The Epidemiology of Acute Asthma Managed by Ambulance Paramedics in the Prehospital Setting in Western Australia.

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ABSTRACT

Aim

This thesis describes the epidemiology and outcome of acute asthma managed by ambulance paramedics, in the metropolitan area of Perth, Western Australia, for the period of 1990 to 2001. The primary aim of this thesis was to determine demographic, socio-economic and clinical trends for ambulance transported patients with asthma, their outcomes and how they have changed over time.

Setting

The Perth metropolitan area, located in the south-western corner of Western Australia (WA), accounts for 72% of the state's population, which was approximately 1.3 million people at Census 2001.

Method

This thesis was structured around the analysis of twelve years of St John Ambulance (WA) data. Ambulance data was linked using probabilistic matching techniques to the Western Australian Data Linkage System, custodian of links to thirty five years of morbidity and mortality data of the state's population. This produced a horizontally and vertically linked dataset of all episodes of care for each patient. Descriptive analysis was undertaken on demographic, socioeconomic, clinical and temporal factors. Comorbidity and socioeconomic status were modelled using multivariate analysis techniques to identify predictors for the outcomes of readmission and short, medium and long-term survival.

Results

In over a million ambulance attendances in twelve years, 15,671 asthma cases were identified, of which ambulance paramedics correctly diagnosed asthma in approximately 57% of cases. Age-standardised rates of patients with asthma transported by ambulance identified a widening differential between females and males during the 12 years, where more than half of the patients transported by ambulance were female, and the highest transport rate was recorded by the 85+ years age group. The

proportion of priority 1 (lights and sirens) transports decreased by 10.4%, and although the proportion of problem urgency codes remained steady over the time of the study, the proportion of cases transported for problem urgency 1 and 2 (ATS 1 and 2) was highest in the early hours of the morning and in the summer months. Ambulance usage by patients with asthma was associated with socioeconomic status, with the highest rate of use in the lowest socioeconomic quintile, and the lowest rate of use in the highest socioeconomic quintile.

Multivariate regression modelling found age (OR = 1.04, 95% CI: 1.03-1.06), comorbidity (OR = 1.36, 95% CI: 1.07-1.72), cumulative length of stay (OR = 1.04, 95% CI: 1.02-1.05) and total number of non-invasive ventilation procedures for any admission (OR = 2.46, 95% CI: 1.25-4.87) to be associated with survival at discharge. Age (OR = 1.05, 95% CI: 1.02-1.07), comorbidity (OR = 1.47, 95% CI: 1.14-1.89) and cumulative length of stay (OR = 1.03, 95% CI: 1.01-1.05) were found to be associated with survival at thirty days, and age (OR = 1.06, 95% CI: 1.05-1.079), comorbidity (OR = 1.37, 95% CI: 1.17-1.59) and cumulative length of stay (OR = 1.02, 95% CI: 1.01-1.03) were found to be associated with survival at one year. Factors associated with readmission at seven days were age (OR = 0.98, 95% CI: 0.98-0.99), being female (OR = 1.46, 95% CI: 1.09-1.95), any type of ventilation procedure for hospital asthma admissions (OR = 1.87, 95% CI: 1.21-2.90) and urgency (OR = 0.70, 95% CI: 0.61-0.80), whereas the only factor associated with readmission at thirty days was being female (OR = 1.84, 95% CI: 1.25-2.71).

Conclusion

Unique geography, a monopolistic ambulance service and access to extensive linked data provided ideal conditions for this population-based epidemiological study of patients with asthma who were transported by ambulance. Observed trends in age and gender characteristics of patients, ambulance codes and temporal variables appear to be consistent over time. Monitoring trends in the use of ventilation procedures recorded in hospital data provided useful indicators for describing the epidemiology of severe, life-threatening asthma in the prehospital setting. Findings from this study were found to be consistent with published literature.

Health planning and policy decisions that seek to improve outcomes of patients with asthma would need to target areas that reduce or ameliorate conditions contributing to increased prevalence and severity of asthma, increased comorbid conditions and the length and frequency of hospital admissions. Whilst prehospital care by the ambulance paramedic is predominantly focussed on managing the acute episode, it has little to offer in terms of ongoing and long-term clinical management.

This study confirms the enormous potential that linked data analysis at the population level has in epidemiological research.

CONTENTS

MEDICAL ABBREVIATIONS AND DEFINITIONS

Atelectasis:

A total or partial collapse of the air sacs (alveoli) in the lung causing a lack of air to the affected area of the lung.

Asphyxia:

The pathological changes due to hypoxia.

Atopy:

an allergy, involving an inherited immunoglobulin of the IgE type, that predisposes a person to certain allergic responses.

Allergic Rhinitis:

An allergen-induced inflammation of the membranes lining the nose.

Bradycardia:

An unusual slowing of the heart rate to 60 beats per minute or less.

Cyanosis:

A physical sign causing bluish discoloration of the skin and mucous membranes, caused by a lack of oxygen in the blood. Cyanosis is associated with cold temperatures, heart failure, lung diseases and smothering.

Eczema:

A group of non-contagious skin conditions which can affect all age groups, of varying severity. In mild forms the skin is dry, hot and itchy, whilst in more severe forms the skin can become broken, raw and bleeding.

Forced Vital Capacity (FVC):

The total volume expired forcefully from maximum inspiration to end-expiration.

Forced Expiratory Volume (FEV):

A measure of how much a person can breathe out during a forced breath.

FEVx is the volume of air expired forcefully in the x^{th} second of FVC.

Hypertension:

High blood pressure, which rarely causes any symptoms, but can lead to heart attack, heart failure, stroke, kidney failure and hardening of the arteries.

Hypoxia:

A reduction in tissue oxygenation.

IgE:

Immunoglobulin E, a group of allergy antibodies produced by the body's immune system.

Metabolic acidosis:

A clinical disturbance characterized by an increase in total body acid; considered a sign of an underlying disease process.

Paradoxical Pulse (Pulsus Paradoxus):

A pulse that weakens abnormally during inspiration and is symptomatic of various abnormalities (eg. pericarditis).

Peak Expiratory Flow Rate (PEFR):

A measure of how fast a person can exhale air. It is one of many tests that measure the function of the airways, which are commonly affected by diseases such as asthma or chronic obstructive pulmonary disease.

Pneumothorax:

Occurs when air leaks from inside of the lung to the space between the lung and the chest wall, causing the lung to collapse.

Pneumomediastinum:

A condition in which air is present in the mediastinum (the space in the chest between the two lungs).

Residual Volume (RV):

The volume of gas in the lungs at the end of maximal expiration. Cannot be measured by spirometry.

Status Asthmaticus:

A medical emergency in which asthma symptoms do not respond to initial bronchodilator therapy in the emergency department.

Tachycardia:

An increased heart rate, that continues to beat above 100 beats per minute.

Tachypnoea (Polypnoea):

An increased respiratory rate.

Urticaria:

An itchy skin eruption characterized by weals with pale interiors and well-defined red margins; usually the result of an allergic response to insect bites or food or drugs.

STATISTICAL ABBREVIATIONS AND DEFINITIONS

Age Standardised Rate:

A figure that is statistically corrected to remove the distorting effect of age when comparing populations of different age structures.

Crude Rate:

The number of cases in a particular population quantity (e.g. per 100,000).

Degrees of freedom (df):

The number of independent units of information in a sample used in the estimation of a parameter or calculation of a statistic.

Discriminant Function Analysis:

A statistical method of predicting membership in groups (the dependent variable) from a set of independent variables.

Homoscedasticity:

Where the variance of one variable is the same at all values of the other variable.

Incidence:

The number of new cases of a particular condition, disease or other occurrence over a given time period.

Outlier:

An extreme observation that is well separated from the remainder of the data. In regression analysis, not all outlying values will have an influence on the fitted function. To test the influence of such values, the Cook statistic is used.

Overdispersion:

Dispersion is a measure of the extent to which data are spread about an average. Overdispersion is the situation that occurs most frequently in Poisson and binomial regression when variance is much higher than the mean (normally, it should be the same). This may be caused by outliers, misspecification of the model, variation between the response probabilities or correlation between the binary responses, and may be taken into account by estimating a dispersion parameter.

Parsimonious:

The simplest plausible model with the fewest possible number of variables.

Prevalence:

The number of existing cases of a particular condition, disease or other occurrence at a given time.

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1.0 INTRODUCTION

Recognized as a major health problem, asthma is currently responsible for significant ill health and suffering worldwide. In the United States, over 12 million people suffer from asthma, the majority of whom are young patients, and acute asthma presentations account for close to 2 million emergency department visits annually.[1] In 1990, costs related to asthma in the United States were estimated to total $6.2 billion. In 2004, these costs have trebled for a total of $16.1 billion dollars, with annual direct health care cost of asthma approximately $11.5 billion and indirect costs another $4.6 billion.[2]

In Australia, the prevalence of asthma is one of the highest in the world, with two million or more Australians having the disease across all age groups.[3] It is one of the top five medical problems referred to hospital by general practitioners and a common cause of presentation to emergency departments.[3] It ranks among the ten most common reasons for seeing a general practitioner, and is the most common medical cause for hospital admission in children in Australia. It is estimated that 40% of all Australians will have respiratory symptoms consistent with asthma at some time in their lives.[4]

Asthma is an important health issue because of the personal burden it places on those with the condition, often with onset in childhood, as well as the financial burden it places on the health system. Asthma has been estimated to be responsible for 2.6% of the total burden of disease in Australia.[5] In addition, the last decade has seen many advances in the care of asthma, including changes in the nature of drug treatments resulting in an increase in expenditure on asthma, particularly pharmaceuticals. The direct health expenditure on asthma was $693 million in 2000-2001, of which more than half was consumed by pharmaceuticals.[6]

Moreover, under-diagnosis and under-treatment of asthma has been identified as a significant factor contributing to reported increases in asthma morbidity and mortality.[7-9] In recognition of this problem, the Australian Government in 1999 established asthma as the sixth National Health Priority Area and developed the National Asthma Action Plan.[10] Asthma-related deaths have steadily declined in Australia from this time, with deaths from asthma falling from 685 in 1998 to 313 in 2004 [11], however asthma

mortality in Australia remains high in comparison to other countries.[6] Australia ranked 22nd highest out of 67 countries with an asthma mortality rate of 0.5 per 100,000 population, compared to Sweden which ranked 64th with an asthma mortality rate of 0.1 per 100,000 population.[12]

As asthma remains a significant cause of unexpected and premature death in our society, there is considerable need to seek solutions that reduce both the incidence, acute exacerbations and associated mortality of this disease. Such solutions would need to be supported by strategies that improve quality of life and health outcomes, reduce the social and economic impact, and optimise clinical management to reduce the risk, prevalence, and severity of asthma.

Despite recognition of the increasing problem of asthma, there remains a paucity of objective information on the pre-hospital treatment, transport and subsequent outcomes of patients with asthma who seek emergency services for their condition. Further, there is a dearth of information about the influences of urgency, socio-economic status or comorbidity on the occurrence, severity, and survival from asthma.

The purpose of this study is to describe the trends and outcomes of acute patients with asthma managed by ambulance paramedics in the pre-hospital setting in Western Australia, and how these may have changed over time. In doing so, this will contribute population-based evidence toward a better understanding of the epidemiology of acute asthma in the pre-hospital setting.

This chapter describes the aims, specific objectives and the thesis approach.

1.1 AIM

The aim of this study is to investigate all asthma cases that were transported to hospital by ambulance in Perth, Western Australia (WA), over the twelve-year period of 1990 to 2001. Secondary aims are to determine demographic, clinical and socio-economic trends for ambulance transported patients with asthma, their outcomes and how they have changed over time.

1.2 SPECIFIC OBJECTIVES

1. To validate the WA Ambulance Dataset for the purposes of matching to the WA Data Linkage System.

The results of this study are based on the analyses of two large administrative data sets that are linked to each other, the WA Data Linkage System and the St John Ambulance (Western Australia) Dataset, the 'WA Ambulance Dataset'.

The WA Data Linkage System contains hospital morbidity data, mortality records and other datasets that are regularly updated, and has previously been validated by sampling techniques. The WA Ambulance Dataset is an electronic database containing information from every ambulance event since late in 1989 and includes demographic data, ambulance service operational data and clinical information. There has been no prior attempt to validate this dataset, so a sample set was randomly selected from each year of the study for the purposes of validation. For each case selected, the data contained in the electronic WA Ambulance Dataset was compared with information recorded by the attending ambulance paramedics on the original paper Patient Care Record (PCR).

2. To determine trends in the rate of ambulance transport to hospital for patients with an acute asthma event over the period 1999 to 2001.

The number of asthma cases transported by ambulance were identified from the WA Ambulance Dataset for each of the study years. Population denominators were derived from the appropriate Australian Bureau of Statistics (ABS) census data, and both crude and age standardised event rates with 95% confidence intervals were calculated for estimate.

3. Describe the demographic, socio-economic and clinical characteristics of patients transported to hospital by ambulance with an acute asthma event.

Demographic, social, geographical and clinical status was derived for each asthma case in the WA Ambulance Dataset. Indicators for variables of interest were derived for each of the study years and compared over the twelve-year period. Where applicable, trend analysis was undertaken to ascertain changes in status over time.

4. Identify predictors for outcomes of patients with asthma who use ambulances.

The linkage of the WA Data Linkage System to the WA Ambulance Dataset provided outcome data including diagnosis on discharge from hospital, length of hospitalisation, comorbidity and survival for each ambulance case that was admitted. Modelling techniques were undertaken to identify predictors of survival and subsequent readmission to hospital, reporting odds ratios and 95% confidence intervals.

1.3 THESIS APPROACH

This thesis is based on the analysis of twelve years of data derived from case records of the St John Ambulance (Western Australia) Dataset, the 'WA Ambulance Dataset', that were linked to Western Australian hospital morbidity and mortality data, the 'WA Data Linkage System'. These data were collected and entered by third parties who are subject to the policies, guidelines, and statutes that define such activities, and not by the candidate. However, the candidate did solely perform all data checking, manipulation and analysis.

It is first necessary to consider the body of knowledge to help understand the disease of asthma. Chapter 2 reviews and explores the causes of asthma, pathological and pathophysiologic changes that occur with asthma, and its relevance to other medical conditions. In particular, severe acute asthma and status asthmaticus are examined, given their potential for unexpected fatal outcomes. This chapter also looks at the history of asthma treatment, in particular prehospital care, and specifically prehospital care and treatment in the Australasian context. A review of outcome studies is described with a focus on both international and Australasian studies of those treated for asthma. The intention is to compare results from the international arena and highlight differences in outcomes to those experienced in Australia.

It is important to understand the unique conditions that make this study possible, and to this purpose Chapter 3 describes the unique geography and demography of Western Australia and the role played by the St John Ambulance service in the emergency treatment of asthma. The methods of record linkage is also introduced, with descriptions of the process of linkage between the key databases used for this study and details of the validation process of the WA Ambulance Dataset, one of the key aims of this study. The statistical methods used, and in particular the multivariate modelling techniques used in this thesis are described in some depth in Chapter 3.

Chapter 4 begins with reporting the descriptive analysis results and then presents the multivariate models. The relationship of comorbidity and socio-economic status on the use of emergency services by patients with asthma is explored using the Charlson Index as a measure of comorbidity, and the Socio-Economic Index For Advantage (SEIFA) index as a measure of socioeconomic status. The results of modelling for predictors of readmission and survival outcomes are reported here. Chapter 5 discusses the results of the analyses performed, compares the findings in the light of other studies, and presents limitations of the study.

This project is unique in that it offers significant advantages over a number of previous studies. High rates of record linkage and large patient numbers in a stable, relatively isolated population allow a highly accurate and realistic description of pre-hospital ambulance usage, emergency and hospital care, and outcome of patients with asthma. Due to the uniqueness of the prehospital environment in Western Australia, this study may help establish platforms on which operational and training directions may be determined in the light of relevant epidemiological data and best available evidence.

2.0 A CRITICAL REVIEW OF THE LITERATURE

This chapter begins with a review of current knowledge regarding the causes and clinical features of asthma, and the care and treatment of asthma. This is followed by a review of the epidemiology of asthma, with the intention of highlighting the importance of asthma as a prevalent disease within our society and a major cause of morbidity. The final section of the chapter focuses on outcome studies and care of the asthmatic in the prehospital context, from both an international and Australasian perspective. The chapter then concludes with research questions that have been formulated as a result of the review of the literature.

2.1 ASTHMA AS A DISEASE

Asthma affects individuals differently and there are variations to the definition of asthma. The Australian National Asthma Action Plan has opted for simplicity and defined asthma thus:

'Asthma is an inflammatory disease of the air passages, making them prone to narrowing and increased mucus production. It becomes difficult to move air in and out of the lungs. Symptoms include wheeze, shortness of breath, chest tightness and cough. Asthma is a chronic condition with attacks occurring at varying intervals and degrees of severity. Over many years, persistent asthma may cause permanent narrowing of the airways resulting in reduced response to available treatments. Severe acute attacks can result in death.[10 (page 1)],

From an aetiological perspective, asthma is a heterogeneous disease, in that it can be initiated by more than one type of stimulus. Historically, the methods of classifying asthma have reflected the existing disease paradigms where, for clinical and epidemiological purposes, it is often classified by the primary stimuli that incites or is associated with an acute episode, e.g. allergic asthma or exercise-induced asthma.[6, 13] However, while each of these groups have some distinguishing features, there is no evidence that such distinctions represent fundamentally different pathophysiological characteristics of asthma.[6]

Currently, existing clinical guidelines tend to classify patients with having either intermittent or persistent asthma [14-16], and although this distinction may not indicate either particular characteristics of the disease, the severity of the episode or the periodic nature of exposure to triggers, it has served to give some indication of long-term prognosis.[17] Other classification schemes have incorporated information about the frequency and severity of disease exacerbations and are usually based on the presence and frequency of daytime or night-time symptoms, the need for medication and levels of lung function.[14, 18] Nonetheless, at a general level, asthma can be broadly classified into two types, allergic and idiosyncratic.[13] In view of its potential for death and the fact it may manifest in either of these types, severe acute asthma also deserves consideration. The role played by each of these types will be discussed in more detail further in this chapter.

Allergic Asthma.

