduction was seen and was statistically significant (p<0.01).

In contrast, no significant improvements were seen in all 3 sub-scales in the control group.
Table 5.4: Changes following pulmonary rehabilitation

<table>
<thead>
<tr>
<th>OUTCOME MEASURE</th>
<th>TIME</th>
<th>TREATMENT (CBT) GRP (n=14)</th>
<th>CONTROL GROUP (n=14)</th>
<th>BETWEEN-GROUP EFFECT SIZE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
<td>Cohen’s d (95% CI)</td>
</tr>
<tr>
<td>6MWT (m)</td>
<td>1-2</td>
<td>32.9 (55.0)*</td>
<td>5.6 (40.1)</td>
<td>0.57 (-0.19 to 1.32)</td>
</tr>
<tr>
<td></td>
<td>1-3</td>
<td>23.4 (35.9)*</td>
<td>4 (46.9)</td>
<td>0.46 (-0.34 to 1.25)</td>
</tr>
<tr>
<td></td>
<td>2-3</td>
<td>-1.3 (50.6)</td>
<td>0.92 (35.3)</td>
<td>-0.05 (-0.9 to 0.8)</td>
</tr>
<tr>
<td>CRQ</td>
<td>1-2</td>
<td>2.1 (6.9)</td>
<td>0.4 (4.4)</td>
<td>0.29 (-0.45 to 1.04)</td>
</tr>
<tr>
<td>Dyspnoea (range 5–35)</td>
<td>1-3</td>
<td>3.1 (6.2)</td>
<td>2.1 (5.9)</td>
<td>0.17 (-0.58 to 0.91)</td>
</tr>
<tr>
<td></td>
<td>2-3</td>
<td>1.1 (4.8)</td>
<td>1.8 (6.2)</td>
<td>-0.13 (-0.87 to 0.61)</td>
</tr>
<tr>
<td>Fatigue (range 4–28)</td>
<td>1-2</td>
<td>2.4 (3.3)**</td>
<td>-1 (4.8)</td>
<td>0.84 (0.06 to 1.61)*</td>
</tr>
<tr>
<td></td>
<td>1-3</td>
<td>1.3 (3.1)</td>
<td>0.2 (3.9)</td>
<td>0.20 (-0.45 to 1.04)</td>
</tr>
<tr>
<td></td>
<td>2-3</td>
<td>-1.1 (4.3)</td>
<td>1.2 (4.1)</td>
<td>-0.56 (-1.31 to 0.20)</td>
</tr>
<tr>
<td>Emotion (range 7–49)</td>
<td>1-2</td>
<td>2.6 (7.2)</td>
<td>0.7 (8.8)</td>
<td>0.24 (-0.51 to 0.98)</td>
</tr>
<tr>
<td></td>
<td>1-3</td>
<td>2.5 (4.9)</td>
<td>1.1 (6.4)</td>
<td>0.24 (-0.51 to 0.98)</td>
</tr>
<tr>
<td></td>
<td>2-3</td>
<td>-0.1 (6.5)</td>
<td>0.4 (6.3)</td>
<td>-0.09 (-0.83 to 0.65)</td>
</tr>
<tr>
<td>Mastery (range 4–28)</td>
<td>1-2</td>
<td>-0.3 (6.3)</td>
<td>1.1 (4.9)</td>
<td>-0.25 (-0.99 to 0.49)</td>
</tr>
<tr>
<td></td>
<td>1-3</td>
<td>0.8 (6.5)</td>
<td>-1.1 (3.8)</td>
<td>0.14 (-0.60 to 0.88)</td>
</tr>
<tr>
<td></td>
<td>2-3</td>
<td>1.1 (4.0)</td>
<td>0 (4.4)</td>
<td>0.56 (-0.20 to 1.31)</td>
</tr>
<tr>
<td>HADS</td>
<td>1-2</td>
<td>-1.1 (2.6)</td>
<td>0.2 (3.6)</td>
<td>-0.41 (-1.16 to 0.34)</td>
</tr>
<tr>
<td>Anxiety</td>
<td>1-3</td>
<td>-1.3 (2.3)</td>
<td>0.4 (3.2)</td>
<td>-0.59 (-1.40 to 0.23)</td>
</tr>
<tr>
<td></td>
<td>2-3</td>
<td>0.3 (2.6)</td>
<td>-0.2 (2.8)</td>
<td>0.16 (-0.65 to 0.96)</td>
</tr>
<tr>
<td>Depression</td>
<td>1-2</td>
<td>-0.9 (3.1)</td>
<td>-0.1 (2.7)</td>
<td>-0.27 (-1.01 to 0.48)</td>
</tr>
<tr>
<td></td>
<td>1-3</td>
<td>0.1 (1.4)</td>
<td>0.3 (2.0)</td>
<td>-0.10 (-0.90 to 0.70)</td>
</tr>
<tr>
<td></td>
<td>2-3</td>
<td>1.1 (2.5)</td>
<td>0.3 (3.0)</td>
<td>0.31 (-0.50 to 1.11)</td>
</tr>
<tr>
<td>DASS</td>
<td>1-2</td>
<td>-4.3 (7.3)*</td>
<td>-1.9 (7.3)</td>
<td>-0.33 (-1.08 to 0.42)</td>
</tr>
<tr>
<td>Depression</td>
<td>1-3</td>
<td>-1.5 (5.2)</td>
<td>0.2 (5.8)</td>
<td>-0.31 (-1.08 to 0.47)</td>
</tr>
<tr>
<td></td>
<td>2-3</td>
<td>3.1 (9.0)</td>
<td>0.6 (7.3)</td>
<td>0.30 (-0.48 to 1.07)</td>
</tr>
<tr>
<td>Anxiety</td>
<td>1-2</td>
<td>-2.6 (7.0)</td>
<td>0.4 (5.7)</td>
<td>-0.47 (-1.22 to 0.29)</td>
</tr>
<tr>
<td></td>
<td>1-3</td>
<td>-3.1 (3.6)**</td>
<td>-1.7 (5.7)</td>
<td>-0.29 (-1.06 to 0.49)</td>
</tr>
<tr>
<td></td>
<td>2-3</td>
<td>-0.3 (6.1)</td>
<td>-2.6 (5.9)</td>
<td>0.38 (-0.40 to 1.16)</td>
</tr>
<tr>
<td>Stress</td>
<td>1-2</td>
<td>-3.9 (5.6)**</td>
<td>0.3 (6.3)</td>
<td>-0.69 (-1.45 to 0.08)</td>
</tr>
<tr>
<td></td>
<td>1-3</td>
<td>-2.6 (6.2)</td>
<td>-1.8 (7.2)</td>
<td>-0.11 (-0.88 to 0.66)</td>
</tr>
<tr>
<td></td>
<td>2-3</td>
<td>1.5 (7.7)</td>
<td>-2.2 (7.7)</td>
<td>0.47 (-0.31 to 1.25)</td>
</tr>
<tr>
<td>PAIS</td>
<td>1-2</td>
<td>-3.7 (17.4)</td>
<td>-6.6 (18.7)</td>
<td>0.16 (-0.57 to 0.89)</td>
</tr>
<tr>
<td></td>
<td>1-3</td>
<td>-7.1 (10.4)</td>
<td>0.5 (17.3)</td>
<td>-0.54 (-1.4 to 0.33)</td>
</tr>
<tr>
<td></td>
<td>2-3</td>
<td>-3.4 (13.3)</td>
<td>6.6 (15.4)</td>
<td>-0.7 (-1.5 to 0.08)</td>
</tr>
</tbody>
</table>
5.3.2 SECONDARY OUTCOMES

Statistically significant improvements in the 6MWT were seen in the CBT group (p<0.05). This was maintained at the 3-month post PR (p<0.05). Improvements were also seen in the control group but were not statistically significant.

In relation to the CRQ, only the fatigue domain had a statistical significant improvement in the CBT group (p<=0.02). There was also a statistical improvement between the two groups (p=0.03). Emotion and dyspnoea improved in both groups, though bigger changes were noted in the treatment group. However, these changes were not significant.

Both anxiety and depression scales in the HADS had reductions following PR in the CBT group, but were not statistically significant. In the control group, reductions were only seen in the depression scale. Again, none of the changes in the control group were statistically significant.

Reductions were seen in PAIS across both groups after completion of PR. None of the changes were statistically significant.
5.4 DISCUSSION

This is one of the few studies looking at strategies beyond physical measures for COPD and shows that with the addition of CBT to PR provides additional benefits. Greater improvements in the CBT group were seen in the 6MWT, HADS, DASS and CRQ (except Mastery). Only the 6MWT, fatigue, depression (DASS component) and stress measures were statistically significant (p<0.05, p<=0.02, p<0.05, p<=0.02 respectively).

The improvements in the 6MWT following PR were sustained at the 3-month post PR timepoint. At the 3-month post PR, the improvement in the anxiety component of the DASS was statistically significant (p<=0.02).

There was significant psychological comorbidity in patients in this study. Approximately half of study patients had depression or anxiety and 14% had stress on the DASS. This may have contributed to the lack of response to PR. This psychological burden was even higher than a previously conducted study in the same centre which showed statistically significant improvements in the walk test and all four domains of the CRQ (170).

Two similar outcome measures (DASS & HADS) were used to measure anxiety and depression. Studies in the traumatic brain injury population reported both measures were valid as screening tools for anxiety and depression (171). In this study, the DASS showed higher prevalence rates than HADS. However, the DASS was more sensitive to changes following PR in the CBT group.

Despite the increasing recognition of psychological burden in patients with COPD, the current Australian Lung Foundation Pulmonary Rehabilitation Guidelines does not recommend any routine screening or the use of psychological interventions (16). It is hoped that this study along with other future studies will offer additional evidence and suggest further modifications to the PR program. This also highlights the importance of providing psychological...
support to everyone participating in the program and not just those diagnosed as anxious or depressed.

The use of CBT has been more commonly used for psychological disorders rather than in the general medical population. Reductions in stress and depression scores following CBT would be expected, however this study showed CBT carries additional benefits to other impairments such as exercise capacity. The CBT program in this study was designed to address not only pre-morbid psychological burden, but also to enhance the concurrent physical exercise and education programs. Given that PR does not change lung function, the ultimate aim of PR would be not only to improve exercise capacity and QOL but also improve self-efficacy and management of their disease (104).

Whilst there are trials evaluating the use of CBT in people with COPD, very few compare the additional benefits of CBT in PR. In a similar study, De Degoy et al compared various PR components such as exercise, education and CBT (172). This showed combined psychotherapy and exercise as well as psychotherapy alone were effective in improving exercise capacity, anxiety, depression and QOL. No statistical analyses were performed to show which group was more effective. Similarly, in this study it was shown that adding a CBT component provided additive benefits to a PR program. Exercise alone in De Degoy et al or PR alone in this study did not improve exercise capacity or QOL. In contrast, a systematic review on the role of physical exercise in COPD showed significant improvements in exercise and QOL (7). The improvements in the 6MWT and six of the seven QOL domains exceeded the MID (7).

The PAIS was used as an outcome measure in this study to determine whether patients’ psychological adjustment changed following PR. With the greater recognition and treatment of psychological disturbance in COPD, it is hoped that patients would have increased psychological adjustment and associated self-coping. Whilst the PAIS scores reduced (indicating improved adjustment), the changes were not statistically significant.
Respiratory studies frequently report on MID. MID attempts to define the smallest difference in score that patients would perceive as important (117). This is usually greater than statistical significance. In this study, the increases in 6MWT and the fatigue subscale of the CRQ, exceeded the MID (117, 168).

This study was a CCT which could create bias. Participants were enrolled to either the CBT or control group based on when they started PR. A randomised controlled trial would provide a higher level of evidence though may be difficult to conduct with the small group sizes. Also, larger sample sizes would be ideal to provide statistically significant data.

PR, in particular exercise training have been shown to produce unequivocal improvements to QOL and exercise capacity (7). This study, in contrast has shown the PR program at this centre does not produce similar results. An analysis involving a larger group of patients (n=88) at this centre has shown statistically significant improvements in the walk test and CRQ (170). A larger sample size in this study may have been able to replicate these results. It would also allow further subanalysis to determine whether certain factors such as the presence of anxiety or depression affects PR performance.

Another key difference is despite a similarity with severity of COPD when compared to other studies, the mean CRQ scores were higher. Another study looking at PR in the same city and a similar cohort showed lower pre PR CRQ scores (116). This means our patients at study entry had a higher QOL and thus further improvements in COPD related QOL may have been limited. Further sub-analyses would be required to confirm this. Other factors that could have impacted on outcomes were beyond the scope of this study.

Data from participants were recorded up to three months following completion of PR. Information beyond three months were not recorded as there was no funding. Further monitoring of participants would track the longevity and duration of gains with CBT. Patients who complete PR would typically return to their premorbid state (170). Furthermore, other factors which may be affected
by PR, including the number or exacerbations or hospitalisations, were not recorded.

5.5 CONCLUSION

This study shows that the addition of a non-exercise intervention improves the efficacy of a PR program. Non-physical exercise interventions should be considered in all PR programs. Further research is required to determine which interventions are most effective.

The next chapter will discuss the outcomes following participation in a PR program and tracking of patients to see whether these changes can be maintained in the long term (beyond 12 months).
CHAPTER 6 LONG TERM STUDY

The systematic review in Chapter 4 has demonstrated the effectiveness of exercise training, which is one of the major components in Pulmonary Rehabilitation (PR) for patients with Chronic Obstructive Pulmonary Disease (COPD). In this Chapter, the Long Term study aims to investigate whether these physical, psychological and Quality of Life (QOL) gains are maintained following completion of the program into the longer term.

6.1 INTRODUCTION

Patients with COPD often experience ongoing impairments with their day to day life despite optimal pharmacological management. Whilst COPD is known to affect the lungs, the associated physical deconditioning and the emotional responses to chronic respiratory disease contribute greatly to the resulting morbidity (133). It has been difficult to determine whether these changes relate to the disease itself or reduced activity levels as a consequence of progressive lung disease (164). Skeletal muscle dysfunction beyond deconditioning has been identified and recognised as a major target for treatment (4). Despite optimal pharmacological treatment, many COPD patients experience substantial functional impairment limiting their normal activities of daily living and affecting their QOL (173, 174). The medical treatment of COPD has been well established, yet very little is known about how the disease progresses to disability (175).

PR is an accepted non-pharmacological intervention for individuals with COPD (176). This consists of an interdisciplinary approach to patients with chronic respiratory impairment that is individually tailored and designed to optimise physical and social performance and autonomy (133). The minimum duration of an effective rehabilitation program is 6 weeks (177). PR should be offered to patients with moderate to severe COPD (13).
Unlike neurological and orthopaedic rehabilitation in which therapy acts as an adjuvant treatment in enhancing recovery, the primary aim of PR is not to improve lung function, but rather to improve self-coping or management of COPD.

Following successful completion of PR, some patients deteriorate further and require repeat stints of PR. Studies that have monitored patients beyond 12 months following PR have shown differing results. Some have shown that benefits such as QOL persist beyond 12 months (112, 178-181). Others have shown that patients often return to baseline or even deteriorate further (113-115). Some studies had small sample sizes with only 16 and 21 patients (181, 182). Many studies included patients in a hospital outpatient setting or patients with less severe COPD. The aim of this study is to look at long term outcomes of patients with moderate to severe COPD attending PR in a community setting. Secondary aims include comparing the demographics and changes in mobility and function following PR.

6.2 METHODS

6.2.1 PARTICIPANTS & SETTING

This was a prospective cohort study of patients who had completed PR conducted at Royal Melbourne Hospital (RMH) and Merri Community Health Service (MCHS). This study was approved by the Human Research Ethics Committee of Melbourne Health.

The diagnosis and severity of COPD was graded according to the Global Initiative for COPD (GOLD) criteria (183) by respiratory and rehabilitation physicians at RMH. Patients who are treated by the respiratory service are referred for ongoing pulmonary management and rehabilitation.

The eight-week pulmonary rehabilitation program consists of multidisciplinary management including medical, nursing and allied health using standardised
therapy protocols. Following patient assessment including goal setting, an individualised exercise plan was created. Each week, participants undertook two 2-hourly sessions consisting of group physical therapy and general education sessions. The 45-minute exercise session consists of 15 minutes treadmill/walking, 15 minutes cycling and 15 minutes circuit exercises. Treadmill speeds were set at 80% of the initial ISWT speed. Patients were educated and monitored to ensure they spend most of their time on the treadmill or bike at a high level of intensity as per current American Thoracic Society guidelines (15). This correlated to a Rating of Perceived Exertion (RPE) of 4-6 on the modified Borg scale. In subsequent sessions, patients were encouraged to either increase treadmill speed or bike resistance provided they remained in the 4-6 on the RPE. Each group contained a maximum of 15 patients. Patients were supervised during the program by their key worker and physician. Group education included topics such as how the lungs work and medication management.

Eligible patients were identified from a centralised database at MCHS. The inclusion criteria were patients with a confirmed diagnosis of COPD and have completed PR between 2003 and 2012. This allowed a minimum period of 12 months follow-up. Patients were excluded if they had severe cognitive impairment or were medically unwell for further assessment and testing.

6.2.2 PROCEDURE

Following consent, eligible patients were invited to attend the community centre for assessment (long term assessment).

The long-term assessment participant interviews and clinical assessments were completed using a structured format. The assessors completed demographic, functional and Quality of Life (QoL) assessments using standardised instruments (see measures). Standardised instructions were given to patients to complete questionnaires. Any additional queries were answered.
6.2.3 DATA COLLECTION

Patient data was extracted from a centralised database. Information was collected at several timepoints, from pre PR, post PR and at 3 monthly intervals post PR until they were discharged from case management. Basic demographic information was collected at the first visit. The main outcome measures including ISWT, CRQ and HADS were recorded at pre PR, post PR and repeated at the long-term assessment.

6.2.4 MAIN OUTCOME MEASURES

Activity was assessed with the Incremental Shuttle Walk Test (ISWT) (73), whilst participation and QOL was measured with the Chronic Respiratory Questionnaire (CRQ) (71) and Hospital Anxiety and Depression Scale (HADS) (72). COPD related measures were obtained from the medical record include: socio-demographic, clinical and treatment data, such as spirometry and severity of COPD.

The primary outcome measure in this study is the Chronic Respiratory Questionnaire (CRQ). The CRQ consists of a 20-item questionnaire with four major domains which patients self-administer. This measures the health-related Quality of Life in respiratory patients. CRQ has been widely used in the respiratory and COPD contexts (15). The Minimal Clinically Important Difference (MCID) is reflected by a change in score of 0.5 on a 7 point scale (117).

Secondary outcome measures include:

ISWT - This is a field based test that progressively increases walking speed and measures the functional capacity of COPD patients (73). ISWT is a true symptom-limited maximal exercise capacity test, and distance walked relates strongly to peak aerobic capacity (15). Normal health subjects are able to complete 810m (119). The MCID for COPD is 47.5m (147). Patients were asked to complete ISWT twice at each timepoint with the best result recorded.
HADS - The HADS is a fourteen-item scale that measures levels of anxiety and depression. Each item is rated on a scale of 0-3. Each domain is totaled, scores 8-10 indicate possible case and greater than 10 indicate probable case(122). HADS is the current recommended screen tool in COPD patients(13). The MCID is 1.5 (169).

6.2.5 STATISTICAL ANALYSES

The data was keyed into Microsoft Excel (Microsoft, WA USA) and exported into Stata12 (StataCorp, TX USA) for data analysis and reporting. Descriptive analysis of study cohort was undertaken and results reported as n(%) for categorical data (e.g. gender, living arrangements, etc.) and mean for continuous data (FEV1, FVC, BMI, etc.).

The change in outcomes of interest between pre and post PR was calculated based on the score at end of PR minus the score at baseline. The long-term change was calculated based on the score at the long-term assessment visit minus the score at baseline. The differences were assessed for normality using Shapiro-Wilks test. An one-sample t-test was used in scores with normal distribution to determine the significance of the change and its magnitude. Multivariate regression analysis was then undertaken to determine the predictors of the change. Level of significance for the study was set at p<0.05. Accounting for multiple comparison and subscale analysis, the change for CRQ subscales was defined as significant if p was <0.01.

6.3 RESULTS

A total of 217 patients commenced PR between 2003 and 2012. 129 patients actually completed rehabilitation and were eligible. 88 patients were included in the analysis. 21 patients were deceased and 20 patients declined participation or could not be contacted.
Table 6.1 shows the basic demographics of the cohort. There was a similar ratio of males to females with a mean age of 71 years. A mean FEV1 of 46% correlates with severe COPD according to the GOLD criteria(32). 94% were either a past or present smoker. 26% of patients were on Long Term Oxygen Therapy (LTOT).

The prevalence of medical comorbidities ranged from 13% to 29%. 8% had previously diagnosed anxiety and 19% had previously diagnosed depression.

