School of Physiotherapy

Burden of Disease and Benefits of Exercise in Fixed Airway Obstruction Asthma

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This thesis is presented for the Degree of

Doctor of Philosophy

of

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Declaration

This thesis contains no material which has been accepted for the award of any other degree or diploma in any university. To the best of my knowledge and belief this thesis contains no material previously published by any other person except where due acknowledgment has been made.

Signature:

Date:

Statement of originality

This thesis is presented for the degree of Doctor of Philosophy at Curtin University of Technology, Western Australia. Studies were undertaken between August 2004 and July 2009, through the School of Physiotherapy at Curtin University of Technology, in association with the Lung Institute of Western Australia and the Physiotherapy Department at Sir Charles Gairdner Hospital.

All of the material presented in this thesis is original. This research project was developed in association with my supervisors who have been involved in editing both this thesis and all associated publications.

Abstract

Background and research questions

The characterization of chronic persistent asthma in an older adult population is not well defined. This is due to the difficulties in separating the diagnosis of asthma from that of chronic obstructive pulmonary disease (COPD), the latter being a condition which primarily consists of emphysema and chronic bronchitis, and in some cases asthma.

The studies in this thesis focus on middle-aged and older adults with chronic irreversible asthma, or 'fixed airway obstruction asthma' (FAOA). Individuals who have FAOA are frequently labeled as having COPD and as such are rarely studied in isolation. As a consequence, little is known about FAOA and to what extent treatment strategies for COPD are relevant to individuals who present with the condition. The specific aims of the studies in this thesis were to: (i) implement and evaluate a supervised exercise training programme in middle-aged and older adults (aged 40 years and over) who had moderate to severe asthma and a degree of fixed airways obstruction; (ii) determine the similarities and differences in cardiorespiratory and dyspnoea responses with exercise testing between this population and in a cohort of subjects with COPD; and (iii) describe the burden of both asthma and COPD on hospital services in Western Australia (WA).

The primary study in this thesis was a randomised controlled trial (RCT) that evaluated the effects of a 6 week supervised exercise training program in subjects with FAOA. The purpose of the study was to determine whether individuals with FAOA achieve significant improvements with a program that adhered to the guidelines for exercise training in COPD.

The second study compared measures commonly collected prior to the prescription of exercise training in a cohort of individuals with COPD and a cohort of individuals with FAOA. This study arose because of unanticipated findings of low dyspnoea and a high 6 minute walk distance (6MWD) at baseline in the FAOA subjects who participated in the RCT. The FAOA and COPD cohorts were matched on the basis of pulmonary hyperinflation, or air trapping, at rest as quantified by the ratio of

residual volume to total lung capacity (RV/TLC), gender and age. Comparisons were made between the groups of cardiorespiratory and dyspnoea data collected during the 6 minute walk test (6MWT), resting lung function and peripheral muscle strength.

The third study utilized geographic information systems (GIS) technology to explore the distribution of respiratory health services throughout WA and hospital admissions secondary to asthma or COPD in adults aged 40 years and over during a 5 year period 2000-2004. The purpose of this study was to: (i) gain insights into issues facing the provision of respiratory services for middle-aged and older adults with asthma and COPD throughout WA; and (ii) explore the burden of asthma and COPD in middle-aged and older adults across the State.

The following research questions were addressed:

1. What are the effects of a 6 week supervised exercise training program in subjects who have FAOA on quality of life (QOL), functional exercise capacity, anxiety and depression, asthma control and peripheral muscle strength?

2. What, if any, characteristics differentiate individuals who have FAOA and individuals with COPD with respect to measures of resting lung function, functional exercise capacity and peripheral muscles strength collected prior to the prescription of exercise and what is the physiological basis for any differences?

3. Does the distribution of hospital admissions for asthma and COPD in middle-aged and older adults relate to the distribution of respiratory support services for these conditions throughout WA, and are there any trends in admissions data for asthma and COPD admissions in relation to age, gender and numbers of admissions during the 5 year period of data collection?

Methods

Study 1

Study 1 was a prospective RCT in which 35 subjects (16 males) were randomised using a stratified process to match for gender into an ‘exercise’ and a ‘control group’.

Subjects initially participated in a 3 week run-in period during which asthma control using the Asthma Control Questionnaire (ACQ), was assessed weekly to ensure stability of the subject's asthma. This was followed by the collection of baseline data prior to the intervention period. The run-in period was extended if a subject reported an increase in asthma symptoms as reflected by their responses to the ACQ, a variation in forced expiratory volume in one second (FEV_1) of >10% or a change in their asthma medications. Health care utilization data, comprising the number of hospitalizations and emergency department visits, exacerbations in the year preceding study entry, medications taken for asthma and co-morbid conditions were recorded.

Subjects randomised to the exercise group participated in a fully supervised 6 week exercise training program consisting of three exercise classes each week at Sir Charles Gairdner Hospital. The control group received standard medical care during this 6 week period. Baseline measures were repeated immediately following the 6 week intervention period (post-intervention assessment) and at 3 months following completion of the intervention period (3 month follow-up).

The measurements collected pre- and post-intervention comprised resting lung function, functional exercise capacity (6MWD), ACQ, QOL [Asthma Quality of Life Questionnaire (AQLQ) and the Medical Outcomes Study 36-item Short-Form Health Survey (SF-36)], anxiety and depression (Hospital Anxiety and Depression Scale; HAD) and peripheral muscle strength (quadriceps force and hand-grip strength). The timing of assessments was delayed if a subject experienced an exacerbation or other medical problem such that all measurements were made when subjects were in a stable condition and taking their usual medications. Health care utilization data and number of exacerbations for a 1 year period that commenced immediately after the 3 month follow-up were also collected.

Study 2

Study 2 was a cross-sectional matched comparison study comparing respiratory function functional exercise capacity, cardiorespiratory and dyspnoea measures obtained during the 6MWT and peripheral muscle strength in 16 subjects (10 male) with a diagnosis of FAOA to 16 subjects (10 male) with COPD. The two groups were chosen on the basis of similar age (±5 years), gender and resting hyperinflation

or air trapping (RV/TLC ±0.05). Resting lung function measurements comprised measures of airflow, lung volumes and single-breath diffusing capacity of the lung for carbon monoxide corrected for alveolar volume (DL_{CO}/VA). All subjects completed the 6MWT during which cardiorespiratory and dyspnea responses and 6MWD were measured. The 6MWT was performed twice and data from the maximum 6MWD were used in the analyses. Quadriceps force was measured in triplicate using a strain gauge and the maximum value obtained on the subjects' dominant leg recorded. Handgrip strength was measured using a Jamar dynamometer, and the maximum force obtained from three measurements on the subject's dominant side recorded. The following data were compared in the two subject cohorts: resting lung function expressed as a percentage of predicted normal value (% predicted); maximum 6MWD; % predicted 6MWD; cardiorespiratory [oxygen saturation (SpO_2) and heart rate] and dyspnoea responses to the 6MWT and peripheral muscle strength expressed as % predicted normal value. Data for the 32 subjects were then combined to investigate relationships between resting lung function and 6MWT data.

Study 3

Study 3 was a record-linked prevalence investigation to define the prevalence, demographic characteristics and regional distribution of asthma and COPD admissions in adults aged 40 years and over in relation to the distribution of respiratory services within WA. Data on the distribution of hospitals, respiratory physicians, pulmonary rehabilitation programs and asthma educators were obtained for WA. Population data of adults aged 40 years and over were then extracted from the 2001 census released by the Australian Bureau of Statistics, and hospital admission data were obtained in a de-identified format from the Health Department of WA for the period 2000-2004 for all asthma and COPD cases. All data were aggregated according to the 30 health service areas for the State of WA which were the administrative boundaries used by the Health Department of WA at the time of data collection. Data were linked together in a geo-database using specialized GIS software and graphically displayed to show the distribution of respiratory services. Thematic maps were developed to show the proportion of adults aged 40 years and over with a primary diagnosis of asthma, a primary diagnosis of COPD, and combined data showing adults with a primary diagnosis of asthma or COPD in order

to determine the proportion of admissions relative to the population size within each health service. Finally, data were aggregated in graphical format and trends in admissions data for each health service over the period 2000-2004 by gender and by age groups were identified.

Results

Study 1

A total of 266 adults matched the selection criteria for the study and of these, 39 adults attended an initial screening interview. Thirty-five subjects were enrolled in the study and randomised to the exercise group or control group, of whom 34 subjects (15 male; exercise group n=19, control group n=15) completed the intervention period. The participation rate for this study was 14.7% which decreased to 12.8% with subject withdrawals. Subjects demonstrated moderate to severe airflow limitation (FEV_1 59.4±15.8% predicted) with evidence of lung hyperinflation and gas trapping (mean RV/TLC 125±19% predicted) at study entry. Subjects were aged 68±11 years. Baseline measures showed subjects to have well preserved peripheral muscle strength but significantly impaired QOL. The physical component summary score for the SF-36 was 38.1±10.0 which was significantly lower than age and gender matched Australian and WA normative data ($p<0.05$). The subjects had a high level of functional exercise capacity with 6MWDs close to predicted values (88±12% predicted). Dyspnoea was not a significant factor limiting performance on the 6MWT. The 6 week exercise intervention improved disease-specific QOL with the improvement being maintained at the 3 month follow-up. The magnitude of improvement in the symptoms domain and the activity limitation domain were significantly greater than any changes seen in the control group ($p=0.001$ and $p=0.04$ respectively). Six minute walk distance and anxiety levels were not significantly changed in relation to the control group though were improved in the exercise group against baseline measures.

Study 2

The main findings of this study were that, despite comparable levels of pulmonary hyperinflation and air trapping, individuals with FAOA were characterized as having

significantly greater 6MWD (571±88m, 95±11% predicted versus 488±11m, 80±16% predicted $p<0.005$), lower scores for dyspnoea at the end of the 6MWT (2.7 ±1.8 versus 5.9±2.5, $p<0.001$) and preserved SpO_2 during the 6MWT (post-exercise SpO_2 94.7±1.9% versus 84.3±2.7%, $p<0.001$) than individuals with COPD. Peripheral muscle strength was similar between the two groups.

Study 3

A total of 4,159 cases with a primary diagnosis of asthma and 19,970 cases with a primary diagnosis of COPD were extracted as respiratory admissions within WA during the years 2000-2004. Maps generated through GIS technology revealed a disproportionate number of hospital admissions in rural and remote areas compared to metropolitan data for adults aged 40 years and over. In addition, many parts of WA lacked the services of a respiratory physician, a hospital emergency department and access to a pulmonary rehabilitation program. Trends in admissions data showed a gradual decline in asthma admissions over the 2000-2004 time period but a rise in COPD admissions. The hospital separations for Aboriginal and Torres Strait Islander adults were high (6.7% of the COPD admissions and 16.1% of the asthma admissions) considering only 3.2% of all adults aged 40 years and over in WA are of Aboriginal and Torres Strait Islander descent. The numbers of admissions for females with asthma were consistently higher than for males within all health services whilst this pattern was reversed for the COPD admissions. With increasing age, the proportion of COPD admissions increased, and in contrast a small decline was observed in asthma admissions with increasing age.

Discussion and conclusions

It is generally assumed that rehabilitation for middle-aged and older adults with chronic asthma should be similar to that prescribed for individuals with COPD subjects as the disability arising from the respiratory disease is considered to be similar. The RCT undertaken in this thesis (study 1) showed that despite the recruitment of asthmatics with fixed airflow limitation, these individuals had a higher functional exercise capacity at baseline as evidenced by 6MWDs that were close to their predicted normal values and better functional capacity than individuals with COPD recruited to studies of pulmonary rehabilitation. Participation in the exercise

program for these subjects with FAOA improved QOL, however compared to a control group, the effects of the program on functional exercise capacity, asthma control, anxiety and depression, and peripheral muscle strength were not significant. A high baseline 6MWD in this cohort may however have limited the responsiveness of the 6MWT to detect a meaningful change in functional exercise capacity following training.

The study comparing subjects with FAOA to those with COPD (study 2) illustrated regardless of the observations of a similar magnitude of pulmonary hyperinflation at rest in these two cohorts, the degree to which functional exercise capacity was limited differed between the two conditions and this was most likely attributable to the preservation of gas transfer in the FAOA cohort.

The record linked prevalence study provided an overview of the distribution of admissions to hospitals for middle-aged and older adults with asthma and COPD and the burden placed on health services particularly in regional WA. The lack of essential respiratory services in many parts of the State and the disproportionate number of hospital admissions in rural areas compared to metropolitan areas highlighted a need for further research. The focus of this research would identify opportunities to improve the provision of health services for middle-aged and older adults with asthma and COPD in regional and remote parts of WA which may follow on to better patient outcomes for these individuals.

The three studies in this thesis highlight the necessity of a correct diagnosis of an individual who has FAOA and distinguishing this from COPD as the assessment and treatment modalities for the two cohorts in terms of exercise differ. The differences in the distribution of hospital admissions data, and trends in this data with time further illustrate that a correct diagnosis of asthma versus COPD in middle-aged and older adults is important to ensure accurate evaluation of the burden of these diseases on the health care system and to plan for future services based on the need for these services in both metropolitan and regional areas.

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Presentations, publications and awards arising from this thesis

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List of Abbreviations and Symbols

ARIA:	Accessibility/Remoteness Index of Australia
ANOVA:	analysis of variance
ACT:	Asthma Control Test
ACQ:	Asthma Control Questionnaire
AQLQ:	Asthma Quality of Life Questionnaire
ATAQ:	Asthma Therapy Assessment Questionnaire
A$:	Australian dollars
ASGC:	Australian Standard Geographic Classification Areas
BP:	bodily pain (domain of the SF-36)
BMI:	body mass index
cm:	centimetres
COPD:	chronic obstructive pulmonary disease
CRDQ:	Chronic Respiratory Disease Questionnaire
CI:	confidence interval
DH:	dynamic hyperinflation
ECG:	electrocardiograph
ED:	emergency department
EELV:	end expiratory lung volume
ESWT:	endurance shuttle walking test
EIA:	exercise-induced asthma
VCO_2:	expired carbon dioxide
FAOA:	fixed airway obstruction asthma
FEV_1:	forced expiratory volume in one second

FEV_1/FVC:	the ratio of forced expiratory volume at one second to forced vital capacity written as a percentage
FRC:	functional residual capacity
FVC:	forced vital capacity
GH:	general health (domain of the SF-36)
GP:	General Practitioner
GIS:	geographic information systems
GINA:	Global Initiative for Asthma guidelines
GOLD:	Global Initiative for Chronic Obstructive Lung Disease
g:	grams
HRQOL:	health-related quality of life
HR:	heart rate
HRCT scan:	high resolution computed tomography scan
HAD Scale:	Hospital Anxiety and Depression Scale
HMDS:	Hospital Morbidity Data System
SWT:	incremental shuttle walking test
ICS:	inhaled corticosteroids
ICD:	International Classification of Diseases
kg:	kilograms
kg/m^2:	kilograms per metre squared
km:	kilometers
km/hr:	kilometers per hour
L:	litres
LABA:	long-acting beta agonists
LIWA:	Lung Institute of Western Australia
HRmax:	maximum heart rate
VE/MVV:	ratio of maximum expired minute ventilation to maximum voluntary ventilation ratio

SF-36:	Medical Outcomes Study 36-Item Short-Form Health Survey
MCS:	mental component summary score of the SF-36
MH:	mental health (domain of the SF-36)
m:	metres
ml/min/mmHg:	millilitres per minute per millimetre of mercury
MCID:	minimal clinical important difference
min:	minutes
N:	newtons
n:	number
SpO_2:	oxygen saturation
VO_2:	oxygen uptake
PEF:	peak expiratory flow
VO_{2peak}:	peak oxygen uptake
r:	pearson's correlation coefficient
%:	percent
% predicted:	percentage of predicted normal value
PCS:	physical component summary score of the SF-36
PF:	physical function (domain of the SF-36)
lb:	pounds
PJT:	Professor PJ Thompson
QOL:	quality of life
RCT:	randomised controlled trial
RPE:	ratings of perceived exertion
VE/MVV:	ratio of maximum expired minute ventilation to maximum voluntary ventilation ratio
RV/TLC:	ratio of residual volume to total lung capacity
rpm:	repetitions per minute

RV:	residual volume
RE:	role-emotional (domain of the SF-36)
RP:	role-physical (domain of the SF-36)
SGRQ:	Saint Georges Respiratory Questionnaire
SABA:	short-acting beta agonists
SIP:	Sickness Impact Profile
p:	significance
DLco:	single breath diffusing capacity of the lung for carbon monoxide
DLco/VA:	single breath diffusing capacity of the lung for carbon monoxide corrected for alveolar volume
SCGH:	Sir Charles Gairdner Hospital
6MWD:	six minute walk distance
6MWT:	six minute walk test
SF:	social functioning (domain of the SF-36)
SEIFA:	socio-economic indices for areas
SD:	standard deviation
SLA:	statistical local area
V_T:	tidal volume
TLC:	total lung capacity
DLCO:	transfer factor for carbon monoxide
12MWT:	twelve minute walk test
UK:	United Kingdom
US:	United States (of America)
VE:	ventilation
VAS:	Visual Analogue Scale
VC:	vital capacity
VT:	vitality (domain of the SF-36)

W/min: watts per minute

WA: Western Australia

WACRRM: Western Australian Centre for Rural and Remote Medicine

CHAPTER 1

Introduction

Asthma is one of the most common chronic diseases in the world, and has been associated with an unprecedented acceleration in social, economic and health burden on individuals, communities and governments (1). Asthma is a chronic inflammatory disease of the airways characterized by widespread but variable airflow obstruction which is reversible spontaneously or with treatment. Airway inflammation results in episodes of wheezing, dyspnoea, chest tightness and coughing. These symptoms have a major impact on an individual who needs to control the disease through medications, avoidance of triggers and frequent monitoring (2, 3)

Older adults with chronic, moderate to severe asthma comprise a considerably under-researched population. Often these individuals present with airway obstruction that is only partially reversible, because repetitive episodes of asthma induced inflammation have caused permanent structural changes to the airways (4, 5). For the purpose of this thesis, the presence of this chronic irreversible form of asthma will be referred to as 'fixed airway obstruction asthma' or FAOA.

This thesis contains three studies which all seek to advance the characterization of the condition FAOA in middle-aged and older adults. The primary focus of this thesis involves the evaluation and implementation of a supervised exercise training program, carried out in a group setting, for individuals with FAOA. This involved a randomised controlled trial (RCT) with 35 subjects randomised to either an intervention group that received a 6 week exercise training program in addition to usual care or to a control group that received usual care only. Exercise training is a

mandatory component of pulmonary rehabilitation and significantly improves exercise tolerance, decreases dyspnoea and fatigue, reduces disability and handicap and improves quality of life (QOL) in individuals with chronic obstructive pulmonary disease (COPD) (6, 7). It is reasonable to assume that middle-aged and older adults who have a diagnosis of FAOA will benefit from exercise training in a similar way to those with COPD, given that symptoms of dyspnoea, reduced exercise tolerance, and impaired QOL have been reported in both patient groups (4, 8).

There is limited research evaluating the benefits of exercise training programmes in older adults with asthma. A Cochrane review of exercise training for individuals with asthma consisted of 13 studies, of which only two were in adults. The authors of this review concluded that exercise training improves cardiopulmonary fitness in the absence of any changes in lung function. Notably, none of these 13 studies included QOL as an outcome measure (9).

Following on from this first study, the secondary aim of this thesis was to compare outcomes in a subgroup of the individuals with FAOA who participated in the RCT with a cohort of subjects with COPD. Care was taken to ensure that both subject groups were comparable with respect to resting pulmonary hyperinflation, age and gender. A retrospective analysis was carried out to compare resting lung function measurements, functional exercise capacity as measured by 6 minute walk distance (6MWD), cardiorespiratory and dyspnoea responses to the 6 minute walk test (6MWT), and peripheral muscle strength measurements between the two groups.

The third component of this thesis involved a study that examined the community burden of asthma and COPD in older adults within Western Australia (WA), particularly in rural and remote areas outside the Perth metropolitan area. A descriptive study was carried out which mapped asthma and COPD admissions of adults aged 40 years and over across the State over a five year period (2000-2004). This study identified trends in the admissions data over this period and located the distribution of support services for individuals with asthma and COPD (such as pulmonary rehabilitation programmes, asthma educators and respiratory physicians) in regional areas. This study identified where services were lacking in regional Western Australia and regional ‘hot spots’ for asthma and COPD could be visualized.

The thesis is divided into five main chapters. The first chapter (chapter 2) presents a critical review of the existing literature relevant to each of the three studies conducted. This chapter is followed by individual chapters for each of the three studies (chapters 3-5). The final chapter (chapter 6) summarises the main findings of the research and discusses their clinical implications. The scope of this thesis is deliberately broad as it focuses on addressing novel issues related to asthma treatment, management and prevalence in middle-aged and older adults. Specifically, the studies aimed to evaluate the efficacy of a clinical intervention, i.e. exercise training, as a means of improving QOL, and to investigate prevalence and service issues related to asthma and COPD management in regional areas in WA. The findings of these studies are clinically relevant and applicable to the management of chronic asthma in middle-aged and older adults around the world.

CHAPTER 2

Literature Review

2.1 Introduction

Asthma is one of the most common chronic diseases world-wide with over 300 million people affected, and represents a significant burden to governments, health care services, family and patients (1). The chronic irreversible airways obstruction resulting from long-term asthma shares many similarities in its clinical presentation and management with chronic obstructive pulmonary disease (COPD), particularly in middle-aged and older individuals (10). The treatment approaches to chronic asthma and COPD do differ, however, which make it important to clearly differentiate between the two conditions. The first line of therapy for the management of COPD is pharmacological, which is used to prevent and control symptoms and to reduce the frequency and severity of exacerbations, however once this is optimised pulmonary rehabilitation, of which exercise is the major component, has been shown to have a substantial effect (7, 11). To date, the role this therapeutic option in middle-aged and older adults with chronic asthma remains unexplored.

This literature review is divided into three sections. Part 1 (Sections 2.2 and 2.3) outlines the definition, characterisation of, and distinction between fixed airway obstruction asthma (FAOA) and COPD. Because there are currently such broad definitions pertaining to asthma and COPD, the difficulties that are faced in the diagnosis of FAOA are explored, as well as the concepts of asthma severity and asthma control.

Part 2 (Sections 2.4 to 2.8) discusses the disability associated with chronic asthma in middle-aged and older adults. The presence of anxiety and depression, dyspnoea, exercise limitation, and a reduced ability to carry out activities of daily living in adults with asthma are reviewed, together with the impact of the condition on quality of life (QOL). This section includes a summary of the management of chronic asthma with an emphasis on the role of exercise training for adults with asthma.

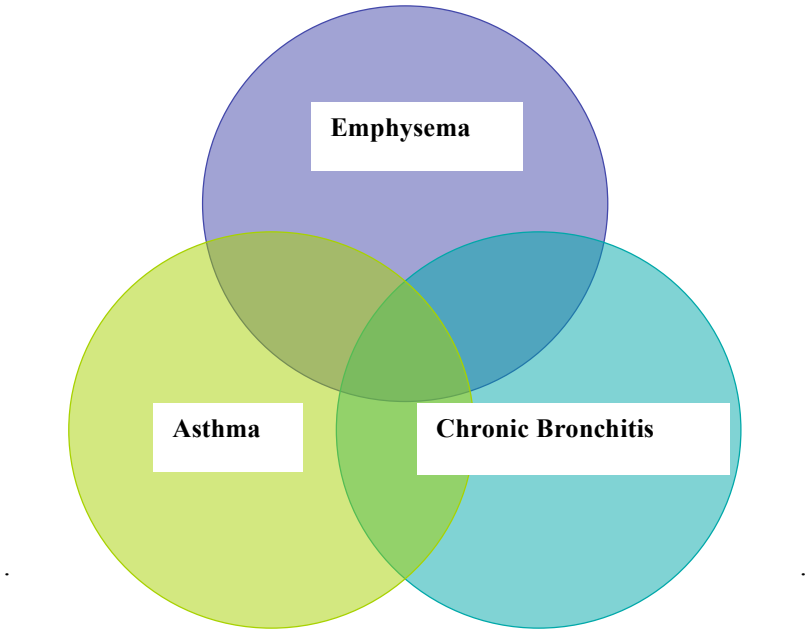
Part 3 (Sections 2.9 and 2.10) explores the impact of asthma at a community level. This includes a summary of the health burden resulting from the ageing Western Australian population, particularly in relation to the burden associated with asthma and COPD. To effectively examine the health burden resulting from chronic asthma in Western Australia (WA), a general overview of the organisation of the health service in the State is provided. Management issues which relate to the delivery of effective care in metropolitan, rural and remote parts of the State are described. The section concludes with an introduction to the use of geographic information systems (GIS) in the health sector and the role GIS can play in understanding health service accessibility issues which might arise for older adults with chronic asthma. Methods by which GIS can assist in health planning and determining areas that are in need of further health services, such as exercise training for individuals with chronic respiratory disease, are also examined.

Part 1

2.2 Obstructive airways diseases

There are three main disease entities that cause limitation to airflow in the lungs. These are asthma, chronic bronchitis and emphysema. Each of these three diseases can be present to a greater or lesser degree in a given individual (Figure 2.1) (12).

Figure 2.1 Obstructive airways diseases



2.2.1 Asthma

Asthma is a chronic inflammatory disease of the airways, characterized by widespread but variable airflow obstruction that is at least partially reversible, either spontaneously or with treatment (1, 3). Inflammation of the airways can cause episodes of wheezing, chest tightness, dyspnoea and coughing (3). The definition of asthma is non-specific, as there are several causes for the aetiology of the disease and there is no unifying pathology by which it can be defined (13).

Understanding the cause of asthma is a key priority area in asthma research (1). Despite improved understanding of the links between genetic determinants and environmental factors such as diet, obesity, lack of physical activity, exposure to allergens, pollutants and viral infections in the development of asthma, the pathophysiological basis for the disease is incompletely understood (14). Numerous epidemiological studies have mapped geographic variations with asthma prevalence

and have shown that changes associated with a move towards Western culture and urbanization contribute significantly to the development of asthma and other atopic diseases (15).

The prevalence of asthma is now of epidemic proportions, and it is one of the most common chronic diseases worldwide (1). Over 300 million people have asthma and it is expected an additional 100 million people will be diagnosed with the disease by 2025 (1). In Australia, it is estimated that over 2 million individuals have current asthma, representing 10.3% of the population (16). In the 2004-2005 financial year, the health expenditure for asthma amounted to A$606 million which represented 1.2% of the total allocated health expenditure in that year (16). Most asthmatics have mild disease, and although they can be affected by acute episodes of bronchoconstriction in response to well-recognised triggers within the environment, they are usually well controlled with pharmacotherapy (1).

It is estimated 10% to 15% of adults in Australia are diagnosed with current asthma and one third of these have moderate or severe disease (16). In children, asthma is more prevalent in males than females, whereas in adults (over 20 years of age) there is a shift towards a higher proportion of women being diagnosed with the condition than males (17, 18). Potential reasons for this shift include hormonal changes (19, 20), a smaller airway calibre size in females (21), or obesity (22). Mortality rates from asthma in Australia reached a peak in the late 1980s and since then rates have fallen by 28% (23). Mortality due to asthma is highest in the elderly (>65 years of age), with statistics from 1999-2003 suggesting average rates of death for males >65 years were 34.45 (95% CI 34.5 - 42) per 100,000 of the population and 60.42 (95% CI 56.1 - 64.4) per 100,000 of the population for women (24).

2.2.2 Emphysema and chronic bronchitis

Emphysema is defined as the permanent dilatation and destruction of air spaces distal to the terminal bronchiole. Respiratory tissue is progressively destroyed, which causes a loss in elastic recoil and the area for gas exchange is reduced. Emphysema is caused by an imbalance in the activity of proteases and protease inhibitors, often in response to contact with inhaled irritants and/or genetic predisposing factors (discussed below). This condition eventually leads to a decrease in gas transfer (12).

Chronic bronchitis is a functional disorder that does not have any characteristic radiologic features, but is diagnosed primarily on an individual's history of "a cough productive of sputum on most days for 3 months of the year for at least 2 successive years". Airway obstruction occurs due to mucus plugging and the narrowing of the lumen (12).

In Australia in 2001, 3.6% of the population (665,000 people) self-reported they had either bronchitis or emphysema (25). There are approximately 14 million cases of chronic bronchitis and 2 million cases of emphysema reported each year in the United States (US) (26).

2.2.3 Chronic obstructive pulmonary disease

Chronic obstructive pulmonary disease is the third most burdensome disease in Australia and the fourth most common cause of mortality. More than 2.1 million Australians are estimated to have the condition and of these individuals, 1.2 million have moderate to severe COPD (27). In 2008 the financial cost of COPD in Australia was $A8.8 billion and it was estimated there were around 16,000 deaths due to COPD (27). Worldwide, it is estimated that 210 million people have COPD and more than 3 million people died from the condition in 2005 (28).

Chronic obstructive pulmonary disease is defined by the Global Initiative for Chronic Obstructive Lung Disease (GOLD) as "a preventable and treatable disease with some significant extrapulmonary effects that may contribute to the severity in individual patients. Its pulmonary component is characterised by airflow limitation that is not fully reversible. Airflow limitation is usually progressive and associated with an abnormal inflammatory response of the lung to noxious particles or gases. The airflow limitation in COPD is caused by a mixture of small airway disease (obstructive bronchiolitis) and parenchymal destruction (emphysema)" (11). This definition has been adopted in the American Thoracic Society and European Respiratory Society guidelines. Chronic obstructive pulmonary disease is therefore an umbrella term which encompasses the more familiar terms of 'chronic bronchitis' and 'emphysema'. Spirometry provides a description of disease severity and is important in the diagnosis of COPD (Table 2.1) (1, 11).

Table 2.1 GOLD (2008) outline of the stages of severity of COPD

Stage	Severity	FEV_1/FVC	FEV_1
Stage I	Mild	<0.70	≥ 80%
Stage II	Moderate	<0.70	50- 80%
Stage III	Severe	<0.70	30-50%
Stage IV	Very severe	<0.70	< 30%*

GOLD: Global Initiative for Chronic Obstructive Lung Disease; FEV_1: forced expiratory volume in one second; FVC: forced vital capacity; *plus chronic respiratory failure (arterial partial pressure of oxygen <60mmHg with or without arterial partial pressure of CO_2 >50mmHg while breathing air at sea level) (www.goldcopd.com) (11).

Exposure to cigarette smoke is the most important cause of COPD and accounts for up to 85% of the risk associated with the development of the disease. Genetic predisposition also plays a role with the best documented genetic risk factor being a hereditary deficiency of alpha-1 antitrypsin deficiency that can result in the early onset of emphysema, even in non-smokers. This is a rare recessive trait that is more often seen in individuals of North European origin. Other risk factors include occupational or environmental pollution and recurrent respiratory infections in childhood (11). Asthma itself may also be a risk factor for the development of COPD, although the evidence is not conclusive (29). Symptoms of COPD are the presence of chronic, progressive dyspnoea, cough and sputum production. Of these symptoms, it is the dyspnoea experienced by an individual with COPD that interferes most with their activities of daily living and health status (11).

2.2.4 Where does fixed airway obstruction asthma fit among the spectrum of obstructive airways disease?

Traditionally, the reversible nature of airway obstruction in asthma has not been considered to cause any long-term damage to the airways, in contrast to emphysema and chronic bronchitis (8, 10). Only in the last decade has it been appreciated that repetitive episodes of inflammation can lead to permanent structural changes in the airways (30). In severe chronic asthma, airway obstruction is persistent despite

optimum pharmacological management, and therefore individuals with severe chronic asthma most often present with both an irreversible and a reversible component to their disease (1, 10, 29, 31).

A challenge is how to define FAOA: that is, is it asthma or COPD or both? The concept of there being a condition such as FAOA is controversial in the light of the historical classification for obstructive lung conditions. Continued widespread differences in opinion about the presentation and definition of both asthma and COPD remain (13, 32).

Because FAOA involves an irreversible degree of airways obstruction, it meets the criteria used to describe COPD. It also shares many clinical similarities, not only in relation to the objective measures of airflow, but also symptoms of dyspnoea on exertion, reduced exercise tolerance and impaired QOL (4, 8). The goals of treatment in both patient groups are also similar: to prevent acute exacerbations, maintain lung function, optimize levels of habitual physical activity and to reduce symptoms. It is logical, therefore, that the primary and secondary intervention strategies for the management of FAOA should be similar to those for COPD. Indeed many older adults who present with FAOA are (rightly or wrongly) diagnosed as having COPD.

The argument remains, however, whether or not the 'FAOA group' should remain distinct from COPD and thus be treated differently. The natural histories of the two conditions are markedly different and their responses to various pharmacological medications are not comparable (4). For example, adults with FAOA display greater therapeutic benefit in response to corticosteroids than those with COPD (4). Disease progression differs for someone with FAOA compared to COPD. For an individual with FAOA, lung function remains stable, a normal life expectancy is forecast and the individual is unlikely to display any of the secondary co-morbidities associated with COPD such as weight loss, skeletal muscle dysfunction and nutritional abnormalities (4). This is in contrast to the accelerated decline in lung function and poorer prognosis following a diagnosis of COPD (11, 33).

Perhaps the biggest reason for the differences seen in the natural progression of the two diseases is their underlying histopathology. Individuals with FAOA may not present with any chronic bronchitic or emphysematous changes in the lung; both of which are usually present to some degree in COPD (33, 34). It is estimated that as

many as one fifth of elderly asthmatic adults have an improper diagnosis of COPD, rather than asthma (35, 36). Large databases in both the US and United Kingdom (UK) suggest there is considerable overlap between the two diseases (37).

2.2.5 Diagnosing fixed airway obstruction asthma

Due to a lack of a gold standard for diagnosing asthma, differential diagnosis of asthma - let alone FAOA - in an older adult population remains a challenging task (38-40). Table 2.2 outlines some of the factors which can assist in differential diagnosis of asthma and COPD in older adults (39). In addition, investigation of trigger factors for exacerbations, family history, bronchial hyper-responsiveness (by histamine or metacholine challenge tests), significant variability in symptoms over time, past bronchodilator reversibility, and the measurement of peak expiratory flow to identify any evidence of diurnal variability are also important (41).

Table 2.2 Differential diagnosis of asthma and COPD in older adults

	Asthma	**COPD**
Age at onset	Any age	Older
Allergy	Often	Sometimes
Sudden symptom onset	Often	Sometimes
Wheezing	Often	Sometimes
Dyspnoea	Often	Often
Coughing	Sometimes	Often
Smoking history	Sometimes	Almost always
Sputum production	Seldom	Almost always

COPD: Chronic obstructive pulmonary disease.

Source: An algorithmic approach to diagnosing asthma in older patients in general practice (39)

Other diagnostic tests include detailed lung function tests which are undertaken when an individual's condition is stable (42). This can confirm the presence of airflow limitation and can assist in excluding other lung conditions. In COPD, particularly in moderate to severe disease, gas exchange is often impaired. This is reflected by a reduction in measurements of gas transfer, in particular the reduction in single breath diffusing capacity of the lung for carbon monoxide corrected for alveolar volume (DLco/VA) which is often <80% of predicted in COPD whilst DLco/VA is either normal or elevated in adults with a history of asthma (42, 43). Asthma is only likely to cause an impairment of gas exchange during severe attacks (1, 10). Spirometry and trial of therapy (to assess an acute bronchodilator response and longer term changes to peak expiratory flow with therapy) can confirm a diagnosis of asthma, however if uncertainty remains, the gold standard of a high resolution computed tomography (HRCT) scan is useful to exclude the presence of underlying structural emphysematous changes or bronchiectatic changes (29, 39).

Despite these imaging and physiological testing techniques mentioned above, individuals with FAOA may still be considered as having a combination of COPD and asthma as the distinction from COPD is often not possible. However, it must be recognised that this subgroup of individuals with asthma may not necessarily present with the progressive lung deterioration or extrapulmonary co-morbidities associated with COPD (11).

2.3 Assessing asthma severity and control

2.3.1 Definition of asthma severity and asthma control

Guidelines developed to assist in grading the severity of asthma commonly incorporate measures of pulmonary function, frequency and intensity of symptoms, bronchodilator response and medication usage. The guidelines used in this thesis to grade the severity of an individual's asthma are those currently recommended by the National Asthma Council of Australia (2). These are based on the Global Initiative for Asthma Guidelines (1) and are provided in Tables 2.3 and 2.4.

Asthma severity is assigned to one of four categories: intermittent, mild persistent, moderate persistent and severe persistent when first diagnosed and prior to treatment (Table 2.3) (2). Once treatment is commenced, severity is then determined by the

requirement and dosage of pharmaceutical medications (inhaled corticosteroids and long acting beta-agonists) to control the disease, in conjunction with clinical symptoms and the results of spirometry (Table 2.4). Severity is classified when an individual's condition is stable, not during an acute episode. Due to the reversible nature of the disease an individual can move between categories in a classification system throughout the course of the disease (1, 2).

The majority of adults with asthma (80%) have mild or very mild disease. It is estimated only 6% have severe or very severe disease (44). The severity of asthma has been shown to influence health-related QOL (HRQOL) (45) and health care utilisation (46). Individuals with the most severe asthma tend to underestimate their symptoms and may present with very severe obstruction but with little perception of any deterioration in their condition (47). Though asthma severity *per se* is not a patient-focused measure, a patient's perception of their severity is influenced by not only their level of symptoms, but also restrictions to physical activity and social life (48). These relationships are explored further in Part 2 of this literature review (Section 2.4).

There is a distinction between an individuals' level of asthma control and underlying severity of the disease (49). Asthma symptoms may be well controlled with appropriate treatment, but an individual may in fact have severe 'underlying' asthma (50). With increasing asthma severity however, achieving the guideline targets for asthma control becomes more difficult despite appropriate treatment (51). It has been postulated that evaluating the clinical features of asthma over the course of a year provides a more valid assessment of disease severity, while assessing symptoms over the preceding month better reflects the degree of asthma control, or disease activity (52). Table 2.5 illustrates the currently accepted definitions of the various levels of asthma control- *i.e.* good, fair and poor that are used in clinical practice within Australia (1, 2). It is estimated that of the adult population in Australia who have been diagnosed with asthma, 45% have asthma that is considered to be poorly controlled (44).

Table 2.3 Classification of asthma severity in an individual with untreated, newly diagnosed asthma

	Day-time asthma symptoms	Night-time asthma symptoms	Exacerbations	Spirometry
Intermittent	Less than weekly	Less than 2 per month	Infrequent Brief	FEV_1 at least 80% predicted FEV_1 variability less than 20%
Mild persistent	More than weekly and less than daily	More than 2 per month but not weekly	Occasional May affect activity or sleep	FEV_1 at least 80% predicted FEV_1 variability 20-30%
Moderate persistent	Daily	Weekly or more often	Occasional May affect activity or sleep	FEV_1 60-80% predicted FEV_1 variability more than 30%
Severe persistent	Daily Physical activity is restricted	Frequent	Frequent	FEV_1 60% predicted or less FEV_1 variability more than 30%

An individual's asthma pattern (intermittent, mild persistent, moderate persistent or severe persistent) is determined by the level in the table that corresponds to the **most severe** feature present. Other features associated with that classification need not be present.
FEV_1: forced expiratory volume in one second
Sources: (1, 2)

Table 2.4 Classification of asthma severity in an individual with treated asthma

Clinical features and lung function	No inhaled ICS	Low dose ICS	Low- to medium dose ICS and LABA	High dose ICS and LABA +/- other agents
Day-time symptoms occurring <1/week Night-time symptoms occurring <1/month Exacerbations are brief FEV_1 between episodes is at least 80% predicted and 90% of personal best	Intermittent	Mild persistent	Moderate persistent	Severe persistent
Day-time symptoms >1/week but not every day Night-time symptoms >2/month but not weekly FEV_1 between episodes is >80% predicted and 90% of personal best	Mild persistent	Moderate persistent	Severe persistent	Severe persistent
Day-time symptoms daily Night-time symptoms at least weekly Exacerbations affect sleep and activity SABA use daily FEV_1 is 60-80% predicted and 70-90% of personal best	Moderate persistent	Moderate persistent	Severe persistent	Severe persistent
Day-time symptoms every day and restrict physical activity Night-time symptoms frequent Exacerbations are frequent FEV_1 is <60% predicted and <70% of personal best	Severe persistent	Severe persistent	Severe persistent	Severe persistent

Asthma severity in an individual with treated asthma is classified according to medications, symptoms and spirometry. ICS: inhaled corticosteroids; LABA: long acting beta agonists; FEV_1: forced expiratory volume in one second; SABA: short acting beta agonists.
Sources: (1, 2)

Table 2.5 Assessment of asthma control

	Level of control		
Parameters	**Good**	**Fair**	**Poor**
Day-time symptoms	None	<3 days/week	>3 days/week
Night-time symptoms	Not woken	<1 night/week	>1 night/week
Physical activity	Normal	Normal	Restricted
Exacerbations	None	Mild, infrequent	Moderate, severe frequent
Missed school/work due to asthma	None	None	Any
Reliever use*	None	<3 doses/week	<3 doses/week
FEV_1, FEV_1/FVC	Normal	>90% personal best	<90% personal best
PEF	Normal	>90% personal best	<90% personal best

FEV_1: forced expiratory volume in one second; FVC forced vital capacity obtained by spirometry; PEF: peak expiratory flow obtained with a portable peak flow meter. *Does not include one dose/day for prevention of exercise induced symptoms.
This assessment classification is applicable to adults and older children.
Lung function parameters are not appropriate measures of asthma control in young children

2.3.2 Evaluating asthma control

A number of questionnaires have been validated to measure the goals of asthma management as defined by international guidelines. Use of these questionnaires enables the identification of individuals whose asthma management is suboptimal and therefore those who have poor asthma control (53).

To achieve good asthma control, an individual is required to have minimal day and night-time symptoms, rarely demonstrate activity limitation and bronchoconstriction, and require minimal use of rescue medication (54). Three questionnaires that have been validated specifically for measuring asthma control are reviewed in this section, two of which, the Asthma Control Questionnaire (ACQ) and the Asthma Control Test (ACT), are recommended by the International Primary Care Respiratory Group in their Users Guide to Asthma Control Tools {http://www.theipcrg.org/}.

The ACQ is a 7 item, self-complete questionnaire developed by Juniper and colleagues (55) with input from 100 asthma physicians who were members of asthma management guidelines committees across 18 countries, and were opinion leaders in asthma management or asthma clinicians with recognised expertise in the measurement of asthma severity. The overall score for the ACQ is the mean of responses to the 7 items with a score of 0 representing totally controlled asthma and a maximum score of 6 representing severely uncontrolled asthma (55).

The ACQ has been shown to be responsive to changes in asthma control, and is able to differentiate between adults who have well controlled and poorly controlled asthma. The cross-over point between an individual considered to have well controlled asthma, as defined by a composite score based on the National Institute for Health and Global Initiative for Asthma Guidelines, to poorly controlled asthma is a mean score of 1 on the ACQ. To accurately separate a given individual with well controlled versus poorly controlled asthma, the suggested value on which to base clinical decisions is ≤ 0.75 for well controlled asthma, and ≥ 1.5 for poorly controlled asthma (56).

The ACT (57) has been validated in 4,313 individuals with asthma and takes 2 to 3 minutes to complete. The instrument uses a 4 week recall period and a 5 point scale {1-5} to grade asthma control in relation to day-time symptoms, night-time symptoms, rescue beta agonist use, daily activity limitation and the individual's

perception of control. An individual with a composite score of 25 has complete control whilst a score of 5 indicates very poor control (57).

The Asthma Therapy Assessment Questionnaire (ATAQ) (52) consists of a self-complete questionnaire with a 5 level measure of asthma control from 0 (no control problems) to 4 (4 control problems). To assess the level of control, questions ask about nocturnal symptoms, missed activities, medication usage, and self-perception of control. Control is assessed relative to the last 4 weeks and also to the preceding 12 months, with separate control scores calculated for each time period. In addition, the questionnaire contains items which relate to health care utilisation and patient attitudes to treatment to assist in the identification of possible disease management problems. However, these items have not been independently validated. Table 2.6 illustrates a comparison of the components of asthma control that these three questionnaires measure.

Table 2.6 Components of asthma control measured in three questionnaires

	ACQ	ACT	ATAQ
Limits daily activity	Yes	Yes	Yes
Shortness of breath	Yes	Yes	No
Disrupts sleep	Yes	Yes	Yes
Rescue medication	Yes	Yes	Yes
Effect on global control	No	Yes	Yes
Frequency of wheeze	Yes	No	No

ACQ: Asthma Control Questionnaire ; ACT: Asthma Control Test ; ATAQ: Asthma Therapy Assessment Questionnaire. Sources: (49, 58)

Part 2

2.4 Impact of chronic asthma on an individual and the role of exercise training

To date, little research has been dedicated to the characterisation of FAOA in middle-aged and older adults. Studies which illustrate the impact of asthma in adult populations are reviewed in this section. Co-morbid conditions such as significant depression, anxiety, disability, impairment of QOL and reduced mobility occur in association with asthma, and the prevalence of these conditions has been shown to increase with age (59, 60). Disability associated with asthma has been reported to be greater in individuals with more severe disease, those who are older and in individuals who have poorer control of their asthma (61). These associations are reviewed in this section, as well as the impact of chronic asthma on an individual's QOL, and the effects of anxiety, depression, dyspnoea and exercise limitation in this population.

The section concludes with a synthesis of the literature related to the benefits of exercise training in adults with asthma and adults with COPD. Due to the lack of studies of exercise specifically in adults with FAOA, studies of exercise training in these two adult populations are used to explore the potential benefits of exercise training in a cohort of individuals who have chronic asthma with irreversible airflow limitation.

2.4.1 Quality of life and health-related quality of life

Quality of life is defined as an individual's perception of health-related issues such as physical, emotional and mental well-being as well as nonmedical aspects of life such as relationships, occupation and social standing (62). Socio-economic and environmental factors as well as the impact of a disease can influence overall QOL (63).

In health, when referring to the concept of QOL, HRQOL is defined as the part of an individual's overall QOL that is determined primarily by the functional effects of an illness and its consequent treatment perceived by that individual (54, 64, 65).

2.4.2 Measurement of health–related quality of life

A number of generic questionnaires and disease-specific questionnaires have been used to measure HRQOL in individuals with asthma in both clinical practice and the research setting (54, 64). The most commonly used questionnaires are outlined in Table 2.7 along with their relative merits and limitations.

Generic questionnaires measure impairment over a broad spectrum of functions and have the advantage of the potential to compare outcomes across a wide range of medical conditions. The broad nature of the questions may, however, mask small but important changes following a given treatment because of the limited depth of the questions. This is because impairments important to individuals with a specific condition may not be addressed (54, 66). In adults with asthma, the most often reported and best validated generic questionnaire is the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36) (67).

Disease-specific questionnaires include items which pertain to symptoms and functional impairments that are most important to an individual with a specific disease. A number of studies have demonstrated these questionnaires to be more responsive to change than generic health profiles (66, 68). Many disease-specific HRQOL questionnaires now have a minimal clinical important difference (MCID) estimate which refers to “the smallest difference in score which patients perceive as beneficial and would mandate, in the absence of troublesome side-effects and excessive cost, a change in the patients management” (69). The most widely used disease-specific questionnaire in adults with asthma is the Asthma Quality of Life Questionnaire (AQLQ) developed by Juniper and colleagues (66, 70, 71). The AQLQ has been shown to have strong evaluative and discriminative properties with high degrees of sensitivity to change shown in numerous drug trials (66, 68, 72, 73).

Table 2.7 Generic and disease-specific instruments for measuring HRQOL in adults

Questionnaire	Description {Domains}	Administration format, time taken to complete and scoring	Advantages	Limitations
Generic				
Medical Ouctomes Study 36-Item Short-Form Health Survey (74)	36 items grouped in 8 domains: • Physical functioning • Role-physical • Bodily pain • General health • Vitality • Social functioning • Role-emotional • Mental health A separate item assesses change in health from the previous year, called 'health transition'	Self-administered 5-10 minutes Score 0-100 (higher score indicates better QOL) Scoring algorithms can be applied to produce combined physical and mental component summary scores	Valid and reliable (67, 75, 76) Normative data available for Australians (77) Domains are responsive to clinical manifestations (physical functioning) and global psychiatric (mental health) conditions, and the instrument is overall responsive to change More commonly used for cross-sectional studies than for evaluating interventions Moderate correlation with lung function in asthma	Internal consistency in individuals with asthma determined and is good for physical functioning, role-physical, bodily pain, general health and vitality domains; moderate for mental health and role-emotional; lower but acceptable for social functioning due to the small number of items (78-80)
Sickness Impact Profile (81)	Generic 136 items in 2 domains with the following dimensions: • Physical: ambulation, mobility and body care • Social: general well-being, work/ social role performance, social support and participation, global social function, personal relationships and global emotional functioning	Self-administered 20-30 minutes Higher scores indicate more severe dysfunction	Good repeatability and internal consistency Moderate or strong correlations with other measures of health status Used most extensively in patients with COPD	Not strictly a QOL questionnaire, instead assesses behaviours, many which are closely related to factors that affect a subject's QOL Good evidence that it is not useful for measuring the impact of asthma on QOL (82, 83)

Questionnaire	Description {Domains}	Administration format, time taken to complete and scoring	Advantages	Limitations
Disease-specific				
Asthma Quality of LifeQuestionnaire-McMaster Juniper *et al* (70)	Measures health-related limitations in QOL experienced during the past two weeks 32 items grouped in 4 domains: • Activity limitation • Symptoms • Emotional function • Environmental stimuli Three versions available: 1) Individualised: items in activity limitations individualised, i.e. activities to be rated are provided by the respondents themselves 2) Standardised version: items in activity limitations standardised (84) 3) Mini AQLQ: shortened version comprises 15 of the 32 items of the standardised AQLQ (85)	Interviewer or self-administered 15 minutes Item scores range from 1(maximal impairment) to 7 (no impairment) Subscale scores expressed as average of all items within each domain Overall QOL score derived by calculating the mean across all subscales.	Optimized for longitudinal designs and responsive to small within-subject changes over time, with good responsiveness to change and longitudinal construct validity Was found to be most sensitive to improvements in health status compared to other QOL measures (LWAQ, SIP) (66) Responsiveness indexes ranged from 1.28 to 1.46 in total scores (86) Effect size shown to be larger for the total AQLQ score and the Activities and Symptoms domains (86) The MCID for subscales is 0.5, changes of 1.0 are considered moderate and changes of 2.0 are large (68) Highly repeatable Has acceptable levels of content and construct validity and reliability (84)	Individualised version less suitable for cross-sectional designs however a standardised version is available Individualised version increases signal-to-noise ratio caused by personalised items which does make it less responsive to within-person change than other survey tools (87) The internal consistency of the scale has not been reported Scores are skewed to less impact on QOL (higher scores) Empirical method was used to select items

Questionnaire	Description {Domains}	Administration format, time taken to complete and scoring	Advantages	Limitations
Asthma Quality of Life Questionnaire - Marks (88) Original version Modified version	Original version- 20 items with domain scores in 4 areas: • Breathlessness and physical restrictions (Breathlessness) • Mood disturbance due to asthma (Mood) • Social disruption from asthma (Social) • Concerns about health and future (Concerns) Changes in modified version are: i) change from a 5 point to 7 point Likert-type response scale ii) 2 items that had 2 indicator activities were separated to produce 4 items. Thus the modified version consists of 22 items overall in the 4 domain areas	Interviewer or self-administered 5 minutes Looks at affect of each item in preceding 3 months Response items 0-not at all to 4-very severely Computation of four asthma specific subscale scores (each subscale scored out of 10 - mean of all items associated with it multiplied by 2.5) Also overall score. Total scales score (out of 10) is the mean of all item scores multiplied by 2.5 Higher scores = more adverse impact on QOL	Responsive to change Reliable and relatively independent of subject characteristics (89) Moderate correlation between total score and other subjective measures of disease severity Discriminates between subjects who would be expected to differ in HRQOL A change of > 0.5 is the MCID in scores (90)	Floor effect (zero values- have fallen within the lowest quartile in all populations studied) Intended for use as outcome measure in clinical trials
St Georges Respiratory Questionnaire (91)	76 items divided into 3 domains: • Symptoms • Activity • Impacts	Telephone or face-to-face interview. 10 minutes Weighting each item and dividing the summed weights by the maximum possible weight and expressing result as a percentage provides respondents score Score 0 (best)-100% (worst)	Reproducible, valid and responsive in both asthma and COPD populations (91-94) MCID found to be 4 points (95, 96) Cross cultural and linguistic considerations are included	Limited coverage of psychological symptoms Most testing and development of questions was done in populations with COPD not asthma

Questionnaire	Description {Domains}	Administration format, time taken to complete and scoring	Advantages	Limitations
Living with Asthma Questionnaire (97)	68 items in 11 domains Items derived from 6 focus groups Major focus is psychological and social aspects of QOL	Self-administered 15 minutes 3 point response option Higher scores indicate more adverse impact on QOL	Main strength is the extensive qualitative research used in developing the questionnaire Correlation with generic Sickness Impact Profile was 0.66	Limited range of response options. Does not measure the physical symptoms of asthma Weak to moderate correlations with clinical measures of asthma (66, 86)
Asthma Impact Record Index (98)	4 domains: • Psychological • Physical activity • Physical symptoms • Social.	Self-administered Items are scores 0 to 1 and summed without weighting Higher scores indicate more adverse impact on QOL	Internally consistent Highly repeatable, intra-class correlation for total scale =0.97 Strongly correlated with other measures of QOL	Performance as a measure of change has not been reported. Longitudinal characteristics not established. Developed in France Distribution skewed towards lower scores

HRQOL: Health-related quality of life; QOL: Quality of life; COPD: chronic obstructive pulmonary disease; MCID: Minimal clinically important difference; AQLQ: Asthma Quality of Life Questionnaire.

2.4.3 Quality of life and asthma

From the perspective of an individual with asthma, measures of HRQOL represent the success of treatment in a more meaningful way than physiological end-points such as spirometric measures of lung function (99). Consequently, optimising HRQOL has become an important component of asthma management, and assessment of HRQOL is now regularly included as an outcome measure in clinical trials (54).

Regardless of age, adults with asthma have been shown to report their health status to be lower than those without asthma (100). Adams and colleagues (101) showed that standardised SF-36 scores adjusted for age, gender and social class were significantly lower in subjects with asthma drawn from a representative population survey consisting of both hospital-based and community-based subjects when compared to population norms. Combined physical component and mental component scores were comparable to those reported by individuals with other chronic diseases such as diabetes and arthritis.

Asthma has been associated with significant medical morbidity, and has also been reported to adversely affect an individual's personal and social life, their employment, finances and relationships (102). Asthma symptoms contributing most to this reduction in HRQOL are dyspnoea, morning symptoms, sleep disturbances and recurrent hospitalisations (103, 104). In an investigation of the determinants of HRQOL in asthma, dyspnoea, rather than measures of lung function, was found to be an independent determinant of HRQOL across all levels of asthma severity (45).

Good asthma control has been associated with improved HRQOL (52, 105). One study (106) showed that regardless of asthma severity, subjects with well controlled asthma had consistently better HRQOL (as measured with the AQLQ). This study, which was primarily evaluating a combination of salmaterol and fluticasone, showed that subjects with well controlled asthma at study entry went on to achieve greater improvements in their HRQOL than the subjects with poorly controlled asthma at study entry. However, the subjects who had poorly controlled asthma at study entry were able to achieve clinically meaningful improvements in their HRQOL with treatment (53).

2.4.4 Anxiety and depression in asthma

There is evidence that anxiety and depression are more common in adults with asthma than in the general population (103, 104, 107-110). The sensations that occur during acute episodes of asthma share many overlapping sensations to those associated with panic disorders. These symptoms include hyperventilation-induced dyspnoea, a sensation of 'being smothered' or choking, and increased anxiety. The prevalence of panic disorders in adults has been estimated to be 1-3% in community populations (111), but as high as 6-24% among individuals with asthma (107, 112-118).

Reasons postulated to explain an apparent increased risk for the development of panic disorder among individuals with asthma include the theory that such individuals generate fearful or catastrophic beliefs about their respiratory symptoms which in turn provoke panic attacks. Alternatively, a biological theory suggests that repetitive experiences of hypoxia and hypercapnia may sensitise the nervous system to over-react to subsequent episodes of hypoxia or hypercapnia. The fact that there is also an association between asthma severity and anxiety supports this notion. Figure 2.2 is adapted from a theoretical model (108) developed to describe the potential adverse impacts of co-morbid anxiety or depression in adults with asthma.

Both depression and anxiety have been associated with a decrease in the level of asthma control including a greater number of doctor's visits, the inability to carry out usual activities and more days during which asthma symptoms are present (119). Further, among individuals with asthma, there appears to be a dose-response relationship between the severity of depression and level of physical inactivity (119). A prospective cohort study of 59 adults who had been hospitalised for asthma showed that symptoms of depression were associated with an 11.4-fold increase (95% confidence intervals 2.2-58.2) in the possibility of poor adherence to therapy on discharge from hospital (120). There is substantial evidence to suggest that poor adherence to therapy leads to severe asthma exacerbations (121). Lavoie and colleagues (122) reported an association between the presence of depression or anxiety and poorer HRQOL in adults with asthma. In addition, these authors found a significant association between depression and poor asthma control.

Figure 2.2 Adverse impact of anxiety/depressive disorder and asthma co-morbidity

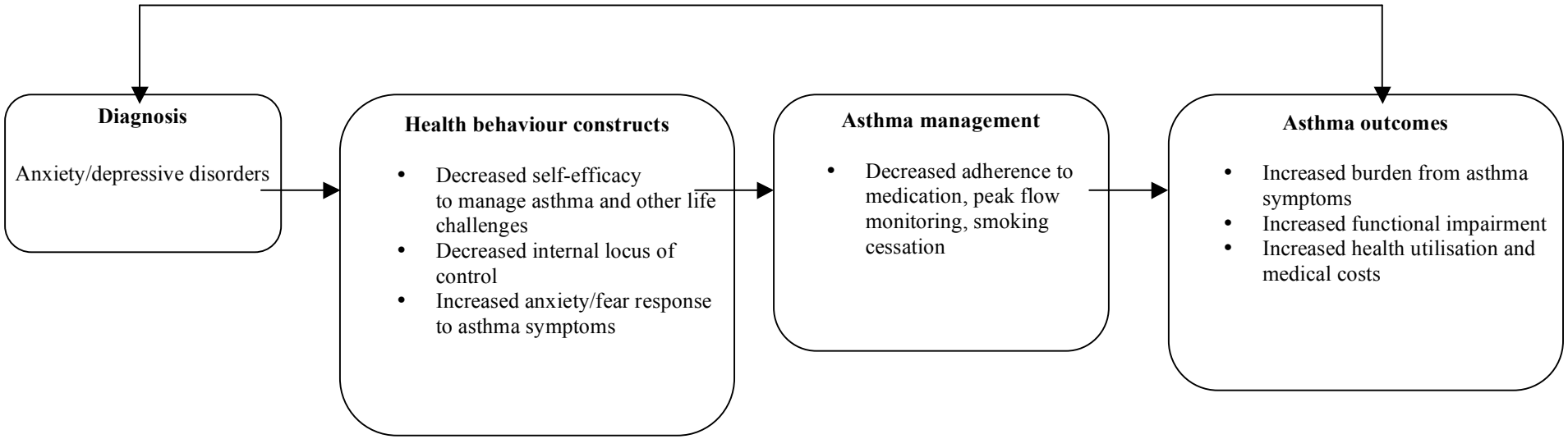


Figure adapted from Katon *et al* (108)

2.4.5 Measuring anxiety and depression in clinical trials

The Hospital Anxiety and Depression (HAD) Scale (123) is a reliable and valid tool for screening clinically significant anxiety and depression in patients attending a general medical clinic. This scale was specifically designed for use in non-psychiatric hospital departments and assesses an individual's mood state through questions about how the individual has felt during the past week. The scale is self-administered and takes 5 to 10 minutes to complete. It contains 14 multiple choice type questions, seven of which are oriented to the detection of anxiety and seven to the detection of depression. All items are based on psychological symptoms. Questions that might also relate to physical illness, such as the presence of dizziness or headaches, are eliminated. A score of more than 10 on either subscale is likely to indicate the presence of an anxiety or depressive disorder (123). The HAD Scale has been shown to reliably detect the severity of anxiety and depression and has demonstrated sensitivity to changes in mood state following pulmonary rehabilitation in subjects with COPD (124, 125).