Atopy is generally considered the single largest risk factor for the development of asthma.[13] Atopy can be defined as a genetically determined state of hypersensitivity to environmental allergens.[19] It involves Type I allergic reactions associated with the IgE antibody and is manifested in a group of diseases, principally asthma, hay fever, and atopic dermatitis.[19] Allergic asthma is often associated with a personal and/or family history of allergic diseases such as rhinitis, urticaria, and eczema.[13] There is increasing evidence that the initiation of atopy and asthma may occur in early life or even during foetal life.[20] Diagnostic criteria associated with an allergic aetiology include positive reactions to intradermal injections of airborne antigens, increased levels of IgE in the blood serum, and/or positive responses to inhalation provocation tests of specific antigens.[13]

Idiosyncratic Asthma.

A large proportion of asthma cases do not present with a personal or family history of allergy, often displaying negative skin tests and normal serum levels of IgE, and so cannot be classified on the basis of their immunological responses.[13] This is considered idiosyncratic asthma, and many cases develop typical symptoms some days after contracting an upper respiratory illness. The signs of wheezing and dyspnoea may often develop after a slight insult such as a common cold, and yet may last for days or months.[21, 22]

As a further complication, many asthma cases fail to fit into either of the described categories, but may exhibit features of each. However, in general, asthma with onset in the early years appears to have a strong allergic aetiology, whereas asthma that develops later in life tends to be of a non-allergic or mixed aetiology.[13]

Acute Severe Asthma.

Acute severe asthma may develop rapidly over a few hours, or more commonly over a number of days [23], and sudden and unexpected death may occur, even in patients with only mild disease.[24]

Clinical factors associated with patients at risk of developing severe asthma include previous life threatening episodes (with previous intubation or respiratory acidosis without intubation), multiple or frequent hospital admissions, recent steroid use, and deterioration whilst on steroids.[25] Population studies have suggested that older age, ethnicity, poor socio-economic status, poor health care, and psychological problems are risk factors for developing life-threatening asthma.[26, 27]

Reasons often cited for this increased risk include the over-reliance on $beta_2$ adrenergic medications, under-use or under-prescription of anti-inflammatory medications, illicit drug use, environmental conditions, and a lack of appreciation of disease severity by both patient and physician.[28, 29]

2.2 CAUSES OF ASTHMA

There are many factors that stimulate, interact with airway responsiveness and incite acute episodes of asthma. These can be grouped into major categories for the purposes of identifying them, which are described below, but the groups are not necessarily mutually exclusive.

Infection

Respiratory infections are the most common stimuli to cause acute exacerbations of asthma.[13] Infections such as common colds, sinusitis, and bronchitis are known non-allergic triggers of asthma.[30] It is also believed that respiratory viruses, and not bacteria or allergy to micro-organisms, may be major aetiological factors in actively and chronically destabilizing asthma.[13] In young children, the respiratory syncytial virus and para-influenza virus are implicated, and for older children and adults, rhinovirus and influenza virus play a role.[13]

It is believed that the mechanism by which viruses cause exacerbations of asthma relates to the production of T cell-created cytokines that assist the infiltration of inflammatory cells into already susceptible airways, resulting in immune pathology.[31]

Allergens

Allergic asthma is often seasonal, and frequently seen in children and young adults.[32, 33] The majority of asthma allergens are airborne, and to incite an asthma episode they must be reasonably abundant for considerable periods of time, but once sensitization has occurred, even tiny amounts of the offending allergen can produce a swift and significant exacerbation of the disease.[13]

Allergic triggers may include pollen from grasses, trees and weeds.[34] Late spring thunderstorms in Melbourne, Australia, triggered epidemics of asthma attacks and the pattern of allergic responses found in affected patients suggested a possible aetiological role for rye grass pollen.[35] Non-seasonal triggers may include dust mite particles, feathers, the skin and saliva of furry animals (such as cats, dogs, horses, rabbits and guinea pigs), moulds, foods (such as milk, eggs, peanuts, fish, wheat, and certain fruit

and vegetables), and other antigens that are continuously present in the environment.[36, 37]

Various inflammatory cells including T cells, B cells, eosinophils, macrophages and mast cells are involved in the complex immune response to antigens in the airway.[38] Current theory suggests small antigenic particles penetrate the lung's defences and come in contact with mast cells on the epithelium and mucosa of the central airways, precipitating an IgE response controlled by B and T lymphocytes.[13] These cells process the antigen and transport an immunogen to local lymph nodes, where T lymphocytes are activated and differentiate into a Th2 subset, whilst B lymphocytes switch antibody production to IgE. The activated T cells of the Th2 subset play a major role in the initiation and maintenance of the allergic inflammation.[31]

Environmental

Airborne pollutants may cause a wide spectrum of immunologically mediated disorders, including asthma.[39] Asthma episodes caused by environmental influences usually relate to climatic conditions that contribute to the concentration of atmospheric antigens and pollutants, usually in densely populated areas and areas of heavy industry, and usually when thermal inversion or stagnant air masses exist.[13] Increased air stagnation has been shown to be more strongly associated with asthma aggravation than any of the individually measured air pollutants.[40]

Air pollution in general, such as high levels of car exhaust fumes, may trigger episodes of asthma, and specific pollutants believed to have this effect include ozone, nitrogen dioxide (NO_2), and sulphur dioxide (SO_2).[41-46]

Natural events such as dust storms may also precipitate episodes of asthma. Days of high respirable, particulate natural dust have been shown to be associated with increased presentation of asthma and shortness of breath in adults [32], whilst dust from volcanic eruptions have precipitated increased admissions for asthma and bronchitis.[47, 48] In Australia, dust plumes that originated from arid inland wind erosion have caused changes in asthma severity as they blew over populated areas.[49]

Infants exposed to cigarette smoke by parents and domestic gas heater use are also associated with increased asthma later in childhood, suggesting that poor indoor air quality may play an important role in the development of childhood asthma.[50]

Genetic Influences

There seems little doubt that asthma has a strong familial tendency [51, 52], and recent research is beginning to identify certain genes that indicate asthma susceptibility.[53] Already, genetic screening of families for candidate genes has identified chromosomal regions that relate to atopy, elevated immunoglobulin E (IgE) levels, and airway hyper-responsiveness.[13]

Atopy, a common familial syndrome underlying allergic asthma and rhinitis, is characterised by sustained IgE responses to common allergens.[54-56] Analysis of maternally derived alleles from 155 sibling-pairs affected by atopy found that high-affinity receptors for IgE also lies on the chromosome that is in close genetic linkage with the gene for atopy.[57] Since then, evidence for genetic linkage of high total serum IgE levels and atopy have been observed on the same chromosomes in a number of populations throughout the world.[58, 59]

Further, regions of the genome that exhibit evidence for linkage to bronchial hyper-reactivity also show evidence for linkage to elevated serum IgE levels, and linkage studies have identified excellent candidate genes for the expression of specific abnormalities in asthma [59, 60], including lung eosinophilia, mucous hyper-secretion, mast cell hyperplasia and bronchial hyper-responsiveness.[61] The same regions also contain the beta-adrenergic receptors and the glucocorticoid receptors, key target areas for drug interventions.

Pharmacologic

Medication-induced asthma can be separated into predictable and unpredictable asthma reactions. Predictable asthma reactions include beta blockers (used in the management of hypertension, cardiac disorders, migraine and glaucoma) cholinergic agents (e.g. carbachol, pilocarpine) and cholinesterase inhibitors (e.g. pyridostygmine), all of which may lead to bronchoconstriction.[14]

Unpredictable reactions include the most common medication-induced asthma exacerbations and medications such as aspirin and other non-steroidal anti-inflammatory drugs are most commonly involved in iatrogenic asthma.[62] Aspirin appears to produce bronchospasm by stimulating over-secretion of cysteinyl leukotrienes that activate mast cells, causing bronchospastic action.[13]

Other drugs implicated include tartrazine, carbemazepine and parenteral drugs (e.g. penicillin, iron dextran complex, hydrocortisone, ipratropium bromide, aminophylline, N-acetyl cysteine), and preservatives such as bisulfites, metabisulfites and benzalkonium chloride.[14]

All these agents have the potential to produce acute airway obstruction in sensitive individuals, although the mechanisms of these agents are not properly known.[13] Drug induced bronchial narrowing is often associated with increased morbidity, often death.[63]

Occupational

Occupational asthma is the most common occupational lung disease in Australia and many other western countries.[14] It has been estimated that up to 15% of new asthma in adults was directly attributable to occupational exposures, and an even greater proportion of workers with pre-existing asthma found that their asthma was aggravated by occupational exposures.[14]

Occupational asthma may develop with a period of latency, often in response to exposure to a high molecular weight compound (usually a protein) such as rat excreta, flour dust and sawdust, or without latency in response to exposure to a low molecular weight compound such as wood resins, pharmaceutical agents, metal salts and isocyanates.[14]

Acute and chronic airway obstruction has been reported to follow exposure to a large number of compounds used in many types of industrial processes. To date, there are more than 200 occupational allergens that have been identified.[63]

Exercise

At least 80% of people with asthma have symptoms triggered by vigorous exercise, including chest tightness, wheezing, dyspnoea and coughing.[14] This cause differs from other stimuli, such as antigens, viral infections and air pollutants, as it tends not to cause any long-term effects or increase airway reactivity. Typically the attacks follow exertion and do not occur during it.[13] Exercise-induced asthma may be the only symptom of asthma in some people, but may also indicate undertreated asthma, so a therapeutic trial of medication is often the most practical way of confirming the diagnosis.[14]

The pathophysiology that makes this group of patients with asthma susceptible to bronchoconstriction after a brief period of exercise remains poorly understood, and despite there being immunopathological differences between asthmatics with and without exercise-induced brochoconstriction [64], the treatment remains essentially the same.

Emotional

A review of the literature suggests an association between asthma and emotion, where psychological factors can worsen or ameliorate asthma.[65-69] Asthmatics tend to report and display a high level of negative emotion, and asthma exacerbations have been linked temporally to periods of heightened emotionality, where causality may be bi-directional.[70]

The extent to which psychological factors participate in the precipitation or continuation of an asthma event is not established, but it likely to vary from patient to patient and from episode to episode.[13] As research continues on the model of asthma and emotion, there may be a role for a focus on the psychological treatment of asthma [70, 71], but there are also risks associated with the suggestion that asthma exacerbations may have a psychological basis, as this may result in patients delaying initial treatment and not seeking early help.

2.3 CLINICAL FEATURES OF ASTHMA

Whilst discussion continues on possible aetiologies to this disease, there is a high level of congruence when it comes to describing the clinical features of asthma.

2.3.1 The Normal Lung.

In a normal lung, small bronchi and bronchioles approximately 2mm in diameter are spread throughout the lung, and connect the larger airways to the alveoli.[72] These are part of the central conducting airways that provide a large cross-sectional area for rapid diffusion of O_2 and CO_2 between the distal conducting airways and the gas-exchanging surface. These airways are the major site of resistance to airflow in the normal lung, which falls sharply as the cross-sectional area of the conducting airways increases.[73, 74]

The tissues found in the conducting airways include epithelium, subepithelial connective tissue, muscle and adventitia. Bronchi have a fibrocartilage layer external to the smooth muscle, whereas bronchioles lack cartilage in their walls.[75] Toward the periphery of the bronchial tree, the percentage of smooth muscle increases from 5% of wall tissue in the central bronchi to about 20% of the total wall thickness in the bronchioles, where it surrounds the entire lumen of the airway (see Figure 1, Normal bronchiole).[75, 76]

As a result, smooth muscle shortening has a smaller effect on the calibre of the trachea and central airways than on the distal bronchi and bronchioles.[77] The adventitial layer consists of collagen, blood vessels, lymphatics, and nerves. This layer, through alveola attachments, has the ability to limit airway narrowing by smooth muscle contraction, particularly at higher lung volumes.[78]

2.3.2 Pathophysiology

In the development of asthma, there are three main components in the pathophysiology of the airway: bronchial hyper-responsiveness, broncho-constriction and airway-remodelling.[79-81]

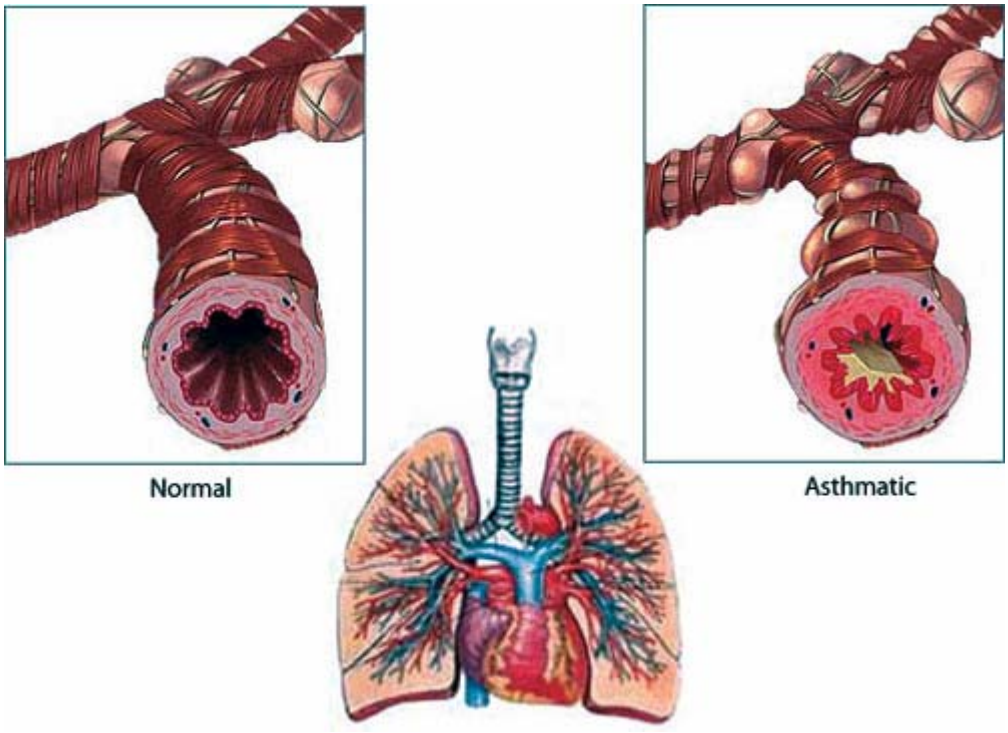
A commonality underlying all asthmatic disease is increased non-specific irritability of the tracheobronchial tree.[82] When this airway reactivity to stimuli is high, then symptoms are more severe and persistent, and fluctuations in lung function are greater.[83] This equates to a greater amount of therapy required to control the symptoms of the asthmatic.[84]

Studies have confirmed that the inflammatory process is present in the small airways, the major site of airway dysfunction.[77, 85-88] It is this persistent state of subacute inflammation of the airways that is thought to play a central role in the pathogenesis of both reversible airflow obstruction and bronchial hyper-responsiveness.[89-94] However, the precise roles that different inflammatory cells and mediators play in the development of pathologic and physiologic changes seen in the lungs of asthmatics are still not fully understood. Changes in the subepithelial connective tissue alter the mucosa, and exudates of plasma proteins, mucus and inflammatory cells present in the airway lumen, even in mild asthma, affect the surface of the airway lumen.[72]

Even in asymptomatic patients, an active inflammatory process has been frequently observed in endobronchial biopsy specimens.[95] Clinically, the degree of bronchial hyper-responsiveness has been shown to correlate with general asthma severity, for the degree of bronchial hyper-responsiveness appears to decrease when asthma is well controlled with medication.[96]

Inhalation of allergens by a patient with allergic asthma causes prompt and significant bronchoconstriction. Normal smooth muscle shortening with an abnormally thickened airway wall narrows the airway lumen, and both central and peripheral airway resistance increases, reducing the function of the conducting airways (see Figure 1, Asthmatic bronchiole).[77]

Figure 1: Cross-section of Normal and Asthmatic bronchiole



After this bronchial allergen challenge, there is a rapid decline in forced expiratory volume that often begins within 10 minutes and generally subsides within one to three hours.[37] This early phase response often resolves spontaneously or with a beta$_2$-agonist, but in about 50% of patients who develop an early asthmatic response, the bronchoconstriction persists and either does not return to baseline values or recurs after three to four hours and reaches a maximum over the next few hours.[97-99] This late asthmatic response appears to be higher in children, but the cause of this higher prevalence, estimated to be 70 to 86% of children sensitized to various allergens, is unknown.[100]

It is believed the early response results from binding of inhaled allergen to mast cell membrane-bound IgE with subsequent release of mediators, e.g. histamine, leukotrienes, and prostaglandins.[96] Among these mediators, the cysteinyl leukotrienes appear to account for a significant part of the early asthmatic response, and combine with histamine to be responsible for bronchoconstriction during the late asthmatic response.[37]

Now, it is known that the inflammation process causes thickening of all of the compartments of the airway wall.[101, 102] Airway-remodelling refers to the development of specific structural changes in the airway wall accompanying long-standing and severe airway inflammation.[81]

Airway-remodelling and fibrosis may be the cause of fixed airflow obstruction in asthma that is not reversible with either steroids or bronchodilators, due to reduced elasticity, increased muscle mass and mucosal oedema.[103] However, both the relationship between the remodelling and inflammatory components, and the cellular and molecular events underlying the remodelling process in asthma remain poorly understood.[96]

2.3.3 Clinical Features

Clinically, the characteristics suggestive of asthma are wheeze, chest tightness, shortness of breath and cough.[6, 14] Diagnosis of asthma is likely if these symptoms usually begin suddenly, are recurrent, worse at night or in the early morning, or obviously triggered by exercise, cold air, irritants, allergens or viral infections.[104] Auscultation of the chest during an episode reveals wheezing, but lung sounds are usually normal between episodes, and often the episode will resolve spontaneously or is relieved by bronchodilators.[104]

The signs and symptoms of asthma can vary widely from person to person and although the absence of typical symptoms does not exclude the diagnosis of asthma, a chronic or recurring cough in the absence of any wheeze or associated atopic feature is unlikely to be asthma, especially in children.[14]

Usually on presentation, forced vital capacity is reduced, residual volume is increased, and a diagnosis of asthma can be established by a demonstrable reversion of airway obstruction, measured as an increase in forced expiratory volume (FEV_1) after treatment with a beta-antagonist.[13] Occasionally spirometry results may be normal, but a diagnosis can often be made by a demonstrable increase in airway responsiveness to challenges such as methacholine or hyperventilation of cold air. Once a diagnosis is

made, progress is usually monitored by regularly measuring peak expiratory flow rates (PEFR) and FEV_1.[13, 83]

Status asthmaticus is a manifestation of acute severe asthma and is a medical emergency in which asthma symptoms do not respond to initial bronchodilator therapy in the prehospital setting or emergency department.[28] The amount of time taken for an acute severe asthma episode to develop and the severity of airway obstruction may vary widely.[105] Subacute changes may develop over several days before the appearance of severe symptoms (slow-onset), or lung function may deteriorate severely in less than an hour (sudden onset).[105, 106]

It is suggested that slow onset asthma crises are mainly related to faults in management such as inadequate treatment or low compliance, whereas massive exposure to common allergens, sensitivity to non-steroidal anti-inflammatory agents, whereas sensitivity to food allergens and sulphites are mainly considered the triggers in sudden onset asthma crises.[107]

Patients with status asthmaticus may complain of chest tightness, rapidly progressive shortness of breath, dry cough, and wheezing, and in prolonged episodes are most likely to exhibit mucous plugging and bronchial oedema.[106] In severe cases, decreased audible wheezing, an ineffective cough, and gasping respirations may indicate extensive mucous plugging and impending suffocation.[108]

Without prompt and appropriate treatment, status asthmaticus may result in respiratory failure and death.[107] Approximately 80 to 85% of deaths from asthma occur in slow onset patients who gradually deteriorate over days and weeks with severe and poorly controlled disease[109-111], and this pattern of asthma death is generally considered preventable.[107, 112] However, in the small proportion of sudden onset patients with asthma, death can be sudden and unexpected without any obvious prior deterioration of asthma control, but when treated they present a faster rate of improvement then patients with slow onset asthma crises.[107, 113]

2.4 TREATMENT OF ASTHMA

Despite advances in understanding the pathogenesis of asthma, argument continues over the optimal clinical management of acute exacerbations of asthma.[114] However, there seems little disagreement that the most effective treatment for acute episodes of asthma is a systematic approach based on the aggressive use of selected medications and continuous monitoring of key indicators of improvement.[13]

Acute episodes of asthma are one of the most common respiratory emergencies seen in medicine, and the importance of recognizing which episodes are life-threatening cannot be underestimated. The following section introduces the principles of emergency treatment for asthma, outlines the asthma management protocol used by St John Ambulance paramedics in Western Australia, and examines the main groups of medication used in the treatment of asthma.