Table 6.1: Baseline demographics

<table>
<thead>
<tr>
<th></th>
<th>(n=88)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>41 (47%)</td>
</tr>
<tr>
<td>Female</td>
<td>47 (53%)</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td>70.7 (SD 7)</td>
</tr>
<tr>
<td><strong>Body Mass Index (BMI – kg/m$^2$)</strong></td>
<td>26.9 (SD 6)</td>
</tr>
<tr>
<td><strong>Lung Function</strong></td>
<td></td>
</tr>
<tr>
<td>FEV1</td>
<td>46% (SD 16)</td>
</tr>
<tr>
<td>Modified Medical Research Council Scale (MMRC)</td>
<td>1.98</td>
</tr>
<tr>
<td>Current/Past smoker</td>
<td>83 (94%)</td>
</tr>
<tr>
<td>Smoking (pack years)</td>
<td>55 (SD31)</td>
</tr>
<tr>
<td>Long Term Oxygen Therapy (LTOT)</td>
<td>23 (26%)</td>
</tr>
<tr>
<td>Ischaemic Heart Disease (IHD)</td>
<td>26 (29%)</td>
</tr>
<tr>
<td>Congestive Cardiac Failure (CCF)</td>
<td>12 (13%)</td>
</tr>
<tr>
<td>Diabetes Mellitus (DM)</td>
<td>14 (16%)</td>
</tr>
<tr>
<td>Previously Diagnosed Anxiety</td>
<td>7 (8%)</td>
</tr>
<tr>
<td>Previously Diagnosed Depression</td>
<td>17 (19%)</td>
</tr>
</tbody>
</table>

Table 6.2 reflects the scores of patients at baseline, end of rehabilitation and their reassessment (long term reassessment). The mean time between the end of PR and the long-term reassessment was 22 months (standard deviation 16 months, range 12-84 months) (See Figure 5.1). At the time of reassessment, some of these patients were already discharged from case management.
Baseline scores revealed 39% of patients had probable anxiety and 28% had probable depression on the HADS.

**Figure 6.1: Data collection timepoints**
Table 6.2: Results at pre-PR, post-PR and at long term assessment

<table>
<thead>
<tr>
<th>OUTCOME MEASURE (SD)</th>
<th>PRE PR</th>
<th>POST PR</th>
<th>LONG TERM POST ASSESSMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incremental Shuttle Walk Test (ISWT)</td>
<td>234.5 (99.4)</td>
<td>263.6 (104.8)</td>
<td>215.2 (116.6)</td>
</tr>
<tr>
<td>CRQ Scores</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total (range 20 – 140)</td>
<td>85.6 (18.9)</td>
<td>98.4 (17.1)</td>
<td>92.6 (21.6)</td>
</tr>
<tr>
<td>Dyspnoea (range 5–35)</td>
<td>16.3 (4.5)</td>
<td>20.1 (5.9)</td>
<td>19.7 (6.9)</td>
</tr>
<tr>
<td>Fatigue (range 4–28)</td>
<td>15.2 (5.5)</td>
<td>18.2 (4.4)</td>
<td>16.7 (5.9)</td>
</tr>
<tr>
<td>Emotion (range 7–49)</td>
<td>33.6 (9.1)</td>
<td>37.3 (7.8)</td>
<td>34.2 (9.8)</td>
</tr>
<tr>
<td>Mastery (range 4–28)</td>
<td>20.4 (5.3)</td>
<td>22.9 (4.3)</td>
<td>21.3 (5.3)</td>
</tr>
<tr>
<td>HADS (n=54)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anxiety Score</td>
<td>6 (4-10)</td>
<td>6 (2-8)</td>
<td>7 (4-9)</td>
</tr>
<tr>
<td>Depression Score</td>
<td>4 (2-8)</td>
<td>3 (2-5)</td>
<td>4 (2-7)</td>
</tr>
<tr>
<td>Prob Anxiety</td>
<td>21 (39%)</td>
<td>14 (26%)</td>
<td>16 (40%)</td>
</tr>
<tr>
<td>Prob Depression</td>
<td>15 (28%)</td>
<td>9 (16%)</td>
<td>8 (20%)</td>
</tr>
</tbody>
</table>
Table 6.3: Immediate and long term assessment changes in functional exercise capacity and quality of life following pulmonary rehabilitation

<table>
<thead>
<tr>
<th>Outcome measure (SD)</th>
<th>Mean change from pre-PR to post-PR</th>
<th>Mean change from pre-PR to long term assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>ISWT (m)</td>
<td>29.0 (64.5)**</td>
<td>-18.5 (100.9)</td>
</tr>
<tr>
<td>CRQ Scores</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dyspnoea (range 5–35)</td>
<td>3.7 (4.6)**</td>
<td>3.3 (7.4)**</td>
</tr>
<tr>
<td>Fatigue (range 4–28)</td>
<td>3.0 (4.5)**</td>
<td>1.5 (5.5)*</td>
</tr>
<tr>
<td>Emotion (range 7–49)</td>
<td>3.6 (6.6)**</td>
<td>0.4 (7.9)</td>
</tr>
<tr>
<td>Mastery (range 4–28)</td>
<td>2.5 (3.8)**</td>
<td>0.8 (5.8)</td>
</tr>
</tbody>
</table>

CRQ Scores

<table>
<thead>
<tr>
<th>HADS</th>
<th>Mean change from pre-PR to post-PR</th>
<th>Mean change from pre-PR to long term assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anxiety</td>
<td>-1.6 (3.7)**</td>
<td>-0.9 (3.5)</td>
</tr>
<tr>
<td>Depression</td>
<td>-0.7 (2.8)</td>
<td>-0.3 (2.9)</td>
</tr>
</tbody>
</table>

*<0.05

**<0.01

*** <0.001

Table 6.3 shows the mean change of outcome measures immediately following rehabilitation and at the long-term reassessment. In the walk test, this showed a statistically significant (p<0.001) increase in the ISWT distance of 29.0 m following rehabilitation but this gain was lost at the long-term reassessment and in fact worsened. CRQ scores showed a statistically significant (p<0.001) improvement in all four domains but only dyspnoea and fatigue remained statistically significant (p<0.001 and p<0.01 respectively) at the long-term reassessment. The mean improvements in dyspnoea and fatigue scores were maintained at the long-term reassessment. The other domains of emotion and mastery maintained some of their gains following rehabilitation but not statically significant.

Both the anxiety and depression component of the HADS scores reduced following rehabilitation but only the anxiety component was statistically significant (p<0.01). Some of these improvements persisted at the long-term reassessment but was not statistically significant.
Multivariate regression analysis was performed to see whether any baseline variables could predict maintenance of gains in the long term. No predictors were seen. Mild to moderate correlation was observed between the change in ISWT and the change in total CRQ ($r=0.27$, $p=0.014$) and emotional CRQ ($r=0.26$, $p=0.018$). Other domains in the CRQ showed no correlation.

6.4 DISCUSSION

This study showed that patients showed improvements immediately following PR but these gains are not maintained in the longer term. At the long-term assessment, only the dyspnoea domain of the CRQ showed sustained gains that were both statistically significant and exceeding the MCID. An improvement in fatigue was statistically significant but did not reach MCID. The other domains of the CRQ, ISWT, and HADS returned to previous level of function. Previously, Griffiths et al demonstrated sustained improvements in CRQ exceeding MCID (115), whilst another showed all improvements following PR were lost at one year (184). Two other studies which monitored patients one year post pulmonary rehabilitation have shown patients returning to baseline in the walk test (115, 184). In HADS, Ige et al did confirm a significant difference three months' post rehabilitation (Anxiety -0.8, Depression -0.69) (185). The demographics such as age and severity of COPD and outcomes following rehabilitation were similar to other cohort studies conducted in Australia and New Zealand (181, 182, 186).

In relation to QOL, statistically significant and exceeding Minimal Clinically Important Difference (MCID) increases were seen in all four domains. These results were similar to a systematic review of PR. Meta-analysis confirmed improvements exceeding MCID in all four CRQ domains (7). In the longer term however, only improvements in one of the four CRQ domains were sustained post PR.
In this study, exercise capacity improved following PR. Other studies of PR showed improvement between 33-88m in the ISWT (112, 115, 184, 187). This study showed a 29m improvement following PR. This is statistically significant (\( p<0.001 \)) but did not reach the MCID of 47.5m (147). However, when patients were reassessed at the long-term assessment their ISWT scores actually worsened though not statistically significant. Whilst our centre’s PR program was developed around current lung foundation guidelines, some patient’s programs could not be uptitrated due to their medical comorbidities or deterioration of their respiratory status (16). This may have contributed to the lower improvement of exercise capacity. Higher intensity of exercise is likely to provide greater benefit, but the exact amount or type remains unknown (187).

Significant underreporting of psychological disorders was noted in this study. Screening of patients showed 39% of patients had probable anxiety and 28% had probable depression. In contrast, only 8% self-reported anxiety and 19% with depression. This highlights the importance of screening psychological disorders in patients with COPD and has been recognised in the COPD-X guidelines produced conjointly by the Thoracic Society of Australia and New Zealand and the Lung Foundation (177). Additional support from their key worker including referral to a psychologist as well as informing their general practitioner were provided where anxiety and depression had been identified. The scores obtained from this centre are similar to that obtained from another study of patients in the same metropolitan region (188). Depression has been shown to influence the adherence to pulmonary rehabilitation program (189) and may impact on effectiveness of PR. A recent systematic review on the effect of comorbidities confirms that patients with anxiety and/or depression are less likely to improve in dyspnoea scales (190).

Ideally, PR would target the significant psychological (anxiety and depression) burden in this group. Following PR, both anxiety and depression scores reduced but only the anxiety component was statistically significant. MCID was not reached. Two studies (Bentsen et al & Ige et al) using the HADS as an outcome measure in PR have shown differing results. Bentsen et al showed no significant difference in anxiety or depression following PR but the baseline
scores were within the normal range (191). In another study, Ige et al showed significant difference in both anxiety and depression (-0.7 & -0.5 respectively) immediately following rehabilitation (185).

The loss of physical gains (as seen in the ISWT) is likely due to patients not maintaining either the intensity or frequency of exercise following PR. The major focus of PR is increasingly focused on changing patients' behaviour or perception of their disease long term. This has been confirmed in this study as two of the four domains in CRQ did maintain their gains. Only the emotional domain of CRQ correlated with exercise capacity. The three other domains had no correlation. Other studies have shown that improvements in QOL were not necessarily related to increases in exercise capacity (187).

This study illustrates the performance of the pulmonary rehabilitation program in this health service and in particular rehabilitation conducted in a community health service rather than a hospital outpatient department. In this particular centre there was 59% (129/217) completion rate. This completion rate is within the 9.7-31.8% range identified previously in a systematic review (189). Patients who smoke or have depression has been identified as factors affecting PR completion rate (192). The rate of depression in this particular cohort was 28% and may have contributed to the high drop out rate (189). Recruitment bias may be possible given that all patients were recruited from this single service. Another limitation is that only those who completed PR were analysed. Those that were initially enrolled but did not commence or did not complete the program were not included. In addition, analysis of a patient’s activity levels following PR was not recorded. As all of these patients received case management, most patients would have been encouraged to participate in either a specialised respiratory maintenance program or other structured activity. Patients who repeated PR during the analysis period were excluded from this study which could potentially bias results. A longer follow-up period would have provided more information. Lastly, hospital readmissions or frequency of exacerbations were not recorded. Further progression of COPD may explain why patient’s function may deteriorate.
6.5 CONCLUSIONS

This study confirms that many of the functional gains achieved in PR are lost in the longer term. Further studies are required to determine which factors affect the longevity of gains following PR. Regular surveillance or monitoring of these patients post PR is important to identify those requiring further intervention.

The next chapter will describe the results of the Healthcare Utilisation Study. Further from the Long Term Study which looked at patient outcomes, this looked at longitudinal data to determine whether integrated disease management and PR reduced patients’ healthcare utilisation.
CHAPTER 7: HEALTHCARE UTILISATION STUDY

This chapter describes a retrospective cohort study using up to 12 year of data research to determine whether patients who enrol in Pulmonary Rehabilitation (PR) and/or Integrated Disease Management (IDM) reduces acute healthcare resources.

7.1 BACKGROUND

Approximately 300,000 people in Australia have Chronic Obstructive Pulmonary Disease (COPD) and it has been predicted that COPD will be the seventh leading cause in Disability Adjusted Life Years lost worldwide by 2030 (193). Despite recent medical advancements, COPD still causes significant morbidity. Patients with COPD may not recognise the increasing symptoms and impairments due to the slow pace of disease(11). Most patients with COPD only present when their Forced Expiratory Volume in 1 second (FEV₁) has reduced to about 1 litre (less than half the normal value) (63). Further deterioration of lung function occurs with time, with those continuing smoking having greater decline than those who stop smoking (63).

In addition to functional decline, substantial financial resources are required to support the long-term management of COPD (1, 3, 11). Acute healthcare utilisation consisting of inpatient and Emergency Department (ED) admissions, outpatient and outreach services are the major contributors to the cost of managing advanced COPD. Inpatient hospitalisation, especially for acute exacerbations of COPD represents the greatest proportion of acute care costs for COPD management (97). Patients with COPD have a high prevalence of cardiovascular and oncology diagnoses and the presence of comorbidities further increases healthcare utilisation (48, 194, 195).

In response to increasing demand for acute health care resources, funding bodies and governments both in Australia and overseas have explored a range of strategies to prevent ED presentations and inpatient admissions (194). Two key strategies are IDM and PR programs.
IDM programs typically include case management and coordination of healthcare services and interventions, patient education and self-management training and strategies to optimise primary care management of chronic conditions (31). IDM has been created to coordinate healthcare interventions and communication between multiple providers in conditions in which patient self-care plays a substantial role in effective long-term management (31). It can also streamline care as well as increasing cost-effectiveness. In a recent Cochrane review, IDM also improved respiratory-specific Heath Related Quality of Life (HRQOL) and exercise capacity. Most of the IDM models of care analysed included an exercise element which may account for the impact on patient exercise tolerance (108). Sub analyses were not performed to assess whether IDM programs with an exercise component performed better than IDM alone. In addition, 15 studies had health care utilisation as an outcome measure. This showed no difference with all hospital admissions but a reduction in respiratory-related admissions. ED admissions and mortality remained unchanged.

PR has been shown to be effective in the management of COPD. Many people with COPD have low levels of physical activity and demonstrate reduced exercise tolerance (3). PR provides physiological, symptom reducing, psychosocial, and health economic benefits in multiple outcome areas. A number of studies have shown that following PR alone, hospital admissions, acute care Length Of Stay (LOS) and specialist outpatient visits were reduced (41, 115, 196).

Major health services may operate one or both of these programs for their patients with COPD. Whilst PR and IDM have immediate physical and HRQOL benefits, whether these changes persist into the long term is unclear. There is strong evidence of positive physical and HRQOL outcomes following enrolment in both IDM and PR, however few studies have evaluated improvements in healthcare utilisation following participation in these programs. The most recent study evaluated healthcare utilisation but showed no difference in hospitalisation rates, however LOS was reduced (115). Some studies have shown reductions in LOS and admissions but they did not distinguish the
difference between the effects of IDM and PR (197). In addition, no studies have looked at whether the addition of PR to IDM can provide greater impact on health care utilisation rates.

7.2 AIMS AND OBJECTIVES

The aims of this study were:

- To identify factors which contribute to increased utilisation of acute health care services.
- To assess whether those patients who commenced or completed an intensive eight-week PR had lower acute health care utilisation than those who did not receive these interventions; and
- To assess whether completion of an exercise PR program was associated with decreased rate of mortality compared to patients who did not complete PR.

7.3 METHODS

7.3.1 STUDY DESIGN

This was a retrospective cohort study of people who were referred to the health service IDM over a 10-year period between 2002 and 2012. This study was approved by the Ethics Committee at Melbourne Health (HREC QA2015130).

7.3.2 SETTING

This study was conducted in the Royal Melbourne Hospital (RMH), as a collaboration between the Respiratory Medicine and Rehabilitation Medicine Departments and a community health centre. These centres run a government–funded community-based IDM for patients with chronic respiratory disease.
Patients discharged from the acute health service following an exacerbation of COPD are assessed and referred to IDM. Patients were referred if they lived within the health service catchment area and the treating clinician assessed that they had COPD that was having an impact on their functional status. COPD was confirmed by spirometry. Following assessment, selected patients were enrolled in an eight-week PR in addition to receiving the IDM program.

The IDM team consisted of respiratory and rehabilitation physicians, respiratory trained nurses and allied health professionals who provided a variety of interventions in both home and centre based settings. The interventions provided as part of the IDM program included: patient specific goal setting and regular re-evaluation, general education on COPD, smoking cessation, generation of a personalised COPD action plan for management of acute exacerbations, regular phone or in person contact and referral to other health professionals if required (108). Patients were allocated a primary case worker who screened and identified issues to be managed during their time in IDM, thus each patient received a personalised program delivered on a 1:1 basis. Also, the frequency of visits and total time in IDM varied dependent on patient’s needs.

All patients receiving IDM were also assessed for PR. Patients who were thought to be able to participate and benefit from PR was placed onto the waitlist for the next cohort of PR (Figure 7.1). The eight-week PR program consisted of multidisciplinary management including medical, nursing and allied health using standardised therapy protocols. This involved twice weekly exercise rehabilitation sessions and education sessions. The 45-minute exercise session consists of 15 minutes treadmill/walking, 15 minutes cycling and 15 minutes’ circuit exercises. In contrast to IDM, group education was given and included topics issues such as how the lungs work and medication management.

Reasons for non-referral to PR included: patients with comorbidities that prevented them from completing walking exercises (severe osteoarthritis,
unstable cardiac disease), patients who were housebound, patients identified for palliative care and patients who refused referral to the program.

**Figure 7.1: Patient referral process**

### 7.3.3 DATA COLLECTION

This study used data linkage to evaluate whether there were differences in the impact of the program on acute health care utilisation between individuals who completed PR versus those who received only the IDM intervention. A database was established at the commencement of the IDM program to capture data on all patients at enrolment into the program. Additional outcomes were collected for patients enrolled in the PR program. Data was entered prospectively for each new patient to the service, this included basic demographic data, severity of COPD characterised according to Global Initiative for Chronic Obstructive Lung Disease (GOLD) COPD severity criteria, Forced Expiratory Volume in 1 second (FEV₁ %) predicted and Forced Expiratory Volume in 1 second /Forced Vital Capacity (FEV₁/FVC \(\text{L}^\text{L}\)) ratio, participation in the PR program and number of PR episodes (11).

Data on all ED and outpatient attendances and acute inpatient admissions between 2001 and 2014. Of interest, were ED attendances and acute care admission data between one year prior to patient referral to the IDM program and one year post referral. Outcome data obtained from the acute health service administrative data set included: number and type of inpatient admissions including LOS and need for high dependency or Intensive care unit
admission, number of ED attendances, number of specialist outpatient appointments and patient mortality. Patient files were reviewed if there were discrepancies between the IDM database and the administrative dataset and mortality data was obtained and cross referenced between both datasets.

Patient comorbidity burden were calculated from the acute health service administrative dataset based on secondary diagnostic codes and pre-existing health conditions to calculate a modified Elixhauser Comorbidity Score. The Elixhauser score is a comorbidity measure used to take into account whenever chronic disease burden is associated with a particular outcome (120). The summary score is a weighted combination of the 30 Elixhauser comorbidities, where a larger comorbidity weight indicates a stronger association between the comorbidity and in-hospital mortality (121). The comorbidities were obtained from ICD-10 diagnoses codes from acute care admissions in the one year prior to enrolment.

7.3.4 OUTCOME MEASURES

Acute health care utilisation was measured as: hospital admissions, ED presentations or admissions, LOS and outpatient appointments. Health utilisation data one year preceding their referral to the program was compared to data one year following enrolment to the program. Mortality was based on death data being recorded in the medical record.

All patients referred to the IDM-respiratory program were grouped according to whether or not they were referred for PR or had IDM alone. Patient survival and acute health care utilisation were compared between the two groups. Secondly a sub-group analysis was performed for the PR group according to whether they completed the PR (PR completers) and those that did not complete the PR (PR non-completers). A PR completer was defined as those who completed >80% of sessions and attended the end of PR assessment.
7.3.5 STATISTICAL ANALYSIS

The mean and standard deviations were reported for continuous demographic data which were approximately normally distributed for variables such as severity of COPD (FEV1), age and the Elixhauser index, with students t-tests applied for differences between groups. Variables which were skewed and non-normally distributed, such as the hospital utilisation data (admissions and LOS), were reported with the median and the interquartile range (IQR), with Mann-Whitney (rank-sum) tests applied. Categorical variables were assessed using the chi-squared test or the Fishers exact test on occasions when counts were fewer than 5 for any group. To assess changes in healthcare utilisation for each outcome and adjust for patient differences at baseline, multivariate Zero-Inflated Negative Binomial regression model (ZINB) analyses were performed. Time to death analysis was also undertaken with comparisons over three groups: 1) patients who received IDM only, 2) patients who PR non-completers and 3) patients who were PR completers. Hazard ratios were reported for survival data.