2.4.6 Dyspnoea

Dyspnoea is the term used to describe the "subjective experience of breathing discomfort that consists of qualitatively distinct sensations that vary in intensity" (126). It has been suggested that the sensation of dyspnoea is related to the activation of sensory systems that are involved with respiration, which in turn relay information to the central nervous system where processing takes place. This information in conjunction with interactions from physiological, social, cognitive and environmental factors can induce secondary behavioural and physiological responses (126).

In COPD, dyspnoea is primarily triggered by exertion due to limiting physiological processes and alterations in lung mechanics (126, 127), and the intensity of dyspnoea is shown to increase with increases in ventilation (127). In asthma, dyspnoea can be triggered by a number of environmental allergens or by exertion (126). The presence of inflammatory mediators such as those present during acute episodes of asthma can lead to an increased sensitivity to respiratory sensations. This in turn contributes to a disproportionate drive to breathe and may culminate in the presence of

hyperventilation syndrome (1, 126). Dyspnoea often limits an individual's level of physical activity and leads to a sedentary lifestyle which in turn decreases fitness and exercise tolerance (128).

The intensity of dyspnoea in adults with asthma has been shown to loosely correlate with the magnitude of expiratory flow limitation as measured by a fall in FEV_1 (129) during metacholine-induced bronchoconstriction. More importantly, dyspnoea is strongly and directly correlated with the development of dynamic lung hyperinflation that occurs because of the increase in work of breathing with this challenge (130-132). Tidal expiratory flow limitation and dynamic hyperinflation during exercise have been reported in stable asthmatics without evidence of exercise-induced bronchoconstriction. The presence of such flow limitation and hyperinflation can contribute to a reduction in exercise capacity (133).

Abnormal breathing patterns are often apparent during hyperventilation and may result in breathlessness, light-headedness, paresthesia and anxiety. These symptoms can occur in all grades of asthma severity and may be related to the increased incidence of anxiety and depression in asthmatic patients (134, 135).

Some individuals with asthma, particularly those with a history of near-fatal asthma and chronic asthmatics whose airway pathology is characterised by inflammation and eosinophilia, have a blunted perception of dyspnoea and report less symptoms than asthmatic subjects whose obstruction is transient and more readily reversible. Such individuals are considered to be poor perceivers of their symptoms (1). This decreased ability to perceive an increase in mechanical load or abnormal gas exchange may be due to temporal adaptations and physiological changes to the feedback mechanism. This in turn can make an individual with asthma more vulnerable to a fatal attack (136-139).

The term dyspnoea is used to characterise a range of qualitatively distinct sensations. Simon and co-workers (140) compiled a list of 19 descriptors of dyspnoea that were experienced by individuals with a variety of lung and cardiac conditions. Examples of some of the descriptors for dyspnoea included "My breathing requires effort", "My chest feels tight", "My chest is constricted" and "I feel out of breath". This list was refined and modified to 15 descriptors and use of this list of descriptors has been validated and shown to have acceptable test-retest reliability (141, 142).

Moy and colleagues (143) showed that the qualitative descriptors of breathlessness changed in eight subjects with mild asthma in response to mild bronchoconstriction through metacholine broncho-provocation versus breathing against an external resistive load which provided resistance on both inspiration and expiration. For example, the language of chest tightness or constriction was chosen to describe dyspnoea in 92% of 26 trials involving a methacholine challenge causing bronchoconstriction, compared to only 3% of 72 trials which required breathing against an external resistance. When breathing against an external resistance, the responses chosen to describe dyspnoea related to the sensation of an increase in "work" and "effort".

2.4.7 The measurement of dyspnoea

A number of instruments are available to assess dyspnoea including structured interviews, self-report questionnaires and visual analogue scales. However few of these are suitable for single point measurement during an exercise test or exercise training (144). The most widely used tools to measure the intensity of dyspnoea during exercise are the Visual Analogue Scale (VAS) and the modified Borg Category Ratio Scale. The VAS requires a subject to place a mark on a 10cm vertical or horizontal line to indicate their level of breathlessness. Although this technique has been validated (145) it lacks test-retest reliability when repeat testing occurs weeks apart, thus questions remain about the reliability of VAS dyspnoea rating across different dyspnoea-inducing exercise tasks (144).

The Category Ratio Scale developed by Borg (1982) (146) is a scale which ranges from 0 (no breathlessness) to 10 (maximum breathlessness) and is a useful indicator of breathlessness because of its relative simplicity (146). This scale was adapted from an original ordinal scale which ranged from 6 to 20 that was developed by Borg in 1970 (147) to measure perceived exertion. In general, scores obtained using the category ratio scale are reliable over short periods of time, are easy to collect, sensitive to change and highly reproducible at peak exercise intensities (148). The recommended MCID for the Borg Dyspnoea Scale is 1-unit. This is based on a retrospective review of a number of published trials which evaluated the response to

an exercise training program. The MCID was calculated using a distribution-based approach based on the effect size (149).

At submaximal exercise intensities (i.e. exercise below peak oxygen uptake) Belman and colleagues (150), assessed the reproducibility of the Borg scale ratings of dyspnoea in nine subjects with COPD, and found that over a 10 day period scores decreased significantly with successive treadmill walking tests. These authors concluded that because oxygen uptake (VO_2), ventilation (VE), heart rate (HR) and tidal volume (VT) stabilised after only one or two practise attempts, the proportionally greater fall in Borg ratings with repetitive testing was independent of a true physiological effect. Because habituation to the task of treadmill walking was complete by the second or third test in the study, the authors proposed that the serial improvement in dyspnoea scores may have resulted from desensitisation to the sensation of dyspnoea, and thus desensitisation may play a role in the improvement of individuals with COPD with exercise training (150).

2.4.8 Measuring the sensation of chest tightness in asthma

To date, a scale does not exist that quantifies the intensity of chest tightness experienced during physical activity in adults with asthma. In such individuals the sensation of chest tightness is often present, but qualitatively distinct from that of an increased work of breathing (151). For this reason it is important to quantify the separate sensations of 'breathlessness' and 'chest tightness' when assessing functional exercise capacity in adults with FAOA during a clinical trial.

A review of the literature revealed one scale that has been used in an attempt to gain an understanding of the subjective feelings surrounding the sensation of dyspnoea in individuals with asthma. This scale includes language descriptors relating to chest tightness used by asthmatics (140, 141). Frequency of chest tightness symptoms were assessed in another study conducted by Teeter and colleagues (152) with a scale that incorporated a 5 point whole integer scoring system (0- no symptoms, to 4- constant symptoms). This study rated the frequency of a number of asthma symptoms including chest tightness, cough, dyspnoea, wheeze, sputum production and nocturnal wakening in 67 adults with chronic asthma, to characterise the relationship between symptoms and degree of airway obstruction as determined by FEV_1. The

time period over which the symptoms were monitored was not specified, however, within the study and therefore the usefulness of using this scale for individuals with FAOA during physical activity is not certain (152).

To date, the only study reporting a measure of the intensity of chest tightness symptoms during exercise was undertaken in individuals with cystic fibrosis (153). This study utilised a VAS to measure the intensity of chest tightness following inhalation of hypertonic nebulised colistin.

Since the Borg Category Ratio Scale (146) has shown to be reliable over short time periods, sensitive to change and reproducible at peak exercise intensities, it could be argued that this scale may be suitably adapted to measure chest tightness in individuals with FAOA due to the close relationship chest tightness has with breathlessness in those who have asthma. The Borg Category Ratio Scale was utilized in the randomized controlled trial conducted in this thesis to measure chest tightness based on this argument (chapter 3).

2.5 Functional exercise capacity in adults with asthma

Research suggests that the risk behaviours of physical inactivity in addition to smoking and obesity have profound effects on asthma severity and these effects are compounded when multiple adverse behaviours exist (154). Several studies have reported lower levels of aerobic fitness in asthmatic adults in comparison to their healthy peers (155). A study of 44 subjects with mild to moderate asthma matched with 64 healthy control subjects showed that the asthmatic subjects had a significantly lower aerobic capacity as measured by peak oxygen uptake (VO_{2peak}), anaerobic threshold and oxygen pulse compared to the healthy controls. Consistent with this finding, young asthmatic males conscripted to military service have been reported to display poorer physical fitness than those without asthma as measured by a 12 minute running test (156).

Intensity of habitual exercise has also been reported to be lower in asthmatic than non-asthmatic subjects. In a US population-based study where, after adjusting for age, respondents with current asthma demonstrated on average their estimated energy expenditure from leisure time physical activity was 206 kilocalories lower than respondents with former asthma, and 91 kcal/week lower than respondents who had

never had asthma ($p<0.001$) (157). In contrast, a study which recruited 27 adults with stable mild to moderate asthma found levels of aerobic fitness were comparable to non asthmatics of average fitness levels measured with a maximal treadmill test (158).

In the study conducted by Garfinkel *et al* (158), a self-complete questionnaire was also administered which was based on a revised version of the Canadian Standardized Test of Fitness Lifestyle Questionnaire. Results from this questionnaire suggested that asthmatics perceive their disease as the limiting factor to improving aerobic fitness. The three main reasons for not exercising more were lack of time (64%), breathlessness/wheezing (52%) and lack of energy (44%). In addition, factors which subjects thought would assist them to increase their exercise levels were better asthma control (64%), more time for exercise (56%), more energy (44%) and people to exercise with (44%).

Potential causes of reduced exercise capacity in adults with chronic persistent asthma include deconditioning as a result of a sedentary lifestyle, exertional dyspnoea, peripheral muscle impairment arising from prolonged corticosteroid usage, decreased lean body mass and fatigue, low self-efficacy and fear, sleep disturbances, psychological impairments such as depression and anxiety and a developed aversion to exercise due to inappropriate restriction when young and a fear of developing asthma symptoms during exercise (121, 159, 160).

2.5.1 Measurement of functional exercise capacity

An objective measure of functional exercise capacity should assess the level of disability experienced by an individual with chronic respiratory disease. Exercise tests are employed in this manner to quantify exercise capacity (161, 162). The determination of baseline exercise capacity enables the prescription of an individualised rehabilitation programme aimed at improving exercise tolerance (7). Regular exercise testing is a useful way to monitor change in an individual's exercise capacity, and such data are used as outcome measures of interventions including exercise training (163).

2.5.2 Laboratory-based exercise tests

The gold standard for determination of exercise capacity is the measurement of peak oxygen uptake (VO_{2peak}) which is usually obtained during a maximal exercise test conducted in a laboratory setting. In this environment, measurements of oxygen saturation (SpO_2), HR, work rate, VE, VO_2 and expired carbon dioxide (VCO_2) can be obtained. Arterial blood samples may also be collected and concentrations of inspired and expired gases can be accurately monitored by breath by breath gas analysis (161, 164).

Laboratory tests are generally administered only once, due to cost and time constraints and because the measurement of exercise capacity through VO_{2peak} is reported to be reliable after just one laboratory test (163). Testing within the laboratory requires sophisticated equipment and trained personnel. The equipment enables monitoring of the patient throughout the exercise test and the identification of the pathophysiological limitations to exercise (163, 164). Laboratory tests are commonly performed using a cycle ergometer or treadmill. Conventionally for the assessment of patients with known or suspected respiratory disease a cycle ergometer is more commonly used, but in cardiac patients a treadmill protocol is employed.

Treadmill tests involve incremental increases in workload by progressively increasing a combination of speed and grade (slope). Balke's protocol, which keeps speed constant at 5-6 kilometers per hour (km/hr) and progressively increases the slope by 1-2% per minute, is an effective and simple testing procedure; this can be modified by using a slower speed for individuals who are unable to tolerate such a high walking speed. This method of increasing workload avoids the problem experienced by some individuals, for example the elderly, being unable to maintain fast walking speeds (164, 165).

Exercise testing performed on a stationary cycle ergometer provides a stable platform for metabolic measurement. It allows easy monitoring of the patient, accurate determination of the workload and enables the patient's body weight to be supported (166, 167). Unlike the treadmill, cycle ergometers provide easily and accurately quantifiable work rates, and at submaximal work rates yield VO_2 values that are less variable than those obtained from a treadmill test (164).

The standard protocols used in exercise tests on a cycle ergometer to assist in the diagnosis of respiratory diseases involve increasing work rate by a specified amount each minute in a step protocol or averaging the increase in work rate over each minute in a ramp protocol (168, 169). Between 8 and 15 minutes of exercise is considered as the ideal duration for a maximal exercise test. In normal subjects, exercising for less than 8 minutes or more than 15 minutes does not produce the typical plateau in VO_2 seen when circulatory factors limit exercise capacity (164).

2.5.3 Field-based exercise tests

Because laboratory-based tests are expensive and often difficult to access, field walking tests have become an important part of the assessment of functional exercise capacity in adults with chronic respiratory disease (170). Field walking tests are easy to conduct, require little preparation and are less expensive than laboratory-based tests (171, 172). Distances walked during field walking tests are reliable after one familiarisation test (171, 173), and the outcome measures from these tests such as distance walked, peak dyspnoea scores and the degree of oxygen desaturation have been used to indicate the level of disability, to prescribe the intensity of a walking programme and to assess outcome following rehabilitation (6, 174, 175). The more common field walking tests used in older adults with respiratory disease are the 6 minute walk test (6MWT), the 10m incremental shuttle walking test (ISWT) and the endurance shuttle walking test (ESWT).

2.5.3.1 The 6 minute walk test

The 6MWT was derived from the 12 minute walk test (12MWT) that was developed to estimate VO_{2peak} in patients with chronic bronchitis (173). The 12MWT was shortened to 6 minutes for disabled populations, as it was shown by Butland *et al* (177) that a test of 6 minutes duration correlated well with the 12MWT (r=0.95). Six minutes has become the most widely accepted length of time for this test as it is better tolerated by patients and usually allows multiple tests to be performed on the same day in the same individual (172). At present, the 6MWT is the most commonly used, non-externally paced field assessment of functional exercise capacity in individuals with COPD (6, 175). The main outcome of this test is the distance walked in the 6 minutes (6MWD).

The testing procedure for the 6MWT requires the subject to cover as much distance as possible in 6 minutes. Stopping to rest is permitted, and subjects must continue to walk again as soon as they are able. Self-selection of the pace at which a subject will walk may consequently result in a sub-maximal performance. The extent to which the subject's cardiopulmonary system is stressed maximally is dependent on his/her level of motivation and whether or not they are encouraged throughout the test (171). Therefore, a 6MWT protocol should allow for a potential learning effect and include standardised instructions and encouragement with the aim of overcoming poor motivation as a potential source of sub-maximal performance (178-181). Standardised encouragement provided throughout the test has been shown to improve 6MWD by 30.5m in 43 subjects with COPD or chronic heart failure or both COPD and chronic heart failure (179).

Comparisons between the distance walked in the 6MWT with measures of lung function and measures derived from a maximal exercise test (such as VO_{2peak} and maximal workload) and subjective measures of functional status have been undertaken in patients with COPD in an attempt to validate the 6MWT. Functional status questionnaires have been shown to correlate more closely to the 6MWT than VO_{2peak} or spirometric measurements (172).

A moderately strong correlation has been found between the distance walked and values obtained from the St George's Respiratory Questionnaire ($r=0.59$, $p<0.0001$) (91). Concurrent validity has also been assessed between the 6MWT and self rating scales such as the Oxygen Cost Diagram ($r=0.68$, $p<0.001$), structured questionnaires regarding patient symptoms such as the Baseline Dyspnoea Index ($r=0.59$), the Rand Instrument ($r=0.31$) and the Chronic Respiratory Disease Questionnaire ($r=0.52$, $p=0.01$) (182, 183). All of these validation studies have been undertaken in subjects who have COPD.

Where coefficients of variation have been calculated for the 6MWT, excellent reproducibility has been demonstrated with variability of 8-9% being reported (184). Familiarisation with the 6MWT procedure significantly increases 6MWD, thus the effect of learning needs to be taken into account when measuring distance in the 6MWT (184, 185). Knox *et al* (186) showed that a 33% improvement occurred over 12 walks of 5 minutes duration in a 3 day period. Half of this improvement occurred between the first and third walk. In comparison an 8.5% improvement occurred when

the tests were carried out over 4 weeks. Thus it appears that one practice walk is necessary to achieve acceptable reproducibility in 6MWD so that changes in performance can be attributed to an intervention or change in disease status rather than to the effects of learning in subjects with COPD (173, 185).

To quantify the magnitude of an individual's disability, 6MWD can be expressed as a percentage of predicted based on reference equations that have been generated in healthy populations (187). Published regression equations can give a 6MWD that varies by up to 175m for the same individual. Reasons for the disparity include variations in walking speeds of individuals from different geographical regions (188, 189) and differences in test protocol (187). Therefore the best regression equation selected provide a valid estimate of the impact of a condition on 6MWD is one which has been generated at the same facility, using the same protocol, and in the population from which the patients arise (187).

The 6MWT is considered a submaximal exercise test in individuals with COPD (178), although a number of studies comparing physiological parameters measured in a laboratory-based test and the 6MWT have shown that peak HR, dyspnoea (181) and VO_{2peak} (190) are similar between tests in subjects who have moderate to severe COPD. Further, 6MWD has a moderate to strong correlation with VO_{2peak} ($r=0.73$, $p<0.001$) (181) and maximum work rate ($r=0.75$, $p<0.001$) in individuals with moderate to severe COPD (191). Thus field walking tests can challenge adults with moderate to severe COPD to a similar level of cardiovascular and respiratory stress as laboratory-based tests (181, 192). Generally the relationship between 6MWD and VO_{2peak} is strongest in adults who have more severe functional limitation (187).

In a recent study, a change of about 35m has been calculated as the change in 6MWD that represents an important effect following treatment for patients with moderate to severe COPD. This corresponds to a 10% change from a baseline 6MWD of 350m (193). This study involved data from nine trials which enrolled COPD subjects with a spectrum of disease severity and measured 6MWD at baseline and following participation in pulmonary rehabilitation programmes (193). A change of 54m had previously been widely reported as the minimal clinically important difference for the 6MWT (194). This minimal clinically important difference was based on one cross-sectional study of 112 COPD patients attending pulmonary rehabilitation. The methodological approach relied on patient comparisons of how they judged their own

walking ability relative to others and the correlations of 6MWD with self-reported categorical scale anchors (194).

2.5.3.2 The 10m incremental and endurance shuttle walking tests

The 10m ISWT is a standardised externally paced incremental field test developed for individuals with COPD. Subjects are required to walk around a 10m course and walking speed is regulated by pre-recorded auditory signals. There are 12 levels within the ISWT. The test starts with a walking speed of 0.5m/s in level one and the pace at which the subject walks is progressively increased by 0.17m/s each minute (180).

Singh *et al* (195) showed a strong relationship (r=0.88) between VO_{2peak} measured on a treadmill and distance walked in the ISWT in 19 subjects with moderate to severe COPD. The treadmill test used a modified Balke protocol which involved increasing the gradient by 2.5% every two minutes while the subjects maintained a constant speed.

Good reproducibility of the ISWT has been demonstrated by Singh and co-workers (180) in 10 subjects with COPD (mean [range] age 63 [52-74] years, FEV_1 1.10 [0.60-2.10]l) with the authors concluding reproducible results could be attained with one practice walk. Good reproducibility has also been demonstrated by Eiser and colleagues (173). In adults with moderate to severe COPD, similar peak HRs and dyspnoea scores were elicited in both a 6MWT using standardised encouragement and an ISWT, and there was a strong correlation shown between the distances walked on the two tests (181).

The ESWT was developed by Revill and co-workers (196) to allow a standardised assessment of submaximal exercise capacity without the need for laboratory-based equipment. However the use of this test is limited because there is a need for the subject to have had a prior maximal exercise test (i.e. the ISWT) to set the workload for the endurance test. The workload for the ESWT is calculated at a percentage (i.e. 85%) of the VO_{2peak} which is estimated from the performance of a prior ISWT.

2.6 The effects of exercise training in adults with asthma

There are many health benefits of exercise. Regular moderate intensity physical activity reduces the risk of coronary heart disease, osteoporosis, colon cancer and type II diabetes mellitus. It can also guard against the risks associated with being overweight or obese, improve mood and reduce anxiety and depression. Physiologically, endurance trained individuals typically demonstrate 10%-50% higher aerobic capacity than their sedentary peers (197, 198).

There is evidence to suggest that regular exercise plays an important role in optimizing asthma management (158, 199, 200). Following an improvement in cardiopulmonary fitness, ventilation is reduced at low to moderate exercise intensities; this may increase the threshold before asthma symptoms are triggered on exertion (199). A study by Hallstrand and colleagues (201) showed that a 10 week aerobic exercise training programme improved maximal voluntary ventilation and decreased ventilation at a given submaximal workload and this was associated with a decreased dyspnoea index and ventilatory equivalent in the five subjects who had mild asthma and five normal control subjects enrolled in the study. Improvements in peripheral muscle function and neuromuscular co-ordination with regular exercise can also lead to an improved ability to perform activities of daily living.

Physiological responses during exercise in an asthmatic with fully reversible lung function are the same as in a healthy individual without asthma. That is, the pattern of oxygen uptake, oxygen pulse, minute ventilation, work capacity, heart rate responses and blood pressure with exercise are similar between the two groups (202).

At present, there are few published studies that have evaluated exercise training programmes in older adults with asthma. The majority of these studies have not included a control group and the frequency, intensity and modes of exercise evaluated have varied widely (202). A Cochrane review (203) on the efficacy and effectiveness of exercise training for asthma concluded that exercise training improved cardiopulmonary fitness, with improvements obtained in VO_{2peak}, work capacity and HRmax, and this occurred in the absence of any changes in lung function. This review included randomised controlled trials performed in subjects aged 8 years or older, and training sessions that lasted at least 20 minutes, twice a week for a minimum of 4 weeks. Of the 13 studies included in the review, only two

carried out the intervention in an adult cohort. One study included adults aged 16-40 years who had mild to moderate asthma (200) and the other study involved subjects with an age range 28-33 years with asthma, recruited through media solicitation (204). A limitation of all 13 studies was the lack of QOL as an outcome measure (203).

To date, only two studies have evaluated the effects of a supervised pulmonary rehabilitation programme in middle-aged and older adults with asthma. Both of these were carried out in Europe and involved intensive multidisciplinary programmes consisting of exercise, education and psychosocial interventions implemented over a 3 month period in a mixed cohort of COPD and asthma subjects (205, 206). In both studies, subjects who had asthma showed improvements in exercise capacity (205, 206).

The study by Cox *et al* (206) involved 27 subjects aged 43.2±13.1 years with asthma randomised to a rehabilitation group and 26 subjects aged 44.3± 13.7 years with asthma in the control group. The rehabilitation group participated in a programme that incorporated team and individual sports, swimming, walking, cycling, skill exercises, co-ordination and relaxation exercises. Each session took 4-5 hours per day for a total of 38 hours per week for a period of 3 months. Results were combined for the asthma and COPD subjects; therefore it is not possible to determine whether the benefits were of a similar magnitude in the two subject cohorts, however improvements in oxygen uptake and endurance time in a cycle ergometer test were observed in the rehabilitation group.

The intervention studied by Cambach *et al* (205) involved 23 subjects with asthma in a randomised controlled trial with a cross-over design. Rehabilitation consisted of pharmaceutical therapy, breathing retraining, airway clearance techniques, upper and lower extremity exercise training 3 times a week for 90 minutes, recreational activities such as swimming, cycling and hockey once a week for 45 minutes, education and relaxation sessions for 45 minutes once a week. The asthmatics involved in this study had an FEV_1 of 86±18% predicted and were aged 46±14 years. The study showed improved 6MWD and endurance time with cycling post rehabilitation. Intensive training programmes such as these two described above would not be feasible within clinical practice in Australia. Given the multi-

component nature of these studies it is difficult to determine the relative benefits of each of the programme components.

To date only one study has examined the long-term effectiveness of a pulmonary rehabilitation programme in adults with asthma. Foglio *et al* (207) investigated the long-term effectiveness (1 year post training) of a pulmonary rehabilitation programme in adults with chronic asthma and COPD. The 35 asthmatic subjects (age 56±10 years) had a mean FEV_1 of 64±16% predicted, and FEV_1/FVC of 52±9%. These subjects participated in three sessions (each of 3 hours duration) every week. The sessions comprised education, a nutritional programme and an exercise programme for 8±10 weeks. The study showed a significant improvement in 6MWD from 471±61m to 508±56m ($p<0.05$) immediately following the intervention and also at one year post-discharge (485±60m). The total, activity, and impact scores of the SGRQ were also significantly improved immediately post-intervention and 1 year later. This study showed that at baseline the asthmatic cohort had a similar impairment in QOL to the COPD subjects. Although the study did not have a control group, the aim of the study was not to assess the clinical benefits of a pulmonary rehabilitation programme in COPD and asthma, but rather to ascertain if long-term benefits could be observed in asthmatics and patients with COPD (207).

Many health benefits can be derived from exercise in asthmatic populations. However, paradoxically, physical exertion can also be a potent stimulus for asthma symptoms if asthma control is suboptimal (159). This is because the increase in ventilation associated with exercise can lead to changes in airway osmolarity that causes smooth muscle constriction in susceptible individuals, i.e. those with heightened bronchial reactivity (208, 209).

This exercise-induced asthma (EIA) is a reversible airway obstruction which can occur during or after exertion. Individuals may exhibit an immediate response after 6 to 8 minutes of vigorous exercise (over and above 80% of the predicted maximum heart rate; HRmax) or, in about 30% of cases, a late response that occurs 6 to 8 hours after the onset of the exercise (210). Symptoms include cough, wheeze, dyspnoea and/or chest tightness. Types of activities that are more likely to provoke EIA are aerobic in nature and require a high minute ventilation such as long distance running and soccer or activities associated with cool and dry climatic conditions such as cross-country skiing. Exercise which involves short bursts of intensity and lower

minute ventilation such as volleyball and tennis, or sports associated with warm and humid climatic conditions such as swimming, are less likely to precipitate EIA (211). The prevalence of EIA in young adults with chronic asthma has been reported to be between 40% and 90% (210, 211). The prevalence of EIA in middle-aged and older adults has not been reported.

2.7 The effects of exercise training in adults with chronic obstructive pulmonary disease

Exercise training programmes are widely accepted as effective treatment strategies for individuals with COPD. In this population, exercise training is recognised to be the mandatory component of a pulmonary rehabilitation programme. Exercise training alone or in combination with education has been shown to significantly improve exercise tolerance, decrease symptoms of dyspnoea and fatigue, reduce disability and handicap, improve QOL and decrease hospital utilization (6, 26, 125, 212, 213). According to the GOLD executive summary, COPD patients at all stages of disease severity benefit from exercise training, with improvements seen in exercise tolerance, and symptoms of dyspnoea and fatigue (11). Individuals need to be motivated to engage in rehabilitation that is demanding in terms of their time as well as physical and psychological investment especially in the case of outpatient programmes (11, 174, 214).

Exercise has been shown to improve fitness of patients with mild COPD, but it has not been shown conclusively to improve QOL or dyspnoea, or have any effect on long-term progression of the disease (215). A study by Babb *et al* (216) showed that in comparison to nine control subjects with normal pulmonary function, 12 subjects who had mild to moderate airflow limitation (FEV_1 72% predicted, FEV_1/FVC% 58%) showed significantly reduced maximal exercise capacity (69% predicted VO_{2peak}), versus the controls (104% predicted VO_{2peak}). However, peak HR and the ratio of maximum expired minute ventilation to maximum voluntary ventilation (VE/MVV) were not significantly different between groups. One interesting observation in this study was that although resting end expiratory lung volumes (EELV) were similar between the groups, at maximal exercise, EELV reduced to 45% of total lung capacity (TLC) in controls, but increased to 58% of TLC in those

with airflow limitation, suggesting dynamic hyperinflation played an important role in limiting exercise capacity even in those with mild lung impairment (216).

In severe COPD, exercise training improves submaximal exercise tolerance in the absence of an increase in VO_{2peak}, and the changes are associated with an increase in inspiratory capacity, improved VE and a significant reduction in breathing frequency, which in turn leads to a reduction in dynamic hyperinflation and contributes to profound improvements in submaximal exercise endurance (217).

One review suggests that adults with asthma characterised by severe or very severe airflow obstruction and with poor or no reversibility should be included in programmes for COPD and that their rehabilitation should be similar to that recommended for COPD patients (202). It is reasonable, however, that those with chronic severe asthma, particularly those with FAOA, would benefit equally from a supervised exercise training programme as an individual with COPD (218).

For adults who have FAOA, that is a fixed airways component in relation to their underlying diagnosis of asthma, the benefits of exercise training are less clear than in adults with a diagnosis of smoking-related COPD, because this patient cohort has not been studied in isolation. Despite the suggestion that when treated appropriately, patients with asthma are not ventilatory limited and therefore can tolerate high intensity training (218), one would assume that the permanent airways obstruction demonstrated in adults with FAOA would result in a comparable ventilatory limitation on exercise as observed in those with mild or moderate COPD.

2.7.1 Factors leading to reduced exercise capacity in chronic obstructive pulmonary disease

A number of mechanisms can operate in combination to bring about a reduction in exercise capacity in individuals with COPD. The factors which determine peripheral muscle function such as oxygen delivery and the presence of peripheral muscle weakness are just as important as variables related to lung mechanics. The contribution of a fall in SpO_2 during exercise as a limiting factor is uncertain. Oxygen desaturation can worsen post-bronchodilator yet a patient may be able to undertake more exercise than prior to administration of the bronchodilator. Although supplementary oxygen decreases the magnitude of desaturation, the improvement in

exercise performance is more a reflection of the reduction in minute ventilation and reduced lactate production (219).

Serres *et al* (220) have shown that skeletal muscle abnormalities are present in those with COPD, often a result of a sedentary lifestyle, which reduce the aerobic capacity of peripheral muscles. The subsequent increase in glycolytic activity at a given load then results in higher lactate levels and this in turn leads to excessive hyperventilation and dyspnoea. Malnutrition is seen in COPD, with a third or more individuals with the condition affected by excessive weight loss and reduced fat free mass, which also appear to be determinants of reduced exercise capacity (220). Peripheral and respiratory muscle weakness can also contribute to limited exercise capacity (221, 222).

2.8 Components of exercise training programmes

To be considered successful, an exercise training programme should result in clinically meaningful improvements. The most meaningful improvements from an individual's perspective relate to functional exercise capacity and QOL (223). Exercise training programmes for asthma or COPD described in the literature vary with respect to the setting (in-patient, out-patient in either a hospital or community facility, or home), the frequency (number of session each week), the modalities of exercise (endurance, strength, upper or lower limb exercises), intensity and programme duration. However within the American Thoracic Society/European Respiratory Society official statement on pulmonary rehabilitation, there is the acknowledgement that "there are no formal evidence-based guidelines regarding the exercise prescription or response to exercise training for patients with respiratory disorders other than COPD" (218).

2.8.1 Safety considerations

Safety is an important consideration in exercise prescription (218). Potentially the most important safety consideration in the exercising of older adults with asthma is for any adult with a diagnosis of EIA to pre-medicate with short-acting beta agonists

or cromolyn sodium, and follow this pre-medication with an extended warm-up (199, 224).

2.8.2 Modalities of exercise

Lower limb endurance exercise is considered a standard component of an exercise training programme for people with chronic lung disease, with strong evidence that lower extremity exercise training at high exercise intensity produces greater physiological benefits than low intensity training in patients with COPD (225). Evidence supports the addition of unsupported upper limb endurance exercise in adults with COPD, which both improves upper limb exercise capacity and reduces VE and VO_2 (225). The effects of unsupported and supported arm exercises have not been assessed in asthmatic subjects.

The use of high resistance and low repetition strengthening exercise increases muscle strength, while a low resistance but high repetition programme increases endurance (226). The addition of resistance training may offer the opportunity to strengthen individual muscle groups in adults with asthma, and there is level 1A evidence that adding strength training to a programme of pulmonary rehabilitation increases muscle strength and muscle mass in COPD (200, 225). Whether the addition of resistance training translates to additional improvements in QOL and functional exercise capacity in adults with asthma remains unknown.

The majority of pulmonary rehabilitation programmes are land-based. Water-based exercise has specifically been recommended in asthmatic populations because EIA is less likely to be triggered by the moist, humid environment. The literature suggests, however, that even when the inspired air is dried, swimming itself causes less asthma symptoms than land-based endurance exercise, this finding is inexplicable because whole-body prone submersion in water does not seem to affect airway hyperactivity, and a person's body posture on land has no meaningful effect on the severity of bronchoconstriction (227). Research to date also shows that swimming itself can potentially worsen asthma and bronchial hyper-reactivity due to the effects of long-term exposure to chlorine, and the possible transmission of infection through the water. It is possible that these adverse effects might outweigh the benefits of

swimming being less likely to provoke EIA than land-based exercise once the disease is present (227).

2.8.3 Frequency and duration of exercise programmes

Formal exercise programmes as short as 4 weeks and as long as 18 months have previously been described, although most programmes range between 6 and 12 weeks in duration. There is level 1A evidence that 6 to 12 weeks of rehabilitation produces benefits in several outcomes in adults with COPD which decline gradually over 12 to 18 months following cessation of the programme (225). Pulmonary rehabilitation for individuals with COPD should involve at least an accumulation of 30 minutes of aerobic exercise on 3 days or more a week for at least 6 to 8 weeks to induce meaningful improvements in functional exercise capacity and QOL (218, 223). Most studies of exercise training in asthma have used three to five sessions each week as the frequency of training in their programmes (224, 228).

2.8.4 Intensity of exercise

Physiological improvements in functional exercise capacity have consistently been demonstrated following exercise training programmes which incorporate supervision of participants, prescription of moderate to high intensity training loads and the regular progression of exercise intensity (218). Both intensity of exercise and the load duration affect the magnitude of the training effect. Training at higher intensities generally demonstrates the greatest physiological improvements in exercise capacity in terms of reduced lactate, VE, HR and VO_2 in COPD (225). A study by Casaburi *et al* (229) which involved COPD subjects training on cycle ergometers at either low [30 watts per minute, (W/min)] or high (71 W/min) intensities showed the higher intensity group demonstrated greater improvements in minute ventilation, oxygen uptake, heart rate and reduced lactate for a constant work rate test after training as compared with before training.

To set the intensity of exercise variables such as external work rate, VO_2, HR, dyspnoea and ratings of perceived exertion (RPE) have been used. For normal subjects, a percentage of predicted HRmax is often used and a commonly prescribed intensity range is between 60% - 85% of HRmax (223). For older adults, care needs

to be taken when setting exercise intensity and symptoms need to be well monitored if intensity is increased, as often elderly patients in an exercise programme are not capable of exercising within the commonly prescribed ranges of intensity and duration. High intensity exercise in some older adults may cause musculoskeletal injury (223).

The traditional approach to exercise prescription involves using a percentage of predicted HRmax. However, measured HR does not bear the same relationship to exercise intensity in COPD subjects as seen in normal subjects. Predictions of maximum HRs are also subject to errors with a standard deviation of 10 beats per minute recognised in cohorts of subjects of the same age. Therefore using this method to prescribe exercise intensity may not be the most appropriate for individuals with chronic lung disease (223).

The most commonly used scale for measuring perceived exertion is the Borg RPE scale which ranges from 6-20. Ratings on this scale increase linearly with exercise intensity, HR and VO_2. On this scale a maximum cardiovascular response is associated with an RPE of 16-18 and metabolic threshold occurs around 12-14 (230). When this scale is to be used for targeting intensity, the desired threshold should be around 12 with an upper limit of 16 (230).

2.8.5 Advantages of supervision and group exercise

The advantages of supervised exercise training programmes for older adults are that exercises can be prescribed on an individual basis, symptoms with exercise are monitored and intensity is progressed within symptom tolerance. Individuals can benefit from the psychosocial support of exercising in a group, and the instruction and supervision of using asthma medications before and during exercise (231). Individuals can also be encouraged to recommence exercising following an exacerbation of asthma that enforces a degree of inactivity (199). Potentially, older adults with chronic asthma may demonstrate a fear of developing asthma symptoms during exercise, particularly when exercising alone and at home, and thus may benefit from the support of a supervised exercise training programme.

Part 3

2.9 Burden of asthma in the community, with a focus on the management of respiratory disease in Western Australia

Part 2 of this literature review describes the burden of asthma on an individual. This section expands on the concept of burden to examine the disease burden on the community. Included in this section is a review of the health care burden in relation to hospital utilisation in WA, and as such a general overview on the current health structure for the provision of services for adults with asthma is provided. In addition, terms which relate to remoteness and health are introduced, given that currently a striking gap remains in the characterization of asthma in middle-aged and older adults on a regional level within WA. Investigation of the spatial distribution of asthma and COPD cases and patient demographics in the state could assist in the alignment of asthma programmes more closely with areas of need. The concept of GIS technology and its role in needs analyses for improved health service planning are also introduced.

2.9.1 Health care burden of asthma

Studies have shown that adults with asthma at the severe end of the disease spectrum rely more heavily on health care resources and accumulate significantly greater costs in the management of their disease (61, 232, 233). Costs not only arise directly, but also indirectly from absenteeism from work and loss of earnings. Intangible costs also relate to living with an impaired QOL (234).

In a study of emergency department (ED) visits for asthma in three countries (Italy, France and Spain), the likelihood of an ED visit increased with asthma severity. The odds ratios for individuals presenting with mild asthma, moderate asthma and severe persistent asthma were 1.6 (95% C.I. 1.1-2.5), 2.3 (95% CI 1.5-3.6) and 5.6 (95% CI 3.2-9.9) respectively (235). Further, a study by Koga *et al* (236) found subjects who had multiple exacerbations of their asthma and who were at increased risk for severe exacerbations were characteristically those who presented with persistent irreversible airflow limitation. Additional risk factors were a history of chronic sinusitis and/or intolerance to non steroidal anti-inflammatory medication.

Increased resource utilisation has also been reported to be greater in those with poor control of their asthma when compared to those with well controlled asthma at the same level of severity (44). It is estimated that the cost savings would be up to 45% if optimal control of asthma was achieved for all asthmatics within Australia (44). Factors associated with a greater reliance on hospital services by people with asthma include socio-economic disadvantage, poor adherence to medical advice, psychological factors such as denial of the condition, the lack of a written asthma action plan, excessive use of reliever medications and inadequate use of medication to control symptoms (61, 237).

2.9.2 Asthma in Australia

Globally, it has been reported that asthma is less common in rural areas compared to urban areas (1) and that growing up on a farm may confer some protection against atopy and the development of allergic asthma (238). However, recent population surveys (2004-2005) show that the prevalence of asthma does not differ significantly between the metropolitan, inner regional and remote areas of Australia (18). It is notable, however, that death rates from asthma from 1997-2001, were significantly higher in outer regional and remote areas among persons aged 35 to 64 years (239). Death rates from asthma among females are reported to be consistently higher than in males in all categories of remoteness except in the outer suburbs of capital cities (240).

Despite similar prevalence statistics, the rates of hospitalisation for adults with asthma have been shown to be significantly higher in rural or remote areas compared with major cities and regional areas (728 patient days versus 331 patient days per 100 000 people). Rates of hospitalisation are also higher in more socioeconomically disadvantaged localities (240).

A descriptive study by Tong and Drake (241) analysed admissions data between 1989 and 1994, and found that hospital admission rates for asthma in New South Wales were 52% to 69% higher for rural residents than their urban counterparts, and in the period from 1983 to 1992 mortality rates were 4% to 43% higher for rural residents than urban dwellers. Although the authors were cautious when interpreting these data as the study was descriptive in nature, they suggested that the findings

could have significant implications for the provision and planning of asthma health care services in rural Australia. A key point of the authors' discussion alluded to the need to investigate the potential influence that the availability of health care services and personnel (such as asthma educators and specialists) may have on admissions data (241).

Jones and colleagues (242) showed that there was an apparent trend between health service accessibility and levels of mortality from asthma in the UK, and that social and geographical isolation contributed to the inappropriate management of asthma (242). This study also showed that those in lower socioeconomic classes and individuals without a car had a higher relative risk of dying from asthma. This is the only reported study that has identified geographical barriers to acute hospital services to be a risk factor for asthma mortality (242).

2.9.3 Population demographics in Western Australia

Western Australia comprises over one third of the land mass of Australia and is highly diverse in many respects: socially, economically, demographically and climatically. Because of the vast land mass involved, health care planners and providers face unique challenges when attempting to provide equality of health services and to improve health outcomes. These objectives are part of the principles of Medicare Australia, which plays a role in delivering Australia's universal health funding programmes (243).

At the end of the June quarter, 2008, the total population of WA was estimated to be 2,163,200 (244). This population distribution is heavily skewed to the Perth metropolitan area with three quarters of the population of WA living in or around Perth (245). The remaining 500,000 people live in an area spanning 2.5 million square kilometres (246).

The demographics of WA show that it is an ageing society, with a trend both in higher life expectancies but also in associated increased levels of morbidity. Eleven percent of the population of WA are aged 65 years and over, and this percentage is expected to double over the next 50 years. Areas in which the proportions of older adult population are greater correspond to those in which increased health services are required (247). The 'sea change' phenomenon is increasingly evident among the

country's retiring population, with city dwellers moving to large rural centres for a 'better, healthier lifestyle', the 'clean country air', reduced noise and traffic congestion. Contrary to general opinion however, people residing in rural and remote areas have many health disadvantages, as evidenced by higher disease and mortality rates due to poor access to health services (239).

A trend also exists for older adults who live in the most remote parts of the State to shift towards larger regional centres. Among the older adult population, the proportion of people aged 55 years and over in remote areas is around half that of metropolitan and rural communities, with higher premature mortality also contributing to these lower proportions (248). Table 2.8 displays the population of West Australians in 2002 by age and gender for adults aged 45 years and over according to Divisions of General Practice.

Table 2.8 Estimated regional residential populations for 2002 by General Practice Division, age and gender

		45-64 years	65-74 years	75+ years
Central Wheatbelt	Male	6666	1943	1045
	Female	5950	1602	1358
Eastern Goldfields	Male	5693	922	503
	Female	4336	867	708
Great Southern	Male	9222	2595	1841
	Female	8536	2517	2464
Greater Bunbury	Male	7449	1751	1320
	Female	6968	1773	1723
Kimberley	Male	3155	497	293
	Female	2581	459	304
Mid West	Male	7556	2039	1135
	Female	6518	1818	1368
Peel South West	Male	16589	5496	3579
	Female	16143	5618	4205
Pilbara	Male	4407	332	185
	Female	2790	239	197

* These figures were calibrated using local government area resident population figures from the 2002 census. Source: (249)

Australia's indigenous population continues to have higher rates of morbidity and mortality than the non-indigenous Australian population. Aboriginal people make up 3.5% of the total population of WA, and of this population, 66% live in rural and remote areas. Fifteen percent of indigenous people living in remote areas and 18% of those living in rural areas were reported to have asthma as a long-term health condition in the 2001 National Health Survey (250).

2.9.4 The medical workforce in Western Australia

The Australian Rural Health Institute has identified a range of problems that rural General Practitioners (GPs) and health workers need to overcome in order to provide effective asthma management for their communities. Limitations in asthma service provision arise from large distances and travel times to health facilities for many patients, a lack of facilities and medical staff, poor access to services such as laboratory testing, lack of funding for asthma educator positions, community apathy towards asthma management, and difficulties providing adequate support for communities that have been affected by a fatal asthma episode (251).

To be effective in developing and delivering improved community support programmes for older adults with moderate to severe asthma, it is essential to: (i) understand current accessibility issues that patients and caregivers encounter in regional areas; and (ii) have a clearer understanding not only of the geographical distribution of asthma services, but also the prevalence and geographical distribution of the disease within WA.

The GP is the key element within most rural health care delivery systems (252). In terms of the medical workforce in 2002, of the estimated 2000 GPs working in WA, 465 (2001 figures) worked in regions classified as rural or remote (249). This number included 16 long-term locums and 57 trainee registrars (249). Data collected at that time suggested a high degree of mobility was required of rural and remote patients to attend a GP for their illness, with only 88% of patient visits in large rural centres being to a doctor who lived in the region, compared to 98% in capital cities. This figure progressively declined to 68% in very remote areas (253).

It was estimated that in 2003, in rural and remote WA, there was a deficit of between 50 and 60 GPs based on the standardised population figures, and with the trend

towards increased population in rural areas it was forecast that an extra 150-160 GPs would be needed over a ten year period to practise in rural WA. Table 2.9 summarises the number of GPs that were working in each of the Divisions of General Practice throughout the State in 2002 (253).

Table 2.9 General Practitioner workforce in rural and remote WA

		Primary model of service provision			
Division of General Practice	**Number of GPs**	**Resident GP**	**Fly-in-fly-out GP**	**Hospital based GP**	**Primary care team GP**
Central Wheat belt	35	89%	0%	0%	0%
Goldfields	53	60%	8%	0%	13%
Great Southern	57	86%	0%	2%	0%
Greater Bunbury	41	90%	0%	0%	5%
Kimberley	44	14%	0%	41%	18%
Mid West	59	56%	0%	15%	8%
Peel South West	129	81%	0%	1%	0%
Pilbara	47	45%	0%	21%	11%
Total	**465**	**67%**	**2%**	**8%**	**6%**

Source: Western Australian Centre for Rural and Remote Medicine General Practitioner Database: November 2002, and adapted from The Analysis of Rural General Practice Workforce in WA (253)

2.9.5 The Western Australian health system

The WA government provides health service to the public of the State through a system which incorporates:

- 5 tertiary health campuses
- 8 public secondary campuses in the metropolitan area
- 2 privately operated hospitals that provide service to public patients under contract from the Department of Health

- 6 regional resource centres
- 20 district health services in rural and regional areas
- 45 small health campuses of which a portion are multipurpose services
- More than 300 community-based and mental health facilities
- More than 250 non-government organisations and statutory authorities.

There are also two privately-run hospitals in the metropolitan area and an additional two in regional centres (254).

2.9.6 Defining remoteness in Western Australia

The term 'remoteness' describes the degree of difficulty in accessing a range of services, whereas 'accessibility' describes the relative ease of accessing such services. It is known that people 'trade off' geographic and non-geographic factors in making decisions about health service use (255). For example, travel for health care is affected by socio-demographic characteristics such as income, age and gender (255).

The Accessibility/Remoteness Index of Australia (ARIA) is the commonly used standard classification scale for remoteness and accessibility to services. It was developed in 1997 by the National Key Centre for Social Applications of Geographic Information Systems for the Commonwealth Department of Health and Aged Care. This is a scoring system which ranges from 0 to 12 that integrates information on physical geography and the distance from every locality in Australia to service centres of various sizes, with the primary aim being the measurement of remoteness solely on the basis of geographical accessibility excluding socioeconomic and population size factors.

The Australian Bureau of Statistics further refined ARIA for the 2001 census and developed the Australian Standard Geographical Classification system based on this measure which group populated localities into one of five levels of remoteness. These five ASGC classifications and the ARIA index scores on which they are based are described in Table 2.10. The ASGC provides an objective measure of remoteness and attempts to distinguish remoteness in terms of accessibility alone (256).

Table 2.10 Australian Bureau of Statistics - classes of remoteness by ASGC and their definition

ASGC classification	ARIA index Score	Definition
Major cities of Australia	0-0.2	Geographic distance imposes minimal restriction upon accessibility to goods and services
Inner Regional Australia	>0.2-2.4	Geographic distance imposes some restriction upon accessibility
Outer Regional Australia	>2.4-5.92	Geographic distance imposes a moderate restriction upon accessibility
Remote Australia	5.92-10.53	Geographic distance imposes a high restriction upon accessibility
Very Remote Australia	>10.53-15	Locationally disadvantaged. Geographic distance imposes the highest restriction upon accessibility

ASGC: Australian Standard Geographical Classification Areas; ARIA: Accessibility/ Remoteness Index of Australia

2.10 Using geographic information systems in health studies

Observations of geographical and temporal variations in health outcomes are one of the foundations of epidemiological analyses (257). Geographic information systems technology can be a powerful tool to assist health planners visualise the nature of a health accessibility problem. Its utility derives from the ability to explore relationships between geographic location and health through mapping, taking into account multiple sources of spatial information (258). Geographic information systems technology can also be used to screen and test hypotheses about disease and environmental factors, and assist in the generation of hypotheses relating to the optimal sites for health services based on areas of need (259).

In the context of health analysis in Australia, data sources that incorporate an address field can be assigned a latitude and longitude, a collector's district and also a statistical local area using purpose built software. It is within such spatial models that health attributes of interest can be incorporated for analyses and mapping (258). For example, hospital data codes, such as admission diagnosis of asthma or COPD can be attached to an 'event' or (de-identified) individual who was admitted to a particular

hospital, because the hospital has a defined latitude and longitude by which it can be described. This information can be accumulated and aggregated in a database containing other possible attributes, such as population figures for the given region that the hospital services.

It is important to note that in using positional data (e.g. to assign a certain latitude or longitude to a hospital), errors can occur in the accuracy of the geo-referencing. This raises the question of how much positional error is tolerable, and the results must be considered in terms of the context of the purpose for which the data will be used.

Errors can also be associated with the collection of attribute data. For example, data accessed may inherently contain coding inaccuracies, not only with a change in coding systems over time, but also in relation to miscoding a diagnosis (260). For example, hospital data were initially coded with International Classification of Diseases (ICD) codes 9 during the period between 1988 and 1999. This changed to a revised coding system - ICD codes 10 from 2000 onwards. Population data sources include population registers, census data, electoral roll and special surveys. The census is completed only every few years, and difficulties may arise in the estimation of data for inter-census years which must consider trends in births, deaths and migration factors - a particular problem in studies of small population sizes in specific geographic areas. In addition, geographic boundaries may change between censuses.

Despite these potential flaws in the initial storing of data in a spatial database, GIS has a potentially important role in the creation of spatially-referenced morbidity data. The technology has the ability to calculate rates of disease or admissions to hospital in relation to the density of the underlying population, and to produce disease maps which allow visualisations of the spatially varying frequencies of disease within a region of interest (259).

2.11 Conclusion

This chapter has reviewed the pathophysiology behind FAOA and its relation to asthma, COPD and other respiratory diagnoses. The burden of asthma on an individual, at a community level and also on the government has been explored, in relation to the associated disability that an older adult with moderate to severe

disease might present as being burdened by. Exercise training as an additional treatment modality to the first line treatment with pharmacological agents has been reviewed for its effectiveness within the literature in both asthmatic and COPD populations. The literature review has concluded with a focus on WA, and the burden of disease experienced by the health system in relation to the unique challenges associated with servicing older adults with asthma in rural and remote areas of the State due to the vast land mass and low population density outside the Perth metropolitan area.

CHAPTER 3

Benefits of exercise training in fixed airway obstruction asthma

3.1 Introduction

Most studies evaluating exercise training as an intervention for chronic respiratory disease have focused on individuals with moderate to severe chronic obstructive pulmonary disease (COPD) (225). The majority of studies that have been carried out in subjects with asthma have been restricted to children or young adults with mild to moderate disease. Most of these studies have methodological limitations such as the lack of a control group, insufficient sample size or lack outcome measures such as quality of life (QOL) (202).

Therefore it remains uncertain whether exercise training is a beneficial intervention in individuals with chronic moderate to severe asthma, and particularly in middle-aged and older individuals in whom the evidence is lacking. One reason that may account for the lack of evidence within the asthma literature is because some of these individuals with asthma exhibit permanent impairments in lung function and there remains some controversy in the way this group is defined (10, 13, 30, 34, 261). In this thesis a decision was made to describe these individuals as having fixed airway obstruction asthma (FAOA).

In order to address the limitations within the literature, there was a need for a randomised controlled trial (RCT) in a cohort of middle-aged and older adults with FAOA that compared outcomes in a group of subjects that participated in an exercise intervention with the outcomes in a control group that continued to receive standard

medical care only. Importantly, assessment of QOL was a necessary outcome measure.

This chapter describes the methodology, results and discussion of a RCT that evaluated a 6 week supervised exercise training programme in a group of middle-aged and older subjects with moderate to severe asthma who had a degree of irreversibility in lung function because of their asthma.

3.2 Methods

3.2.1 Overview

Section 3.2 of this chapter describes the study hypothesis, aims and objectives. Subject recruitment strategies, sample size and study design are outlined, and the study methodology including procedures for data collection, outcome measures and the methods used in data reduction and analyses are described.

3.2.2 Research hypothesis

The hypothesis for this study was that adults aged 40 years and over with FAOA would significantly benefit from a 6 week supervised exercise training programme. Compared to a matched group of control subjects who received standard medical care only, subjects who participated in the exercise program would demonstrate benefits through statistical and clinically significant improvements in:

i) QOL;
ii) functional exercise capacity;
iii) anxiety and depression; and
iv) asthma control

immediately post-intervention (6 week assessment) and at a 3 month follow-up.

3.2.3 Aim

The aim was to implement and evaluate a supervised exercise training programme in middle-aged and older adults (aged 40 years and over) who had moderate to severe asthma and a degree of fixed airways obstruction.

3.2.4 Objectives

The primary research objectives were to evaluate the effects of the exercise training programme on:

i) health-related QOL (HRQOL);
ii) QOL;
iii) functional exercise capacity;
iv) levels of anxiety and depression; and
v) asthma control.

These variables were measured immediately after the training (6 week assessment) and at 3 months following cessation of the intervention period.

Secondary research objectives of this study were to:

i) determine the extent of impairment in pulmonary function, peripheral muscle strength, functional exercise capacity and QOL in this cohort;
ii) define any relationships between baseline measures of pulmonary function, functional exercise capacity, asthma control, QOL and anxiety and depression;
iii) evaluate feedback from subjects regarding the exercise training programme; and
iv) collect data on health care utilisation for the 12 months prior to and following the intervention period.

3.2.5 Subjects

3.2.5.1 Inclusion criteria

Subjects were selected for the study on the basis that they had moderate to severe chronic asthma diagnosed by a respiratory physician (i.e. following investigations by their respiratory physician to determine disease variability, trigger factors, atopy and responsiveness to medications) and satisfied at least two of the following lung function criteria after a trial of maximum bronchodilator therapy and a trial of oral corticosteroids of at least 3 weeks duration:

i) Forced expiratory volume in one second (FEV_1) <80% of the predicted normal value (% predicted);
ii) FEV_1/ forced vital capacity (FVC) ratio less than 80% predicted; or
iii) residual volume (RV) >120% predicted.

These criteria aimed to capture a population of asthmatics who had a degree of fixed obstruction affecting the small and/or large airways. It was conjectured that there was a risk that subjects with asthma affecting the small airways alone might have been excluded if the selection criteria defined moderate to severe asthma on the commonly used basis of FEV_1 alone (262).

In addition, subjects were required to satisfy the following criteria:

i) aged 40 years or over;
ii) be on stable asthma medication;
iii) smoking history of ≤15 pack years;
iv) demonstrate a normal or raised gas transfer (DLCO/VA >80% predicted) to exclude significant smoking related disease; and
v) demonstrate a restriction in activities of daily living secondary to asthma determined by the subjects' responses to the activity limitation domain of the Asthma Quality of Life Questionnaire (AQLQ) (70).

3.2.5.2 Exclusion criteria

Subjects were excluded from the study if any of the following criteria applied:

i) evidence of co-existing respiratory conditions (e.g. emphysema, chronic bronchitis, bronchiectasis or pulmonary fibrosis);
ii) smokers or ex-smokers who had ceased smoking within the previous 2 years;
iii) participation in an average of more than 30 minutes a day of moderate or vigorous exercise;
iv) involvement in a pulmonary rehabilitation programme in the previous 12 months;
v) inability to understand written and/ or spoken English;

vi) co-morbid conditions limiting or likely to reduce exercise capacity (e.g. cardiovascular disease, neurological impairment, severe inflammatory joint disease, severe claudication pain, poorly controlled diabetes, or severe cognitive impairment); or

vii) existence of a serious psychiatric disorder such as schizophrenia or bipolar disorder.

3.2.5.3 Withdrawal criteria

Subjects could be withdrawn from the study in the event of any of the following:

i) withdrawal of consent;

ii) two or more asthma exacerbations requiring a change in medication lasting more than 7 days;

iii) development of any new medical condition which interfered with the subject's ability to perform the assessments or participate in the exercise training programme, and

iv) for the exercise group (to reflect non-adherence) failure to attend at least 14 out of 18 exercise classes.

The data from any subject who withdrew from the study was included in the intention-to-treat analyses.

3.2.5.4 Sources for subject recruitment

To minimise recruitment bias and variations in asthma management, recruitment was restricted to patients from one respiratory physician (Professor PJ Thompson [PJT]) at a single metropolitan hospital and one private clinic where patients were managed by either one of two respiratory physicians (Dr Q Summers and Dr P Bremner). The records of patients were screened if they were considered likely to meet the selection criteria and brought to the attention of the respiratory physician in charge of their care to determine suitability for participation in the study. The respiratory physician could also directly pass on the details of patients who satisfied the inclusion criteria. Patients who met the inclusion criteria were then sent a letter of invitation to

participate in the randomised controlled trial. These patients were contacted by telephone 1 week later.

The aim was to recruit a study population that consisted of asthmatics who had stable chronic asthma and in whom fixed airways disease from other respiratory pathologies would have been eliminated. Full lung function measurements including those of patients recruited from the private clinic were reviewed by PJT to ensure study criteria had been met prior to study entry. This systematic approach to the recruitment process was aimed at reducing selection bias, and allowed accurate identification of the participation rate for this study.