The principles governing the care for asthma remain the same for both prehospital and emergency department situations, and the area of prehospital treatment of asthma will be explored in more detail later in this chapter.

2.4.1 Emergency Treatment of Asthma

There is a high level of agreement that inhaled $beta_2$ agonist bronchodilators are the first-line therapy for the management of asthma in the emergency department. $Beta_2$ agonists are a group of bronchodilator medicines that opens the airways by relaxing the muscles around the airways that may tighten during an asthma attack or in chronic obstructive pulmonary disease. They work by activating the $beta_2$ receptor on the muscles surrounding the airways, which relaxes the muscles surrounding the airways and opens the airways, thus relieving the symptom of shortness of breath.[115]

The action of beta-2 agonists starts within minutes after inhalation and lasts for about 4 hours. Because of their quick onset of action, beta-2 agonists are especially helpful for patients who are acutely short of breath but, because of their short duration of action, several doses of beta-agonists are often necessary each day. The side effects of beta-2

agonists include anxiety, tremor, palpitations or tachycardia, and low blood potassium.[116-119] The cornerstone of most treatment regimes is multiple inhalations of a short acting beta$_2$ agonist such as salbutamol.[120]

The mode of delivery does not appear critical, for salbutamol administered either by nebulizer, metered dose inhaler or dry powder inhaler all provide equal resolution in acute situations.[120] Intravenous salbutamol is not normally used in the emergency setting, however it has been successfully tested in the early management of acute asthma in children.[121, 122] Studies have shown that asthma attacks in approximately two thirds of patients will terminate with beta$_2$-agonists alone, with a further 5-10% benefiting from the addition of other broncho-dilator drugs such as aminophylline.[13]

Anticholinergic drugs such as atropine and ipratropium are usually not used as first-line therapy because of the long time they take to act, however they may be added to beta$_2$ agonist treatment in severe and life threatening asthma.[13, 123] Ketamine, midazolam and succinylcholine may be used for rapid intubation in life-threatening cases, and adrenaline and intravenous salbutamol may be considered as alternatives to conventional therapy in non-responsive life-threatening cases.[122, 124]

Measurements of the severity of airflow restriction are used to monitor the effectiveness of treatment, with FEV1 and PEFR measured before and after treatments, and at discharge.[44] All patients are considered candidates for corticosteroid therapy on discharge, and inhaled corticosteroids are recommended for all patients discharged on oral corticosteroids.[125, 126] Patients should be given a discharge treatment plan and clear instructions for follow-up care.[4]

2.4.2 SJA-WA Asthma Management Protocol

During the period of this study, the management of asthma by ambulance paramedics in Perth was covered by specific clinical practice guidelines that relate to the emergency treatment of dyspnoea and respiratory distress. Asthma is considered a lower airways obstruction and the St John Ambulance management protocol by ambulance paramedics for asthma is outlined in Table 1 below.[127]

The protocol adheres closely to the concepts of emergency treatment discussed in the previous section, and there has been little in the way of change to this clinical practice guideline over the period of the study, other than the inclusion of oxygen saturation measurements in the year 2002, and the addition of the use of intramuscular adrenaline for status asthmaticus in recent years (500 micrograms for adults, 300 micrograms for children).

Table 1: SJA Clinical Practice Guideline for Asthma

Indication: LOWER AIRWAY OBSTRUCTION Reactive Airways, eg Asthma, Expiratory Wheezing
Specific Management: • Oxygen, high concentration or 100% or 8-10 litres per minute with mask if cannot tolerate demand valve. • Administer salbutamol by nebuliser, if trained and authorised, even if patients have used their own aerosol or nebuliser. • Pre and post nebuliser Peak Flow measurements when possible, and record. • Beware the 'silent chest' in a breathless asthmatic patient – a serious sign. • If patient deteriorating, impaired consciousness, respiratory shock, consider intramuscular adrenaline, if trained and authorised. Monitor cardiac rhythm. • Monitor patient carefully. Record dose, time, effects, route. • Monitor vital signs and oxygen saturation.* • Transport URGENTLY, Priority 1. Do not delay to await results of medication. • Advise hospital (form 'K2 DeMIST' format).
Specific precautions/notes: • If you are unable to differentiate the cause of the respiratory distress, the proper course is to administer oxygen, and transport in the position of comfort. • Wheezing in older persons may be due to pulmonary oedema, not asthma. Your patient may make the wrong diagnosis. Consider also pulmonary embolus. • Children with croup, epiglottis or laryngeal oedema, who develop respiratory arrest, usually do so due to exhaustion or spasm. You will still be able to ventilate gently with mouth-to-mouth, or using resuscitation equipment, eg. mouth-to-mask. • Children achieve higher oxygen concentrations because of lower inspiratory rate, tidal volume, and dead space. Even a 'Hudson' type mask can give 60-70% oxygen in a child. • Sudden complete obstruction due to epiglottitis may respond to tipping the child steep head down, and using back-blows to dislodge the swollen epiglottis. In extremis, consider cricothyrotomy, if trained and authorised.

Ref: SJA Clinical Practice Guideline 15, June 2002

* Oxygen saturation measured by pulse oximeters, available only from 2002 on.

2.4.3 Ongoing Treatment of Asthma

These groups of medications can be readily divided into reliever medications, preventer medications and symptom controllers.

Reliever Medications

These medications are also known as bronchodilators, which cause dilation of the bronchi and bronchioles by inhibiting smooth muscle contraction.[115] They are taken to give immediate relief for asthma symptoms or before exercise in people who experience asthma symptoms when exercising. When inhaled, they usually provide relief within 10 to 15 minutes.[120]

The most common adrenergic stimulants used are the $beta_2$ agonist group, of which the most widely used is salbutamol[120], but include other drugs such as albuterol, metaproterenol and terbutaline. Short-acting anti-cholinergic drugs can also be used for this purpose.[6] Some of these medications also come in oral formulations such as tablets and syrup but take longer to work, but because dosages are usually larger, the likelihood of aforementioned side effects is increased.[119]

Oral corticosteroids have long been the mainstay of treatment for exacerbations of asthma.[6] They are usually either prednisone or prednisolone and are most commonly used in short courses during episodes of wheezing which are not controlled with reliever medications, and occasionally need to be used in children with persistent asthma. They work by reducing the inflammation and mucous produced in the airway, and also increase the effectiveness of the reliever medication.[125]

Preventer Medications.

The role of all preventer medications is to reduce the frequency and severity of asthma attacks and to prevent regular asthma symptoms between attacks.[128] There are two major groups of these medications, those that do or do not contain corticosteroids, with the type used depending on the severity of the asthma.[128]

Non-corticosteroid medications protect the airways from triggers that cause them to become narrowed, and also prevent exercise-induced asthma.[128] To be effective, these medications must be taken every day, even when symptom free.[4]

Inhaled corticosteroids decrease the inflammation and swelling and reduce the sensitivity of the airway.[128] There is evidence from systematic reviews that they are highly effective in minimising symptoms and preventing exacerbations.[129-131] These medications may include beclomethasone, budenoside, and flunisolide, amongst others. Recent clinical trials have demonstrated that most people with asthma can be well controlled with relatively low doses of inhaled corticosteroids, resulting in a low risk of adverse effects.[132]

Leukotriene antagonists are a fairly new group of medications that work by blocking the effects of leukotrienes, one of the chemicals that are released in the allergic reaction.[128] This helps the airways to stay relaxed and reduces the inflammation in the airways.[133] Indications for the use of these medications are still under debate, as they are considered less effective than inhaled corticosteroids.[13]

Symptom Controllers.

This group of medications are considered for the long-term control of asthma and produce bronchodilation for up to 12 hours after administration, and as such are known as long acting relievers or long acting beta-agonists.[4] As the onset of bronchodilation is delayed, these drugs are not used to treat acute asthma symptoms, and patients are advised to carry a short-acting $beta_2$ agonist with them for use when acute symptom relief is needed.[4]

The addition of long-acting beta agonists to inhaled corticosteroids, now available in a combined formulation, allows equivalent or greater effectiveness in disease control with lower doses of inhaled corticosteroids and appear to protect against a wide range of bronchoconstricting stimuli including exercise, allergen, histamine and methacholine.[6]

They are prescribed for people who continue to experience regular asthma symptoms despite using inhaled corticosteroids or regular oral corticosteroids.[128] They are taken daily, even if the asthmatic becomes unwell, and the side effects are the same for the reliever group of medications that include muscle tremors, nervousness or excitability, an increased heart rate and occasionally headache.[4]

Continuing Treatment.

The goal of asthma treatment is to achieve a stable, symptom-free state with the best pulmonary function possible using the least amount of medication.[6] Assessment of the severity of illness should use objective measures of lung function, a plan should be in place for the treatment of acute episodes and chronic management of the disease, and regular follow up should be essential.[13]

The Australian Centre for Asthma Monitoring recommends patients with asthma only use medication, such as a $beta_2$ agonist like salbutamol, for infrequent symptoms when required.[6] If symptoms worsen, such as increased nocturnal and daytime symptoms, then the addition of inhaled steroids and/or a mast cell stabilising preventer, such as cromolyn sodium or nedocromil sodium, may be indicated. If symptoms continue, then an increased dosage of inhaled steroids may be required, with the addition of a long acting $beta_2$ agonist or similar.[6]

Once the initial presenting asthma attack has been managed, the ongoing aims of asthma management are to minimize the symptoms, maximize lung function and maintain best lung function at all times, identify trigger factors and minimize side-effects from medication.[4] This is in order to achieve the best quality of life for the person with asthma, reduce morbidity and mortality, and prevent the development of permanently abnormal lung function.[4]

These long-term aims of successful asthma management and best patient outcome are more likely to be achieved when there is a close working relationship between the patient and doctor, pharmacist, and other health professionals such as nurses and asthma educators, who also have an important educational role.[6] These aims of asthma management have been incorporated into the Six Step Asthma Management Plan developed by the National Asthma Council of Australia, which is summarized below in Table 2.[4]

Table 2: Summary Table for the Six Step Asthma Management Plan.

SUMMARY OF THE SIX STEP ASTHMA MANAGEMENT PLAN	
Assess Asthma Severity	Assess overall severity **when the patient is stable,** not during an acute attack.
Achieve Best Lung Function	Treat with intensive asthma therapy until the 'best' lung function is achieved. Back titrate to lowest dose that maintains good symptom control and best lung function.
Maintain Best Lung Function **Avoid Trigger Factors**	Identify and avoid trigger factors and inappropriate medication.
Maintain Best Lung Function **with Optimal Medication**	Treat with the least number of medications and use minimum doses necessary. Ensure the patient understands the difference between 'preventer', 'reliever' and 'symptom controller' medications. Take active steps to reduce the risk of adverse effects from medication.
Develop an Action Plan	Discuss and write an individualised plan for the management of exacerbations. Detail the increases in medication doses and include when and how to gain rapid access to medical care.
Educate and Review Regularly	Ensure patients and their families understand the disease, the rationale for their treatment and how to implement their Action Plan. Emphasise the need for regular review, even when asthma is well controlled. Review inhaler technique at each consultation. Review adherence at each consultation.

Source: Asthma Management Handbook 2002, National Asthma Council Australia

2.5 EPIDEMIOLOGY OF ASTHMA

This section of the chapter explores the epidemiology of asthma as a prevalent disease within our society and a major cause of morbidity. The prevalence, incidence and mortality due to asthma is examined firstly in the international, and then in the Australasian context.

2.5.1 The Global Burden of Disease Project

Efforts to enumerate the global epidemiology of disease, including asthma, have long been thwarted for a variety of reasons. These include inconsistent and varying methods of measuring mortality and morbidity, the influence of advocacy by interest groups on health policies and interventions, and a lack of quantification to effectively appraise the economic impact of disease.[134] In 1993, the Harvard School of Public Health collaborated with the World Bank and the World Health Organisation (WHO) to assess the Global Burden of Disease (GBD).[135] This study generated a comprehensive and consistent set of estimates of mortality by sex, age and regions of the world for the first time.[136]

The GBD project also introduced a new metric, the disability-adjusted life year (DALY), that could quantify the burden of disease.[137, 138] The DALY is a summary measure of population health that combines, in a single indicator, the years of life lost from premature death and years of life lived with disability. In recent years, considerable international effort has been made to develop summary measures of population health that combine information on both mortality and non-fatal health outcomes into a single measure, and international policy interest in such indicators is increasing.[139-141]

The contribution of the GBD project to the understanding and description of the epidemiology of asthma is considerable. Asthma is a multi-factorial problem, and as seen from previous discussion, the wide variations in asthma rates nationally and internationally cannot be adequately explained by single factors such as measurement variations or geographical differences.[142, 143]

By quantifying the burden of premature mortality and disability for 135 major causes of disease and injury, internally consistent estimates have been developed for the prevalence, incidence, duration and case fatality for over 500 sequelae resulting from these causes.[134] As a result, the GBD study has been able to describe and value health states associated with these sequelae, analyse the burden of major risk factors, and develop projected scenarios of mortality and non-fatal health outcomes over the next few decades.[134]

For geographic separation of the global burden of disease, the six WHO regions of the world (Africa, The Americas, Eastern Mediterranean, Europe, South-East Asia and Western Pacific) have been further divided into 14 subregions, based on levels of child (under five years) and adult (15-59 years) mortality for WHO Member States. Five mortality strata ranging from very low to very high child/adult mortality were defined in terms of quintiles of the distribution of WHO analyses of mortality rates for 1999, based on UN Population Division population estimates.[144] The Western Pacific (A) region includes Australia, Japan, Brunei Darussalam, New Zealand, and Singapore, where Australia is rated as a low child and low adult mortality stratum.[134]

To emphasize the usefulness of the GDB project, an extract from two of the GBD tables is shown below, highlighting how dissimilar regions and mortality strata can be compared with each other in a meaningful way. Table 3 shows a hierarchical structure with a total for a major cause of disease, sub-totals for sub-sections such as respiratory diseases and then further sub-totals for specific items such as chronic obstructive pulmonary disease and asthma. It can be seen from the highlighted areas of the table that the Western Pacific region has not only the highest number of estimated deaths from asthma in the low child/ low adult mortality stratum (33,000 deaths), but also the highest burden of disease for any region in the same mortality stratum (2,952,000 DALY's).[134]

By developing comparable, valid and reliable epidemiological information on disease and its associated risk factors, the GBD has the potential to become an important underpinning for programs that can target asthma, and provide evidence to support global health policy.

Table 3: Deaths and DALY's cause and mortality stratum in WHO Regions, estimates for 2001.

CAUSE	TOTAL	%	AFRICA		THE AMERICAS			EASTERN MED.		EUROPE			S/EAST ASIA		WEST PACIFIC	
Mortality stratum			High child, high adult	High child, very high adult	Very low child, very low adult	Low child, low adult	High child, high adult	Low child, low adult	High child, high adult	Very low child, very low adult	Low child, low adult	Low child, high adult	Low child, low adult	High child, high adult	Very low child, very low adult	Low child, low adult
Population (000)	*6 122 210*	*%*	*301 878*	*353 598*	*328 176*	*437 142*	*72 649*	*141 835*	*351 256*	*412 512*	*219 983*	*241 683*	*297 525*	*1 262 285*	*154 919*	*1 546 770*
TOTAL DEATHS (000)	56 554	100	4 365	6 316	2 748	2 619	544	707	3 449	4 076	1 969	3 658	2 194	12 273	1 161	10 475
I. Communicable diseases; maternal, perinatal and nutritional conditions	18 374	32.5	2 968	4 615	172	485	198	126	1 700	236	193	157	644	5 171	138	1 572
II. Noncommunicable conditions	33 077	58.5	1 098	1 264	2 400	1 810	288	475	1 454	3 643	1 664	3 048	1 275	5 913	939	7 805
Respiratory diseases	3 560	6.3	105	129	186	163	20	19	125	213	80	126	130	693	59	1 513
Chronic obstructive pulmonary disease	2 672	4.7	53	63	133	84	5	10	78	140	49	96	66	548	23	1 324
Asthma	226	0.4	9	15	6	10	2	3	15	13	11	16	21	66	6	33
III. Injuries	5 103	9.0	298	437	176	324	57	106	295	197	113	453	275	1 188	84	1 098
TOTAL DALYs (000)	1 467 257	100	147 899	209 985	46 520	81 270	17 427	23 007	113 214	53 075	38 936	59 212	61 290	357 554	16 430	241 438
I. Communicable diseases; maternal, perinatal and nutritional conditions	615 737	42.0	105 097	156 359	3 250	17 105	6 761	5 691	61 446	2 579	7 029	4 999	20 403	167 749	1 064	56 205
II. Noncommunicable conditions	672 865	45.9	30 030	36 075	38 642	50 328	8 432	13 282	39 329	46 259	27 473	42 170	31 866	144 703	13 720	150 556
Respiratory diseases	62 842	4.3	3 126	4 144	2 986	4 848	761	674	3 125	3 195	1 699	2 149	2 366	14 042	1 053	18 674
Chronic obstructive pulmonary disease	29 917	2.0	505	608	1 552	1 359	86	178	828	1 777	737	1 201	895	6 441	380	13 372
Asthma	15 010	1.0	943	1 300	777	1 539	282	304	999	706	369	290	543	3 630	375	2 952
III. Injuries	178 656	12.2	12 771	17 551	4 628	13 837	2 235	3 960	12 439	4 237	4 434	12 042	9 021	45 102	1 646	34 677

* Extracted from Annexe Table 2: 'Deaths by cause, sex and mortality stratum in WHO Regions, estimates for 2001' and Annexe Table 3: :Burden of disease in DALYs by cause, sex and mortality stratum in WHO Regions, estimates for 2001', being part of 'Global burden of disease 2002: version 2 methods and results. Global programme on evidence for health policy discussion paper number 50.', World Health Organisation, October 2002.