Statistical analyses were performed using Stata, version 12.1 (StataCorp, College Station, TX, USA). A two-sided alpha value of less than 0.05 was assumed to indicate statistical significance.

7.4 RESULTS

Between 2002 and 2012, there were 670 acute care discharges that were referred to IDM. This included 517 patients who had at least one inpatient admission for COPD. 365 (71%) patients were referred to IDM once, 125 (19%) patients were referred twice, 22 (3%) were referred three times and 5 (0.8%) patients were referred four times (See figure 7.2). Patients were divided into those who were not referred to PR (IDM only) and those that referred and commenced a PR program (rehab referred). Following referral to the service, 315 patients (61%) were assessed for PR and of those, 220 patients (70%) completed the rehabilitation program (Table 7.1). Patients in the rehab referred
group were younger when compared to the IDM only group (mean age 71.7 vs 75.3, p<0.001) and had less comorbidities (reduced Elixhauser score, 4.46 vs 7.43, p<0.001). There was no difference in FEV$_1$ % predicted between the two groups (p=0.0979).

The second section of Table 7.1 shows patients’ acute healthcare utilisation in the 12 months prior to referral to the service. This showed that the group referred to PR had significantly lower utilisation of acute health services in the 12 months prior to referral to the program compared to those who received the IDM intervention alone (all p=values <0.001). There was no difference between groups in the number of outpatient appointments in the 12 months prior to enrolment in the program (p=0.836).
Figure 7.2: Flow diagram of included patients

Patient episodes referred to IDM, n = 670

Individual patients referred to IDM, n = 517

 Patients with multiple episodes
   (Two = 125)
   (Three = 22)
   (Four = 5)

IDM patients assessed for pulm rehab, n = 315

Patients had IDM Only
   n= 202

Not completed pulm rehab
   (n= 95)

Completed pulm rehab
   n= 220
Table 7.1: Baseline characteristics

**Patient Characteristics**

<table>
<thead>
<tr>
<th></th>
<th>IDM only</th>
<th>Rehab referred</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Patients</td>
<td>202</td>
<td>315</td>
<td></td>
</tr>
<tr>
<td>Age (years), Mean ± SD</td>
<td>75.3 ± 9.34</td>
<td>71.7 ± 9.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Female</td>
<td>80 (39.6)</td>
<td>133 (42.2)</td>
<td>0.555</td>
</tr>
<tr>
<td>FEV1, Mean ± SD</td>
<td>45.9 ± 14.5</td>
<td>45.9 ± 15.8</td>
<td>0.979</td>
</tr>
<tr>
<td>GOLD Severity Category</td>
<td></td>
<td></td>
<td>0.195</td>
</tr>
<tr>
<td>2</td>
<td>76 (37.6)</td>
<td>118 (37.5)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>102 (50.5)</td>
<td>142 (45.1)</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>24 (11.9)</td>
<td>55 (17.4)</td>
<td></td>
</tr>
<tr>
<td>Elixhauser Score, Mean ± SD</td>
<td>7.43 ± 7.24</td>
<td>4.46 ± 5.42</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

**Acute Health Care Utilisation**

<table>
<thead>
<tr>
<th></th>
<th>IDM only</th>
<th>Rehab Referred</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Bed-days</td>
<td>6.5 (3 - 17)</td>
<td>3 (0 - 9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Emergency admissions only</td>
<td>6 (2 - 12)</td>
<td>3 (0 - 8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total Inpatient admissions</td>
<td>2 (1 - 3)</td>
<td>1 (0 - 2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Emergency admissions only</td>
<td>1 (1 - 2)</td>
<td>1 (0 - 1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total ED Encounters</td>
<td>1 (1 - 2)</td>
<td>1 (0 - 2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total Outpatient Appointments</td>
<td>1 (0 - 4)</td>
<td>1 (0 - 3)</td>
<td>0.836</td>
</tr>
</tbody>
</table>

FEV1 = Forced Expiratory Volume in 1 second
GOLD = Global Initiative for Chronic Obstructive Lung Disease
7.4.1 ACUTE HEALTHCARE UTILISATION OVER 12 MONTHS FOLLOWING REFERRAL

Table 7.2 shows the changes to healthcare utilisation in the 12 months prior to enrolment compared to the 12 months following enrolment into the program within each group. Both groups show statistically significant reductions in both ED and inpatient measures. There was a larger reduction in median total bed-days per annum and ED attendances in the IDM only group compared to the rehab referred group. Reductions in outpatient appointments were noted in both the exercise rehabilitation referred cohort (p<0.001) and in the IDM only group (p=0.015).

Table 7.2: Change in acute health care utilisation over 12 months

<table>
<thead>
<tr>
<th>Reductions in acute health care utilisation 12 months Pre to 12 months Post Median (IQR)</th>
<th>IDM only</th>
<th>p-value</th>
<th>Rehab Referred</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Bed-days</td>
<td>2 (-2 to 8)</td>
<td>&lt;0.001</td>
<td>0 (-1 to 6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Emergency admissions only</td>
<td>2 (-2 to 7)</td>
<td>0.004</td>
<td>0 (0 to 6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total Inpatient admissions</td>
<td>0 (0 to 1)</td>
<td>&lt;0.001</td>
<td>0 (0 to 1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Emergency admissions only</td>
<td>1 (0 to 1)</td>
<td>&lt;0.001</td>
<td>0 (0 to 1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total ED Encounters</td>
<td>1 (0 to 1)</td>
<td>&lt;0.001</td>
<td>0 (0 to 1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total Outpatient Appointments</td>
<td>0 (-2 to 1)</td>
<td>0.015</td>
<td>0 (-2 to 1)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

IQR = Interquartile Range

Multivariate analysis was conducted to assess whether the differences in acute health care utilisation between the IDM only and rehab referred group remained significant after adjusting for differences in patient baseline characteristics (Table 7.3). The Incidence Rate Ratio (IRR) in total bed-days of 0.71 (95% Confidence Interval (CI): 0.48 - 1.06) indicates that patients who were assessed for rehab had fewer bed-days in the 12 months post referral by a factor of 0.71 after adjusting for prior bed-days, age, COPD severity and Elixhauser scores, although this was not statistically significant (p=0.095). IRRs which were lower than 1.0, indicating a reduction in health service utilisation for the rehab referred
group, were also obtained for total inpatient episodes (IRR 0.85, 95% CI: 0.67-1.10) and emergency presentations (IRR 0.81, 95% CI:0.61-1.08), although as indicated by the confidence bounds, no statistically significant differences in changes in health care utilisation from pre to post referral were found between the groups.

Table 7.3: Multivariate analysis of changes in healthcare utilisation: Rehab referred vs IDM only*

<table>
<thead>
<tr>
<th></th>
<th>IRR</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total bed-days post</td>
<td>0.71</td>
<td>0.48 - 1.06</td>
<td>0.095</td>
</tr>
<tr>
<td>Total Inpatient Episodes</td>
<td>0.85</td>
<td>0.67 - 1.10</td>
<td>0.216</td>
</tr>
<tr>
<td>Total Emergency Presentations</td>
<td>0.81</td>
<td>0.61 - 1.08</td>
<td>0.152</td>
</tr>
</tbody>
</table>

IRR – Incident Rate Ratio, CI = Confidence Intervals
* = Adjusted for prior bed days, age, COPD severity and Elixhauser scores

7.4.2 MORTALITY

To assess differences in patient mortality, patients were further stratified into three groups: 1) patients who received IDM only, 2) IDM patients who were referred and commenced PR but did not complete the program (PR non-completers) and 3) IDM patients who were referred and completed the PR program (PR completers), (Table 7.4). As indicated in Figure 7.3, there was a survival benefit (Hazard Ratio (HR) 0.68, 95% Confidence Interval (CI): 0.50 to 0.92) for those who were PR completers, compared to patients who received IDM only. PR non-completers had an HR of 0.83 (95% CI: 0.57 to 1.19) suggestive of a benefit but this was not statistically significant (p=0.309). Risk factors independently associated with decreased survival were older age (HR 1.04, 95% CI: 1.03 to 1.06), FEV1 (HR 0.99, 95%CI: 0.98 to 0.99) and the number of comorbidities (Elixhauser Score) (HR 1.06 95% CI: 1.04 to 1.08).
Table 7.4: Survival analysis based on rehabilitation status

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariate</th>
<th></th>
<th></th>
<th></th>
<th>Multivariate</th>
<th></th>
<th></th>
<th></th>
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</thead>
<tbody>
<tr>
<td></td>
<td>HR</td>
<td>95% CI</td>
<td>p-value</td>
<td>HR</td>
<td>95% CI</td>
<td>p-value</td>
<td>HR</td>
<td>95% CI</td>
</tr>
<tr>
<td><strong>Rehab Status</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IDM Only</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PR Non-Completers</td>
<td>0.70</td>
<td>0.49 – 1.01</td>
<td>0.056</td>
<td>0.83</td>
<td>0.57 – 1.19</td>
<td>0.309</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PR Completers</td>
<td>0.48</td>
<td>0.36 – 0.65</td>
<td>&lt;0.001</td>
<td>0.68</td>
<td>0.50 – 0.92</td>
<td>0.014</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>1.05</td>
<td>1.03 – 1.07</td>
<td>&lt;0.001</td>
<td>1.04</td>
<td>1.03 – 1.06</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>0.80</td>
<td>0.61 – 1.05</td>
<td>0.103</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FEV₁</td>
<td>1.00</td>
<td>0.99 – 1.01</td>
<td>0.448</td>
<td>0.99</td>
<td>0.98 – 0.99</td>
<td>0.005</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GOLD 2</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GOLD 3</td>
<td>0.95</td>
<td>0.72 – 1.27</td>
<td>0.747</td>
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<td></td>
<td></td>
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<tr>
<td>GOLD 4</td>
<td>0.91</td>
<td>0.61 – 1.36</td>
<td>0.649</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elixhauser Score,</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>1.07</td>
<td>1.05 – 1.09</td>
<td>&lt;0.001</td>
<td>1.06</td>
<td>1.04 – 1.08</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
7.5 DISCUSSION

To the best of our knowledge, this is the first study not only looking at the effect of IDM on healthcare utilisation and survival but whether IDM in conjunction with PR provides an additive effect. Readmission rates following a COPD related admission are becoming a major focus as insurers drive to reduce costs (198). IDM and PR are examples of programs which aim to keep patients well and out of hospital. The isolation of the exercise component (i.e. PR) from the general IDM program in this study allowed a comparison between the two groups. IDM alone reduced healthcare utilisation and when compared with the rehab referred group had greater reductions in admissions and total bed day utilisation, however this was not statistically significant.
A systematic review has shown that IDM alone can reduce respiratory related admissions and total hospital stays (108). Compared with the systematic review, this study showed a reduction in all acute health care utilisation measures. Respiratory-related admissions were not recorded in this study. Elements in a typical IDM program such as educating on the use of action plans and regular contact and advice by a clinician may have contributed to these reductions. Some of the analyses in the systematic review only included as few as two studies, so further studies are required.

In relation to survival data, patients who commenced and completed PR had a survival benefit. Age, severity of COPD (FEV₁) and comorbidity loading were other factors affecting survival. Previous research has shown that physical activity was linked with mortality (67). It is possible that those who complete PR are more likely to have higher levels of physical activity, but further research is needed to establish this link. It was interesting to note that whilst completing PR conferred a survival benefit, yet healthcare utilisation was not further reduced. PR alone has been shown to reduce admission rates. It is difficult to determine the reasons for this in the study. It could be postulated that differences in healthcare utilisation may not appear within one year post IDM and that a longer period of follow-up is required. This would also determine further the relationship between lower healthcare utilisation and life expectancy. Alternatively, healthcare utilisation within the rehab referred group was already at a lower level when compared with the IDM only group, so further decreases in healthcare utilisation may be difficult. It may be also possible that factors which are common to both IDM and PR programs, such as education are significant contributors to reducing healthcare utilisation, so patients who undertake both programs do not receive an additive benefit. Other studies that included mortality as an outcome measure have shown mixed results (96, 106). IDM alone also yielded similar results (199-202).

Patients who were assessed or commenced for PR were younger, had less comorbidities, beddays, inpatient and ED admissions. Whilst there were no criteria set for which patients should be referred to PR, it appears clinicians
used prior admission and presentation data as well as the number of comorbidities as consideration factors. The current PR guidelines do not however recommend patients should be excluded due to their comorbidities (16). The presence of comorbidities does not affect PR performance (203). Severity of their disease however was not a factor and research has shown patients with severe COPD have similar positive responses from PR than those with less severe disease (99).

7.5.1 STRENGTHS AND LIMITATIONS

The greatest strength of this study was analysing all patients enrolled in a working pulmonary service over a 10-year period, rather than a carefully selected and controlled group of patients typically seen in pilot studies. This real-world data may allow for greater generalisation of the results to other respiratory centres.

As this was a retrospective study reflective of a community pulmonary program, patients who were enrolled to either IDM or PR were not randomised. Apart from patients living within the hospital catchment area and were consenting to participate, clinicians enrolled patients who they felt would benefit with either an IDM or PR program. In addition, patients who were enrolled to IDM were not obligated to participate in PR, so PR may not have been offered to all patients. Multivariate analyses were performed in order to adjust for confounders and therefore improve accuracy of results. The study design was reliant on hospital data, and an assumption was made that patients would attend the same hospital for any acute illness. It is possible that some patients may have chosen to attend other acute hospitals or have moved away during the time of data collection. Accurate mortality data was dependent on the patient’s final admission at the same hospital. COPD is a complex disease with multiple triggers and comorbidities so it would be difficult to attribute all admissions to their respiratory disease (204). The exact cause of hospitalisations, in particular whether they were respiratory related, is unknown. Similarly, further analyses of the exact type and severity of comorbidities would provide additional information. Comorbidities such as cardiovascular disease can affect the ability to participate in a PR program (189).
Patients with COPD who successfully complete PR in addition to participating in an IDM program have improved survival. IDM alone was effective in the reduction of healthcare utilisation, however the addition of PR did not reduce healthcare usage further. This study provides the information for further studies, so research in individual components of IDM and PR (and in combination) which contribute to clinical efficacy can be explored.

This study as well as the Long Term study (Study 3, Chapter 6) has described patients physical, QOL and healthcare usage following participation in rehabilitation programs. The next and final chapter summarises the findings of studies 1-4 and discusses the implication of these findings and future directions.
CHAPTER 8 DISCUSSION

This chapter aims to discuss the findings of Studies 1 to 4 (Chapters 4-7) including the limitations of the studies and future implications for clinical practice and research. The aims originally set in Chapter 1 will be revisited and reviewed.

8.1 OVERVIEW OF THESIS

Four clinical studies were conducted and each incorporated specialised methodical designs to address the specific aims and objectives in each study. The original objective was to evaluate the effectiveness of Pulmonary Rehabilitation (PR) for persons with Chronic Obstructive Pulmonary Disease (COPD), including the optimal components and intensity of therapy.

8.2 KEY ISSUES ADDRESSED AND SUMMARY OF FINDINGS

The following aims were initially devised and discussed in chapter 1, hypothesis and objectives:

1. To describe the current evidence base for the non-pharmacological, non-surgical management of persons with COPD.
2. To determine whether the addition of Cognitive Behavioural Therapy (CBT) to a PR program is associated with improved physical and Quality of Life (QOL) outcomes.
3. To describe the long-term outcomes in persons with COPD attending PR in a community setting.
4. To identify factors which contribute to increased utilisation of acute healthcare services.

5. To compare the effectiveness between PR and Integrated Disease Management (IDM) in reducing acute healthcare utilisation and mortality.

Each aim will be addressed individually in the following sections.

8.2.1 EVIDENCE BASE FOR THE NON-PHARMACOLOGICAL, NON-SURGICAL MANAGEMENT OF PERSONS WITH COPD

Key Issue 1

PR has been shown to be effective in the management of COPD. Most studies have been centred on the effects of physical therapy in COPD, but evidence for other modalities are lacking (133). There is minimal evidence to show which components offer the most benefit or the ideal duration or intensity (133). Systematic reviews of individual interventions used in COPD have been widely published, however none have incorporated common interventions in one single review. This review aims to present, investigate and compare the different types of interventions available in the PR setting.

Summary of findings

In Study 1 (Chapter 4), an overview of systematic reviews was conducted for non-pharmacological, non-surgical interventions in COPD. Several interventions were analysed. This showed physical exercise as an intervention has the most number of studies and the strongest evidence base. Other interventions such as inspiratory muscle training, self-management and integrated disease management have systematic reviews confirming their effectiveness, but are not yet commonly utilised in practice. Techniques such as breathing exercises and psychological interventions have yet to show consistent improvements between trials.
Comparison with other reviews

This was the first type of review of its type which described commonly used interventions for COPD in a single review. Other systematic reviews published for COPD have only included single intervention techniques. Further large trials are required for some interventions. Following the publication of systematic reviews, there is now an increasing emphasis on the use of overviews of systematic reviews to provide ready comparison of interventions available for a given condition. To date there is no such type of review for the management of COPD or the use of PR. In contrast, there is already a review of systematic reviews for cardiac rehabilitation (205).

8.2.2 ASCERTAIN WHETHER THE ADDITION OF COGNITIVE BEHAVIOURAL THERAPY TO A PULMONARY REHABILITATION PROGRAM IS ASSOCIATED WITH IMPROVED PHYSICAL AND QUALITY OF LIFE OUTCOMES.

Key Issue 2

Comorbid psychological disorders are a significant burden for patients with COPD, in whom there is an increased prevalence of depression (36%) and anxiety (40%) (55). Patients with psychological co-morbidities are more likely to have reduced engagement and participation, and subsequently reduced QOL (3). Despite this, the treatment and rehabilitation of these patients commonly focuses only on the physical characteristics of the disease.

The objectives of the Cognitive Behavioural Therapy (CBT) Study (Study 2, Chapter 5) were to: conduct a Clinical Controlled Trial (CCT) comparing the current PR regime with a program adding CBT to the existing schedule and that a directed psychological intervention consisting of CBT improves patient participation and clinical outcomes in PR.
The study recruited patients about to undertake PR and allocated them to either the control group consisting of PR alone or to the treatment group receiving PR and an additional six sessions of group based CBT. Assessments consisting of questionnaires and walk tests were conducted pre and post PR.

Summary of findings
The CBT group had significant improvements in exercise capacity following PR which was maintained at 3 months post PR. Patients in the CBT group showed significant short term improvements in fatigue, stress and depression and a 3-month post PR improvement in the anxiety score. No significant changes were seen in the control group.

Comparison of other reviews
This is one of the few studies looking at strategies beyond physical measures for COPD and shows that the addition of CBT to PR provides additional benefits. A systematic review of various psychological interventions showed some improvements in psychological outcomes when these were analysed together. However, when CBT was analysed as an intervention alone, there were significant improvements in psychological but not for physical outcomes (8). Ultimately, the optimal type or intensity of psychological interventions remains unknown (8).

8.2.3 DESCRIBING THE LONG-TERM OUTCOMES IN PERSONS WITH COPD ATTENDING PULMONARY REHABILITATION IN A COMMUNITY SETTING

Key Issue 3
Key Issue 1 has identified that physical exercise, which is the biggest component of PR, is successful in improving physical and QOL outcomes. Following successful completion of PR, some patients deteriorate further and
require repeat stints of PR. Studies which have monitored patients beyond 12 months following PR have shown differing results.

The aim of the Long Term Study (Study 3, Chapter 6) was to look at long term (beyond 12 months) outcomes in patients with COPD attending PR in a community setting.

Summary of findings

Firstly, in this study, improvements in both exercise capacity and QOL were seen following participation in PR and was similar to studies reviewed in key issue 1. However, when these patients were followed up in the long term (mean duration 22 months), many of these functional gains were lost. This included improvements in exercise capacity and QOL. In addition, anxiety and mood symptoms improved following PR but these gains were not maintained at the long-term follow-up. Further studies are required to determine which factors affect the longevity of gains following pulmonary rehabilitation.

Comparison of other reviews

This is a unique study in looking at long term outcomes following PR in a community rather than in a hospital based setting. Also unlike other studies, this had a relatively large sample size (88 patients).