3.2.6 Study design

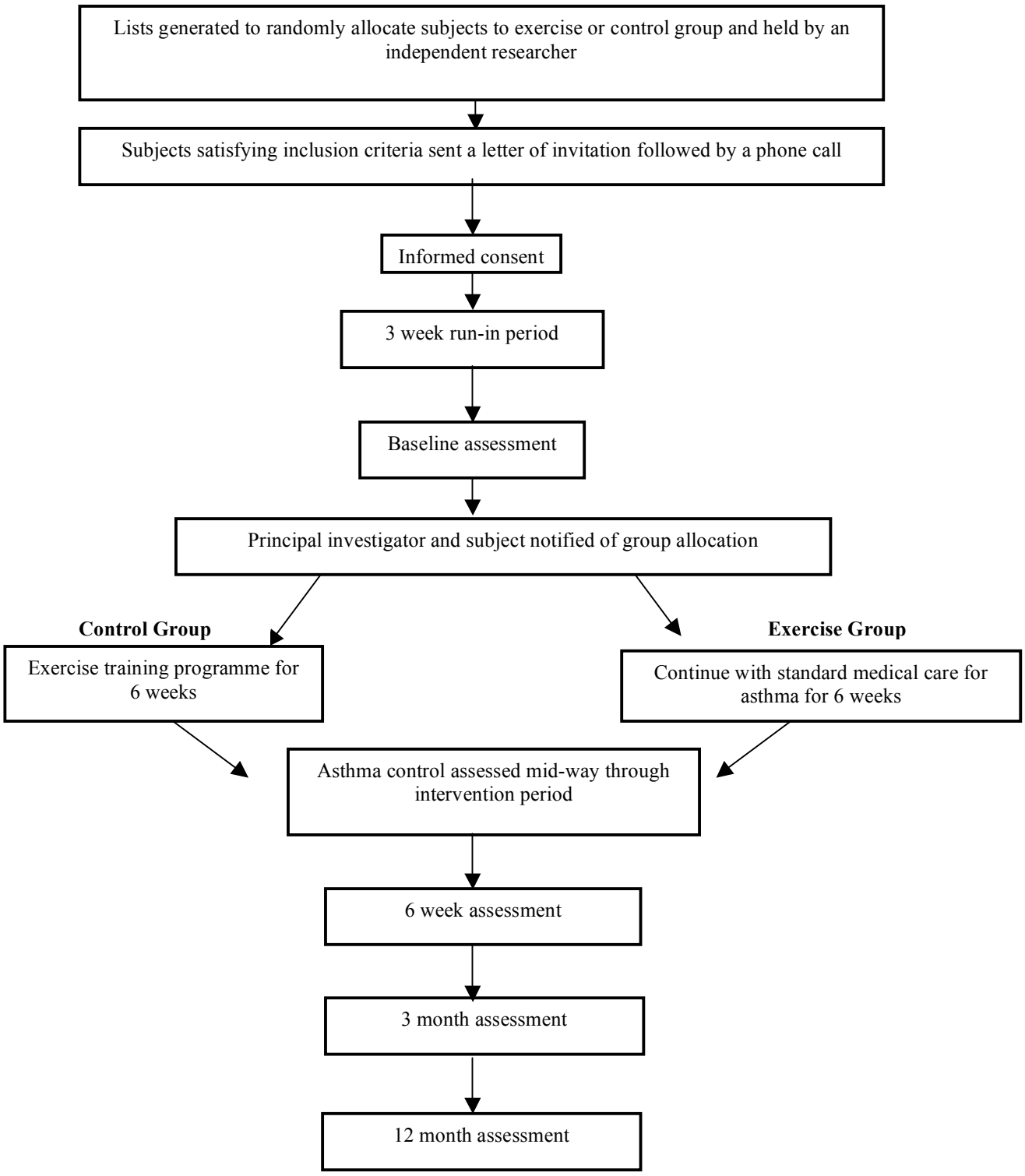
A prospective RCT was carried out. Subjects were randomised using a stratified process matching by gender (http://www.randomizer.org) into an 'exercise group' and a 'control group'. Two computer lists separated by gender were generated by an independent medical researcher (Dr J Woods) at the Lung Institute of Western Australia (LIWA), that consisted of random permutations of the numbers 0 (control group) and 1 (exercise group) for 20 subjects per group. Subjects were allocated to the exercise or control group at the time of informed consent, however the group allocation was not revealed by Dr Woods to the principal investigator or to the subject until after the subject had completed the 3 week run-in period and baseline assessment. This procedure was designed to ensure the principal investigator did not bias the process of recruitment of subjects into groups based on the assessment findings. The subjects and investigators were, however, aware of which arm of treatment (exercise or control) they were allocated to from this point.

It is acknowledged that if possible outcome assessments should be made by a 'blinded' assessor in a trial such as this and double blinding is ideal. For this study, blinding of the investigator beyond the initial assessment was not feasible due to the financial restraints of the study which prevented additional staff other than the principal investigator being involved in the exercise training and conducting the assessments. Successfully blinding participants from an intervention such as exercise training is also not possible.

The exercise group participated in a 6 week programme of supervised exercise training. The control group received standard medical care over this time period. Prior to randomisation, subjects entered a 3 week run-in period during which the Asthma Control Questionnaire (ACQ) (55) was completed each week. The run-in period was extended if a subject reported an increase in asthma symptoms as reflected by their responses to the ACQ, a variation in FEV_1 of >10% or a change in their asthma medication lasting >7 days.

Figure 3.1 illustrates the design and timeline of the study.

Figure 3.1 Design and timeline



3.2.7 Procedures for data collection

3.2.7.1 Informed consent

Individuals who expressed interest in participating in the study following telephone contact were invited to a face-to-face meeting lasting approximately 45 minutes with the principal investigator (Sian Turner) who explained in detail the research aims, methods, risks and benefits and time commitment. Only subjects who gave written, informed consent were included in the study.

3.2.7.2 Three week run-in period

To confirm stable disease prior to commencing the intervention phase of the study subjects were asked to attend a weekly assessment for a minimum of 3 weeks to undergo spirometry and to complete the ACQ (55). All assessments of lung function were carried out using a portable spirometer (Vitalograph 2120, Vitalograph Ltd, Maids Moreton House, Buckingham, UK.) using a standard technique (260). The spirometer was calibrated each week by the principal investigator.

After completion of the run-in phase, subjects were given a form to complete which asked for details of the respiratory medications they were currently taking, any unplanned hospital, emergency department (ED), respiratory physician or General Practitioner (GP) visits for their asthma and number of courses of oral corticosteroids for asthma exacerbations in the preceding year (Appendix A).

3.2.7.3 Assessments

Lung function

Respiratory function tests were performed in the Pulmonary Physiology Department at Sir Charles Gairdner Hospital (SCGH). The following measures of spirometry were made pre- and post-bronchodilator: FVC, FEV_1, FEV_1/FVC. Gas transfer (single breath diffusing capacity of the lung for carbon monoxide [DLCO], single breath diffusing capacity of the lung for carbon monoxide corrected for alveolar volume [DLCO/VA]) and lung volumes (total lung capacity [TLC], RV, functional residual capacity [FRC], and vital capacity [VC]) were also measured.

Measurement of lung function was repeated immediately after the 6 week intervention period (i.e. appointments were requested for the week following the

intervention, and if this was not possible they were scheduled as soon as possible and no later than 4 weeks after the intervention ceased).

Baseline and follow-up assessments

The baseline assessment lasted approximately 2 hours and required collection of the following data: generic and disease-specific QOL, anxiety and depression, functional exercise capacity, and peripheral muscle strength. This assessment was repeated immediately following the intervention period (6 week assessment) and again 3 months post-intervention (3 month assessment). Measures were taken in the following order:

1. Subjective history
2. Measurement of height, weight, and resting blood pressure
3. Spirometry measured and completion of the ACQ
4. First 6 minute walk test (6MWT)
5. Completion of the AQLQ, Hospital Anxiety and Depression (HAD) Scale and the Medical Outcomes Study 36-Item Short-form Health Survey (SF-36)
6. Repeat 6MWT

The following sections provide further detail of these measures.

3.2.8 Outcome measures

3.2.8.1 Primary outcome measures

Health-related quality of life

Health-related QOL was measured using the self-administered Australian-English individualised version of the AQLQ (69, 70). This questionnaire assessed the four domains of activity limitation (11 items) in which five of the questions specified individualised answers, asthma symptoms (12 items), emotional function (5 items) and environmental exposure (4 items). The activity domain requires subjects to identify their five most important activities that have been limited by asthma in the previous 2 weeks. The AQLQ was administered in written format for all three

assessments and took 15-20 minutes for the subject to complete. Permission to use this questionnaire was granted prior to the commencement of the study (Juniper, 6.5.03).

Functional exercise capacity

Functional exercise capacity was measured using the 6MWT. This test was used because the test outcome [i.e. 6 minute walk distance (6MWD)] has been shown to be responsive to changes following exercise training and other interventions in adults with COPD and asthma and is considered to better reflect the ability to undertake physically demanding activities of daily living than performance in a laboratory-based exercise test (175, 205, 207).

The 6MWT was conducted in accordance with current recommendations (178). The test protocol was modified from the American Thoracic Society guidelines to include standardized instructions prior to the test and standardized verbal encouragement at the start of each minute throughout the test. In addition, each minute subjects were informed of the elapsed time, and if a subject rested, verbal encouragement "begin walking as soon as you are able" was provided at 15 second intervals.

The 6MWT was performed over a straight 45m level course within an enclosed corridor. The 45m course was marked with two cones. A chair was located at each end of the course and at the mid-point for subjects to use if required. To allow for familiarization with the protocol at the baseline assessment, subjects completed two 6MWTs, separated by between 20 and 60 minutes rest (264). At all follow-up assessments two 6MWTs were also performed (265). At each time point the greater of the two 6MWDs was used in the analyses.

The 6MWT protocol is described below:

- A heart rate (HR) monitor (Polar A1, Polar Electro Oy, Kempele, Finland) was applied to the subject's chest. The polar watch was applied to the back of the subject's left shoulder using a safety pin to ensure HR readings could be taken without interfering with test performance. Strong correlations between HR readings obtained from the polar monitor and electrocardiograph (ECG) recordings have been reported (266, 267). Throughout the test, HR was continuously monitored and recorded at the end of each minute.

- Pre-exercise blood pressure and time of test were recorded. Subjects who had been instructed by their respiratory physician to take prophylactic bronchodilators prior to exercise took their bronchodilators prior to the 6MWT and the dose, time taken and medication were recorded. On all subsequent visits the subject took the same medication and dose prior to the 6MWT.
- The Borg (0-10) Dyspnoea Scale with standard instructions was introduced and pre-exercise dyspnoea was recorded (146).
- Resting oxygen saturation (SpO_2) was measured using a Tuffstat Pulse Oximeter and finger sensor (Datex-Ohmeda, Louisville, USA).
- The Borg (0-10) Dyspnoea Scale was modified to also record the perception of chest tightness (Appendix B). This scale was developed because no published scale was found for recording this symptom.
- The subject was given a description of the 6MWT course and instructed to turn immediately in front of the cones as if they had approached a wall.
- This distance walked was measured to the nearest 0.5m using a metre measurer.
- The number and duration of rest periods were also recorded.

End-point data

At the end of the sixth minute, heart rate (HR), dyspnoea and chest tightness, SpO_2 and leg fatigue were recorded. Leg fatigue was measured using a modified version of the Borg (0-10) dyspnoea scale (Appendix C) (146). After the first test the subject was asked: **"Was that the most you could do? Do you think you could do better another time?"** The Borg 6-20 Rating of Perceived Exertion (RPE) scale (147) was introduced, and subjects were asked to rate the level of effort or physical stress experienced during the test.

3.2.8.2 Secondary outcome measures

Generic quality of life

The standardised Australian version of the SF-36 (version 1) was used to assess health status. Permission to use this questionnaire was granted by Quality Metric

following registration and licensing (Appendix D). The data obtained were compared with age and gender-matched Australian (77) and West Australian normative data (75). The SF-36 was a self-administered scale and took 10 minutes for subjects to complete.

Peripheral muscle strength

Quadriceps strength

Knee extension strength was measured using a strain gauge (Falls Assessment Kit, Prince of Wales Medical Research Institute, NSW, Australia). The subject was seated on a high chair with hips and knees flexed to 90 degrees. The testing procedure was adapted from Andrews *et al* (268) to include the use of a strain gauge attached proximal to the subject's ankle to a horizontal metal bar connecting the two rear legs of the chair via a velcro strap.

In three separate trials, separated by a rest period of 1 minute, the subject was encouraged to pull against the strap assembly with maximal force, and the greatest force for each leg was recorded. If the highest reading was not within 10% of the other two readings then additional trials were carried out. Both legs were assessed and subjects were questioned as to their favored leg for kicking a ball. The measurement obtained on this leg was used in the analyses.

This technique for measuring quadriceps strength has been described by Lord *et al* (269). Normative data using the technique and strain gauge described by Lord and colleagues have not been published, therefore quadriceps strength was compared to reference data published by Bohannon *et al* (270).

Grip strength

A hand-held Jamar 5030 J1 dynamometer (Sammons Preston Inc. Bolingbrook, Illinois, United States of America) was used to measure grip strength. Grip strength was measured with the subject seated. The subject's arm was positioned with the shoulder adducted and neutrally rotated, elbow flexed at 90 degrees, and the forearm and wrist position were neutral. A minimum of three measures were taken with at least 1 minute rest between each effort. The single highest value achieved that was within 5% of at least two other measures was recorded on the subjects dominant side and compared with normative data (271-273).

Anxiety and depression

The HAD scale was used to screen for the presence of anxiety and depression and to assess for changes in mood states following the intervention period (124). The scale was self-administered and took 5-10 minutes for the subject to complete.

This well validated scale has been shown to be a reliable tool for detecting states of anxiety and depression and has demonstrated responsiveness to changes in mood state following pulmonary rehabilitation in patients with COPD (125, 126). A score of >10 for either subscale was used to identify cases of anxiety or depression among the subjects. This threshold value is recommended when the aim is to detect cases of anxiety or depression with a low probability of false positives (124). Although the scale is reliable for detecting states of anxiety and depression, it is not recommended as the sole means of making a diagnosis of altered mood state (124),

Asthma control

Asthma control was assessed each week using the ACQ (55) during the run-in period to ensure stable asthma before the collection of baseline data and was also measured at all follow-up assessments to determine whether any change in asthma control occurred during or following the intervention period.

Health care utilisation

Data were collected on hospital admissions, length of stay, ED visits and unscheduled GP consultations for asthma over the previous 12 months. This was collected via a self-report questionnaire and validated against hospital records where possible (Appendix A).

Subject feedback

Subject feedback following the exercise programme was assessed using a self-complete questionnaire. The questionnaire was developed specifically for this study and is provided in Appendix E.

3.2.8.3 Controlled measures

Testing procedures were controlled using the following methods:

- standardised protocols and instrumentation were used for all measurements;
- the venue was constant and the time of day of assessments was maintained as constant as possible;
- subjects were asked to refrain from eating or drinking any caffeinated products in the 2 hour period prior to testing to avoid any adverse effects on exercise performance (274);
- subjects were requested to wear the same footwear and similar clothing on each testing occasion;
- the order in which subjects performed tests and completed the questionnaires was kept consistent at each assessment;
- pre-medication for exercise was administered at the same time before the 6MWT on all assessments as the administration of a bronchodilator can affect 6MWD (86, 275); and
- repetitions of the 6MWT were conducted at least 20 minutes and no more that 60 minutes apart.

3.2.9 The intervention period

3.2.9.1 Exercise group

Subjects attended three exercise classes each week for 6 weeks. The classes lasted for 80-90 minutes and were supervised by a physiotherapist. Exercise was prescribed in accordance with the recommendations for individuals with COPD (218). An indoor air-conditioned corridor within SCGH and a gym in the Physiotherapy Department at SCGH were used for the walking programme and exercise circuit respectively.

Specifically, classes commenced with a 10-15 minute warm-up period comprising a slow 400m walk followed by stretches (triceps, pectoralis, trunk side-flexors, gastrocnemius and soleus, and a hamstring stretch).

The warm-up was immediately followed by a 20 minute walk prescribed at an initial intensity equivalent to 80% of the average walking speed achieved on the 6MWT performed at the baseline assessment (218). For example, a 6MWD of 500m would

be considered to have been completed at an average walking speed 5.0kph. Thus the prescribed walking intensity would be 4.0kph. This exercise prescription was provided to subjects in the format of a target distance to walk in 20 minutes within the 200m hospital corridor, therefore in this example the prescribed distance would be 1.3 to 1.4km or 1300-1400m. Subjects were encouraged to take regular rests if they experienced intolerable dyspnoea/chest tightness, or intolerable leg fatigue. Chairs were located approximately 10-15m apart throughout the hospital corridor (200m course).

The walking training was followed by an exercise circuit comprising cycle ergometry training for 10 minutes, step-ups, wall squats and unsupported and supported upper limb endurance training (arm ergometry and unsupported bilateral arm elevation) for a total of approximately 45 minutes. Details of each of these training stations are provided in Appendix F.

The target training intensity for the circuit exercises was a RPE of between 12 and 14 (146). When subjects reported a higher RPE they continued to exercise at this intensity if their symptoms were tolerable. The intensity of the walking training and circuit exercises was increased each week within symptom tolerance (218). Following the circuit, the subjects repeated stretches described above and HR and SpO_2 were re-measured at the end of the class.

At the end of the training period each subject was provided with a home exercise programme based on the exercise intensities achieved during their final training week and instructed to exercise on at least 3 days each week.

All subjects randomised to the exercise group continued to receive standard medical care for their asthma and any subjects requiring prophylactic bronchodilators prior to exercise were instructed to take their medication immediately prior to each class. The percentage of individuals with exercise induced asthma (EIA) in an older adult population with FAOA is unknown. However, exercise has been shown to induce bronchoconstriction in up to 80% of individuals with asthma (276). The incorporation of a prolonged warm up, controlled temperature of the indoor facilities in which the exercise training took place and the encouragement to those with known EIA to use beta 2 agonist pre-training helped to reduce the potential for such a phenomenon to occur. A portable spirometer was available to measure FEV_1 if

necessary post-training. A prolonged warm-up and the provision of pre-medication to help prevent a potential asthmogenic effect has also been advocated within the literature in exercise training programmes for adults with asthma (277).

The period over which the exercise programme was run was extended to a maximum of 10 weeks for any subject who experienced an exacerbation of their asthma, or other problems, with the aim of subjects completing at least 14 supervised training sessions within a maximum of 10 weeks.

3.2.9.2 Control group

Subjects randomised to the control group were instructed to continue with their current daily activities and management of their asthma in the usual manner (standard medical care). These subjects were not supervised during the 6 week intervention period; however each subject attended an appointment for measurement of spirometry and completion of the ACQ mid-way through the 6 week period. At this appointment they were asked if they had changed their asthma medication due to illness or an exacerbation.

3.2.10 Pilot study

To determine the feasibility of conducting this study, a pilot study was performed. Six subjects (four females) with moderate or severe asthma completed an 8 week supervised exercise training programme at SCGH. The subjects were aged 65.3±4.4 years and post-bronchodilator FEV_1 was 53±6.8% predicted. Subjects attended classes twice a week and completed a home exercise programme on an additional 2 days each week. Six minute walking distance and QOL (measured with the Chronic Respiratory Disease Questionnaire (278)) were measured prior to and immediately following the exercise programme (Table 3.1). This study confirmed the feasibility of the training protocol used in the main study.

Table 3.1 Data from six subjects pre- and post-training

	Pre	Post	Significance
6MWD (m) *n = 5	410±84	448±91	p=0.21
Distance walked in 20 min	1333±186	1525±211	p<0.01
QOL - total CRDQ score	86.5±8.1	109±5.7	p<0.01

*Data are mean±SD, pre- and post data compared using paired t-tests.
6MWD: 6 minute walk distance, m: metres; min: minutes; QOL: quality of life, CRDQ: Chronic Respiratory Disease Questionnaire

3.2.11 Sample size

In designing this study, consideration was given as to how many patients would need to be recruited to evaluate the efficacy of the treatment. It is acknowledged that the answer to this question is not a simple one as it is dependent on not only the size of effects which are likely to be observed between the exercise and control group, the statistical requirements related to Type I and Type II errors (which are related to size and power) and on the success or failure of the types of simple comparisons which are to be made between the measurements made in each group.

In this study, an anticipated clinical difference in the AQLQ and the 6MWT were measures chosen with an appropriate level of statistical significance to determine sample size. The pre-specified sample size of 32 subjects was calculated for this study based on detecting a clinically significant change (0.5 points per item) in the activity domain of the AQLQ and a 54m change in 6MWD between groups with 80% power (α=0.05) (66, 69, 194, 207).

3.2.12 Data management and statistical analyses

Data that were not normally distributed were transformed using a natural logarithmic scale and non-parametric analyses performed when normality was violated.

Baseline SF-36 data, 6MWD and muscle strength were compared with published norms or predicted values using paired t-tests.

Data were analysed according to both per-protocol analyses and the intention-to-treat principle. For missing data, the last observation carried forward method was utilised (279). Baseline equivalence of the exercise group and control group for each of the outcome measures was tested using unpaired t-tests, Mann-Whitney U-tests and Chi-

squared depending on the distribution of the data and its conformity with assumptions of normality.

Data for the primary outcome measures were principally analysed using a 3 (time) x 2 (group) repeated measures analysis of variance (ANOVA) and post-hoc tests. If a significant interaction was observed, simple contrasts were specified for differences between groups at the post-intervention assessment and 3 month follow-up. Main effects for each group were also analysed using a simple t-tests post-intervention compared with baseline measures if a non-significant difference was observed in the 3 x 2 ANOVA.

Differences between groups are expressed as mean±standard deviation (SD) or 95% confidence intervals (95% CIs). All statistical analyses were performed using SPSS software (Version 16.0) for Windows.

The relationships between the following baseline measures for the subject cohort (n=34) were investigated: %predicted FEV_1, magnitude of air-trapping or pulmonary hyperinflation at rest represented through the measurement of the ratio of residual volume to total lung capacity (RV/TLC), 6MWD and body mass index (BMI) with scores on the following questionnaires: ACQ, AQLQ, HAD and the SF-36 physical component summary scores (PCS) and mental component summary scores (MCS).

3.2.13 Ethical considerations and safety issues

Ethics approval for this study was obtained from the Human Research Ethics Committees of Curtin University of Technology (HR120/2004) and SCGH (Trial 2003-149). Subjects gave written informed consent prior to participating in the study. In the event of respiratory distress occurring during any of the study assessments or exercise training, an emergency protocol was put in place to ensure subject safety throughout the study.

Subjects were under no obligation to release their information for the study and were free to withdraw at any time without prejudice. Confidentiality was maintained by allocating each subject an identification number with the subject's identity known only to the principal investigator and project supervisors. All data were stored electronically on a computer in LIWA and access was password protected. Hard copies of the data were stored in a locked filing cabinet in LIWA. Access to the

electronic data was via a password known only to the principal investigator, and the project files were accessed only by the principal investigator and project supervisors. Currently the data obtained for this study are stored in a secure place where it will remain for 5 years, after which it will be destroyed in accordance with the requirements of Curtin University of Technology.

3.3 Results

3.3.1 Overview

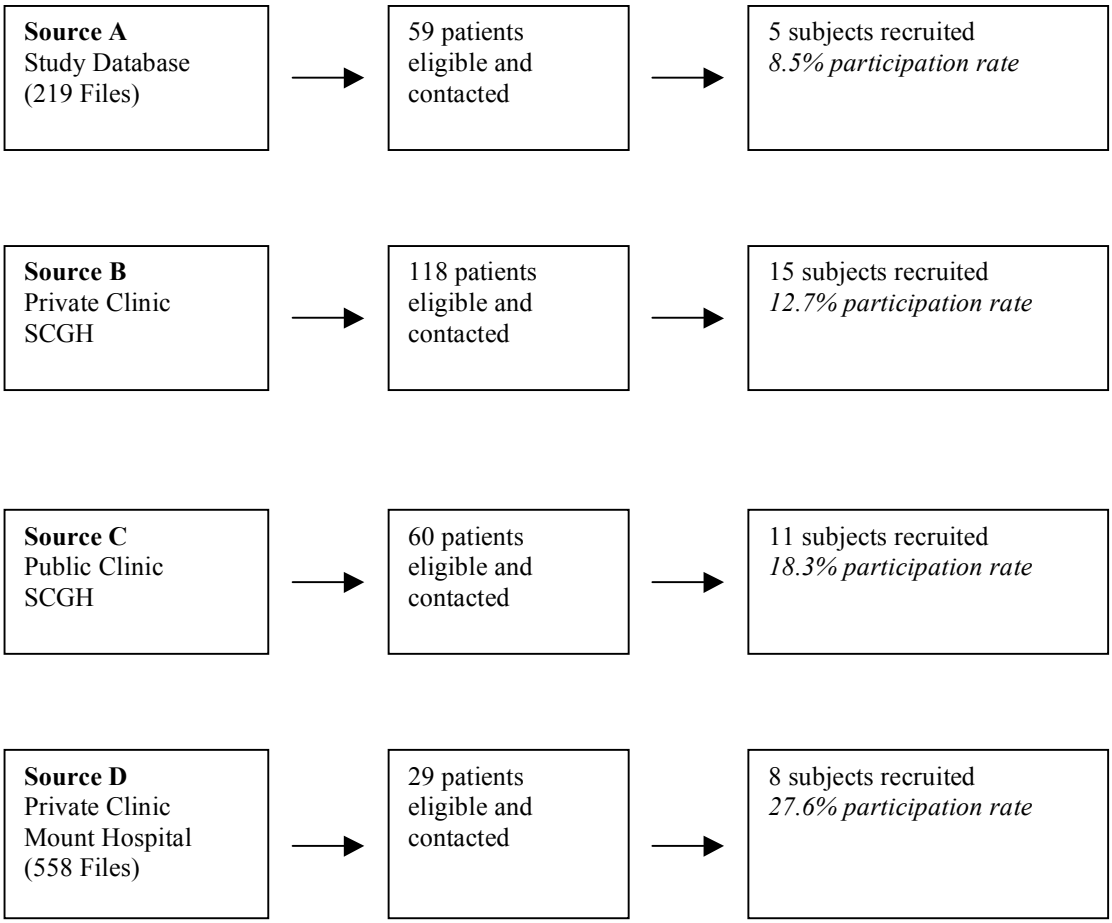
These results are divided into three parts. Part 1 describes baseline data for the exercise and control groups. Part 2 describes exercise training data pertaining to adherence with training and training loads achieved during the 6 week programme. Part 3 evaluates the efficacy of the exercise intervention in relation to changes in QOL, 6MWD, anxiety and depression and asthma control using intention-to-treat and per-protocol analyses as well as subject feedback regarding the exercise programme. Group data are presented as mean±SD unless otherwise stated.

PART ONE: BASELINE DATA

3.3.2 Subjects

Participant recruitment took place between 23rd of August 2004 and 3rd of July 2007. During this period, over 1,200 medical files of adults with asthma were reviewed by the principal investigator. Two hundred and sixty-six patients satisfied the inclusion criteria and were invited to participate in the study. Of these, 40 expressed interest and attended an initial screening interview (Figure 3.2). The participation rate was 14.7%, which decreased to 12.8% with subject withdrawals. Figure 3.3 describes the flow of subjects through the study.

Figure 3.2 Recruitment process and subject participation by source



Subject Source Details

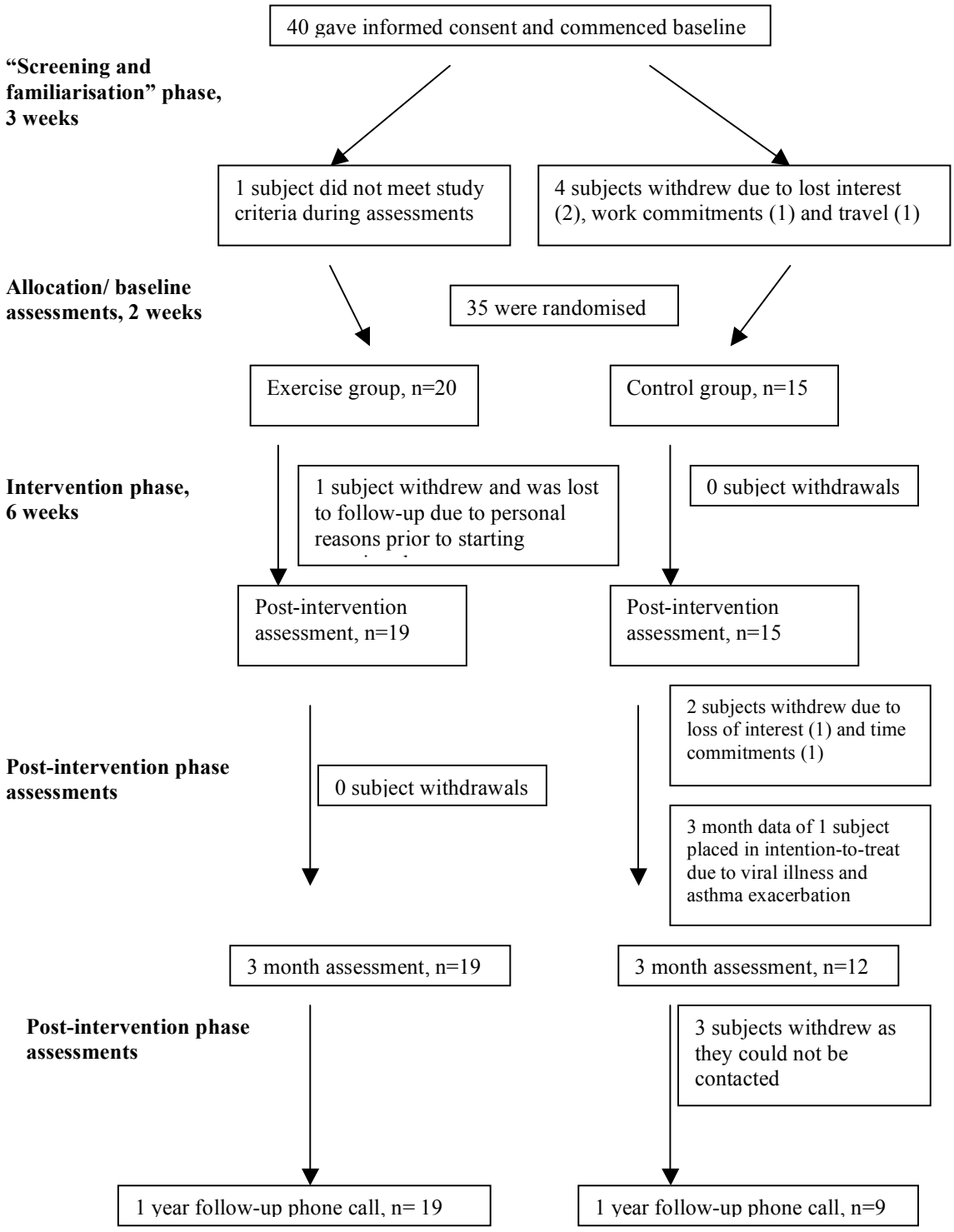
Source A (Patients managed by PJT) Patients on a respiratory database held at SCGH

Source B (Patients managed by PJT) A systematic review of the files of all patient seen privately at SCGH

Source C (Patients managed by PJT) A review of the files of all patients attending respiratory appointments with PJT at a public outpatient clinic between January 2005 through to August 2006

Source D (Patients with 'asthma diagnosis' managed by respiratory physician) attending a single private clinic between 1st January 2004 to 13th April 2006

Figure 3.3 Study design as per CONSORT guidelines (280)



Patients who declined to participate in the study cited the following reasons for non-participation: no interest; work commitments; too far to travel to appointments; too much of a time commitment, and musculoskeletal problems. Four subjects withdrew before the baseline assessment and one subject in the exercise group withdrew due to personal reasons before the intervention phase commenced but after collection of baseline data. Data from this subject were included only in the analysis of the effect of test repetition on 6MWD. Results are presented for 34 subjects (15 male) for baseline comparisons between groups in the intention-to-treat analyses (19 subjects in exercise group, 15 in control group), and with data from 31 subjects (15 male) included in the per-protocol analyses (19 subjects in exercise group, 12 in control group).

3.3.3 Baseline characteristics

Demographic, anthropometric and lung function data for the two groups were not significantly different (all $p>0.05$). These data are presented in Tables 3.2 and 3.3. The lung function data for both groups demonstrated moderate airflow limitation (mean FEV_1 ≤60% predicted) with evidence of lung hyperinflation and gas trapping (Table 3.3).

Twelve subjects (five of whom were ex-smokers) had a high resolution computer tomography (HRCT) scan in the previous year that excluded the presence of other pulmonary diseases. The remaining six ex-smokers had smoking histories which ranged from of 0.5 to 13.3 pack years (median 7 pack years).

Subjects in both groups demonstrated a high level of functional exercise capacity with 6MWDs close to predicted values (88±12%) (281) and had well preserved peripheral muscle strength (Table 3.2). The percentage of subjects who reported taking regular exercise, defined as walking at a leisurely pace for 30 minutes on at least 3 days each week, was 53% and 60% in the exercise and control groups respectively.

Table 3.2 Anthropometrics and demographic data at baseline

	Study cohort (34 subjects)	Exercise Group (19 subjects)	Control Group (15 subjects)
Gender (male: female)	15:19	8:11	7:8
Age (years)	67.8±10.6	65.3±10.8	71.0±9.7
Height (cm)	168.2±10.8	169.1±9.0	167.3±12.8
Weight (kg)	79.0±19.2	81.7±12.7	75.8±25.3
Smoking history (never:former) (n)	23:11	14:5	9:6
Pack years	3.1±7.1	2.0±4.5	4.5±9.3
CT scan (n)	12	7	5
BMI (kg/m^2)	27.8±6.2	28.6±5.0	26.8±7.6
BMI 18.5-24.9 (n)	12	3	9
BMI 25-30 (n)	13	12	1
BMI>30 (n)	9	4	5
Quadriceps strength (N)	258±117	264±104	251±136
% predicted	81±29	84±30	78±30
Hand-grip strength (lb)	72±27	72±20	72±35
% predicted	109±25	109±23	110±27
6MWD	548±100	569±88	522±111
% predicted	88±12	91±10	85±15
Lived alone (n)	12	6	6
Retired (n)	23	11	12
Working part-time (n)	5	3	2
Working full-time (n)	6	5	1
Exercise Advice (n)			
No previous instructions received by subject (n)	8	5	3
General encouragement given by a doctor (n)	21	10	11
Specific instructions given by physiotherapist or doctor (n)	5	4	1

Mean±SD. BMI: Body mass index; n: number; cm: centimetres; kg: kilograms; N: newtons; %: percent; lb: pounds.

Table 3.3 Resting lung function at baseline

	Study cohort (34 subjects)	Exercise Group (19 subjects)	Control Group (15 subjects)
Resting Lung function			
FEV_1 (L)	1.6±0.6	1.7±0.6	1.6±0.7
FEV_1 % predicted	59.4±15.8	58.9±15.9	60.0±16.2
FVC (L)	3.1±1.1	3.1±1.0	3.1±1.2
FVC % predicted	85.0±15.7	83.4±16.4	87.2±15.0
FEV_1/FVC %	59.7±16.1	53.8±8.3	53.1±12.9
FEV_1/FVC % predicted	53.4±10.4	71.0±9.8	71.2±16.6
VC (L)	3.2±1.1	3.3±1.0	3.2±1.3
VC % predicted	100.9±17.1	99.9±18.6	102.1±15.7
FRC (L)	3.8±1.0	3.8±0.8	3.9±1.2
FRC % predicted	159.4±56.2	161.5±58.4	157.0±55.3
TLC (L)	6.2±1.6	6.3±1.3	6.2±1.9
TLC % predicted	114.3±12.8	113.4±11.5	115.3±14.7
RV (L)	3.0±0.8	3.1±0.6	3.0±1.0
RV % predicted	142.3±26.3	144.3±22.0	139.7±31.6
RV/TLC	49.8±8.7	49.9±8.9	49.6±8.7
RV/TLC % predicted	124.8±19.0	127.6±19.2	121.1±18.7
DL_{CO}/VA (ml/min/mmHg/)	4.1±0.6	4.3±0.7	3.9±0.5
DL_{CO}/VA % predicted	99.5±13.7	101.6±16.1	96.9±9.6

Mean±SD. n: number; FEV_1: forced expiratory volume in one second; FVC: forced vital capacity; VC: vital capacity; FRC: functional residual capacity; TLC: total lung capacity; RV: residual volume; DLco/VA: single breath diffusing capacity for carbon monoxide corrected for alveolar volume; L: litres; %: percent; ml/min/mmHg: millilitres per minute per millimetre of mercury.

Appendices G-J illustrate physical activity levels, asthma triggers, and asthma management at study entry for the exercise and control groups (n=34). Specifically, Appendix G depicts the number of times/week, on average, subjects reported walking at a leisurely pace for periods of at least 30 minutes. In addition, 2 subjects (1 exercise group, 1 control group) played lawn bowls twice a week, and 1 subject (control group) played golf 3 times a week.

Asthma triggers were grouped into one of 10 categories based on perceived triggers for worsening asthma symptoms listed by the subjects. These are given in Appendix H. Appendix I displays the asthma management profiles, specifically the number of subjects who owned a written asthma action plan, nebuliser, peak flow meter and the number of subjects who had been reviewed by a trained asthma educator in the past year (excluding the subject's GP or specialist). For the group as a whole, of those who owned a peak flow meter, 14.7% used it daily while 41.2% never used it. These data are presented by group in Appendix J.

3.3.4 Medications and health care utilisation in the preceding year

Table 3.4 provides a summary of the respiratory medications taken by subjects and the number of hospital and ED presentations in the year preceding recruitment to the study for the exercise and control groups.

For the cohort, nine subjects had visited a respiratory physician once, one subject had visited twice and three subjects visited three times secondary to worsening asthma symptoms. Seven subjects had attended an ED secondary to asthma symptoms, of whom five were admitted to hospital. The numbers of medical attendances with a GP due to an exacerbation of asthma are given in Appendix K.

Table 3.4 Respiratory medications and health care utilisation data

Class	Exercise (n=19)	Control (n=15)
Long-acting beta-agonists	18 (95%)	15 (100%)
Anticholinergics	2 (11%)	3 (20%)
Inhaled corticosteroids	18 (95%)	15 (100%)
Maintenance oral corticosteroids	1 (5%)	1 (7%)
Leukotriene receptor antagonists	4 (21%)	1 (7%)
Cromoglycate	2 (11%)	2 (13%)
Theophylline	2 (11%)	2 (13%)
Courses of oral corticosteroids in last 12 months	8 (42%)	7 (47%)
ED presentations in last 12 months	3 (16%)	4 (27%)
Hospital admissions in last 12 months	2 (11%)	3 (20%)

Data are numbers of subjects with the number in parentheses denoting the percentages of subjects. ED: Emergency Department; %: percent

3.3.5 Asthma control

At the start of the run-in phase, 14 subjects (73%) in the exercise group and eight subjects (53%) in the control group met the criteria for inadequately controlled asthma (ACQ score > 1.5) (56). These data are shown in Table 3.5.

In five subjects (4 exercise group) the run-in period was extended due to worsening asthma symptoms. For each of these subjects, the best three consecutive asthma control scores were used in analyses as that subject's 'first, second and third' run-in data. There were no significant differences between groups in asthma control scores measured at the first, second or third baseline assessments (p=0.44, 0.78 and 0.99 respectively). The last asthma control score measured in the run-in period was used as the baseline measure for comparison with measures of asthma control following the intervention period.

Table 3.5 Asthma control data collected during the run-in period

	Exercise (n=19)	Control (n=15)
First baseline ACQ score	2.1±0.7 (14)	1.9±1.0 (8)
Second baseline ACQ score	2.0±0.7 (14)	1.9±1.1 (9)
Third baseline ACQ score	1.7±0.7 (11)	1.7±1.0 (8)

ACQ: Asthma Control Questionnaire. The number in parentheses denotes the number of subjects who had an ACQ score >1.5, and therefore by definition poorly controlled asthma (56).

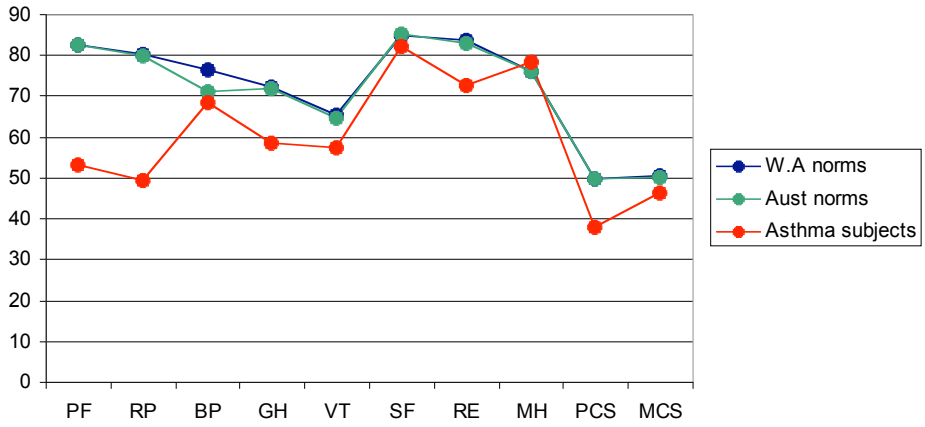
3.3.6 Quality of life at baseline

There were no significant differences in the AQLQ scores between groups in any of the domains (all $p>0.05$).

There were also no significant differences between groups in the PCS or MCS of the SF-36 at baseline. The PCS and MCS are calculated using data from the eight subscales of the SF-36 and incorporate the general population norm into the scoring algorithm (282). In this thesis, PCS and MCS were calculated using means, SDs and factor score coefficients obtained from the (unweighted) 1995 National Health Survey of Australia (77) (Appendix L).

The PCS for the subject cohort at baseline was 38.1±10.0, which was significantly lower ($p<0.05$ one-sample t-test) that the normative mean value reported for both Australians and West Australians (49.7 reference PCS score). The MCS score (52.6±11.5) was not significantly different from the mean MCS scores reported for either the Australian (50.1, $p=0.22$), or WA populations (50.2 $p=0.24$). Figure 3.4 illustrates the SF-36 scores for the subject cohort together with age-standardised population data for Australia and WA.

Figure 3.4 SF-36 profiles by group: athma subjects and Australian and WA norms (age-standardised)



PF: physical function; RP: role-physical; BP: bodily pain; GH: general health; VT: vitality; SF: social functioning; RE: role-emotional; MH: mental health; PCS: physical component summary score; MCS: mental component summary score

3.3.7 Effects of test repetition on 6 minute walk distance

Data for the 34 subjects who performed two 6MWTs at baseline assessment showed an increase in 6MWD from 524±99m to 549±101m ($p<0.0001$) on the second 6MWT. This equates to a 5.2±7.0% improvement. 6 minute walk distance increased on the second 6MWT by 22.7±29.8m in the exercise group, and by 28.5±32.8m in the control group, but there was no significant difference in the magnitude of increase between the groups ($p=0.60$). Data were excluded for one subject (control group) in this analysis due to irregularities in this subject's HR detected using a Polar monitor during her second 6MWT.

3.3.8 Relationships between baseline measures

Correlations between physiological and QOL data measured at baseline for the subject cohort are displayed in Table 3.6. The strongest correlation was found between the magnitude of air trapping or pulmonary hyperinflation, as evidenced by RV/TLC, and 6MWD ($r=-0.66$). Asthma control scores were negatively and significantly correlated with the total score on the AQLQ. Forced expiratory volume in one second showed a significant negative correlation with BMI. Disease-specific QOL (AQLQ) was moderately and significantly correlated with SF-36 data (MCS and PCS) and with levels of anxiety and depression.

Table 3.6 Correlations (r) between physiological and QOL measurements taken at baseline for the study cohort (n=34)

	6MWD	ACQ baseline score	AQLQ total score	SF-36 PCS	SF-36 MCS
FEV_1 (% predicted)	0.34†	-0.44*	0.19	0.16	0.10
RV/TLC	-0.66$^{\#}$	0.23	-0.13	-0.28	-0.24
BMI	-0.15	0.50*	-0.40†	-0.28	-0.29
HAD anxiety score	-0.08	0.31	-0.54$^{\#}$	0.05	-0.57$^{\#}$
HAD depression score	-0.17	0.34	-0.54$^{\#}$	-0.09	-0.74$^{\#}$
AQLQ total score	0.24	-0.69$^{\#}$	1.0	0.37†	0.73$^{\#}$

FEV_1: forced expiratory volume in one second; %: percent; RV: residual volume; TLC: total lung capacity; BMI: body mass index; HAD: Hospital Anxiety and Depression scale; 6MWD: 6 minute walk distance; ACQ: Asthma Control Questionnaire; AQLQ: Asthma Quality of Life Questionnaire; SF-36: Short-Form 36 Health Survey; PCS: physical component score; MCS: mental component score; r: Pearson's correlation coefficient; $^{\dagger}p<0.05$, *$p<0.01$, $^{\#}p<0.001$.

PART TWO: EXERCISE TRAINING PROGRAMME

3.3.9 Training attendance

Of the 19 subjects randomised to the exercise group, 11 attended all 18 sessions. Six subjects with an incomplete attendance record worked full-time. These six subjects attended 15 sessions (n=2) and 14 sessions (n=4).

One subject developed knee pain on session 9 (due to the recall of the medication Vioxx) but attended a total of 16 sessions, and another subject developed a viral illness which limited full participation (15 sessions attended). No severe episodes of wheezing or chest tightness requiring medical intervention occurred in any of the subjects during the supervised training sessions.

The intervention period was extended for five subjects in the exercise group due to an asthma exacerbation or viral illness (two subjects), problems attending classes because of work commitments (two subjects), and as a result of a foot injury (infection) (one subject). The intervention was extended in two subjects in the control group because of asthma exacerbations resulting from viral illness.

3.3.10 Adverse events

One subject randomised to the exercise group developed cervical pain from the unsupported bilateral upper limb exercise in the first week of training. This subject had a history of cervical pain. No progression of this exercise occurred and the subject received a course of physiotherapy treatment to relieve symptoms.

3.3.11 Exercise training loads

Twenty minute walk distance and training loads achieved during all of the exercise stations, with the exception of the wall squats, are presented in Figures 3.5 to 3.8. Over the course of the 6 week training programme, 20MWD increased by 17.8±9.6% from baseline (282±145m, $p<0.001$). Data points are displayed as the mean±2 standard errors of the mean change from baseline at each of the time points, i.e. sessions 3, 6, 9, 12 etc.

Figure 3.5

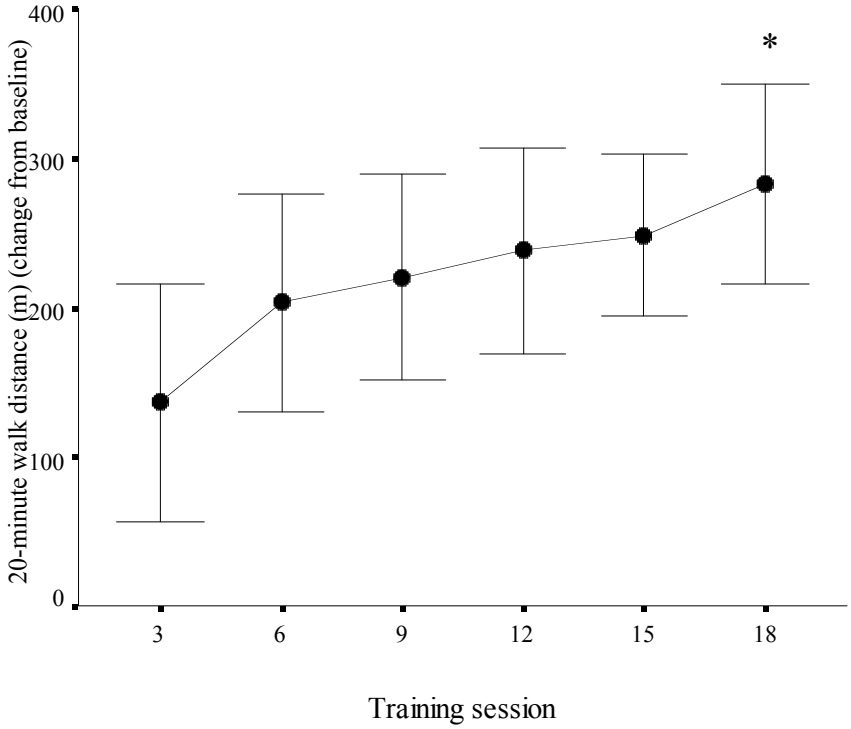
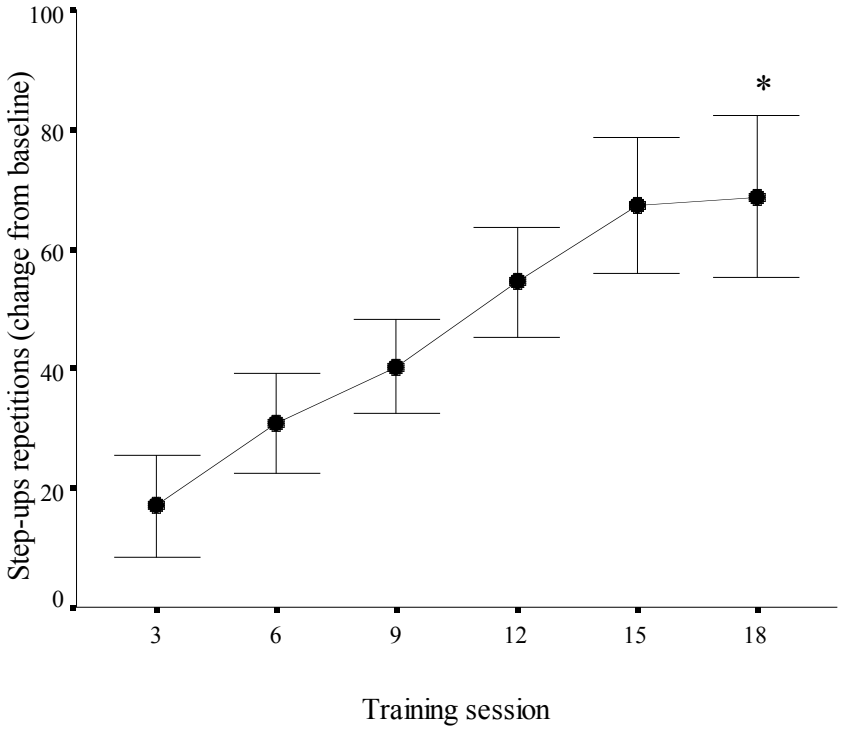


Figure 3.6



Figures 3.5 - 3.6 Change in training load (mean±2 standard errors of the mean) over the 18 training sessions for 20-minute walk distance (Figure 3.5) and step-ups (Figure 3.6). Data points are the mean change from baseline for that session for the participating subjects *:$p<0.05$ vs training session 1.

Figure 3.7

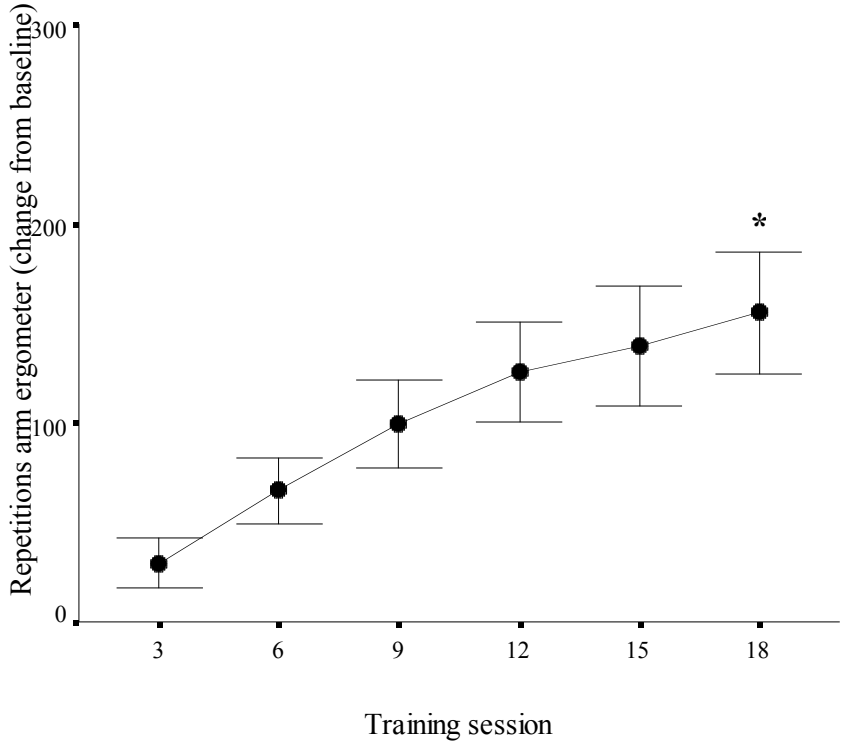
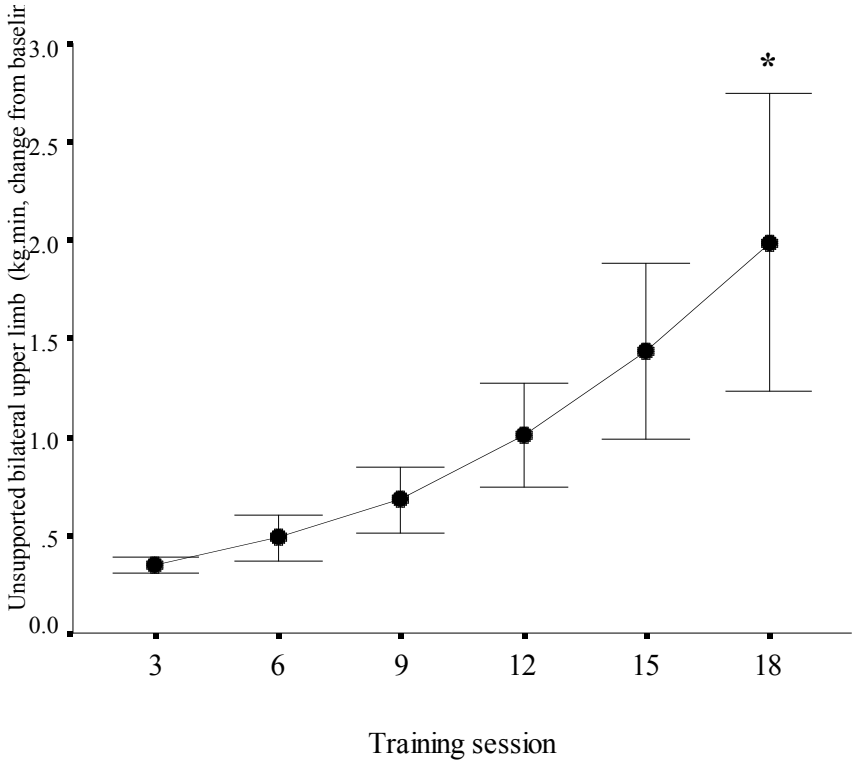


Figure 3.8



Figures 3.7 - 3.8 Change in training intensity (mean±2 standard errors of the mean) over the 18 training sessions for arm ergometry training (Figure 3.7) and unsupported upper limb exercise (Figure 3.8). Data points are the mean change from baseline for that session for the participating subjects *:$p<0.05$ vs training session 1.

PART THREE: EFFICACY OF THE INTERVENTION

3.3.12 Resting lung function and anthropometrics

There were no significant changes in any measures of lung function at the 6 week follow-up versus baseline, nor any significant changes in BMI, handgrip and quadriceps strength measured at baseline, 6 week and 3 month follow-up in either group (Tables 3.7 and 3.8).

3.3.13 Asthma control

During the 6 week intervention period, two subjects (randomised to the control group) and one subject in the exercise group reported an asthma exacerbation. As none of these subjects experienced a change in medication lasting more than seven days and all reported full recovery by their 6 week follow-up, data from all of these subjects were included in the per-protocol analyses. Seven subjects experienced a clinically significant improvement in their asthma control immediately post-intervention compared to baseline, and six of these subjects were in the exercise group.

Figures 3.9 and 3.10 illustrate the mean and 95% CIs for ACQ scores recorded at baseline and at the 6 week and 3 month follow-up in the two groups. The change in ACQ scores at 6 weeks compared to baseline was -0.26±0.36 in the exercise group and -0.11±0.51 in the control group, and at 3 months was -0.19± 0.42 for the exercise group and 0.02±0.37 in the control group with per-protocol analyses. Analyses using intention-to-treat showed a change of -0.04±0.49 at 6 weeks and -0.07±0.37 at 3 months in the control group. Improvements in asthma control scores therefore did not reach the minimal clinically significant difference of 0.5 in either group, and repeated measures ANOVA showed changes were also not statistically significant.

Table 3.7 Resting lung function at baseline and immediately post-intervention (6 weeks)

	Exercise group (n=19)		Control group (n=15)	
Resting Lung Function	**Baseline**	**6 weeks**	**Baseline**	**6 weeks**
FEV_1 (L)	1.7±0.6	1.8±0.6	1.6±0.7	1.5±0.6
FEV_1 % predicted	58.9±15.9	62.1±15.4	60.0±16.2	59.6±16.7
FVC (L)	3.1±1.0	3.2±1.0	3.1±1.2	3.0±1.1
FVC % predicted	83.4±16.4	84.3±16.4	87.2±15.0	86.3±16.2
FEV_1/FVC %	53.8±8.3	54.5±8.1	53.1±12.9	52.3±13.2
FEV_1/FVC % predicted	71.0±9.8	72.0±10.0	71.2±16.6	70.1±17.0
VC (L)	3.3±1.0	3.3±1.1	3.2±1.3	3.1±1.4
VC % predicted	99.9±18.6	100.7±20.7	102.1±15.7	100.3±15.3
FRC (L)	3.8±0.8	3.9±1.0	3.9±1.2	3.8±1.0
FRC % predicted	161.5±58.4	166.9±63.8	157.0±55.3	156.5±66.2
TLC (L)	6.3±1.3	6.4±1.4	6.2±1.9	6.0±1.8
TLC % predicted	113.4±11.5	113.9±12.9	115.3±14.7	112.5±13.6
RV (L)	3.1±0.6	3.1±0.8	3.0±1.0	2.9±0.7
RV % predicted	144.3±22.0	142.0±32.8	139.7±31.6	137.1±24.9
RV/TLC	49.9±8.9	48.6±10.4	49.6±8.7	50.1±8.4
RV/TLC % predicted	127.6±19.2	124.7±22.0	121.1±18.7	122.0±15.0
DL_{CO}/VA (ml/min/mmHg/)	4.3±0.7	4.1±0.6	3.9±0.5	3.8±0.7
DL_{CO}/VA % predicted	101.6±16.1	98.2±17.6	96.9±9.6	93.7±12.4

Mean±SD. n: number; FEV_1: forced expiratory volume in one second; FVC: forced vital capacity; VC: vital capacity; FRC: functional residual capacity; TLC: total lung capacity; RV: residual volume; DLco/VA: single breath diffusing capacity of the lung for carbon monoxide corrected for alveolar volume.