2.5.2 International.

Prevalence

During the 1980's and 1990's, the results of a series of studies with similar methodology suggested that substantial increases in the prevalence of wheeze and asthma had occurred over past decades in western countries.[145-147] At the same time, hospital admission rates for childhood asthma were increasing[148] and there was an increasing prevalence of bronchial hyper-responsiveness, hay fever and atopic eczema in affluent countries.[149]

These events prompted concern about a possible 'asthma epidemic', and had the effect of stimulating worldwide efforts to promote awareness about the diagnosis, prevention and treatment of asthma.[150] However, ambiguous definitions of asthma have made both estimates of the prevalence of asthma and comparisons between studies difficult to interpret.[151-153]

Methodological differences between studies make it difficult to compare the size of the differences in an asthma prevalence between countries, but reported trends of increasing prevalence have been consistent among populations of widely varying lifestyles and ethnic groups.[143] In addition, there is evidence to suggest that substantial geographical differences in asthma prevalence exist that cannot just be attributed to different methods of measurement.[142, 143]

These differences emphasize the need for a standard method of measuring and comparing asthma prevalence, yet to date there have been too few international and regional multi-centred prevalence comparisons. The European Community Respiratory Health Survey (ECRHS)was the first such study in adults[154] and the International Study of Asthma and Allergies in Childhood (ISAAC) was the first such study in children.[155, 156]

Involving approximately 140,000 adults between 20 and 44 years old, the ECRHS assessed the prevalence of asthma in 22 countries using an identical and standardised protocol. Using a screening questionnaire, the ECRHS documented up to a tenfold regional difference in the prevalence of respiratory symptoms such as asthma, atopic

sensitisation, and bronchial responsiveness. The highest percentage prevalence rates of asthma were found in the United States (7.1%), the United Kingdom (7.5 to 8.4%), New Zealand (9.0 to 11.3%) and Australia (11.9%).[142] The ECRHS concluded that the prevalence of asthma varied widely, even within some countries, and the fact that the geographical pattern was consistent with the distribution of atopy and bronchial hyper-responsiveness supported the conclusion that the geographical variations in the prevalence of asthma were true and most likely due to environmental factors.[157]

Phase 1 of the ISAAC studied approximately 460,000 children aged 13-14 years in 155 collaborating centres (56 countries), and approximately 260,000 children aged 6 to 7 years in 91 centres (38 countries).[156] It found differences of between 20 to 60 fold between centres in the prevalence of symptoms of asthma, allergic rhino-conjunctivitis and atopic eczema. For asthma symptoms, the highest twelve-month prevalence were identified from centres in the Republic of Ireland (28%), Australia (25-34%), New Zealand (27-32%), and the United Kingdom (19-37%).[158] It was also concluded that the differences between populations in the ISAAC are likely to be due to environmental factors.[156]

A comparison of the findings of these two studies was conducted for the 17 countries in which both surveys were taken, and it was found that there was strong correlation between the ECRHS and ISAAC data in the prevalence of 'wheeze within the last 12 months', and generally good agreement in the international pattern observed in the two studies for 'self-reported asthma', 'self-reported asthma before age 14 years' 'hay fever' and 'eczema'.[143] The authors have been happy to accept 'good overall agreement' between the two studies with regard to international prevalence patterns[143], but this must be viewed in light of the fact that there were large differences in the absolute levels of prevalence observed in the two surveys, and that the two studies focussed on different age groups (the ECRHS is unable to directly analyse the effect of childhood exposure).

Whether these findings really do lend support to the validity of the two studies remains a matter of conjecture. It had previously been concluded that an international comparison of childhood asthma symptom prevalence, using simple standardised instruments, was feasible [155], and since then, the standardised questionnaire developed

for use in the ISAAC has been used as a tool for other studies to assess point prevalence [159], validate other questionnaires for the determination of asthma symptoms [160] and assess predictive values of parental questionnaire responses.[161] However, limited sample sizes [161] (especially adult samples [160]), narrow age groups [159, 161], potential selection bias [159, 161] and restricted geographical areas [159-161] all limit the scope of conclusions drawn by the authors.

Although these studies have supported the validity of the questionnaire as an instrument, they contribute little to the investigation of factors that lead to the variation in asthma prevalence internationally. So far, the results from the ECRHS and ISAAC, the two largest multi-centred studies conducted on asthma prevalence to date, have only been able to conclude that the prevalence of asthma varies widely [157, 158], and that geographical differences in asthma prevalence may exist.[142] It has been hypothesized that these differences may be due to differences in exposure to risk factors and differences in the management of asthma [155], but so far these differences have not been identified.

Phase 2 of the ISAAC will investigate possible aetiological factors, and Phase 3 will be a repetition of Phase 1 to assess trends in prevalence.[156] A planned follow-up study to the ECRHS, the ECRHS II, will also provide further evidence of changes in prevalence.[157] Perhaps, when results from these and other prevalence studies are available, possible explanations for the trends and differences in reported asthma prevalence may be a little clearer.

In the United States, the National Health Interview Survey (NHIS) was a multi-purpose health survey conducted by the National Centre for Health Statistics (NCHS), Centres for Disease Control and Prevention (CDC), and is the principal source of data for the estimation of asthma prevalence in the United States.[162] This survey, and four other national databases, supported new evidence that childhood asthma mortality and morbidity rates may be beginning to plateau.[163] Childhood asthma prevalence increased on average 4.3% per year from 1980 to 1996, and remained level from 1997 to 2000. The general practitioner visit rate increased on average 3.8% per year between 1980 and 1999, and the hospitalisation rate increased by 1.4% per year from 1989 to 1998.[163]

Unfortunately, revisions to the NHIS from 1997 on precludes the direct comparison of responses to questionnaires given prior to 1997, thus there is not a continuous estimate of asthma prevalence trends in the United States.[164] As a result, comparisons cannot be easily drawn to data reported from other international centres. However, overall trends reported for 'lifetime asthma' and 'attack rate' prevalence from 1997 to 2003 in the United States reflected a temporary decrease in rates for the 1997 to 1999 period, but increases of 25% in the lifetime asthma prevalence rate for 2001 [165] and 10% in the asthma attack rate for 2002.[162] This data suggests that there has been a net increase in lifetime asthma prevalence overall in the United States since 1997, and that the idea of an 'asthma epidemic' being over may be a little premature.

Regardless, asthma is still recognised as a major public health problem. In the United States in the year 2002, asthma accounted for an estimated 3 million lost working days for adults and 10.1 million lost school days for children. Asthma ranked within the top ten prevalent conditions causing limitation of activity, and cost the United States $US12.7 billion in health care costs.[165]

It has also been noted in the United States that ethnic minorities of low socio-economic status (such as Hispanics and African-Americans) are disproportionately represented in the trends of increasing asthma prevalence, morbidity, and mortality.[166, 167] In comparison, the prevalence of asthma in China and Africa was quite low (approximately 0.5% to 5%) and was comparable to other indigenous populations whose rates range between 0.5% and 12%, whereas there was a much higher rate (approximately 20 to 25%) in countries such as Australia and New Zealand, where people's ancestors migrated from distant areas.[168] A recent systematic review and meta-analysis of epidemiological studies within the United Kingdom found that despite originating from low risk areas internationally, South Asians and Afro-Caribbeans experienced significantly poorer asthma outcomes than do whites.[169]

In addition, a meta-analysis of the data on asthma rates in various populations revealed a statistically significant higher rate of asthma among immigrants to another country than natives of that country, with elevated blood IgE concentration in these immigrant populations suggesting that immigration may influence, along with other factors, the incidence and prevalence of IgE-mediated asthma in the world.[168]

Incidence

It remains uncertain that the perceived increase in prevalence represents an increase in incidence or a longer duration of disease.[170, 171] As knowledge of the natural history and the risk factors of asthma rely heavily on prevalence data, confirming an increase in asthma incidence as a cause of increasing asthma prevalence is important. Both the ECRHS and ISAAC are prevalence studies and have not been designed to measure incidence, and in the United States none of the national survey tools employed, including the NHIS, measure asthma incidence.[164] Therefore, the three largest international multi-centred studies of asthma offer little opportunity to explore and compare trends in asthma incidence.

Reports from various countries regarding asthma incidence are drawn from a wide range of age, ethnic and racial backgrounds, and their findings are diverse. Some parts of the world report a decrease in incidence, especially in children, such as Rome, Italy [172]; Saskatchewan, Canada [173]; and Melbourne, Australia [174], whereas other areas such as Saudi Arabia [175], South Australia and Patras, Greece [176] continue to notice an increase. Varying definitions of asthma and methodological differences between studies make it difficult to compare the reported asthma incidence between countries.

A retrospective analysis of the data of the ECRHS elicited age and sex-specific incidences of asthma in men and women across several countries, and found that during childhood, girls had a significantly lower risk of developing asthma than boys (RR: 0.74 (0 to 5 years), 0.56 (5 to 10 years)); at puberty the risks were almost equal (RR: 0.84); and after puberty the risk in women was always significantly higher than in men (RR: 1.38 to 5.91).[177] Particular care was taken to control for the potential effect of cohort effect (where the incidence pattern could have changed over generations) and recall bias, and a nested case-control study within the analysis showed that airway calibre at least partly explained the greater incidence of asthma in young women (OR: decreased from 2.04 to 1.47). Smoking did not appear to increase the risk of asthma. The authors suggested that smaller airway calibre in girls, in addition to hormonal factors, could play an important role in explaining the different patterns of incidence in men and women.[177] The reversal of sex-related incidence around the time of puberty has also been reported separately for studies of British adolescents [178] and United States children and adolescents.[179]

It has also been reported that atopic symptoms and family history of atopy were strongly associated with incidence of adult-onset asthma.[180] A Swedish study estimate the incidence rate of adult-onset asthma in relation to atopy, age, sex and smoking in a random sample (n = 15,813) of the population. It was found that the incidence rate of adult-onset asthma among females was 130 per 100,000 PY compared with 100 per 100,000 PY for males, with a high incidence rate 300 per 100,000 PY among females aged 16-20 years. It was considered that tobacco smoking may be associated with an increased incidence rate of adult-onset asthma, especially among women.[180]

Conversely, a follow-up study of random subjects (n = 1,640) who participated in the ECRHS was conducted in Spain, where the prevalence of asthma is considered low to medium.[181] The incidence of asthma was 553 per 100,000 PY (688 in females, 404 in males), where incidence was highest in subjects who at the baseline survey had bronchial hyper-responsiveness (incidence rate ratio (IRR), 3.85), in those with positive IgE against timothy grass (IRR, 3.16), and in females (IRR, 1.80). There was no significant association with atopy defined by reactivity to any allergen, high total serum IgE, smoking, occupational exposure or maternal asthma.[181]

The ECRHS only examined adults to 44 years old, and there are few studies that describe patients with onset of asthma after 65 years old, despite asthma being common in the elderly. A study in Rochester, Manitoba, concluded that asthma could begin late in life at an incidence rate comparable to the incidence rates previously reported in young and middle-aged adults in the community [179], and that age-specific incidence rates declined with age in the elderly (103 per 100,000 PY for residents aged 65 to 74 years, 81 per 100,000 PY for those aged 75 to 84, and 58 per 100,000 PY in residents older than 85 years), with the incidence of asthma significantly higher in men.[182] Despite this being a population based study, small sample numbers (n = 98), the retrospective nature of the study, and the fact that study subjects were mostly a white population of a small city limit the extrapolation of these results to populations of different backgrounds or geography.

The widely varying reported incidence rates above simply serve to confirm variations in reported annual figures from other cohort studies on asthma incidence [183-188], and

highlights the need for studies that can explore comparative trends in asthma incidence over long periods of time.

However, very few longitudinal studies exist on the incidence of asthma.[171] An early study in England and Wales reported an increase in asthma incidence from 10.2 to 27.1 per 100,000 patients per week over the period of 1976 to 1987, with increases most marked in children.[189] However, this study only used simple correlation statistical methodology within a paired-conditions format for analysis, which created doubt that adequate controls were in place for misclassification or changes in patient consulting behaviour. Supporting these findings in part, the study in Rochester, Manitoba (described above), also found that increases in incidence rates seen from 1964 to 1983 occurred only in children and in adolescents [182], but this study remains constrained by limitations mentioned previously

In Finland, from 1986 to 1993, the annual incidence of persistent asthma in adults aged 15 to 64 years increased 21%, with a 43% increase in new cases for women, and the number of new cases stable in men.[190] However, in the age group 15 to 29 years, the increase was 91% for women and 87% for men. Suggestions for the increase among women included the concurrent increase in the proportion of regular smokers, especially among young women, and increased exposure to domestic indoor allergens such as pets, mites and moulds. In the same period, the annual incidence of occupational asthma increased 70% for both men and women (4.8% of all new cases of asthma), with more than half of the new cases of occupational asthma found in the farming population and in bakeries.[190]

Another Finnish study on twins conducted over a similar period (1975 to 1990) found that the pattern of increase in asthma and hay fever prevalence with time were similar, with hay fever being a strong predictor of asthma, but these diseases showed no significant increase in incidence.[188] The authors used very different methods to derive prevalence, calculated at three different time periods of the study, compared to incidence, which was calculated separately for two follow-up periods and only those aged 24 to 44 years at the beginning of each follow-up period were included in the analyses. The intention of the authors to make the age distributions of the two follow-

up periods as comparable as possible resulted in reducing the external validity of the results.

An eleven year study of approximately one-third of the Mexican population found that asthma incidence steadily increased from 1991 to 1995, followed by a plateau from 1995 to 1997 and a subsequent decline from 1997 to 2001, where there was an early trend toward decreased health-care utilization by asthmatic patients.[191] This study was only able to access health claims data from a nationwide database of the third of the population with health insurance, so even if the decreased health care utilization may be due to a decrease in the incidence of asthma, the results cannot be extrapolated to the remainder of the population without health insurance.

A multi-centred study in the United Kingdom (number of cases not reported) set out to determine trends in the incidence of new episodes of asthma presented to general practitioners, covering ten years from 1989 to 1998 of reported data from 92 practices.[192] After initial increases, the study found a gradual decrease in the incidence of asthma episodes and of acute bronchitis presenting to general practitioners since 1993. This prompted the authors to conclude that secular trends they had described provided strong evidence that the 'asthma epidemic' had peaked.

However, the basis of the above study relied on general practitioner reporting, and no attempt had been taken to compare their results to hospital data, especially emergency department episodes where admissions may not take place, or to take into account that general practitioner consulting patterns and registration routines may have changed over time. Further, a new episode and a repeat consultation may be difficult to discern, given the chronic nature of asthma. The authors were also quick to discount the effect of practice nurses, however it was possible that the introduction of specialist nurses with subsequent improved management of asthma and bronchitis patients may have reduced both the number of asthma exacerbations and also the number of presentations of acute bronchitis. Given that a strong relationship has been shown between asthma and chronic bronchitis [193] and that the number of practice nurses had concurrently increased three-fold during the time of the above study [194], not controlling for these variables challenges the validity of the study conclusions.

There are few studies that have estimated the adult incidence of asthma. A Norwegian group of researchers reviewed general population studies published worldwide on the incidence of asthma to provide an estimate of the adult incidence of asthma, and to determine how the incidence of adult asthma varied by age[195]. They found that the adult incidence of asthma was higher in women than men, and that there was a trend towards a higher incidence rate with age. It was thought that this was likely due in part to misclassification with chronic obstructive pulmonary disease (COPD), however findings from their study implied that the incidence of asthma in the elderly has previously been underestimated. Further, it was noted that the estimates of adult asthma incidence tended to be higher in later studies, implying a rise in asthma incidence in adults, at least within the timeframe of observation. In fact, for those studies with a wide age span, the estimates of asthma incidence were unchanged or increased with greater age, and for those studies that included adjusted risk estimates of the effect of age on the adult incidence of asthma, the risk increased with greater age, most significantly in the highest age group[195].

However, despite many studies finding rises in asthma prevalence [147, 196-198], it would appear that a convincing trend of either increasing or decreasing asthma incidence has yet to be established. It could be concluded that an increasing prevalence and a stable incidence could suggest that the remission rate of asthma is decreasing or asthma severity is increasing. However, caution must be exercised in drawing any interpretation from these results as there are impediments to comparison, including differences in diagnostic criteria of the disease, case definitions, survey techniques, periods of study and population characteristics.

Mortality

Asthma was not considered a significant cause of death during the early years of the twentieth century, with the frequency of asthma and especially death from asthma considered to be rare.[199] This perception changed in recent years when evidence showed the mortality rate for asthma was increasing worldwide. From the mid-1970's to mid-1980's, substantial increases in deaths due to asthma were reported in patients aged 5 to 34 years old, and remained disproportionately high for this group, especially in industrialized countries.[199]

Several studies have showed that there was a failure to recognize the severity of a fatal episode of asthma by either the patient or health care practitioner.[200-205] However, the majority of these studies were uncontrolled and solely relied on retrospective analysis of events by an expert group of physicians. Despite this, the results are of concern.