This study highlights that regular surveillance or monitoring post PR is important to identify those requiring further intervention. To maintain these gains some patients may require another “burst” of PR. Repeating PR produces clinically significant improvements in exercise tolerance and QOL though it is still unclear which patients are most likely to decline and need repeat PR (116).
8.2.4 IDENTIFYING FACTORS WHICH CONTRIBUTE TO INCREASED UTILISATION OF ACUTE HEALTH CARE SERVICES

Key Issue 4

Substantial financial resources are required to support the long term management of COPD (1, 3, 32). Acute healthcare utilisation consisting of inpatient and Emergency Department (ED) admissions, outpatient and outreach services are the major contributors to the cost of managing advanced COPD. Inpatient hospitalisation, especially for acute exacerbations of COPD represents the greatest proportion of acute care costs for COPD management (6). Two key strategies to reduce healthcare utilisation are Integrated Disease Management (IDM) programs and PR programs.

The aim of the Healthcare Utilisation Study (Study 4, Chapter 7) was to identify factors which contribute to increased utilisation of acute health care services and to assess whether those patients who commenced or completed PR had lower acute health care utilisation than those who did not receive these interventions.

Summary of findings

This retrospective cohort study analysed data of patients who participated in an IDM program over a 10-year period. Patients who were referred to PR were younger and had less comorbidities. Both groups (IDM only and IDM+PR referred) had reductions in healthcare utilisation. This included outpatient presentations and emergency and inpatient admissions. The incidence rate ratios were independently adjusted for bed days, age, COPD severity and the number of medical comorbidities.

Comparison of other reviews

The greatest strength of this study was analysing all patients enrolled in a working pulmonary service over a 10-year period, rather than a carefully
selected and controlled group of patients typically seen in pilot studies. This real-world data may allow for greater generalisation of the results to other respiratory centres, both locally and worldwide.

8.2.5 COMPARING THE EFFECTIVENESS BETWEEN PULMONARY REHABILITATION AND INTEGRATED DISEASE MANAGEMENT IN REDUCING ACUTE HEALTHCARE UTILISATION AND MORTALITY

Key Issue 5

Similar to Key Issue 4, healthcare utilisation remains a significant topic of interest for not only clinicians but also hospital administrators and policy makers who are keen on reducing the ever escalating costs of managing patients with COPD (198). Two common strategies are PR and IDM.

The Healthcare Utilisation Study not only analysed reductions in healthcare utilisation in a COPD population, its study design allowed a comparison between those that received only IDM and those who received both IDM and PR interventions. The second group were assessed and enrolled into PR during their IDM intervention. The outcomes of interest were similar to Key Issue 3, namely emergency and inpatient admissions.

Summary of findings

IDM alone was effective in the reduction of healthcare utilisation, however the addition of PR did not reduce healthcare usage further. A survival benefit was seen in those who were PR completers compared to patients who received IDM only. In those participants who commenced a PR program but who did not finish, no survival benefit was seen.
Comparison of other reviews

To the best of our knowledge, this is the first study not only looking at the effect of IDM on healthcare utilisation and survival but whether IDM in conjunction with PR provides an additive effect. The isolation of the exercise component (i.e. PR) from the IDM program in this study allowed a comparison between the two groups. Compared with a systematic review, this study also showed a reduction in all health care utilisation measures (108). Some of the analyses in the systematic review only included as few as two studies.

8.3 LIMITATIONS WITH METHODOLOGY

These sections aims to discuss in broad terms the limitations associated with the various projects in this thesis. Please refer to the individual chapters for a more detailed discussion.

8.3.1 STUDY DESIGN

In the studies conducted for this thesis, the sample sizes were relatively small, especially when compared to studies from acute medicine settings. However, this issue is not isolated in rehabilitation research and has been discussed earlier in Chapter 3 (Methodology). Larger sample sizes will likely require multi centre recruitment which may cause heterogeneity with the patient population or the delivery and structure of the PR program. Alternatively, a longer recruitment period could be utilised, though the need for additional resources such as in the CBT Study (Study 2, Chapter 5) may make it difficult to run for longer periods.

None of the study designs for projects in this thesis were randomised. Whilst it is acknowledged in biomedical research that randomised controlled trials have
the highest level of evidence, this is not always feasible in the rehabilitation setting. This was described in further detail in Chapter 3. Similarly, a placebo controlled trial was not undertaken to determine the effectiveness of PR. The results of the systematic review (Study 1, Chapter 4), showed that the evidence of PR is so strong and overwhelming that it would not be ethical to run a placebo controlled trial and delay starting PR. In addition, many patients who would be enrolled into PR in a period where their COPD management has been optimised and is stable. Patients could develop exacerbations or other medical conditions that may preclude them from starting PR at a later point (192).

Lastly, neither the participants or the clinicians were blinded to the additional intervention that was offered in the CBT Study. As this study was designed to compare the usual PR program with another group who undertook the normal PR as well as CBT, it would be difficult to blind study participants as the extra intervention requires them to attend further classes. Sham therapy could be offered to the usual treatment group, however it would also be difficult to completely exclude potential effects (either positive or negative) (125). Also, both groups would co-mingle during the other elements of PR and so could potentially unblind such a study design.

8.3.2 GENERALISABILITY

The limitations common to all the clinical studies (studies 2-4) were that they were all based in the one geographical catchment area, namely the inner North West of metropolitan Melbourne and of one tertiary health service (Royal Melbourne Hospital). The data may be generalisable to other similar catchment areas and tertiary health services in Australia, but further studies are required to ensure the validity of these results in other clinical services.

In addition, throughout the world, the concept of PR is not standardised (15). The delivery format of PR can be given in many formats, from inpatient acute and subacute to hospital outpatient and community settings (9). Additionally, the
intensity and frequency varies dramatically between programs. Any clinician wanting to improve their current PR programs will need to be aware of this and take note of any potential differences and were beyond the scope of these studies.

8.3.3 LIMITATIONS IN OUTCOME MEASUREMENT

Lastly, an economic or financial analysis was not performed in any of these studies. It was evident in the Healthcare Utilisation Study that IDM could reduce acute healthcare utilisation such as admission and attendance rates but no economic analysis was done to confirm that this resulted in reduced cost of managing COPD. The costs of managing COPD are not just direct hospital costs but also indirect costs such as nursing care, carers, home oxygen hire, transport and equipment that may be difficult to define and calculate.

Given that COPD is a chronic and progressive disease, it would have been ideal to track patients beyond the 10 years follow-up that occurred in the Healthcare Utilisation Study and to perform additional analyses on physical, QOL, financial and other health related outcomes. The Healthcare Utilisation Study did incorporate 12 years and 517 patients of “real world” data. Significantly more resources would have been required to further expand the study and capture patients who rarely presented to hospital. Many longitudinal studies including this one only tracked negative aspects of their health (hospitalisations, presentations to ED and outpatient clinics). Positive aspects (such as patients’ ability to mobilise, perform usual day to day tasks and even work or study) have not been assessed or included.
8.4 RECOMMENDATIONS FOR OPTIMAL PULMONARY REHABILITATION CARE

The findings of this thesis support the recommendations of the current COPD X plan (206). The COPD-X plan was developed jointly by the Australian Lung Foundation and the Thoracic Society of Australia and New Zealand to guide health care professionals in the management of patients with COPD.

The following points of the guidelines were confirmed (206):

*Pulmonary rehabilitation reduces dyspnoea, fatigue, anxiety and depression, improves exercise capacity, emotional function and health-related quality of life and enhances patients’ sense of control over their condition*

The systematic review (Study 1, Chapter 4) confirmed that exercise training, which is one major component of PR, does improve QOL and exercise capacity. Other components of PR such as inspiratory muscle training and self-management do not have the same strength of evidence. These results following participation in PR were also replicated in the Long Term Study (Study 3, Chapter 6).

*Pulmonary rehabilitation reduces hospitalisation and has been shown to be cost-effective*

The Healthcare Utilisation Study has shown either IDM alone or IDM combined with commencement of PR reduces admissions and outpatient attendances. Economic analyses were not performed and this was described in the previous section (Chapter 8, Section 3).
Anxious and depressive symptoms and disorders are common comorbidities in people with COPD

Both the CBT and Long Term Studies assessed patients for the presence of anxiety and depression. Self-reporting indicated anxiety was present in 7-14% and depression in 29-36% of individuals. However, when the same patients were screened prior to PR involvement this increased to 39% for anxiety and 28% for depression. This highlights the importance of not only reviewing patients’ medical history but also the need for screening with simple tools such as the Hospital Anxiety and Depression Scale (HADS).

8.4.1 COMMUNITY SUPPORT GROUPS

Consumer organisations are vital for any chronic disease as the needs of persons with COPD does not only rest with clinicians or health services. The community and voluntary sectors have much to offer and allow the services to be offered in the community rather than in hospital settings. Consumer organisations play a number of roles including:

- Provision of information to clinicians, patients and their families through brochures, booklets, websites and telephone hotlines
- Hosting and providing ongoing support of local support groups in the community
- Raising the profile and awareness of COPD in the Australian community including the identification and diagnosis of COPD
- Promoting and encouraging persons with COPD to participate in PR
- Acting on behalf of persons with COPD to engage and lobby various levels of government for increased levels of funding and policy change

The local consumer groups in Australia are Lung Foundation Australia and Lung Health Alliance. When compared with other chronic disease consumer groups such as MS (Multiple Sclerosis) (previously MS Society) or the Motor Neurone
Disease Foundation of Australia, there remains significant areas that would benefit from further improvement. These include:

- Carer education and support programs
- Remote or tele rehabilitation programs for those who cannot access conventional centre based PR programs
- Employment support
- Provision of services and equipment to persons with COPD

8.5 IMPLICATIONS FOR CLINICAL PRACTICE

The projects completed in this thesis have provided a framework for guiding future clinical practice in the management of persons with COPD. Firstly, the results confirm that the current PR program as recommended by the Australian Lung Foundation is effective in a few aspects, including QOL and functional exercise capacity (16). The evidence is strong enough currently to even suggest that no further trials are required in this area. In addition, reductions in healthcare utilisation and improved survival were seen following PR completion.

Secondly, the effects of successful completion of PR are short lived, so it is essential that these patients are not discharged from support services following completion. Even though self-management sometimes feature in PR and IDM programs, the level of evidence is not strong and therefore should not be used as a substitute for traditional clinician monitoring. Either regular centre or home based visits should be offered to all PR completers to ensure participants maintain their level of activity and function in the community. Participation in maintenance programs or even repeating PR should be considered if there is decline in function or recent exacerbation. In addition, patients who were unable to complete a PR program after starting should be encouraged to repeat PR when able.
Thirdly, most centres already incorporate physical exercise and education components based on available evidence. It is now time to consider adding other interventions to complement the effects of physical exercise. Strategies vary broadly and it may be impractical to offer some or all of these interventions due to financial, clinician expertise or time constraints. Certainly, some interventions such as inspiratory muscle training, self-management and integrated disease management have stronger evidence than other interventions.

Fourthly, there remains a significant psychological burden in the COPD cohort. Patients with COPD have higher prevalence rates of anxiety and depression than the general population. A significant proportion of these patients are undiagnosed. This highlights the importance of screening patients for the presence of anxiety and depression. It is important to note that screening tools such as HADS are not diagnostic so clinicians will need to do further workup for a definitive diagnosis. Patients who are diagnosed with anxiety or depression should receive appropriate follow-up and treatment. Depending on the unit structure, this could include in-house psychology referral or referral back to the patient’s general practitioner or respiratory physician.

The presence of anxiety or depression needs to be taken into account when enrolling patients to a PR program. There is potentially a relationship between the presence of psychological disorders and poorer PR response. Interventions such as CBT given in conjunction with physical exercise not only improve anxiety, depressive or stress symptoms but also improve QOL and functional exercise capacity.

In summary, the evidence behind mainstream components of PR is undisputable (9). However, despite this not all patients who would benefit from PR are being referred. Further work must be done to address this gap and ensure PR is accessible to all patients in a timely manner.
8.6 IMPLICATIONS FOR FUTURE RESEARCH

Further targeted research would provide immense benefit for people with COPD. The projects that were conducted in this thesis have provided some answers to questions posed in the management of COPD but has also led to other, newer questions that are beyond the scope of this thesis.

Firstly, the COPD group would benefit with further, more detailed longitudinal analysis following either successful or unsuccessful completion of PR. Risk factors or certain demographics will need to be mapped out to identify which patients are at greater risk of rapid deterioration or need earlier intervention. The level of activity or presence of psychological disorders may affect long term outcomes. PR studies cannot occur in a “silo” but will need to further integrate with acute respiratory research.

COPD is one of the first chronic diseases to describe and delineate phenotype characteristics into the “pink puffer” and “blue bloater”. Currently the guidelines for the management of COPD does not differ between the two types and the latest GOLD guidelines have been changing to better describe patients in terms of their symptomatology and activity or mobility level. So, the future may be that pharmacological treatments will be individualised and likewise rehabilitation will need to be individualised. Patient profiling and an individualised prescription of PR will be given at the start of the PR program and components offered may vary according to patient needs (99).

This project, especially in the systematic review, has confirmed that methods such as the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) and the Assessment of Multiple Systematic Reviews (AMSTAR) can be used in the analysis of studies and other systematic reviews. Other methodological models such as the RE-AIM framework can be used to
analyse interventions such as PR in such a format that various programs can be compared easily at a glance (129).

Similarly, further research and development needs to be made on the exact “formula” of PR. In order to achieve greater benefits of PR, it may be no longer appropriate to just offer the standard PR program. The interventions available are vast and clinicians will soon need to decide which combinations would be the best going forward. Several, common combinations will need to be compared and a strong, prospective trial with a large sample size may be required. Interventions should not be limited to traditional rehabilitation strategies but also involve components such as psychological interventions, case management and self-management. These strategies will play an important role given COPD is a chronic disease and patients will need to be empowered to manage not only their disease but its manifestations in the community away from the hospital setting.
CHAPTER 9 CONCLUSION

This thesis confirms the main hypothesis that mainstream PR programs are effective in improving the QOL and wellbeing of persons with COPD.

This thesis for the first time presents all common rehabilitation interventions not just physical exercise in stable COPD. This was presented as a comprehensive systematic review of the current literature. The Long Term and Healthcare Utilisation studies accurately mapped patients exercise, QOL and acute healthcare utilisation following PR and IDM. The Cognitive Behavioural Therapy Study demonstrated that an intervention which complements the pre-existing PR program can further improve outcomes.

COPD is a complex, chronic condition and this thesis highlights the systemic nature of the disease. A multifaceted approach is required for the management of COPD and not just limited to only acute or pharmacological management. Rehabilitation strategies act to complement but not replace optimal pharmacological and surgical therapy. The ICF model on which the thesis is based upon allows the accurate documentation and mapping of the disability associated with the disease.

This body of work has led to changes in practice at the local health service (Royal Melbourne Hospital) and more focus on PR. The interventions found effective in PR and COPD provides a basis for future research projects currently being planned. It is a golden opportunity at this time for research to guide future physicians on the best “formula” of PR. An individualised prescription and approach is required to produce maximal functional and QOL outcomes for this cohort of patients.
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193. COPD — chronic obstructive pulmonary disease Canberra2015 [ ]


APPENDIX

Appendix A Worksheet for Long Term Study (Study 2, Chapter 5)

Pulmonary Rehabilitation Long Term Follow-up

PATIENT NAME: ___________________________  BRADMA

PATIENT UR: ___________________________

DATE OF VISIT  ___________  _________  _________
    DAY      MONTH      YEAR

DATE OF BIRTH  ___________  _________  _________  _________  _________  _________
    AGE
    DAY      MONTH      YEAR

GENDER:  Male  ☐  Female  ☐

Part A – Patient Demographics

MARITAL STATUS  ☐ Married/partner  ☐ divorced/separated  ☐ single  ☐ widowed

LIVING ARRANGEMENTS  ☐ Alone  ☐ With others  ☐ HLC  ☐ LLC  ☐ Other supported accom

Education level:  Primary  Secondary  Tertiary

Weight (kg):   Height (m):

Respiratory Clinic/Specialist: _____________________________

COPD HISTORY
**Spirometry**

Yes  
No

Date of last test:
FEV1: (<80%)
FVC:
FEV1/FVC: (<0.70)
DLCO

**Smoking**

Yes  
No

Still smoking?  
Yes  
No
Total Pack Years (cigarettes/day x years):
Year quit?

**Home O2 use**

Yes  
No

O2 type  
Concentrator  
Cylinder

O2 rate

**MEDICAL COMORBIDITIES**

IHD  
Yes  
No
CCF  
Yes  
No
Other lung pathology  
Yes  
No
Diabetes  
Yes  
No
Depression  
Yes  
No
Anxiety  
Yes  
No
Anti-depressant use  
Yes  
No
Anti-anxiolytic use  
Yes  
No

**MEDICATIONS**

RESP

**OTHER**
COPD SEVERITY
Modified Medical research council rating of dyspnoea (circle best description) – (for BODE index)

0 not troubled with breathlessness except with extreme exercise

1 troubled by shortness of breath when hurrying on the level or walking up a slight hill

2 walks slower than people of the same age on the level because of breathlessness or has to stop for breath when walking at own pace on the level

3 stops for breath after walking about 100 yards after a few minutes on the level

4 too breathless to leave the house or breathless when dressing or undressing
PLANNED OUTCOME EVALUATION

First session PRP Date  I__I__I  I__I__I  I__I__I__I__I
                      DAY       MONTH      YEAR

Last session PRP Date  I__I__I  I__I__I  I__I__I__I__I
                     DAY       MONTH      YEAR

PRP Sessions attended _______________ (of total 16 sessions/group)
Total PRP Groups attended______________
Subsequent PRP/TEP Sessions attended:

ACTIVITY LIMITATION

b) Six minute walk test (6MWT) _______________ metres
Or
Incremental Shuttle Walt Test (ISWT) _______________ metres

GAIT AID USED

☐ NO  ☐ YES  If yes, what type:  ☐ SPS  ☐ 4PS  ☐
          FAC/ AC

☐ 4WF  ☐ 3WF
☐ PUF
☐ Other ________________
### Scoring for CRQ – SR

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<th>Questions</th>
<th>Minimum Score (worst function)</th>
<th>Maximum Score (best function)</th>
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</tr>
<tr>
<td>Fatigue</td>
<td>8, 11, 15, 17</td>
<td>4</td>
</tr>
<tr>
<td>Emotional Function</td>
<td>6, 9, 12, 14, 16, 18, 20</td>
<td>7</td>
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<tr>
<td>Mastery</td>
<td>7, 10, 13, 19</td>
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</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td>20</td>
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</tbody>
</table>

**QUESTION**  
**SCORE**  
1 (D)  
2 (D)  
3 (D)  
4 (D)  
5 (D)  
6 (E)  
7 (M)  
8 (F)  
9 (E)  
10 (M)  
11 (F)  
12 (E)  
13 (M)  
14 (E)  
15 (F)  
16 (E)  
17 (F)  
18 (E)  
19 (M)  
20 (E)  

D=  
F=  
E=  
M=  
**Total =**
b) Hospital Anxiety and Depression Scale (HADS)

Each Question is scored 0–3, and totalled

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<tr>
<td>Depression Questions</td>
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<td>TOTAL SCORE</td>
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Scoring Guide:

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<th>Description</th>
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<td>0–7</td>
<td>normal</td>
</tr>
<tr>
<td>8-10</td>
<td>mild</td>
</tr>
<tr>
<td>11-14</td>
<td>moderate</td>
</tr>
<tr>
<td>15-21</td>
<td>severe</td>
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Appendix B: Worksheet for Cognitive Behavioural Therapy Study (Study 4, Chapter 7)

Pulmonary Rehabilitation Study

RESEARCHER NAME: ________________________ Date: ____________

PARTICIPANT CODE: ________________________

PATIENT NAME: ____________________________ BRADMA

PATIENT UR: ______________________________

DATE OF VISIT I__I__I I__I__I I__I__I__I__I 
DAY MONTH YEAR

DATE OF BIRTH I__I__I I__I__I I__I__I__I__I AGE
_______ years
DAY MONTH YEAR

GENDER: Male ☐ Female ☐

Part A – Patient Demographics

MARITAL STATUS ☐ Married/partner ☐ divorced/separated ☐ single ☐widowed

LIVING ARRANGEMENTS ☐ Alone ☐ With others ☐ HLC ☐ LLC
☐ Other supported accom

Education level: Primary Secondary Tertiary

Weight (kg): ____________________ Height (m):

Respiratory Clinic/Specialist: __________________________

COPD HISTORY
### Spirometry

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<tr>
<th></th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date of last test:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FEV1: (&lt;80%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FVC:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FEV1/FVC: (&lt;0.70)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DLCO</td>
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<td></td>
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### Smoking

<table>
<thead>
<tr>
<th></th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Still smoking?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Total Pack Years (cigarettes/day x years):</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Year quit?</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Home O2 use