Table 3.8 Anthropometrics at baseline, 6 weeks and 3 months follow-up

	Exercise n=19			Control n=12 (per-protocol)			Control n=15 (intention-to-treat)		
	Baseline	**6 weeks**	**3 months**	**Baseline**	**6 weeks**	**3 months**	**Baseline**	**6 weeks**	**3 months**
Anthropometrics									
BMI (kg/m^2)	28.6±5.0	28.4±4.7	28.2±4.6	26.7±6.8	26.6±6.9	26.7±7.1	26.8±7.6	26.7±7.6	26.8±7.8
BMI 18.5-24.9 (n)	3	4	4	7	7	7	9	9	9
BMI 25-30 (n)	12	12	12	1	1	1	1	1	1
BMI>30 (n)	4	3	3	4	4	4	5	5	5
Quadriceps strength (N)	264±104	279±95	293±90	283±134	269±141	285±148	251±136	240±139	253±147
% predicted	84±30	88±24	92±23	85±29	81±33	86±34	78±30	75±32	79±33
Hand-grip strength (lb)	72±20	73±21	72±24	80±34	83±32	76±34	72±35	75±34	69±34
% predicted	109±23	109±20	108±25	116±24	122±22	110±25	110±27	115±29	105 ±28

Mean±SD. BMI: body mass index; n: number; N: newtons; lb: pounds

Figure 3.9 Mean±95% confidence intervals for asthma control scores: per-protocol analyses (n=31)

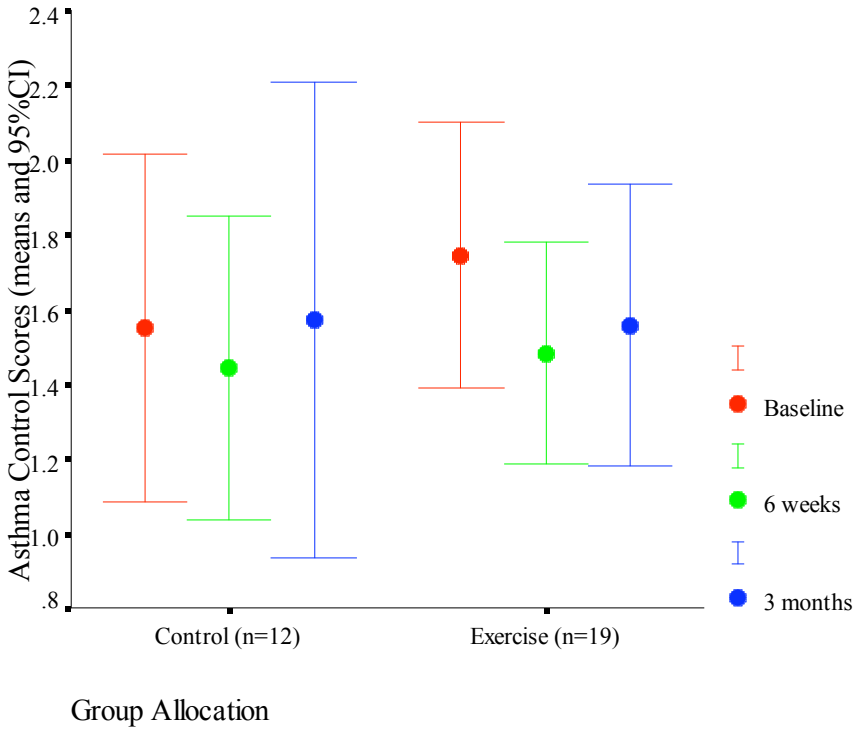
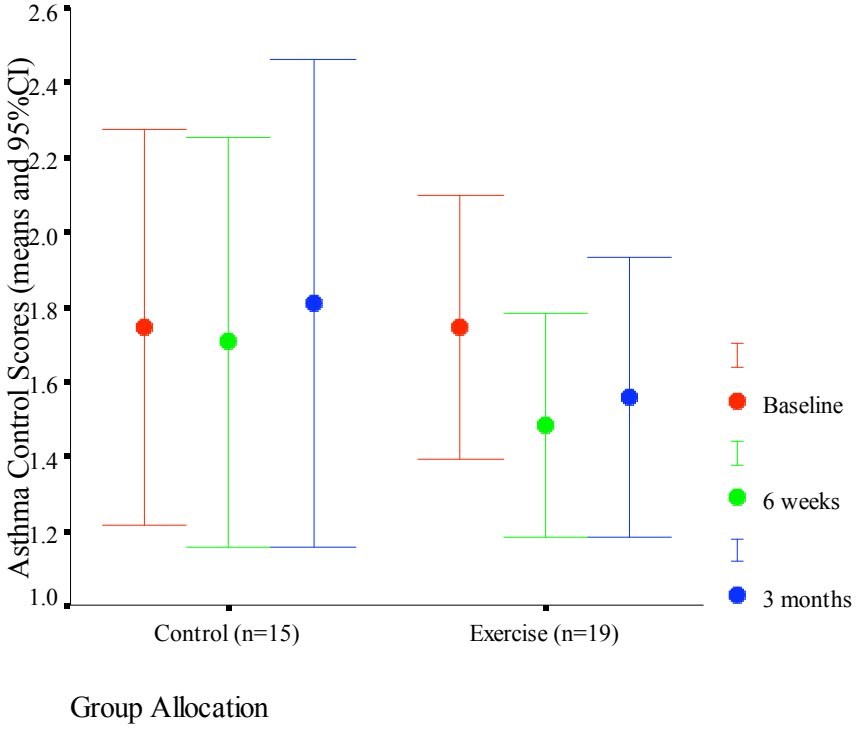


Figure 3.10 Mean±95% confidence intervals for asthma control scores: intention-to-treat analyses (n=34)



3.3.14 Quality of life, anxiety and depression

Scores for the four domains of the AQLQ are given in Tables 3.9 (per-protocol analyses) and 3.10 (intention-to-treat analyses). Overall, 3x2 ANOVAs showed significant improvements in symptoms, activity and total scores with intention-to-treat analyses and a significant improvement in symptom scores with per-protocol analyses for the exercise group. The changes in the total AQLQ score and the activity and symptom domains were also clinically significant immediately post-intervention and at the 3 month follow-up when compared to baseline scores.

The interpretation of SF-36 data is facilitated with norm-based scoring and the use of summary scales. Norm-based scoring uses general population norms which provide a basis for meaningful comparisons across the scales in the SF-36 profile and assist with the interpretation of differences.

Eighty to 85% of the reliable variance in the eight separate SF-36 subscales are accounted for in the combined physical and mental component summary scores. These two summary measures are interpretable as the physical and mental dimensions of health and their use reduce the number of statistical analyses down from eight to two without any loss of information. In addition, the scores obtained in the role-physical, bodily pain, social functioning and role-emotional domains were not normally distributed, therefore because of the presence of floor and ceiling effects on the subscales (282), statistical analyses on these subscales would not be easily interpretable. Statistical analyses, therefore, were only performed on the PCS and MCS scores. SF-36 data are given in Tables 3.9 and 3.10.

Overall the effect of group randomisation on PCS scores was not significant ($p=0.06$ with intention-to-treat, $p=0.27$ with per-protocol analyses). Simple contrasts performed in the 3x2 ANOVA with intention-to-treat analyses showed there was a significant positive change in PCS scores at 6 weeks ($p=0.003$) in the exercise group, but this improvement declined at 3 months ($p=0.05$) such that the overall 3x2 ANOVA was not significant.

Mean PCS and MCS scores at baseline, 6 weeks and 3 months for both groups are shown in Figures 3.11-3.14. The PCS and MCS scores incorporate norm-based scoring. This means a linear transformation has been applied to standardise the data against population norms that have a mean of 50 and SD of 10. This transformation

enables the scores for each group to be easily interpreted as being above or below the norms (283).

Anxiety and depression profiles for the exercise and control groups are reported in Tables 3.9 and 3.10. Only two subjects (one exercise group) recorded a score of >10 for anxiety and one subject (control group) recorded a score of >10 for depression at baseline.

Repeated measures analyses of variance showed a significant improvement in anxiety scores in the exercise group compared to the control group over the course of the study ($p=0.04$) in per-protocol analyses, but not in intention-to-treat analyses ($p=0.09$). There were no significant improvements in depression scores with either per-protocol ($p= 0.13$) or intention-to-treat analyses ($p=0.17$).

Table 3.9 Quality of life, anxiety and depression: per-protocol analyses

	Exercise (n=19)			Control (n=12)		
AQLQ (points per item)	**Baseline**	**6 weeks**	**3 months**	**Baseline**	**6 weeks**	**3 months**
Symptoms [ξ]	5.2±0.9	5.9±0.7*†	5.8±0.7*†	5.7±1.3	5.8±1.1	5.7±1.4
Activity	4.7±1.0	5.7±0.8*†	5.8±0.9*†	4.9±0.9	5.6±1.0*	5.5±1.1*
Emotional	5.1±1.5	5.8±0.9*	5.8±0.9*	5.5±1.6	5.8±1.4	5.8±1.5
Environmental	4.9±1.3	5.7±1.1*	5.7±0.8*	5.3±1.5	5.6±1.4	5.6±1.3
Total score	5.0±01.0	5.8±0.7*†	5.8±0.7*†	5.3±1.1	5.7±1.1*	5.7±1.1*
SF-36 (range 0-100) [#]						
Physical functioning	56.1±21.6	71.3±16.4	73.4±14.7	54.6±25.1	63.3±22.2	61.3±29.2
Role-physical	46.1±32.6	86.8±22.6	81.6±27.4	58.3±41.7	62.5±42.0	55.6±31.4
Bodily pain	79.4±21.9	83.4±18.5	80.6±20.8	55.6±31.5	68.0±24.5	64.8±25.5
General health	61.0±21.5	66.3±14.9	66.8±22.2	58.2±21.4	63.3±18.3	60.2±20.1
Vitality	60.5±18.7	69.2±14.5	67.4±16.2	59.6±16.6	68.3±10.9	64.6±14.1
Social functioning	86.2±22.4	93.4±11.3	87.7±17.9	85.4±18.3	77.1±33.2	82.3±27.9
Role-emotional	80.7±35.7	84.2±30.2	87.7±27.7	69.4±41.3	69.4±41.3	75.0±40.5
Mental health	82.3±12.5	85.3±10.3	86.5±12.2	76.0±20.0	80.0±16.2	82.3±12.1
Health transition	2.6±1.2	2.0±1.1	2.3±1.0	2.6±1.3	2.5±1.1	2.8±0.8
Physical component summary score	39.2±9.8	47.1±6.9*	46.2±6.2*	38.0±11.4	41.8±9.2	40.0±11.8
Mental component summary score	54.9±10.4	55.0±7.0	55.0±8.9	52.4±12.0	52.2±10.7	54.0±10.3
HAD						
Anxiety [ξ]	5.2±3.5	3.4±3.2*†	3.9±3.2*	5.4±3.1	6.1±3.8	4.8±4.0
Depression	3.3±2.8	1.8±1.8	2.2±2.8	3.8±2.6	3.6±2.6	2.8±2.7

AQLQ: Asthma Quality of Life Questionnaire; SF-36: Short Form-36 Health Survey; HAD: Hospital Anxiety and Depression scale. *$p<0.05$ compared with baseline; [†]$p<0.05$ compared with control group; [ξ]$p<0.05$ 3x2 ANOVA factor*randomisation; [#]: statistics performed only on the physical and mental component scores

Table 3.10 Quality of life, anxiety and depression: intention-to-treat analyses

	Exercise (n=19)			Control (n=15)		
AQLQ (points per item)	**Baseline**	**6 weeks**	**3 months**	**Baseline**	**6 weeks**	**3 months**
Symptoms $^{\xi}$	5.2±0.9	5.9±0.7*†	5.8±0.7*†	5.6±1.3	5.7±1.2	5.6±1.4
Activity $^{\xi}$	4.7±1.0	5.7±0.8*†	5.8±0.9*†	4.7±1.1	5.3±1.2*	5.3±1.3*
Emotional	5.1±1.5	5.8±0.9*	5.8±0.9*	5.2±1.7	5.5±1.7	5.5±1.8
Environmental	4.9±1.3	5.7±1.1*	5.7±0.8*	5.1±1.5	5.4±1.6	5.4±1.5
Total score $^{\xi}$	5.0±1.0	5.8±0.7*†	5.8±0.7*†	5.2±1.2	5.5±1.3*	5.5±1.3
SF-36 (range 0-100) $^{\#}$						
Physical functioning	56.1±21.6	71.3±16.4	73.4 ±14.7	49.3±26.3	55.3±25.9	53.7±30.4
Role-physical	46.1±32.6	86.8±22.6	81.6±27.4	53.3±39.9	50.0±45.3	50.0±46.3
Bodily pain	79.4±21.9	83.4±18.5	80.6±20.8	54.1±28.2	66.2±23.0	63.6±23.6
General health	61.0±21.5	66.3±14.9	66.8±22.2	54.7±21.8	57.5±20.8	54.9±21.4
Vitality	60.5±18.7	69.2±14.5	67.4±16.2	53.0±20.9	59.3±21.4	56.3±21.5
Social functioning	86.2±22.4	93.4±11.3	87.7±17.9	76.7±24.5	73.3±31.3	77.5±27.6
Role-emotional	80.7±35.7	84.2±30.2	87.7±27.7	62.2±45.2	62.2±45.2	66.7±45.4
Mental health	82.3±12.5	85.3±10.3	86.5±12.2	73.1±19.3	80.3±15.7	82.1±12.5
Health transition	2.6±1.2	2±1.1	2.3 ±1.0	2.9±1.4	2.8±1.2	3 ±0.9
Physical component summary score	39.2±9.8	47.1±6.9*†	46.2±6.2*	36.7±10.4	38.4±11.0	37.0±12.4
Mental component summary score	54.9±10.4	55.0±7.0	54.9±8.9	49.6±12.5	51.1±10.8	52.4±10.6
HAD (range 0-21)						
Anxiety	5.2±3.5	3.4±3.2*†	3.9±3.2*	5.9±3.1	6.0±3.5	4.9±3.8
Depression	3.3±2.8	1.8±1.8	2.2±2.8	4.6±3.3	4.1±2.9	3.5±3.1

AQLQ: Asthma Quality of Life Questionnaire; SF-36: Short Form-36 Health Survey; HAD: Hospital Anxiety and Depression scale. *$p<0.05$ score compared with baseline; $^{\dagger}p<0.05$ change between groups significant; $^{\xi}p<0.05$ 3x2 ANOVA factor*randomisation. $^{\#}$: statistics performed only on the physical and mental component summary scores

Figure 3.11 Mean PCS scores at baseline, 6 weeks and 3 months: per-protocol analyses (n=31)

*** denotes a significant improvement (p<0.05) from baseline**

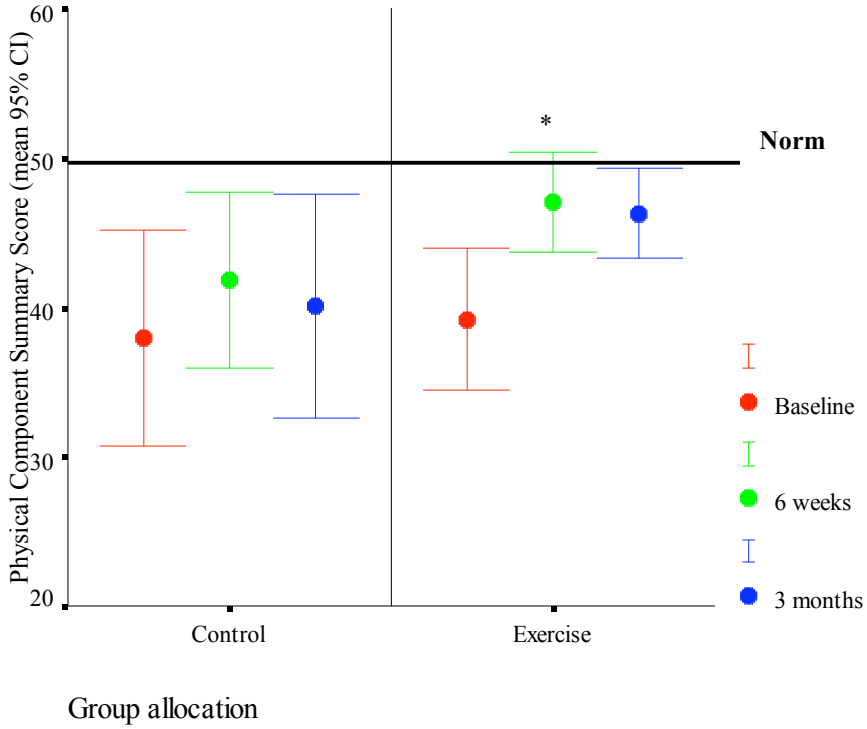


Figure 3.12 Mean MCS scores at baseline, 6 weeks and 3 months: per-protocol analyses (n=31)

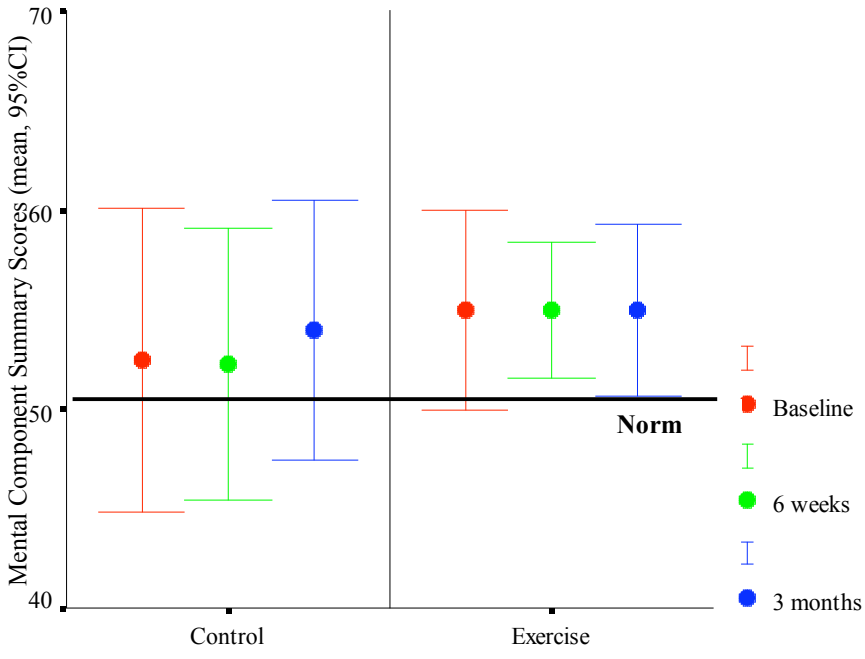


Figure 3.13 Mean PCS scores at baseline, 6 weeks and 3 months: intention-to-treat analyses (n=34)

- **denotes a significant improvement (p<0.05) from baseline**

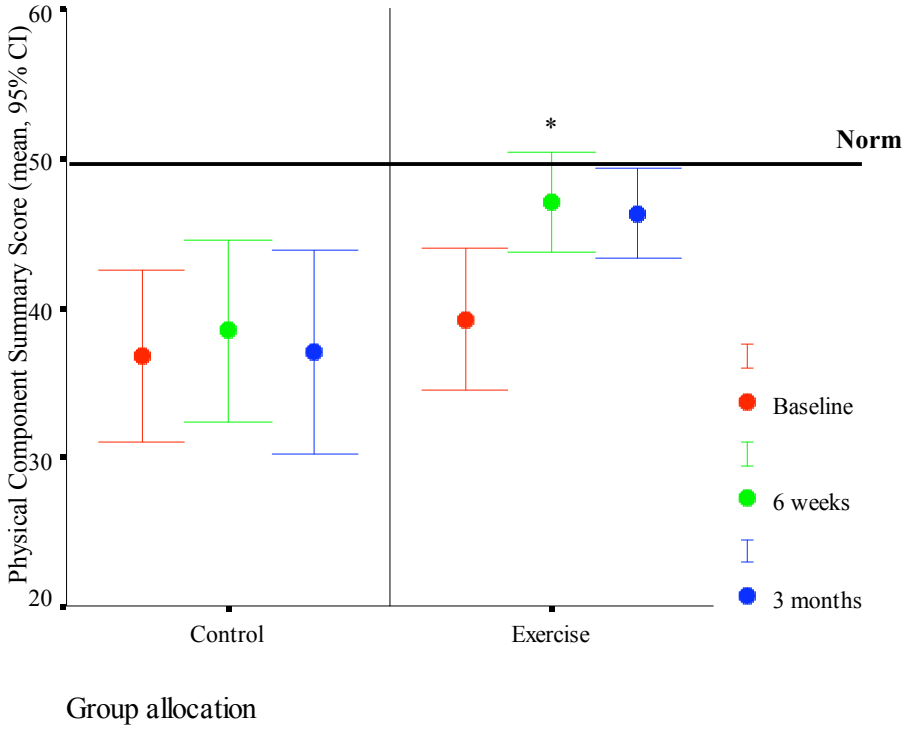
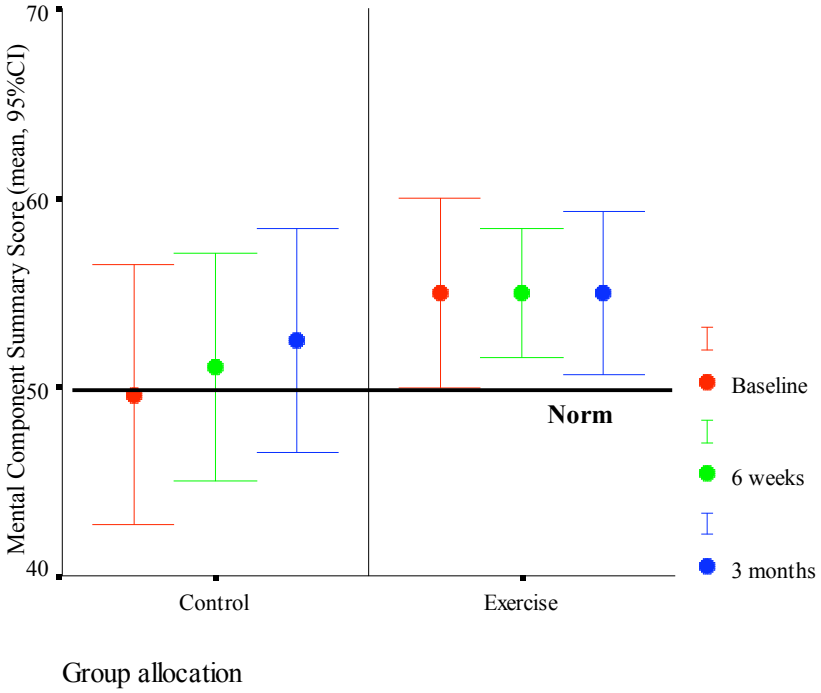


Figure 3.14 Mean MCS scores at baseline, 6 weeks and 3 months: intention-to-treat analyses (n=34)



3.3.15 Six minute walk distance

Table 3.11 displays the 6MWT data at baseline, 6 week and 3 month follow-up using both per-protocol and intention-to-treat analyses. In the exercise group, 6MWD increased by 35.8±37.3m at 6 weeks (p=0.001) and 33.6±44.7m at 3 months (p=0.004) compared to baseline. In the control group, per-protocol analyses showed an increase in 6MWD of 22.0±26.6m (p=0.01) at 6 weeks and 31.2±34.9m (p=0.01) at 3 months. With intention-to-treat analyses, however, the mean change in the control group was not significant at either 6 weeks (6.3±38.3m, p=0.54) or 3 months (13.0±45.6m, p=0.29).

Although the magnitudes of improvement in walk distance were significant from baseline in both groups at 6 weeks and 3 months, the differences between the exercise and control groups were not significant at either follow-up assessment ($p>0.05$, i.e. 3x2 ANOVAs not significant).

Table 3.11 Functional exercise capacity

	Exercise n=19			Per-protocol: Control n=11			Intention-to-treat: Control n=15		
6MWT (best of 2 tests)	**Baseline**	**6 weeks**	**3 months**	**Baseline**	**6 weeks**	**3 months**	**Baseline**	**6 weeks**	**3 months**
6MWD (m)	569±88 (430-703)	555±101 (418-733)	522±111 (333-733)	555±101 (418-733)	577±84* (460-716)	586±94* (456-747)	522±111 (333-733)	528±114 (317-716)	535±122 (317-747)
6MWD (% pred)	91±10 (74-108)	88±12 (72-111)	85±15 (57-111)	88±12 (72-111)	92±9 (74-108)	93±11 (74-111)	85±15 (57-111)	86±14 (54-108)	87±16 (54-111)
Dyspnoea- pre	0.5±1.0 (0-3)	0.5±1.0 (0-2)	0.5±1.0 (0-2)	0.5±1.0 (0-2)	0.5±1.0 (0-2)	0.5±0.5 (0-2)	0.5±1.0 (0-2)	0.5±1.0 (0-2)	0.3±0.5 (0-2)
Dyspnoea- end	3.0±1.0 (0.5-7)	2.0±3.0 (0-4)	2.5±2.8 (0-4)	2.0±3.0 (0-4)	2.0±2.0 (0.5-4)	2.0±1.0 (0.5-5)	2.5±2.8 (0-4)	2.5±1.8 (0.5-4)	2.0±1.0 (0.5-5)
Chest tightness- pre	0.0 ±0.5 (0-2)	0.5±1.0 (0-2)	0.5±1.0 (0-2)	0.5±1.0 (0-2)	0.0±0.5 (0-2)	0.0±0.5 (0-3)	0.5±1.0 (0-2)	0.0±0.9 (0-2)	0.0±0.9 (0-3)
Chest tightness- end	1.0±2.0 (0-3)	0.5±2.0 (0-4)	0.8±2.0 (0-4)	0.5±2.0 (0-4)	1.0±2.0 (0-3)	0.5±2.0 (0-6)	0.8±2.0 (0-4)	1.0±2.0 (0-3)	0.8±2.0 (0-6)
Leg fatigue	2.0±3.0 (0.5-9)	3.0±1.0 (0-7)	3.0±1.0 (0-7)	3.0±1.0 (0-7)	3.0±3.0 (0-9)	2.0±2.0 (0-7)	3.0±1.0 (0-7)	2.0±3.0 (0.5-9)	2.5±2.0 (0-7)
RPE	13.0±3.0 (11-17)	13.0±6.0 (7-19)	14.0±6.0 (7-19)	13.0±6.0 (7-19)	13.0±1.0 (9-19)	13.0±4.0 (9-17)	14.0±6.0 (7-19)	13.0±1.8 (9-19)	13.0±3.3 (9-17)
HR- pre (bpm)	86±12	89±12	85±13	89±12	96±14	92±10	85±13	92±15	89±11
HR- peak (bpm)	129±16	131±20	127±20	131±20	133±19	137±18	127±20	127±20	132±21
%pred HRmax	84 ±11	87 ±12	85±10	87 ±12	88±9	91±10	85±10	85±10	86±12
SpO_2- pre (%)	96±1.5	95.8±0.9	95.5±1.6	95.8±0.9	96.4±0.9	96.1±1.0	95.5±1.6	95.9±1.5	96.1±0.9
SpO_2- end (%)	95.6±2.0	95.0±2.2	93.8±4.7	95.0±2.2	95.3±2.1	95.2±2.7	93.8±4.7	93.7±5.3	94.7±2.8

Mean± SD. 6MWT: 6 minute walk test; 6MWD: 6 minute walk distance; % pred: percent predicted; RPE: rating of perceived exertion; HR: heart rate; bpm: beats per minute; SpO_2: arterial oxygen saturation; %pred HRmax: percent predicted maximum heart rate; IQR: interquartile range; * $p<0.05$ compared with baseline measures.
Percent predicted HRmax calculated from formula 220-age.
Predicted 6MWDs were calculated using the equation derived in healthy West Australian adults.
Dyspnoea, chest tightness, leg fatigue and RPE are reported as medians±IQRs. Data in parentheses are ranges.

3.3.16 Subject feedback

Responses to the feedback questionnaire (Appendix E) from subjects randomised to the exercise group are given in Table 3.12. The walking component was the most-liked component of the training (n=16), followed by step-ups (n=14), bike and arm ergometry (n=13). Subjects made the following suggestions for changes to the training programme: increasing the duration of the classes; including an education component; changing the class time for people who worked; incorporating water-based exercise and increasing the class size.

Subjects also reported that participation in the exercise training programme:

- reduced phlegm and nasal symptoms (n=4)
- improved mental health (n=4)
- increased energy (n=7)
- improved physical fitness (n=8)
- reduced asthma symptoms (n=4)
- decreased the need for reliever medication, improved tone, balance, body posture and sleeping (n=1 for each).

Table 3.12 Feedback following the 6 week exercise training programme (n=19)

	Strongly agreed	Agreed	Unsure	Disagreed	Strongly disagreed
More confident to undertake physical activities	11 (58%)	7 (37%)	1 (5%)		
Improved ability to deal with problems caused by the lung disease	7 (37%)	11 (58%)	1 (5%)		
Satisfied with the place the classes were held	12 (63%)	6 (32%)			1 (5%)
Times of classes suited	12 (63%)	5 (26%)	1 (5%)	1 (5%)	
Length of time of each class was right	13 (68%)	6 (32%)			

Data denote the number of subjects

3.3.17 Twelve month follow-up data

The data collected at 12 months involved a recall of unscheduled medical attendances due to worsening of asthma symptoms collected via self-report in the format of a telephone interview. Table 3.13 illustrates the health care utilisation of the remaining 28 subjects (19 exercise, 9 control) at 12 months.

Table 3.13 Health care utilisation at 12 month follow-up

	Exercise (n=19)	**Control (n=9)**
Courses of oral corticosteroids in last 12 months	7 (37%)	4 (44%)
ED presentations in last 12 months	2 (11%)	2 (22%)
Hospital admissions in last 12 months	2 (11%)	2 (22%)
Nil RP attendances	16 (84%)	7 (78%)
RP attendances (once)	3 (16%)	0 (0%)
RP attendances (2 times)	0 (0%)	2 (22%)
Nil GP attendances	10 (53%)	5 (56%)
GP attendances (1-3 times)	8 (42%)	3 (33%)
GP attendances (4 or more times)	1 (5%)	1 (11%)

ED: Emergency Department; RP: Respiratory Physician; GP: General Practitioner; n: number; %: percent

3.4 Discussion

3.4.1 Overview

This study has demonstrated that a 6 week supervised exercise training programme significantly improves HRQOL and anxiety scores (per-protocol analyses) in individuals with FAOA. Though improvements in other outcomes measured (functional exercise capacity, generic QOL, asthma control and depression scores) were evident in the exercise group immediately post-intervention, a non-significant treatment effect was observed for each of these outcomes in relation to the control group when 3 month follow-up data were included in the analyses.

Compared with previous studies that have investigated the effects of land-based exercise training in asthma, this study has a number of novel aspects and strengths:

i) the study cohort comprised middle-aged and older adults with FAOA - a demographic not previously examined in the literature;

ii) the study was rigorously designed as a RCT with an exercise and control group and the inclusion of a 3 week run-in period that ensured all subjects had stable asthma prior to randomisation and collection of baseline data;

iii) familiarisation with the 6MWT was ensured at baseline and on all subsequent assessments with the aim of confirming that changes in 6MWD were not due to a learning effect for the test; and

iv) the study included assessments of HRQOL, QOL and mood state, outcomes that have been lacking in published RCTs of exercise training in asthma.

The following sections of this chapter discuss the major findings of the study.

3.4.2 Baseline characteristics

3.4.2.1 Subject demographics

Thirty-four subjects participated in this study, all of whom had moderate to severe asthma and a degree of irreversibility in their lung function. The lung function data for the group demonstrated moderate airflow limitation (FEV_1 ≤60%) with evidence of lung hyperinflation and air trapping (RV/TLC 125% and FRC 159%) but normal gas transfer (DLCO/VA 100%). There was a slight preponderance of females in the

study (19 females, versus 15 males), reflecting the gender difference noted in population studies of adults with asthma carried out in Australia (18).

Fifty-six per cent of the cohort reported a diagnosis of atopic asthma that was identified by a positive skin prick test, a raised concentration in serum for specific immunoglobin E or a history of typical rhino-conjunctivitis. Although this information was obtained via self-report, this proportion is similar to previous studies (284, 285).

Subjects randomised to the exercise and control groups were similar in all demographic and anthropometric measures such as age, BMI, gender and in the severity of lung function impairment. Both groups had well preserved peripheral muscle strength and a high level of functional exercise capacity with baseline 6MWDs close (91%) to predicted 6MWDs derived from studies in healthy middle-aged and elderly West Australians (281). More subjects in the exercise group (n=5, 26%) were engaged in full-time work than in the control group (n=1, 7%).

3.4.2.2 Body mass index

The mean BMI for the subject cohort was 27.8±6.2. A BMI within the range of 20-24.9 is considered normal, a BMI 25-29.9 is considered overweight, and a BMI over 30 is equivalent to a classification of obesity, which is 20% above the upper limit of desirable weight (286). However, abdominal circumference is generally a better measure of obesity than BMI due to differences in fat distribution between men and women. Measurement of BMI also fails to take into consideration individuals with a high component of muscle mass (287).

Although recruitment to this study did not target individuals with a high BMI , 65% of the subjects were classified overweight (n=13) or obese (n=9). This percentage is reflective of population statistics for obesity among middle-aged and older adults in Australia. In 2004 - 2005, more than half (54%) of adults aged >18 years were overweight or obese and, more specifically, in adults aged 55-64 years the proportion of males and females classified as overweight was 72% and 58% respectively (288).

Guerra *et al* (289), in a nested case-control study from the longitudinal cohort of the Tuscan Epidemiologic Study of Airways Obstructive Diseases, showed that being overweight or obese significantly increases the risk of developing asthma in females

(adjusted odds ratio [OR], 3.45; 95% CI, 2.10 to 5.67) but not males (adjusted OR, 1.69; 95% CI 0.88 to 3.27). In this study, controls comprised 1,475 subjects who reported no diagnoses of respiratory disease and respiratory symptoms at enrolment and during the study period. A large prospective study in the USA showed that an increased BMI was significantly associated with the risk of 'incident' asthma over a 10 year period, with the strength of the association being similar in males and females (290). 'Incident' asthma was described as a new diagnosis of asthma, or the report of previously diagnosed asthma (i.e. diagnosed in childhood) that had reactivated. Because this information was gathered by self-report, it is uncertain whether these individuals had a diagnosis of asthma or reported respiratory symptoms that were misdiagnosed as asthma.

Similar findings to these have been observed in other population studies in the USA (291) and Sweden (287, 292). Further, the relationship between obesity and asthma in one study was almost exclusively confined to subjects with non-atopic rather than atopic asthma (287).

Several studies have demonstrated a direct association between increasing BMI and asthma morbidity as measured by increased health care utilisation, the frequency of exacerbations, persistent asthma symptoms and the use of inhaled corticosteroids (154, 293, 294). A higher BMI has also been reported to be associated with worse asthma control and a greater impairment in QOL (295). Conversely, asthma severity as defined by the level of bronchial hyper-reactivity (293, 296), airflow obstruction (297) or using the Global Initiative for Asthma (GINA) guidelines (295) does not appear to be associated with increasing BMI (after controlling for age and gender).

Potential mechanisms behind the link between obesity and asthma are multifactorial and could relate to a sedentary lifestyle, diet, histological changes in the lung, or the effect of obesity on immune function (290). It remains unclear whether obesity is a result of asthma rather than the cause of asthma. Regardless, there appears to be a direct relationship between severity of symptoms and health care utilisation and levels of obesity in adults with asthma. This observation is relevant to the present study which targeted adults with moderate to severe disease and evaluated the effects of an exercise intervention on measures of asthma morbidity.

3.4.2.3 Self-management

Asthma Action Plans

The National Asthma Council of Australia recommends that all individuals with asthma should have a written individualised plan of how to treat deteriorating asthma. This should be provided in conjunction with self-management education and training on how to adjust medications (2). A Cochrane review showed that asthma self-management education programmes coupled with regular reviews by a health practitioner was associated with a reduction in hospital admissions, ED presentations, unscheduled visits to the GP, a reduction in the number of days off work and improved quality of life. Measures of lung function were unchanged (298). The provision of an asthma action plan and self-management eduction has also been shown to decrease the risk of asthma mortality by 70% (299).

Forty-four per cent of the subject cohort in this study stated that they had been provided with an asthma action plan. This is higher than data from an Australia-wide study carried out in 2001 that reported between 12.9% and 16.4% adults with asthma had a written asthma action plan (25). Individuals with more severe asthma and those with recent asthma symptoms were more likely to have an action plan, although there was some geographical variation in the data with a lower prevalence reported from WA than some other States (18). Other cross-sectional epidemiological studies have reported the ownership of an asthma action plan to be 13.3% in a Melbourne study (300), 30% in a South Australian cohort (104), and 34.7% in a New South Wales cohort (18).

Peak Flow Meter Ownership

The majority of subjects recruited to this study (n=24, 76%) owned a peak flow meter, however only eight subjects used their peak flow meter at least once a week. Studies carried out elsewhere in Australia report that between 10% and 15% of adults with asthma owned a peak flow meter, however only a minority (<1%) of individuals used their peak flow meter on most days (104, 300).

Habitual exercise

More than half of the study group (56%) reported walking at a moderate pace for 30 minutes, or an equivalent form of exercise on three or more days a week. This proportion is higher than the WA data collected as part of the National Health Survey

(2004-2005). West Australian statistics showed that 52% of adults aged 45-64 years reported walking for exercise with 81% of these engaging in this activity on more than seven occasions during a 2 week period. The findings were similar in those aged over 65 years (i.e. 50% walked for exercise with 76% reporting walking on more than seven occasions during a 2 week period) (301). Of all individuals (all age groups) surveyed in the 2004-2005 National Health Survey, West Australians reported a slightly higher participation rate (51%) for walking compared to the national average (49%) (302).

The level of habitual exercise was higher than expected in the study cohort, and this may have been due to the attractiveness of this type of study to individuals with a positive attitude towards exercise. It is also possible that since this information was obtained through self-report (303), the accuracy of the data may be questionable with a bias towards overestimation of physical activity levels (303).

3.4.2.4 Peripheral muscle strength

The subject cohort showed well preserved peripheral muscle strength at baseline compared to predicted values based on age and gender (268, 270). Peripheral muscle strength did not change in either group during the course of the study.

Skeletal muscle dysfunction is recognised to contribute to exercise limitation in COPD (222) and in subjects with COPD, the presence of muscle weakness has been associated with a greater response to exercise training than in subjects with preserved muscle strength (304). In the early stages of the design of the present study, it was postulated that individuals with FAOA might show signs of peripheral muscle weakness based on long-term oral or inhaled corticosteroid usage. In the year preceding the commencement of this study, 42% of the exercise group and 47% of the control group required treatment with oral corticosteroids to treat at least one asthma exacerbation and two subjects (one control) were receiving maintenance oral corticosteroids.

Further review of the literature suggests that long-term corticosteroid usage may not necessarily be associated with peripheral muscle weakness. One study examining the quadriceps femoris muscles of patients with bronchial asthma on long-term treatment with prednisolone (mean daily dose 17.3mg) did not find clinical

symptoms of myopathy, significant muscle weakness or significant changes in the muscle histology. In the quadriceps muscles of these subjects, however, the glycogen concentration and activity of main regulatory enzymes of glycogen metabolism were modified compared with controls. The significance of these changes are unknown (305).

Inhaled corticosteroid usage is also not linked to muscle myopathy in asthmatics, though little research has been reported in this area. The available studies appear to have focused on the associations between corticosteroid use and loss of bone mineral density and risk of fractures, two consequences which have been associated with long-term oral corticosteroid use (306, 307), but were not observed in individuals prescribed inhaled corticosteroids (308).

3.4.2.5 Six minute walk distance

Familiarisation

In this study, 6MWD increased from 523.5±99.3m to 548.6±101.4m ($p<0.0001$) on the second 6MWT at baseline, which translated to a 5.2±7.0% improvement. There are no reported data on the effects of test repetition on 6MWD in subjects with asthma. Six minute walk distance is influenced by the process of conducting repeat tests on different days (daily variability) (309) and is dependent on the testing protocol (178) (i.e. inclusion of encouragement) (179). Specifically, the magnitude of increase in 6MWD with test repetition at baseline assessment is likely to be protocol dependent.

Two studies have used the identical test protocol to that used in this study and reported the magnitude of the increase in 6MWD with test repetition (281, 310). In healthy middle-aged and elderly subjects (n=109), 6MWD increased by 20±31m (3±5%) in males and 21±24m (4±4%) in females (both $p<0.001$) on the second 6MWT (281). The other study tested 121 individuals with stable COPD referred for pulmonary rehabilitation (310). Subjects in this study were stratified into three groups according to their 6MWD (best of two tests expressed as %predicted 6MWD, i.e. <60%, 60-80% and >80% pred 6MWD). The increase in 6MWD in the three groups was 28±31m, 37±31m and 44±29m respectively which translates into percentage increases in 6MWD of 12%, 9% and 9% (310). Thus in the COPD cohort

the effect of test repetition on 6MWD was greater than in the healthy subjects and this may be explained by the subjects with COPD experiencing anxiety related to dyspnoea which is reduced with habituation on the second test. Using the same 6MWT protocol the increase in 6MWD with test repetition in the FAOA cohort was greater than in the healthy subjects but less than observed in the COPD cohort. This might be anticipated given the FAOA cohort reported some dyspnoea but it was of a lower intensity to that observed in the COPD cohort (310).

Consistent with many other studies, subjects in this study undertook a single practise 6MWT as there is evidence that when a highly standardised 6MWT protocol is used and repeat testing performed on the same day, then any increases in 6MWD with a second practise walk are small (173, 179, 264, 311, 312).

Best distance

At the baseline assessment, subjects demonstrated a high level of functional exercise capacity with 6MWD close to predicted values (88±12%) (281). A 6MWD greater than 82% of predicted has been suggested to represent a normal 6MWD (312). The finding of a high level of functional exercise capacity at baseline was unexpected based on the data obtained in the pilot study. However, exercise capacity as measured by a maximal test such as a laboratory-based cycle or treadmill test may not have been within the normal range in the study cohort. One study demonstrated a noticeable difference in maximal exercise capacity, measured through VO_{2peak} between normal subjects and patients who had mild heart failure but little variation in the distances covered in the 6MWT in the two groups (313).

The baseline 6MWD recorded in the FAOA subjects (548±100m) is higher than has been reported in COPD subjects in studies which have used that same 6MWT protocol (181, 314). In subjects with COPD, Hill *et al* (311) reported baseline 6MWDs of 446±112m in a group of 16 subjects (11 males, mean FEV_1 37±12%), and 508±88m in a group of 17 subjects (11 males, mean FEV_1 37±12%) prior to undertaking an intervention of high-intensity inspiratory muscle training or sham inspiratory muscle training respectively. The principal investigator in this thesis previously reported a study of 20 COPD subjects (15 males, mean FEV_1 29±8%) in whom 6MWD was 475±88m (181). Both of these studies report higher baseline 6MWD than many published studies of individuals with COPD with similar levels of

severity, which may in part be explained by the 6MWT protocol used that is aimed at maximising test performance (179, 187, 207, 309, 315).

Cardiorespiratory responses

The RPE (score of 13) at the end of the 6MWT indicated that the subjects achieved a submaximal but reasonable intensity of exercise. In healthy subjects, an RPE of 16-18 is generally associated with a maximal cardiovascular response with ratings of between 12-14 being reported to be at the level of the anaerobic threshold (230).

The peak HR reached by the subjects during their baseline 6MWT was 84±11% of predicted. This is slightly higher than attained by subjects with moderate to severe COPD using the same 6MWT protocol (81.6±11.4%) (181), but comparable to those recorded in healthy middle-aged and elderly subjects (281). One study in 12 healthy (six males) subjects aged 60-70 years who performed a 6MWT and a maximal laboratory-based treadmill test also showed comparable peak HR's to that recorded in the current study, however comprised an older subject cohort, and utilised a different 6MWT protocol. In this study, the intensity of the 6MWT corresponded to 79.6±4.5% of the VO_{2max} measured in the treadmill test (316). The authors concluded that in healthy older individuals the 6MWT represented submaximal exercise, but the intensity at which the test was performed exceeded the ventilatory threshold.

Despite the subjects with FAOA reaching a high peak HR at the end of the 6MWT, the intensity of dyspnoea was lower than reported in some studies of subjects with moderate to severe COPD. Dyspnoea scores (3 on the Borg scale) at the end of the 6MWT were equivalent to a mild to moderate intensity, compared to studies in COPD subjects performed by the principal investigator and other researchers using the identical 6MWT protocol, that reported dyspnoea intensities corresponding to severe to very severe dyspnoea (181, 191).

The presence of dyspnoea can provide an important warning to an individual with asthma that there may be deterioration in their lung function (317). It has been shown that asthmatic subjects who frequently develop acute airflow obstruction acquire a degree of tolerance that reduces the perception of dyspnoea. Asthmatics with long-standing airflow obstruction also tend to be report less dyspnoea for any given reduction in FEV_1 than asthmatics with complete reversibility in FEV_1 (318). It is

possible that the subject cohort in the present study may have included a large number of individuals with a blunted perception of dyspnoea.

Chest tightness was not a significant symptom for any of the subjects in the 6MWT and the well preserved SpO_2 at the end of the 6MWT was anticipated given that gas transfer was within normal limits in all subjects (319).

3.4.2.6 Asthma control

Fourteen subjects in the exercise group (74%) and eight in the control group (53%) had an ACQ score above 1.5 at baseline which is indicative of poorly controlled asthma (56). The avoidance of environmental triggers and an overall level of good asthma control are considered prerequisites for assisting subjects to achieve a good tolerance to exercise (1).

The international guidelines for complete asthma control recommend that patients should have no symptoms, no activity limitation, no rescue bronchodilator therapy and normal airway calibre (1). The goal of achieving normal airway calibre is not realistic in asthmatics that have permanent lung function irreversibility. Poor asthma control has been reported in up to 70-95% of asthmatics in Western Europe and the Asia-Pacific region (1).

Levels of asthma control and patient adherence to asthma treatments have been shown to decline with age and increasing severity of asthma. One study of 5,107 females with physician diagnosed asthma (mean age 63±7 years), found that adherence to medication guidelines was 57% in those with mild persistent asthma, 55% if moderate persistent asthma was present but only 32% for those with severe persistent asthma (320). It has been reported that as many as 50% of asthmatics do not comply regularly with their medication regimen and that poor compliance contributes to a reduction in HRQOL (321).

3.4.2.7 Quality of life

The study cohort demonstrated impaired QOL compared to age and gender matched Australian and WA normative data. In particular, there were impairments in the SF-

36 domains of physical functioning, role-physical, general health and role-emotional. The PCS score was significantly lower when compared to Australian norms.

Worse QOL and HRQOL have been identified in subjects with asthma compared to healthy subjects in several studies (18, 68, 322), as has a trend for those with moderate to severe persistent asthma to have significantly worse QOL compared to individuals with mild asthma (285). Significant impairments in QOL were reported for all domains of the SF-36 in a community sample of 293 adults with asthma when compared to the Australian norms, with the impairments being more pronounced in the domains relating to physical health (101) consistent with the findings in the present study.

3.4.2.8 Relationships between baseline measures

This study investigated relationships between baseline measures and found that the magnitude of air trapping or pulmonary hyperinflation (RV/TLC) was the strongest correlate (r=-0.66) of functional exercise capacity (i.e. 6MWD). Post-bronchodilator FEV_1, a measure of large airway calibre, also had a positive (but weaker) correlation with 6MWD (r=0.34). This differs from one study in mild to moderate asthmatics, which showed no association between resting measurements of FEV_1 measured pre- and post bronchodilator and cardiovascular fitness (i.e. VO_{2max}, maximum oxygen pulse or anaerobic threshold) measured by a progressive cycle ergometer test. In this study all subjects had well controlled asthma that was less severe than subjects in the present study. The authors of this study concluded that the lack of any correlation between airway obstruction and measures of physical fitness in the asthmatic subjects suggested that factors other than the severity of asthma were responsible for lack of fitness (323).

A moderately strong and significant negative correlation (r=-0.69) was observed between asthma control and total score on the AQLQ in the current study (a higher ACQ score indicates poorer control, whereas a higher AQLQ score indicates better QOL). The magnitude of this relationship is similar to that reported in other studies of asthmatic subjects (84, 324). Two other studies (52, 106) have reported associations between better asthma control and QOL, however in these studies asthma control was not measured using the ACQ. Specifically, asthma control was

defined using the GINA guidelines in the study by Bateman *et al* (106), while the Asthma Therapy Assessment Questionnaire was used in the study by Vollmer *et al* (52).

There was no relationship between scores on the AQLQ and FEV_1 (r=0.19), consistent with the findings of other studies (45, 68, 325). Ehrs *et al* (325) found a relationship between lower QOL and high usage of inhaled corticosteroids and suggested that corticosteroids may be more potent at normalising lung function than improving symptoms and QOL. Moy *et al* (45) also found no significant correlation between FEV_1 and HRQOL in adults with moderate to severe asthma and that the strength of the association between symptom intensity and HRQOL was lower in this cohort when compared to subjects with mild asthma. Weaker associations between HRQOL and physiological measures such as FEV_1 may suggest that psychosocial factors such as coping styles, as well as socioeconomic factors such as education or employment status can also influence QOL (45). Another theory is that the perception of airway narrowing varies greatly between patients with asthma (318), and this may have an influence on HRQOL (68).

3.4.3 Efficacy of the intervention

3.4.3.1 Lung function and baseline demographics

There were no significant changes in any measures of lung function at the 6 week follow-up compared to baseline. This is in agreement with other studies of exercise training which reported no changes in lung function (200, 207, 277, 326, 327) or bronchial reactivity (206) following an exercise intervention. It has been suggested any improvements in lung function after exercise training would more likely be attributed to improved compliance and the optimisation of asthma treatment as a result of increased medical supervision provided during the intervention (202).

No significant changes in BMI were found at the 6 week or 3 month follow-up in either group. Although regular exercise can contribute to weight loss, the benefits from short-term exercise programmes (less than 6 months duration) are minimal unless accompanied by strict dietary control (328). Subjects in the current study were instructed not to change their dietary habits throughout the intervention period to avoid any confounding influences on the study findings.

3.4.3.2 Asthma control

The present study did not show any statistically significant improvements in asthma control following exercise training. Seven subjects did, however, exhibit a clinically significant improvement in their ACQ scores immediately post-intervention, six of whom were randomised to the exercise group. The question remains as to which components of asthma control could be improved in response to an exercise intervention? This study found no change in FEV_1 following exercise training, and since all subjects recruited to this study had a degree of fixed obstruction this finding was expected. The other six items on the ACQ pertain to night waking, activity limitation, morning symptoms, dyspnoea, wheeze and the frequency of rescue medication usage. Of these, the components of asthma control most likely to change secondary to an exercise intervention are activity limitation and dyspnoea. It is also possible that any overall changes in asthma control in the study participants may have been a result of improved adherence to medications, as this in turn is a component of asthma control (18, 52).

There is limited evidence which shows regular exercise is associated with fewer exacerbations, a decreased need for asthma medications and less absenteeism from school or work, but overall the relationship between exercise and asthma control remains unclear (1). In a study by Garfinkel *et al* (158) more than two thirds of the participants held a belief that if they improved their physical fitness this would result in improved asthma control.

3.4.3.3 Quality of life, anxiety and depression

Both immediately post-intervention and at 3 month follow-up, statistically and clinically significant improvements were observed in the total score, symptoms and activity domains of the AQLQ in the exercise group compared to the control group. A significant improvement in anxiety was also observed with per-protocol analyses over the course of the study. These findings illustrate the positive psychological benefits of exercise training. The Cochrane review of exercise training in asthma consisted of 13 trials, however none of these trials included measures of QOL or anxiety and depression. The present study is the first to examine the effects of exercise training on QOL using both generic and disease-specific QOL measures (9).

An intervention programme, such as that conducted in this study can, by nature of the supervision and group interaction, bring about a positive change in the subject's emotional well-being.

Signficant improvements in QOL were reported by Foglio *et al* (207), in a mixed cohort of asthmatics and COPD subjects, following a 6 week exercise training programme. These authors showed significant improvements in the activity and impact scores on the St George's Respiratory Questionnaire, however no changes in symptom scores were found. These improvements were maintained at the long-term follow-up (12 months) in the asthmatic cohort. A major limitation of this study, however, was the lack of a control group.

One other study of subjects with asthma reported improvements in QOL following rehabilitation. In a RCT with a crossover design conducted by Cambach *et a*l (205), 43 subjects with COPD (FEV_1 59% predicted) and 23 with asthma (FEV_1 86% predicted) who received a 3 month pulmonary rehabilitation programme were compared with a control group. Significant improvements in QOL were reported using the Chronic Respiratory Disease Questionnaire immediately following the rehabilitation programme, that were still present when subjects were assessed 3 months later.

3.4.3.4 Six minute walk distance

There were no statistically significant improvements in 6MWD in the exercise group compared to the control group over the course of the study. Baseline 6MWD in the exercise group was 569±88m and for the control group was 555±101m. These distances increased to 605±89m and 528±114m respectively immediately after the intervention period (intention-to-treat analysis). With the per-protocol analysis these distances were 605±98m and 577±84m respectively. This change in 6MWD (35.8±37.3m) was significant compared to baseline in the exercise group, however the difference between the groups was not significant. The threshold for the minimal clinical important difference (MCID) in 6MWD has not been determined for subjects with asthma.

In subjects with COPD, the first study to determine the MCID for the 6MWD following pulmonary rehabilitation concluded that a change of 54m was perceived by

subjects to be clinically important (194). However the change in 6MWD in many RCTs of pulmonary rehabilitation in this population fails to reach this threshold value (6). A recent study calculated that a change of about 35m in 6MWD, represented an important effect following rehabilitation for patients with moderate to severe COPD (193). Data were used from nine trials which enrolled COPD patients with a wide spectrum of severity to calculate this value of 35m. Guyatt *et al* (329) estimated a similar MCID with an increase of 30m or more in 6MWD being associated with an important improvement in exertional dyspnoea.

In subjects with asthma, there are only three studies that have used 6MWD to measure outcomes following an intervention that included exercise training. Improvements in 6MWD have been reported following exercise training both immediately post-intervention and at long-term follow-up in individuals with asthma (205, 207, 330). In the study by Foglio *et al* (207) which consisted of 35 subjects with asthma and 26 subjects diagnosed with COPD, 6MWD significantly improved immediately following an 8 to 10 week exercise programme, an improvement that was partially lost at 1 year follow-up in the asthmatic cohort (6MWD=471±61m at baseline, 508±56m post-intervention and 485±60m at 1 year follow-up, $p<0.05$). A major limitation of this study however was the lack of a control group.

In the RCT with a crossover design reported by Cambach *et a*l (205), an improvement of 55m occurred in 6MWD in the asthmatic subjects following the 3 month pulmonary rehabilitation programme. The increase in 6MWD following rehabilitation was significant when compared to the control period which comprised usual care only. Emtner *et al* (330) used the 12 minute walk test in a study of adults with mild to moderate asthma who underwent an intensive 10 week programme of exercise training and education that commenced with a 2 week inpatient period. Subjects were followed up for 3 years. The authors reported an improvement in 12MWD following the intervention and 12MWD remained above baseline when assessed at the 3 year follow-up.

In the present study it is feasible that no significant changes were observed in 6MWD post-intervention between the exercise group and control group because the intervention was not effective in improving functional exercise capacity in this cohort. However, because signficant ($p<0.05$) improvements in 6MWD were seen immediately post-intervention in the exercise group, but not in the control group, it is

more likely that the lack of any intervention between the 6 week and 3 month follow-up weakened the strength of the treatment effect calculated in the 3x2 ANOVA. Additionally the positive benefits observed in the activity and symptoms domain of the AQLQ in the exercise group strengthens the likelihood that the exercise training was beneficial in this group, at least in the short-term.

Unexpectedly, a high 6MWD was measured at baseline in this FAOA cohort. This was not expected based on the small pilot study carried out and reported earlier in this chapter. The high baseline 6MWD may have limited the responsiveness of the 6MWT to detect a meaningful change in functional exercise capacity on further testing due to mechanical factors that limit the ability to increase stride length (331).

In the current study, the 6MWT was used to measure functional exercise capacity for several reasons. The following section discusses the rationale for choosing the 6MWT, and other walking tests that were considered as outcome measures.

The exercise intervention involved a large component of ground-based walking training. This is because walking is a very functional form of exercising, often avoided by people who are breathless, it is simple to undertake as it does not require any equipment and thus could be carried out long-term by the subjects. A further reason for selecting the 6MWT was to enable a comparison to be made of any changes in 6MWD in the FAOA cohort with the magnitude of change reported following exercise training in subjects with COPD. Lastly, the intent of this study was to develop an exercise programme that could be implemented in other centres within metropolitan, regional and rural WA and thus an exercise test that required no sophisticated equipment was necessary.

It is possible that an alternative field walking test may have been a more responsive measure in this subject population. Tests to consider include the 12MWT, the incremental shuttle walking test (ISWT) and the modified shuttle walking test. To date, no studies have compared the responsiveness of these tests with that of the 6MWT in subjects with FAOA. The 12MWT is seldom used in the current literature, due in part to the time consuming nature of the test. However, this test may have provided an indication of exercise endurance capacity and as such may have shown a change in the exercise group given that the distance walked in 20 minutes during the programme increased by 18±10%.

The ISWT has been tested in healthy older individuals (332). All of the subjects stopped the ISWT due to mobility limitations, suggesting that the inability to increase gait speed may have also limited the responsiveness of this test in the FAOA subjects such as occurred in the 6MWT. The latter stages of the modified ISWT (333) allow the subject to run and hence this test does not rely on the ability to increase stride length or walking cadence to show an improvement. A decision was made, however, not to use a test that involved running in this FAOA cohort due to safety reasons including the possibility of causing a musculoskeletal injury.

In the COPD cohort, there is some evidence that the endurance shuttle walking test (ESWT) may be a more responsive measure to change following pulmonary rehabilitation than either the 6MWT or the ISWT (196, 334). However, disadvantages of the ESWT include the necessity of a prior ISWT and the difficulties achieving appropriate test duration at baseline to allow improvements following an intervention to be detected within the 20 minute time limit allowed for the ESWT. Further, the ESWT has not been studied in the FAOA population.

Finally, laboratory-based tests such as a walking test using a treadmill may have been more responsive than the 6MWT as they allow workload to be increased by adding an incline and thus are not solely reliant on ability to change stride length and cadence. Similarly, performance on a maximal bike test is not subject to the same limitations as field walking tests. However, for the reasons stated earlier, these tests were not considered as outcome measures.

3.4.3.5 Comparison of study results to mild and moderate chronic obstructive pulmonary disease

It could be proposed that literature and outcomes from exercise training in individuals who have mild and moderate COPD may be more appropriate to consider in relation to this study population who had a component of fixed obstruction, as opposed to studies of asthmatics with fully reversible disease. Although there is a large body of literature investigating the effects of exercise training in moderate to severe COPD, the number of studies in mild to moderate COPD are much less numerous and have shown some mixed results. One study has reported no effect on exercise tolerance, dyspnoea or QOL after a 2 month exercise programme (335),

another showed improved exercise tolerance but no difference in dyspnoea after an 18 month programme (336) and another showed improvements in exercise tolerance after a 3 month exercise programme (337).

A systematic review of exercise training for adults with mild to moderate COPD included five RCTs (215). These studies included only subjects with an FEV_1 between 47-77% predicted. Four of the studies reported an improvement in exercise tolerance following training. A variety of measures were used comprising the 6MWT, maximal cycle ergometry test and an endurance walking test. The one study that failed to show an improvement had a low dose of supervised training (two sessions a week for 8 weeks) (335). The review showed no clear effect on dyspnoea or QOL, which in part may have been due to the relatively low numbers of subjects in these studies (215). The authors concluded that exercise training improves exercise tolerance in mild to moderate COPD. Further, the review did not provide evidence of any consistent effect could be found on dyspnoea or QOL, nor could exercise training be shown to significantly affect long-term disease progression (215).

One other study (338) stratified COPD subjects based on their impairment in FEV_1 and compared outcomes following a 12 week exercise programme. Subjects with mild disease (FEV_1 >49% predicted) demonstrated a significant increase in 6MWD, endurance treadmill time and a reduction in dyspnoea assessed using the Chronic Respiratory Disease Questionnaire. The magnitude of change in these outcome variables was not significantly different from those observed in subjects with moderate or severe disease with the exception of treadmill endurance time which did not increase in those with very severe disease. Limitations of this study were the lack of a control group and the lack of a practice 6MWT at the baseline assessment.

Patients in the early stages of COPD have been described as not recognising the presence of their disease and not considering the associated disability to be sufficient to necessitate rehabilitation, and this may explain why QOL and dyspnoea do not appear to improve in this cohort to the same extent as seen in individuals with more severe COPD (225).

3.4.3.6 Feedback from the exercise training programme

The feedback from the subjects who participated in the exercise training programme was positive, and highlighted that participation in the programme increased the confidence of participants to undertake physical activity. The majority of the subjects felt their ability to deal with problems caused by their asthma was improved, thus indicating an effect of the programme on self-management despite no asthma education being provided during the training sessions.