It had been suggested that there was an excess mortality in asthma, other than non-preventable deaths, that was associated with poor assessment, underestimation of severity, inappropriate treatment and delays in obtaining help.[202] A confidential panel for the British Thoracic Society investigating deaths from asthma found that some aspect of care or supervision was deficient in 98% of the deaths reviewed.[206] Problems varied from failure to diagnose asthma (10%) to gross under-treatment (92%), with patients not acting appropriately 77% of the time.[206, 207]

It had also been recognized that speed of onset and prognosis of the patient after discharge appeared to be dependent on the asthma control status prior to the acute episode [208], and that predisposing factors identified for severe acute asthma included a lack of appropriate treatment, lack of compliance, and poor preventative measures.[112] In view of this, the influence of the management of asthma in the pre-hospital period on satisfactory outcome cannot be underestimated.

Yet, despite finding that the majority of severe asthma attacks were due to management errors and were preventable by currently available strategies [27, 209, 210], the rates of death from asthma continued to rise in many countries, including Australia, England and Wales, Canada, the Netherlands, Sweden, France, West Germany, Israel, the United States, and Denmark.[199] Deaths rates due to asthma have only begun to decline in some countries in recent years.

A longitudinal study in Denmark examined asthma mortality in children and young adults from 1973 to 1994 and studied the validity of death certificates.[211] Asthma mortality rates in Denmark increased in adolescents from 1973 to 1987 and decreased from 1988 to 1994, one possible reason being an increased awareness of asthma symptoms combined with a steadily improved treatment of asthma.[211] However, this well-constructed study highlighted the difficulties in ensuring adequate certification of

the cause of death, even in children and young adults [212], and the potential for inaccuracies, even in national mortality statistics.[211]

A retrospective study conducted in Cape Town, South Africa, over the period of 1980 to 1997 concluded that the incidence of fatal and non-fatal asthma had declined over the period and that this may have reflected improved asthma management.[213] The authors reported higher relative asthma mortality rate in people of mixed race, and the predominance of deaths outside health facilities and on weekends suggested that there may be problems with access to care. Like the Danish study described above, this study also suffered limitations in using death certification to investigate trends in mortality, and in attempting to correct misclassification of death by only using death certificates where asthma is reported as the sole cause of death or in association with respiratory failure, the mortality rates are likely to be underestimated. Further, data was restricted to people under 55 years to control for potential confounding by diagnostic transfer from patients with chronic obstructive pulmonary disease (COPD), and this will limit the comparability of results to other studies.

In the United States, the childhood asthma death rate increased by 3.4% per year from 1980 to 1998, then dropped approximately 3% in 1999, compared to1998.[163] Overall, the lifetime prevalence rate of childhood and adult asthma had decreased 4% and the asthma attack prevalence had decreased 7.4% between 1997 and 1999, however hospital discharges increased between 1998 and 1999.[165]

There are considerable differences in the reported asthma mortality rates of different countries [214], with barriers to effective comparison including changes in ICD classifications, inaccuracies in certification and coding of death certificates, and changes in diagnostic criteria. However, it is considered that these barriers do not appear to be sufficient explanation for these differences [214], therefore the reality may be that many countries have actually failed to decrease asthma mortality.

An increasing asthma prevalence, especially in children and young adults, may partly explain the unchanged pattern of asthma mortality observed in some countries [214, 215], but it would appear that even the interpretation of national trends require caution [211], and validity problems will continue to make comparisons between countries difficult.

2.5.3 Australia.

Prevalence

The prevalence of asthma in Australia is among the highest in the world.[143], and asthma is particularly prevalent in young Australians.[153] Over the last decade there has been a range of population health surveys measuring the prevalence of asthma in Australia, including the Australian Bureau of Statistics' (ABS) National Health Survey and some state and territory health surveillance programs.[6]

In Australia, a National Health Survey (NHS) was conducted in 1989-90, 1995, 2001 and 2004-05, with prior Australian Health Surveys conducted in 1977-78 and 1983. The 2001 and 2004-05 NHS are the first two in a series of proposed trienniel health surveys, collecting information about the health status of Australians, their use of health services and facilities, and health related aspects of their lifestyle.[216]

The NHS is the only nationally representative household survey in which the prevalence of asthma in Australia has been measured [6], but it is important to note that results reported in the NHS are based on self-reported answers by householders in response to questions from interviewers. With regard to asthma, a variety of self-reported measures may include a self or parent-reported doctor diagnosis of asthma [217], symptoms such as wheeze [218-220], shortness of breath [142, 174], cough at night [221], wheezing with exercise [161, 221, 222], and taking treatment for asthma.[142]

In view of this, caution must be exercised in the interpretation of the results, for there is great potential for misclassification associated with differential diagnosis of asthma as well as recall bias. For example, a householder who may have had asthma as a child may not recall such events as an adult, and as there is no universally applied definition for asthma [6], results may be subject to changes in the tendency of doctors to apply the diagnostic label 'asthma'. For example a householder may recall a wheezy episode associated with bronchitis where the doctor suggested that it might be asthma, and when questioned if they ever had asthma medically diagnosed, they may consider this to have been an episode of asthma and report it as such.

Moreover, there are limited time series data available from these surveys, with some having been conducted only once, or where there are repeated measures, the definition used to identify people with asthma has changed.[6] However, despite these limitations, the best opportunity to explore trends in asthma prevalence lies with examining the prevalence of asthma reported in successive surveys.

In 2001 it was estimated that approximately 12% of Australians (2.2 million people) currently had long-term asthma, where it had lasted or was expected to last for six months or more, an increase from 8.5% in 1989-1990 and 11% in 1995.[223] However, these estimated increases need to be considered in the light of the introduction of the National Asthma Campaign in 1990, which led to increased awareness and vigilance by doctors and patients, and may have resulted in increased diagnosis and reporting of the disease.[224]

By 2004-05, there were approximately 10% of Australians with asthma as a current and long term condition (9% of males and 11% of females), a decrease from 2001.[216] Among children and young adults, respiratory conditions remained the most commonly reported conditions (19% of children under 15 years and 30% of persons aged 15–24 years), with asthma remaining the most prevalent among children under 15 years (12%), and hayfever and allergic rhinitis remaining the most prevalent condition for young people aged 15–24 years (19%).[5, 216]

For 2004-05, asthma was most prevalent in younger age groups affecting 12% of those in the 0–14 and 15–24 years age groups combined, and 11% in the 25–34 years age group. The prevalence of asthma in most other age groups was around 9-10%. Children aged 0 to 4 years were the group that most commonly visited general practitioners, emergency departments or were hospitalised for asthma [6], and nearly one quarter (24%) of adults with asthma were also current smokers.[216] Changes in percentage of the most commonly reported conditions from 2001 to 2004-05 can be seen in Table 4 below.

Table 4: Australian National Health Surveys, most commonly reported conditions

Australian National Health Survey, 2001 [a]					
0-4 YEARS	**%**	**5-14 YEARS**	**%**	**15-24 YEARS**	**%**
Asthma	8	**Asthma**	16	Hayfever/allergic rhinitis	19
Allergy	4	Hayfever/allergic rhinitis	9	Short-sightedness	17
Dermatitis/eczema	3	Allergy	6	**Asthma**	16
Otitis Media	3	Chronic sinusitis	6	Back pain/problems	16
Hayfever/allergic rhinitis	3	Long-sightedness	5	Chronic sinusitis	9

Australian National Health Survey, 2004-05 [b]			
0-14 YEARS*	**%**	**15-24 YEARS**	**%**
Asthma	12	Hayfever/allergic rhinitis	19
Hayfever/allergic rhinitis	8	Short-sightedness	18
Allergy	6	**Asthma**	12
Long Sightedness	4	Long Sightedness	9
Short Sightedness	4	Back pain/problems	9

Source:

[a] Year Book Australia 2003, Health, Asthma. Australian Bureau of Statistics. 1301.0-2003

[b] Year Book Australia 2006, Health, Asthma. Australian Bureau of Statistics. 1301.0-2006

* Note: Summary results of the 2004-05 NHS did not differentiate between 0-4 and 5-14 year age groups.

The International Study of Asthma and Allergy in Childhood (ISAAC) reported an estimated prevalence rate of approximately 25% in 6-7 year old Australian children and 29% in 13-14 year olds.[225, 226] A repeat survey of 6-7 year olds conducted in Melbourne in 2002 using the ISAAC protocol found a decrease in the proportion of children reporting ever had asthma (1993, 28.6%; 2002, 25.5%) as well as a decrease in reported wheeze within the preceding 12 months (1993, 27.2%; 2002, 20.0%).[227] However there is little satisfactory national data, for not only does the prevalence of asthma vary between different parts of the country, but it also has been unstable over time.[228]

A cross-sectional community survey (n = 4,500) conducted in Melbourne, Australia, determined the prevalence of self-reported asthma and respiratory symptoms among young adults and whether there had been any change since a previous survey, using the European Community Respiratory Health Survey (ECRHS) survey questionnaire.[229] It was found that the prevalence of current asthma had not increased significantly since a

previous survey in 1990. However, the prevalence of nocturnal chest tightness, nocturnal cough, and use of asthma medications had increased significantly over the same period.[229]

Multiple population studies conducted in south-western Sydney, Australia, found the prevalence of diagnosed asthma in Australian adolescents across all three studies to be 16.5%, and prevalence declined in males but increased in females from the ages of 12-15 years.[230] This age-dependent gender differential has been reported in other studies.[5, 6, 231]

Overall in Australia, asthma is more common among indigenous Australians, particularly adults, than among other Australians.[6] The prevalence of asthma is higher among Aboriginal and Torres Straight Islander women than among Australian women, especially in women aged 35 years or older.[6] However, there are conflicting findings from studies which have reported asthma prevalence in remote Aboriginal communities.[232-234] Further, with regard to socioeconomic status, those living in the most socioeconomically disadvantaged localities did not exhibit a substantially different prevalence of asthma to those in the most advantaged localities.[6]

Although asthma is less common among Australians who were born in non-English-speaking countries than among other Australians, the dramatic influx of immigrants from South-East Asian countries into Australia over the past 20 years has been associated with an increase in asthma and allergic diseases amongst these immigrants.[6] Many of this group only developed these conditions after their arrival in Australia, suggesting that the environment may play an important role in the pathogenesis of asthma and allergy.[235]

A wide range of both objective and subjective measures, used either alone or in tandem, have been used in various studies to estimate asthma prevalence in a variety of settings [153], however it is difficult to interpret the reported rates and variations in asthma prevalence because of the lack of a standard definition for asthma. As previously mentioned, limitations to comparing the results of surveys include variation in the survey methods used, age ranges surveyed and sample sizes. Therefore, data from these

surveys cannot directly be used to compare prevalence rates among states or other population subgroups.

However, an examination of the range of values obtained in these surveys can at least suggest a likely prevalence of asthma in the population. The Australian National Health and Medical Research Council (NH&MRC) estimated the prevalence of asthma in Australian children to be in the range of 10-20%.[228] The Australian Institute of Health and Welfare (AIHW) reported that among adults, the prevalence of reporting ever having been diagnosed with asthma ranged from 17% to 25%, with most estimates between 19% and 21%.[6] Overall, the prevalence of current asthma among adults has ranged from 9% to 15%, with most estimates falling between 10% and 12%, and in four major surveys conducted among children, estimates of the number who had ever been diagnosed with asthma ranged from 20% to 26%, with most estimates of the proportion of children with current asthma ranging between 14% and 16%, based on self-report.[6]

In the light of these results, the Australian Centre for Asthma Monitoring has cautiously concluded that, geographically, the prevalence of asthma overall does not differ substantially among the states and territories, or between major cities, inner regional, outer regional or remote areas of Australia.[6] Moreover, since the early 1990's, a decline in hospitalization rates and general practitioner consultation rates for asthma among children has also been noted.[236] It remains to be seen whether this trend, coupled with suggested evidence of a decrease in asthma prevalence for children, will translate into a favourable trend for adult asthma prevalence.

Incidence

In the early 1980's the prevalence of asthma in Australian children was less than 10%, but by the late 1990's it was close to 20%, whereas in adults it had risen from approximately 7% to 12% in the same time.[237] The lower rate in adults suggested there was either a reduced incidence of adult-onset asthma or a decreased rate of expression of asthma symptoms in adult life. Comprehensive data on the incidence of asthma over time would provide valuable evidence, however there is a dearth of incidence studies for asthma in Australia.

The National Health Surveys (NHS) have provided information over time on self-reported asthma from a probability sample representing the whole Australian population, reporting results such as 'recent asthma' (in the previous two weeks), 'long-term' asthma (6 months or more) or 'ever doctor diagnosed asthma'.[238] Although these were primarily prevalence studies, the authors have derived a frequency that measures the proportion of individuals getting asthma, and have reported this as the cumulative incidence of asthma (the ratio of incident cases of asthma to the number of individuals at risk.[239]).

Changes in cumulative incidence can be seen in Table 5 below for the 1989-90 and 2001 NHS, where the cumulative incidence of asthma appears to have at least doubled or trebled for each age group over time. These results are counter-intuitive to those published internationally (discussed previously), and as they also reflect responses to different asthma definitions from separate surveys, the utility of using these results to explain changing trends of prevalence in Australia remains questionable.

Table 5: Australian National Health Surveys, reported cumulative incidence of asthma

Australian National Health Survey, 1989-90 (people with 'long-term or recent asthma')										
Age (years)			**0-14**	**15-24**	**25-34**	**35-44**	**45-54**	**55-64**	**65-74**	**75+**
Cum Inc (%)			13.9	10.4	6.9	5.7	5.8	5.7	6.8	4.2
Australian National Health Survey, 2001 (people with 'ever doctor diagnosed asthma')										
Age (years)	**0-4**	**5-9**	**10-14**	**15-24**	**25-34**	**35-44**	**45-54**	**55-64**	**65-74**	**75+**
Cum Inc (%) Males	14.5	30.4	34.5	29.9	20.3	15.4	13.7	11.9	12.4	11.1
Cum Inc (%) Females	11.2	21.6	28.3	30.6	25.8	19.0	18.8	17.5	16.9	13.7

* Source: National Health Survey 1989-90, ABS 4378.0 and National Health Survey 2001, ABS 4364.0

For the 2004-05 NHS, cumulative incidence was no longer reported, and only estimates of prevalence of asthma (as a long term condition) were reported at points of time during the survey period. Special note was made by the authors that the data did not refer to the incidence of asthma occurring in the survey period.[240]

As exposure to occupational allergens has been conclusively linked to the development of asthma and progression of the disease [241], the incidence of occupational asthma could be explored as proxy for the disease burden of asthma in the workplace. The exposure to occupational allergens and the occurrence of occupational asthma are important targets for surveillance, and it would be expected that asthma cases were reported for workers compensation and other legal purposes. However, there is also a paucity of comprehensive data on the incidence or prevalence of occupational asthma in Australia [242], and an absence of a nationally coordinated surveillance scheme.[243] Recently, notification schemes have commenced in some states of Australia, and the most common condition reported by physicians in Victoria and Tasmania has been asthma, comprising 33% of the occupational respiratory events reported, which were found to be similar to those reported in overseas physician notification schemes.[244]

Another method of examining asthma incidence is to explore Global Burden of Disease measures, which have been widely accepted for monitoring health by various organisations such as the World Health Organization.[134] The estimation of incident years lost to due to disability (YLDs) forms the major component of disability adjusted life years (DALYs) for asthma, the primary metric used to compare disease burden.[245] This estimation is based on expected future disability in incident cases of asthma arising during the study period, but knowledge about asthma incidence in Australia is limited because incident cases are not routinely reported.

There are other uncertainties in the estimation of DALYs attributable to asthma. The calculation of incident YLDs is based on estimation of both incidence and duration of asthma, and both of these are derived from primary data on the prevalence, age-specific mortality and remission rates from asthma.[245] As there is no universally agreed definition of prevalence of asthma, estimates vary substantially depending on the definition that is applied.[242, 246]

As a result, the Australian Burden of Disease Study has estimated asthma incidence from the best available data, being prevalence and remission data from the United States.[247] It remains uncertain whether these are reliable for estimating asthma incidence in Australia.

Nevertheless, comparison of prevalent and incident YLDs in the Australian Burden of Disease Study showed that the two estimates were broadly similar but prevalent YLDs were lower than incident YLDs in the youngest age group and higher than incident YLDs in the older age groups.[247] This suggested that children are generally more likely to have incident conditions while a larger proportion of the elderly population have prevalent conditions. If so, this has ramifications for the allocation of health resources in future to address the issue of preventing new cases of asthma in the young and relapses in the elderly.

The Australian Burden of Disease Study has showed the burden of disease attributable to asthma was dominated by disabled years, especially in the youngest age group.[247] This is consistent with the natural history of asthma, a chronic disease with highest incidence in childhood and low rates of mortality and remission [245], however it is noted that these estimates of life-long burden are sensitive to incidence data, which are not well described for asthma in Australia.

Mortality

The most recent peak in asthma deaths in Australia occurred in 1989, and standardised death rates for asthma have been declining since then.[5] Deaths due to asthma accounted for 0.3% of deaths (169 males, 285 females) in 2000 and 0.2% of deaths (108 male, 206 female) in 2003, most occurring in older age groups.[248] Changes to coding practices with the introduction of ICD-10 coding rules from 1997 onwards resulted in decreased recording of asthma as the underlying cause of death compared with previous years [248], so comparison to earlier years are not reliable.