<table>
<thead>
<tr>
<th></th>
<th>Yes</th>
<th>No</th>
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</thead>
<tbody>
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<td>O2 type</td>
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<td>Cylinder</td>
</tr>
<tr>
<td>O2 rate</td>
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### MEDICAL COMORBIDITIES

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<th></th>
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<th>No</th>
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<tbody>
<tr>
<td>IHD</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>CCF</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Other lung pathology</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Diabetes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Depression</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Anxiety</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Anti-depressant use</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Anti-anxiolytic use</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

### MEDICATIONS

**RESP**

### OTHER
COPD SEVERITY

**Modified Medical research council rating of dyspnoea** (circle best description) – (for BODE index)

0  not troubled with breathlessness except with extreme exercise

1  troubled by shortness of breath when hurrying on the level or walking up a slight hill

2  walks slower than people of the same age on the level because of breathlessness or has to stop for breath when walking at own pace on the level

3  stops for breath after walking about 100 yards after a few minutes on the level

4  too breathless to leave the house or breathless when dressing or undressing
PLANNED OUTCOME EVALUATION

RESEARCHER ________________________________

PARTICIPANT CODE NUMBER: ____________________

DATE OF VISIT  I__I__I  I__I__I  I__I__I__I
        DAY      MONTH      YEAR

Time interval of current evaluation?
☐ Baseline  ☐ Follow up 1 (End of PRP)  ☐ Follow up 2 (3mths post end of PRP)

Next review date  I__I__I  I__I__I  I__I__I__I
        DAY      MONTH      YEAR

ACTIVITY LIMITATION

b) Six minute walk test (6MWT) ___________ metres

GAIT AID USED

☐ NO  ☐ YES  If yes, what type:  ☐ SPS  ☐ 4PS  ☐ 4WF  ☐ 3WF  ☐ FAC/ AC  ☐ Other ___________
b) Functional Assessment Measure (FAM)

**Scale:**
7 Complete Independence (timely, safely)
6 Modified Independence (extra time, devices)
5 Supervision (cuing, coaxing, prompting)
4 Minimal Assist (performs 75% or more of task)
3 Moderate Assist (performs 50%-74% of task)
2 Maximal Assist (performs 25%-49% of task)
1 Total Assist (performs less than 25% of task)

<table>
<thead>
<tr>
<th>ITEM</th>
<th>Score</th>
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</thead>
<tbody>
<tr>
<td>Self Care</td>
<td></td>
</tr>
<tr>
<td>1. Feeding</td>
<td></td>
</tr>
<tr>
<td>2. Swallowing</td>
<td></td>
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<tr>
<td>3. Grooming</td>
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<tr>
<td>4. Bathing</td>
<td></td>
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<tr>
<td>5. Dressing Upper Body</td>
<td></td>
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<tr>
<td>6. Dressing Lower Body</td>
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<tr>
<td>7. Toileting</td>
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<tr>
<td>Sphincters</td>
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<tr>
<td>8. Bladder management</td>
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<tr>
<td>9. Bowel management</td>
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<tr>
<td>Mobility</td>
<td></td>
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<tr>
<td>10. Transfer (bed, chair, wheelchair)</td>
<td></td>
</tr>
<tr>
<td>11. Transfer (toilet)</td>
<td></td>
</tr>
<tr>
<td>12. Transfer (tub or shower)</td>
<td></td>
</tr>
<tr>
<td>13. Car Transfer</td>
<td></td>
</tr>
<tr>
<td>14. Walking/Wheelchair (circle)</td>
<td></td>
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<tr>
<td>15. Stairs</td>
<td></td>
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<tr>
<td>16. Community Mobility</td>
<td></td>
</tr>
<tr>
<td>car = c, taxi = t, PT = p</td>
<td></td>
</tr>
<tr>
<td>Communication</td>
<td></td>
</tr>
<tr>
<td>17. Comprehension</td>
<td></td>
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<tr>
<td>18. Expression</td>
<td></td>
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<tr>
<td>19. Reading</td>
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<tr>
<td>20. Writing</td>
<td></td>
</tr>
<tr>
<td>21. Speech Intelligibility</td>
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<tr>
<td>Psychosocial</td>
<td></td>
</tr>
<tr>
<td>22. Social Interaction</td>
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<td>23. Emotional Status</td>
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<tr>
<td>24. Adjustment to Limitations</td>
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<tr>
<td>25. Leisure Activities</td>
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<tr>
<td>Cognition</td>
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<tr>
<td>26. Problem Solving</td>
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<tr>
<td>27. Memory</td>
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<tr>
<td>28. Orientation</td>
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<tr>
<td>29. Concentration</td>
<td></td>
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<tr>
<td>30. Safety Awareness</td>
<td></td>
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<tr>
<td><strong>Total</strong></td>
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RESTRICTION IN PARTICIPATION

Scoring for CRQ – SR

<table>
<thead>
<tr>
<th>Questions</th>
<th>Minimum Score (worst function)</th>
<th>Maximum Score (best function)</th>
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</thead>
<tbody>
<tr>
<td>Dyspnoea</td>
<td>1, 2, 3, 4, 5</td>
<td>5</td>
</tr>
<tr>
<td>Fatigue</td>
<td>8, 11, 15, 17</td>
<td>4</td>
</tr>
<tr>
<td>Emotional Function</td>
<td>6, 9, 12, 14, 16, 18, 20</td>
<td>7</td>
</tr>
<tr>
<td>Mastery</td>
<td>7, 10, 13, 19</td>
<td>4</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>20</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>QUESTION</th>
<th>SCORE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (D)</td>
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<tr>
<td>2 (D)</td>
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<td>3 (D)</td>
<td></td>
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<tr>
<td>4 (D)</td>
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<tr>
<td>5 (D)</td>
<td></td>
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<tr>
<td>6 (E)</td>
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<td>7 (M)</td>
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<td>8 (F)</td>
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<td>9 (E)</td>
<td></td>
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<tr>
<td>10 (M)</td>
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<td>11 (F)</td>
<td></td>
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<tr>
<td>12 (E)</td>
<td></td>
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<td>13 (M)</td>
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<td>14 (E)</td>
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<td>15 (F)</td>
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<td>16 (E)</td>
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<td>17 (F)</td>
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<tr>
<td>18 (E)</td>
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<tr>
<td>19 (M)</td>
<td></td>
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<tr>
<td>20 (E)</td>
<td></td>
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<tr>
<td>D=</td>
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<tr>
<td>F=</td>
<td></td>
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<tr>
<td>E=</td>
<td></td>
</tr>
<tr>
<td>M=</td>
<td></td>
</tr>
<tr>
<td>Total =</td>
<td></td>
</tr>
</tbody>
</table>
b) Hospital Anxiety and Depression Scale (HADS)

Each Question is scored 0 – 3, and totalled

<table>
<thead>
<tr>
<th>Anxiety Questions</th>
<th>Depression Questions</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0 – 3</td>
</tr>
</tbody>
</table>

**Scoring Guide:**

<table>
<thead>
<tr>
<th>Score Range</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 - 7</td>
<td>normal</td>
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<tr>
<td>8-10</td>
<td>mild</td>
</tr>
<tr>
<td>11-14</td>
<td>moderate</td>
</tr>
<tr>
<td>15-21</td>
<td>severe</td>
</tr>
</tbody>
</table>
c) Depression Anxiety Stress Scale (DASS)

Please read each statement and circle a number 0, 1, 2 or 3, which indicates how much the statement applied to you over the past week. There are no right or wrong answers. Do not spend too much time on any statement.

The rating scale is as follows:
- 0 Did not apply to me at all
- 1 Applied to me to some degree, or some of the time
- 2 Applied to me to a considerable degree, or a good part of time
- 3 Applied to me very much, or most of the time

<p>| | | | | | |</p>
<table>
<thead>
<tr>
<th></th>
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<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>I found it hard to wind down</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>2</td>
<td>I was aware of dryness of my mouth</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>3</td>
<td>I couldn’t seem to experience any positive feeling at all</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>4</td>
<td>I experienced breathing difficulty (eg. excessively rapid</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>breathing, breathlessness in the absence of physical exertion)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>I found it difficult to work up the initiative to do things</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>6</td>
<td>I tended to overreact to situations</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>7</td>
<td>I experienced trembling (e.g. in the hands)</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>8</td>
<td>I felt that I was using a lot of nervous energy</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>9</td>
<td>I was worried about situations in which I might panic and</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>make a fool of myself</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>I felt that I had nothing to look forward to</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>11</td>
<td>I found myself getting agitated</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>12</td>
<td>I found it difficult to relax</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>13</td>
<td>I felt down -hearted and blue</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>14</td>
<td>I was intolerant of anything that kept me from getting on with</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>what I was doing</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>I felt I was close to panic</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>16</td>
<td>I was unable to become enthusiastic about anything</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>17</td>
<td>I felt I wasn’t worth much as a person</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>18</td>
<td>I felt that I was rather touchy</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>19</td>
<td>I was aware of the action of my heart in the absence of</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>physical exertion (eg, sense of heart rate increase, heart</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>missing a beat)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>I felt scared without any good reason</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>21</td>
<td>I felt that life was meaningless</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>
d) Psychosocial Adjustment to Illness Scale (PAIS)

INSTRUCTIONS

Please select your responses to each question that best describes your experience. The timeframe referred to is the past 30 days including today.

In Section II it will ask questions about your job performance. If you are currently working, then please answer in terms of your job. If you are a student, answer in terms of your schoolwork. If you are housewife, answer as though your housework is your work environment.
Maintaining Gains Following Pulmonary Rehabilitation

Edwin K. Luk¹ · Fary Khan¹ · Louis Irving²

Abstract

Purpose Pulmonary rehabilitation (PR) is an accepted intervention for individuals with chronic obstructive pulmonary disease. Despite initial improvements following PR, many patients eventually return to baseline function or decline even further. The aim of this study is to look at long-term (>1 year) outcomes following PR.

Methods This was a prospective cohort study of patients who had completed PR. Participants were invited for an assessment consisting of participant interviews and clinical assessments using standardised instruments.

Results 129 patients between 2003 and 2012 completed rehabilitation and were eligible. 88 patients were included in the analysis. The mean time of the long-term assessment was 22 months following PR. The mean age was 71 years. Mean FEV1 was 46%. There was a statistically significant ($p < 0.001$) increase in the incremental shuttle walk test distance of 29.0 m following PR but this gain was lost at the long-term reassessment. Chronic Respiratory Questionnaire (CRQ) scores showed a statistically significant ($p < 0.001$) increase in all four domains but only the domains of dyspnoea and fatigue remained statistically significant ($p < 0.001$, $p < 0.01$, respectively) at the long-term reassessment. Hospital Anxiety and Depression Scale scores reduced following rehabilitation but only the anxiety component was statistically significant ($p < 0.01$). These improvements persisted at the long-term reassessment but were not statically significant.

Conclusions This study confirms that many of the functional gains achieved in PR are lost in the longer term. Regular surveillance or monitoring of these patients post-PR is important to identify those requiring further intervention.

Keywords Pulmonary disease · Chronic obstructive · Pulmonary rehabilitation · Exercise

Introduction

Patients with chronic obstructive pulmonary disease (COPD) often experience ongoing impairments with their day-to-day life despite optimal pharmacological management. Whilst COPD is known to affect the lungs, the associated physical deconditioning and the emotional responses to chronic respiratory disease contribute greatly to the resulting morbidity [1]. It has been difficult to determine whether these changes relate to the disease itself or reduced activity levels as a consequence of progressive lung disease [2]. Skeletal muscle dysfunction beyond deconditioning has been identified and recognised as a major target for treatment [3]. In spite of optimal pharmacological treatment, many COPD patients experience substantial functional impairment limiting their normal activities of daily living and affecting their quality of life (QOL) [4, 5]. The medical treatment of COPD has been well established, yet very little is known about how the disease progresses to disability [6].

Pulmonary rehabilitation (PR) is an accepted non-pharmacological intervention for individuals with COPD [7]. This consists of an interdisciplinary approach to
patients with chronic respiratory impairment that is individually tailored and designed to optimise physical and social performance and autonomy [1]. The minimum duration of an effective rehabilitation program is 6 weeks [8]. PR should be offered to patients with moderate to severe COPD [9].

Unlike neurological and orthopaedic rehabilitation in which therapy acts as an adjuvant treatment in enhancing recovery, the primary aim of PR is not to improve lung function, but rather to improve self-coping or management of COPD.

Following successful completion of PR, some patients deteriorate further and require repeat sintes of PR. Studies that have monitored patients beyond 12 months following PR have shown differing results. Some have shown that benefits such as QOL persist beyond 12 months [10–14]. Others have shown that patients often return to baseline or even deteriorate further [15–17]. Some studies had small sample sizes with only 16 and 21 patients [14, 18]. Many studies included patients in a hospital outpatient setting or patients with less severe COPD. The aim of this study is to look at long-term outcomes of patients with moderate to severe COPD attending PR in a community setting. Secondary aims include comparing the demographics and changes in mobility and function following PR.

Methods

Participants and Setting

This was a prospective cohort study of patients who had completed PR conducted at Royal Melbourne Hospital (RMH) and Merri Community Health Service (MCHS). This study was approved by the Human Research Ethics Committee of Melbourne Health.

The diagnosis and severity of COPD was graded according to the Global Initiative for COPD (GOLD) criteria [19] by respiratory and rehabilitation physicians at RMH. Patients who are treated by the respiratory service are referred for ongoing pulmonary management and rehabilitation.

The 8-week PR program consists of multidisciplinary management including medical, nursing and allied health using standardised therapy protocols. Following patient assessment including goal setting, an individualised exercise plan was created. Each week, participants undertook two 2-hour sessions consisting of group physical therapy and general education sessions. The 45 min exercise session consists of 15 min treadmill/walking, 15 min cycling, and 15 min circuit exercises. Treadmill speeds were set at 80% of the initial incremental shuttle walk test (ISWT) speed. Patients were educated and monitored to ensure they spend most of their time on the treadmill or bike at a high level of intensity as per current American Thoracic Society guidelines [20]. This correlated to a rating of perceived exertion (RPE) of 4–6 on the modified Borg scale. In subsequent sessions, patients were encouraged to either increase treadmill speed or bike resistance provided they remained in the 4–6 on the RPE. Each group contained a maximum of 15 patients. Patients were supervised during the program by their key worker and physician. Group education included topics such as how the lungs work and medication management.

Eligible patients were identified from a centralised database at MCHS. The inclusion criteria were patients with a confirmed diagnosis of COPD and have completed PR between 2003 and 2012. This allowed a minimum period of 12 months follow-up. Patients were excluded if they had severe cognitive impairment or were medically unwell for further assessment and testing.

Procedure

Following consent, eligible patients were invited to attend the community centre for assessment (long-term assessment).

The long-term assessment participant interviews and clinical assessments were completed using a structured format. The assessors completed demographic, functional, and QOL assessments using standardised instruments (see measures). Standardised instructions were given to participants to complete questionnaires. Any additional queries were answered.

Data Collection

Patient data were extracted from a centralised database. Information was collected at several time points, from pre-PR, post-PR and at 3 monthly intervals post-PR until they were discharged from case management. Basic demographic information was collected at the first visit. The main outcomes measures including ISWT, CRQ and Hospital Anxiety and Depression Scale (HADS) were recorded at pre-PR, post-PR and repeated at the long-term assessment.

Main Outcome Measures

Activity was assessed with the ISWT [21], whilst participation and QOL was measured with the Chronic Respiratory Questionnaire (CRQ) [22] and HADS [23]. COPD-related measures were obtained from the medical record which include socio-demographic, clinical and treatment data, such as spirometry and severity of COPD.

The primary outcome measure in this study is the CRQ. The CRQ consists of a 20-item questionnaire with four major domains which patients self-administer. This
measures the health-related Quality of Life in respiratory patients. CRQ has been widely used in the respiratory and COPD contexts [20]. The Minimal Clinically Important Difference (MCID) is reflected by a change in score of 0.5 on a 7-point scale [24].

Secondary Outcome Measures Include

ISWT This is a field-based test that progressively increases walking speed and measures the functional capacity of COPD patients [21]. ISWT is a true symptom-limited maximal exercise capacity test, and distance walked relates strongly to peak aerobic capacity [20]. Normal health subjects are able to complete 810 m [25]. The MCID for COPD is 47.5 m [26]. Patients were asked to complete ISWT twice at each timepoint with the best result recorded.

HADS The HADS is a fourteen-item scale that measures levels of anxiety and depression. Each item is rated on a scale of 0–3. Each domain is totaled; scores 8–10 indicate possible case and greater than 10 indicate probable case [27]. HADS is the current recommended screen tool in COPD patients [9]. The MCID is 1.5 [28].

Statistical Analyses

The data were keyedi into Microsoft Excel (Microsoft, WA USA) and exported into Stata12 (StataCorp, TX USA) for data analysis and reporting. Descriptive analysis of study cohort was undertaken and results were reported as N(%) for categorical data (e.g. gender, living arrangements, etc.) and mean for continuous data (FEV1, FVC, BMI, etc.).

The change in outcomes of interest between pre- and post-PR was calculated based on the score at end of PR minus the score at baseline. The long-term change was calculated based on the score at the long-term assessment visit minus the score at baseline. The differences were assessed for normality using Shapiro–Wilk test. An one-sample test was used in scores with normal distribution to determine the significance of the change and its magnitude. Multivariate regression analysis was then undertaken to determine the predictors of the change. Level of significance for the study was set at p < 0.05. Accounting for multiple comparison and subscale analysis, the change for CRQ subscales was defined as significant if p was < 0.01.

Table 1 shows the basic demographics of the cohort. There was a similar ratio of males to females with a mean age of 71 years. A mean FEV1 of 46 % correlates with severe COPD according to the GOLD criteria [29]. 94 % were either a past or present smoker, 26 % of patients were on Long-Term Oxygen Therapy (LTOT).

The prevalence of medical comorbidities ranged from 13 to 29 %, 8 % had previously diagnosed anxiety and 19 % had previously diagnosed depression.

Table 2 reflects the scores of patients at baseline, end of rehabilitation and their reassessment (long-term reassessment). Graph 1 illustrates the mean time between the end of PR and the long-term reassessment was 22 months (standard deviation 16 months, range 12–84 months). At the time of reassessment, some of these patients were already discharged from case management. Baseline scores revealed 39 % of patients had probable anxiety and 28 % had probable depression on the HADS (Table 1).

Table 3 shows the mean change of outcome measures immediately following rehabilitation and at the long-term reassessment. In the walk test, this showed a statistically significant (p < 0.001) increase in the ISWT distance of 29.0 m following rehabilitation but this gain was lost at the long-term reassessment and in fact worsened. CRQ scores showed a statistically significant (p < 0.001) improvement in all four domains but only dyspnoea and fatigue remained statistically significant (p < 0.001 and p < 0.01, respectively) at the long-term reassessment. The mean improvements in dyspnoea and fatigue scores were maintained at the long-term reassessment. The other domains of emotion and mastery maintained some of their gains following rehabilitation but not statistically significant.

Both the anxiety and depression component of the HADS scores reduced following rehabilitation but only the anxiety component was statistically significant (p < 0.01). Some of these improvements persisted at the long-term reassessment but was not statistically significant.

Multivariate regression analysis was performed to see whether any baseline variables could predict maintenance of gains in the long term. No predictors were seen. Mild to moderate correlation was observed between the change in ISWT and the change in total CRQ (r = 0.27, p = 0.014) and emotional CRQ (r = 0.26, p = 0.018). Other domains in the CRQ showed no correlation.