Similar benefits have been reported by Emtner *et al* (330) following a 10 week programme which incorporated education and physical training in adults with mild and moderate asthma (FEV_1 >75% post bronchodilator). Following the exercise component of the programme, all 21 subjects interviewed retrospectively as part of a study on long-term follow-up indicated that the training improved their ability to exercise to a maximal level. In addition, 19 subjects felt they had an improvement in their asthma status, 13 claimed to have benefited from the sense of security from exercising at a hospital, and 12 of the subjects believed that they had benefited from the use of pre-medication and a long warm-up in conjunction with the exercise.

3.4.3.7 Health care utilisation and 12 month follow-up data

Seven of the 34 subjects (20.5%) had visited an ED because of their asthma in the 12 months prior to the study and of these five had been hospitalised. The present subject cohort reported a high level of utilisation of medical services for their asthma prior to study entry in comparison to that reported in other studies of asthmatic populations within Australia. A cross-sectional study carried out in Melbourne found 2% of the asthmatics interviewed had visited the ED because of their asthma in the preceding year, 28% had seen their GP and 2.3% had visited a specialist (300). In a random survey of a population with self-reported asthma conducted in South Australia in 1997 (over 3,000 interviews carried out), approximately 5% of individuals reported a previous hospitalisation (not confined to the preceding year) (104).

Risk factors for visits to the ED reported in asthmatics include the suboptimal use of preventative medication (61), the absence of a predetermined crisis plan or asthma action plan, previous visits to an ED and inadequate use of prophylactic medication during an exacerbation (339).

In a study of inner city minority populations, in which a prospective cohort of 198 individuals was interviewed over a period of 1 year, patients who were followed by an asthma specialist were significantly more likely to present to an ED or have been hospitalized during the 6 month follow-up period (p=0.002). Care of a specialist was associated with increased resource utilization and probably reflected the fact that sicker patients were more likely to be referred to specialists, as opposed to indicating differences in asthma management (340).

One of the secondary objectives of the current study was to assess health care utilisation at 12 months following cessation of the intervention period. However as this was a secondary objective the study was not powered for this variable.

In the current study, there was a significant attrition at 12 months and this was greater in the control group (20% versus 5%) and thus limited any opportunities for comparison between the groups for these data.

Although exercise training in COPD patients has been associated with a reduction in health care utilisation (7, 341), this has not been studied in subjects with FAOA (207). One study in individuals with mild to moderate asthma (post-bronchodilator FEV_1 >75%) reported that the number of ED visits decreased from 28 episodes in the year before participation in a 10 week pulmonary rehabilitation programme (exercise, education and physiotherapy) to 15 episodes during the following year (330). However this study lacked a control group for comparison.

Previous studies have shown recall for hospital care and visits to respiratory specialists are fairly reliable, but may be unreliable for other types of health care utilisation, such as visits to the GP (342). Because data on health care utilisation are often based on self-report, it is possible that there may be recall bias, with those who report poorer asthma control (i.e. in response to the Asthma Therapy Assessment Questionnaire) also more likely to recall their health care utilisation history than someone who has better control over their asthma (52).

3.4.4 Sample size issues and statistical power

Forty subjects were initially recruited and randomised for the study. Based on power calculations it was anticipated this number would have been of sufficient size to detect a significant change in the primary outcome measures as the calculations prior

to the study showed that a sample size of 32 subjects was required to detect a clinically significant change (0.5 points per item) in the activity domain of the AQLQ and a 54m change in 6MWD between groups with 80% power ($\alpha = 0.05$) (66, 69, 194, 207).

Only 20 subjects remained in the exercise group and 15 in the control group at the baseline assessment. This reduced to 19 subjects (95%) in the exercise group and 15 in the control group at 6 weeks (100%). Two subjects in the control group withdrew prior to the 3 month assessment, and at 12 months, only nine of the control group subjects (60%) could be contacted. This level of attrition seems reasonable in comparison with the few published RCTs of exercise training in adults with asthma. For example, the attrition rate in the crossover study by Cambach *et al* (205) was 33% and 20% in the two subject groups. Although there was no attrition in the study by Cochrane and Clark (200), (18 subjects in the exercise group, 18 in the control), over the course of this study six subjects in the exercise group (33%), and three of the control subjects (17%) had an alteration to their asthma medication - an outcome which would have resulted in these subjects being included in only intention-to-treat analyses had they been involved in the current study.

Reasons for the low participation rate in this study may have related to the time involved, which included both attendance at assessments (2 hours) at intervals throughout the study period and the necessity to attend classes if randomised to the exercise group (three times a week with each class lasting 1.5 hours and taking place during normal office hours, which limited participation by subjects who were employed). In addition to the travel time required for participants, there were also often problems for subjects in finding car-parking spaces at the hospital where the study was conducted. Attempts to overcome some of these problems included the provision of free parking and hospital transport if required. However, use of the hospital transport added greatly to the time commitment involved, as to attend a 1.5 hour class the subject would have to be ready for pick-up at least 2 hours prior to the class and may have waited up to 2 hours for return transport.

3.4.5 Limitations of the study

There are a number of limitations with this study. Despite being a RCT, the study subjects could not be blinded as to which group they were randomised to after the baseline assessment. This may have influenced responses to the self-complete questionnaires. Further, resource limitations limited the use of a blinded assessor and thus measurement bias was also possible since the principal investigator completed all assessments and also supervised the training programme. Attempts to overcome some of this bias involved the investigator not reviewing any of the baseline data for the primary and secondary outcome measures prior to any follow-up visits.

It was inevitable that the nature of conducting a study involving exercise was likely to attract subjects who are already keenly motivated to either make a change in their current management or were already converted to the positive benefits of exercise, which may have reduced the potential for a positive treatment effect in some of the outcomes measured. The overall effect size between groups was smaller than expected, therefore more subjects were needed to gain adequate study power.

Individuals who were randomised to the control group, although instructed to continue with their normal management for their asthma and asked not to change their exercise habits, were not monitored for their exercise habits. The majority of those who entered the study stated that they were enthusiastic about the chance of participating in a supervised exercise programme, and it is likely that improvements seen in the control group (i.e. significant improvements in 6MWD from baseline), were a result of the Hawthorne effect, with some individuals in the control group admitting at the 6 week assessment they had increased the amount of exercise they were taking at home. In contrast, some individuals randomised to the control group seemed to lose interest in the study, and withdrew before completing the 3 month follow-up. This high level of attrition was not expected in this group, and limited the overall power of the study.

Because exercise classes utilising the physiotherapy department facilities at SCGH could only be held during office hours, a number of participants in the exercise group had difficulties attending classes due to work commitments. The study population included a proportion of adults who worked either full or part-time. In the screening phase many of these workers were not interested in participating in the study in the

knowledge that if they were randomised to the exercise group they would have to withdraw due to work commitments. However, some subjects who were still working and recruited to the study attempted to change their working hours to participate in the study in the event of being randomised to the exercise group, and in some cases this resulted in an incomplete number of class attendances (<18 sessions).

In this study, baseline functional exercise capacity measured by the 6MWT was not remarkably different from normative data, nor was dyspnoea a significant factor limiting performance on the test. This suggests the possibility that the 6MWT was not as responsive as other measures for detecting change in the exercise group with the training, and also highlights that individuals with FAOA present differently to individuals with COPD in terms of their physical limitations and symptom severity. In retrospect, the inclusion of a maximal exercise test may have detected improvements following exercise that were not evident with the 6MWT.

The literature shows that the 6MWT has been applied in many patient populations other than those with COPD. Examples include individuals undergoing surgical procedures, adults with congestive heart failure, cystic fibrosis, pulmonary hypertension, interstitial lung disease or peripheral vascular disease, and thus it was reasonable to assume that its applicability could be translated to older individuals who had a component of fixed obstruction as a result of asthma (311). Further research is necessary to evaluate its discriminative properties amongst individuals with conditions other than COPD (178).

A limitation of this study arose because of the lengthy and difficult process in subject recruitment. Because it was such a select group of individuals, the numbers of subjects involved in the exercise programme at any one time were small, which reduced the positive benefits of peer support that may occur when subjects train in a group setting.

Finally, due to the expense associated with procedural assessments, it was not possible to test all subjects via HRCT scans for evidence of emphysema or chronic bronchitis and so, although subjects had minimal or no smoking history, it is not possible to rule out a degree of co-existent COPD being present. In addition, a recommendation for future studies of exercise training studies in this subject

population is that objective assessment of activity levels using a physical activity monitor be performed.

3.5 Implications and conclusion

In summary, a 6 week exercise intervention produced a positive change in disease-specific QOL and anxiety that was maintained at 3 months and was significant in comparison to the control group. Improvements in 6MWD, asthma control, depression scores and generic QOL, although significant against baseline measures in the exercise group, had either declined at 3 months or were not of a statistically significant magnitude compared with the control group.

Although exercise training is of benefit in adults with FAOA, any improvements tend to decline as training ceases. Further studies are recommended to ascertain the costs versus benefits of providing programmes for older adults with chronic asthma and to assess whether improvements in functional exercise capacity translate into a reduction in GP attendance, ED visits or hospital stays (as is the case for COPD).

Clinical implications of the findings of this study are that first, individuals with FAOA referred to pulmonary rehabilitation programmes are likely to tolerate higher intensities of exercise than their counterparts with COPD. A 6MWT may not be an appropriate measure for functional exercise capacity in this group due to a potential ceiling effect at baseline, and this should be taken into consideration in the assessment of these patients when they are referred to a pulmonary rehabilitation programme.

The high baseline 6MWD in individuals who have FAOA and the low levels of dyspnoea experienced by these subjects during the 6MWT, particularly in relation to the past experience of the investigators in assessing individuals who had been referred to pulmonary rehabilitation with COPD, prompted the development of a further study which is presented in the following chapter. The study that follows compared outcomes measured in a group of individuals with COPD who had a similar level of pulmonary hyperinflation and air trapping, and were age and gender matched with those of obtained in a sample drawn from individuals with FAOA who participated in this RCT.

CHAPTER 4

Differences in resting lung function and functional exercise capacity in a fixed airway obstruction asthma and chronic obstructive pulmonary disease cohort

4.1 Introduction

Older individuals with more severe asthma and an irreversible component of their lung function measurements (fixed airway obstruction asthma, FAOA) are more likely to be referred to hospital or community-based pulmonary rehabilitation programs than those with mild asthma. This referral trend arises because it is acknowledged that many of the clinical features which are associated with chronic obstructive pulmonary disease (COPD) and FAOA overlap, such as similarities in measures of airflow, symptoms of dyspnoea and reduced exercise tolerance (4, 343, 344).

An unexpected finding in the FAOA cohort studied in Chapter 3 was their relatively low level of dyspnoea at the end of the 6 minute walk test (6MWT) and high 6 minute walk distance (6MWD). This questions the responsiveness of the 6MWT in these individuals and raises the possibility of a 'ceiling effect' with this test. The physiological basis for this finding is examined in the following chapter by comparing cardiorespiratory and dyspnoea responses to the 6MWT in a FAOA

cohort and COPD cohort selected on the basis of the severity of their resting pulmonary hyperinflation, age and gender.

The COPD cohort were obtained from a randomised controlled trial (RCT) investigating the benefits of inspiratory muscle training that was carried out in the same research facility and utilised the same protocols for the 6MWT and for assessments of peripheral muscle strength, and for measurements of lung function. To ensure a cohort who clearly had air trapping was recruited, the resting ratio of residual volume to total lung capacity (RV/TLC) was the primary measure used to match the two groups. This was for a number of reasons:

1) RV/TLC showed a much stronger correlation with 6MWD ($r=-0.66$, $p<0.001$) than forced expiratory volume in one second (FEV_1) with 6MWD ($r=0.34$, $p<0.05$) in the RCT of exercise training in the FAOA cohort as outlined in Chapter 3 (Table 3.6);

2) matching of the subject cohorts primarily on their FEV_1 could pose problems, given the potential for more day-to-day variability in this measure within the FAOA cohort; and

3) there is evidence that RV/TLC is more strongly correlated to exercise capacity than FEV_1 in both COPD subjects and subjects with moderate to severe asthma (345).

4.2 Methods

4.2.1 Objectives

The primary objective of this study was to compare functional exercise capacity (i.e. 6MWD) and resting lung function in a cohort of subjects with FAOA matched with a cohort of COPD (emphysema/chronic bronchitis) subjects.

4.2.2 Research hypothesis

The study hypothesis was that the preservation of gas transfer in the FAOA subjects would result in better exercise performance than their matched counterparts with COPD, even though the cohorts have a similar magnitude of air trapping and hyperinflation.

4.2.3 Aims

To compare, in a matched cohort of subjects with FAOA and COPD:

- resting lung function;
- functional exercise capacity [6MWD, peak heart rate (HR), oxygen saturation (SpO_2) and dyspnoea post-exercise]; and
- peripheral muscle strength (handgrip and quadriceps strength).

4.2.4 Study design

A cross-sectional matched comparison study was conducted.

4.2.5 Subjects

Inclusion criteria

The COPD subjects were drawn from a cohort who had participated in a RCT of inspiratory muscle training (346) and met the following criteria:

- a diagnosis of COPD;
- smoking history > 20 pack years; and
- FEV_1 < 80% of the predicted normal value.

The FAOA cohort was drawn from a group of moderate to severe asthmatics who had participated in the RCT of exercise training (Chapter 3) and met the following criteria:

- minimal or no smoking history (<15 pack years); and
- single-breath diffusing capacity of the lung for carbon monoxide corrected for alveolar volume (DL_{CO}/VA) > 80% of the predicted normal value

and at least two of the following:

- FEV_1 <80% of the predicted normal value;
- FEV_1/ forced vital capacity (FVC) <80% of predicted ratio; or
- RV >120% predicted.

These criteria aimed to capture a cohort of asthmatics who had a degree of fixed obstruction affecting the small and/or large airways. It was conjectured that there was a risk that subjects with asthma affecting the small airways alone might have been

excluded if the selection criteria defined moderate to severe asthma on the commonly used basis of FEV_1 alone (262).

Subjects with FAOA were under the long-term management of a respiratory physician with a special interest in asthma Professor PJ Thompson (PJT) and had undergone detailed investigations to determine disease variability, trigger factors, atopy and responsiveness to medications.

To confirm stable disease prior to commencing the intervention phase of the study the asthmatic subjects were asked to attend a weekly assessment for a minimum of 3 weeks to undergo spirometry and to complete the Asthma Control Questionnaire (ACQ) (55).

Both COPD and FAOA subjects were free from major musculoskeletal, cardiovascular and neurological conditions likely to adversely affect exercise performance. Ethical approval was obtained from the Human Research Ethic Committees of Sir Charles Gairdner Hospital (SCGH), (Ethics approval numbers: 2003-149 and 2001-149) and Curtin University of Technology (Ethics approval numbers: HR120/2004, and HR 210/2002). Written, informed consent was obtained from all subjects.

4.2.6 Matched variables in the fixed airway obstruction asthma and chronic obstructive disease cohorts

Subjects within the population were evaluated and selected to ensure comparability of:

- gender,
- age (± 5 years), and
- the severity of air trapping and pulmonary hyperinflation at rest measured by RV/TLC (± 0.05).

All measurements in both groups were made within a 4 week period when subjects were in a stable condition. Specific details of the methodology are given in Chapter 3 and are outlined in brief below.

4.2.7 Resting lung function

Measurements obtained were:

- FEV_1 and FVC (digital pneumotachograph, Vertek Series Hewlett-Packard, Palo Alto, CA, USA);
- resting lung volumes (Medgraphics Elite Series DX plethysmograph; Medical Graphics Corporation, St Paul, Minnesota, USA); and
- DL_{CO}/VA (P.K. Morgan Ltd, Chatham, UK).

The American Thoracic Society Guidelines (263) were followed for calibration, quality control and correction for haemoglobin concentration. To normalise all of the data, measurements were compared to predicted normal values obtained from published regression equations as outlined in Table 4.1. Full details of these measurements are given in Section 3.2.7.3 of Chapter 3.

Table 4.1 Predicted normal values for resting lung function measurements: regression equations

Gender	Variable	Equation
Males	TLC	8.67*height-8.49 (347)
	VC	5.2*height-0.022*age-3.6 (348)
	RV	2.7*height + 0.017*age-3.45 (349)
	FRC	5.78*height+0.016*age-0.04*weight-4.24 (350)
	FEV_1	$0.5536+(-0.01313*age)+(0.000172*age^2)+(0.00014098*height^2)$ (351)
	FVC	$0.1933+(0.00064*age)+(-0.000269*age^2)+(0.00018642*height^2)$ (351)
	DL_{CO}/VA	10.0882-2.244*height-0.0309*age for non-smoker
		9.72-2.244*height-0.0309*age for ex smokers and
		9.3214- 2.244*height-0.0309*age for current smokers (352)
Females	TLC	7.31*height-0.016*age-6.29 (350)
	VC	4.17*height-0.021*age-2.87 (353)
	RV	3.2*height + 0.009*age-3.9 (349)
	FRC	5.59*height-0.03*weight-4.91 (350)
	FEV_1	$0.4333+(-0.00361*age)+(-0.000194*age^2)+(0.00011496*height^2)$ (351)
	FVC	$0.356+(0.0187*age)+(-0.000382*age^2)+(0.00014815*height^2)$ (351)
	DL_{CO}/VA	8.3297-1.811*height-0.0157*age for non/ex smokers
		7.5732-1.811*height-0.0157*age for smokers (352)

TLC: total lung capacity; VC: vital capacity; RV: residual volume; FRC: functional residual capacity; FEV_1: forced expiratory volume in one second; FVC: forced vital capacity; DL_{CO}/VA: transfer factor for carbon monoxide corrected for alveolar volume. Height is measured in metres in all equations apart from the FEV_1 and FVC where it is expressed in centimetres.

4.2.8 Six minute walk test

The 6MWT was performed using a 45m straight course within a temperature-controlled corridor within the hospital. Tests were supervised by one of two physiotherapists [Sian Turner (asthma cohort), Dr Kylie Hill (COPD cohort)]. Chairs were placed at both ends to enable seated rests if required. The specific instructions given to subjects and full details of the protocol have been described in Chapter 3, Section 3.2.8.1. The 6MWT was performed in accordance with current recommendations (178), but modified to include standardised encouragement to recommence walking every 15 seconds during any rest periods. Additionally, heart rate (HR) was recorded prior to commencing the test and was continuously monitored throughout the test (Polar a1 HR monitor; Polar Electro Oy, Kempele, Finland). The HR at the end of each minute was recorded. The peak HR achieved during the test was used in the analyses. Arterial SpO_2 was measured prior to and immediately following test completion using a pulse oximeter and finger probe (Ohmeda 3700; GE Health care, Louisville, CO, USA or Tuffstat monitor (Datex Ohmeda, GE Health care, Louisville, CO, USA). The end-exercise SpO_2 was recorded.

Dyspnoea was measured prior to and at the end of each 6MWT using the Borg (0-10) dyspnoea scale (146). This same scale was used to determine the severity of leg fatigue at the end of the test. In the protocol followed by the COPD subjects, SpO_2 was monitored continuously throughout the test for safety reasons and dyspnoea scores were collected at the end of each minute. The end-exercise data for SpO_2 and dyspnoea were used to compare the responses in the COPD cohort with those of the subjects with FAOA .

Two 6MWTs were performed, separated by between 20 and 60 minutes rest. Supplementary oxygen was not used by any subject during the tests. Data from the greatest 6MWD were used in the analyses. Predicted values for the 6MWD were obtained from a recent study carried out in healthy West Australian adults (281).

4.2.9 Peripheral muscle strength

4.2.9.1 Quadriceps strength

Quadriceps force was measured using a strain gauge (Fall assessment Kit, Prince of Wales Medical Research Institute, NSW, Australia) following a standard protocol with the subject seated with the hips and knees flexed to 90 degrees (269). Subjects were instructed to generate a maximal isometric contraction. Measurements were made in triplicate on both legs and the maximal value obtained was recorded. Measurements from the subject's dominant leg were converted into newtons and expressed as a percentage of predicted values (268). The protocol is described in detail in Chapter 3, Section 3.2.8.2.

4.2.9.2 Handgrip strength

A hand-held Jamar 5030 J1 dynamometer (Sammons Preston Inc. Bolingbrook, Illinois, USA) was used to measure grip strength using the protocol described by Mathiowetz *et al* (1985) (271). The subject was seated with their shoulder abducted and mid prone, elbow flexed at 90 degrees and the forearm and wrist position were neutral. A minimum of three measures were taken and the single highest value achieved was recorded on the subject's dominant side. Full details are given in Chapter 3, Section 3.2.8.2.

4.2.10 Strategies to minimize variability during the measurement period

To ensure subjects with FAOA had stable asthma, measurements of FEV_1 were recorded once a week for a minimum of 3 consecutive weeks and at the same time subjects completed the ACQ (55). Current smokers in the COPD cohort were asked to refrain from smoking on each day of testing and all subjects were requested to refrain from ingesting food and drinks containing caffeine for 2 hours prior to the tests. All subjects were under the care of a respiratory physician and were receiving optimal medical management.

4.2.11 Statistical analyses

Data were analysed using SPSS (Version 16.0). The distributions of anthropometric, lung function data and 6MWD data were examined using visual plots and the

Shapiro-Wilks test of normality, and natural log transformations applied where necessary.

Independent t-tests were then used to compare the following data between the two cohorts:

- resting lung function expressed as % predicted normal value;
- maximum 6MWD, % predicted 6MWD, pre- and peak values of HR, and pre- and post-exercise SpO_2; and
- peripheral muscle strength measurements expressed in absolute values for handgrip and %predicted normal value for quadriceps strength.

End-exercise dyspnoea scores were categorised into binary format (0 to ≤ 3 and > 4) and a Chi-square test of association was employed to analyse these data (using McNemar's test for significance). The same analyses were used for ratings of leg fatigue**.**

For all comparisons the level of statistical significance was set at $p \leq 0.05$. Data are presented as mean±standard deviation (SD).

Data from the 32 subjects were combined (both FAOA and COPD cohorts), for the analyses of relationships between exercise variables and resting lung function. Spearman's rank correlation coefficients (r_s) were used to examine associations between dyspnoea scores recorded at the end of the 6MWT with resting lung function measures (RV/TLC, DLCO/VA and FEV_1) and post-exercise SpO_2.

Pearson-product moment correlation coefficients (r) were used to compare 6MWD with lung function measures (RV/TLC, DLCO/VA and FEV_1) and with post-exercise SpO_2. The relationships between post-exercise SpO_2 and RV/TLC, DLCO/VA and FEV_1 were also examined using Pearson-product moment correlation coefficients. For each of these relationships, the level of statistical significance was set at $p \leq 0.05$.

4.3 Results

4.3.1 Sample size

A total of 32 subjects participated in this study; 16 with stable moderate to severe FAOA (10 males) and 16 subjects with moderate to severe stable COPD (10 males).

4.3.2 Anthropometric and lung function data

Anthropometric and resting lung function data for the FAOA and COPD subjects are summarized in Table 4.2. Compared with the FAOA group, COPD subjects had lower FEV_1 ($p<0.001$), FEV_1/FVC ($p=0.002$) and DLCO/VA ($p<0.001$). Twelve (75%) of the FAOA subjects were life-time non-smokers, and the remaining four subjects had a smoking history of 2, 11, 12, and 14 pack years respectively.

4.3.3 Six minute walk test

The 6MWD and cardiorespiratory and dyspnoea responses to the 6MWT are presented in Table 4.3. None of the subjects with FAOA rested during the 6MWT whereas three subjects (18.8%) in the COPD cohort rested during the tests. Total rest times were 22, 102 and 17 seconds respectively. The mean 6MWD was significantly greater in the FAOA subjects than the COPD subjects (571m ± 89m versus 488m ± 111m respectively, $p=0.005$). The mean difference (95% confidence interval) between the two groups in 6MWD was 84 (11.2, 155.8)m.

There were no significant group differences in peak HR either as an absolute value or as % predicted HRmax (220-age). There was also no difference in ratings for leg fatigue between the two subject cohorts. A significant correlation was noted between the 6MWD and %predicted HRmax in both groups ($r=0.61$, $p=0.012$, FAOA and $r=0.54$, $p=0.03$, COPD).

Peak dyspnoea scores were significantly higher in the COPD cohort ($p<0.0001$) and the magnitude of oxygen desaturation was significantly greater in this cohort compared to the FAOA subjects ($p<0.001$) (Table 4.3). Post-exercise SpO_2 was below 90% in all of the COPD subjects and remained above 90% in all subjects with FAOA (Table 4.3).

Table 4.2. Demographic and lung function data for the 32 subjects

	Asthma	**COPD**
	n=16	**n=16**
Gender (male:female)	10:6	10:6
Age (years)	68.7±8.2	68.0±8.3
Height (cm)	169.9±8.6	169.1±6.5
Weight (kg)	77.0±11.9	71.3±14.9
BMI (kg/m^2)	26.6±3.4	24.8±4.4
FEV_1 (litres)	1.7±0.7	1.0±0.3#
FEV_1 (%pred)	58.3± 16.9	37.7±10.9*
FVC (litres)	3.2±1.0	2.9±0.9
FVC (%pred)	84.1±13.4	78.2±17.5
FEV_1/FVC	51.0±10.3	37.0±12.2#
FEV_1/FVC (%)^	68.3±13.2	49.9±16.9#
VC (litres)	3.3±1.0	3.2±0.8
VC (%pred)	95.9±15.2	96.0±17.4
FRC	4.1±0.9	4.7±1.2
FRC (%pred)	136.2±36.2	153.4±46.4
RV	3.3±0.8	3.5±1.1
RV (%pred)^	148.0±28.7	161.6±48.9
TLC	6.6±1.4	6.7±1.4
TLC (% pred)^	113.4±9.7	118.9±24.2
RV/TLC	0.51±0.10	0.52±0.10
RV/TLC (%pred)	129.9±18.8	132.4±20.4
DL_{CO}/VA (mm/min/mmHg/L)	4.2±0.5	2.1±0.6*
DL_{CO}/VA (%pred)	102.1± 15.1	55.3±18.5*

All data are mean±SD. TLC: total lung capacity; VC: vital capacity; RV: residual volume; FRC: functional residual capacity; FEV_1: forced expiratory volume in one second; FVC: forced vital capacity; DL_{CO}/VA: transfer factor for carbon monoxide corrected for alveolar volume; n: number; y: years; cm: centimetres; kg: kilograms; kg/m^2: kilograms per metre squared; %: percent predicted; mm/min/mmHg/L: millimetres per minute per millimetres of mercury per litre; ^Log transformations applied to these variables before t-tests performed;

*$p<0.001$, # $p<0.05$.

Table 4.3 Six minute walk test data for the 32 subjects

Variable	Asthma n=16	COPD n=16
6MWD (m)	571 ± 88	488 ± 111[#]
6MWD (%pred)	95 ± 11	80 ± 16[#]
Number of Subjects who rested	0	3
HR pre-test (bpm)	88.6 ± 14.3	90.1 ± 9.9
Peak HR(bpm)	130.4 ± 19.7	130.4 ± 13.6
Peak HR (%predHR$_{max}$)	86 ± 12	86 ± 10
SpO_2 pre-test (%)	95.8 ± 1.1	94.4 ± 1.2
SpO_2 post-test (%)	94.7 ± 1.9	84.3 ± 2.7*
SpO_2 < 90% post-test (n)	0	16
SpO_2 fall >4% (n)	1	16
Dyspnoea	2.7 ± 1.8	5.9 ± 2.5*
Leg fatigue	2.2 ± 1.6	1.9 ± 1.6

Data are mean±SD or numbers of subjects (n). All statistical comparisons are between group comparisons (independent t-tests) and for dyspnoea scores McNemar's test. 6MWT: 6 minute walk test; 6MWD: 6 minute walk distance; m: metres; %pred: percent predicted; bpm: beats per minute; HR: heart rate; %predHRmax: percent predicted maximum heart rate; SpO_2: oxygen saturation; n: number; % percent. [+]p=0.018, [#]p≤0.005, *p≤0.001

4.3.4 Peripheral muscle strength

Hand grip strength and quadriceps strength were not significantly different between the two cohorts (Table 4.4).

Table 4.4 Handgrip strength and quadriceps force

Variable	Asthma n=16	COPD n=16	Significance
Handgrip (Lb)	77 ± 24	74 ± 20	p=0.67
Range	40 - 116	43 – 107	
Quadriceps (N)	256.0 ± 91.3	246.2 ± 88.4	p=0.76
Range	125 - 500	157 - 412	
%predicted quads	76 ± 16	80 ± 27	p=0.63
Range	50 – 113	40 – 135	

Data are mean±SD. N: number; COPD: chronic obstructive pulmonary disease; FAOA: fixed airway obstruction asthma; Lb: pounds; N: newtons %: percent

4.3.5 Relationships between exercise variables and measures of lung function

Table 4.5 provides the correlations between post-exercise dyspnoea, 6MWD and post-exercise SpO_2 with RV/TLC, DL_{CO}/VA and FEV_1 in the 32 subjects. Moderately strong and significant relationships were found between DL_{CO}/VA with both dyspnoea and SpO_2. There was a significant inverse relationship between 6MWD and RV/TLC. Six minute walk distance was also significantly related to FEV_1. The relationship between post-exercise SpO_2 and dyspnoea was inversely and moderately strong (r_s=-0.61, $p<0.001$), and was significant (r=0.44, $p<0.05$) between 6MWD and post-exercise SpO_2.

Table 4.5 Correlations between dyspnoea, 6MWD and post-exercise SpO2 with measures of resting lung function in the 32 subjects

	Dyspnoea	**6MWD**	**Post-exercise SpO_2**
RV/TLC	0.05	-0.39#	-0.09
DL_{CO}/VA	-0.60*	0.30	0.75*
FEV_1	0.22	0.51#	0.59*

RV/TLC: residual volume on total lung capacity, DL_{CO}/VA: transfer factor for carbon monoxide corrected for alveolar volume, FEV_1: forced expiratory volume in one second, 6MWD: 6 minute walk distance, SpO_2: oxygen saturation, *$p<0.001$, #$p<0.05$

4.4 Discussion

The main findings of this study were that, despite having comparable baseline pulmonary hyperinflation, compared to subjects with COPD, those with FAOA were characterized as having: (i) a significantly greater 6MWD; (ii) less dyspnoea during the 6MWT; and (iii) preservation of oxygen saturation during the 6MWT. It is most likely that these findings can be attributed to the well-preserved gas transfer in the FAOA group, although it is also possible that differences in the degree of dynamic hyperinflation (DH) between groups, which were not measured in the present study, could also contribute to the different responses.

4.4.1 Demographic variables

The two cohorts participating in this study were matched for gender and comparable with respect to age, weight and height. For each of the lung function variables measured, comparisons between groups were also made after normalising these values using reference equations which took into consideration demographic variables such as age, weight and height. Increased age results in decreased lung recoil due to changes in the connective tissue matrix of the lung. At rest, RV/TLC is increased with age, inspiratory capacity is reduced, and elderly subjects can experience DH at a high intensity of exercise in a manner similar to, but of a lesser magnitude than that seen in subjects with COPD (354). In individuals with airflow limitation, a higher ventilatory demand due to these mechanical derangements contributes to higher levels of dyspnoea in an older individual compared to a younger individual (354). Age, weight and short stature have also been shown to be associated with a decreased 6MWD (178, 187, 355). .

4.4.2 Gas exchange and oxygen desaturation

In the present study, a significantly lower DL_{CO}/VA was observed in the COPD subjects when compared with the FAOA subjects. This measurement represents the ability of the lungs to exchange respiratory gases between the alveoli and pulmonary circulation (356). Since the gas transfer is corrected for alveolar volume it is more sensitive to the level of appropriately matched perfusion and any inhibition of gas

diffusion across the alveolar capillary membrane. It is expected that in a progressive condition such as emphysema, a reduction in DL_{CO}/VA will occur due to the pathological destruction of air spaces distal to the terminal bronchioles, causing both reduced diffusion of gas and poor perfusion *per se* (357). In asthma, DL_{CO}/VA remains relatively well preserved (356) despite the repetitive inflammation that can cause permanent airway obstruction in chronic severe asthma (262). This presumably occurs because of an intact alveolar-capillary membrane and, if anything, increased perfusion.

In earlier studies, DL_{CO} has been shown to be a significant predictor of functional performance and oxygen uptake (319, 343). A lower DL_{CO}/VA constrains oxygen transport to the metabolically active cells, and this can lead to an early shift in energy pathways from aerobic to anaerobic pathways during exercise, with the net result of the early production of lactic acid (192, 358). Lactic acidosis occurring during low intensity exercise provides an additional ventilatory stimulus and can accentuate the symptom of dyspnoea and lead to a premature cessation of exercise (354).

The level of ventilation required to provide adequate alveolar ventilation for homeostatic acid-base regulation in an individual with FAOA is likely to be lower than for individuals with emphysematous changes given that hypoxia does not play a significant role in FAOA and that these individuals will have a lower level of lactic acid production.

In the present study, significant oxygen desaturation did not occur in the FAOA cohort at the end of the 6MWT in contrast to the finding of marked desaturation in the COPD subjects. A normal SpO_2 is likely to reflect preserved oxygen transfer (DL_{CO}/VA), as DL_{CO} has been shown to be a predictor of arterial oxygen desaturation during exercise (319).

To date, there is little evidence that the severity of oxygen desaturation *per se* has a major impact on exercise performance (219, 359). However, in single laboratory-based assessments of exercise, supplementary oxygen (short-term) has been demonstrated to increase endurance exercise capacity, reduce dyspnoea (at iso-time) and improve oxygen saturation (360-363). This was the conclusion of a Cochrane review which included 31 studies comparing an exercise test breathing oxygen or air in subjects with moderate to severe COPD (360). A Cochrane review (364)

investigating the use of ambulatory oxygen during exercise training in individuals with COPD who did not meet the criteria for long-term oxygen therapy, concluded that the evidence for the benefits of this therapy (i.e. effect on symptom alleviation, HRQOL or ambulation) was uncertain due to the availability of only a small number of included studies, which could not allow a conclusion to be drawn. There is a need for studies with larger numbers of participants and a strong design.

In COPD subjects, the proposed mechanisms by which supplementary oxygen improves exercise tolerance, is by lowering the ventilatory requirement as a result of direct peripheral chemoreceptor inhibition, which in turn slows breathing frequency and thus decreases dynamic lung hyperinflation (365). Supplementary oxygen may also have an effect on reducing skeletal muscle lactate production (366).

4.4.3 Relationship between resting lung function and functional exercise capacity

It is well recognised that the ability to predict exercise capacity using anthropometric or physiological variables alone in individuals with COPD and asthma is low, however the severity of respiratory impairment measured through resting lung function measurements does partially contribute to the limitation in exercise capacity (183, 345, 367, 368). The present study demonstrated a significant relationship between resting pulmonary hyperinflation (RV/TLC) and 6MWD (r_s=-0.39, $p<0.05$). A similar finding was also observed by Marin *et al* (343) who reported a correlation of 0.38 ($p<0.001$) between mean 6MWD and resting pulmonary hyperinflation (RV/TLC) in 72 males with COPD (FEV_1 45±13.3% pred).

Another study (369) in 27 males with severe COPD (FEV_1 40±2.6%pred) reported a significant correlation ($r=0.46$, $p<0.01$) between the degree of resting pulmonary hyperinflation and the tolerability (or time to end) of an interval exercise test performed on a cycle ergometer at 100% of peak work capacity which alternated 30 seconds of pedalling with 30 seconds of rest.

In the present study, the level of large airway obstruction (%pred FEV_1) at rest explained a small but significant part of the variability in 6MWD ($r=0.51$, $p=0.003$). Normalising FEV_1, by expressing this variable as a percentage of predicted ultimately removes the effects of age and height to this relationship and thus tends to

lower the correlation coefficient (345). This may account somewhat for conflicting results in the degree to which FEV_1 contributes to exercise intolerance in COPD (176, 367, 370) and asthma (345, 368). An interesting trend observed by Lo Russo *et al* (371) is that the more severely disabled a group of patients are, the better the prediction between FEV_1 and exercise capacity. The correlation between FEV_1 and peak oxygen uptake (VO_{2peak}) for a group of patients with mild COPD (FEV_1 2.78 ±0.77l) was 0.69 compared to a correlation of 0.87 for a group of patients with severe COPD (FEV_1 1.06± 0.47l). These authors did note, however, that although the correlations between resting pulmonary function tests and measures of maximal exercise capacity were significant, a large variance precluded the use of resting lung function tests such as FEV_1 to accurately predict exercise cpacity in individual patients.

In studies which have included asthmatic populations that do not have a component of fixed airways obstruction, FEV_1 is likely to account for a lower percentage of the variability in exercise capacity that occurs in COPD because of the reversibility demonstrated in this lung function measure post-bronchodilator. The study by Foglio *et al* (345) evaluated the physiological and symptom determinants of exercise performance as measured by 6MWD and VO_{2peak} from a symptom limited cycle ergometer test in a group of 44 subjects with COPD (age 63±7yrs, FEV_1 48±19%pred) and 55 subjects with asthma (age 55±10yrs, FEV_1 65±17%pred). The authors showed that RV/TLC, age and Baseline Dyspnoea Index were the strongest and most consistent correlates of exercise performance whilst FEV_1 was not a significant predictor of exercise performance (6MWD or VO_{2peak}). This may have been because all of the asthmatics were receiving inhaled bronchodilators and all had variable airflow limitation with reversible obstruction, which is likely to have weakened the significance between the degree of airflow obstruction and exercise performance.

In the present study, the FAOA and COPD groups were not comparable with respect to FEV_1, as our hypothesis of similar responses occurring during the 6MWT in the FAOA and COPD cohorts was based on resting pulmonary hyperinflation rather than large airways obstruction being matched.

4.4.4 Dynamic hyperinflation with exercise

End-expiratory lung volumes typically increase during strenuous exercise in individuals with mild to moderate airflow limitation, in contrast to healthy controls in whom end-expiratory lung volume decreases during exercise (217, 372). In the present study, it was hypothesised that because subjects with FAOA and COPD had similar resting pulmonary hyperinflation, a similar degree of DH would develop in both cohorts during the 6MWT. This is because the presence of air trapping at rest increases the work of breathing and causes a higher ventilatory demand with activity (343) which may lead to further hyperinflation with exercise in both individuals with FAOA (133, 136) and those with COPD (373).

One of the characteristic pathological changes that has occurred in an individual who presents with low diffusing capacity is an irreversible destruction of one of the major connective tissue components in the lung called elastin (374). This loss of elastin, which is mediated by proteases, results in a loss of alveolar attachments which contributes to early peripheral airway closure (375). Early airway closure leads to further DH with exercise and results in greater inefficiency of the lung and chest wall contributing to dyspnea and impaired exercise tolerance (374).

Dynamic hyperinflation has been shown to be inversely related to the level of resting lung hyperinflation in individuals with COPD (376), but it is not currently known whether this also applies to individuals with FAOA. The present study did not measure the development of DH during the 6MWT and therefore it is not possible to comment on whether the magnitude of exercise-induced DH differed between the two groups.

The development (or absence) of DH during exercise is generally measured in a laboratory by taking serial measurements of inspiratory capacity, first practicing the measurement protocol at rest before the exercise begins (130, 373). Errors in the measurement of inspiratory capacity can occur if inspiration begins before the patient's normal end-expiratory lung volume is reached (130). It is assumed that TLC is constant during exercise therefore the change in inspiratory capacity reflects the degree of DH (130, 377). Pre- and post- measures of inspiratory capacity recorded with calibrated pneumotachography have also been used to measure DH during a

6MWT in individuals with COPD to indicate the development of DH during a 6MWT in this population (343).

One study (133) which measured DH during exercise in 20 stable asthmatics, of whom only three exhibited an FEV_1 below normal limits at rest, reported that 13 of these subjects developed DH in a symptom-limited cycle ergometer test, and exercise capacity was significantly reduced in these subjects (maximum exercise work rate 75±9% pred) compared to those who did not develop DH (maximum exercise work rate 95±13% pred). It is possible, however, that during short bouts of exercise (i.e. an exercise test of short duration such as the 6MWT) or submaximal exercise tests, the development of DH is less of a contributor to exercise limitation and dyspnoea intensity in asthmatic populations (136, 378).

Several studies have reported the presence of DH in asthmatic subjects during metacholine-induced bronchoconstriction (131, 379-381). The DH that develops during a metacholine challenge is likely to be attributed to increased expiratory resistance as a result of persistent activity of the inspiratory muscles (130). In a study of 21 subjects with mild stable asthma, Lougheed et al (379) showed that an increase in end-expiratory lung volume was the single most important contributor to dyspnoea occurring during a methacholine challenge. Furthermore, airway obstruction and hyperinflation have been found to be the best predictors of dyspnoea in individuals with asthma during a methacholine challenge (381).

In the present study, the reduced DL_{CO}/VA in the COPD cohort may have accelerated the rise in breathing frequency at an earlier time point during the 6MWT, leading to a greater ventilatory demand in this cohort compared to the FAOA subjects. If so, the magnitude of DH would be greater in the COPD subjects than would occur in the individuals with FAOA with normal gas transfer (376). If DH is exacerbated during exercise in an individual with COPD to a greater degree than in an individual with FAOA, the end result will be a greater limitation in functional exercise capacity and a higher intensity of dyspnoea (382).

4.4.5 Expiratory flow limitation

Also related to the physiological concept of DH is expiratory flow limitation, ‘the maximum expiratory flow achievable by an individual during tidal breathing’ (130).

The gold standard for the measurement of expiratory flow limitation is by the determination of iso-volume relationships between flow and transpulmonary pressure using the passage of an oesophageal balloon, but more commonly, is detected by superimposing a flow-volume loop of a tidal breath with a maximal flow-volume curve (130). The presence of expiratory flow limitation promotes DH and may contribute to dyspnoea, with the rate of development of DH being reported to be greatest in subjects with the most severe expiratory flow limitation, the lowest DL_{CO}/VA and the highest ventilatory demand (376).

Although the presence of expiratory flow limitation has been observed in stable asthmatics with normal spirometry, potentially contributing to reduced exercise capacity in these individuals (133), its occurrence has been reported more frequently in COPD populations than asthmatic populations (130).

4.4.6 Relationship between dyspnoea and resting lung function

In the present study dyspnoea scores recorded at the end of the 6MWT were significantly correlated with DL_{CO}/VA, but not with FEV_1. A study by Marin *et al* (383), showed that exertional dyspnoea measured by a visual analogue scale during a symptom-limited cycle ergometer test was not correlated with any resting spirometric or plethysmographic measurements (including FEV_1), nor with measures of anthropometry or respiratory muscle function in 26 patients with severe COPD (FEV_1 27.1±10.7% predicted). These authors instead found a significant relationship between exertional dyspnoea and the subject's resting respiratory drive and the response of the central output to increased carbon dioxide stimuli. These authors did not measure resting levels of DL_{CO}/VA, however it is possible their findings might also be reflective of impaired gas transfer, particularly as this may impact on respiratory drive as alluded to earlier in this discussion.

The present study also found no significant correlation between dyspnoea and RV/TLC, and as has previously been highlighted, it is possible that RV/TLC does not necessarily reflect the degree of DH that develops during exercise. This may explain the reason for this poor relationship between these two variables.

4.4.7 Dyspnoea on exertion in individuals with chronic obstructive pulmonary disease and asthma

The present study showed significantly greater dyspnoea at the end of the 6MWT in subjects with COPD when compared to the cohort with FAOA. The pathophysiology of dyspnoea is multifactorial (126), and to date, the exact mechanisms which underlie this sensation in individuals with asthma are not fully understood (139, 381). The sensation of dyspnoea is most often triggered by exertion in an individual with stable COPD (219), but in asthma, other stimuli which give rise to bronchoconstriction can be the cause of dyspnoea (384). It has been reported that a given ventilatory threshold needs to be reached before both asthmatics and COPD subjects perceive dyspnoea (138).

A study by Laveneziana *et al* (2006) (381) which involved 22 subjects (19 with mild asthma, two with moderate asthma (FEV_1 60-80% pred) and one with severe asthma (FEV_1 ≤60%pred) showed the descriptors of dyspnoea that subjects chose varied for the two tasks, one being an incremental (6-8 minute) cardiopulmonary exercise test and the other a methacholine challenge. Specifically, chest tightness was more often reported during the metacholine challenge, whereas an increase in effort was the method by which the individuals described their dyspnoea during the exercise test. As such the underlying mechanisms of dyspnoea are likely to be different depending on the task (381). This finding has also been reflected in two other studies (143, 385).

4.4.8 Blunted dyspnoea response

All of the subjects with asthma who participated in this study had evidence of airway obstruction, as measured by resting lung function. Asthmatics with airway obstruction at rest have been reported to have an impaired perception of external resistive loads which is not observed asthmatics with normal airway calibre (386). Barriero *et al* (136) showed subjects with severe and long standing asthma tended to have a poor recognition of their symptoms and perception of the severity of their disease.

It has previously been mentioned in the discussion of study 1 (Chapter 3, Section 3.4.2.5), that some individuals with chronic asthma, who in the past have had a near

fatal asthma attack, suffer from significantly more hospitalisations, asthma exacerbations and deaths as a result of this reduced perception of dyspnoea (387, 388). Another study showed less dyspnoea measured using a category scaling technique occurred during histamine challenge in a subset of subjects with asthma who had airflow obstruction present at the start of the challenge compared to subjects with normal lung function prior to the challenge. This study also showed a significant relationship between the degree of bronchial hyper-responsiveness and the level of dyspnoea (318).

It is difficult to estimate how many subjects in the FAOA cohort had experienced a near fatal asthma attack, given that information on such a history was not collected. A future study that investigates the prevalence and effect of this condition on dyspnoea in individuals who have FAOA would be of interest. Because all of the asthmatics in this study had fixed obstruction at rest, it is possible that a blunted dyspnoea response with exercise may have (at least in part) accounted for the lower intensities of dyspnoea at the end of the 6MWT compared to the COPD subjects, however this was not demonstrated through clinical signs of disproportionate level of work of breathing in relation to their dyspnoea scores in these subjects at the end of the 6MWT. Further research is required to better understand the differences in dyspnoea in individuals with FAOA versus COPD.

4.4.9 Systemic differences between COPD and asthma: peripheral muscles and BMI

In this study, both cohorts showed similar levels of quadriceps strength and handgrip strength, though the cohort size was relatively small for making such comparisons. Peripheral muscle strength has been shown to be reduced in individuals with COPD and contributes to impaired exercise tolerance (221, 222). The proximal arm muscles are more affected by peripheral muscle weakness and wasting than distal hand muscles in individuals with moderate to severe COPD, although the impairments in upper limb muscle strength are of a lesser magnitude than the changes in quadriceps strength (389).

Associated with the disease process in COPD are the mediators of hypoxaemia and oxidative stress which contribute to the pathophysiology of skeletal muscle

dysfunction in these individuals (390). In COPD, shifts in fibre type distribution of the vastus lateralis muscles (391) and a reduction in fibre size (392) have been documented, as well as impairment in the oxidative metabolism of these muscles with a reported increase in glycolytic enzymes and a reduction in aerobic metabolism (393). This presence of a reduction in skeletal muscle strength and a loss of muscle mass in individuals with advanced COPD is one of the systemic consequences of COPD (374). The increased concentration of inflammatory mediators such as TNFα and IL6 and presence of oxygen derived free radicals may also contribute to the development of osteoporosis, chronic anemia, depression and an increased risk of cardiovascular disease (374).

Reduced physical activity in individuals with moderate to severe COPD can also lead to muscle atrophy through disuse (390) and steroid-induced myopathy from the prolonged treatment with corticosteroids in individuals with COPD has been documented, which again leads to reduced peripheral muscle strength (394). As alluded to in the discussion of Chapter 3, long-term corticosteroid usage may not necessarily be associated with peripheral muscle weakness in individuals who have asthma, with one study demonstrating normal muscle strength and function of the quadriceps femoris muscle in individuals with bronchial asthma on chronic treatment with prednisolone (mean daily dose 17.3mg) (305).

Two other factors which have been shown to have a negative effect on muscle strength and aerobic capacity are reduced body mass, which is often a co-morbidity associated with advanced COPD (395), and ageing (390). Malnutrition and weight loss can reduce muscle strength and endurance by reducing respiratory muscle mass and the strength of the remaining respiratory muscles (374). The BMI of the FAOA cohort and the COPD cohort in the present study were similar however one limitation of the current study was no measures of fat-free mass body composition were recorded.

4.5 Conclusion

The most important findings of this study were that, despite a similar magnitude of air trapping and hyperinflation at rest, the FAOA subjects achieved a significantly higher 6MWD and experienced less dyspnoea and desaturation than the subjects with

COPD. Overall therefore, adults with FAOA are likely to tolerate much higher exercise intensities than their counterparts with COPD, regardless of their resting pulmonary hyperinflation. This is explained at least in part by their well preserved gas transfer, which is reflected in normal SpO_2 levels during the 6MWT. This study lead to a discussion which illustrated that, regardless of the similar resting pulmonary hyperinflation between the cohort of subjects with FAOA and those with COPD, the structural abnormalities behind these two conditions lead to different mechanical derangements (such as lower DL_{CO}/VA in the COPD cohort) which limit maximal ventilation and hence functional exercise capacity to a different degree in these two disease cohorts.

CHAPTER 5

Respiratory services and hospital admissions for asthma and chronic obstructive pulmonary disease in Western Australia

5.1 Introduction

In order to develop improved community support programmes for middle-aged and older adults with asthma and chronic obstructive pulmonary disease (COPD) in Western Australia (WA), it is important to define the current geographical distribution of health services throughout the State and highlight areas which experience a greater burden of hospital admissions secondary to these conditions. Geographic information systems (GIS) technology is able to manage spatially referenced data that describe human health outcomes and can assist in the visualisation of issues relating to health accessibility. This chapter utilises GIS technology to explore the current distribution of respiratory health services in WA, and hospital admissions secondary to asthma or COPD from 2000-2004 in adults aged 40 years and over.

5.2 Methods

5.2.1 Research aims

The aims of this section of the thesis were to: (a) determine accessibility to respiratory health services in WA, (b) spatially represent and analyse the distribution

of hospital admissions for asthma and COPD, and (c) investigate trends in hospital admissions over a 5 year time period (2000-2004).

5.2.2 Objectives

Using GIS, the objectives were to:

1. Map the current distribution of the following respiratory health services in WA:
    - hospitals;
    - emergency departments (EDs);
    - respiratory physician clinics;
    - pulmonary rehabilitation programmes; and
    - asthma educators.
2. Determine the proportion of admissions to hospital (2000-2004) for adults aged 40 years and over with asthma or COPD within each health service relative to the population size within that health service by thematic mapping. Thematic maps would show:
    - admissions with a primary diagnosis of asthma;
    - admissions with a primary diagnosis of COPD; and
    - admissions with a primary diagnosis of both asthma and COPD.
3. Define trends in admissions data for both asthma and COPD for each health service area over the time period 2000-2004, by gender and by age groups.

5.2.3 Study design

A record-linked prevalence study was undertaken to obtain prevalence, demographic characteristics and regional distribution of asthma and COPD admissions for adults aged 40 years and over in relation to respiratory services in WA. The following steps were followed:

1. obtain data on:
    a) all hospital services (HOSPITAL DATASET);
    b) respiratory physician services (SPECIALIST DATASET);

c) pulmonary rehabilitation programmes (REHAB DATASET); and

d) practising asthma educators (EDUCATOR DATASET).

2. Extract population data of adults aged over 40 years from the 2001 census using CDATA 2001, a CD Rom released by the Australian Bureau of Statistics (POPULATION DATASET).

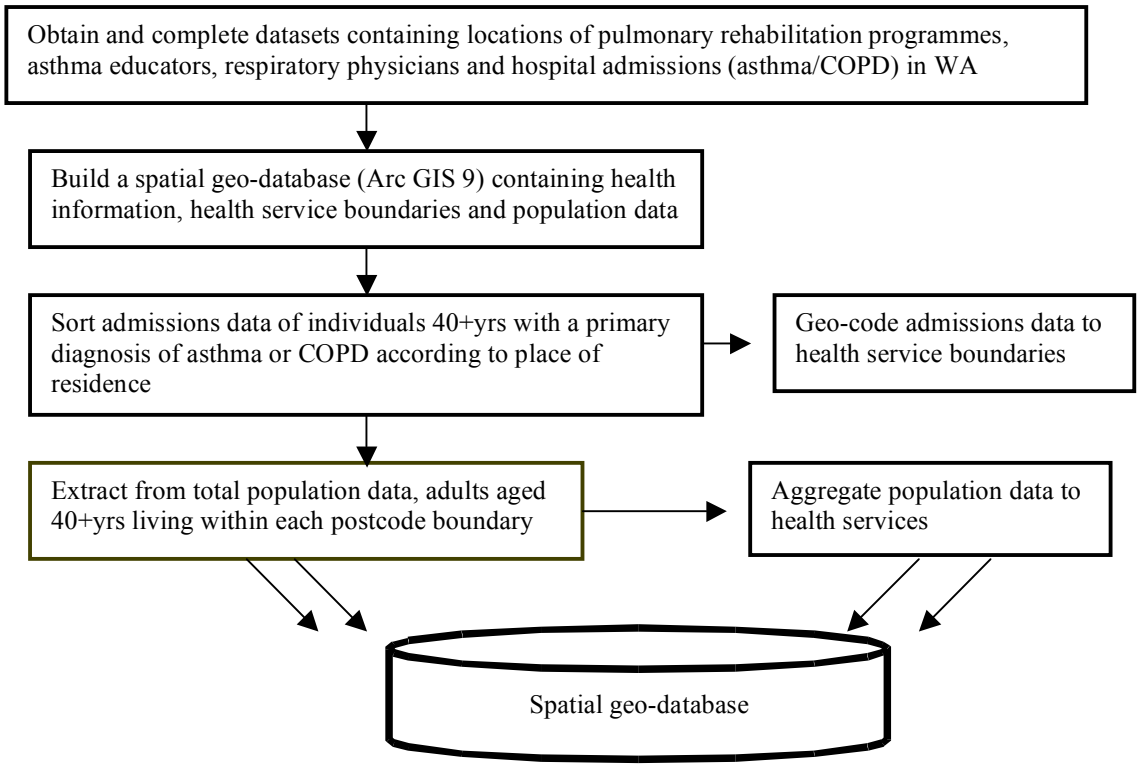
3. For each hospital admission during the time period 2000-2004, sort and geo-code the data for asthma and COPD. These data were accessed from the Health Department of WA in a de-identified format (ADMISSIONS DATASET).

4. Build a geo-database linking each of these datasets using GIS software.

Detailed information on these data sets is provided in Section 5.2.6 (page 157).

A geo-database refers to an object-orientated data model produced with GIS technology which removes redundant data and provides a means of understanding the organisation of the data in a systematic structure. Figure 5.1 outlines the geo-database data input required to visualise hospitals, asthma educators, respiratory physicians, pulmonary rehabilitation programmes and asthma and COPD admissions of adults aged 40 years and over for regional and remote WA.

Figure 5.1 Structure chart for building the geo-database



5.2.4 Selection of geographic information systems software and data model

The programmes ArcMap, Arc Catalogue and Arc Info were chosen to develop the GIS database. These ArcGIS programmes allow the discovery of patterns, relationships, and trends in data through their management and integration in a visual format, i.e. displayed as points on a map.

MapInfo Professional[8], a GIS programme, was also accessed within the framework of a customised application called CDATA 2001. CDATA is a CD-ROM that is released conjointly by the Australian Bureau of Statistics and MapInfo Australia and which allows manipulation of census data within a GIS environment. CDATA with MapInfo include a range of digital maps such as postcode boundaries, census boundaries and the Australian Standard Geographical Classification (ASGC) Areas for WA. The population data contained in the CD-ROM were collected during the 2001 census. Digital maps of the study area, postcodes, and ASGC Areas as well as attribute data from the census, were imported into the Arc GIS programme in the form of shape-files as part of the process of building the geo-database.

A vector data model was used to store and manipulate the spatial data. Geographic entities that are encoded in this type of model are referred to as features and represented by 'polygons', 'lines' and 'points'. For the current study, polygons represented the study area of WA, postcode boundaries, and health service catchment areas and point data comprised the positions of hospitals, asthma educators, pulmonary rehabilitation programmes, and respiratory physician clinics.

5.2.5 Identification of the study area

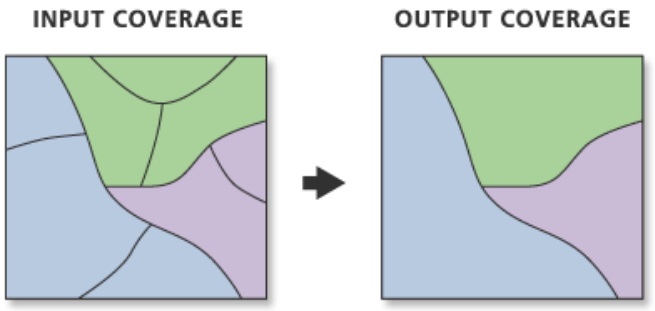
The state of WA was chosen as the study area boundary. Western Australia spans 2.525 million km^2 and covers one third of the Australian continent. Latitudes range from 14° to 35° south. This study area was divided initially into postcodes and then merged (or 'dissolved', to use the Arc GIS terminology) into 30 larger health service areas for the basic spatial unit for analysis. Initially it was anticipated that data would be coded according to the individual residential postcodes of each asthma and COPD admission that occurred during the time period 2000-2004. However, Health Department data did not allow this level of identification to be released for research purposes due to ethical issues. Further, post office box addresses, 'lot' numbers and

'care-of' addresses could potentially have been given as address details for asthma and COPD admissions that lived in rural and remote areas. Such addresses are not easily able to be geo-coded and this would have resulted in a high percentage of missing data in rural areas, and have led to inaccurate estimates of the extent of COPD and asthma within the area. In addition, in more remote parts of WA, the use of postcodes and census districts as the areal unit would have generated very small catchments, and may have led in some instances to the admission of an individual being able to be identified based on the area of residence. Therefore the larger, but more clinically relevant health service boundaries were chosen as the areal unit on which to carry out mapping.

The WA public health system has multiple levels of administration including the Health Department of WA, metropolitan and country health services and individual health units and hospitals. In 2004, Dr Jim Coddee within the public health division of the Health Department of WA was approached to provide information on the administrative boundaries for the provision of health services in WA for this study. Appendix M lists the spatial relationships between health services, to health districts, local government areas and statistical local areas for WA.

The digital map of postcode areas supplied in the CDATA programme was imported into the Arc GIS programme in the form of a shape-file. Using a computer software programme command called 'dissolve' which is located within the Arc GIS toolbox, the postcodes that corresponded to each health service boundary could be amalgamated together into the larger boundary areas of health services (Figure 5.2). 'Dissolve' is a command that is used to create a simplified coverage from one that is more complex. Although the input coverage may contain information concerning many feature attributes, the output coverage contains information only about the 'dissolve' item. The merging of polygons with Dissolve is the counterpart of intersecting polygons in overlays.