The risk of dying from asthma was highest in the elderly, and mortality was more common in females than males in people aged 65 years and over. However deaths occurred in all age groups and were more common among people living in less well-off localities of Australia.[6] Australia's age standardised death rates for chronic bronchitis, emphysema, and asthma collectively have been ranked eleventh when compared to twenty other OECD countries[249], with the mortality rate due to asthma in Australia being considered moderately high by international standards.[12]

The decrease in deaths has largely been attributed to a combination of asthma management, education and treatment changes over time, e.g. better use of preventer medications, provision of asthma management plans and a greater awareness of asthma, meaning people are getting help earlier.[250] However, there is little evidence of improved management of asthma in the general practice setting, with a recent survey of general practice activity indicating a significant reduction in rates of presentation for asthma among children but not adults, with no change in severity indicators over time.[251] Recent research in Sydney, Australia, examining uptake of the National Asthma Council's Asthma 3+ Visit Plan[252] suggests a reluctance on the part of both general practitioners and their patients to participate in the plan.[253] Alarmingly, it has been estimated that up to 60% of asthma deaths may have been associated with avoidable factors, and that death from asthma was preventable in many cases.[250]

To highlight this, a study in 1992 examined random samples of children (n = 8,753) from 33 Australian primary schools and their parents (n = 13,945) and concluded that asthma was consistently being under treated.[254] This was highlighted by the fact that preventative asthma medications were only used regularly by 25.5% of the children with probable asthma, 44.3% of the children who had asthma symptoms more than twice a week and only slightly higher rates for those with diagnosed asthma. In the adult group, only 39% were using preventative medications, only 34% had their ventilatory function assessed in the last year, and only 7% had both a peak flow meter and an asthma action plan.[254] Initially, there was an increase in the number of people who had these plans in the early 1990s, however the number of people with asthma who had written asthma action plans has decreased since 1995 to present. Further, many people with asthma who would benefit from use of inhaled corticosteroids have not been using them regularly, and a commensurate steady decline in the use of spirometry in the 5 to 34 years age group has occurred since 1998.[6] It would appear that steps that could be taken to greatly improve the outcomes of asthma and reduce potentially fatal acute asthma episodes are not being embraced by those who would benefit most from them.

Summary

The prevalence of asthma has appeared to rise steadily in both the developed and undeveloped world over the last forty years, with Australia enjoying one of the highest

prevalence rates of asthma in the world.[255] Recent evidence has shown there has been a decline in reported symptoms and reduced hospitalizations in Melbourne children since 1993 [256], supporting the suggestion that asthma prevalence worldwide may have peaked.[257] However, caution needs to be exercised in interpreting these results for wide variations in asthma prevalence have previously been reported across Australian centres in large international prevalence studies.[143, 158]

An absence of reliable incidence data prevents an estimation of the effect new cases of asthma had on prevalence trends, with incidence data so poorly described in Australia that the Australian Burden of Disease Study required the use of international data to estimate disability components.[247] The Australian Burden of Disease study estimated asthma contributed 2.6% of all DALY's in Australia in 1996 with an estimated financial burden of $4.3 billion, and was the ninth leading contributor to the overall burden of disease. For children aged 0 to 14 years, asthma was the leading contributor to the burden of disease accounting for 18% of DALY's for this age group in 1996.[245]

Australian mortality rates due to asthma have been steadily falling for more than a decade, however the risk remains high compared with other nations.[6] It is clear that under-treatment and suboptimal management of asthma remains an important problem in Australia [227, 254, 258], and that deaths may be prevented with better asthma management.[250] Recent surveys confirm that inhaled corticosteroid therapy is not being optimally targeted and people who would benefit from regularly using this treatment are not doing so, despite being the cornerstone of drug therapy for asthma. Others are receiving doses higher than they need, and risking the consequences of long-term side effects.[6] Despite the introduction of an incentive scheme introduced nationally in 2001 to promote structured asthma care in general practice, only 3.9% of all people with asthma have utilised the Asthma 3+ Visit Plan.[6]

In the Australian 2000-2001 financial year, expenditure on asthma was $693 million, representing 1.4% of total allocated health expenditure, of which more than half was expended on pharmaceuticals.[6] Expenditure was highest among children, particularly boys aged 5 to 14 years, and per capita expenditure increased 21% between 1993-94 and 2000-2001.[6] Among adults, expenditure was higher for females than males, reflecting the higher prevalence of asthma in females.[245]

2.6 REVIEW OF OUTCOME STUDIES

The aim of this section is to review international and Australasian literature where studies concerned with asthma place particular emphasis on clinical outcomes in the context of pre-hospital care. In the outcome studies reviewed, there is a diversity of defined populations and outcome measures, and wide variation in study design and strategy. However, in view of the varied aetiology, pathogenesis and diversity of treatment options for asthma, this is not unexpected.

The 'effectiveness' of a service can be defined as the level by which it achieves its objectives, whereas 'quality' is the degree to which it conforms to pre-set standards of care.[259] It follows that the ideal measure of quality would be an outcome measure that can evaluate whether or not care delivered results in the desired standard. Historically, the use of outcome measures has not been successfully built into the assessment of clinical practice, except from work performed in research settings.[260] This can be explained in part by the political drive to measure short-term expedients such as waiting lists and waiting times, and the use of performance measurement instruments that are either process orientated, ambiguous or simply inappropriate.[261]

Recently there has been a shift away from management systems that have been preoccupied with measuring cost and efficiency, toward a greater emphasis on clinical outcome and quality.[262] There is broad agreement about the need to measure the outcome of disease, and as health systems worldwide come under increasing scrutiny, the pressure for health outcomes in current managed-care environments help to stimulate clinical research.[263]

The modern concept of asthma now differs markedly from earlier ideas [264] and as understanding of the pathogenesis of asthma improves, so does the selection of therapies and the way in which they should be used. The presence of a vast amount of information about an ever increasing number of new drugs and delivery devices for asthma make it difficult to establish the most appropriate drug or regimen to use in any given clinical situation.[265] However, it is now clear that evidence provided by outcome

studies is required to not only determine the clinical efficacy of these therapies, but also guide the training requirements and management practices of asthma care teams.[266]

Outcomes research has become an integral part of sweeping changes occurring in the United States health care system [266] and the United Kingdom's National Health Service, and in view of increasing prevalence and cost of asthma to health systems worldwide, efforts to identify and improve asthma outcomes are being encouraged.[262]

2.6.1 International

Direct measures of outcome are not easy to construct and information systems capable of providing data are not always widely available. To overcome this, analysts often develop indicators that are pointers or markers to a desired outcome, rather than a direct measure of it.

Of the majority of studies reviewed in the international literature, interventions for asthma could be readily grouped into either drug therapies or education programs. A third, but less significant group, included lifestyle changes, environmental changes and alternative therapies. Outcome measures and indicators developed from these interventions were readily grouped into those measuring mortality, morbidity and quality of life.

Although mortality is relatively easy to measure, morbidity may include any number of variations in type and scale of indicators. Measurements of lung capacity such as forced expiratory volume in one second (FEV1) and peak expiratory flow rate (PEFR) were the most frequently used outcomes in studies reviewed, but an exhaustive list of outcome indicators were also noted in the literature.

Examples of morbidity outcome indicators included airway hyper-responsiveness [267], the number of corticosteroid bursts [132], asthma related physician visits [268], emergency room visits [269], hospitalisations [270], health care utilizations [271], number of asthma episodes [272], inflammatory markers [273], exacerbation rates [274], frequency of daytime and nocturnal symptoms [171], symptom free days [275], relapse and readmission.[231]

Examples of quality of life outcome indicators included quality of life scores [276, 277], a caregiver's assessment of quality of life [275], self-reported levels of fear, panic and bother [278], compliance to drug therapies [279] and other psychological measures of health.[67, 280]

However, robust outcome indicators not only require the establishment of an appropriate numerator and denominator, but also the provision of clear definitions about the context in which an indicator can be used and interpreted.[262] In an attempt to simplify the measurement of health outcomes, the United States' National Centre for Health Outcomes Development (NCHOD) responded by concentrating on 10 conditions and identifying outcome indicators that were simple enough to define and record so that they could be used in routine clinical practice. Patient-focussed outcome indicators for asthma were developed, and feasibility studies measuring their sensitivity and reliability suggested utility within different health care settings.[262, 281]

This approach to measuring outcome has potential to be widely used and would serve the interests of both patients, carers and physicians, however such a system has yet to be embraced internationally.[281, 282] In the absence of standardized outcome indicators, varying definitions of outcome measures and methodologies between studies will continue to make it difficult to compare reported asthma outcomes between centres nationally and internationally.

However, the popular growth of systematic reviews has helped in part to address this problem. Systematic reviews are scientific investigations in themselves, that use pre-planned strategies and methods to synthesize the results of multiple primary investigations, and help health practitioners keep abreast of medical literature by summarizing large bodies of evidence and helping to explain differences among studies of the same clinical question.[283] These strategies include comprehensive searches of all potentially relevant articles and the use of explicit, reproducible criteria in the selection of studies for review. For each included study, the research designs and characteristics are appraised, data are synthesized and results are interpreted.[284]

A quantitative systematic review, or meta-analysis, is a systematic review that uses statistical techniques to combine the results of two or more independent studies [283, 285],

and is most often used to assess the clinical effectiveness of healthcare interventions by combining data from two or more randomized control trials.[286] An international initiative known as the Cochrane Collaboration has evolved to prepare, maintain and disseminate the results of systematic reviews of health care interventions.[287, 288] Cochrane systematic reviews are a highly regarded source of evidence about the effects of healthcare interventions, partly because they are regularly updated as more information becomes available and in response to comments and criticisms.[284]

Criticism leveled at many studies on the treatment of asthma and outcomes published in peer reviewed journals, and those funded by industry, has been for the presence of serious methodological flaws that limit their value to guide decisions.[289] Systematic reviews have been reported to incorporate strategies to minimize bias and maximize precision [290-293], however caution needs to be exercised in interpreting these claims as systematic reviews are fundamentally limited by the quality of the underlying studies. If the original data is flawed, then results of the systematic reviews cannot be regarded as trustworthy [294], and as the review process itself is subject to bias [283], a balanced assessment of these deficiencies is required by the health practitioner before accepting conclusions of research evidence and health care.

Nonetheless, despite ongoing debate regarding the quality of primary trials included in systematic reviews and meta-analyses [295-297], systematic reviews of randomized controlled trials are ranked as the best evidence for demonstrating the therapeutic efficacy of clinical interventions.[289, 298] Exploring systematic reviews of randomized controlled trials in the context of asthma outcomes allows an overview of the most current evidence in the framework of the three main areas of asthma intervention mentioned previously, namely drug therapies; education programs; and lifestyle and environmental changes and alternative therapies.

Drug Therapies

It is noted that of the many systematic reviews identified that related to outcome indicators for the asthma patient, e.g. admission rates and/or pulmonary capacity, none were directly related to action taken by ambulance paramedics in the prehospital setting. However, interventions and outcomes that were identified and reviewed in context of

acute care in the emergency department may translate directly to changes in the management of patients with asthma in the pre-hospital setting.

Table 6 below highlights three such systematic reviews dealing with drug therapy and delivery in the acute setting. Two of these reviews (19 included studies, 1239 cases) were concerned with the use of inhaled and systemic corticosteroids in the emergency department [126, 299], whilst the other review (31 included studies, 2921 cases) was concerned with delivery techniques of medication.[300] Outcome indicators for these studies included readmission rates and measures of pulmonary capacity. Conclusions found on the timeliness and method of administration of these selected drugs has implications for changes to pre-hospital treatment protocols.

For example, one of the first treatments given to an asthmatic patient by St John Ambulance paramedics is salbutamol, a $beta_2$ agonist medication, via nebuliser. If, as a result of a well-designed controlled trial or systematic review, it was shown that it was advantageous to also initiate a corticosteroid adjunct, it would be expected that changes to pre-hospital treatment regimes would be considered to reflect the new evidence.

There were many more systematic reviews identified that involved clinical measures and outcomes for drug therapies in the asthma patient. Although of great interest for areas concerning both acute and chronic asthma, these reviews were more concerned with treatment initiated in the emergency department or on admission and not directly associated with the area of prehospital care. These have been summarized and can be found in Appendix 1.

Table 6: Systematic Reviews for Clinical Measures and Outcomes, Drug Therapies

Author, Date of Review	Topic	Results & Conclusions
Edmonds, M.L. Camargo, C.A. et. al. 27 May 2003	Early use of inhaled corticosteroids (ICS) in the emergency department treatment of acute asthma.	Included studies: 10 (587 cases). Patients treated with ICS were less likely to be admitted to hospital (OR 0.32; 95% CI: 0.18, 0.54), significant in patients not receiving concomitant systemic steroids (CS) (OR 0.27; 95% CI: 0.14, 0.52). Patients receiving ICS also demonstrated small, significant improvements in peak expiratory flows (PEFR WMD: 7%; 95% CI: 4, 11%) and forced expiratory volumes (FEV1 WMD: 6%; 95% CI: 2, 10%). Inhaled steroids reduced admission rates in patients with acute asthma, but it is unclear if there is a benefit of ICS when used in addition to systemic steroids. There is insufficient evidence that ICS therapy results in clinically important changes in pulmonary function or clinical scores when used in acute asthma.
Rowe, B.H. Spooner, C.H. et. al. 22 Jan 2001	Early emergency department treatment of acute asthma with systemic corticosteroids (CS).	Included studies: 12 (863 cases). Early use of CS for acute asthma in the ED significantly reduced admission rates (N=11; OR 0.40; 95%CI: 0.21, 0.78), with the benefit more pronounced for those not receiving systemic CS prior to ED presentation (N=7; OR 0.37; 95% CI: 0.19, 0.70) and those with more severe asthma (N=7; OR 0.35; 95% CI: 0.21, 0.59). Oral CS therapy in children was particularly effective (M=3; OR: 0.24; 95% CI: 0.11, 0.53). Use of systemic corticosteroids within 1 hour of presentation to an ED significantly reduces the need for hospital admission in patients with acute asthma. Benefits are greatest in patients with more severe asthma and those not currently receiving steroids. Children appear to respond well to oral steroids.
Cates, C.J. Crilly, J.A. et. al. 4 Jan 2006	Holding chambers versus nebulisers for beta-agonist treatment of acute asthma.	Included studies: 31 (2921 cases). Method of delivery of beta2-agonist did nit appear to affect hospital admission rates. The relative risk of admission for spacer versus nebuliser in adults was 0.97 (95% CI: 0.62, 1.49) and for children was 0.65 (95% CI: 0.4, 1.06). Length of stay in ED was similar for adults for the two delivery methods, but significantly shorter in children when the spacer was used (Mean diff -0.47 hours; 95% CI: -0.58, -0.37). PEFR and FEV were also similar for the two delivery methods. Metered-dose inhalers with holding chambers produced outcomes that were at least equivalent to nebuliser delivery. Holding chambers may have some advantages compared to nebulisers for children with acute asthma.

Legend:

PEFR	Peak Expiratory Flow Rate
FEV1	Forced Expiratory Volume (1 second)
WMD	Weighted Mean Difference
OR	Odds Ratio
RR	Risk Ratio
95% CI	95% Confidence Interval
ICS	Inhaled Corticosteroids
LOS	Length of Stay

Education programs

Although it would appear from the number of systematic reviews reported above and in Appendix 1 that drug therapies occupy the majority of asthma research interest, recent trends indicate increased activity in the area of patient education. It has been reported for some time that education interventions directed at the prehospital and preventative care stage for asthma can result in improved outcomes [301-303], and it has recently been concluded that the presence of the simplest education programs for patients with asthma can result in decreases in the rate of readmission, resource use and costs.[304-308]

Also, though not education programs per se, the implementation of actively managed structured asthma programs for patients with asthma and clinical pathways have been shown to significantly decrease length of stay and overall costs, without an increased rate of readmission.[309, 310] Also, it was found readmissions could be avoided with the use of follow-up visits after recent treatment in emergency departments.[311-313]

There were a number of systematic reviews identified that involved clinical measures and outcomes for educational programs with the asthma patient. Once again, there were no clearly identified reviews that dealt directly with the pre-hospital component of asthma care, however there were interesting conclusions drawn from many reviews which have implications for the frequency of use of emergency services by the asthma patient, such as emergency department presentations and hospital admissions (Table 7).

However, it was noted that although there was no firm evidence to support asthma education for children already attending emergency departments in reducing subsequent visits or admissions [314], asthma self-management education programs improved a wide range of outcomes in both children and adults.[315, 316] It would appear that limited asthma education programs may not translate into better outcomes, but when self-management takes the form of either a written action plan or regular medical review, then health outcomes can be improved in adults.[317, 318]

The benefits of primary-care based clinics for asthma have been cautiously proposed, but until further trials have been carried out, effectiveness is yet to be established.[319] Similarly, the use of written individualized asthma management plans for both children and adults was inconclusive due to the small number of trials.[320]

It would appear that education and self-management programs have the potential to reduce emergency presentations, subsequent admissions and other outcomes, but until further trials are carried out, the influence of these measures on the pre-hospital use of emergency services remains unknown.