Results

A total of 217 patients commenced PR between 2003 and 2012. 129 patients actually completed rehabilitation and were eligible. 68 patients were included in the analysis. 21 patients were deceased and 20 patients declined participation or could not be contacted.
Table 1  Baseline
Demographics

<table>
<thead>
<tr>
<th></th>
<th>(n = 88)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>41 (47 %)</td>
</tr>
<tr>
<td>Female</td>
<td>47 (53 %)</td>
</tr>
<tr>
<td>Age</td>
<td>70.7 (SD 7)</td>
</tr>
<tr>
<td>Body mass index (BMI—kg/m²)</td>
<td>26.9 (SD 6)</td>
</tr>
<tr>
<td>Lung function</td>
<td></td>
</tr>
<tr>
<td>FEV1</td>
<td>46 % (SD 16)</td>
</tr>
<tr>
<td>Modified Medical Research Council Scale (MMRC)</td>
<td>1.98</td>
</tr>
<tr>
<td>Current/past smoker</td>
<td>83 % (94 %)</td>
</tr>
<tr>
<td>Smoking (pack years)</td>
<td>55 (SD31)</td>
</tr>
<tr>
<td>Long-term oxygen therapy (LTOT)</td>
<td>23 % (26 %)</td>
</tr>
<tr>
<td>Ischaemic heart disease (BHD)</td>
<td>26 % (29 %)</td>
</tr>
<tr>
<td>Congestive cardiac failure (CCF)</td>
<td>12 % (13 %)</td>
</tr>
<tr>
<td>Diabetes mellitus (DM)</td>
<td>14 % (16 %)</td>
</tr>
<tr>
<td>Previously diagnosed anxiety</td>
<td>7 % (8 %)</td>
</tr>
<tr>
<td>Previously diagnosed depression</td>
<td>17 % (19 %)</td>
</tr>
</tbody>
</table>

Table 2  Results at pre-PR, post-PR and at long-term assessment

<table>
<thead>
<tr>
<th>Outcome measure (SD)</th>
<th>Pre-PR</th>
<th>Post-PR</th>
<th>Long-term post-assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incremental shuttle walk test (ISWT) (m)</td>
<td>234.5 (99.4)</td>
<td>263.6 (104.8)</td>
<td>215.2 (116.6)</td>
</tr>
</tbody>
</table>

CRQ scores:
- Total (range 20–140) 85.6 (18.9) 98.4 (17.1) 92.6 (21.6)
- Dyspnoea (range 5–35) 16.3 (4.5) 20.1 (5.9) 19.7 (6.9)
- Fatigue (range 4–28) 15.2 (5.5) 18.2 (4.4) 16.7 (5.5)
- Emotion (range 7–49) 33.6 (9.1) 37.3 (7.8) 34.2 (9.8)
- Mastery (range 4–28) 20.4 (5.3) 22.9 (4.3) 21.3 (5.3)

HADS
- Anxiety score 6 (4–10) 6 (2–8) 7 (4–9)
- Depression score 4 (2–8) 3 (2–5) 4 (2–7)
- Prob anxiety 21 (39 %) 14 (26 %) 16 (40 %)
- Prob depression 15 (25 %) 9 (16 %) 8 (20 %)

Graph 1  Data collection time points

Pre Rehab  End Rehab  Long Term Ax

Mean 22mths
(SD 16 mths)

the MCID. An improvement in fatigue was statistically significant but did not reach MCID. The other domains of the CRQ, ISWT and HADS returned to previous level of function. Previously, Griffiths et al. demonstrated sustained improvements in CRQ exceeding MCID [17], whilst another showed all improvements following PR were lost at 1 year [30]. Two other studies which monitored patients 1 year post-PR have shown patients returning to baseline in the walk test [17, 30]. In HADS, Ige et al. did confirm a significant difference three months’ post-rehabilitation.
Table 3 Immediate and long-term assessment changes in functional exercise capacity and quality of life following pulmonary rehabilitation (PR)

<table>
<thead>
<tr>
<th>Outcome measure (SD)</th>
<th>Mean change from pre-PR to post-PR</th>
<th>Mean change from pre-PR to long-term assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>ISWT (m)</td>
<td>29.0 (64.5)***</td>
<td>18.5 (100.9)</td>
</tr>
<tr>
<td>CRQ scores</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dyspnoea (range 5–35)</td>
<td>3.7 (4.6)***</td>
<td>3.3 (7.4)***</td>
</tr>
<tr>
<td>Fatigue (range 4–28)</td>
<td>3.0 (4.5)***</td>
<td>1.5 (5.5)**</td>
</tr>
<tr>
<td>Emotion (range 7–49)</td>
<td>3.6 (6.6)***</td>
<td>0.4 (7.9)</td>
</tr>
<tr>
<td>Mastery (range 4–28)</td>
<td>2.5 (3.8)***</td>
<td>0.8 (5.8)</td>
</tr>
<tr>
<td>HADS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anxiety</td>
<td>−1.6 (3.7)**</td>
<td>−0.9 (3.5)</td>
</tr>
<tr>
<td>Depression</td>
<td>−0.7 (2.8)</td>
<td>−0.3 (2.9)</td>
</tr>
</tbody>
</table>

*p < 0.05; **p < 0.01; ***p < 0.001

(Angiography −0.8, Depression −0.69) [31]. The demographics such as age and severity of COPD and outcomes following rehabilitation were similar to other cohort studies conducted in Australia and New Zealand [14, 18, 32].

In relation to QOL, statistically significant and exceeding MCID increases were seen in all four domains. These results were similar to a systematic review of PR. Its meta-analysis confirmed improvements exceeding MCID in all four CRQ domains [31]. In the longer term, however, only improvements in one of the four CRQ domains were sustained post-PR.

In this study, exercise capacity improved following PR. Other studies of PR showed improvement between 33 and 88 m in the ISWT [11, 17, 30, 34]. This study showed a 29 m improvement following PR. This is statistically significant (p < 0.001) but did not reach the MCID of 47.5 m [26]. However, patients reassessed at the long-term assessment their ISWT scores actually worsened though not statistically significant. Whilst our centre’s PR program was developed around current lung foundation guidelines, some patient’s programs could not be uprated due to their medical comorbidities or deterioration of their respiratory status [35]. This may have contributed to the lower improvement of exercise capacity. Higher intensity of exercise is likely to provide greater benefit, but the exact amount or type remains unknown [34].

Significant underreporting of psychological disorders was noted in this study. Screening of patients showed 39% of patients had probable anxiety and 28% had probable depression. In contrast, only 8% self-reported anxiety and 19% self-reported depression. This highlights the importance of screening psychological disorders in patients with COPD and has been recognised in the COPD-X guidelines produced conjointly by the Thoracic Society of Australia and New Zealand and the Lung Foundation [8]. Additional support from their key worker including referral to a psychologist as well as informing their general practitioner was provided where anxiety and depression had been identified. The scores obtained from this centre are similar to that obtained from another study of patients in the same metropolitan region [36]. Depression has been shown to influence the adherence to PR program [37] and may impact on effectiveness of PR. A recent systematic review on the effect of comorbidities confirms that patients with anxiety and/or depression are less likely to improve in dyspnoea scales [38].

Ideally, PR would target the significant psychological (anxiety and depression) burden in this group. Following PR, both anxiety and depression scores reduced but only the anxiety component was statistically significant. MCID was not reached. Two studies (Bentsen et al. and Ige et al.) using the HADS as an outcome measure in PR have shown differing results. Bentsen et al. showed no significant difference in anxiety or depression following PR but the baseline scores were within the normal range [39]. In another study, Ige et al. showed significant difference in both anxiety and depression (−0.7 and −0.5, respectively) immediately following rehabilitation [31].

The loss of physical gains (as seen in the ISWT) is likely due to patients not maintaining either the intensity or frequency of exercise following PR. The major focus of PR is increasingly focused on changing patients’ behaviour or perception of their disease long term. This has been confirmed in this study as two of the four domains in CRQ did maintain their gains. Only the emotional domain of CRQ correlated with exercise capacity. The three other domains had no correlation. Other studies have shown that improvements in QOL were not necessarily related to increases in exercise capacity [34].

This study illustrates the performance of the PR program in this health service and in particular rehabilitation conducted in a community health service rather than a hospital outpatient department. In this particular centre, there was 59% (129/217) completion rate. This is within the 9.7–31.8% range identified in a systematic review [37]. Patients who smoke or have depression have been identified as factors affecting PR completion rate. The rate of depression in this particular cohort was 28% and may have contributed to the high dropout rate [37]. Recruitment bias may be possible given that all patients were recruited from this single service. Another limitation is that only those who completed PR were analysed. Those that were initially enrolled but did not commence or did not complete the program were not included. In addition, analysis of a patient’s activity levels following PR was not recorded. As all of these patients received case management, most patients would have been encouraged to participate in either a specialised respiratory maintenance program or
other structured activity. Patients who repeated PR during the analysis period were excluded from this study which could potentially bias results. A longer follow-up period would have provided more information. Lastly, hospital readmissions or frequency of exacerbations were not recorded. Further progression of COPD may explain why patient's function may deteriorate.

Conclusions

This study confirms that many of the functional gains achieved in PR are lost in the longer term. Further studies are required to determine which factors affect the longevity of gains following PR. Regular surveillance or monitoring of these patients post-PR is important to identify those requiring further intervention.

Acknowledgments

We are grateful to all participants in this study. We thank the team at Melbourne Easy Breathers and Dr. S. Kofod for patient assessment, Ms A. Gouloukli for statistical analysis and Dr. L. Ng for assistance with ethics submission.

Conflict of interest

None.

References

Appendix D  Published journal article – Cognitive Behavioural Therapy Study

ORIGINAL REPORT

EFFECTIVENESS OF COGNITIVE BEHAVIOURAL THERAPY IN A COMMUNITY-BASED PULMONARY REHABILITATION PROGRAMME: A CONTROLLED CLINICAL TRIAL

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From the 1Department of Rehabilitation Medicine, 2Department of Medicine, the University of Melbourne, *Melbourne EpCentre and 3Department of Respiratory and Sleep Medicine, Royal Melbourne Hospital, Melbourne, Australia

Objective: To investigate whether the use of cognitive behavioural therapy in pulmonary rehabilitation addresses the depression and anxiety burden and thereby improves rehabilitation outcomes.

Design: Prospective controlled clinical trial.

Patients: A total of 70 patients with chronic obstructive pulmonary disease who were referred to a community centre for pulmonary rehabilitation.

Methods: Patients were allocated to either the control group, consisting of pulmonary rehabilitation alone, or to the treatment group, receiving pulmonary rehabilitation and an additional 6 sessions of group-based cognitive behavioural therapy. Assessments consisting of questionnaires and walk tests were conducted pre- and post-pulmonary rehabilitation.

Results: A total of 28 patients were enrolled. The cognitive behavioural therapy group had significant improvements in exercise capacity following pulmonary rehabilitation (mean change 32.9 m, p = 0.043), which was maintained at 3 months post-pulmonary rehabilitation (mean change 23.4 m, p = 0.045). Patients in the cognitive behavioural therapy group showed significant short-term improvements in fatigue, stress and depression (mean change 2.4, p = 0.016; 3.9, p = 0.024 and 4.3, p = 0.047, respectively) and a 3-month post-pulmonary rehabilitation improvement in anxiety score (mean change 3.1, p = 0.01). No significant changes were seen in the control group.

Conclusion: The addition of cognitive behavioural therapy improved patients’ physical, psychological and quality of life results. Cognitive behavioural therapy should be considered for inclusion in a pulmonary rehabilitation programme to enhance outcomes.

Key words: pulmonary disease, chronic obstructive; pulmonary rehabilitation; cognitive therapy; psychotherapy.

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Chronic obstructive pulmonary disease (COPD) is a major cause of mortality, morbidity and health service use worldwide. COPD affects both the ability of patients to perform their activities of daily living and their quality of life. It is projected that COPD will be the seventh leading cause of loss of disability-adjusted life years (DALYs) worldwide by 2030 (1).

COPD affects not only the lungs, but is a systemic disease causing other body system pathology, such as skeletal muscle dysfunction (2). Patients with COPD often experience limitations in physical and functional activity, but it is difficult to determine whether these changes relate to the disease itself or to reduced activity levels as a consequence of progressive lung disease (3).

Pulmonary rehabilitation (PR) involves patient assessment, exercise training, education, behaviour change, nutritional intervention and psychosocial support (4). Benefits of PR include improved exercise tolerance, improved quality of life and lowered perception of dyspnoea (5). Exercise programmes alone have clear benefits, while the benefits of education or psychosocial support without exercise training are less well documented (6). Comprehensive programmes incorporating all 3 interventions (exercise, education and psychosocial support) have the greatest benefits.

Comorbid psychological disorders are a significant burden for patients with COPD, in whom there is an increased prevalence of depression (36%) and anxiety (40%) (7). Patients with psychological co-morbidities are more likely to have reduced engagement and participation and subsequently reduced quality of life (6). The presence of anxiety or depression worsens the degree of dyspnoea and, consequently, patients are more likely to be sedentary at home (8).

Despite this, the treatment and rehabilitation of these patients focuses only on the physical characteristics of the disease. A systematic review of various psychological interventions showed some improvements in psychological outcomes when these were analysed together. However, when CBT was analysed as an intervention alone, there were significant improvements in psychological, but not physical, outcomes (9). Ultimately, the optimal type or intensity of psychological interventions remains unknown (9).

The objectives of this study were to: (i) conduct a clinical controlled trial (CCT) comparing the current PR regime with a programme adding cognitive behavioural therapy (CBT) to the existing schedule; and (ii) confirm that a directed psychological intervention consisting of CBT improves patient participation and clinical outcomes in PR.

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MATERIAL AND METHODS

Participants and setting

This was a prospective CCT conducted at Royal Melbourne Hospital (RMH) and Merri Community Health Service (MCHS). Approximately 100 patients with stable COPD undertake outpatient PR each year at MCHS. Patients who were diagnosed with COPD and treated by the RMH respiratory service were referred to MCHS for ongoing pulmonary management and rehabilitation. The diagnosis and severity grading of COPD was based on the Global Initiative for COPD (GOLD) criteria, as assessed by the respiratory and rehabilitation physicians at RMH (10). This study was approved by the Human Research Ethics Committee at Melbourne Health (HREC Approval 2012.174).

Procedure

All patients who were referred to the ambulatory PR programme during the 18-month trial were screened and consented for participation into the study. The multidisciplinary team, consisting of respiratory and rehabilitation specialists, physiotherapists and nurses, screened each patient according to the criteria. Patients were eligible for this study if they had stable COPD, ability to comprehend English and the consent to the study, and were able to attend regular PR sessions. Stable COPD was defined as no exacerbations within the previous 6 weeks and an optimal pharmacological therapy. Exclusion criteria included previous psychological treatment within the past 3 months and any significant psychiatric history, such as psychosis, bipolar disorder, schizophrenia, mental retardation, borderline personality disorder, chronic suicidal behaviour or major depressive disorder with previous episodes of hospitalization. The patient’s general practitioner was contacted if the psychiatric diagnosis was unclear.

Patients were allocated to either the treatment group, consisting of additional group-based CBT and the usual PR, or the control group, consisting of PR alone. Allocation was not randomized. Once patients were referred and assessed to be eligible for PR, they were enrolled into the next PR group. Due to resources, the CBT programme was delivered to consecutive patients in 2 PR cohorts during the 18-month period. Patients who were recruited outside of these times did not receive CBT and were allocated to the control group.

Treatment schedules

Patients in both groups received the usual PR programme. This 8-week programme consisted of multidisciplinary management including medical, nursing and allied health using standardized therapy protocols. Each week included 2 sessions of 2-hour duration, consisting of group physical therapy and general education sessions. The 45-min exercise session consisted of 15 min treadmill-walking, 15 min cycling and 15 min circuit exercises. Patients were educated and monitored to ensure they spent most of their time on the treadmill or bike at a high level of intensity as per current American Thoracic Society guidelines (4). Group education was provided on issues such as how the lungs work, nutrition, advanced care planning and medication management. Whilst patients were educated on the link between dyspnoea and COPD, no specific information was provided in relation to recognizing triggers of dyspnoea or the use specific breathing strategies. An a priori compliance with outpatient treatment was participant attendance in >80% of treatment sessions.

The CBT programme in the treatment group consisted of an additional 6 sessions of group-based CBT delivered by a psychologist. The psychologist did not take part in patient assessment. The content was designed in conjunction with the treating team to complement the pre-existing exercise and education programmes. The programme was not specifically directed at anxiety and depression, but incorporated common issues facing a PR participant. Table 1 lists the themes in the CBT group.

Table 1. Themes in the cognitive behavioural therapy programme

<table>
<thead>
<tr>
<th>Theme</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breathing and relaxation</td>
<td>Methods of relaxation</td>
</tr>
<tr>
<td>Anxiety management</td>
<td>Understanding symptoms, strategies to cope</td>
</tr>
<tr>
<td>Monitoring and responding to thoughts/self-talk</td>
<td>Combating negative thoughts, changing thinking patterns</td>
</tr>
<tr>
<td>Barriers to changing behaviour</td>
<td>Identifying barriers, setting goals</td>
</tr>
<tr>
<td>Goals, objectives and problem-solving</td>
<td>Setting goals, solving problems</td>
</tr>
<tr>
<td>Understanding and responding to the risk of relapse</td>
<td>Recognizing relapse triggers, coping strategies</td>
</tr>
</tbody>
</table>

The outcome measures were all baseline participant interviews and clinical assessments were completed using a structured format. Demographic, functional, and quality of life (QOL) assessments were completed using standardized instruments. Assessors did not prompt patients, but provided assistance for those who had difficulty completing the questionnaires. COPD-related measures, such as socio-demographic, clinical and treatment data, were obtained from the medical record.

The primary outcome measure in this study was the Depression Anxiety Stress Scale (DASS) (short form). This is a 21-item self-reported questionnaire that measures the 3 related negative emotional states of depression, anxiety and tension/stress (11). Participants rated the extent to which they experienced each state over the past week on a 4-point Likert rating scale. When totalled, 3 domain scores are given. Scores greater than 9, 7 and 14 are suggestive of depression, anxiety and stress, respectively (11).

Secondary outcome measures included:

- The 6-min walk test (6MWT). This test measures the distance patients can walk in 6 min and is a measure of functional exercise capacity (12). The best score out of 2 attempts is recorded. The minimal important difference (MID) is 25 m (13).
- Chronic Respiratory Questionnaire (CRQ). The CRQ consists of a 20-item questionnaire with 4 major domains: Dyspnoea, Fatigue, Emotion, Mastery, which patients self-administer. This measures the health-related QOL in respiratory patients. The MID is reflected by a change in score of 0.5 on a 7-point scale (14).
- Hospital Anxiety and Depression Scale (HADS). The HADS is a 14-item scale that measures levels of anxiety and depression. Each item is rated on a scale of 0–3. Total scores greater than 8 indicate anxiety or depression (15). The MID is 1.5 (16).
- Psychological Adjustment to Illness Scale (PAIS). This is a 46-item self-report questionnaire that assesses psychosocial adjustment to chronic illness (17). It measures psychosocial adjustment to illness in terms of 7 primary domains of adjustment: Health Care Orientation, Dyspnoea Environment, Domestic Environment, Sexual Relationships, Extended Family Relationships, Social Environment and Psychological Distress.
Each PAIS item is rated on a 4-point (0–3) scale of adjustment, with higher ratings indicating poorer adjustment status.

Statistical analysis

Data were keyed into Microsoft Excel (Microsoft, WA, USA) and exported to Stata12 (StataCorp, TX, USA) for data analysis and reporting. Descriptive analysis of study cohort was undertaken and results reported as n (%) for categorical data (e.g. sex) and mean (interquartile range; IQR) for continuous data (Forced Expiratory Volume in one second (FEV1), forced vital capacity (FVC), body mass index (BMI), etc.).

The change in outcomes of interest between pre- and post-PR was calculated based on the score at end of PR minus the score at baseline. The 3-month post-PR change was calculated based on the score at the 3-month post-PR visit minus either the score at baseline or end of rehabilitation. Cohen’s d test was used to measure effect size. The differences were assessed for normality using Shapiro-Wilk’s score. Scores that were normally distributed, a 1-sample t-test was utilized to determine the significance of the change and its magnitude. Level of significance for the study was set at p < 0.05.

RESULTS

A total of 70 patients were screened for the study, 34 patients were consented (Fig. 1). Twenty-eight patients completed PR and completed all their assessments.

![Diagram showing the recruitment process](Fig. 1). CBT: cognitive behavioural therapy; PR: pulmonary rehabilitation.

Table II. Baseline characteristics

<table>
<thead>
<tr>
<th>Variables</th>
<th>Control group (n = 14)</th>
<th>Treatment (CBT) group (n = 14)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD)</td>
<td>70.5 (7.5)</td>
<td>74.2 (7.2)</td>
</tr>
<tr>
<td>Body mass index (kg/m²), mean (SD)</td>
<td>24.1 (12.3)</td>
<td>22.3 (8.0)</td>
</tr>
<tr>
<td>FEV1 (%), median (IQR)</td>
<td>61.5 (39-67)</td>
<td>49 (37-77)</td>
</tr>
<tr>
<td>Current smoker/past smoker, n</td>
<td>4/13</td>
<td>3/11</td>
</tr>
<tr>
<td>Smoking (pack years), median (IQR)</td>
<td>48 (30-55)</td>
<td>38 (30-56)</td>
</tr>
<tr>
<td>Baseline oxygen therapy, n (%)</td>
<td>2 (14)</td>
<td>4 (29)</td>
</tr>
<tr>
<td>Ischaemic heart disease, n (%)</td>
<td>4 (29)</td>
<td>4 (29)</td>
</tr>
<tr>
<td>Competing cardiac failure, n (%)</td>
<td>1 (7.1)</td>
<td>2 (14)</td>
</tr>
<tr>
<td>Diabetes mellitus, n (%)</td>
<td>4 (29)</td>
<td>1 (7)</td>
</tr>
<tr>
<td>Previously diagnosed anxiety, n (%)</td>
<td>3 (21)</td>
<td>1 (7)</td>
</tr>
<tr>
<td>Previously diagnosed depression, n (%)</td>
<td>4 (29)</td>
<td>5 (36)</td>
</tr>
</tbody>
</table>

CFT: Cognitively-based pulmonary rehabilitation

There were 14 patients in the CBT (treatment) group and 14 in the control group. Of the 6 non-completers, 5 were male; otherwise there were no statistical differences between the completers and non-completers.