Figure 5.2 The 'dissolve' command used to change the postcode coverage to health service boundary areas

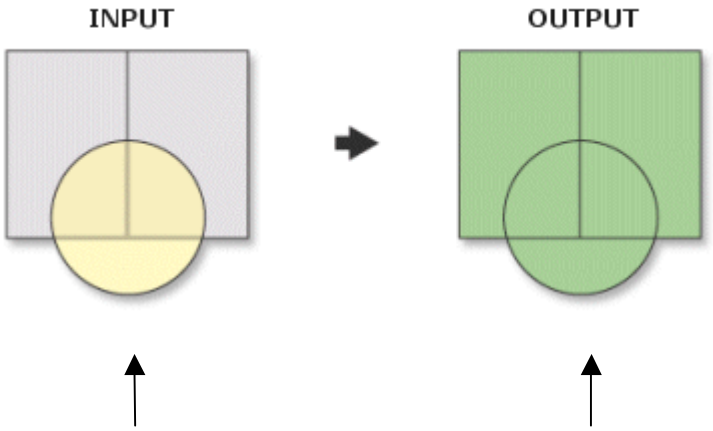


'Dissolve' creates a new coverage by merging adjacent polygons, lines or regions that have the same value for a specific item

Meta-data provided from the Health Department of WA for the point locations of hospitals used the following co-ordinate systems: Australian GDA 1994 Spheroid, GCS_GDA_1994, D_GDA_1994 and Prime meridian was Greenwich 0. These coordinate systems were used to reference all other point and polygon data which were imported into the geodatabase.

Maps which contained the attributes of health services for middle-aged and older adults with asthma and COPD were overlayed onto the base study area using the 'Overlay' command that is located within the Arc Toolbox of Arc GIS-9. Overlay operations (Figure 5.3) merge spatial features on separate data layers to create a new feature class.

Figure 5.3 Illustration of the 'spatial overlay' command in Arc GIS-9



The three separate layers in this figure which are illustrated by two separate rectangles and circle become combined in the input so that all three layers are visual in the output simultaneously

Trends in admissions data were analysed by importing the data sets into SPSS version 16.0 and separating the data using a cross tabulation technique.

5.2.6 Data sources

5.2.6.1 Hospitals

Attributes of hospitals throughout WA were imported into the health geo-database. The original source document supplied from the Health Department of WA contained the following attributes relevant to the study: hospital ID number, name of hospital, address of hospital, poscode, town, whether the hospital was a public or private hospital, the presence of an ED at the hospital, whether the hospital was located in a regional or metropolitan area, and the grid references to spatially locate the hospitals within a GIS setting.

The 102 hospitals which admit adults with respiratory symptoms (i.e. asthma and COPD cases) are provided in Table 5.1. Hospitals which do not provide this type of care (i.e. children's hospitals or hospitals which provide only maternity care, dental treatment or specialist eye hospitals) were excluded from the original list provided by the Health Department before importing into the geo-database. Table 5.2 provides a list of the 29 hospitals which were excluded.

Table 5.1 Attributes of the 102 hospitals in WA providing care for adults with respiratory disease

ID	NAME	ADDRESS	TOWN	POSTCODE	CLASS	WA_GRID	GDA_LAT	GDA_LONG
	Hospitals in Perth or Surrounding Metro Area							
203	Armadale/Kelmscott District Memorial	Albany Highway	ARMADALE	6112	PUBLIC	E20	-32.13316800	116.01945900
623	Attadale Hospital	21 Hislop Road	ATTADALE	6156	PRIVATE	D20	-32.02957400	115.81077600
255	Bentley Hospital	33 Mills Street	BENTLEY	6102	PUBLIC	D20	-32.00688100	115.92730700
602	Bethesda Hospital	25 Queenslea Drive	CLAREMONT	6010	PRIVATE	D19	-31.98761800	115.77903600
632	Cambridge Private Hospital	187 Cambridge Street	WEMBLEY	6014	PRIVATE	D19	-31.94097500	115.82417000
102	Fremantle Hospital	Alma Street	FREMANTLE	6160	PUBLIC	D20	-32.05776600	115.75485800
630	Fremantle Kaleeya Hospital	Staton Road	EAST FREMANTLE	6158	PRIVATE	D20	-32.03632800	115.76636900
647	Galliers Private Hospital	3056 Albany Highway	ARMADALE	6112	PRIVATE	E20	-32.15019500	116.02309700
633	Glengarry Hospital	53 Arnisdale Road	DUNCRAIG	6023	PRIVATE	D19	-31.83424900	115.78458800
641	Hollywood Private Hospital	Monash Avenue	NEDLANDS	6009	PRIVATE	D19	-31.97022100	115.80898500
642	Joondalup Health Campus	Shenton Ave.	JOONDALUP	6027	PRIVATE	D19	-31.73898300	115.77128400
454	Kalamunda District Community Hospital	Elizabeth Street	KALAMUNDA	6076	PUBLIC	E19	-31.96850000	116.06139000
629	Mercy Hospital	Thirlmere Road	MOUNT LAWLEY	6050	PRIVATE	D19	-31.93652400	115.88396100
608	Mount Hospital	150 Mounts Bay Road	PERTH	6000	PRIVATE	D19	-31.95847800	115.84575900
607	Mount Lawley Private Hospital	14 Alvan Street	MOUNT LAWLEY	6050	PRIVATE	D19	-31.93432100	115.87419100
626	Niola Private Hospital	61-69 Cambridge Street	WEST LEEDERVILLE	6007	PRIVATE	D19	-31.94037800	115.83683600
239	Osborne Park Hospital	Osborne Place	STIRLING	6021	PUBLIC	D19	-31.88538400	115.80477500
639	Rockingham Family Hospital	221 Willmott Drive	WAIKIKI	6169	PRIVATE	D20	-32.31033200	115.76342900
277	Rockingham - Kwinana District Hospital	Elanora Drive	ROCKINGHAM	6168	PUBLIC	D20	-32.29205800	115.77048800
101	Royal Perth Hospital	Wellington Street	PERTH	6000	PUBLIC	D19	-31.95482400	115.86648700
616	St John of God Health care Subiaco	175 Cambridge Street	SUBIACO	6008	PRIVATE	D19	-31.94124900	115.82538600
640	St John of God Health care Murdoch	100 Murdoch Drive	MURDOCH	6150	PRIVATE	D20	-32.06805300	115.84481400
105	Sir Charles Gairdner Hospital	Verdun Street	NEDLANDS	6009	PUBLIC	D19	-31.96822500	115.81652800
618	South Perth Community Hospital	76 South Terrace	COMO	6152	PRIVATE	D19	-31.98799400	115.86700400
244	Swan District Hospital	Eveline Road	MIDDLE SWAN	6056	PUBLIC	E19	-31.87655700	116.00600300

ID	NAME	ADDRESS	TOWN	POSTCODE	CLASS	WA_GRID	GDA_LAT	GDA_LONG
	Hospitals in Rural or Remote WA							
201	Albany Regional Hospital	Warden Ave.	ALBANY	6330	PUBLIC	F23	-35.00417200	117.90475600
204	Augusta District Hospital	Donovan Street	AUGUSTA	6290	PUBLIC	D22	-34.30593700	115.15816100
401	Beverley District Hospital	Sewell St.	BEVERLEY	6304	PUBLIC	E20	-32.10288900	116.92247000
402	Boddington District Hospital	Hotham Avenue	BODDINGTON	6390	PUBLIC	E20	-32.80358100	116.47562400
432	Boyup Brook Hospital [Upper Blackwood]	Hospital Drive	BOYUP BROOK	6244	PUBLIC	E21	-33.83900300	116.39135000
444	Bridgetown District Hospital	Peninsula Road	BRIDGETOWN	6255	PUBLIC	E21	-33.95180300	116.13183800
206	Broome District Hospital	Robinson St.	BROOME	6725	PUBLIC	K5	-17.96060900	122.23669200
403	Bruce Rock Memorial Hospital	Dunstal St.	BRUCE ROCK	6418	PUBLIC	G19	-31.87352000	118.14655300
208	Bunbury Regional Hospital	Bussell Hwy.	BUNBURY	6230	PUBLIC	D21	-33.36678500	115.64759400
209	Busselton District Hospital	Mill Road	BUSSELTON	6280	PUBLIC	D21	-33.65390600	115.31961000
210	Carnarvon Regional Hospital	Cleaver Street	CARNARVON	6701	PUBLIC	B12	-24.88654400	113.65932800
211	Collie District Hospital	Deakin Street	COLLIE	6225	PUBLIC	E21	-33.35153000	116.16258000
404	Corrigin District Hospital	Kirkwood St.	CORRIGIN	6375	PUBLIC	F20	-32.32450400	117.87846100
405	Cunderdin District Hospital	Cubbine street	CUNDERDIN	6407	PUBLIC	F19	-31.65510600	117.24460000
406	Dalwallinu District Hospital	Myers St.	DALWALLINU	6609	PUBLIC	E18	-30.27678600	0.00000000
214	Denmark District Hospital	Strickland Street	DENMARK	6333	PUBLIC	F22	-34.95918200	117.35362100
215	Derby Regional Hospital	Loch Street	DERBY	6728	PUBLIC	L5	-17.30594300	123.63321900
476	Dongara Health Service	48 Blenhein Street	DONGARA	6525	PUBLIC	C17	-29.26501600	-29.26501600
271	Donnybrook District Hospital	Bentley Street	DONNYBROOK	6239	PUBLIC	D21	-33.57508100	115.81890100
408	Dumbleyung District Memorial Hospital	McIntyre St	DUMBLEYUNG	6350	PUBLIC	F21	-33.31029100	117.74045400
218	Esperance District Hospital	Hicks Street	ESPERANCE	6450	PUBLIC	J21	-33.85650400	121.89215000
219	Exmouth District Hospital	LEFROY Street	EXMOUTH	6707	PUBLIC	C9	-21.93363500	114.12600700
127	Fitzroy Crossing Hospital	Fallon Road	FITZROY CROSSING	6765	PUBLIC	N6	-18.19139200	125.56265900
220	Geraldton Regional Hospital	Shenton Street	GERALDTON	6530	PUBLIC	C16	-28.78293500	114.61069600
410	Gnowangerup District Hospital	Yougenup Road	GNOWANGERUP	6335	PUBLIC	G21	-33.93060000	118.00319400
411	Goomalling District Hospital	Forrest Street	GOOMALLING	6460	PUBLIC	E19	-31.30369200	116.83109800
128	Halls Creek Hospital	70 Roberta Avenue	HALLS CREEK	6770	PUBLIC	P6	-18.22590200	127.66655900
412	Harvey District Hospital	45 Hayward St.	HARVEY	6220	PUBLIC	D21	-33.07777800	115.89711400
475	Kalbarri Health Service	Kaiber Street	KALBARRI	6536	PUBLIC	C15	-27.71287800	114.16140400

ID	NAME	ADDRESS	TOWN	POSTCODE	CLASS	WA_GRID	GDA_LAT	GDA_LONG
	Hospitals in Rural or Remote WA							
226	Kalgoorlie Regional Hospital	Piccadilly Street	KALGOORLIE	6430	PUBLIC	J18	-30.74046500	121.47006300
227	Katanning District Hospital	Clive Street	KATANNING	6317	PUBLIC	F21	-33.68294200	117.56372400
409	Kellerberrin Memorial Hospital	51-63 Gregory St.	KELLERBERRIN	6410	PUBLIC	F19	-31.62904400	117.71739900
445	Kojonup District Hospital	Spring Street	KOJONUP	6395	PUBLIC	F21	-33.82920900	117.15343500
413	Kondinin District Hospital	Graham St.	KONDININ	6367	PUBLIC	G20	-32.48905200	118.26547600
257	Kununurra District Hospital	96 Coolibah Drive	KUNUNURRA	6743	PUBLIC	Q3	-15.77538800	128.73473200
414	Kununoppin District Hospital	Leake St.	KUNUNOPPIN	6489	PUBLIC	F19	-31.10988400	117.92268100
230	Lake Grace District Hospital	Stubbs Street	LAKE GRACE	6353	PUBLIC	G21	-33.10206800	118.45310600
272	Laverton District Hospital	Beria Road	LAVERTON	6440	PUBLIC	K16	-28.62395500	122.39624500
273	Leonora District Hospital	Sadie Canning Drive	LEONORA	6438	PUBLIC	J16	-28.89436600	121.33730100
233	Margaret River District Hospital	Farrelly Street	MARGARET RIVER	6285	PUBLIC	D21	-33.95233700	115.07097900
234	Meekatharra District Hospital	Savage Street	MEEKATHARRA	6642	PUBLIC	G14	-26.59118600	118.49144500
235	Merredin District Hospital	Kitchener Road	MERREDIN	6415	PUBLIC	G19	-31.48500600	118.27660000
417	Moora District Hospital	Dandaragan Road	MOORA	6510	PUBLIC	E18	-30.63955300	116.00103200
418	Morawa District Hospital	Caufield rdt.	MORAWA	6623	PUBLIC	E17	-29.21318000	116.00320600
419	Mullewa District Hospital	Elder St.	MULLEWA	6630	PUBLIC	D16	-28.53625600	115.51036200
420	Murray District Hospital [Pinjarra]	McKay St.	PINJARRA	6208	PUBLIC	D20	-32.63933300	115.87146500
422	Nannup District Hospital	Carey Street	NANNUP	6275	PUBLIC	D21	-33.98291500	115.76693500
423	Narembeen District Hospital	Ada Street	NAREMBEEN	6369	PUBLIC	G20	-32.06156100	118.39127400
236	Narrogin Regional Hospital	Williams Road	NARROGIN	6312	PUBLIC	F20	-32.93646900	117.16883500
260	Newman District Hospital	Mindarra Drive	NEWMAN	6753	PUBLIC	H11	-23.35500100	119.73614600
460	Nickol Bay Hospital [Karratha]	Millstream Road	KARRATHA	6714	PUBLIC	E8	-20.73639400	116.84893600
424	Norseman District Hospital	Talbot St.	NORSEMAN	6443	PUBLIC	J20	-32.19973400	121.77077800
237	Northam Regional Hospital	Robinson Street	NORTHAM	6401	PUBLIC	E19	-31.64924400	116.65829400
425	Northampton District Hospital	Stephen St.	NORTHAMPTON	6535	PUBLIC	C16	-28.35142300	114.63521600
426	North Midlands District Hospital [Three Springs]	Station Street	THREE SPRINGS	6519	PUBLIC	D17	-29.53450600	115.75927800
238	Onslow District Hospital	Second Avenue	ONSLOW	6710	PUBLIC	D9	-21.64313000	115.11549100
267	Paraburdoo District Hospital	Rocklea Road	PARABURDOO	6754	PUBLIC	F11	-23.20356500	117.67188300
645	Peel Health Campus	110 Lakes Road	MANDURAH	6210	PRIVATE	D20	-32.53253600	115.76322000

ID	NAME	ADDRESS	TOWN	POSTCODE	CLASS	WA_GRID	GDA_LAT	GDA_LONG
	Hospitals in Rural or Remote WA							
427	Pemberton District Hospital	Hospital Avenue	PEMBERTON	6260	PUBLIC	E22	-34.44462900	116.03250900
428	Pingelly District Hospital	Stratford Street	PINGELLY	6308	PUBLIC	F20	-32.53208100	117.08675300
429	Plantagenet District Hospital [Mt Barker]	Langton Road	MOUNT BARKER	6324	PUBLIC	F22	-34.62595900	117.65443400
240	Port Hedland Regional Hospital	Kingsmill Street	PORT HEDLAND	6721	PUBLIC	G8	-20.30993100	118.58113200
446	Quairading District Hospital	Harris Street	QUAIRADING	6383	PUBLIC	F20	-32.01413600	117.40251500
430	Ravensthorpe District Hospital	Martin Street	RAVENSTHORPE	6346	PUBLIC	I21	-33.58500600	120.04541100
243	Roebourne District Hospital	42-44 Hampton Street	ROEBOURNE	6718	PUBLIC	F8	-20.77618500	117.14352900
612	St John of God Health care Bunbury	Lot 800 Bussell Highway	BUNBURY	6230	PRIVATE	D21	-33.36648700	115.64753500
613	St John of God Health care Geraldton	Hermitage Street	GERALDTON	6530	PRIVATE	C16	-28.78419400	114.61604800
431	Southern Cross District Hospital	Coolgardie Road	SOUTHERN CROSS	6426	PUBLIC	H19	-31.23044100	119.33764500
256	Tom Price District Hospital	Mine Road	TOM PRICE	6751	PUBLIC	F10	-22.72581700	117.77650700
245	Wagin District Hospital	Warwick Street	WAGIN	6315	PUBLIC	F21	-33.30497900	117.34731300
433	Warren District Hospital [Manjimup]	Hospital Avenue	MANJIMUP	6258	PUBLIC	E22	-34.24028900	116.15372500
266	Wickham District Hospital	Mulga Way	WICKHAM	6720	PUBLIC	F8	-20.67531800	117.14233200
437	Wongan Hills District Hospital	Ackland Street	WONGAN HILLS	6603	PUBLIC	E18	-30.89409400	116.72459700
438	Wyalkatchem - Koorda District Hospital	Honour Avenue	WYALKATCHEM	6485	PUBLIC	F19	-31.17600300	117.38607600
249	Wyndham District Hospital	Lot 1270 Minderoo Street	WYNDHAM	6740	PUBLIC	Q3	-15.47896500	128.12706600
439	Yarloop District Hospital	Barrington-Knight Road	YARLOOP	6218	PUBLIC	D20	-32.95556400	115.90243700
251	York District Hospital	Trews Road	YORK	6302	PUBLIC	E19	-31.89408500	116.75765600

Footnote; WA_GRID refers to the Western Australian Grid reference identity for each hospital, GDA_lat and GDA_long refer to the global latitudes and longitudes of each hospital defining their location on the earth's surface with respect to the Royal Observatory at Greenwich (United Kingdom), the centre of mass for the earth and the axis of rotation of the earth with a reference radius of -9.

Table 5.2 Attributes of the 29 hospitals in WA which do not provide care for adults with respiratory disease

ID	NAME	ADDRESS	TOWN	POSTCODE	CLASS	WA_GRID	GDA_LAT	GDA_LONG
	Hospitals in Perth or Surrounding Metro Area							
459	Central Drug Unit [Next Step]	32 Moore Street	EAST PERTH	6004	PUBLIC	D19	-31.95318500	115.86896000
691	Colin Street Day Surgery	51 Colin Street	WEST PERTH	6005	PRIVATE	D19	-31.94941400	115.84172500
638	Concept Fertility Centre	374 Bagot Road	SUBIACO	6008	PRIVATE	D19	-31.95052600	115.82007400
695	Cottage Hospice	15 Bedbrook Place	SHENTON PARK	6008	PRIVATE	D19	-31.95275000	115.79993900
694	Eye Surgery Foundation	42 Ord Street	WEST PERTH	6005	PRIVATE	D19	-31.95013400	115.83976500
648	General Practice Divisions of WA [Home Ward]	130 Royal Street	EAST PERTH	6004	PRIVATE	D19	-31.95311300	115.87692900
698	GI Clinic	20 Fortune Street	SOUTH PERTH	6151	PRIVATE	D19	-31.98787700	115.86375100
935	Graylands Hospital (MHS)	Brockway Road	MT CLAREMONT	6010	PUBLIC	D19	-31.96220300	115.79106800
699	Harborne Dental Clinic	286 Harborne Street	GLENDALOUGH	6016	PRIVATE	D19	-31.92114900	115.82035400
686	Ian Rosenberg Oral Surgery	235 Wanneroo Road	TUART HILL	6060	PRIVATE	D19	-31.88698900	115.83667000
104	King Edward Memorial Hospital For Women	374 Bagot Road	SUBIACO	6008	PUBLIC	D19	-31.94989500	115.81897100
685	Lions Eye Institute Day Surgery	2 Verdun Street	NEDLANDS	6009	PRIVATE	D19	-31.96731900	115.81416100
682	McCourt Street Day Surgery	28 McCourt St.	WEST LEEDERVILLE	6007	PRIVATE	D19	-31.94139500	115.82784000
696	Marie Stopes Midland	8 Sayer Street	MIDLAND	6056	PRIVATE	E19	-31.89192100	116.01043200
644	Midland Dialysis Centre	46 Helena St.	MIDLAND	6056	PRIVATE	E19	-31.88914400	116.00291000
684	Murdoch Community Hospice	100 Murdoch Drive	MURDOCH	6150	PRIVATE	D20	-32.06804900	115.84484700
681	Murdoch Surgicentre	100 Murdoch Drive	MURDOCH	6150	PRIVATE	D20	-32.06804900	115.84484700
631	Ngala Family Resource Centre	9 George Street	KENSINGTON	6151	PRIVATE	D19	-31.98495200	115.88629400
643	Perth Clinic	29 Havelock St.	WEST PERTH	6005	PRIVATE	D19	-31.95121500	115.84402000
103	Princess Margaret Hospital For Children	Roberts Road	SUBIACO	6008	PUBLIC	D19	-31.94582100	115.83760700
100	Royal Perth Rehabilitation Hospital	Selby Street	SHENTON PARK	6008	PUBLIC	D19	-31.95438600	115.80430700
158	Selby Authorised Lodge (MHS)	2 Selby Street	SHENTON PARK	6008	PUBLIC	D19	-31.95829400	115.80279400
692	Serapis Day Hospital	57 Burroughs Road	KARRINYUP	6018	PRIVATE	D19	-31.87632300	115.77516400
690	Southbank Clinic	38 Meadowvale Avenue	SOUTH PERTH	6151	PRIVATE	D19	-31.97589200	115.87176500
689	Westminster Day Surgery	476 Wanneroo Road	WESTMINSTER	6061	PRIVATE	D19	-31.86364900	115.82818600
247	Woodside Maternity Hospital	18 Dalgety Street	EAST FREMANTLE	6158	PUBLIC	D20	-32.04126700	115.77174700
697	Woodvale Private Hospital for Women	231 Timberlane Drive	WOODVALE	6026	PRIVATE	D19	-31.78313800	115.78801400

ID	NAME	ADDRESS	TOWN	POSTCODE	CLASS	WA_GRID	GDA_LAT	GDA_LONG
	Hospitals in Regional or Remote WA							
687	Albany Hospice	Diprose Crescent	ALBANY	6330	PRIVATE	F23	-35.00426700	117.90485800
680	Busselton Hospice	Mill Road	BUSSELTON	6280	PUBLIC	D21	-33.65390600	115.31961000

Footnote; WA_GRID refers to the Western Australian Grid reference identity for each hospital, GDA_lat and GDA_long refer to the global latitudes and longitudes of each hospital defining their location on the earth's surface with respect to the Royal Observatory at Greenwich (United Kingdom), the centre of mass for the earth and the axis of rotation of the earth with a reference radius of -9.

5.2.6.2 Respiratory physicians

The medical specialist outreach assistance programme was accessed from the Western Australian Centre for Rural and Remote Medicine (WACRRM) to identify all respiratory physicians working in areas outside of the metropolitan area. In addition, the Medical and Surgical Specialist Referral Directory of WA, (2004) compiled and published by Dr Stephen Hobdy and the St John of God Clinical Services Directory, a referral guide for General Practitioners (2005) were also sourced to identify specialists working in the private system who may not have been included in the WACRRM database.

5.2.6.3 Pulmonary rehabilitation programmes

For the purpose of this study, a pulmonary rehabilitation programme was defined as a supervised group exercise training programme provided specifically for individuals with chronic respiratory disease. Data sources used to create a comprehensive picture of the location of pulmonary rehabilitation programmes across the state were:

(1) telephone survey of the Physiotherapy Departments within public and private hospitals conducted from June 2005-Sept 2005;
(2) data from a project carried out by a physiotherapist at Fremantle Hospital in 2005;
(3) The Australian Lung Foundation website (http://www.lungfoundation.com); and
(4) the Australian Physiotherapy Association.

Physiotherapists have the knowledge and skills to provide education and one-on-one rehabilitation for individuals with a chronic disease, and it must be acknowledged that any private physiotherapy practice is able to offer this service, and many do offer an informal type of service to individuals with chronic respiratory disease. However, the added benefits of a supervised exercise programme in a group setting have been discussed in Chapter 2 (section 2.8.5) of this thesis.

5.2.6.4 Asthma educators

To complete the asthma-educators dataset, the Asthma Foundation of WA provided the postcodes of all practising asthma educators within metropolitan and rural areas

who had given their consent to have their details on a database held by the Asthma Foundation in 2005. It was estimated that this database included one third of all educators in WA. In addition, hospitals and nursing posts around WA were contacted by phone over a 3 week period in August 2005 and contact was made with any individual at that hospital or post who was trained as an asthma educator or provided formal asthma education to patients. Through this contact it was ascertained if the individual was employed in part, or full as an asthma educator. Asthma educators in regional areas were then asked if they outsourced and provided this service to other parts of the district.

5.2.6.5 Hospital admissions data

Hospital admissions data from patient discharge summaries are coded by professional coders within the Health Department of WA. It is notable that hospital admissions represent only a small percentage of all cases of asthma and COPD. Only the most severe exacerbations are included in hospital admissions data. From 2000, the 10th Edition of the International Classification of Diseases Coding System (ICD-10) were used to code diagnoses during hospital admissions across WA. This was an update to the previous ICD-9- CM coding system in use prior to 2000. Therefore for the purpose of this study, a five year period (2000-2004) was selected as the time period in which to study hospital admissions, because it was the most up-to-date dataset available and the older ICD-9 coding system was no longer in use from 2000. The Health Department of WA holds the State's Hospital Morbidity Data System (HMDS) which contains discharge data for every admission to acute hospitals in WA. Information accessible from the HMDS includes age, gender, race and clinical information such as primary diagnoses, length of stay and complications from the admission. Table 5.3 lists the attributes of the data that were retrieved with permission from the Health Department of WA in a de-identified format on 22nd of August 2005.

Table 5.3 Attributes of hospital admissions data

Abbreviation	Definition
EVE ID	Unique identifier
FIN YEAR	2000/2001, 2001/2002, 2002/2003, 2003/2004 financial years
HSRES	Health service of residence: patient admitted to
AGE GROUP	five year age strata groups 40 years and over
SEX	Male or Female
ETHNICITY	Aboriginal or Torres Strait Islander or other
ASTHMA	Asthma flags showing either as a principal diagnosis, additional diagnosis, or no asthma
ASTHMA_CODE	ICD 10 codes: J45 Asthma and or J46 status asthmaticus
COPD	Flagging those with a principle diagnosis, additional diagnoses or no diagnosis of COPD
COPD_CODE	ICD 10 codes J40-44.9 codes as follows: J40 Bronchitis not specified as acute or chronic, J41 simple and mucopurulent chronic bronchitis, J41.0 Simple chronic bronchitis, J41.1 Mucopurulent chronic bronchitis, J41.8 Mixed simple and mucopurulent chronic bronchitis, J42 unspecified chronic bronchitis, J43 Emphysema, J43.0 MacLeod's syndrome, J43.1 Panlobar emphysema, J43.2 Centrilobar emphysema, J43.8 Other emphysema, J43.9 Emphysema unspecified, J44 Other Chronic obstructive pulmonary disease, J44.0 Chronic obstructive pulmonary disease with acute lower respiratory infection, J44.1 Chronic obstructive pulmonary disease with acute exacerbation, unspecified, J44.8 Other specified chronic obstructive pulmonary disease, J44.9 Chronic obstructive pulmonary disease unspecified.

The hospital admissions data obtained from the Health Department of WA were provided in a spreadsheet generated in Excel, which was converted into a database file to allow import into Arc GIS. The source file contained 46,356 records for either a principle or additional diagnosis of asthma or COPD.

5.2.6.6 Baseline population data

MapInfo for Windows is a compatible programme for CDATA 2001 to access census data and digital boundaries. Before the census information could be used, relevant MapInfo coverages were converted into shape-files using the Map-Info toolbox and these were imported into the health geo-database for this study.

Data obtained included population data (males and females) for each health service area and for the ASGC Remoteness Areas. This latter dataset refers to the five classification areas (major cities, inner regional, outer regional, remote and very remote) that census districts are allocated to, around Australia, based on road

distance from a locality to the closest service centre in each of the five classes of population size.

5.2.7 Ethical considerations

Ethics approval was granted from the Human Research Ethics Committee of Curtin University of Technology (HR120/2004) prior to the commencement of this study.

5.3 Results

5.3.1 Overview

This section describes the location of health services in WA for asthma and COPD and illustrates the distribution of the asthma and COPD admissions data between 2000 and 2004. These data are presented in a graphical format, to aid the visualisation of service and admissions data. The objective of this study was to use the tools within GIS to provide information that could be further tested through epidemiological studies, hence no further analyses have been conducted on these results. The results are divided into two main parts, the first part, (5.3.2) focuses on services and the second (5.3.3) on admissions data.

5.3.2 Health services

5.3.2.1 Hospitals and their selective attributes

Maps illustrating the distribution of hospitals, EDs, respiratory physicians, pulmonary rehabilitation programmes and asthma educators are located in Figures 5.4 through to 5.8.

Health services without a visiting respiratory physician included the Pilbara, Northern Goldfields and Vasse-Leeuwin. The Midwest-Murchison Regions and Kimberley were among those without access to pulmonary rehabilitation. Asthma educators could be contacted within almost all health service boundaries. Table 5.4 illustrates the location and frequency of respiratory physician visits to regional areas within WA and Table 5.5 illustrates the location of pulmonary rehabilitation programmes in regional WA.

Figure 5.4 Distribution of hospitals within WA

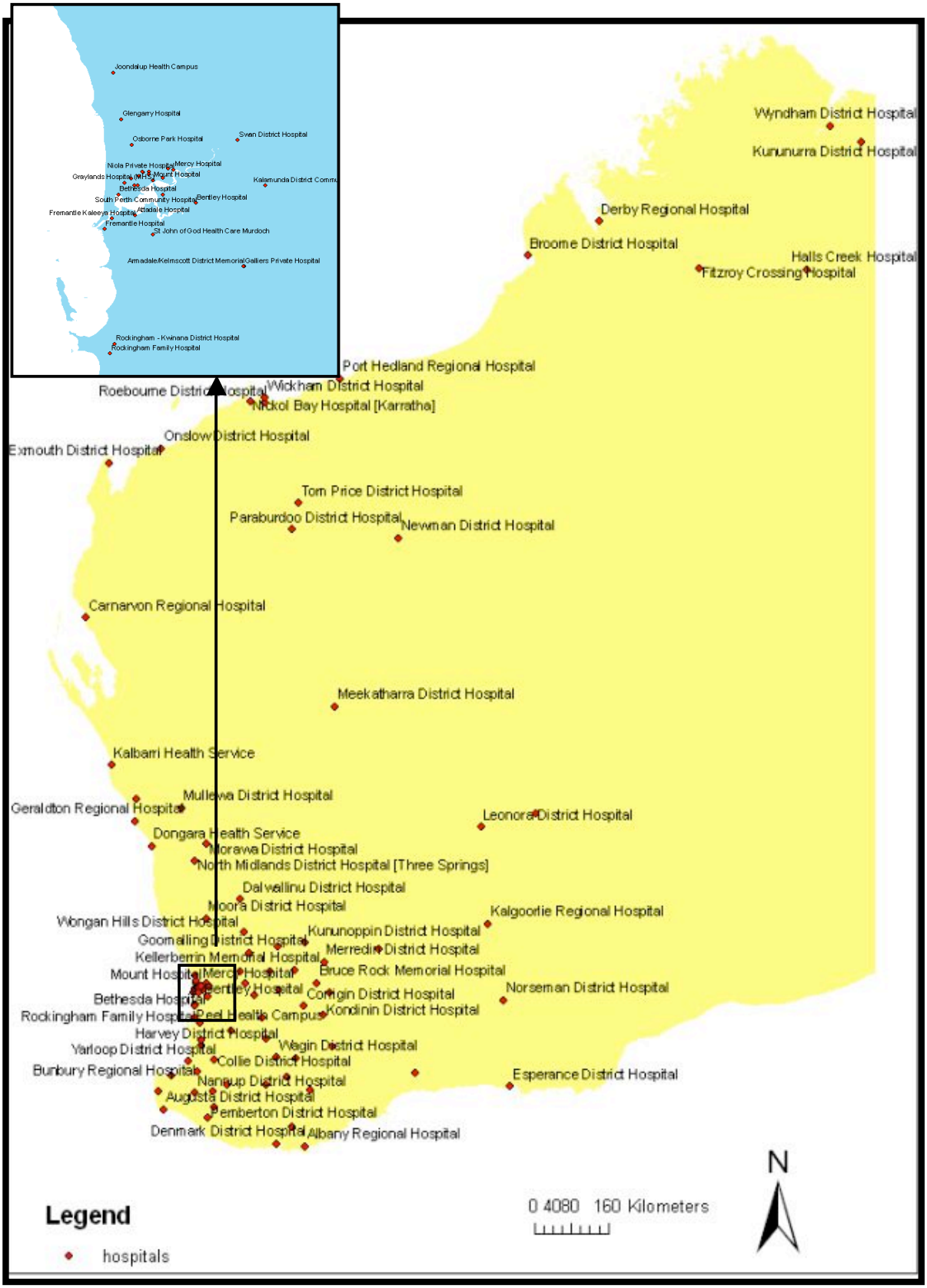


Figure 5.5. Hospitals with an emergency department within WA

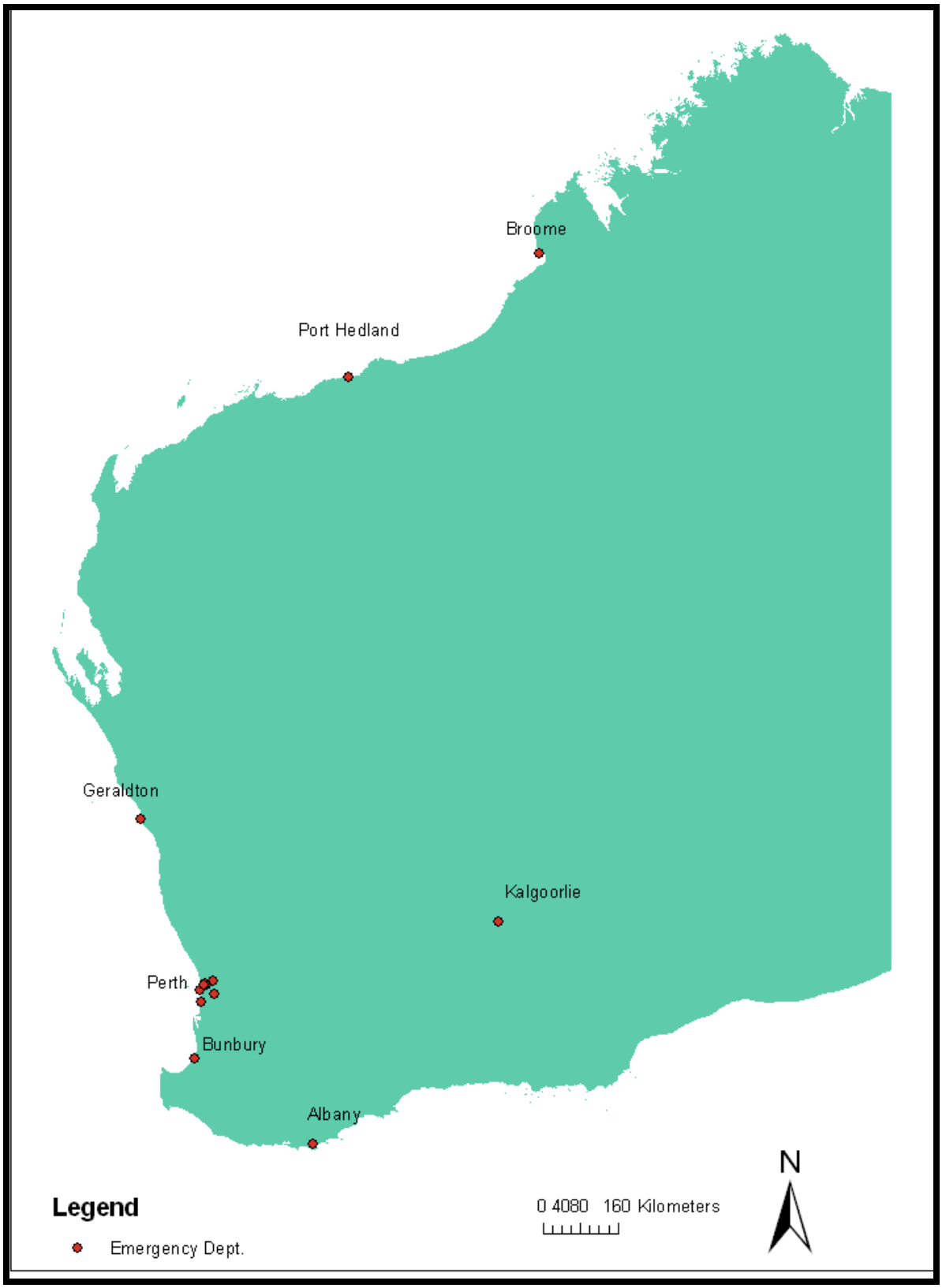


Figure 5.6 Hospitals with pulmonary rehabilitation programmes within WA

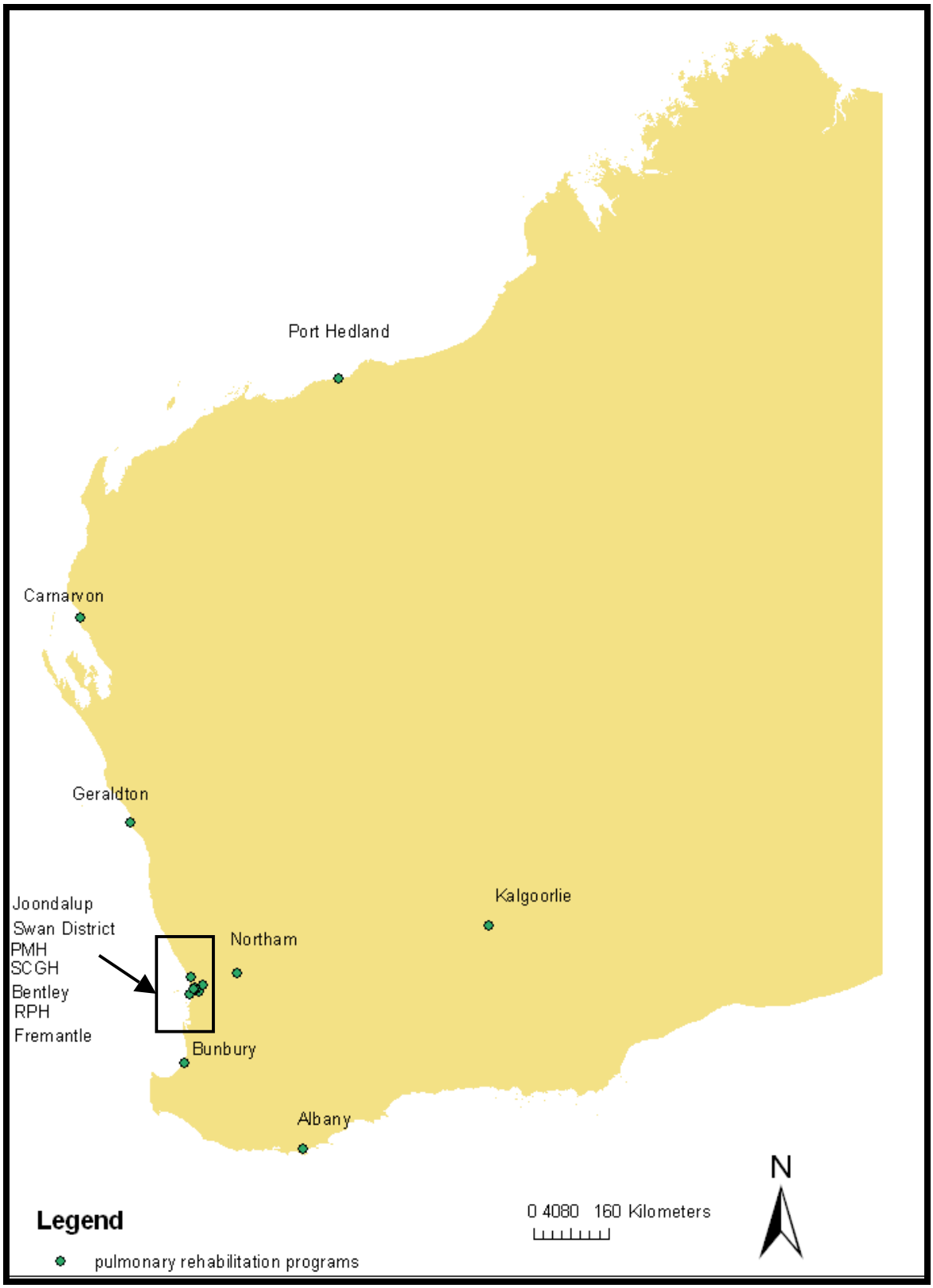


Figure 5.7 Towns with a visiting respiratory physician within rural WA

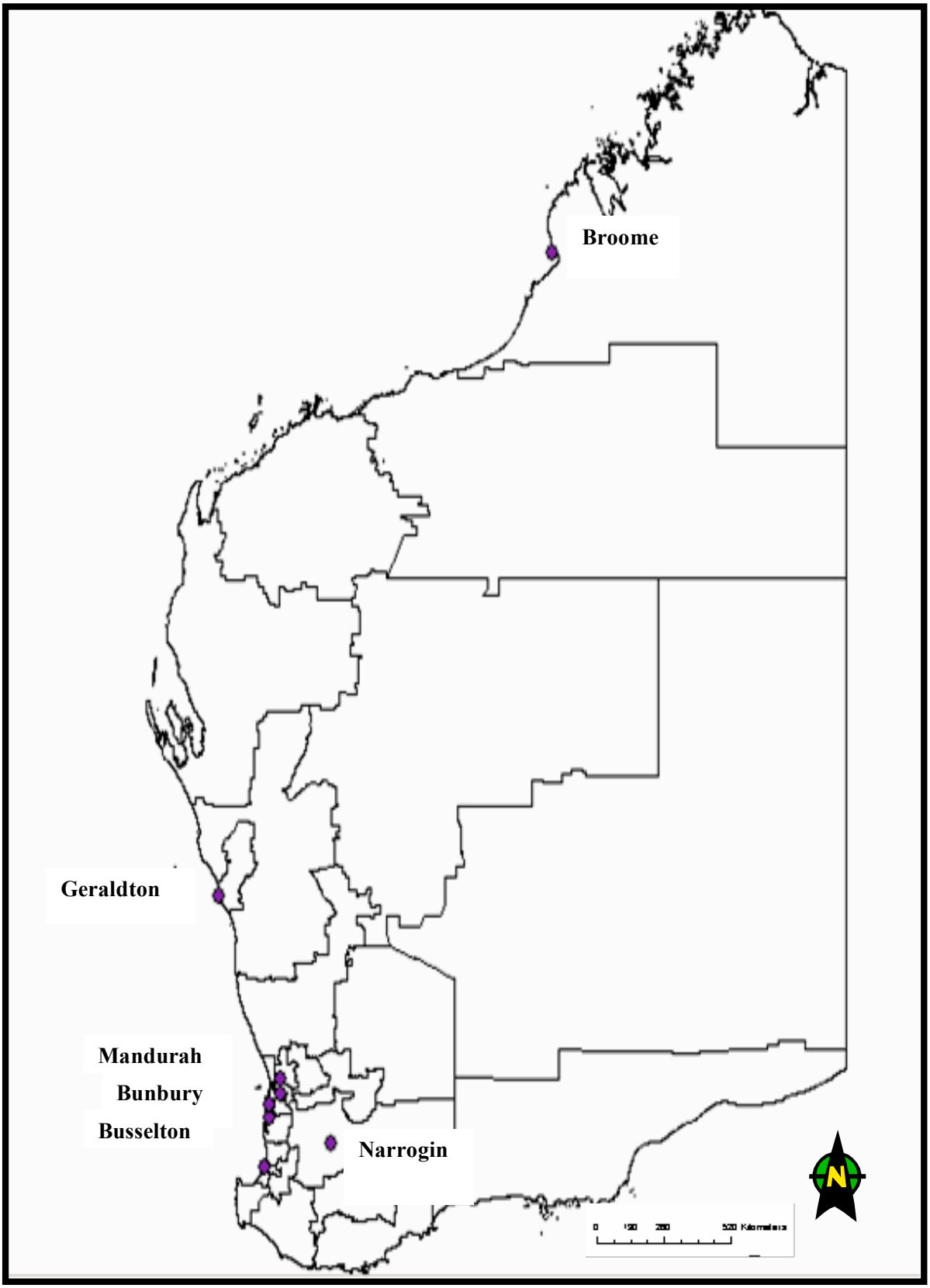


Figure 5.8 Distribution of asthma educators in relation to Australian Standard Geographical Classification (ASGC) areas

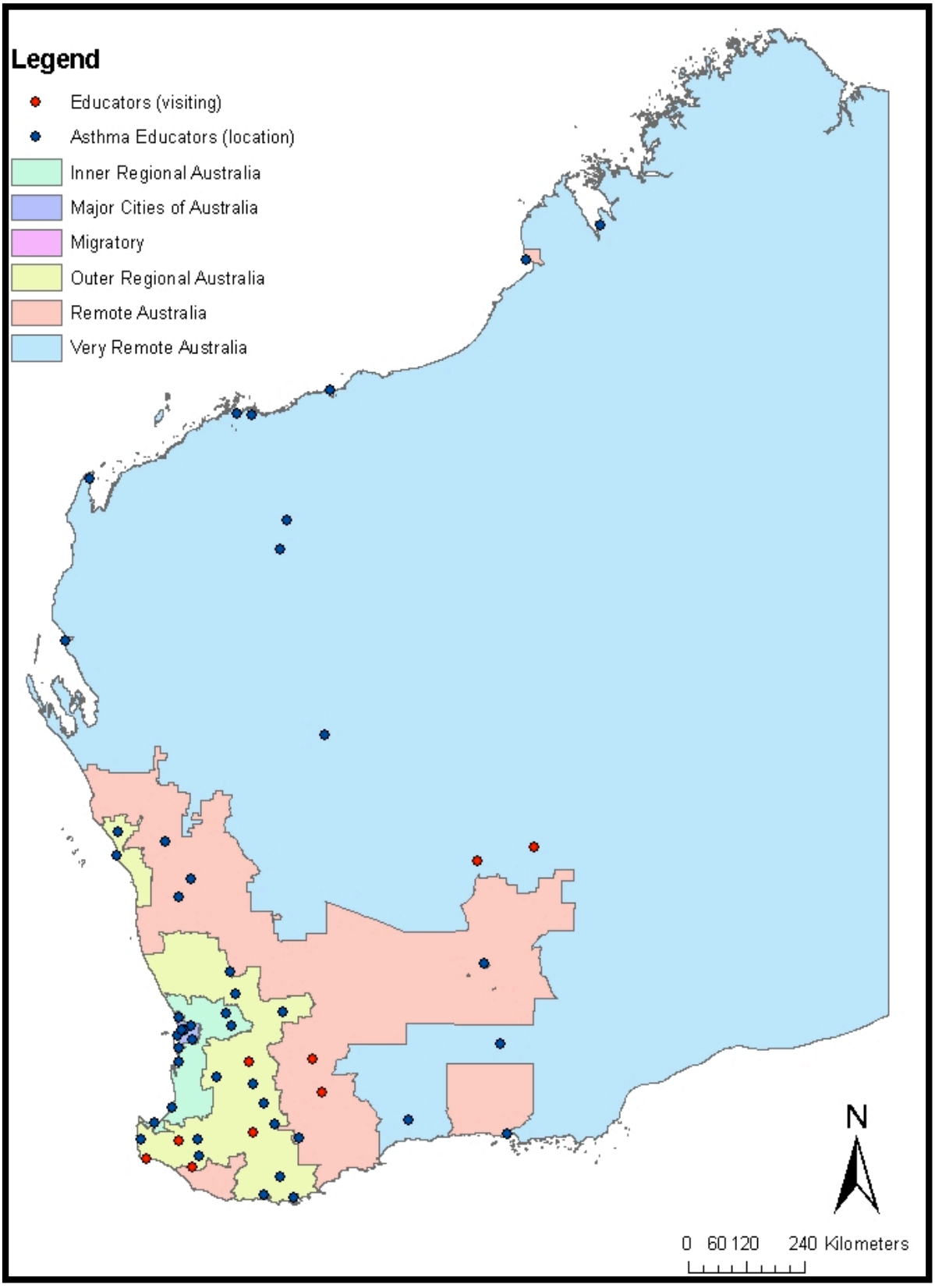


Table 5.4 Location and frequency of respiratory physician visits within regional WA

Location	Number of physicians	Frequency of clinics
Broome	1	Full-time
Bunbury	2	Once a month, once every 2 months
Busselton	1	Once a month
Geraldton	2	Both clinics once every 3 months
Mandurah	2	Once a fortnight, once a month
Narrogin	1	Once a month
Northam	1	Once a month
Rockingham	1	Full-time

Table 5.5 Location of pulmonary rehabilitation programmes within regional WA

Location	Number of classes per week when a block programme is held
Albany	2
Bunbury	2
Carnarvon	On demand
Geraldton	2
Kalgoorlie	2
Mandurah	2
Northam	1
Port Hedland	3

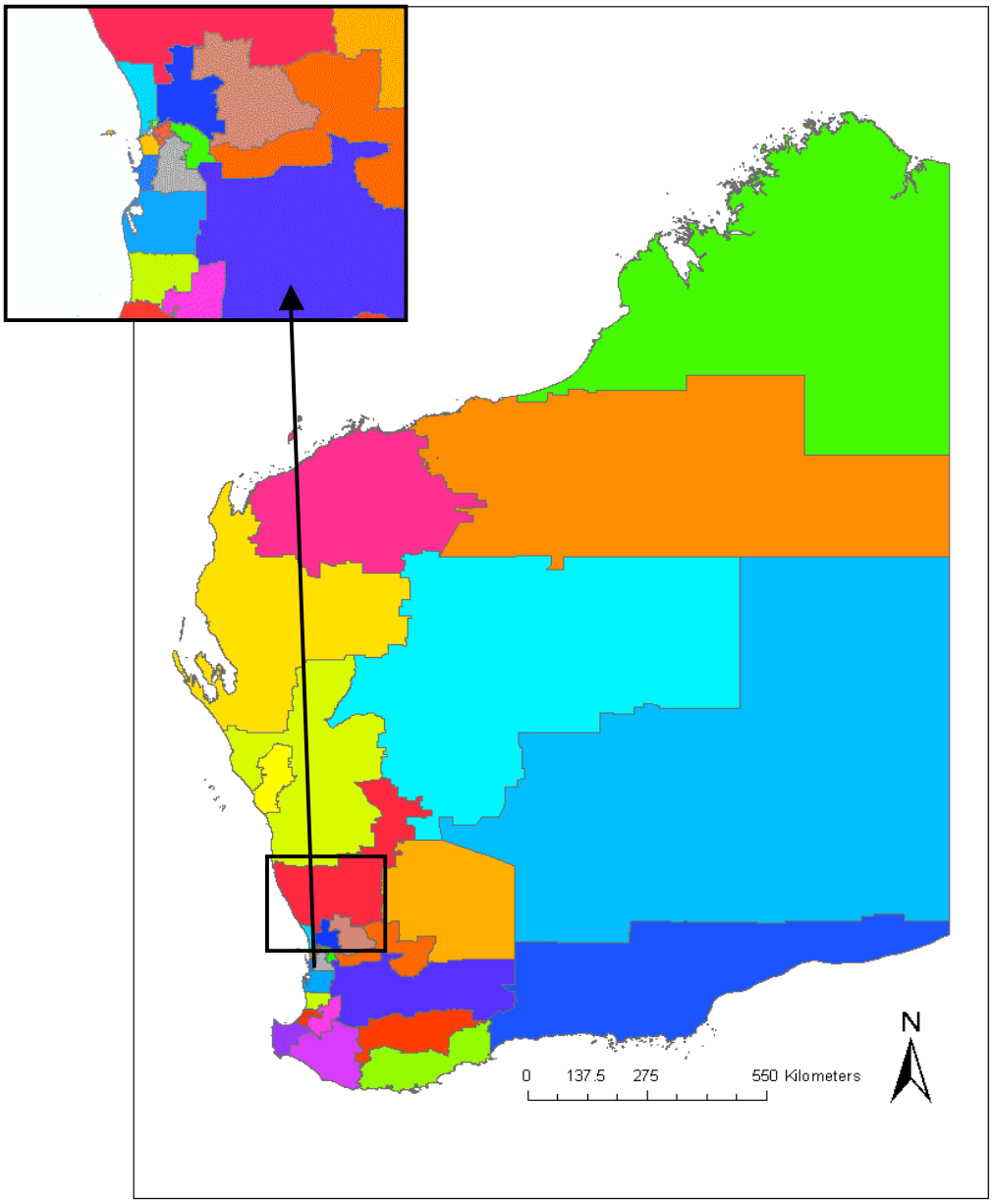
5.3.3 Hospital admissions data

5.3.3.1 Distribution of admissions across Western Australia

A total of 23,049 admissions were recorded with a primary diagnosis of asthma or COPD (4,159 asthma and 18,890 COPD) in adults aged over 40 years between 2000 and 2004. Individuals of Aboriginal or Torres Strait Islander descent comprised 1,262 of the COPD admissions (6.7%), and 670 of the asthma admissions (16.1%). In 2001, indigenous individuals, however, represented only 3.2% of the total population of WA (396). Across the State, 55% of asthma admissions and 41% of COPD admissions were in adults residing in health services outside the metropolitan area.

Figure 5.9 illustrates the health service boundaries in WA used to analyse the distribution of asthma and COPD cases relative to baseline population data (40 years and over) within each catchment area. Figure 5.10 shows the percentage of admissions in adults aged 40 years and over recorded between 2000-2004 with a diagnosis of asthma by health service boundary. Figure 5.11 illustrates these percentages relative to the number of adults aged 40 years and over counted in the 2001 Australian Bureau of Statistics census for each health service boundary. Figures 5.12 and 5.13 illustrate the data for COPD admissions in each health service and figure 5.14 combines the number of asthma and COPD cases and presents these data relative to baseline population data for each health service boundary. In Figure 5.11, it is evident that Geraldton and the Wheatbelt recorded the highest number of admissions for asthma in relation to baseline population data between 2000 and 2004. In Figure 5.13, Geraldton, the Eastern Pilbara health service, Kalgoorlie-Boulder and the Wheatbelt show the greatest percentage of COPD admissions in relation to baseline population data. Table 5.6 depicts the relationship between the number of respiratory physician clinics per year outside the metropolitan area and pulmonary rehabilitation programmes, to the average number of combined asthma and COPD admissions from 2000-2004, the population of adults aged 40 years and over within each health service and the health service area size.

Figure 5.9 Health service boundaries for Western Australia*



*'Health services' in the legend correspond to the 31 administrative boundaries, both regional and metropolitan, that the Health Department of WA has defined in 2005 to provide the State with comprehensive health care.