Table 7: Systematic Reviews for Clinical Measures and Outcomes, Educational Programs

Author, Date of Review	Topic	Results & Conclusions
Wolf, F.M. Guevara, J.P. et. al. 7 Jan 2003	Educational interventions for asthma in children.	Included Studies: 32 (3706 cases). Asthma education programs were associated with moderate improvement in measures of airflow (SMD 0.50, 95% CI: 0.25 to 0.75) and self-efficacy scales (SMD 0.36, 95% CI: 0.15 to 0.57). Education programs were associated with modest reductions in days of school absence (SMD -0.14, 95% CI: -0.23 to -0.04), days of restricted activity (SMD -0.29, 95% CI: -0.49 to -0.08), and emergency room visits (SMD -0.21, 95% CI: -0.33 to -0.09). Effects of education were greater for most outcomes in moderate-severe, compared with mild-moderate asthma, and among studies employing peak flow versus symptom-based strategies. Effects were evident within the first six months, but for measures of morbidity and health care utilization, were more evident by 12 months. Asthma self-management education programs in children improve a wide range of measures of outcome. Self-management education directed to prevention and management of attacks should be incorporated into routine asthma care.
Haby, M.M. Waters, E et. al. 22 Jan 2001	Interventions for educating children who have attended the emergency room for asthma.	Included Studies: 8 (1407 cases). Compared to control (usual care or lower intensity education) education did not reduce subsequent emergency department (ED) visits [4 trials; relative risk (RR)= 0.87, 95% confidence interval (CI) 0.37 to 2.08], hospital admissions [5 trials; RR=0.74, 95% CI 0.38 to 1.46] and unscheduled doctor visits [5 trials; RR= 0.74, 95% CI 0.49 to 1.12). Each analysis showed evidence of heterogeneity among the studies (P<0.01). Subgroup analyses by the overall difference in scale of intervention between treatment and control groups (comprehensive programme versus information only) or the timing of the intervention/recruitment (early versus delayed) gave similar results to the main analysis and still revealed significant heterogeneity between trials. There is no firm evidence to support the use of asthma education for children who have attended the emergency department for asthma as a means of reducing subsequent ED visits, hospital admissions or unscheduled doctor visits.
Gibson, P.G. Powell, H. et. al. 21 Jan 2002	Limited (information only) patient education programs for adults with asthma.	Included Studies: 12. Limited asthma education did not reduce hospitalisation for asthma (WMD -0.03 average hospitalisations per person per year, 95% CI: -0.09 to 0.03). No significant effect on doctor visits, lung function and medication use. The effects on asthma symptoms were variable. No reduction in days lost from normal activity, but in two studies, perceived asthma symptoms did improve after limited asthma education (OR 0.44, 95% CI: 0.26 to 0.74). In one study, limited asthma education was associated with reduced emergency department visits (reduction of -2.76 average visits per person per year, 95% CI -4.34 to 1.18). Use of limited asthma education as it has been practiced does not appear to improve health outcomes in adults with asthma although perceived symptoms may improve. Provision of information in the ED may be effective, but needs to be confirmed.
Powell, H. Gibson, P.G. et al 9 Jan 2003	Options for self-management education for adults with asthma.	Included Studies: 15. 6 studies compared optimal self-management allowing self-adjustment of medications according to an individualised written action plan to adjustment of medications by a doctor. These two styles of asthma management gave equivalent effects for hospitalisation, emergency room (ER) visits, unscheduled doctor visits and nocturnal asthma. 6 studies found self-management using a written action plan based on PEF was equivalent to self-management using a symptoms based written action plan. 3 studies compared self-management options. In one, that provided optimal therapy but tested the omission of regular review, the latter was associated with more health centre visits and sickness days. In another, comparing high and low intensity education, the latter was associated with more unscheduled doctor visits. In a third, no difference in health care utilisation or lung function was reported between verbal instruction and written action plans. Optimal self-management may be conducted by either self-adjustment with the aid of a written action plan or by regular medical review. Individualised written action plans based on PEF are equivalent to action plans based on symptoms.
Gibson, P.G. Powell, H. 12 Mar 2002	Self-management education and regular practitioner review for adults with asthma.	Included Studies: 36. When compared with usual care, self-management education reduced hospitalisations (RR 0.64, 95% CI: 0.50 to 0.82); emergency room visits (RR 0.82, 95% CI: 0.73 to 0.94); unscheduled visits to the doctor (RR 0.68, 95% CI: 0.56 to 0.81); days off work or school (RR 0.79, 95% CI: 0.67 to 0.93); nocturnal asthma (RR 0.67, 95% CI: 0.0.56 to 0.79); and quality of life (SMD 0.29, 95% CI: 0.11 to 0.47). Measures of lung function were little changed. Education in asthma self-management which involves self-monitoring by either peak expiratory flow or symptoms, coupled with regular medical review and a written action plan improves health outcomes for adults with asthma. Training programmes that enable people to adjust their medication using a written action plan appear to be more effective than other forms of asthma self-management.
Toelle, B.G. Ram, F.S.F. 10 Oct 2003	Written individualized management plans for asthma in children and adults.	Included Studies: 7. The written management plans were either peak flow or symptom based, which were compared against each other or compared to no written management plan. Reported outcomes included: medication adherence, hospitalisation, emergency department visits, oral corticosteroid use, lung function, days lost from school/work, unscheduled doctor visits and respiratory tract infections. There was no consistent evidence that written plans produced better patient outcomes than no written plan. For some outcomes, there appeared to be an advantage of one type of plan over the other, but there was no consistency - one type of plan was not consistently more effective than another. The available trials are too small and the results too inconsistent to form any conclusions as to the contribution of written self management plans in the known beneficial effects of a comprehensive asthma care programme.
Ram, F.S.F. Jones, A.,et.al 26 Nov 2001.	Primary care based clinics for asthma.	One trial provided 11 outcome measures of which two showed a significant effect of the intervention. More patients in the intervention group had peak flow meters (RR 1.30; 95%CI: 1.05,1.61) and fewer patients in the intervention group were likely to wake up at nights due to their asthma (RR 0.30; 95%CI: 0.16, 0.81). There is limited evidence of benefit for primary care based clinics, but firm conclusions cannot be formed until good quality trials have been carried out.

Lifestyle changes, environmental changes and alternative therapies

The final area of focus for systematic reviews was that of lifestyle changes, environmental changes and alternative therapies. With few exceptions, the majority of these reviews stated that no reliable conclusions could be drawn on whether these therapies had value, due to insufficient or little evidence. One study involving the use of non-invasive positive pressure ventilation showed promising results in status asthmaticus, but randomized controlled studies were required to determine the role of this intervention in both the emergency and pre-hospital settings.[321] These reviews have been summarized and can be found in Appendix 2.

2.6.2 Australia

In Australia, there has been a dearth of studies that specifically address outcomes of patients with asthma transported by ambulance, but recent years have seen an increase in studies exploring the effects of asthma on morbidity [155, 254, 322], readmission [323-327] and other outcome indicators.[328-331] However, to what extent prehospital care has affected these outcomes remains unknown. By comparison to other health disciplines and medical specialties, prehospital and emergency medical systems (EMS) research continues to lag behind.[332] This shortfall has been recognised, and efforts have been made to identify gaps in the current research effort to identify targets for future research.[332-334]

The Asthma Management Plan (AMP) was developed by the Thoracic Society of Australia and New Zealand in 1989 to provide a more uniform approach to asthma care, aimed at reducing mortality, morbidity and emergency presentations.[329] Launched in Australia in 1990 by the National Asthma Council, the AMP appears to have been successful in raising awareness about asthma in the community.[335-337]

However, whilst research had shown a continued uptake of written asthma action plans and a decrease in the use of inhaled bronchodilator medications [338], there also remained an under-utilisation of preventative therapy by people with asthma [322], especially children where more than one third of children with asthma continue to have sleep

disturbances, and 60% have missed school or experienced other restrictions in their activities.[153] Nevertheless, it is believed that the sustained effect of the activities of the National Asthma Council has contributed to reduced mortality and hospital readmission rates.[322]

Readmission has been used in studies as both an outcome in its own right and also as an indicator of asthma morbidity and the quality of management of patients with asthma in the population.[324, 339] When trends in hospital readmission for asthma in South Australia were examined in relation to the implementation of the National Asthma Campaign, it was concluded the decline in the risk of readmission may reflect changes in asthma severity or improved management practices.[327] What this study highlighted was the fact that readmission rates still remained high, and to further reduce readmissions for asthma there was a need to identify factors related to the presentation for asthma at emergency departments.[327]

There have been efforts to characterise presentations to emergency departments for acute asthma, with the Snapshot of Asthma Study Group project collecting data from 38 emergency departments throughout Australia, examining demographics, severity, treatment and disposition of patients with asthma.[340] It was revealed that 67% of all presentations were for children under 15 years, only 6% were considered 'severe' and less than 1% of patients required ventilation assistance, of which half was non-invasive mechanical ventilation. Overall adherence to treatment guidelines was good, and the majority of patients were treated and discharged from the emergency department.[340]

Similar to results from international studies, Australian studies confirm that despite asthma being the most common preventable reason for hospitalisation, a small proportion of patients with asthma account for a disproportionate number of acute health care episodes.[341, 342] The greatest increase in readmissions occur in the 0 to 4 years group [343-345] and it is suggested that early readmission occurs in two main groups, namely a subset of children with greater disease severity [346] and the elderly [270, 347] This is despite evidence suggesting a fall in admissions for asthma overall.[6]

Factors associated with hospital admissions and repeat emergency department visits have been identified as seasonal changes [324, 344], length of stay for a previous admission

for asthma [324], possessing a written asthma action plan [336], poor patient adherence to inhaled corticosteroids [348] and avoidance coping and attitudes to self-management.[341]

Further, it was found that follow-up visits to a physician reduced asthma relapses in people recently treated in emergency departments [349], and either the presence of an asthma management plan or clinical pathways within emergency departments were found to have a positive influence on asthma management [350], similar to conclusions found in international studies.

However, despite written asthma management plans becoming a core component of asthma management in Australia, the use of these plans by patients remain too low.[336] Importantly, caregivers with written instructions were more knowledgeable about asthma and more likely to report following the management plan during an asthma attack [336], so there is potential to improve outcomes through these plans. It appears that unless the use of written plans by patients increase, this potential may never be realised.

In Australia, the Australian Institute of Health and Welfare (AIHW) has taken a holistic approach to the issue of clinical outcomes and measures for asthma.[10] They proposed a comprehensive list of asthma indicators in consultation with consumers and representatives from clinical, academic, statistical, health policy and health prevention backgrounds.[242] These indicators relate to the overall burden of disease due to asthma in specific areas such as health status and outcomes, determinants of health and health system performance and were designed to highlight factors that have potential to influence the rate and severity of asthma.[10]

The inclusion of these indicators broadens the focus from just clinical and physiological outcomes to also include humanistic and psychosocial outcomes, and the complete list of indicators proposed by the AIHW can be found in Appendix 3. Many of these indicators can be derived directly from administrative datasets routinely collected, those of interest including emergency department attendance, hospital separations and death rates.[10]

These indicators in particular are of great relevance, for these variables are available from the linked dataset created for this study and will be used in statistical analyses

performed later in this thesis. Factors of interest highlighted previously such as the effect of seasonal change, length of stay and mechanical ventilation on outcomes such as readmission and mortality will also be explored in the regression modelling section of this thesis.

2.7 PREHOSPITAL CARE OF ASTHMA

The principles of the prehospital care of asthma differ little from those discussed previously in the emergency treatment of asthma. However, there are two distinct phases involved: home-managed and self-administered care received by the patient before emergency medical services (EMS) are sought, and care received from EMS on attendance.

It has been previously mentioned that an important component of the treatment of asthma in the community is a management or 'action' plan that can be followed by a patient and their family prior to a decision to attend emergency department or call for EMS.[217, 224, 336, 337] However, regardless of the presence of a written asthma plan, effective management of asthma relies on the compliance of the asthma patient to their prescribed medication regimes and the regular measurement of lung function. Poor compliance will often lead to the use of EMS services, and it has been suggested that admission to hospital due to an exacerbation of asthma may represent a failure of prehospital management to prevent an attack or bring about its remission.[351]

Therefore, emergency department visits by asthmatic patients can not only be considered a measure of the severity of asthma, but also a reflection of the degree of control of asthma in the community. For example, in Australia it has been estimated that approximately 8% of people treated for asthma at an emergency department or in hospital have re-attended within 28 days.[6] These re-attendance rates are lower in children and in those aged over 65 years, compared to other adults.[6] It can be seen that, even without knowing the proportion of these patients transported by ambulance, or whether the treatment they received by ambulance paramedics was effective, the frequency of visits and rates of admission and relapse still become an important factor in determining and understanding the demand for EMS.[352]

The following sections explore the role played by emergency medical services in both the international and Australasian prehospital setting for the treatment and transport of the asthmatic patient.

2.7.1 International

Internationally, studies published during the 1990's have shown the prehospital care of asthma by emergency services to be less than optimal. A 1993 retrospective review (n = 383) of advanced life support (ALS) found that asthma constituted the majority of paediatric emergencies in the prehospital setting an inner city EMS system, yet factors that influenced the paramedic judgement in treating asthma in children were frequently inappropriate.[301]

A 1995 study of paediatric asthmatics requiring hospitalisation in Nevada, USA [353], revealed only 63% of cases had a marker of asthma severity noted on the EMS record, 26% of cases did not receive oxygen in the field and 30% of cases were hypoxic at emergency department presentation. None of the hypoxic patients had received albuterol in the field and one did not even receive oxygen. A small sample size (n = 27) restricts the extent to which these results can be extrapolated, but a larger 1996 audit (n = 252) of patients treated by the London Ambulance Service revealed similar results in the form of under-recognition of asthma, underestimation of the severity of attacks and a lack of objective measurements by ambulance crews.[354] A re-audit in 1999 using the same protocol (n = 532) showed under-recognition and under-treatment of severe asthma remained, and pre-hospital documentation of key observations did not improve.[355] In view of the reliability of the audit instrument used, and the fact that training had been initiated for all operational staff after the first audit, this result remains cause for concern.

A recent German study analysed transports of patients with respiratory emergencies and also found that only 41% of the patients with asthma transported received anti-obstructive inhalation therapy.[356] Given the fact that acute asthma exacerbations can be life threatening, recognition of the severity of asthma by EMS personnel is paramount. However, even if a patient's condition is correctly assessed, EMS personnel have often been limited in choice of therapy and medication.[357] This situation highlighted the need for increased training and standard protocols for the pre-hospital management of acute asthma. This has happened with the evolution and acceptance of asthma management

guidelines [358], growing momentum for increased levels of training for ambulance paramedics [359, 360], and an increased repertoire of treatment options.[357, 361-363]

Early studies had showed that ALS providers could successfully be trained within a standard curriculum to identify and safely treat patients with asthma with inhaled metaproterenol [364] and nebulised isoetharine ($beta_1$ and $beta_2$ agonist) [365] in the prehospital environment. Similar studies showed that non-ALS trained ambulance staff could also safely administer salbutamol [366, 367], which subsequently improved patient comfort and morbidity.[368]

Therefore, as ambulance paramedics and EMS staff became increasingly empowered with the responsibility for first-line management of acute asthma, the decision to initiate treatment and medication was now being made on initial ambulance attendance. As it is often some time before the patient reaches the emergency department, it was no longer a question of whether ambulance paramedics were capable or qualified to treat, but rather what choice of treatment and medication was most appropriate for the asthmatic patient.

In recent years, efforts to ascertain optimal treatment regimes in the prehospital setting have been initiated. One such study examined the merits of the use of $beta_2$ agonists by ambulance crews and the best methods of delivery. A prospective comparison across three districts in South Wales concluded that for wheezy and breathless patients (n = 130), 5mg of salbutamol given by oxygen-driven nebuliser was more effective than either 5mg of terbutaline via Nebuhaler (a type of mechanical device to deliver medication to the lungs) or 200mg salbutamol via a pressurised inhaler.[369] There were greater reductions in respiratory rate and breathlessness score and more improvement in PEFR in the group receiving nebulised salbutamol than in the other two groups.[369] Although a small sample, the use of objective measures and a significantly improved pulmonary capacity in the nebulised group provided strong evidence of the effectiveness of $beta_2$ agonists via nebulisers. This was corroborated in a separate study which found nebulised salbutamol to be an effective and safe treatment for acute asthma when administered by ambulance personnel.[367]

A United States study explored the effectiveness of epinephrine (adrenaline) and metaproterenol via different treatment regimes for asthma in adults in the prehospital

setting, concluding that nebulised metaproterenol was as effective as subcutaneous epinephrine in the prehospital treatment of adult patients with acute asthma.[370] Further studies confirmed that the administration of metaproterenol was more effective using a nebuliser than a metered-dose inhaler.[371]

Since these studies, the strategy of oxygen and bronchodilators has became standard prehospital protocols for many EMS systems, but trials involving new drug and treatment regimes have also been conducted in the prehospital setting. For example, in an attempt to reduce both mortality and the need for hospital care for asthmatic patients, an emergency mobile asthma treatment programme in Sweden was set up where ambulance crews gave 24 hour treatment with bronchodilators, followed by injections of corticosteroids by day nurses if there was no improvement.[372] In 53% of cases (n = 240), two or more treatments were given, and out of all the cases, more than 70% improved after treatment. Of the 6% that were unconscious on attendance, 71% survived after therapy.[372] This study suggested that EMS personnel in a pre-hospital environment were quite capable of successfully administering complex treatment. Further, and despite the ongoing debate over the use of adrenaline in acute asthma [373, 374], regional EMS systems in New York have implemented the administration of adrenaline and intravenous methylprednisolone (a corticosteroid) to patients with asthma as one of their medical options following telephone consultation with medical control physicians.[375]

Practice based on the evidence of studies such as these has given EMS personnel more autonomy to select a choice of treatments, and to initiate them in a timely and appropriate manner. However, there are still issues remaining with patient utilization of EMS services and the initiation of treatment by EMS personnel.

Nowadays, ambulances equipped with nebulised bronchodilators provide the optimal mode of transport to hospital with acute asthma, but it has previously been shown that there is a noticeable shortfall in the administration of bronchodilators and corticosteroids for acute asthma before arrival at hospital, although it is noted that in some cases this is due to constraints placed on EMS personnel [357] and not always errors in judgement.

However, an Edinburgh study did find that for those patients referred to hospital (n = 150) who were transported by ambulance and received nebulised $beta_2$ agonists, airflow obstruction had improved upon arrival at hospital, but 25% of ambulance-transported patients arrived without having nebulised $beta_2$ agonists, and 37% without having corticosteroids.[376] It must be mentioned that a significant proportion of the population with asthma referred to hospital did not use the ambulance and instead travelled to hospital by car, perhaps in the mistaken belief that personal transport would reduce the journey time to hospital. More worrying though, is that patients enrolled in an asthma management program were the least likely to have received nebulised $beta_2$ agonists, and the most likely to have travelled to hospital by car rather than ambulance.[376]

This highlights two main issues in the prehospital arena: inadequate management by EMS personnel, and poor self-treatment by patients with asthma via a lack of understanding or lack of compliance to protocols within management plans. Ironically, these are frequently the group of patients most likely requiring timely and adequate treatment.[336, 377] Of the two issues mentioned above, identifying the reasons for under treatment by EMS personnel would seem the simplest to achieve, yet the accuracy of diagnosis and quality of care by ambulance paramedics has remained largely unreported. To examine the area of accuracy of diagnosis, this thesis will calculate and report the sensitivity and specificity of the St John Ambulance paramedics' diagnosis of asthma by comparing it to the hospital principal discharge diagnosis. However, adequacy of treatment modalities given by ambulance paramedics cannot be reported due to incomplete data.

One other group of patients with asthma warrants consideration, and that is those who present with severe asthma. With early and aggressive management the majority can be managed without the need for intubation and ventilation [108], and very few people admitted to hospital with asthma required mechanical ventilation.[6] However, if required, mechanical ventilation can be life saving (by resting the patient and their respiratory muscles, re-oxygenating, and correcting acidosis), but there is an associated high incidence of morbidity and mortality, usually due to the consequences of hyperinflation [108], and despite optimum therapy and management, deaths do occur.[378]

New strategies for the treatment of severe asthma in the prehospital setting continue to be explored. For example, there is anecdotal evidence for the technique of mechanical external chest compression (MECC), a technique historically used in the intensive care situation, to be used for patients suffering from severe, sudden-onset, asphyxic asthma in the prehospital setting [379], but there are no published trials of the technique yet. Moreover, the current role of prehospital treatment, and in particular that provided by emergency medical services, on the survival of severe asthma group of patients has yet to be determined. Hence, in the modelling section of this thesis, ventilation is used as an indicator for severe asthma to explore the relationship between pre-hospital management by ambulance paramedics and the outcomes of survival and readmission.