Table II shows the baseline characteristics between the 2 groups. The mean age of study participants was 72.4 years (standard deviation (SD) 7.4), with 100% being smokers (past or present), mean FEV1 was 57.4% (SD 23.4) and 21% were on long-term oxygen therapy. Forty-three percent of participants lived alone and 7% of participants had only a primary education. There were no statistical differences between the 2 groups.

Table III. Outcome measures at baseline

<table>
<thead>
<tr>
<th>Outcome measure</th>
<th>Control group (n = 14)</th>
<th>Treatment (CBT) group (n = 14)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6-min walk test, mean (SD)</td>
<td>346.9 (105.7)</td>
<td>329.4 (111.1)</td>
</tr>
<tr>
<td>CRQ, median (IQR)</td>
<td>87.5 (60-104)</td>
<td>97.5 (79-111)</td>
</tr>
<tr>
<td>Dyspnoea (range 5-10)</td>
<td>16 (14-20)</td>
<td>15 (14-23)</td>
</tr>
<tr>
<td>Fatigue (range 4-28)</td>
<td>15 (15-22)</td>
<td>15.5 (13-23)</td>
</tr>
<tr>
<td>Emotion (range 7-49)</td>
<td>36.5 (20-44)</td>
<td>36.5 (26-41)</td>
</tr>
<tr>
<td>Memory (range 4-28)</td>
<td>22 (18-23)</td>
<td>23 (19-25)</td>
</tr>
<tr>
<td>HADS, median (IQR)</td>
<td>4.5 (1-6)</td>
<td>5.5 (3-7)</td>
</tr>
<tr>
<td>Anxiety score</td>
<td>3.5 (3-6)</td>
<td>4 (1-8)</td>
</tr>
<tr>
<td>Depression score</td>
<td>3 (2-4)</td>
<td>3 (2-4)</td>
</tr>
<tr>
<td>Probable anxiety (score 8-21)</td>
<td>1 (1-2)</td>
<td>1 (1-2)</td>
</tr>
<tr>
<td>Probable depression (score 6-21)</td>
<td>1 (1-2)</td>
<td>1 (1-2)</td>
</tr>
<tr>
<td>DASS</td>
<td>4 (2-6)</td>
<td>4 (2-6)</td>
</tr>
<tr>
<td>Depression</td>
<td>Median (IQR)</td>
<td>7 (0-14)</td>
</tr>
<tr>
<td>Normal (0-4)</td>
<td>6 (37.1)</td>
<td>7 (50.0)</td>
</tr>
<tr>
<td>Moderate/severe/extreme (&gt;9)</td>
<td>6 (42.9)</td>
<td>7 (50.0)</td>
</tr>
<tr>
<td>Anxiety</td>
<td>Median score (IQR)</td>
<td>7 (2-10)</td>
</tr>
<tr>
<td>Normal (0-7)</td>
<td>7 (50.0)</td>
<td>9 (50.0)</td>
</tr>
<tr>
<td>Moderate/severe/extreme (&gt;7)</td>
<td>7 (50.0)</td>
<td>9 (50.0)</td>
</tr>
<tr>
<td>Stress</td>
<td>Median score (IQR)</td>
<td>6 (0-12)</td>
</tr>
<tr>
<td>Normal (0-14)</td>
<td>12 (85.7)</td>
<td>12 (85.7)</td>
</tr>
<tr>
<td>Moderate/severe/extreme (&gt;14)</td>
<td>2 (14.3)</td>
<td>2 (14.3)</td>
</tr>
<tr>
<td>DASS, mean score (SD)</td>
<td>31 (17)</td>
<td>37 (22)</td>
</tr>
</tbody>
</table>

SD: standard deviation; IQR: interquartile range; CRQ: chronic respiratory questionnaire; HADS: Hospital Anxiety and Depression Scale; DASS: Depression Anxiety Stress Scale; PAIS: Psychological Adjustment to Illness Scale; CBT: cognitive behavioural therapy.
Table III describes participant’s outcome measures at baseline. There were no statistical differences between the 2 groups. DASS scores showed approximately half of the participants had probable depression and anxiety in both groups. These rates are higher when compared with the HADS scores or self-reporting.

**Primary outcome**
In the CBT group, statistical reductions were seen in depression and stress scores of the DASS (p < 0.05, p < 0.02 respectively; Table IV). These improvements were not sustained at 3 months post-PR. In the anxiety sub-scale, a reduction was seen immediately post-PR, but was not statistically significant. By 3 months post PR, a larger reduction was seen and was statistically significant (p < 0.01).

**Table IV. Changes following pulmonary rehabilitation**

<table>
<thead>
<tr>
<th>Outcome measure</th>
<th>Treatment (CBT group) (n=14) Mean (SD)</th>
<th>Control group (n=14) Mean (SD)</th>
<th>Between-group effect size Cohen’s d (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6MWT (m)</td>
<td>1-2 32.9 (35.0)**</td>
<td>4.6 (36.2)</td>
<td>0.57 (-0.19 to 1.32)</td>
</tr>
<tr>
<td></td>
<td>1-3 23.4 (35.9)*</td>
<td>4 (46.9)</td>
<td>0.46 (-0.34 to 1.25)</td>
</tr>
<tr>
<td></td>
<td>2-3 -1.3 (35.6)</td>
<td>0.92 (35.3)</td>
<td>-0.05 (-0.9 to 0.8)</td>
</tr>
<tr>
<td>CRQ</td>
<td>1-2 2.1 (6.9)</td>
<td>0.4 (4.2)</td>
<td>0.29 (-0.45 to 1.04)</td>
</tr>
<tr>
<td>(range 0-35)</td>
<td>1-1 3.1 (6.2)</td>
<td>2.1 (5.5)</td>
<td>0.17 (-0.50 to 0.91)</td>
</tr>
<tr>
<td></td>
<td>2-2 1.1 (6.8)</td>
<td>1.8 (6.2)</td>
<td>0.12 (-0.87 to 0.62)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>1-2 2.4 (3.3)**</td>
<td>-1.4 (4.0)</td>
<td>0.84 (0.09 to 1.61)**</td>
</tr>
<tr>
<td>(range 0-62)</td>
<td>1-2 1.2 (3.1)</td>
<td>0.2 (5.8)</td>
<td>0.20 (-0.45 to 0.94)</td>
</tr>
<tr>
<td></td>
<td>2-2 -1.1 (4.3)</td>
<td>1.2 (4.1)</td>
<td>-0.55 (-1.31 to 0.20)</td>
</tr>
<tr>
<td>Emotion</td>
<td>1-2 2.6 (7.2)</td>
<td>0.7 (6.8)</td>
<td>0.24 (-0.51 to 0.98)</td>
</tr>
<tr>
<td>(range 7-49)</td>
<td>1-1 2.5 (4.6)</td>
<td>1.1 (6.4)</td>
<td>0.24 (-0.51 to 0.98)</td>
</tr>
<tr>
<td></td>
<td>2-2 -0.1 (6.5)</td>
<td>0.4 (6.3)</td>
<td>-0.09 (-0.83 to 0.65)</td>
</tr>
<tr>
<td>Mastery</td>
<td>1-2 -0.3 (6.3)</td>
<td>1.1 (4.9)</td>
<td>-0.25 (-0.95 to 0.49)</td>
</tr>
<tr>
<td>(range 0-28)</td>
<td>1-1 0.8 (5.5)</td>
<td>-1.1 (3.8)</td>
<td>0.14 (-0.60 to 0.88)</td>
</tr>
<tr>
<td></td>
<td>2-2 1.1 (6.0)</td>
<td>0 (4.4)</td>
<td>0.56 (-0.20 to 1.31)</td>
</tr>
<tr>
<td>HADS</td>
<td>Anxiety</td>
<td>1-2 -1.1 (2.6)</td>
<td>0.2 (3.4)</td>
</tr>
<tr>
<td></td>
<td>1-1 -1.3 (2.3)</td>
<td>0.4 (2.2)</td>
<td>-1.31 (-1.45 to 0.23)</td>
</tr>
<tr>
<td></td>
<td>2-2 0.3 (2.6)</td>
<td>-0.2 (2.8)</td>
<td>-0.16 (-0.45 to 0.96)</td>
</tr>
<tr>
<td>Depression</td>
<td>1-2 -0.8 (1.7)</td>
<td>-0.1 (1.7)</td>
<td>-0.09 (-1.31 to 0.38)</td>
</tr>
<tr>
<td></td>
<td>1-1 0.1 (1.5)</td>
<td>0.3 (2.0)</td>
<td>-0.10 (-0.90 to 0.70)</td>
</tr>
<tr>
<td></td>
<td>2-2 1.1 (2.5)</td>
<td>0.3 (3.0)</td>
<td>0.31 (-0.50 to 1.11)</td>
</tr>
<tr>
<td>DASS</td>
<td>Depression</td>
<td>1-2 -4.3 (7.3)**</td>
<td>-1.9 (7.3)</td>
</tr>
<tr>
<td></td>
<td>1-1 -1.5 (6.3)</td>
<td>0.2 (5.8)</td>
<td>-0.31 (-1.38 to 0.47)</td>
</tr>
<tr>
<td></td>
<td>2-2 3.1 (0.9)</td>
<td>0.6 (7.3)</td>
<td>0.30 (-0.48 to 1.07)</td>
</tr>
<tr>
<td>Anxiety</td>
<td>1-2 -2.6 (7.0)</td>
<td>0.4 (5.7)</td>
<td>-0.47 (-1.23 to 0.29)</td>
</tr>
<tr>
<td></td>
<td>1-1 -3.1 (6.4)**</td>
<td>-1.7 (5.7)</td>
<td>-0.29 (-1.36 to 0.09)</td>
</tr>
<tr>
<td></td>
<td>2-2 -0.3 (6.1)</td>
<td>2.0 (5.9)</td>
<td>0.38 (-0.40 to 1.16)</td>
</tr>
<tr>
<td>Stress</td>
<td>1-2 -3.9 (0.0)**</td>
<td>0.6 (5.2)</td>
<td>-0.49 (-1.45 to 0.06)</td>
</tr>
<tr>
<td></td>
<td>1-2 -2.6 (6.2)</td>
<td>-1.8 (7.2)</td>
<td>-0.11 (-0.88 to 0.66)</td>
</tr>
<tr>
<td></td>
<td>2-2 1.5 (7.7)</td>
<td>-2.2 (7.7)</td>
<td>0.47 (-0.31 to 1.25)</td>
</tr>
<tr>
<td>PAIS</td>
<td>1-2 -3.7 (17.4)</td>
<td>-6.6 (18.7)</td>
<td>0.16 (-0.57 to 0.89)</td>
</tr>
<tr>
<td></td>
<td>1-3 -2.3 (10.4)</td>
<td>0.5 (17.3)</td>
<td>0.64 (-1.44 to 0.33)</td>
</tr>
<tr>
<td></td>
<td>2-3 -3.4 (13.3)</td>
<td>6.5 (15.4)</td>
<td>-0.71 (-1.5 to 0.08)</td>
</tr>
</tbody>
</table>

*p<0.05; **p<0.01; ***p<0.01.

In contrast, no significant improvements were seen in all 3 sub-scales in the control group.

**Secondary outcomes**
Statistically significant improvements in the 6MWT were seen in the CBT group (p < 0.05). This was maintained at the 3-month post PR (p < 0.05). Improvements were also seen in the control group, but were not statistically significant. In relation to the CRQ, only the fatigue domain had a statistically significant improvement in the CBT group (p < 0.02). There was also a statistically significant improvement between the 2 groups (p = 0.03). Emotion and dyspnoea improved in both groups, though bigger changes were noted in the treatment group. However, these changes were not significant.

Both anxiety and depression scales in the HADS had reductions following PR in the CBT group, but were not statistically significant. In the control group, reductions were seen only in the depression scale. Again, none of the changes in the control group were statistically significant.

Reductions were seen in PAIS across both groups after completion of PR. None of the changes were statistically significant.

**DISCUSSION**
This is one of the few studies to examine strategies beyond physical measures for COPD. The results show that the addition of CBT to PR provides additional benefits. Greater improvements in the CBT group were seen in the 6MWT, HADS, DASS and CRQ (except Mastery). Only the 6MWT, fatigue, depression (DASS component) and stress measures were statistically significant (p < 0.05, p < 0.02, p < 0.05, p < 0.02, respectively).

The improvements in the 6MWT following PR were sustained at the 3-month post-PR time-point. At the 3-month post-PR, the improvement in the anxiety component of the DASS was statistically significant (p < 0.02).

There was significant psychological comorbidity in patients in this study. Approximately half of study patients had depression or anxiety and 14% had stress on the DASS. This may have contributed to the lack of response to PR. This psychological burden was even higher than a previously conducted study in the same centre, which showed statistically significant improvements in the walk test and all 4 domains of the CRQ (18).

Two similar outcome measures (6MWT and HADS) were used to measure anxiety and depression. Studies in the traumatic brain injury population reported both...
measures were valid as screening tools for anxiety and depression (19). In this study, the DASS showed higher prevalence rates than HADS. However, the DASS was more sensitive to changes following PR in the CBT group.

Despite the increasing recognition of psychological burden in patients with COPD, current Australian Lung Foundation Pulmonary Rehabilitation Guidelines do not recommend any routine screening or the use of psychological interventions (20). It is hoped that this study, along with other future studies, will offer additional evidence and suggest further modifications to the PR programmes.

The use of CBT has been used more commonly for psychological disorders than in the general medical population. Reductions in stress and depression scores following CBT would be expected; however, this study showed CBT carries additional benefits to other impairments, such as exercise capacity. The CBT programme in this study was designed to address not only pre-morbid psychological burden, but also to enhance concurrent physical exercise and education programmes. Given that PR does not change lung function, the ultimate aim of PR would be not only to improve exercise capacity and QOL, but also improve self-efficacy and management of their disease (21).

Whilst there are trials evaluating the use of CBT in people with COPD, very few compare the additional benefits of CBT in PR. In a similar study, De Degoy et al. compared various PR components, such as exercise, education and CBT (22). This showed combined psychotherapy and exercise as well as psychotherapy alone were effective in improving exercise capacity, anxiety, depression and QOL. No statistical analyses were performed to show which group was more effective. Similarly, in this study it was shown that adding a CBT component provided additive benefits to a PR programme. Exercise alone in De Degoy et al. or PR alone in this study did not improve exercise capacity or QOL. In contrast, a systematic review on the role of physical exercise in COPD showed significant improvements in exercise and QOL (23). The improvements in the 6MWT and 6 of the 7 QOL domains exceeded the MID (23).

The PAIS was used as an outcome measure in this study to determine whether patients' psychological adjustment changed following PR. With the greater recognition and treatment of psychological disturbance in COPD, it is hoped that patients would have increased psychological adjustment and associated self-coping. Whilst the PAIS scores reduced (indicating improved adjustment), the changes were not statically significant.

Respiratory studies frequently report on MID. MID attempts to define the smallest difference in score that patients would perceive as important (14). This is usually greater than statistical significance. In this study, the increases in 6MWT and the fatigue subscale of the CRQ, exceeded the MID (13, 14).

This study was a CCT, which could create bias. Participants were enrolled to either the CBT or control group based on when they started PR. A randomized controlled trial would provide a higher level of evidence though may be difficult to conduct with the small group sizes. Also, larger sample sizes would be ideal to provide statistically significant data.

PR, in particular exercise training has been shown to produce unequivocal improvements to QOL and exercise capacity (23). This study, in contrast has shown the PR programme at this centre does not produce similar results. An analysis involving a larger group of patients (n=88) at this centre has shown statistically significant improvements in the walk test and CRQ (18). A larger sample size in this study may have been able to replicate these results. It would also allow further sub-analysis to determine whether certain factors, such as the presence of anxiety or depression, affects PR performance.

Another key difference is despite a similarity with severity of COPD compared with other studies, the mean CRQ scores were higher. Another study looking at PR in the same city and a similar cohort showed lower pre-PR CRQ scores (24). This means our patients at study entry had a higher QOL and thus further improvements in COPD-related QOL may have been limited. Further sub-analyses would be required to confirm this. Other factors that could have impacted on outcomes were beyond the scope of this study.

Data from participants were recorded up to 3 months after completion of PR. Information beyond 3 months were not recorded due to lack of funding. Further monitoring of participants would track the longevity and duration of gains with CBT. Patients who complete PR would typically return to their premorbid state (18). Furthermore, other factors which may be affected by PR, including the number or exacerbations or hospitalizations, were not recorded.

In conclusion, this study shows that the addition of a non-exercise intervention improves the efficacy of a PR programme. Non-physical exercise interventions should be considered in all PR programmes. Further research is required to determine which interventions are most effective.

ACKNOWLEDGEMENTS

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REFERENCES


Appendix E Published journal article – Health Care Utilisation Study

COPD: Health Care Utilisation Patterns with Different Disease Management Interventions

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Abstract

Purpose The management of COPD is a significant and costly issue worldwide, with acute healthcare utilisation consisting of admissions and outpatient attendances being a major contributor to the cost. Pulmonary rehabilitation (PR) and integrated disease management (IDM) are often offered. Whilst there is strong evidence of physical and quality of life outcomes following IDM and PR, few studies have looked into healthcare utilisation. The aims of this study were to confirm whether IDM and PR reduce acute healthcare utilisation and to identify factors which contribute to acute health care utilisation or increased mortality.

Methods This was a retrospective cohort study of patients with COPD who were referred to IDM over a 10-year period. Patients were also offered an 8-week PR program.

Data collected were matched with the hospital dataset to obtain information on inpatient, ED and outpatient attendances.

Result 517 patients were enrolled to IDM, 315 (61%) also commenced PR and 220 (43%) completed PR. Patients who were referred to PR were younger and had less comorbidities (p < 0.001). Both groups (IDM only and IDM + PR referred) had reductions in healthcare utilisation but the IDM-only group had greater reductions. A survival benefit (HR 0.68, 95% CI 0.50-0.92) was seen in those who were PR completers compared to patients who received IDM only.

Conclusion Patients with COPD who successfully complete PR in addition to participating in IDM have improved survival. IDM alone was effective in the reduction of healthcare utilisation; however, the addition of PR did not reduce healthcare usage further.

Keywords Pulmonary disease, chronic obstructive - Disease management - Rehabilitation - Hospitalisation - Readmission

Introduction

Approximately 65 million people worldwide have Chronic Obstructive Pulmonary Disease (COPD) and it has been predicted that COPD will be the seventh leading cause in Disability Adjusted Life Years lost by 2030 [1, 2]. Substantial resources are required to support the management of COPD [3–5]. Acute healthcare utilisation consisting of inpatient and Emergency Department (ED) admissions, outpatient and outreach services are the major contributors to the cost of managing advanced COPD [6].

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In response, funding bodies and governments have explored a range of strategies to prevent ED presentations and inpatient admissions [7]. Two such key strategies are Integrated Disease Management (IDM) and Pulmonary Rehabilitation (PR) programs.

IDM programs typically include case management and coordination of services and interventions, patient education and self-management training and strategies to optimise management of chronic conditions [8, 9]. In a recent Cochrane review, IDM improved respiratory-specific Health-Related Quality of Life (HRQOL) and exercise capacity. Most of the IDM models analysed included an exercise element which may account for the impact on exercise tolerance [10]. Sub-analyses were not performed to assess whether IDM programs with an exercise component performed better than IDM alone. In addition, 15 studies analysed health care utilisation. This showed a reduction in respiratory-related admissions, but ED presentations and mortality remained unchanged.

PR has been shown to be effective in the management of COPD. PR provides physiological, symptom reducing, psychosocial and health economic benefits. A number of studies have shown that following PR, hospital admissions, acute care Length Of Stay (LOS) and outpatient visits were reduced [11–13]. Major health services may operate one or both programs for their patients. Whilst PR and IDM have immediate physical and HRQOL benefits, whether these changes persist into the long term is unclear. Few studies have evaluated improvements in healthcare utilisation following participation in these programs. In addition, no studies have looked at whether the addition of PR to IDM can provide greater impact on health care utilisation rates.

The aims of this study were:

- To identify factors which contribute to increased utilisation of acute health care services;
- To assess whether those patients who commenced or completed an intensive 8-week PR had lower health care utilisation than those who did not receive these interventions and;
- To assess whether completion of a PR program was associated with decreased rate of mortality compared to patients who did not complete PR.

Methods

Study Design

This was a retrospective cohort study of people referred to IDM over a 10-year period between 2002 and 2012. This study was approved by the Ethics Committee at Melbourne Health (HREC QA2015130).