Legend

Health Services

- Armadale- Kelmscott
- Avon
- Bentley
- Bunbury
- Central Great Southern
- Central Wheatbelt
- East Pilbara
- Eastern Wheatbelt
- Fremantle
- Gascoyne
- Geraldton
- Harvey Yarloop
- Inner City
- Kalamunda
- Kimberley
- Lower Great Southern
- Mid West
- Murchison
- North Metropolitan
- Northen Goldfields
- Peel
- Rockingham Kwinana
- South East Coastal
- Swan
- Upper Great Southern
- Vasse-Leeuwin
- Warren-Blackwood
- Wellington
- West Pilbara
- Western Health Service
- Unknown WA

Figure 5.10 Percentage of admissions with a primary diagnosis of asthma (2000-2004) by health service boundary

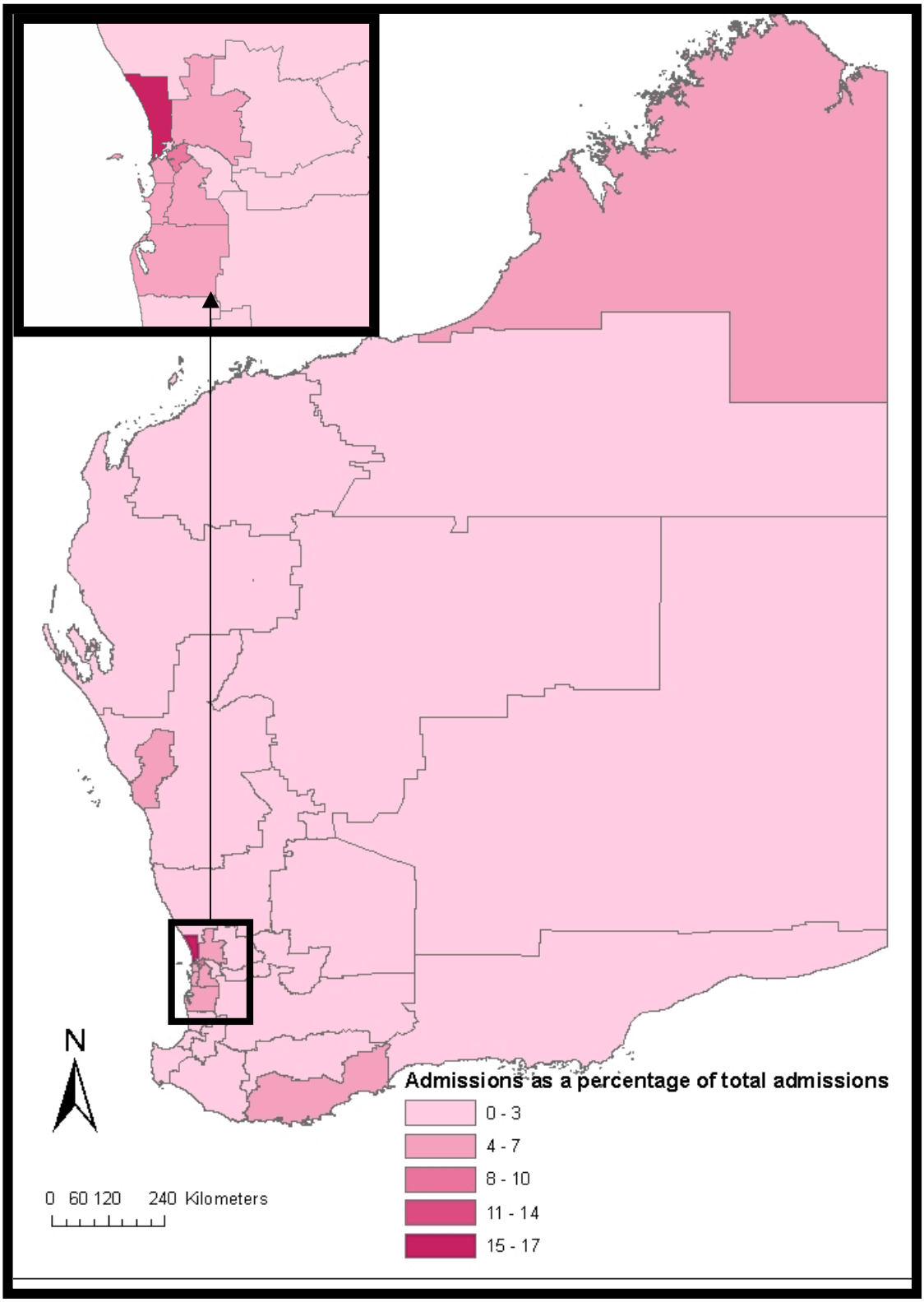


Figure 5.11 Asthma admissions (2000-2004) relative to baseline population aged 40 years and over

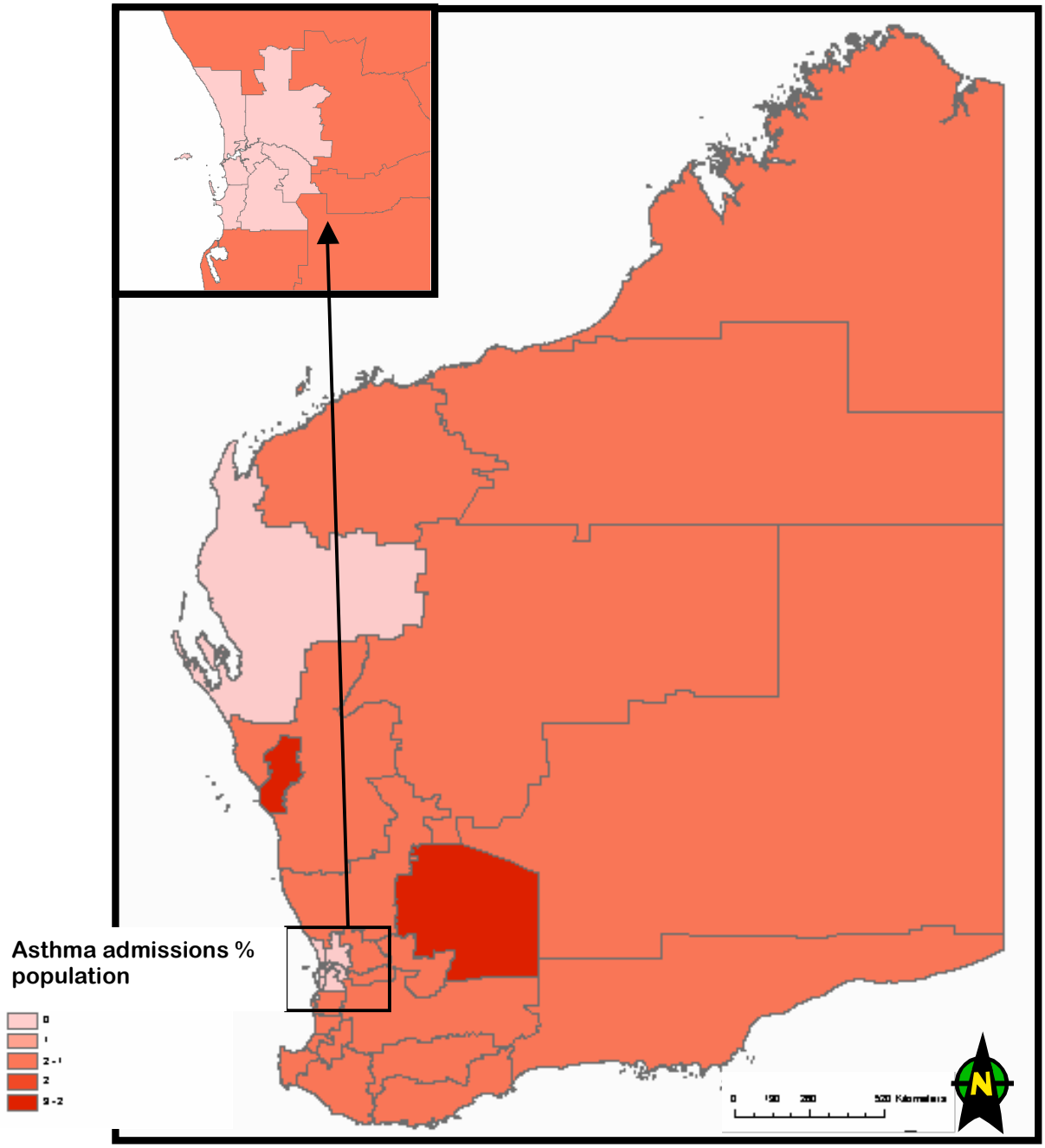


Figure 5.12 Percentage of admissions with a primary diagnosis of COPD (2000-2004) by health service boundary

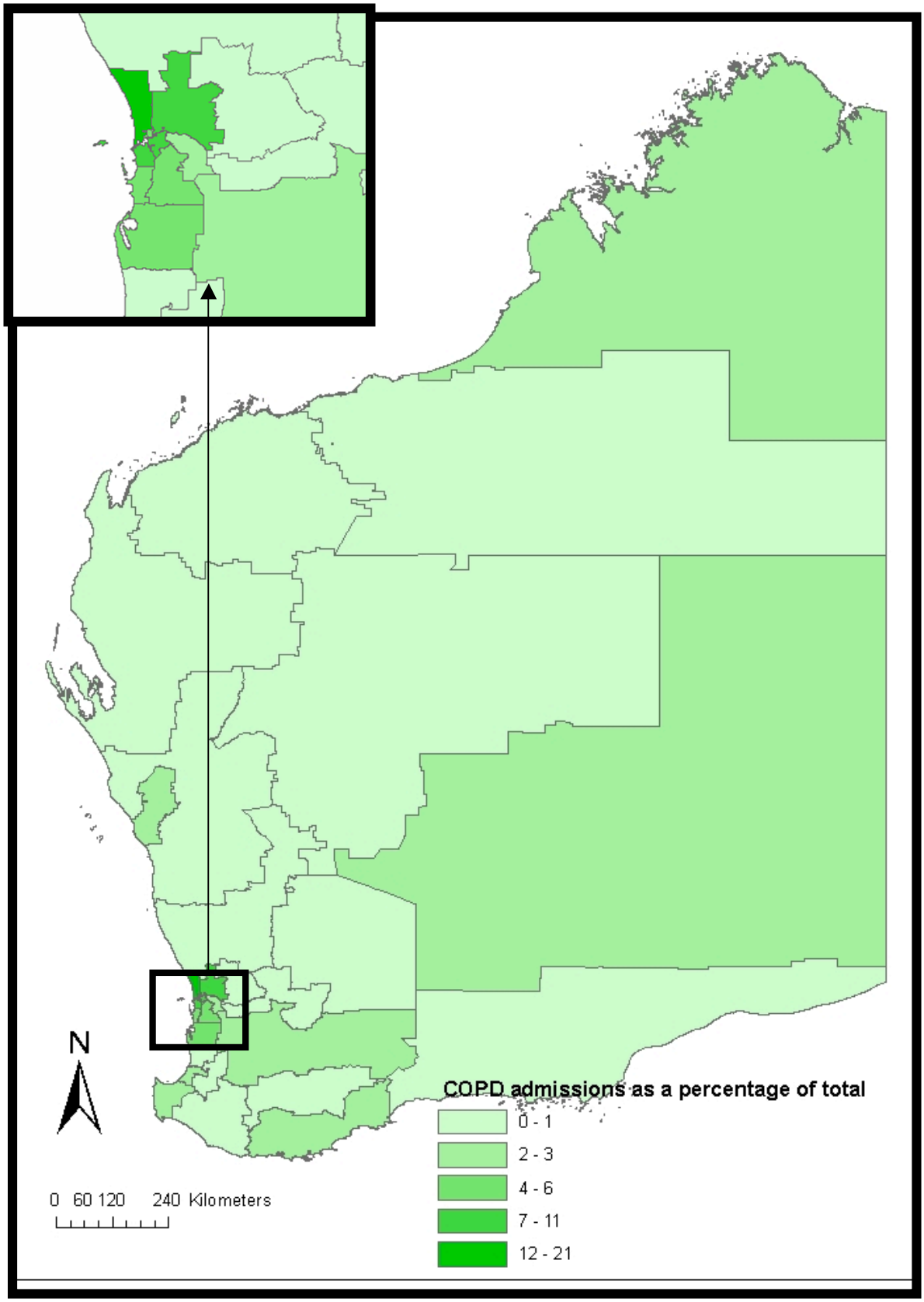


Figure 5.13 Chronic obstructive pulmonary disease admissions (2000-2004) relative to baseline population aged 40 years and over

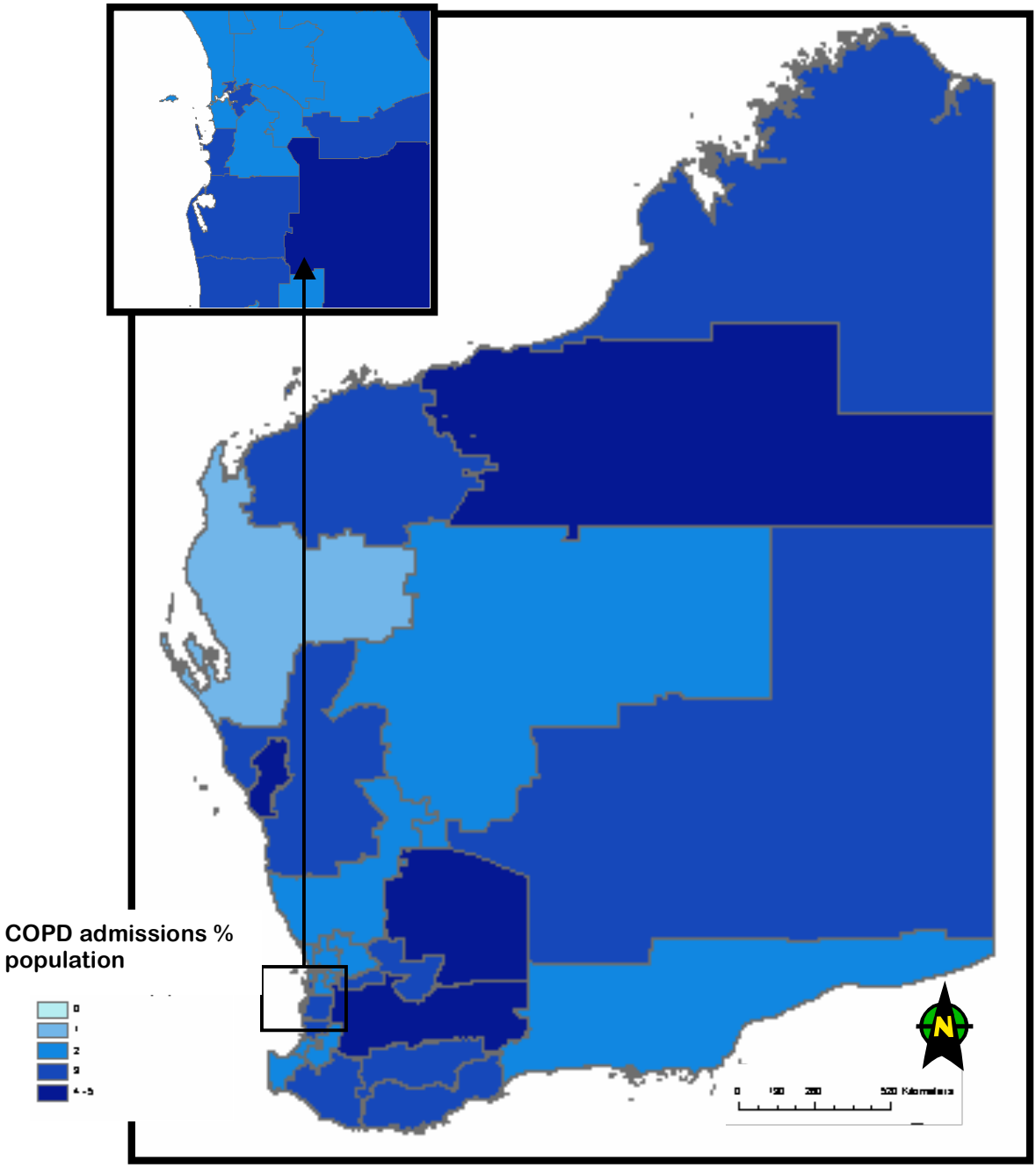


Figure 5.14 Asthma and COPD admissions (2000-2004) combined in relation to baseline population aged 40 years and over

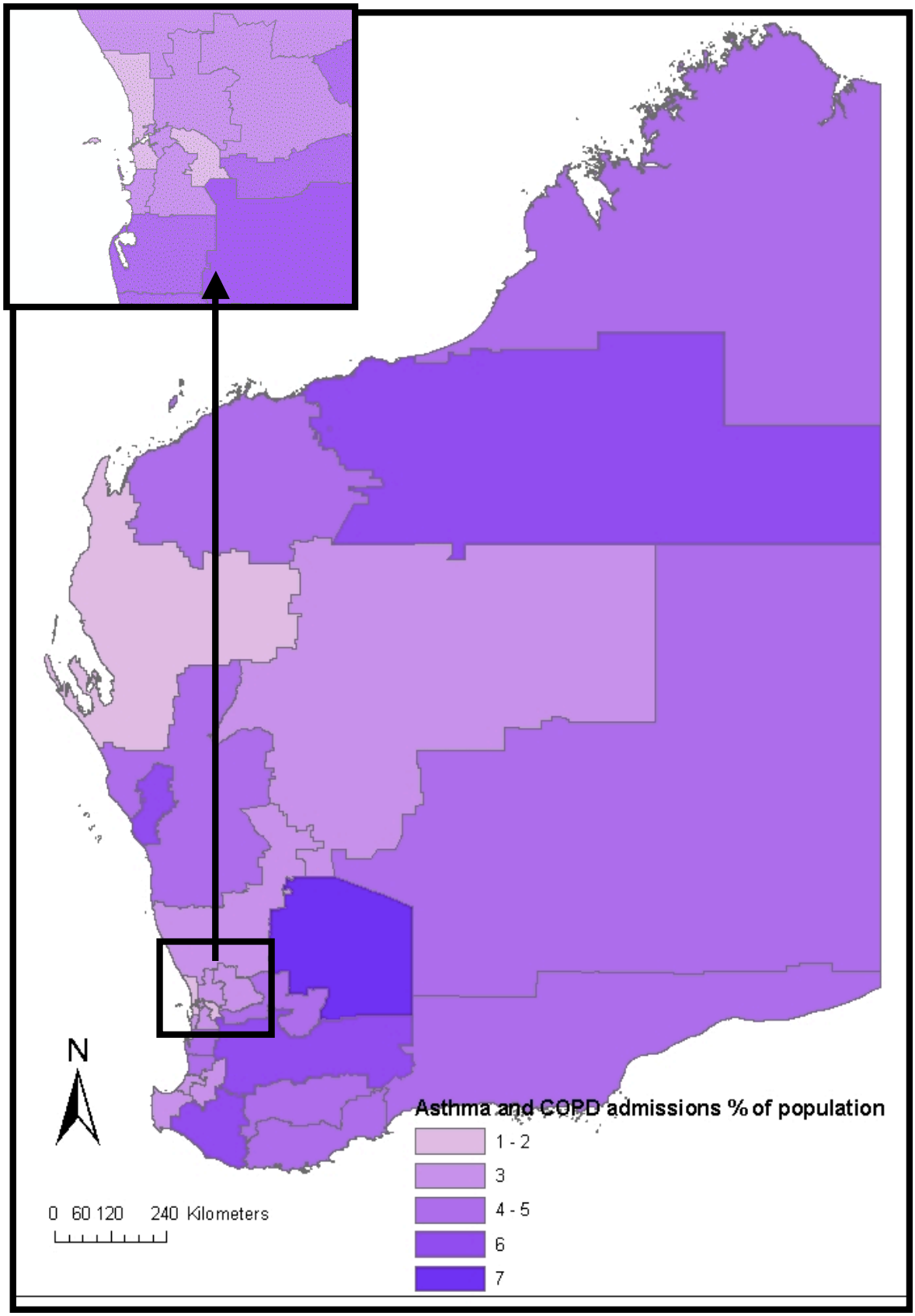


Table 5.6 Respiratory physician clinics and pulmonary rehabilitation programmes in relation to numbers of admissions for asthma and COPD in adults aged 40 years and over, the population (40 years and over) and size of each of the rural health service boundaries within WA

Health Service	Respiratory Physicians (RP)	RP availability total no. clinics/year	Pulmonary Rehabilitation (PR)	Average no combined Asthma/COPD 2000-2004	Population (≥40 yrs)	Health service area size (km^2)	RP clinics for every 1000 admissions	RP clinics for every 1000 people ≥40 yrs	RP clinics for every 1000 km^2	PR for every 1000 admissions/yr	PR for every 1000 people ≥40 yrs	PR for every 1000 km^2
Avon	1 RP visits monthly	12	1	50	7275	5, 255	241.2	1.6	2.3	0	0	0
Bunbury	1 visits 1/month, 1visits 2monthly	18	1	121	17608	623	149.4	1.0	28.9	8.3	0.1	1.6
Central Great Southern	0	0	0	45	3995	18, 114	0	0	0	0	0	0
Central Wheatbelt	0	0	0	34	3085	12, 771	0	0	0	0	0	0
East Pilbara	0	0	1	88	6675	396, 559	0	0	0	11.4	0.1	0.0
Eastern Wheatbelt	0	0	0	78	4506	59, 103	0	0	0	0	0	0
Gascoyne	0	0	(1) On demand	31	8340	136, 288	0	0	0	32	0.1	0.0
Geraldton	2 RP visit 3 monthly, 1 visits once/month	16	1	178	13002	1, 796	90.0	1.2	8.9	5.6	0.1	0.6
Harvey/ Yarloop	0	0	0	66	6828	2, 258	0	0	0	0	0	0
Kimberley	F/T	260	0	164	16070	421, 451	1590.2	16.2	0.6	0	0	0

Health Service	Respiratory Physicians (RP)	RP availability total no. clinics/year	Pulmonary Rehabilitation (PR)	Average no combined Asthma/COPD 2000-2004	Population (≥40 yrs)	Health service area size (km^2)	RP clinics for every 1000 admissions	RP clinics for every 1000 people ≥40 yrs	RP clinics for every 1000 km^2	PR for every 1000 admissions/yr	PR for every 1000 people ≥40 yrs	PR for every 1000 km^2
Lower Great Southern	0	0	1 combined	329	18438	20, 863	0	0	0	3.0	0.1	0.0
Midwest	0	0	0	60	6242	95, 444	0	0	0	0	0	0
Murchison	0	0	0	17	2142	373, 409	0	0	0	0	0	0
Northern Goldfields	0	0	1	137	12549	637, 218	0	0	0	7.3	0.1	0.0
Peel	1 RP visits fortnightly, 1 visits monthly	38	1	275	28442	2, 716	138.3	1.3	14.0	3.6	0.0	0.4
South East Coastal	0	0	0	58	6465	151, 507	0	0	0	0	0	0
Upper Great Southern	1 RP visits monthly	12	0	97	7913	43, 724	124.0	1.5	0.3	0	0	0
Vasse Leeuwin	1RPvisits 1/month	12	0	100	13543	2, 242	119.7	0.9	5.3	0	0	0
Warren/Blackwood	0	0	0	85	7425	14, 231	0	0	0	0	0	0
West Pilbara	0	0	0	80	7888	116, 276	0	0	0	0	0	0
Western	0	0	0	61	7131	31, 753	0	0	0	0	0	0

RP: respiratory physician, PR: pulmonary rehabilitation programmes, COPD: chronic obstructive pulmonary disease, km^2: kilometeres squared, 40+yrs: adults aged 40 years and over

5.3.3.2 Data analyses of hospital admissions with a diagnosis of asthma o chronic obstructive pulmonary disease as a co-morbidity

The data provided in Section 5.3.3.1 *excluded* any admissions for which a primary diagnosis of asthma was recorded as the reason for admission but for which (i) the hospital stay was further complicated by a **secondary or additional** diagnosis of COPD as a co-morbidity, or (ii) the admissions in which a primary diagnosis of COPD was recorded along with a **secondary or additional** diagnosis of asthma as a co-morbidity which complicated the hospital admission. These data were analysed separately as they provide an indication of the degree of overlap or cross-over between these two conditions in adults aged 40 years and over.

Between 2000 and 2004 there were 152 admissions recorded that had a primary diagnosis of asthma with the additional diagnosis of COPD, and 102 admissions reported with a primary diagnosis of COPD along with an additional diagnosis of asthma. These data are presented in relation to health service boundary area in Table 5.7, together with data on the numbers of admissions for individuals that had either asthma or COPD as an additional diagnosis, but the primary reason for the hospital stay was for an unrelated condition (e.g. diabetes, fracture).

Aboriginal and Torres Strait Islanders made up 16 of the 152 admissions (10.5%) that occurred with a primary diagnosis of asthma along with complicating additional diagnosis of COPD, and 17 of the 102 admissions (16.7%) with a primary diagnosis of COPD along with the complicating additional diagnosis of asthma.

Table 5.7 Admissions with asthma and/or COPD as a co-morbidity (2000-2004) by health service boundaries in WA, for adults 40 years and over

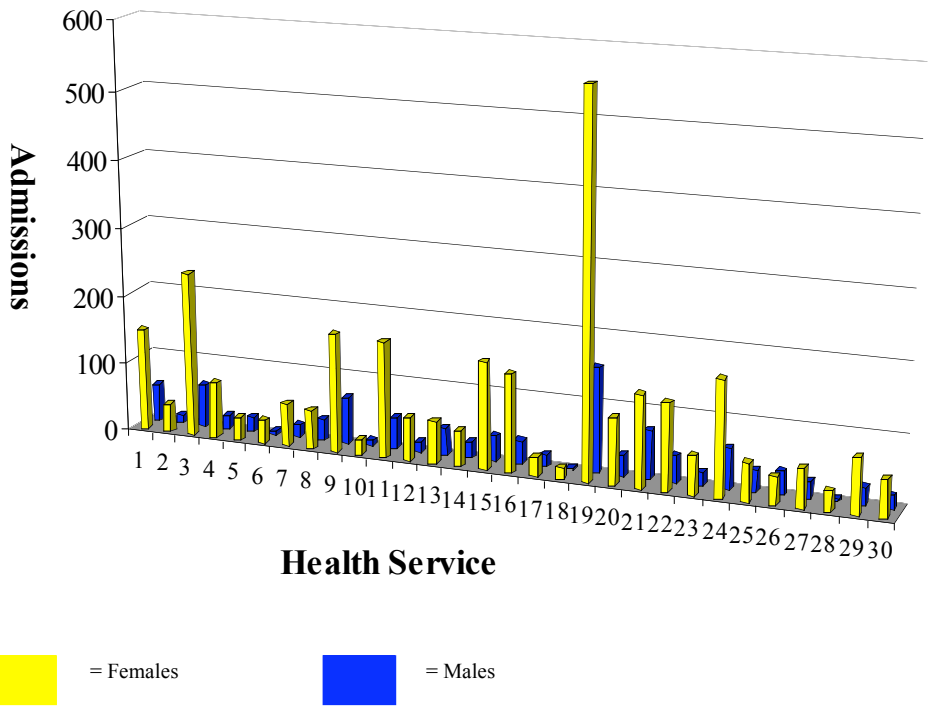
Health Service	Asthma as primary diagnosis + COPD as additional diagnosis (n)	COPD as primary diagnosis + asthma as additional diagnosis (n)	Other condition as primary diagnosis + Asthma as additional diagnosis only (n)	Other condition as primary diagnosis + COPD as additional diagnosis only (n)
Perth metropolitan area and surrounding suburbs				
Armadale/ Kelmscott	3	1	165	965
Bentley	9	6	347	22181
Fremantle	7	15	324	1724
Inner City	16	2	104	726
Kalamunda	-	4	110	450
North Metropolitan	14	8	741	4355
Rockingham/Kwinana	2	3	115	820
Swan	8	3	422	1997
Wellington	-	-	52	169
Regional and Remote				
Avon	3		44	319
Bunbury	3	2	186	527
Central Great Southern	7	4	39	82
Central Wheatbelt	-	-	14	79
East Pilbara	2	-	33	121
Eastern Wheatbelt	3	5	61	201
Gascoyne	2	-	58	150
Geraldton	6	6	204	540
Harvey/Yarloop	3	-	44	177
Kimberley	-	10	115	264
Lower Great Southern	21	2	266	543
Midwest	2	-	64	153
Murchison	-	-	9	45
Northern Goldfields	1	9	85	302
Peel	9	4	159	824
South East Coastal	4	11	96	190
Upper Great Southern	18	3	52	244
Vasse Leeuwin	-	1	77	484
Warren/Blackwood	7	-	45	276
West Pilbara	2	1	36	116
Western	-	-	42	183
Other				
Unknown WA	-	2	42	89
Metro Post Box	-	-	1	3
Total	**152**	**102**	**4152**	**19399**

(n): number, COPD: chronic obstructive pulmonary disease

5.3.3.3 Asthma and chronic obstructive pulmonary disease admissions by gender within each health service boundary in Western Australia (40 years and over)

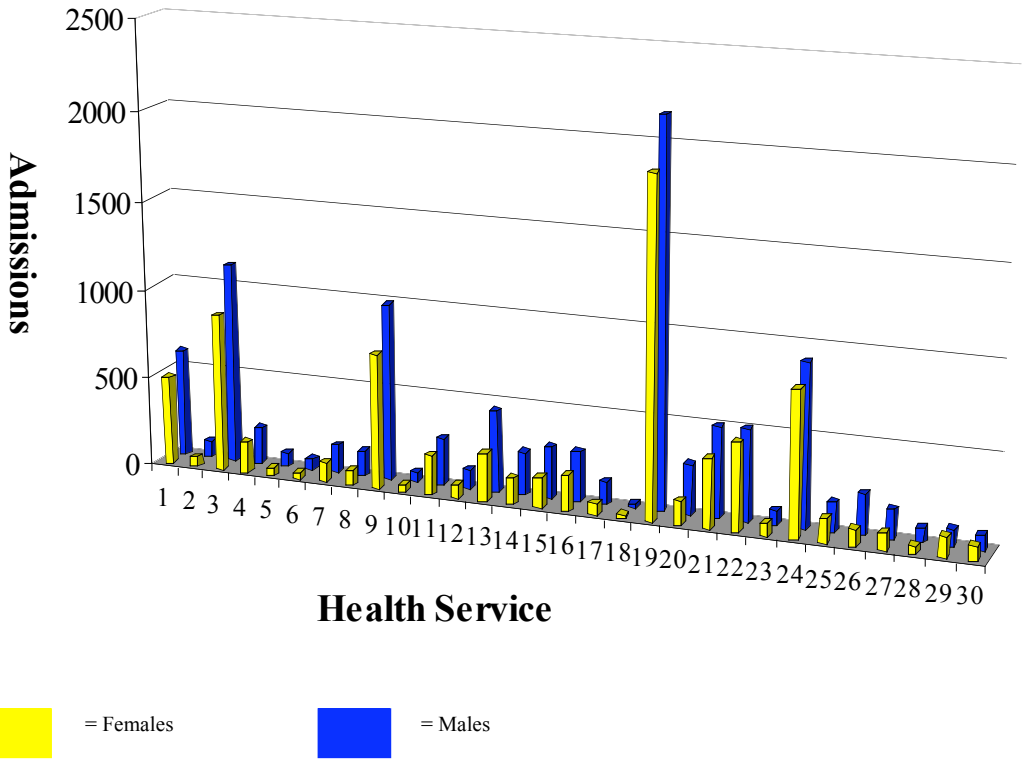
Data concerning the proportions of asthma and COPD admissions across each health service by gender are interrogated in Figures 5.15 and 5.16. In these figures the yellow bars represent the cumulative number of females admitted with a primary diagnosis of asthma (Figure 5.15) or a primary diagnosis of COPD (Figure 5.16) in each health service from 2000-2004, while the blue bars represent the number of males admitted with asthma or COPD in this time period. The names of each health service that correspond to the number Id '1 through to 33' are located within the legend of each figure.

Figure 5.15 Total numbers of asthma admissions by gender in each health service (40 years and over)



1: Armadale/Kelmscott, 2: Avon, 3: Bentley, 4: Bunbury, 5: Central Great Southern, 6: Central Wheatbelt, 7: East Pilbara, 8: Eastern Wheatbelt, 9: Fremantle, 10: Gascoyne, 11: Geraldton, 12: Harvey-Yarloop, 13: Inner-city, 14: Kalamunda, 15: Kimberley, 16: Lower Great Southern, 17: Midwest, 18: Murchison, 19: North metro, 20: Northern Goldfields, 21: Peel, 22: Rockingham/Kwinana, 23: South East Coastal, 24: Swan, 25: Upper Great Southern, 26: Vasse Leeuwin, 27: Warren/Blackwood, 28: Wellington, 29: West Pilbara, 30: Western health service

Figure 5.16 Total numbers of COPD admissions by gender in each health service (40 years and over)

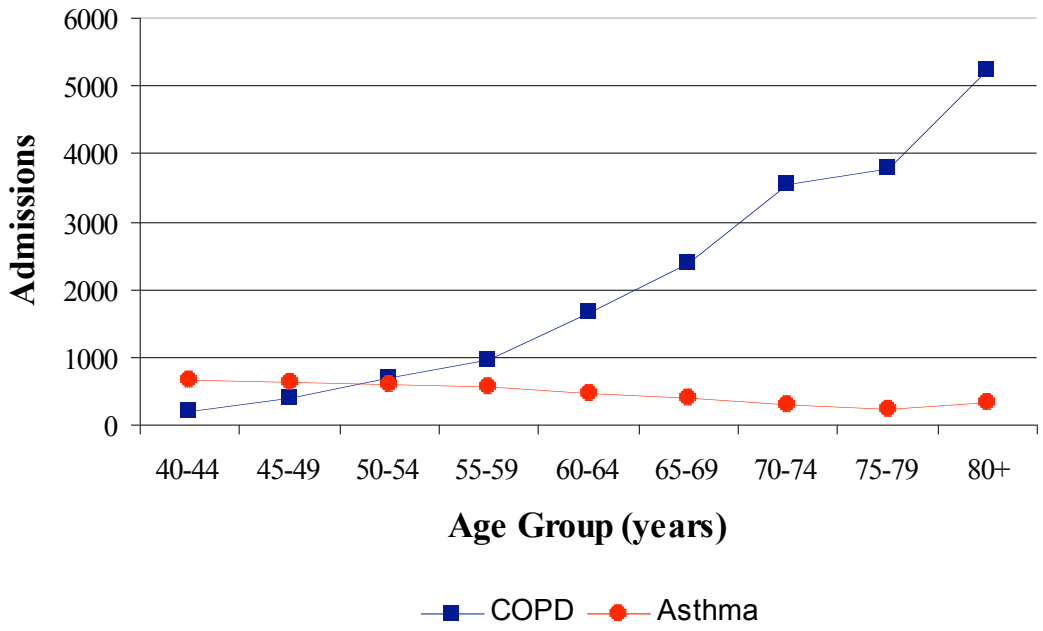


1: Armadale/Kelmscott, 2: Avon, 3: Bentley, 4: Bunbury, 5: Central Great Southern, 6: Central Wheatbelt, 7: East Pilbara, 8: Eastern Wheatbelt, 9: Fremantle, 10: Gascoyne, 11: Geraldton, 12: Harvey-Yarloop, 13: Inner-city, 14: Kalamunda, 15: Kimberley, 16: Lower Great Southern, 17: Midwest, 18: Murchison, 19: North metro, 20: Northern Goldfields, 21: Peel, 22: Rockingham/Kwinana, 23: South East Coastal, 24: Swan, 25: Upper Great Southern, 26: Vasse Leeuwin, 27: Warren/Blackwood, 28: Wellington, 29: West Pilbara, 30: Western health sevice

5.3.3.4 Age distribution of asthma and chronic obstructive pulmonary disease admissions (2000-2004)

When admissions were analysed in relation to the ages of the patients, there was an increase in the number of admissions with a primary diagnosis of COPD with increasing age. In contrast there was a trend towards a decline in asthma admissions with increasing age (Figure 5.17).

Figure 5.17 Total number of asthma and COPD admissions by age (2000-2004)



5.3.3.5 Time trends in asthma and chronic obstructive pulmonary disease admissions (2000-2004)

A gradual decline in the total number of asthma admissions was observed across the 2000-2004 time period (Figure 5.18), with 1,129 admissions reported in 2000-2001 and 934 admissions in 2003-2004. This equates to a 17.3% fall in admissions over this time period. In contrast, a large increase in the number of COPD admissions was recorded between 2000 and 2004 (Figure 5.19). There were 4,594 admissions in 2000-2001, while 4,971 admissions were recorded in 2003-2004. This equates to an 8.2% rise in the total number of admissions.

Figure 5.18 Total number of asthma admissions for adults aged 40 years and over by financial year (2000-2004)

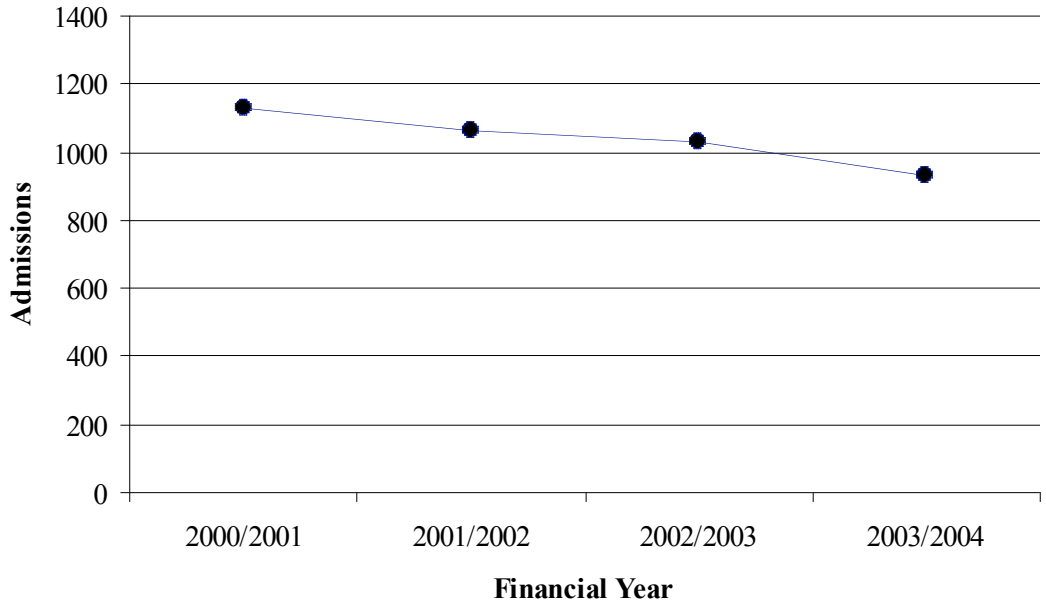
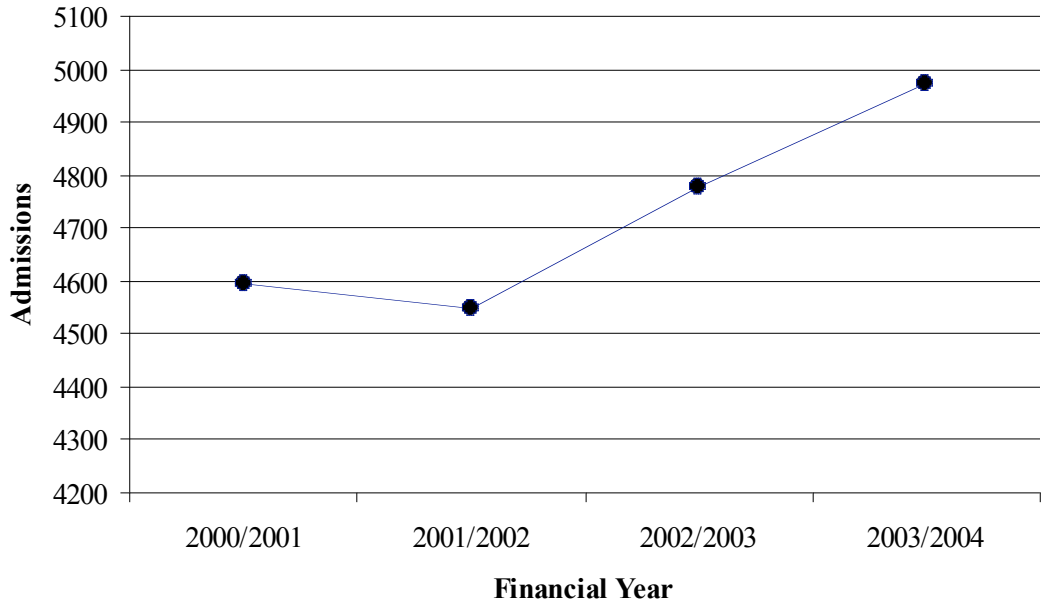


Figure 5.19 Total number of COPD admissions for adults aged 40 years and over by financial year (2000-2004)



5.3.4 Summary of results

These analyses have illustrated the distribution of services and admissions data for asthma and COPD in adults aged 40 years and over in WA. The maps provided illustrate a disproportionate number of hospital admissions in rural and remote areas comparative to baseline population data within this age group. In addition, many parts of the state are without a respiratory physician, pulmonary rehabilitation programme and ED for the management of acute and chronic asthma and COPD. The trends in admissions data show a gradual decline in asthma admissions over the 2000-2004 time period. This was in marked contrast to COPD admissions which increased over the period. Differences in trends within the admissions data when analysed according to age and gender were also observed for asthma and COPD. For example, there was an increase in the number of admissions for COPD as age increased, with more males than females admitted with this diagnosis. Conversely the number of admissions for asthma was fairly steady or declined slightly as age increased and occurred more frequently in females.

5.4 Discussion

The purpose of this study was to provide descriptive data to allow the spatial representation of respiratory services for middle-aged and older adults with chronic asthma and COPD throughout WA, and also to provide a visual comparison of hospitalisation data in relation to health service boundaries for this group of individuals. To achieve these aims, GIS technology was implemented to map hospital admissions data and health services. The findings of this study identified that: i) access for individuals in rural and remote regions of WA to respiratory physicians, pulmonary rehabilitation programmes and an ED was limited in many parts of regional WA; ii) there was a disproportionate number of hospital admissions due to asthma and COPD in regional areas compared to the Perth metropolitan area for adults aged 40 years and over relative to baseline population data for these areas; iii) hospital separations for Aboriginal and Torres Strait Islander adults aged 40 years and over were high comparative to the percentage of total population that this group represented; iv) the number of admissions for females with asthma was consistently higher than for males across all health services, and this pattern was reversed when looking at the numbers of admissions with a primary diagnosis of COPD; and v) there has been a gradual decline in asthma admissions, and a rise in COPD admissions over the time period 2000-2004, with the proportion of individuals admitted with COPD increasing with age. The study was observational and descriptive in its nature and therefore it is not possible to test specific epidemiological hypotheses without further data collection and analyses.

5.4.1 Services for asthma and chronic obstructive pulmonary disease in Western Australia

The GP is the key element in most rural health care delivery systems as it is this person who controls referral to higher levels of care and allied support services (252). Because of limited access to specialist services in regional areas and the constraint of patients not willing or able to travel long distances to Perth for appointments, the GP is often required to provide a higher level of care in addition to basic care. From a review of the literature (Chapter 1), it is apparent that the availability of GPs in regional and remote WA has not kept pace with the size and thus health demands of

the population. Hence there is an increasing need for individuals in these areas to access other specialist and support services.

Optimal access to health care involves providing the right service at the right time and in the right place (397). The locations of hospitals, EDs, respiratory specialist services, pulmonary rehabilitation programmes and asthma educators in WA were identified in this study. The population distribution of WA is such that the majority of people live in Perth and surrounding areas, and therefore in relation to the land mass that regional and remote WA encompasses there is low overall population density. Due to such demographic characteristics, it is often not feasible for the level of services provided for individuals with asthma and COPD to be equivalent in all parts of the State. There are many areas outside the Perth metropolitan area that do have sufficient population density, and also based on the numbers of hospital admissions for asthma and COPD, enough of the population affected by respiratory disease to warrant at least an outreach service by a specialist if a full-time service is not feasible.

The four largest towns without access to a respiratory physician, pulmonary rehabilitation programme or an ED at the time of data collection (2005) were:

- *Albany in the Lower Great Southern Health Service which did not have a respiratory physician or a dedicated pulmonary rehabilitation programme (only a combined exercise programme for patients with cardiovascular and other conditions was available). The town had a resident population of 22,256 in 2001.
- Port Hedland in the Pilbara Health Service, with a resident population of 12,697 in 2001, did not have access to a respiratory physician.
- Esperance with a resident population of 9,365 in 2001 in the South East Coastal Health Service did not have access to a respiratory physician, pulmonary rehabilitation programme or ED.
- Carnarvon with a resident population of 7,189 in the Gascoyne Health Service did not have an emergency department, respiratory physician and only provided pulmonary rehabilitation ‘on demand’.

Research, policy making and practical implementations have been made at both a community and State level to improve access to health services in rural areas (398). Poor accessibility to medical services can lead to reduced use of services and possibly

poorer health outcomes (399). One study in the United States (US) reported the pattern of ED use in a rural area and showed that although many ED patients may travel long distances for medical care, the majority come from nearby areas, with larger hospitals drawing more inpatients from afar than smaller hospitals (400). This pattern was also observed in a study performed in the United Kingdom (UK) where standardised episode ratios decreased as distance increased for acute emergency admissions (401). Another study conducted in New Zealand showed that individuals with asthma who lived in close proximity to an acute district hospital were three times more likely to use the ED and be admitted than those living distant (402).

Health needs increase and the social conditions become increasingly poorer for inhabitants in geographical areas that are more remote and less accessible to health services, according to a study carried out in the UK (399). Jones and colleagues (242) observed an apparent association between health service accessibility and levels of mortality from asthma in the UK. Social and geographical isolation played a part in suboptimal management of asthma (242).

The lack of respiratory specialists in regional and remote areas in WA may reflect an increasing urban orientation of this specialist training and the attractiveness of metropolitan medical practices with support facilities and personnel which are lacking in regional areas (252). An alternative to having a respiratory specialist providing a full-time clinic within a smaller township is to have a structured and organised outreach programme. In rural and remote areas to date, outreach services have most often been organised ad-hoc and without a systematic approach to determine the needs of the towns or current availability of services (403). For outreach to be effective, visits need to be regular and predictable, and patients need to have prior notification (403).

Outreach services can be demanding for specialists as they entail early departures, late return, overnight stays and often combine travel over large distances with days of consulting (403), therefore significant remuneration or other type of incentive would most likely need to be provided to make the provision of an outreach service attractive to the respiratory physician providing the service. A study in rural New South Wales showed that the provision of health and community services in small rural towns was more likely to be provided secondary to funding allocations based on historical funding rather than identified community needs. This study highlighted the need for a

holistic approach to service delivery and better co-ordination which was not focused on one particular professional group, as well as an improved understanding of the context and culture of individual towns (404).

Utilisation of a specialist in the management of chronic disease often results in improved patient care and satisfaction, as well as a greater likelihood of discharge from care (403). One study which specifically investigated the care of COPD patients in an inner city hospital studied a random sample of 80 medical records and showed that the involvement of a respiratory specialist in the patient's care resulted in management that was more consistent with the Global Initiative for Chronic Obstructive Disease (GOLD) guidelines than if the patient had treatment from only a generalist during their hospital admission (405).

Access to pulmonary rehabilitation was also limited in many parts of regional WA. If a service was provided it was not necessarily operational throughout the year and was dependent on staff availability, funding and numbers of referrals. The 'Pulmonary Rehabilitation Toolkit' is an online information resource designed to help health professionals establish pulmonary rehabilitation programmes with or without an education component in metropolitan, regional and rural settings throughout Australia. An initiative of The Australian Lung Foundation and Australian Physiotherapy Association, the toolkit states that the minimum requirement for staff for a pulmonary rehabilitation programme is a health professional that has the expertise to run an exercise training programme and has been trained in cardiopulmonary resuscitation (406).

Community-based pulmonary rehabilitation programmes are usually implemented in areas of population density large enough to support a group exercise programme, thus it is unrealistic to suggest that all small town centres should have this service in operation. For example the Murchison Health Service, which spans 373,409 km^2, has a population of 2,142 adults aged 40 years and over and had a combined average number of only 16.75 asthma and COPD admissions during the 2000-2004 period, would not be able to recruit sufficient numbers to effectively provide a group pulmonary rehabilitation programme (Table 5.5). Allied health services such as physiotherapy which run pulmonary rehabilitation programmes in rural and remote areas of Australia are faced with chronic workforce shortages as a result of high staff turnover, a mobile workforce, and an increased demand for services (407). This

reduces the time commitment these services are able to allocate to providing the regular classes needed for a supervised rehabilitation programme.

One study conducted by Grimmer *et al* (1998) looked at eight public hospitals in South Australia, Queensland and Tasmania and compared the allied health services in metropolitan areas compared to country areas. The authors reported that small numbers of therapists, usually only one or two, provided the service in rural areas compared to up to 20 therapists working together in city sites. The standardised rates of through-put were similar for country and metropolitan allied health services despite the smaller numbers of staff in country areas providing services to larger geographical areas. The patients seen by allied health staff in country areas were older than their metropolitan counterparts and were more reliant on government support for income. Fewer patients were eligible for private health rebates for their treatment. There was also a tendency to greater chronicity of a condition, possibly related to the older age of the patients (408). This study provided an argument for similar funding opportunities for country and metropolitan ambulatory health services.

At a world wide level, it has clearly been shown that regardless of the region in which one lives, the cost of primary care for asthma is less expensive than hospital care, emergency treatment is more expensive than planned treatment, and the cost of managing acute attacks is far greater than the cost of providing preventative management (1). The breakdown of the direct medical expenditure for asthma in Australia in 2001 showed that out-of-hospital medical expenses - which included GPs, specialists and imaging and pathology services – comprised only a small fraction of the total medical costs for the disease (16% combined). Pharmaceuticals accounted for 54% of the budget and 24% was allocated to hospital expenses (inpatient, emergency and outpatient care) (409). A Dutch study in 1993 investigating the burden and cost of illness of asthma and COPD, illustrated that the smallest component of the overall direct medical costs for asthma was taken up by physicians (which included GPs and specialists). This equated to 7% of the total breakdown of asthma costs for GPs and 6% for respiratory specialists. The largest cost components were medications, which accounted for 45% of the total costs, and hospitalisations accounting for 27% of the costs. For COPD, inpatient hospital care costs accounted for 57% of the total direct medical costs for the disease, medications accounted for 23%, GP's 3% and respiratory specialists 4% of the total medical costs (410).

5.4.2 Regional variations in hospital separation rates

The present study identified a disproportionate number of hospital admissions for both asthma and COPD in regional and remote health services compared to health services situated in metropolitan areas.

Fifty-five percent of asthma admissions and 41% of COPD admissions resided in health services outside the metropolitan area, despite 75% of the population of WA residing within this metropolitan area, so a much smaller percentage of admissions in rural and remote WA were expected.

Reasons for differing hospital admission rates in rural areas are multi-factorial and, as this study was descriptive, one can only postulate on reasons for this. These preliminary findings for WA are not isolated, as a study conducted in country Victoria (Australia) showed that four local government areas in the Loddon Mallee Region had close to double the state average number of hospital admission rates for asthma (398). In New South Wales, Tong and Drake (241) showed hospital admission rates for asthma were 52% - 69% higher for rural residents than their urban counterparts.

Hospital admissions are a consequence of a complex relationship between disease severity, illness behaviour and utilisation of health care services (257). Admissions over time can be influenced by factors independent of disease status. These could be differences in diagnostic practices, management practices in the ED, alterations in the access patients have to services, different financing of health care, and diversity in admission policies (411). There are a number of reasons which might also explain why length of stay, or separation rates, are higher for rural and remote patients. These may include the necessity of keeping patients who are returning to very remote areas longer because of a lack of support services in the region. In contrast, access to some services (such as nursing care provided in a patient's residence) may lead to earlier discharge for patients who live in metropolitan areas while these services may not be available in regional areas, so there is a greater need to ensure the patient is clinically stable and unlikely to require immediate medical attention on return to the community due to lack of a tertiary hospital in the region.

The demographic make-up of residents within one region compared to another region may also vary, for example socio-economic factors, lifestyle characteristics, genetic

or ethnic factors. A study of participants, aged 18-70 years, attending a public hospital ED for asthma showed many patients did their own "cost-benefit analyses" by altering the dosage of their medications, not adhering to specific guidelines or not take medication to save on cost (102). Some stated they would reduce the use of preventative medications based on their cost and this was likely to have precipitated the hospital presentation in a number of the participants. For 63% of the participants (38/61), cost was an issue determining adherence to asthma management guidelines (102).

A WA study (412) investigating the relationship between socio-economic status measured using the socio-economic indices for areas (SEIFA), and hospital utilisation at a census district level, showed that higher rate ratios of hospital admission occurred in more disadvantaged quintiles based on socio-economic status. The study showed individuals in census districts with lower SEIFA indices were higher users of hospital services but had worse outcomes following hospitalisation, which was consistent with their worse health status. The SEIFA values for census districts are determined through population censuses conducted by the Australian Bureau of Statistics. Other studies have shown that potentially avoidable hospitalisations and adverse outcomes were more frequent in individuals who had a lower income or lacked private health insurance (413-415)

The number of individuals living in remote areas is relatively small but these individuals represent the most disadvantaged groups, both in terms of location and in terms of socio-demographic characteristics. Therefore, in rural and regional areas there is an over-representation of people living in less advantaged areas due to small population numbers. The majority of people, however, who are living in disadvantaged areas reside in major urban centres. Western Australia has 10 of the 64 'most disadvantaged' statistical local areas (SLAs) in Australia- these are Ngaanyatjarraku, Laverton and Menzies in the Northern Goldfields Health Service, Halls Creek and Derby in the Kimberley Health Service, Upper Gascoyne in the Gascoyne Health Service, Cue and Murchison in the Murchison Health Service, Kwinana in the Rockingham/Kwinana Health Service and Nannup in the Warren-Blackwood health service (416).

The boundary areas for rural health services in WA as a whole do not, however, have a significant percentage of their population in either the highest or lowest SLAs of

socio-economic disadvantage. The exception to this is the Kimberley region, which has considerably lower than average SEIFA index. The average indices of relative social disadvantage for rural regions in 2001 were as follows: Kimberley 905.8, Peel/Southwest 958.7, Central Wheat-belt 978.2, Eastern Goldfields 978.7, Great Southern 986.6 and Greater Bunbury 979.1 (246). The national average for the index of relative disadvantage in 2001 was 999.0, and for Western Australia was 977.0 (417).

The highest average number of combined admissions for adults aged 40 years and over with asthma and COPD over the years 2000-2004 occurred in the Lower Great Southern Health Service (329 admissions), followed by Peel with 275 admissions and then Geraldton (178 admissions on average each year). The presence of environmental variations, in the form of climatic differences or the use of agricultural or other industrial aerosols, which might precipitate exacerbations of asthma or COPD in these rural health services relative to other areas, are potential mechanisms that could be explored further in future research.

For patients with chronic respiratory disease, hospitalisations often indicate a decline in health status as a result of deterioration in quality of life and accelerated disease progression (418). Hospitalisation usually represents the largest component of health care costs and is a reflection of advanced disease, increased frequency and severity of exacerbations for both COPD and asthma, and poor disease control (61, 418, 419).

A US study showed that the prognosis for COPD patients (aged 50-54 years) who required a hospital admission was poor, with only 50% surviving to retirement age. The estimated cumulative survival after 10 years was much higher for those patients admitted with a diagnosis of asthma. Survival after 10 years for men and women admitted with asthma was 83.5% and 93.2% respectively, but in contrast only 60.1% for men and 78% for women with COPD. Women had a better prognosis than men for both asthma and COPD in all age groups (420). This study indicated a need for active prevention and treatment following a first admission to hospital, particularly for COPD (420). Within Australia, approximately two-thirds of deaths that were attributed to asthma in 2003 occurred among people aged 65 years and over (421).

It has also been shown that a small proportion of patients with asthma account for a disproportionate number of acute health service events. In a study by Adams *et al*

(232) in which 293 patients with moderate to severe asthma were surveyed, only 23% of these patients had a single admission to hospital over a 12 month period whereas 16% had two or more admissions over this time frame. Hospital admissions data appear to represent less than 1.5% of asthmatics as most with mild disease self-manage and only the most severe exacerbations are reflected through hospitalisation data. Geelhoed *et al* (418) also showed that more than 50% of hospital admissions with a primary diagnosis of COPD lead to a readmission within a year.

One strategy that has been suggested to improve asthma management in regional areas is a regional asthma management model that is based on a uniform approach to asthma management. This model includes formal ED protocols and written instructions that are provided to patients to follow for the ensuing 24-48 hours after presenting to an ED with an asthma attack (422). It is widely acknowledged that improved management leads to reduced severity and frequency of asthma exacerbations.

5.4.3 Aboriginal and Torres Strait Islanders

In the present study, individuals of Aboriginal or Torres Strait Islander descent comprised 1,262 of the 18,890 (6.7%) COPD admissions for adults aged 40 years and over, and 670 of the 4,159 (16.1%) asthma admissions. This was despite indigenous individuals representing only 3.2% of the total population of WA in 2001 (396).

The 2004-2005 National Aboriginal and Torres Strait Islander Health Survey which involved approximately 1/45th of Australia's total indigenous population (10,439 people) showed that indigenous individuals were 1.6 times more likely to report asthma as a long-term condition than individuals who were non-indigenous. Asthma was more prevalent in older indigenous adults (19%) than younger individuals (12-16%) (396). After adjusting for age differences, indigenous individuals were 1.3 times more likely to be hospitalised in the 12 months prior to the survey than non-indigenous people and hospital admissions were more common in indigenous adults 55 years and over (396).

In a retrospective analysis of hospitalisations for Aboriginal and non-Aboriginal patients for respiratory tract diseases between 1988 and 1993 in WA, Williams *et al* (423) showed indigenous people were admitted to hospital two to 16 times more

frequently for a respiratory complaint than non-Aboriginals of the same age. Asthma was a frequent cause of admission among Aboriginal children and hospitalisation rates were much higher in non-metropolitan than metropolitan areas. Asthma was the second leading cause of admissions in young adults, and amongst Aboriginals, comprised 19% of respiratory admissions.

In WA, most of the State's indigenous people live in the Kimberley region with 34.1% of the population of this health service area being indigenous. In regional and remote WA, 8% of the population is indigenous compared with only 3.2% of the State as a whole (249).

The causes of poor health among indigenous people are multifactorial. In addition to problems of poor education, poverty, harsh environments and crowded households, they participate more frequently in risk-taking behaviours such as smoking and the under-use of medications. Barriers which lead to the misuse or under-use of medications include the distance required to travel to services, lack of ownership of a car, the cost of the medication and culturally inappropriate services (424).

In 1999, in an attempt to improve access to pharmaceuticals (including those which are required for asthma) in designated remote areas, the Aboriginal Medical Services was given the authority to order pharmaceuticals from benefit scheme items and distribute them directly as needed to patients. This led to an improvement in health outcomes in locations where the scheme was in place (425). This legislation only applies to remote areas. Indigenous individuals who live in regional and urban areas still need to obtain their medications through the standard delivery systems such as visiting the GP and then the pharmacist. It has been suggested that widening the legislation to apply to indigenous people in regional and urban areas would provide a benefit to a much larger proportion of indigenous people (425).

A study involving an interview of 17 remote health practitioners, three indigenous patients, five specialists and five regional health administrators highlighted that the barriers faced by remote indigenous people in accessing hospital-based specialist services (403). These barriers included geographical remoteness which resulted in transport and accommodation issues, disorientation and fear in urban centres, and dislocation from the family. In addition, specialist services are often culturally inappropriate and there is often poor doctor-patient communication due to limited proficiency in English and insufficient or no access to an interpreter. Other barriers

highlighted were the lack of family in attendance at consultations, poverty, the inflexibility of the health service structure in terms of appointment times, rushed consultations, and inadequate communication between the hospital and the remote clinic (403).

5.4.4 Trends in admissions for asthma and chronic obstructive pulmonary disease

A gradual decline in the number of asthma admissions was seen across the 2000-2004 time period in WA (Figure 5.17), with a 17.3% fall in admissions over this period. A population health survey carried out between 1994 and 1997 involving 3,000 interviews with individuals residing in metropolitan Adelaide and major country areas in South Australia with populations >1,000 also observed a downward trend in hospitalisation rates for asthma (104). Since the 1980s in the US there has been a decrease in hospital rates for asthma in older adults but a modest increase in children and young adults (426). It has been suggested that changes in health care practice influences the rate of hospital admissions and may influence the decline in rates. Reduced rates may also be attributed to the increased use of inhaled glucocorticoids and other anti-inflammatory medication (1). Hospital separations and average length of stay have been decreasing since the late 1990s (1999-2003) for asthma (427).

In the present study, in contrast to the fall in asthma admissions, an increase in the total number of COPD admissions was recorded between 2000 and 2004, which equated to an 8.2% rise in the total number of admissions. On a national level, the age standardised rate of hospitalisations for COPD as a principal diagnosis remained stable from 1999-2004 for adults aged 55 years and over (427).

The trends in increased numbers of admissions for COPD observed in the present study are consistent with an ageing demographic profile and an increasing population in WA. However, the data reflect overall numbers of admissions rather than age-standardised rates and therefore the figures do not take into consideration the overall change in the baseline population. The estimated residential population of Perth in 2001 was 1,393,002; this had increased to 1,478,039 by 2005, whilst the rest of the State had an estimated population of 508,157 in 2001, which had increased to 532,925 in 2005. If standardised rates were calculated it is possible that the increase in

admissions observed may be explained by the growth in population over this time period.

In a recent WA study examining the long-term trends in COPD admissions using data from the WA data linkage system, the rate of hospital admissions with a primary diagnosis of COPD declined between 1980-1998 except in elderly women, and the decrease in the rate of hospitalisations was particularly evident for men and women under 70 years (418). The rate/100,000 in 1980 was 435.3 for males aged 40-69 years and 2698.3 for males aged 70 years and over, and in 1998 was 208.3 for males aged 40-69 years and 2406.9 for males aged 70 years and over. The rate/100,000 in 1980 for females aged 40-69 years was 227.8 and 642.2 for females aged 70 years and over and in 1998 was 146.2 for females aged 40-69 years and 440.6 for females aged 70 years and over. However, consistent with an ageing population, the total annual number of admissions increased by 50% over the same time period. The authors postulated that reduced trends in COPD admissions within WA may be a reflection of a lower smoking prevalence as disease trends for COPD are largely a result of tobacco exposure (418).

The data obtained in the current study illustrated that there was a clear trend for the number of admissions to increase with age for COPD, but not with asthma, and that a greater number of males were admitted with COPD than females across all health services. However, this pattern was reversed when considering the data for asthma. The US 'NHANES' study showed an increase in hospitalisation rates between 1990-1999, and this was higher for males than for females in the years prior to 1995. From 1995-200 the rate of hospitalisation for COPD in the US was similar with respect to gender. Since 1990 the largest increase in hospitalisation rates for COPD has been observed in people aged 65 years and over (426). Another study reporting trends in hospital admissions for asthma and COPD in the Netherlands showed that the number of admissions and length of stay increased with age for those with COPD, while both the number of admissions and length of stay decreased with age for asthma (410).

A limitation of the present study is that it failed to analyse length of stay. One study carried out in the US which analysed data from 1991-1997 showed that a decline in length of stay from an average (± standard deviation) of 7.5±6.6 days to 5.4±5.6 days for individuals diagnosed with COPD (428). For individuals with COPD who were given an early 'do not resuscitate' order (i.e. within the first couple of days of

admission), post discharge mortality was higher, while for the individuals who were not given a 'do not resuscitate' order, the reduced length of stay was not associated with worse post-discharge outcomes (428).

5.4.5 Overlap between asthma and chronic obstructive pulmonary disease

In the current study, there were 152 admissions registered with a primary diagnosis of asthma that also had an additional diagnosis of COPD, and 102 admissions with a primary diagnosis of COPD that also had an additional diagnosis of asthma. As previously discussed, in older people with either asthma or COPD, it is often difficult to distinguish the two conditions and there can be substantial overlap in both the clinical manifestation of the diseases and the approaches to disease management. The potential for diagnostic misclassifications between asthma and COPD has been estimated to be about 10% based on the long-term data analyses of hospital admissions collected by Geelhoed *et a*l (418).