Setting

This study was conducted in the Royal Melbourne Hospital, as a collaboration between the Respiratory and Rehabilitation departments and a community health centre. These centres run a community-based IDM for patients with chronic respiratory disease. Patients discharged from the acute service following an exacerbation of COPD were assessed and referred to IDM. Patients were referred if they lived within the health service catchment area and the treating clinician assessed that they had COPD that was having an impact on their functional status. COPD was confirmed by spirometry. Following assessment, selected patients were enrolled in an 8-week PR in addition to receiving the IDM program.

The IDM team consisted of respiratory and rehabilitation physicians, respiratory nurses and allied health professionals who provided a variety of interventions in both home- and centre-based settings. The interventions provided as part of IDM included goal setting and regular re-evaluation, general education, smoking cessation, generation of an action plan for management of exacerbations and regular contact [10]. Patients were allocated a primary case worker who screened and identified issues to be managed during their time in IDM, thus each patient received a personalised program delivered on a 1:1 basis. Also, the frequency of visits and total time in IDM varied dependent on patient’s needs.

All patients receiving IDM were also assessed for PR. Patients who were thought to be able to participate and benefit from PR were placed into the next available cohort of PR. The 8-week PR program consisted of multidisciplinary management using standardised therapy protocols. This involved twice weekly exercise and education sessions. The 45-min exercise session consists of 15-min treadmill/walking, 15-min cycling and 15-min circuit exercises. In contrast to IDM, group education was given and included topics and issues such as how the lungs work and medication management.

Reasons for non-referral to PR included patients with comorbidities that prevented them from completing exercises (severe osteoarthritis, unstable cardiac disease), housebound patients, patients identified for palliative care and patients who refused referral to the program.

Data Collection

This study used data linkage to evaluate whether there were differences in the impact of the program on acute health
care utilisation between individuals who completed PR versus those who received only the IDM intervention. A database was established at the commencement of the IDM program to capture data on all patients. Data collected included basic demographics, severity of COPD characterised according to Global Initiative for Chronic Obstructive Lung Disease (GOLD) COPD severity criteria, Forced Expiratory Volume in 1 s (FEV1 %) and the number of PR episodes [3].

Data were obtained on all ED and outpatient attendances and inpatient admissions and mortality between 2001 and 2014. Of interest, were ED attendances and admission data between 1 year prior to patient referral to IDM and 1 year post referral. Patient files were reviewed if there were discrepancies between the IDM database and the administrative dataset.

Patient comorbidity burden was obtained from the hospital service administrative dataset based on ICD-10 diagnoses codes from admissions in the 1 year prior to enrolment. This was used to calculate a modified Elixhauser Comorbidity Score. The Elixhauser score is a comorbidity measure used to take into account whenever chronic disease burden is associated with a particular outcome [14]. The summary score is a weighted combination of the 30 Elixhauser comorbidities, where a larger comorbidity weight indicates a stronger association between the comorbidity and in-hospital mortality [15].

Outcome Measures

Acute health care utilisation was measured as hospital admissions, ED encounters, LOS and outpatient visits. Health utilisation data 1 year preceding their referral was compared to data 1 year following enrolment in the program. Mortality was based on death data in the medical record.

All patients referred to the IDM-respiratory program were grouped according to whether or not they were referred for PR or had IDM alone. Patient survival and acute health care utilisation were compared between the two groups. Secondly, a sub-group analysis was performed for the PR group according to whether they completed PR (PR completers) and those that did not complete PR (PR non-completers). A PR completer was defined as those who completed >80% of sessions and attended the end of PR assessment.

Statistical Analysis

The mean and standard deviations were reported for continuous demographic data which were normally distributed for variables such as FEV1 %, age and the Elixhauser index, with students t tests applied for differences between groups. Variables which were skewed and non-normally distributed, such as the hospital utilisation data, were reported with the median and the Interquartile Range (IQR), with Mann-Whitney (rank-sum) tests applied. Categorical variables were assessed using the x2 test or the Fishers exact test on occasions when counts were fewer than 5 for any group. To assess changes in healthcare utilisation for each outcome and adjust for patient differences at baseline, multivariate Zero-Inflated Negative Binomial regression model (ZINB) analyses were performed.

Time to death analysis was also undertaken with comparisons over three groups: (1) patients who received IDM only, (2) PR completers and (3) PR non-completers. Hazard Ratios (HR) were reported for survival data. Statistical analyses were performed using Stata, version 12.1 (StataCorp. College Station, TX, USA). A two-sided alpha value of less than 0.05 was assumed to indicate statistical significance.

Results

Between 2002 and 2012, there were 670 patients that were referred to IDM. This consisted of 517 patients who had at least one IDM episode. 365 (71%) patients were referred to IDM once and 152 (29%) were referred multiple times (Fig. 1). Patients were divided into those who were not referred to PR (IDM only) and those that commenced PR (rehab referred). Following referral to the service, 315 patients (61%) were assessed for PR and of those, 220 patients (78%) completed PR (Table 1). Patients in the rehab-referred group were younger when compared to the IDM-only group (71.7 vs 75.3, p < 0.001) and had less comorbidities (Elixhauser score, 4.46 vs 7.43, p < 0.001). There was no difference in FEV1 % between the two groups (p = 0.979).

![Flow diagram of included patients](https://example.com/image.png)

**Fig. 1** Flow diagram of included patients

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Table 1  Baseline characteristics

<table>
<thead>
<tr>
<th>Patient characteristics</th>
<th>IDM only</th>
<th>Rehab referred</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>202</td>
<td>315</td>
<td></td>
</tr>
<tr>
<td>Age (years), mean ± SD</td>
<td>75.3 ± 9.34</td>
<td>71.7 ± 9.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Female</td>
<td>80 (39.6)</td>
<td>133 (42.2)</td>
<td>0.555</td>
</tr>
<tr>
<td>FEV1, mean ± SD</td>
<td>45.9 ± 14.5</td>
<td>45.9 ± 15.8</td>
<td>0.999</td>
</tr>
<tr>
<td>GOLD severity category</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>76 (37.6)</td>
<td>118 (37.5)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>102 (40.5)</td>
<td>142 (45.1)</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>24 (11.9)</td>
<td>55 (17.4)</td>
<td></td>
</tr>
<tr>
<td>Elixhauser score, mean ± SD</td>
<td>7.43 ± 7.24</td>
<td>4.46 ± 5.42</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Acute health care utilisation

<table>
<thead>
<tr>
<th>Within 1 year prior to referral date (median IQR)</th>
<th>IDM only</th>
<th>Rehab referred</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total bed-days</td>
<td>6.5 (3-17)</td>
<td>3 (0-9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Emergency admissions only</td>
<td>6 (2-12)</td>
<td>3 (0-8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total inpatient admissions</td>
<td>2 (1-3)</td>
<td>1 (0-2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Emergency admissions only</td>
<td>1 (1-2)</td>
<td>1 (0-1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total ED encounters</td>
<td>1 (1-2)</td>
<td>1 (0-2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total outpatient appointments</td>
<td>1 (0-4)</td>
<td>1 (0-3)</td>
<td>0.836</td>
</tr>
</tbody>
</table>

The second section of Table 1 shows patients’ health-care utilisation in the 12 months prior to referral to the service. This showed that the group referred to PR had significantly less healthcare utilisation compared to those who received the IDM intervention alone (all p < 0.001). There was no difference in the number of outpatient appointments between the two groups (p = 0.836).

Table 2 shows the changes to healthcare utilisation in the 12 months following enrolment compared to the 12 months prior to enrolment into the program. Both groups show statistically significant reductions in both ED and inpatient measures. There was a larger reduction in median total bed-days per annum and ED attendances in the IDM-only group compared to the rehab-referred group. Reductions in outpatient appointments were noted in both the rehabilitation referred cohort (p < 0.001) and in the IDM-only group (p = 0.015).

Multivariate analysis was conducted to assess whether the differences in health care utilisation between the IDM-only and rehab-referred group remained significant after adjusting for differences in patient baseline characteristics (Table 3). The Incidence Rate Ratio (IRR) in total bed-days of 0.71 (95% Confidence Interval (CI) 0.48-1.06) indicates that patients who were referred for rehab had fewer bed-days in the 12 months post referral by a factor of 0.71 after adjusting for prior bed-days, age, COPD severity and Elixhauser scores, although this was not statistically significant (p = 0.095). IRRs which were lower than 1.0, indicating a reduction in health service utilisation for the rehab-referred group, were also

Table 2  Change in acute health care utilisation over 12 months

<table>
<thead>
<tr>
<th>Reductions in acute health care utilisation 12 months pre to 12 months post median IQR</th>
<th>IDM only</th>
<th>p value</th>
<th>Rehab referred</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total bed-days</td>
<td>2 (~2 to 8)</td>
<td>&lt;0.001</td>
<td>0 (~1 to 6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Emergency admissions only</td>
<td>2 (~2 to 7)</td>
<td>0.004</td>
<td>0 (0 to 6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total inpatient admissions</td>
<td>0 (0 to 1)</td>
<td>&lt;0.001</td>
<td>0 (0 to 1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Emergency admissions only</td>
<td>1 (0 to 1)</td>
<td>&lt;0.001</td>
<td>0 (0 to 1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total ED encounters</td>
<td>1 (0 to 1)</td>
<td>&lt;0.001</td>
<td>0 (0 to 1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total outpatient appointments</td>
<td>0 (~2 to 1)</td>
<td>0.015</td>
<td>0 (~2 to 1)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Table 3 Multivariate analysis of changes in healthcare utilisation: Rehab referred vs ID only

<table>
<thead>
<tr>
<th></th>
<th>RRR</th>
<th>95% CI</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total bed-days post</td>
<td>0.71</td>
<td>0.48–1.06</td>
<td>0.095</td>
</tr>
<tr>
<td>Total inpatient episodes</td>
<td>0.83</td>
<td>0.67–1.01</td>
<td>0.216</td>
</tr>
<tr>
<td>Total emergency presentations</td>
<td>0.81</td>
<td>0.61–1.08</td>
<td>0.352</td>
</tr>
</tbody>
</table>

RRR incident rate ratio, CI confidence intervals
* Adjusted for prior bed-days, age, COPD severity and Elixhauser scores

Obtained for total inpatient episodes (RRR 0.85, 95% CI 0.67–1.10) and emergency presentations (RRR 0.81, 95% CI 0.61–1.08), although as indicated by the confidence bounds, no statistically significant differences in changes in health care utilisation from pre to post referral were found between the groups.

Mortality

To assess differences in mortality, patients were further stratified into three groups: (1) patients who received IDM only, (2) IDM patients who were referred and commenced PR but did not complete the program (PR non-completers) and (3) IDM patients who were referred and completed the PR program (PR completers), (Table 4). There was a survival benefit (HR 0.68, 95% CI 0.50–0.92) for those who were PR completers, compared to patients who received IDM only. PR non-completers had a HR of 0.83 (95% CI 0.57–1.19) suggestive of a benefit but this was not statistically significant (p = 0.309). Risk factors independently associated with decreased survival were older age (HR 1.04, 95% CI 1.03–1.06), lower FEV1 % (HR 0.99, 95% CI 0.98–0.99) and the number of comorbidities (Elixhauser Score) (HR 1.06 95% CI 1.04–1.08).

Discussion

To the best of our knowledge, this is the first study not only looking at the effect of IDM on healthcare utilisation and survival but whether IDM in conjunction with PR provides an additive effect. Readmission rates following a COPD-related admission are becoming a major focus as insurers drive to reduce costs [16]. IDM and PR are examples of programs which aim to keep patients well and out of hospital. The isolation of the exercise component (i.e. PR) from the IDM program in this study allowed a comparison between the two groups. IDM alone reduced healthcare utilisation and when compared with the rehab-referred group had greater reductions in admissions and total bed day utilisation; however, this was not statistically significant. Compared with a systematic review, this study also showed a reduction in all health care utilisation measures [10]. Some of the analyses in the systematic review only included as few as two studies, so further studies are required.

In relation to mortality, patients who commenced and completed PR had a survival benefit. Age, severity of COPD and comorbidity loading were other factors affecting survival. As stated in the earlier paragraph, this survival benefit in those commencing PR was accompanied by greater reductions in healthcare utilisation but was not statistically significant. PR alone has been shown to reduce admission rates. It could be postulated that differences in healthcare utilisation may not appear within 1 year of IDM and that a longer follow-up period is required. This would

Table 4 Survival analysis based on rehabilitation status

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariate HR</th>
<th>95% CI</th>
<th>p value</th>
<th>Multivariate HR</th>
<th>95% CI</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rehab status</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IDM only</td>
<td>1.00</td>
<td></td>
<td></td>
<td>1.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PR non-completers</td>
<td>0.70</td>
<td>0.49–1.01</td>
<td>0.056</td>
<td>0.83</td>
<td>0.57–1.19</td>
<td>0.309</td>
</tr>
<tr>
<td>PR completers</td>
<td>0.48</td>
<td>0.36–0.65</td>
<td>&lt;0.001</td>
<td>0.66</td>
<td>0.50–0.92</td>
<td>0.014</td>
</tr>
<tr>
<td>Female</td>
<td>1.05</td>
<td>1.03–1.07</td>
<td>&lt;0.001</td>
<td>1.04</td>
<td>1.03–1.06</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>FEV1</td>
<td>1.00</td>
<td>0.99–1.01</td>
<td>0.448</td>
<td>0.99</td>
<td>0.98–0.99</td>
<td>0.005</td>
</tr>
<tr>
<td>GOLD 2</td>
<td>1.00</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GOLD 3</td>
<td>0.95</td>
<td>0.72–1.27</td>
<td>0.747</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GOLD 4</td>
<td>0.91</td>
<td>0.61–1.36</td>
<td>0.649</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Elixhauser score, mean ± SD

1.07 ± 1.05–1.09 | 0.001 |
1.06 ± 1.04–1.08 | <0.001 |
also determine the relationship between lower healthcare utilisation and life expectancy. Alternatively, healthcare utilisation within the rehab-referred group was already at a lower level when compared with the IDM-only group, so further decreases may be difficult. It may be also possible that elements which are common to both IDM and PR, such as education are significant contributors to reducing healthcare utilisation, so patients who undertake both programs do not receive an additive benefit. Other studies that included mortality as an outcome measure have shown mixed results [17, 18]. IDM alone also yielded similar results [19–22]. Further research to confirm the relationship between healthcare utilisation and survival would be of benefit.

Patients who were assessed or commenced PR were younger, had less comorbidities, bed-days, inpatient and ED admissions, whilst there were no criteria set for which patients should be referred to PR, it appears clinicians used prior admission and presentation data as well as the number of comorbidities as consideration factors. Severity of disease however was not a factor. Current PR guidelines do not however recommend patients should be excluded due to their comorbidities [23].

**Strengths and Limitations**

The greatest strength of this study was analysing all patients enrolled in a working pulmonary service over a 10-year period, rather than carefully selected and controlled subjects typically seen in pilot studies. These real world data may allow for greater generalisation of results to other respiratory centres.

As this was a retrospective study reflective of a community pulmonary program, patients who were enrolled to either IDM or PR were not randomised. Clinicians enrolled patients who they felt would benefit. In addition, patients who were enrolled to IDM were not obligated to participate in PR, so PR may not have been offered to all patients. This could create a selection bias. Multivariate analyses were performed in order to adjust for confounders and therefore improve accuracy of results. The study design was reliant on hospital data, and an assumption was made that patients would attend the same hospital for any acute illness. It is possible that some patients may have chosen to attend other hospitals or have moved away during the time of data collection. COPD is a complex disease with multiple triggers and comorbidities so it would be difficult to attribute all admissions to their respiratory disease [24]. The exact cause of hospitalisation, in particular whether they were respiratory related, is unknown. Similarly, further analyses of the exact type and severity of comorbidities would provide additional information.

**Conclusion**

Patients with COPD who successfully complete PR in addition to participating in an IDM program have improved survival. IDM alone was effective in the reduction of healthcare utilisation; however, the addition of PR did not reduce healthcare usage further. This study provides the information for further studies, so research in individual components of IDM and PR (and in combination) which contribute to clinical efficacy can be explored.

**Acknowledgements**

We thank the team at Melbourne Easy Breathe and the RMH respiratory department for patient assessments.

**Compliance with Ethical Standards**

**Conflict of Interest**

Dr Luk, Prof Hutchinson, Mr Tacey, Prof Irving and Prof Khan declare that they have no conflict of interest.

**Ethical Approval**

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

**Informed Consent**

For this type of study, formal consent is not required.

**References**

Nose to the grindstone: The hidden dangers of long-term oxygen therapy

Edwin Luk

Published journal Article – Burns in COPD patient

Case Report

A 66-year-old man with chronic obstructive pulmonary disease on long-term oxygen treatment presented with facial burns and shortness of breath. He described using an angle grinder to dismantle an air conditioner while wearing nasal prongs. Burns were sustained in the patient's nostrils and nasal passages (Figure 1), with corresponding melted oxygen tubing (Figure 2). His respiratory status remained stable. After localised treatment, including dressing care, the patient was discharged the same day. The patient was further monitored via regular phone contact by his case worker. He remained stable and no deterioration was noted. Further education and reinforcement about the use of long-term oxygen therapy around ignition sources was provided by his case worker and respiratory physician.

DISCUSSION

Oxygen is essential for cell metabolism. Humans are reliant on a complex system in order to acquire enough oxygen from the air, which is then transported via the bloodstream to every cell. Gas exchange is affected in people with chronic obstructive pulmonary disease, though the exact mechanism has yet to be established (Hodgkin et al, 2009). A reduction in partial pressure arterial oxygen (PaO₂) is not seen until forced expiratory volume in 1 second (FEV₁) is decreased to less than 50% of predicted. Further changes, such as an increase in partial pressure of carbon dioxide (PaCO₂), does not occur until FEV₁ is less than 25% of predicted (10).

Symptoms from acute hypoxia are well known (Hodgkin et al, 2009), but given the chronic and insidious nature of chronic obstructive pulmonary disease, most patients will not present with specific symptoms. Hypoxaemic respiratory failure is an independent predictor of mortality in chronic obstructive pulmonary disease. Two major methods have been described: long-term oxygen therapy and intermittent oxygen therapy. The use of long-term oxygen therapy (oxygen at least 15 hours per day) increases survival to about 50% with nocturnal oxygen (Medical Research Council Working Party, 1981), and to about 60% with oxygen administration for more than 15 hours a day (Nocturnal Oxygen Therapy Trial Group, 1980). Long-term oxygen therapy is recommended when PaO₂ is ≤55 mmHg at rest (McDonald et al, 2005). Intermittent oxygen therapy is most commonly prescribed for patients who desaturate on exertion, though the evidence is inconclusive (Ram and Wedzicha, 2002).

Supplemental oxygen near an open flame acts to accelerate combustion. However, the author believes this is the first case of burns using heavy machinery. Other cases of burns while using long-term oxygen therapy have been described. Most (70%) patients admitted to a burns unit with burns associated with long-term oxygen therapy were due to smoking (Chung et al, 2001; Lacasse et al, 2006; Muribit and Tredget, 2012). Approximately 20% of patients on long-term oxygen therapy still smoke, with some clinicians prescribing long-term oxygen therapy despite their smoking status (Lacasse et al, 2006).

APPLICATION TO PRACTICE

This case serves as a timely warning to remind patients not to use equipment that may cause a spark in the immediate vicinity. Most guidelines...
in relation to long-term oxygen therapy neglect to state the risks of fire associated with smoking (List et al., 2012). It is important that general guidelines are issued for users of long-term oxygen therapy, including the need to keep oxygen at least 8-10 feet away from heat or ignition sources (Anonymous, 2014).

Education provided by members of the multidisciplinary team, including the prescriber (medical specialist), nurse and occupational therapist, is essential to ensuring oxygen safety (Peckham et al, 1998). Discussions should begin at the initiation of therapy and at follow-up visits (Chang et al., 2001). Lastly, long-term oxygen therapy should not be offered to current smokers, not only due to increased fire risk but also minimal treatment benefit (McDonald et al., 2005).

The dangers of long-term oxygen therapy should be mentioned in all current guidelines, as well as the importance of regular education and surveillance of patients using this treatment modality. Future research should be directed at specific interventions that would be helpful in reducing this risk.

Conflicts of interest: None declared.


KEY POINTS

- A detailed history of the patient's environment and activities should be undertaken before prescribing long-term oxygen therapy
- Ongoing education should be provided at the commencement and at regular intervals regarding the safe use of long-term oxygen therapy
- Smokers should not be provided with long-term oxygen therapy not only due to increased fire risk but also minimal treatment benefit.

**Figure 1. Burn areas around the nose and nasal passages**

**Figure 2. Nasal prongs (top) and patient's singled nasal prongs (bottom)**

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