National statistics for Australia showed that in the year 2003-2004 there were 283 admissions registered with asthma as the primary diagnosis in conjunction with COPD as an additional diagnosis, and 480 admissions with asthma as the additional diagnosis and COPD the primary diagnosis for hospitalised people aged 55 years and over (421). One discussion point this report highlighted was that since COPD is overwhelmingly the more common condition, misclassification of asthma as COPD only has a small impact on COPD statistics but has a substantial impact on asthma statistics even if potentially a small proportion of COPD is miscoded. The authors reasoned however that the overall decreasing trend in the number of asthma admissions over the time period of data collection was unlikely to be a result of misclassification issues because this trend had also been seen among younger age groups in whom misclassification from COPD was unlikely (421).

5.4.6 Limitations in the methodology and data

5.4.6.1 Health outcome data

The Western Australian HMDS consists of discharge extracts from all admissions to public and private hospitals in WA since 1970. Data includes demographic details for each patient, medical and clinical information and referral and discharge destinations. For the HMDS there are 21 separate quality checks in place to maintain data quality and periodic audits of hospital assigned codes. Hospitals are encouraged to provide accurate and timely data through financial incentives (429). The data collected in the current study through the HMDS did not have the capacity to distinguish between admissions that were repeat admissions.

The next logical step in the analysis of this data would be to take advantage of the WA Health Services Research Linked Database. This allows amalgamation of information from two or more admissions that are believed to be attributable to the same individual (260), and thus can enhance the information gained in the current study by tracking individuals and obtaining data related to readmission rates for asthma and COPD. This would assist in defining the percentage of individuals who account for this burden on the health system through recurrent hospitalisations. It would also allow the identification of individuals who might have been diagnosed with asthma during one admission, but then diagnosed with COPD on a subsequent admission, as there is a potential for diagnostic misclassification to occur on admission by the reviewing doctor and thence at the subsequent review by the medical coders. In terms of utilising data linkage methods, the study design would need to have the following desirable criteria: the population being relatively stable, of adequate size (i.e. greater than 1 million) and with adequate longitudinal coverage (10 years or longer) (260).

For the present study, it was decided the analyses of trends in the data pertaining to additional diagnoses of asthma or COPD may not be valid given the alteration in coding practices of additional diagnoses around the time the data were collected (this arose from the release of new guidelines for the coding system). From the 1st of January 1998, diseases were classified according to the ICD- 10-AM. For this coding system, a revised set of guidelines was released in July 2000 which clarified the details regarding when a condition should be recorded as an additional diagnosis. These guidelines emphasised that an additional diagnosis should *only* be included if that second diagnosis was a significant factor for that particular hospital stay (430).

These guidelines had an impact on the coding of an additional diagnoses, particularly immediately following the release of the guidelines, although further decreases in the recording of additional diagnoses occurred in subsequent years. It was identified that among the conditions for which additional diagnoses substantially declined were the codes J45, J46 for asthma and J44 for COPD only. For example, the number of asthma diagnoses as a secondary condition fell by 68% between 1999-2000 and 2002-2003 within Australia and for COPD decreased by 47%. This change was consistent across most States (421).

5.4.6.2 Boundary effects

The original postcode boundaries used to create the maps in this study were digitised postcode boundaries current to the year 2001. These postcode boundaries were acquired from the CDATA programme, and were originally boundaries that were captured by the Australian Surveying and Land Information Group. Because the hospital admissions data were collected between 2000 and 2004, there may be a slight spatial mismatch in the overall position of the health service boundaries during this time period as postcode boundaries have since changed with the expansion of WA's population and the creation of new suburbs. Changes to existing suburb boundaries may have also resulted in changes to postcode boundaries even when these changes may not result in the creation of new postcodes. As this study was descriptive in nature and did not involve further spatial analyses, any small positional changes that may have occurred to the boundaries from the reference map of 2001 to 2004 were not considered a major limitation.

Since completion of this study, these 30 health service boundaries have since been aggregated by the Department of Health for WA into seven larger regional Health Services which are all under control of the WA Country Health Service (Goldfields, Great Southern, Kimberley, Midwest, Pilbara, South West and Wheatbelt regions) and three larger Health Services servicing the metropolitan area (North Metropolitan Health service, South Metropolitan Health service and the Princess Margaret Hospital for children). In the current study, the original 30 Health Service boundaries that were in operation at the time that the hospital admissions data were collected were used to display the admissions data for this study as they were temporally relevant. Furthermore, it was considered that the much larger amalgamated seven regional areas and three metropolitan areas (of which only two are relevant to asthma and

COPD admissions of older adults) would potentially conceal any spatial patterns in the data and that the geographical (areal) unit might become too broad for meaningful interpretation of the data.

5.4.6.3 Baseline population estimates

In terms of population fluxes in various SLAs, Rockingham recorded one of the highest increases in population growth with a 3.9% increase from 2001-2005. Moora, Coolgardie, Manjimup, Narrogin and Northam all experienced declines in population of between 1.4 to 1.7%. Over this time period, in general, the growth rate of the city of Perth was 1.4%, inner regional areas in WA grew by 4%, outer regional areas grew by 0.2%, remote areas decreased their population size by 0.4% and very remote areas increased their number of residents by 0.8% (431). The 2001 census data was used to reference the baseline population data in the maps generated in the current study and thus do not illustrate the change in the size of the baseline population within each Health Service in subsequent years.

5.4.6.4 Identification of health services and providers

The positions of hospitals, pulmonary rehabilitation programmes, respiratory physicians and asthma educators were all point data located through geocoded addresses. Although sources of error can exist in the positional accuracy for geocoded addresses, geocoding for the most part is very accurate (i.e. within 100m). For this study, it was considered that any slight positional errors, potentially resulting in errors of spatial resolution, were negligible (432).

The original asthma educator data set is likely to have been incomplete due to the inability of tracking and geocoding asthma educators who were working only in individual private practice clinics in both rural and metropolitan areas. This was due to the difficulty of accessing these professionals through The Asthma Foundation of WA due to confidentiality issues, and also the impracticality of contacting every existing medical practice in WA to identify educators. This study did not take into consideration health professionals who may have completed additional training, such as GPs who had developed an interest in respiratory medicine and were therefore more qualified to provide specialist care. In addition, the study did not incorporate other important components of the holistic care for older adults with respiratory disease such as locations of pharmacies, pathology services, and laboratories for lung function testing.

5.5 Conclusion

The changing epidemiology associated with respiratory disease and the consequences that this places on public health policy has increased the need for studies monitoring health outcomes (433). By locating current resources for middle-aged and older adults with asthma and COPD in WA, the present study provides spatial information which could assist in identifying opportunities for improved patient outcomes and optimisation of resource planning in WA. The analyses provide an overview of the distribution of admissions to hospital for adults with asthma and COPD across the State, and thus the burden placed on health services in both regional and metropolitan WA.

CHAPTER 6

Recommendations and Conclusions

The studies in this thesis have improved our understanding of the characterization of fixed airway obstruction resulting from chronic asthma and management issues which confront middle-aged and older adults with this condition. Three studies were conducted. Firstly, a randomised controlled trial (RCT) investigated the efficacy of exercise training on quality of life (QOL), functional exercise capacity, anxiety and depression, asthma control and peripheral muscle strength in individuals with fixed airway obstruction asthma (FAOA). Secondly, a comparative study contrasted resting lung function, functional exercise capacity and peripheral muscle strength in individuals with FAOA with individuals with chronic obstructive pulmonary disease (COPD). Finally, a spatial study mapped and analysed hospital admissions data of middle-aged and older adults with asthma and COPD in Western Australia (WA) and the distribution of support services for respiratory disease. This chapter summarises the novel findings presented in this thesis and discusses the implications of these findings for clinical practice and future research.

6.1 Summary of the first and second studies

A major finding of this thesis is that a 6 week supervised exercise programme in subjects with FAOA improves health-related quality of life (HRQOL) (intention-to-treat and per-protocol analyses) and anxiety (per-protocol analyses) when measured immediately following the exercise programme and when measured again at 3 months

after cessation of the programme. A strength of this study was the inclusion of a well matched control group who did not participate in the exercise programme. Following training, the improvements in all domains of the Asthma Quality of Life Questionnaire (AQLQ) exceeded the threshold for a clinically important change, highlighting the fact that exercise training improved not only symptoms and activity limitation but also was associated with improved emotional function and a reduction in asthma symptoms in response to environmental stimuli. Improvements in both anxiety levels and QOL indicate that an intervention programme, such as that conducted in this study can, by nature of the supervision and group interaction, bring about a positive change in the subject's emotional well-being. To date, there are no other RCTs in adults with asthma that have used the AQLQ to assess the outcomes of an exercise training programme.

For all outcomes measured in the RCT, any benefits observed in the exercise group tended to decline in the 3 month period following cessation of the exercise training programme, despite subjects being provided with a home exercise programme at the end of the supervised training period. It is possible that the tendency for outcome measures to return to baseline levels following training could have been avoided had subjects been offered a formal maintenance programme. At present the role and recommended format of such maintenance programmes in patients with chronic lung disease is unclear (225). The control group was not given any exercise advice. However, by participating in a study of exercise training, these subjects may have increased their activity levels or experienced improved well-being (i.e. Hawthorne effect). Indeed, this effect may account for the improvement seen in the activity limitation domain of the AQLQ in this group at the 6 week follow-up assessment.

In the RCT, it was found that the baseline functional exercise capacity in the FAOA cohort as measured using the 6 minute walk test (6MWT) was not different from normative data and while an increase was observed in 6 minute walk distance (6MWD) immediately post-intervention, this improvement was not statistically significant compared to the control group. These findings suggest the possibility that the 6MWT may not be the most responsive measure for detecting change in functional exercise capacity following exercise training in this patient cohort and this should be taken into consideration in the assessment of patients with FAOA if they are referred to a pulmonary rehabilitation programme.

A high 6MWD in individuals with FAOA was again emphasised in the second study of this thesis which compared resting lung function and 6MWT data in a cohort of subjects with FAOA and a cohort of subjects with COPD. This study showed significantly higher 6MWDs in the FAOA cohort compared to distances achieved in the COPD cohort despite comparable levels of baseline pulmonary hyperinflation and subjects being matched for age and gender.

Dyspnoea is one of the most disabling symptoms in COPD and has been shown to improve with exercise training (434), yet for the subjects with FAOA involved in the first two studies in this thesis, this symptom was not a significant factor limiting their performance on the 6MWT. Though the symptom of dyspnoea has been reported as a common complaint in individuals with chronic asthma, it may in fact be more of an issue to these individuals during exacerbations rather than when their disease is stable.

A number of potential mechanisms may have been responsible for the high 6MWDs and relatively low dyspnoea reported by the subjects with FAOA, and these mechanisms were explored in the second study in this thesis. Transfer factor is inversely related to 6MWD in COPD subjects (319, 343) and thus in part the well-preserved single breath diffusing capacity for carbon monoxide corrected for alveolar volume (DL_{CO}/VA) may have explained the high 6MWDs seen in the subjects with FAOA. The development of dynamic hyperinflation (DH) has been shown to correlate with the increased perception of dyspnoea during the 6MWT in COPD subjects and, together with DL_{CO} and Medical Research Council Dyspnoea Grade, explained 51% of the variance in 6MWD (343). The addition of forced expiratory volume in one second (FEV_1) to this regression model was associated with very little increase in the amount of variance explained (343). Although the subjects involved in this study had evidence of hyperinflation at rest, inspiratory capacity was not measured and thus the magnitude of DH and its contribution to the sensation of dyspnoea on exercise is unknown.

There is accumulating evidence that deconditioning and muscle weakness are important elements in the functional deficit displayed during activities of daily living in individuals with COPD (435, 436). Exercise training addresses this functional deficit, yet these impairments are not necessarily such an important factor for individuals with FAOA since well preserved peripheral muscle strength was observed in these subjects. In addition, the systemic consequences of COPD which are

important in the morbidity and prognosis of this condition (390) may not necessarily occur to the same effect (if at all) in individuals who have FAOA, and hence this preserved function influences the ability of these individuals to exercise.

6.2 Clinical implications and recommendations of the first and second studies

In clinical practice, adults with moderate to severe asthma are sometimes referred to pulmonary rehabilitation programmes, with the assumption that the training protocol and benefits provided for patients with COPD can be extrapolated to individuals with asthma, due to the similarities in the symptoms and impairments in these patient groups (4, 8). The findings from the studies in this thesis demonstrate that this may not necessarily be an appropriate assumption as individuals with FAOA are likely to be able to tolerate higher intensities of exercise than their counterparts with moderate to severe COPD and will require less supervision during exercise than many patients who currently attend such programmes.

Managing individuals with FAOA in a mixed pulmonary rehabilitation programme with adults with COPD therefore does pose a number of problems. Strategies which are taught and practised to manage moderate to severe dyspnoea and oxygen desaturation in individuals with COPD are not always relevant for those with FAOA, and whilst some individuals with COPD require oxygen for training, this is rare for patients with stable asthma. For individuals with bronchiectasis who are involved in pulmonary rehabilitation, there is an emphasis on airway clearance, again an issue which is not relevant for subjects with FAOA. Some components of exercise training for COPD such as inspiratory muscle training in individuals with COPD who are unable to take part in whole-body exercise training (314), or unsupported upper limb training which can improve upper limb endurance, reduce ventilation and oxygen uptake cost during arm activity (225) and has shown a trend towards improvements in dyspnoea in individuals with COPD (437), are less likely to be of benefit to individuals with FAOA because these individuals rely less on accessory muscles for respiration and thus are likely to experience less dyspnoea during upper limb activities.

For individuals with asthma, there is a prolonged warm-up and an emphasis on pre-medication prior to exercise to prevent worsening asthma symptoms, yet for those with COPD a 'prolonged warm-up' may be all they can manage for a walking session. Patients with COPD are encouraged not to reach for their reliever medication when dyspnoeic on exercise but instead to take a short rest and adopt recovery positions. In addition, if education sessions that focus on self management are formal components to pulmonary rehabilitation, there needs to be specifically tailored sessions for individuals who are required to manage their asthma and exacerbations of their condition.

In many countries there is a shortage of pulmonary rehabilitation programmes (438-440). The subjects with FAOA involved in the RCT reported activity limitations due to their asthma and therefore met the criteria for referral for pulmonary rehabilitation (218). One suggestion arising from these study findings is that the role of pulmonary rehabilitation specialists for patients with FAOA is to screen for complicating factors, provide reassurance to these subjects that exercise is safe and effective when their condition is stable and, if available, offer referral to community-based exercise programmes such as those which may exist for middle-aged and older individuals with arthritis and diabetes.

Long-term adherence remains a significant issue for pulmonary rehabilitation programmes provided for individuals with COPD (441). The declines in benefits observed from the exercise training programme at the 3 month follow-up in the RCT highlight adherence is also likely to be an issue in individuals with FAOA. Supervised programmes of at least 3-6 months in duration tend to have more success in reporting extended benefits (442), however these are costly to provide. Further, given the limited access to pulmonary rehabilitation within Australia (438-440), programmes of longer duration will result in a restriction of the numbers of patients who can receive rehabilitation. For older adults with asthma, further studies are recommended to ascertain the costs versus benefits of providing short term exercise programmes and to assess whether improvements in functional exercise capacity translate into a reduction in General Practitioner (GP) attendances, emergency department (ED) visits or hospital stays (as is the case for COPD) (218, 225).

6.3 Summary of the third study and its implications

The prevalence study undertaken as part of this programme of research clearly indicated the disproportionate numbers of admissions from both asthma and COPD in regional WA compared to the metropolitan area. Many factors may account for this finding, including different thresholds for hospital admission versus discharge from the ED due to greater isolation or distances traveled by rural patients and potential consequences if such an individual was discharged back to the community early without adequate follow-up, different hospital practices, and potentially a greater community reliance on hospital services due to a lack of or poor access to other resources and professionals that provide care for these individuals in rural areas.

Western Australia has a population that is heavily skewed towards Perth city, and hence the provision of services such as pulmonary rehabilitation, respiratory physicians, and asthma educators are often not feasible in outlying areas of low population densities. That being said, this study showed that a number of regional towns in WA which have sufficient population to warrant the provision of these services, were lacking in their access to key components for respiratory care. This is likely to place greater pressure on the acute hospital services in these areas, as well as primary care in terms of the role of GPs who are already known to be overworked in these areas. Further investigation on the needs of rural and remote communities in WA is warranted based on these preliminary findings and such investigation would need to utilise specific spatial epidemiological studies and surveillance of chronic respiratory disease in WA.

6.4 Conclusion

In conclusion, though the need for an accurate diagnosis of chronic asthma leading to permanent airway obstruction in older adults versus ‘COPD’ remains contentious amongst the medical fraternity, this thesis highlights that differentiating those who have developed fixed airway obstruction from their asthma from individuals who have COPD has a number of clinical implications related to the prescription of, and provision of, exercise training for this population. In addition ‘getting the diagnosis right’ improves the accuracy of the evaluation of disease burden, not just at the

individual level but also at the community and government levels in terms of health care provision and utilisation.

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Appendix A Medications and health care utilisation questionnaire

Please answer the questions on this form and bring it with you when you come for assessment.
Thank you

Participant ID number: _____

*Please list **ALL MEDICATIONS** you are currently taking (include both asthma medications and any other medications) and the way in which you take each medication – eg. tablets, puffer, nebuliser, spacer device.*

Name of medication	Dose	Number of times taken per day	Tablet, puffer, nebuliser, etc

How many courses of prednisolone have you had in the last 12 months?

_____

Do you always go to the same GP or GP Practice?

YES / NO

Please write below the name, address and telephone number of your regular GP

_____

_____

How many times have you visited your GP in the last 12 months because of worsening asthma symptoms? (we are asking about any unplanned visits not routine appointments)? _____

How many times have you seen your respiratory specialist in the last 12 months because of worsening asthma symptoms? (we are asking about any unplanned visits not routine visits)_____

How many times in the last 12 months have you had an attack of asthma that was so bad that you had to go to a hospital emergency department?

_____

Please give details of any emergency department visits in the last 12 months. If you cannot remember exact dates please give as much information as you can.

Date	Name of hospital

How many times in the last 12 months have you had an attack of asthma that was so bad that you had to be admitted to a hospital ward and stay there for at least one night? _____

Please give details of any hospital stays for asthma in the last 12 months. If you cannot remember exact dates please give as much information as you can.

Date of admission	Number of days in hospital	Name of hospital

Appendix B Scale for measuring chest tightness

Instructions

This is a scale for rating the tight feeling in your chest.

The number 0 represents no tight feeling.

The number 10 represents the most severe or greatest chest tightness you have ever experienced.

Tell me the number which represents your level of chest tightness at this moment in time. Use the descriptions to the right to help guide your selection.

"Tight' Feeling in Chest

0	Not at all
0.5	Very, Very Slight (Just Noticeable)
1	Very Slight
2	Slight
3	Moderate
4	Somewhat Severe
5	Severe
6	
7	Very Severe
8	
9	Very, Very Severe (Almost Maximal)
10	Maximal

Appendix C Scale for rating leg fatigue

Instructions

This is a scale for rating the tight feeling in your chest.

The number 0 represents no tight feeling.

The number 10 represents the most severe or greatest chest tightness you have ever experienced.

Tell me the number which represents your level of chest tightness at this moment in time. Use the descriptions to the right to help guide your selection.

"Tight' Feeling in Chest

0	Not at all
0.5	Very, Very Slight (Just Noticeable)
1	Very Slight
2	Slight
3	Moderate
4	Somewhat Severe
5	Severe
6	
7	Very Severe
8	
9	Very, Very Severe (Almost Maximal)
10	Maximal

Appendix D Permission to use the SF-36 Health Survey

Dear Sian,

Thank you for returning the signed agreement and payment to license the QualityMetric SF-36® Health Survey. Attached are the surveys in Microsoft Word (.doc) and Adobe Acrobat (.pdf) formats, and the corresponding Test Data Set. If you are hand-scoring your data, this Test Data Set will allow you to verify that your algorithm has been programmed correctly.

Note: If you have licensed other languages besides US English, please print a hard copy of the Adobe Acrobat file for each translation. Please compare the Microsoft Word file against the Adobe Acrobat file before administering to assure that they are identical. If you do not have Adobe Acrobat Reader installed on your computer, you can download if for free at http://www.adobe.com/support/downloads/main.html/.

As part of your academic license, you are entitled to scientific support for the duration of your study. In order to efficiently provide this service when needed, please fill out the attached Scientific Support Request Form and email it to my attention or fax it to 401-642-9349. I will ensure that your questions are responded to by the appropriate QualityMetric resource in a timely manner.

If you purchased Scoring Software 2.0™, you will receive the download link, activation key and installation manual in a separate email.

If you purchased any scoring manual(s), they will be mailed to you by United Parcel Service (UPS).

Best wishes with your study!

Kind Regards,

Lynda

Lynda LaPlante
Senior Administrator
Office of Grants and Scholarly Research (OGSR)
640 George Washington Hwy, Suite 201 | Lincoln, RI 02865
Phone: 401.334.8800 ext 249 | Fax: 401.642.9349
www.QualityMetric.com

Appendix E Asthma study feedback form

We are committed to developing the most appropriate exercise program for people with asthma and to help us we would like you to answer this questionnaire which asks you about your experience of the exercise classes. Please answer the questions and be honest with your answers.

Participant ID ……

Answer the questions on this page by putting a tick in the box that best describes how you feel.

	Strongly Agree	Agree	Unsure	Disagree	Strongly Disagree
I now feel more confident to undertake physical activities					
The exercise program has improved my ability to deal with problems caused by my lung disease					
I was very satisfied with the place where the classes were held					
The times of the classes suited me well					
The length of time of each class was just right					

Please continue overleaf

Please answer the following questions in the space provided

What parts of the exercise class were most helpful to you? Please be as specific as you can.

_____
_____
_____
_____

Were there any parts of the exercise class that you did not like? Please give reasons for your answer.

_____
_____
_____
_____

How can these classes be improved? Please think for a moment and write down your suggestions.

_____
_____
_____
_____

Do you have any other comments?

_____
_____
_____
_____

Thank you for taking the time to complete this questionnaire. We appreciate receiving your feedback.

Appendix F Exercise protocol for circuit training

Station 1

Step-ups: A 15 cm step was used for this station. The exercise sequence was up-up-down-down leading with alternate legs. Subjects were asked to count the steps they managed initially within a 1.5 minute time interval. After a 2 minute rest, this station was repeated. Subjects were progressed in the following sequence:

1. increase time interval to 2 minutes for first set
2. increase time interval to 2 minutes for both sets
3. increase time interval to 2.5minutes for first set
4. increase time interval to 2.5 minutes for both sets
5. increase time intervals to 3.0 minutes
6. add in the use of upper limb hand weights

The number of repetitions achieved in each time interval and Ratings of Perceived Exertion (RPE) scores were monitored.

Station 1

Station 2

Unsupported bilateral arm elevation: The subject sat upright on a chair facing the wall. An 84 x 2.5cm bar weighing 200g was held with both hands, shoulder width apart. The bar was lifted to one level below maximal reach, touching a coloured band or the space between the bands, and back to rest on thighs. Cadence was paced by a metronome (30rpm). The task was commenced for a 1 minute time interval, and then increased in 30 second increments to 3 continuous minutes. The weight of the bar was then increased and time was decreased when the task was no longer challenging for the subject. For example, once the subject reached 200g weight lifted continuously for 3 minutes, they were progressed to lifting a 500g bar for 2 minutes. Once 3 minutes was again reached, the task was progressed in the following sequence:

1. lift 1kg weight for 2 minutes
2. lift 1kg weight for 3 minutes
3. lift1.5kg weight for 2 minutes
4. lift1.5kg weight for 3 minutes
5. lift 2kg weight for 2 minutes
6. lift 2kg weight for 3 minutes

Station Two

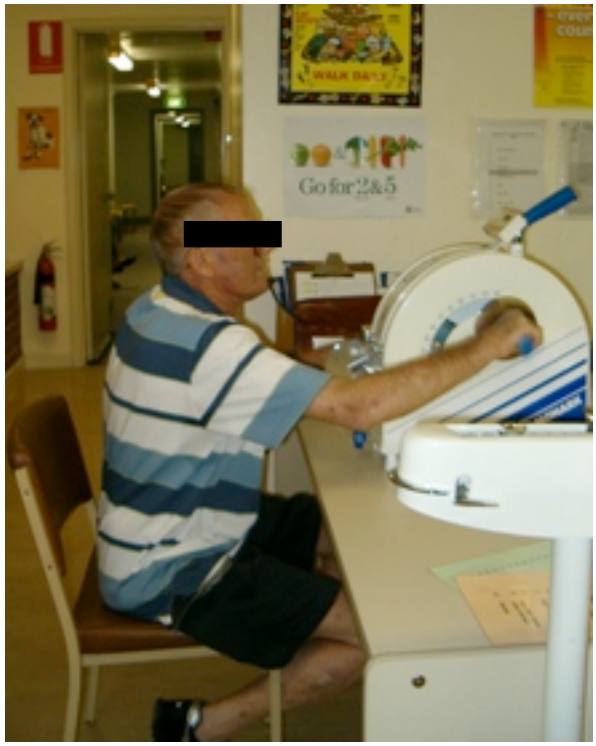
Station 3

Wall Squats: For this task the subject stood with their feet approximately 30cm away from a wall, arms by their sides, and back against the wall. They had to bend their knees and slide slowly down the wall and then back to the starting position. Each subject started with 3 sets of 4 to 6 repetitions and this was progressed by increasing the number of repetitions to a maximum of 8 in each set and then to include holding light hand weights during the squat.

Station 4

Arm Ergometer: For this station the subject sat in a supportive chair in front of an arm ergometer positioned just below 90 degrees of shoulder elevation. Careful instruction on correct sitting posture and scapulo-humeral stability was given to all subjects. A pillow was given for back support if necessary. Subjects were instructed to cycle on the arm ergometer for 1.5 minutes initially against a 20 watt resistance. After resting, this time interval was repeated. The total number of revolutions displayed on the ergometer was recorded on the exercise sheet. Cycling time was increased in 30 second intervals up to a maximum 3 minute interval. This was progressed again according to the RPE levels and dyspnoea scores recorded. Subjects were screened for upper limb gleno-humeral dysfunction and pain prior to performing this exercise.

Station 4

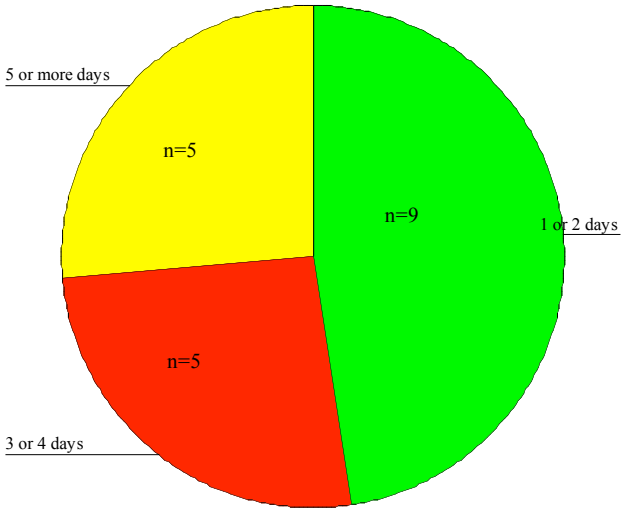


Station 5

Stationary Bicycle: This station was performed on a stationary bicycle. Subjects began cycling for a 3 minute time interval. Dependent on levels of RPE (target intensity 12-14), they were progressed by increasing time in either 30 second or 1 minute intervals to a maximum of 10 minutes. Subjects who reported leg fatigue of >5 on the Borg scale on more than two consecutive occasions had their initial time interval split into two halves and separated by a rest. Subjects were prompted to record leg fatigue, chest tightness, dyspnoea and RPE following the station.

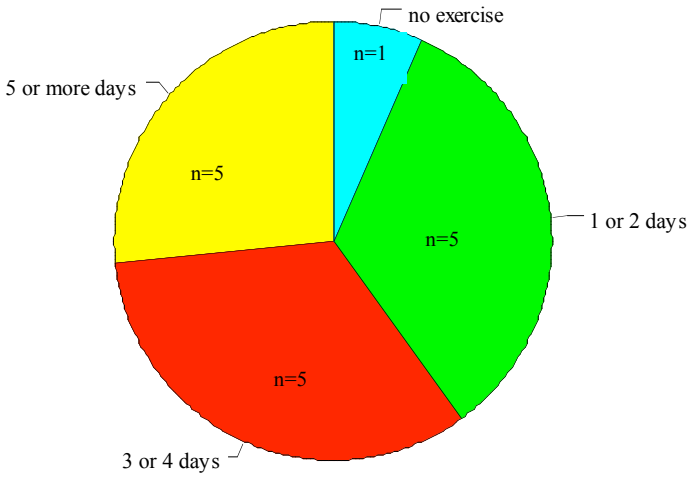
Appendix G Self-reported physical activity levels for 30 minute walking sessions throughout a typical week by group status

Exercise Group (n=19)



Pie segments denote numbers of subjects (n)

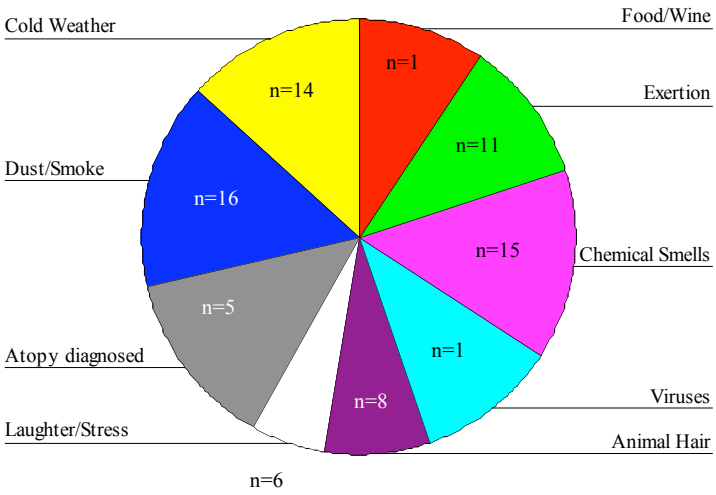
Control group (n=15)



Pie segments denote numbers of subjects (n)

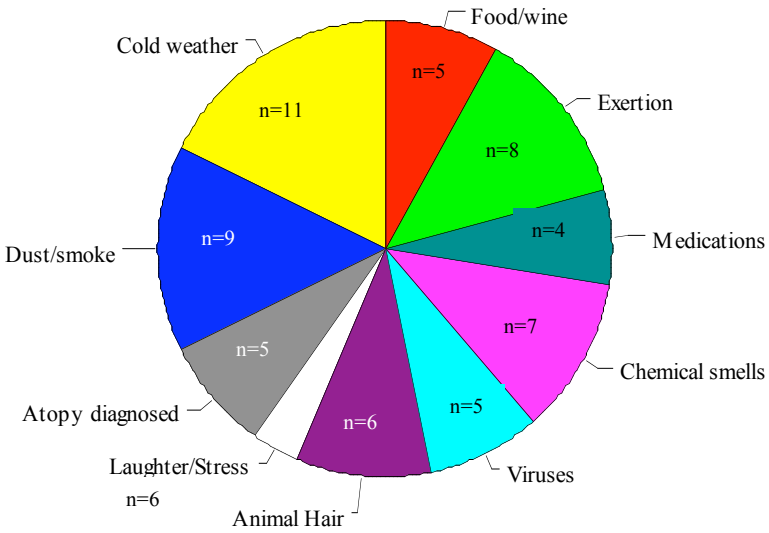
Appendix H Self-reported triggers for asthma exacerbations by group status

Exercise Group (n=19)



Pie segments denote numbers of subjects (n). Subjects could report >1 trigger

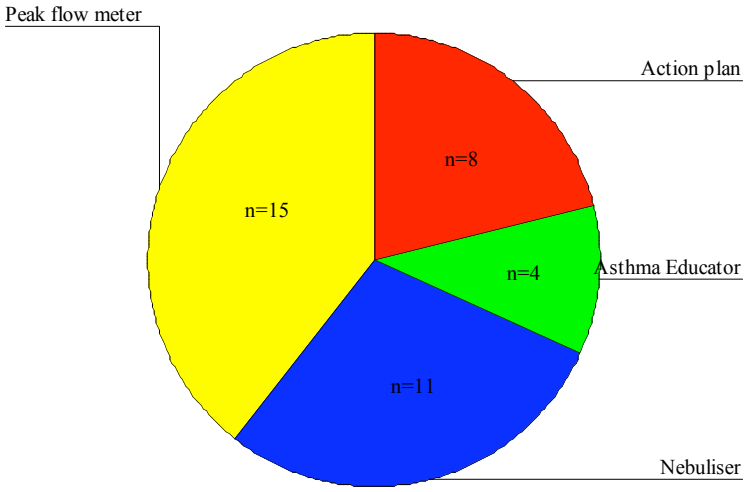
Control Group (n=15)



Pie segments denote numbers of subjects (n). Subjects could report >1 trigger

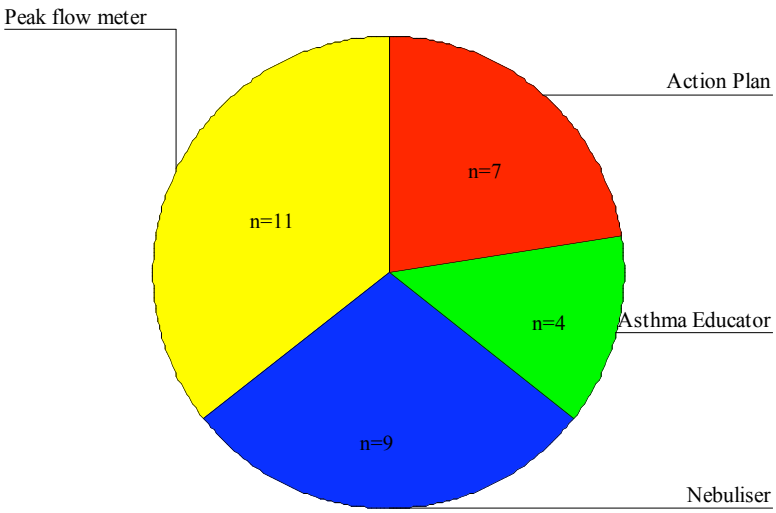
Appendix I Methods of managing asthma symptoms by group status

Exercise Group (n=19)



Pie segments denote numbers of subjects (n)

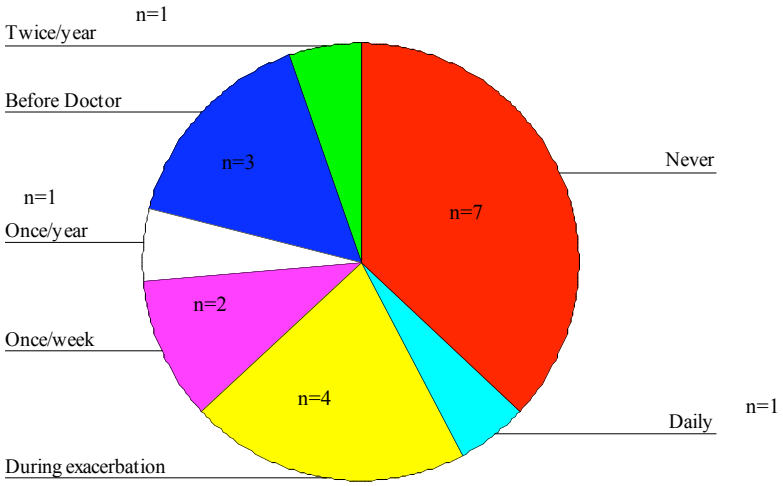
Control Group (n=15)



Pie segments denote numbers of subjects (n)

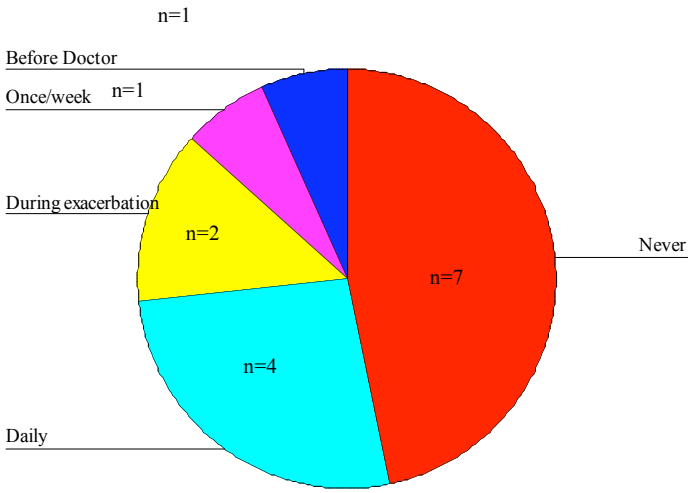
Appendix J Regularity of peak flow meter usage by group status

Exercise Group (n=19)



Pie segments denote numbers of subjects (n)

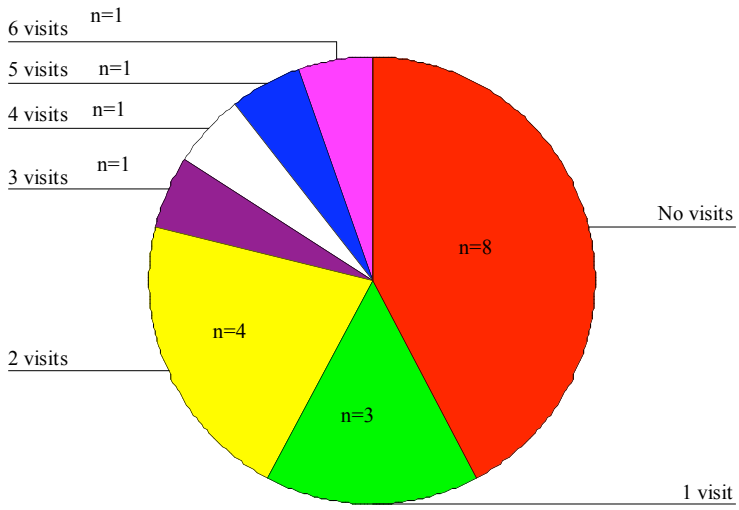
Control Group (n=15)



Pie segments denote numbers of subjects (n)

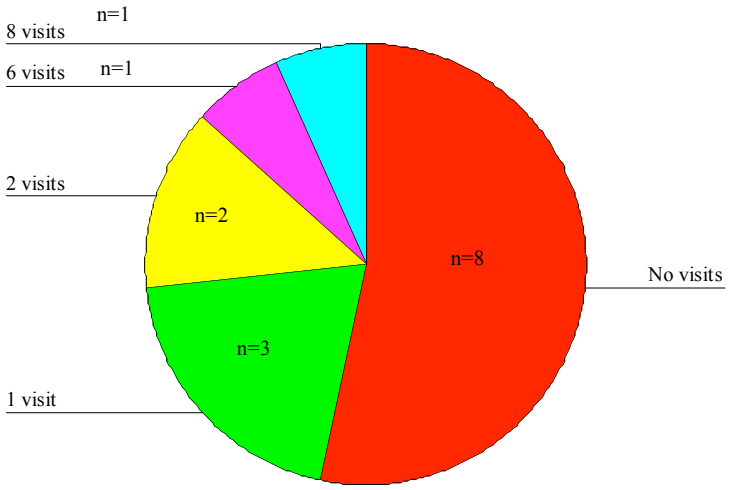
Appendix K Number of GP visits secondary to an asthma exacerbation in the preceding year by group status

Exercise Group (n=19)



Pie segments denote numbers of subjects (n)

Control Group (n=15)



Pie segments denote numbers of subjects (n)

Appendix L SF-36 Health Survey factor score coefficients for Australia used to calculate the physical component summary scores and mental component summary scores

Derivation of PCS Scores and MCS scores for the population norms for Australia

			FACTOR SCORE COEFFICIENTS	
	Mean	**Standard Deviation**	**PCS**	**MCS**
Physical function	83.46290	23.22864	0.47268	-0.24358
Role-limits physical	80.28166	34.83783	0.38210	-0.13410
Bodily pain	76.94163	24.83714	0.36750	-0.12414
General health	71.81575	20.35165	0.18993	0.05271
Vitality	64.47694	19.77187	-0.01883	0.27100
Social function	85.05929	22.29047	-0.01324	0.26460
Role limits emotional	83.19165	32.15215	-0.14971	0.35922
Mental health	75.97772	16.96210	-0.27145	0.48753

PCS: Physical Component Summary Score; MCS: Mental Component Summary Score.
Source: Australian Bureau of Statistics (75)

Appendix M Spatial relationships between health services, to health districts, local government areas and statistical local areas for Western Australia

Area Health Services	Health Districts	Local Government Areas	SLA Description	SLA_Main	SPLIT
North Metro	NMAHS - Central	Bassendean (T)	Bassendean (T)	505100350	1
North Metro	NMAHS - Central	Bayswater (C)	Bayswater (C)	505100420	0
North Metro	NMAHS - Central	Bayswater (C)	Bayswater (C)	505100420	1
North Metro	NMAHS - Central	Stirling (C)	Stirling (C) - Central	505157914	0
North Metro	NMAHS - Central	Stirling (C)	Stirling (C) - Central	505157914	1
North Metro	NMAHS - Central	Stirling (C)	Stirling (C) - South-Eastern	505157916	1
North Metro	NMAHS - Central	Swan (C)	Swan (C)	505108050	0.457
North Metro	NMAHS - Central	Wanneroo (C)	Wanneroo (C) - South	505158767	0.873
North Metro	NMAHS - Coastal	Joondalup (C)	Joondalup (C) - North	505154171	1
North Metro	NMAHS - Coastal	Joondalup (C)	Joondalup (C) - South	505154174	0
North Metro	NMAHS - Coastal	Joondalup (C)	Joondalup (C) - South	505154174	1
North Metro	NMAHS - Hills	Kalamunda (S)	Kalamunda (S)	505104200	0
North Metro	NMAHS - Hills	Kalamunda (S)	Kalamunda (S)	505104200	1
North Metro	NMAHS - Hills	Mundaring (S)	Mundaring (S)	505106090	0.626
North Metro	NMAHS - Lower	Cambridge (T)	Cambridge (T)	505051310	0.827
North Metro	NMAHS - Lower	Claremont (T)	Claremont (T)	505051750	1
North Metro	NMAHS - Lower	Cottesloe (T)	Cottesloe (T)	505052170	1
North Metro	NMAHS - Lower	Mosman Park (T)	Mosman Park (T)	505055740	1
North Metro	NMAHS - Lower	Nedlands (C)	Nedlands (C)	505056580	1
North Metro	NMAHS - Lower	Peppermint Grove (S)	Peppermint Grove (S)	505056930	1
North Metro	NMAHS - Lower	Stirling (C)	Stirling (C) - Coastal	505157915	1
North Metro	NMAHS - Midlands	Mundaring (S)	Mundaring (S)	505106090	0.374
North Metro	NMAHS - Midlands	Swan (C)	Swan (C)	505108050	0.375
North Metro	NMAHS - Perth City	Cambridge (T)	Cambridge (T)	505051310	0.173
North Metro	NMAHS - Perth City	Perth (C)	Perth (C) - Inner	505057081	1

Area Health Services	Health Districts	Local Government Areas	SLA Description	SLA_Main	SPLIT
North Metro	NMAHS - Perth City	Perth (C)	Perth (C) - Remainder	505057082	0
North Metro	NMAHS - Perth City	Perth (C)	Perth (C) - Remainder	505057082	1
North Metro	NMAHS - Perth City	Subiaco (C)	Subiaco (C)	505057980	1
North Metro	NMAHS - Perth City	Vincent (T)	Vincent (T)	505058570	0
North Metro	NMAHS - Perth City	Vincent (T)	Vincent (T)	505058570	1
North Metro	NMAHS - Upper	Wanneroo (C)	Wanneroo (C) - North-East	505158761	1
North Metro	NMAHS - Upper	Wanneroo (C)	Wanneroo (C) - North-West	505158764	1
North Metro	NMAHS - Upper	Wanneroo (C)	Wanneroo (C) - South	505158767	0
North Metro	NMAHS - Upper	Wanneroo (C)	Wanneroo (C) - South	505158767	0.127
North Metro	NMAHS - Valley	Swan (C)	Swan (C)	505108050	0.168
South Metro	SMAHS - Armadale	Armadale (C)	Armadale (C)	505250210	1
South Metro	SMAHS - Armadale	Gosnells (C)	Gosnells (C)	505253780	0
South Metro	SMAHS - Armadale	Gosnells (C)	Gosnells (C)	505253780	1
South Metro	SMAHS - Armadale	Serpentine-Jarrahdale (S)	Serpentine-Jarrahdale (S)	505257700	0
South Metro	SMAHS - Armadale	Serpentine-Jarrahdale (S)	Serpentine-Jarrahdale (S)	505257700	1
South Metro	SMAHS - Bentley	Belmont (C)	Belmont (C)	505250490	0
South Metro	SMAHS - Bentley	Belmont (C)	Belmont (C)	505250490	1
South Metro	SMAHS - Bentley	Canning (C)	Canning (C)	505251330	0
South Metro	SMAHS - Bentley	Canning (C)	Canning (C)	505251330	1
South Metro	SMAHS - Bentley	South Perth (C)	South Perth (C)	505257840	1
South Metro	SMAHS - Bentley	Victoria Park (T)	Victoria Park (T)	505258510	0
South Metro	SMAHS - Bentley	Victoria Park (T)	Victoria Park (T)	505258510	1
South Metro	SMAHS - Fremantle	Cockburn (C)	Cockburn (C)	505201820	1
South Metro	SMAHS - Fremantle	East Fremantle (T)	East Fremantle (T)	505203150	1
South Metro	SMAHS - Fremantle	Fremantle (C)	Fremantle (C) - Inner	505203431	1
South Metro	SMAHS - Fremantle	Fremantle (C)	Fremantle (C) - Remainder	505203432	0
South Metro	SMAHS - Fremantle	Fremantle (C)	Fremantle (C) - Remainder	505203432	1
South Metro	SMAHS - Fremantle	Melville (C)	Melville (C)	505205320	0
South Metro	SMAHS - Fremantle	Melville (C)	Melville (C)	505205320	1
South Metro	SMAHS - Peel	Mandurah (C)	Mandurah (C)	510015110	1

Area Health Services	Health Districts	Local Government Areas	SLA Description	SLA_Main	SPLIT
South Metro	SMAHS - Peel	Murray (S)	Murray (S)	510016230	0
South Metro	SMAHS - Peel	Murray (S)	Murray (S)	510016230	1
South Metro	SMAHS - Peel	Waroona (S)	Waroona (S)	510108820	1
South Metro	SMAHS - Rockingham-Kwinana	Kwinana (T)	Kwinana (T)	505204830	1
South Metro	SMAHS - Rockingham-Kwinana	Rockingham (C)	Rockingham (C)	505207490	1
South West	SWAHS - Blackwood	Boyup Brook (S)	Boyup Brook (S)	510200770	1
South West	SWAHS - Blackwood	Bridgetown-Greenbushes (S)	Bridgetown-Greenbushes (S)	510200840	1
South West	SWAHS - Blackwood	Nannup (S)	Nannup (S)	510206300	1
South West	SWAHS - Bunbury	Bunbury (C)	Bunbury (C)	510031190	1
South West	SWAHS - Bunbury	Capel (S)	Capel (S) - Pt A	510031401	1
South West	SWAHS - Bunbury	Capel (S)	Capel (S) - Pt B	510101404	1
South West	SWAHS - Busselton	Busselton (S)	Busselton (S)	510151260	1
South West	SWAHS - Leeuwin	Augusta-Margaret River (S)	Augusta-Margaret River (S)	510150280	1
South West	SWAHS - Leschenault	Dardanup (S)	Dardanup (S) - Pt A	510032661	1
South West	SWAHS - Leschenault	Dardanup (S)	Dardanup (S) - Pt B	510102664	1
South West	SWAHS - Leschenault	Harvey (S)	Harvey (S) - Pt A	510033991	1
South West	SWAHS - Leschenault	Harvey (S)	Harvey (S) - Pt B	510103994	1
South West	SWAHS - Warren	Manjimup (S)	Manjimup (S)	510205180	1
South West	SWAHS - Wellington	Collie (S)	Collie (S)	510101890	1
South West	SWAHS - Wellington	Donnybrook-Balingup (S)	Donnybrook-Balingup (S)	510102870	1
WA Country	WACHS - Central Great Southern	Broomehill (S)	Broomehill (S)	515051050	1
WA Country	WACHS - Central Great Southern	Gnowangerup (S)	Gnowangerup (S)	515053640	1
WA Country	WACHS - Central Great Southern	Katanning (S)	Katanning (S)	515054340	1
WA Country	WACHS - Central Great Southern	Kent (S)	Kent (S)	515054480	1
WA Country	WACHS - Central Great Southern	Kojonup (S)	Kojonup (S)	515054550	1
WA Country	WACHS - Central Great Southern	Tambellup (S)	Tambellup (S)	515058120	1
WA Country	WACHS - Central Great Southern	Woodanilling (S)	Woodanilling (S)	515059380	1
WA Country	WACHS - East Pilbara	East Pilbara (S)	East Pilbara (S)	540053220	1

Area Health Services	Health Districts	Local Government Areas	SLA Description	SLA_Main	SPLIT
WA Country	WACHS - East Pilbara	Port Hedland (T)	Port Hedland (T)	540057280	1
WA Country	WACHS - Eastern Wheatbelt	Bruce Rock (S)	Bruce Rock (S)	525151120	1
WA Country	WACHS - Eastern Wheatbelt	Kellerberrin (S)	Kellerberrin (S)	525154410	1
WA Country	WACHS - Eastern Wheatbelt	Merredin (S)	Merredin (S)	525155460	1
WA Country	WACHS - Eastern Wheatbelt	Mount Marshall (S)	Mount Marshall (S)	525155880	1
WA Country	WACHS - Eastern Wheatbelt	Mukinbudin (S)	Mukinbudin (S)	525155950	1
WA Country	WACHS - Eastern Wheatbelt	Narembeen (S)	Narembeen (S)	525156370	1
WA Country	WACHS - Eastern Wheatbelt	Nungarin (S)	Nungarin (S)	525156860	1
WA Country	WACHS - Eastern Wheatbelt	Trayning (S)	Trayning (S)	525158400	1
WA Country	WACHS - Eastern Wheatbelt	Westonia (S)	Westonia (S)	525159030	1
WA Country	WACHS - Eastern Wheatbelt	Yilgarn (S)	Yilgarn (S)	525159660	1
WA Country	WACHS - Gascoyne	Carnarvon (S)	Carnarvon (S)	535051540	1
WA Country	WACHS - Gascoyne	Exmouth (S)	Exmouth (S)	535053360	1
WA Country	WACHS - Gascoyne	Shark Bay (S)	Shark Bay (S)	535057770	1
WA Country	WACHS - Gascoyne	Upper Gascoyne (S)	Upper Gascoyne (S)	535058470	1
WA Country	WACHS - Geraldton	Geraldton (C)	Geraldton (C)	535033500	1
WA Country	WACHS - Geraldton	Greenough (S)	Greenough (S) - Pt A	535033851	1
WA Country	WACHS - Geraldton	Greenough (S)	Greenough (S) - Pt B	535153854	1
WA Country	WACHS - Kimberley	Broome (S)	Broome (S)	545100980	1
WA Country	WACHS - Kimberley	Derby-West Kimberley (S)	Derby-West Kimberley (S)	545102800	1
WA Country	WACHS - Kimberley	Halls Creek (S)	Halls Creek (S)	545053920	1
WA Country	WACHS - Midwest	Carnamah (S)	Carnamah (S)	535151470	1
WA Country	WACHS - Midwest	Chapman Valley (S)	Chapman Valley (S)	535151610	1
WA Country	WACHS - Midwest	Coorow (S)	Coorow (S)	535152030	1
WA Country	WACHS - Midwest	Irwin (S)	Irwin (S)	535154060	1
WA Country	WACHS - Midwest	Mingenew (S)	Mingenew (S)	535155530	1
WA Country	WACHS - Midwest	Morawa (S)	Morawa (S)	535155670	1
WA Country	WACHS - Midwest	Mullewa (S)	Mullewa (S)	535156020	1

Area Health Services	Health Districts	Local Government Areas	SLA Description	SLA_Main	SPLIT
WA Country	WACHS - Midwest	Murchison (S)	Murchison (S)	535106160	1
WA Country	WACHS - Midwest	Northampton (S)	Northampton (S)	535156790	1
WA Country	WACHS - Midwest	Perenjori (S)	Perenjori (S)	535157000	1
WA Country	WACHS - Midwest	Three Springs (S)	Three Springs (S)	535158260	1
WA Country	WACHS - Kimberley	Wyndham-East Kimberley (S)	Wyndham-East Kimberley (S)	545059520	1
WA Country	WACHS - Lower Great Southern	Albany (C)	Albany (C) - Central	515100081	1
WA Country	WACHS - Lower Great Southern	Albany (C)	Albany (C) Bal	515100084	1
WA Country	WACHS - Lower Great Southern	Cranbrook (S)	Cranbrook (S)	515102240	1
WA Country	WACHS - Lower Great Southern	Denmark (S)	Denmark (S)	515102730	1
WA Country	WACHS - Lower Great Southern	Jerramungup (S)	Jerramungup (S)	515054130	1
WA Country	WACHS - Lower Great Southern	Plantagenet (S)	Plantagenet (S)	515107210	1
WA Country	WACHS - Northern Goldfields	Coolgardie (S)	Coolgardie (S)	530051960	1
WA Country	WACHS - Northern Goldfields	Kalgoorlie/Boulder (C)	Kalgoorlie/Boulder (C) - Pt A	530014281	1
WA Country	WACHS - Northern Goldfields	Kalgoorlie/Boulder (C)	Kalgoorlie/Boulder (C) - Pt B	530054284	1
WA Country	WACHS - Northern Goldfields	Laverton (S)	Laverton (S)	530054970	1
WA Country	WACHS - Northern Goldfields	Leonora (S)	Leonora (S)	530055040	1
WA Country	WACHS - Northern Goldfields	Menzies (S)	Menzies (S)	530055390	1
WA Country	WACHS - Northern Goldfields	Ngaanyatjarraku (S)	Ngaanyatjarraku (S)	530056620	1
WA Country	WACHS - South East Coastal	Dundas (S)	Dundas (S)	530103080	1
WA Country	WACHS - South East Coastal	Esperance (S)	Esperance (S)	530103290	1
WA Country	WACHS - South East Coastal	Ravensthorpe (S)	Ravensthorpe (S)	530107420	1
WA Country	WACHS - Murchison	Yalgoo (S)	Yalgoo (S)	535109590	1
WA Country	WACHS - Murchison	Cue (S)	Cue (S)	535102380	1
WA Country	WACHS - Murchison	Meekatharra (S)	Meekatharra (S)	535105250	1
WA Country	WACHS - Murchison	Mount Magnet (S)	Mount Magnet (S)	535105810	1
WA Country	WACHS - Murchison	Sandstone (S)	Sandstone (S)	535107630	1
WA Country	WACHS - Murchison	Wiluna (S)	Wiluna (S)	535109250	1

Area Health Services	Health Districts	Local Government Areas	SLA Description	SLA_Main	SPLIT
WA Country	WACHS - Southern Wheatbelt	Boddington (S)	Boddington (S)	510100630	1
WA Country	WACHS - Southern Wheatbelt	Brookton (S)	Brookton (S)	520050910	1
WA Country	WACHS - Southern Wheatbelt	Corrigin (S)	Corrigin (S)	520102100	1
WA Country	WACHS - Southern Wheatbelt	Cuballing (S)	Cuballing (S)	520052310	1
WA Country	WACHS - Southern Wheatbelt	Dumbleyung (S)	Dumbleyung (S)	520053010	1
WA Country	WACHS - Southern Wheatbelt	Kondinin (S)	Kondinin (S)	520104620	1
WA Country	WACHS - Southern Wheatbelt	Kulin (S)	Kulin (S)	520104760	1
WA Country	WACHS - Southern Wheatbelt	Lake Grace (S)	Lake Grace (S)	520104900	1
WA Country	WACHS - Southern Wheatbelt	Narrogin (S)	Narrogin (S)	520056510	1
WA Country	WACHS - Southern Wheatbelt	Narrogin (T)	Narrogin (T)	520056440	1
WA Country	WACHS - Southern Wheatbelt	Pingelly (S)	Pingelly (S)	520057140	1
WA Country	WACHS - Southern Wheatbelt	Wagin (S)	Wagin (S)	520058610	1
WA Country	WACHS - Southern Wheatbelt	Wandering (S)	Wandering (S)	520058680	1
WA Country	WACHS - Southern Wheatbelt	West Arthur (S)	West Arthur (S)	520058890	1
WA Country	WACHS - Southern Wheatbelt	Wickepin (S)	Wickepin (S)	520059100	1
WA Country	WACHS - Southern Wheatbelt	Williams (S)	Williams (S)	520059170	1
WA Country	WACHS - West Pilbara	Ashburton (S)	Ashburton (S)	540100250	1
WA Country	WACHS - West Pilbara	Roebourne (S)	Roebourne (S)	540107560	1
WA Country	WACHS - Western Wheatbelt	Beverley (S)	Beverley (S)	525100560	1
WA Country	WACHS - Western Wheatbelt	Chittering (S)	Chittering (S)	525051680	1
WA Country	WACHS - Western Wheatbelt	Cunderdin (S)	Cunderdin (S)	525102450	1
WA Country	WACHS - Western Wheatbelt	Dalwallinu (S)	Dalwallinu (S)	525102520	1
WA Country	WACHS - Western Wheatbelt	Dandaragan (S)	Dandaragan (S)	525052590	1
WA Country	WACHS - Western Wheatbelt	Dowerin (S)	Dowerin (S)	525102940	1
WA Country	WACHS - Western Wheatbelt	Gingin (S)	Gingin (S)	525053570	1
WA Country	WACHS - Western Wheatbelt	Goomalling (S)	Goomalling (S)	525103710	1

Area Health Services	Health Districts	Local Government Areas	SLA Description	SLA_Main	SPLIT
WA Country	WACHS - Western Wheatbelt	Koorda (S)	Koorda (S)	525104690	1
WA Country	WACHS - Western Wheatbelt	Moora (S)	Moora (S)	525055600	1
WA Country	WACHS - Western Wheatbelt	Northam (S)	Northam (S)	525106720	1
WA Country	WACHS - Western Wheatbelt	Northam (T)	Northam (T)	525106650	1
WA Country	WACHS - Western Wheatbelt	Quairading (S)	Quairading (S)	525107350	1
WA Country	WACHS - Western Wheatbelt	Tammin (S)	Tammin (S)	525108190	1
WA Country	WACHS - Western Wheatbelt	Toodyay (S)	Toodyay (S)	525108330	1
WA Country	WACHS - Western Wheatbelt	Victoria Plains (S)	Victoria Plains (S)	525058540	1
WA Country	WACHS - Western Wheatbelt	Wongan-Ballidu (S)	Wongan-Ballidu (S)	525109310	1
WA Country	WACHS - Western Wheatbelt	Wyalkatchem (S)	Wyalkatchem (S)	525109450	1
WA Country	WACHS - Western Wheatbelt	York (S)	York (S)	525109730	1

(S): Shire; (T): Town; (C): Council; SLA: Statistical local area.
'Split' is the proportion of the SLA in the selected area. This figure is derived from census population counts at the Collection District level and used to apportion the SLA's population between areas that share the SLA.

Data sources: Epidemiology Branch web-site, Monday, 22 August 2005 and Australian Bureau of Statistics (ABS) - SLA and LGA boundary files (2001), Department of Land Information (DLI) - Australia Post postcode boundaries (Nov 2004).