2.7.2 Australia and New Zealand

Australia has one of the highest prevalence of asthma in the world, yet suboptimal management and under-treatment of asthma remain important problems.[5, 6, 254] Therefore, correct recognition and treatment of acute exacerbations, and correct prehospital management of asthma has the potential to reduce an enormous burden on the health system and contribute to a reduction in morbidity and mortality.[3]

Internationally, there have been two major areas of concern in the prehospital management of asthma; poor management of asthma treatment by the patient, and inadequate management of acute asthma episodes by EMS personnel. However, it remains difficult to ascertain to what extent this shortfall in prehospital management has been addressed in the Australian context, as there is little information available in the literature.

Poor management of asthma treatment by the patient

In 1992, one Australian study interviewed parents of children with asthma (n = 100) sequentially admitted to hospital to determine the frequency of the use of asthma action plans and the intensity of prehospital treatment.[380] Results showed that 51% of parents possessed some form of action plan, and 84% of this group used their plan prior to the child's admission to hospital. It also showed that of those children with more than two prior admissions to hospital for asthma, 79% had an action plan. There was a widespread possession of nebuliser units, with regular bronchodilator use, but it was found steroid use was inadequate, and overall prehospital management was considered to be suboptimal, despite a concurrent national asthma campaign.[380] The small convenience sample and single hospital centre of this study limits external validity, but it did highlight the phenomena noted earlier where it seems that patients who have had successive admissions for asthma more readily embrace the ownership and use of action plans. It would appear that patients might not take self-management of their asthma seriously until their condition has deteriorated.

The 1996 South Australian Health Omnibus Survey (a multistage, systematic, clustered area sample of people who lived in metropolitan Adelaide and major country centres), surveyed a sample of people aged 15 years or older (n = 3,010) to examine the relationships between ownership of written asthma action plans, asthma morbidity, use of devices, and patients' perceptions of their asthma management.[377] It found that having a written asthma action plan was associated with regular corticosteroid use, understanding asthma, having enough information and owning a peak flow meter, but the ownership of asthma action plans by people with self-reported asthma was only 33% and had declined since 1995 (42%), and 1992 (51%).[380] The survey concluded that ownership of asthma action plans in South Australia was suboptimal.

The most recent AIHW report on asthma in 2005 [6] has since concluded that although written asthma action plans have been shown to greatly improve the outcomes of asthma and reduce attacks, recent surveys (1998 to 2001) show the proportion of adults with current asthma who possess an asthma action plan only ranged from 15% to 22% and children ranged from 21% to 25%.[6] Hence, despite an initial increase in the use of

action plans during the early part of the 1990s, coinciding with the public awareness campaigns of the National Asthma Council [381], this trend has not been sustained.

A recent study in New South Wales interviewed adult asthmatics (n = 79) admitted to a tertiary hospital and found that during an exacerbation of asthma and prior to hospital attendance, only 27% of subjects had measured their PEFR, 19% had commenced or increased the dose of inhaled steroids, and only 22% had commenced oral steroids.[382] Despite the small sample size, this lends support to the argument that the failure of prehospital management to prevent the necessity of hospital attendance in most cases stemmed from a failure to implement currently recommended actions or treatments for exacerbations.[382]

In New Zealand, the same conclusions were being reached by researchers regarding poor prehospital management by patients, and although conclusions drawn from overseas studies may not be entirely applicable to the Australian environment, given the similar epidemiology of asthma in both Australia and New Zealand and the limited number of studies in Australia, it would seem reasonable to report these results.

In fact, evidence of inconsistent prehospital treatment of asthma in Australia and New Zealand [383] was one reason for the development of the Asthma Management Plan (AMP), an initiative of the Australian National Asthma Council [384] and developed by the Thoracic Society of Australia and New Zealand in 1989 to provide a more uniform approach to asthma care, aimed at reducing mortality, morbidity and emergency presentations.[329]

In New Zealand, early studies investigated mortality rates from asthma and compared them to a similar group of patients in England, finding the verified asthma mortality rate in New Zealand was over twice that in England, despite many characteristics of patients and management being quantitatively similar in the two countries.[202] These included poor compliance with treatment and deficiencies in emergency and long-term care. New Zealand had an apparently higher rate of non-preventable deaths from asthma, suggesting a greater severity of asthma, however it was concluded that in both countries, most deaths were associated with poor assessment, underestimation of severity, inappropriate treatment and delays in obtaining help.[202, 383]

Nearly ten years later in 1995, the New Zealand National Asthma Mortality Study associated mortality with severe asthma, underassessment of severity, under-treatment with corticosteroids, over-reliance on bronchodilators, discontinuity of medical care and delay in seeking help.[385] It would seem that the lack of self management by the patient in the prehospital setting remained a problem.

These results simply mirror the same themes identified in Australia, where an audit of the assessment and treatment of acute asthma and the subsequent application of the AMP identified suboptimal assessment and treatment of acute asthma and deficits in implementation of the AMP.[386] It was clear that mortality, and morbidity increased not only as a result of patients under-treating themselves [386], but also not being provided with adequate skills to manage future asthma attacks.

Concerns about the education and management of asthma in schools led to the convening of the Asthma Special Interest Group, a subcommittee of the Thoracic Society of Australia and New Zealand, to draft a national guideline for school staff to provide optimal management of asthma in the school setting.[387] Issues identified included the availability of an asthma first aid kit; correct use of bronchodilator aerosols by puffer and spacer devices; and clear instructions as to when to notify parents and when to call an ambulance to the school.[387]

A series of studies in New Zealand have also helped to draw focus on the problem of inadequate prehospital treatment and patient education. A questionnaire was developed to determine the level of practical knowledge a patient held for the self-management of acute asthma, via a series of hypothetical scenarios. The errors that patients frequently made in their hypothetical responses were parallel to errors reported in real clinical situations, despite the patient population receiving considerable education and training about how to manage asthma.[388]

This raised the question of whether asthma education, despite increased knowledge, actually influenced patient behaviour. It seemed that there were differences between a patients' knowledge of self-management and their actual behaviour, particularly in terms of life-saving actions.[389] It was found that psychological (e.g. having something

stolen in the last year, concern about having to take time off), health-care (e.g. concern about medical expenses), and socio-economic factors (e.g. lack of paying job,) had a powerful and differential influence on knowledge and behaviour.[27] This was borne out by subsequent studies confirming that despite recent educational advances, serious management errors were common in those admitted to hospital with acute severe asthma. Further, most treatment errors were related to patient self-management behaviour, and could also be predicted by a variety of socio-economic and psychological factors.[390]

The studies described above support the widely held belief that most acute asthma attacks are preventable, but the challenge faced is to change patient behaviour in the light of adverse socio-economic and psychological factors [27], poor asthma knowledge and other barriers to medication use.[391] If asthma sufferers are either unable or unwilling to proactively manage their asthma, then this will continue to contribute substantially to the perceived shortfall in prehospital care.

Inadequate management by EMS personnel

The second major area of concern in the prehospital management of asthma is the degree of inadequate management of acute asthma episodes by EMS personnel. As noted previously, the few international studies that focussed on prehospital care provided evidence that ambulance paramedics may make management errors [301, 353-357], but in Australia there is insufficient evidence to indicate number or scale.

Although there is a body of knowledge regarding general practice encounters [6] and visits to hospital emergency departments for patients with asthma [6, 340], there is a dearth of Australian and New Zealand studies in the area of ambulance transportation of patients with asthma and the form or standard of treatment they received by ambulance paramedics. Hence, in the absence of local evidence, and despite the wide variation in the epidemiology of asthma worldwide and differences between emergency medical systems, it is reasonable to assume that problem areas identified in the prehospital treatment of patients with asthma internationally and discussed previously, may also be applicable to the Australian scenario.

Therefore, the elevation of asthma in Australia to a National Health Priority Area [6] and the development of the Asthma Management Plan [10] will provide opportunities to close the gap between knowledge of treatment and actual practice, if barriers to uptake of recommendations are removed. Methods to remove the barriers to effective prehospital treatment might include appropriate patient education and engagement in self-management [334], improving doctor-patient relationships [392] and addressing disincentives to promote organised asthma care in general practice (e.g. improving the general practitioner uptake of the Asthma 3+ Visit Plan).[253]

Further, until further local research in the area of prehospital care of patients with asthma is undertaken, evidence presented internationally should be considered in providing relevant evidence-based knowledge to guide continual training and evaluation of clinical skills by ambulance paramedics. This will provide the opportunity to provide timely and appropriate prehospital emergency care to patients with asthma.

2.8 RESEARCH QUESTIONS

The previous review of the literature has provided information on a variety of aspects of the epidemiology, prehospital care and treatment of patients with asthma. The value of the contribution of this information to the body of knowledge is without dispute. However it offers little insight into the relationship between the use of ambulance services by patients with asthma, and their outcomes. Lack of knowledge in this relationship raises the following research questions with regard to the WA Data Linkage System and the Ambulance Database.

- What are the age and gender characteristics of patients suffering asthma transported by ambulance, and have trends in these characteristics changed over time ?

- What is the sensitivity and specificity of ambulance paramedic-diagnosed asthma cases ?

- Has the priority code and problem urgency of asthma transported patients changed over time ?

- Is there a circadian, weekly or seasonal variation in the number of patients with asthma transported by ambulance, and have these changed over time ?

- What is the outcome, in terms of survival and readmission to hospital? Specifically, is outcome influenced by problem urgency, co-morbidity or socio-economic factors ?

This study was designed to address these questions and, in doing so, develop an understanding of the epidemiological trends and outcomes of patients with asthma who access ambulance services in the prehospital setting.

3.0 METHODS

3.1 INTRODUCTION

The aim of this chapter is to first describe the physical context of the study by describing the geographic and demographic characteristics of Perth, Western Australia (WA), and then provide a methodological framework for the research undertaken in this thesis.

The St John Ambulance Western Australia (SJA-WA) service provides the sole source of prehospital emergency care in Perth. To provide perspective on the prehospital management of asthma within the Perth metropolitan area, the role of SJA-WA ambulance paramedics in the clinical care of patients with asthma is discussed. As the major source of data that supports the research objectives of this thesis, the collection and processing of data in the WA Ambulance Dataset is described.

Vital components of this thesis depend on results derived from data linkage, so the process of data matching and linking is also described and discussed. Data validation has not previously been performed on the information contained in the WA Ambulance Dataset, so details of the design and results of validation are reported here along with calculation of the sensitivity and specificity of the ambulance data.

The development of comorbidity and socioeconomic indices are also described in this chapter, along with a description of statistical modelling techniques and the development and choice of suitable models for analysis of the linked data.

3.2 PERTH GEOGRAPHY AND DEMOGRAPHY

Australia comprises a land area of about 7,692,024 square kilometres. The land lies between latitudes 10 degrees 41 minutes south (Cape York, Queensland) and 43 degrees 38 minutes south (South East Cape, Tasmania) and between longitudes 113 degrees 09 minutes east (Steep Point, Western Australia) and 153 degrees 38 minutes east (Cape Byron, New South Wales). The most southerly point on the mainland is South Point (Wilson's Promontory, Victoria) 39 degrees 08 minutes south. The latitudinal distance between Cape York and South Point is about 3,180 km, while the latitudinal distance between Cape York and South East Cape is 3,680 km. The longitudinal distance between Steep Point and Cape Byron is about 4,000 km. The area of Australia is almost as great as that of the United States of America (excluding Alaska), about 50% greater than Europe (excluding the former USSR) and 32 times greater than the United Kingdom.[393]

Western Australia is one of the six states of Australia, occupies the western 33% of Australia, has an area of 2,529,875 square kilometres, and a coastline of 20,781 kilometres. Approximately 37% of Western Australia is considered tropical, the remainder temperate.[394] At Census 2001 there were 1,832,008 persons living in Western Australia, of which 1,323,392 (72%) lived in the statistical division of the capital city, Perth, located in the south west of Western Australia.[395] Table 8 below shows a breakdown of the Perth Census 2001 population by age and sex.

Table 8: Population of Perth, WA 2001, by Age and Sex

Age Group	0-14 years	15-24 years	25-44 years	45-64 years	65 years and over	Total
Male	141,046	100,828	192,600	151,230	64,346	650,050
Female	133,303	98,670	203,202	154,829	85,338	675,342
Total	274,349	199,498	395,802	306,059	149,684	1,325,392
Percent	20.7%	15.1%	29.9%	23.1%	11.3%	100%

Note: Overseas visitors are excluded from these counts
Source: ABS 2001 Census, Perth Statistical Division.

3.3 WA AMBULANCE SERVICE

The SJA-WA is a private organization employing both full-time and volunteer staff and deploying resources throughout Western Australia, and represents the largest geographical area in the world covered by a single emergency ambulance service.

This service is available to both members of the public who are seriously ill or injured and non-emergency services for patients who need medical, surgical or convalescent stretcher transport. St John provides paid ambulance services in the metropolitan area and a mixture of paid and volunteer services in eight country locations. Volunteer services are provided in over 150 other locations and are responsible for providing a state-wide emergency ambulance service. In 2001, SJA-WA attended 142,708 calls throughout Western Australia, an increase of 3.4% from the previous year, with 115,608 calls attended within the Perth metropolitan area.[396]

The provision of ambulance services by SJA-WA is based on a fee-for-service basis, with revenues in 2001-2002 totalling $65.3 million. Of the metropolitan revenue, 65% was received from ambulance services, 9% from first aid training, and 23% from the Health Department of Western Australia, who contracts SJA-WA to provide emergency ambulance services for all of Western Australia. In 2001-2002, SJA-WA ambulance workload consisted of 27% emergency cases, 28% urgent cases, and 45% non-urgent or booked cases. The cost of ambulance services is not covered by Medicare, and it is not free to Healthcare, Pharmaceutical or Pensioner Benefit card holders. However, patients are able to insure against the cost of ambulance transport, but a co-payment is applicable for insured patients where they are not taken to an emergency department.[396]

The Ambulance Operations Centre (AOC) is the hub of SJA-WA communications, and operates at headquarters situated in suburban Belmont, WA. All emergency calls are directed through the AOC where dispatch operators use a Computer Aided Dispatch (CAD) system to take details, and dispatch ambulances at various priorities, depending on problem urgency (Table 9).

Problem urgency is assessed by ambulance paramedics on attendance, and approximately equates to the Australasian Triage Score, a scale for rating the clinical urgency of the person's need for medical and nursing care. ATS is also assessed by a designated ED staff member immediately after the arrival of the patient to ED. It is used primarily as a clinical tool for ensuring that patients are seen in a timely manner, commensurate with their clinical urgency.[397]

Table 9: SJA-WA Priority Codes

Priority	Urgency	Example Cases
1	Life-threatening (Lights and Sirens)	cardiac arrest, chest pain, trauma, and collapse
2	Urgent, but not life-threatening (No Lights and Sirens)	severe dyspnoea, ankle or wrist fractures, abdominal pain
3	Non-urgent (Non-booked cases)	chronic disorder, rash, back pain
4	Non-urgent (Booked cases)	nursing home transfers, booked treatments
5	Sporting Events Standby	football matches, public events

Source: Personal Communication, Data Manager, St John Ambulance (Western Australia), 2002

In addition to receiving the call and dispatching ambulances accordingly, time specific information is also automatically recorded by the CAD, and is updated by radio-transmitted information from the ambulance. This time information provides critical information that form the basis of performance indicators, such as response-time and arrival time, and will be discussed in greater detail in the section dealing with the validation of the WA Ambulance Dataset.

The number and location of metropolitan ambulance stations have varied over time, however at the conclusion of this study period there were 20 twenty-four hour ambulance crews stationed at 19 locations (two crews at Perth central station), with a further 11 ambulances providing coverage during day shift. There were also three

volunteer ambulance crews available at the northern, eastern, and southern extremes of the metropolitan area.

Two ambulance paramedics staff each ambulance, at least one being trained to the qualification of paramedic. Duties are undertaken on a rotation basis, alternating driving and patient care. Backup ambulances are called for if a patient's condition requires the attention of both ambulance paramedics, or where there are multiple patients.

The St John College of Prehospital Care collectively covers the various requirements of Ambulance Officer Training, First Aid Training, and Industrial Paramedic Services and Training. Ambulance staff undergoes three years of training and practical work experience before they qualify as an Ambulance Paramedic, then undergo regular refresher programs. Their training consists of formal in-house training, fieldwork, clinical experience supervised by qualified Ambulance Officers and clinical placements in hospitals. Recent additions to curricula include advanced airway management skills and intravenous cannulation techniques.[396]

3.4 RECORD LINKAGE

3.4.1 History of Medical Record Linkage

'Record linkage' may be defined as the bringing together in a single file, of records derived from different sources, but relating to the same individual or event.[398]

Record linking has a number of important applications in the area of public health and injury surveillance.[399] Often necessary in epidemiological research, accumulation of information by record linkage is not a new concept. However, with the advent of advanced automatic data processing, the potential and scale of linkage operations has been greatly increased. Before the use of computer technology, specific studies required manual linkage of data, whereas now it is possible to routinely link together large data files relating to whole populations.

The value of record linkage for epidemiological purposes has been previously described. These included a prospective study where questionnaire replies were linked to death certificates to describe the effect of smoking on lung cancer [400], the linkage of hospital and death records to industrial exposure records to show a relationship between chemicals and bladder cancer [401, 402], and the linkage of episodes of radiotherapy and diagnostic irradiation to childhood malignancies.[403, 404] Without computer assistance, these studies involved a huge amount of persistence and clerical effort, and underlined the problem that, although simple in concept, many studies may never come to fruition either due to the effort required, or because of inaccessibility of data.[398]

Since then, ad-hoc linkage of health records has been used for many purposes, including public health surveillance, primary prevention research, natural history and prognostic research, and the utilisation, adverse effects and outcomes of health services.[405] Record linkages in areas such as taxation and criminal research are well established [406, 407], but serve administrative purposes rather than the objective of population based research. The few examples of comprehensive and sustained record linkage systems included the Oxford Record Linkage Study, Scottish Record Linkage System, Rochester Epidemiology Project, and the Manitoba Population Health Information System.[405]

Oxford Record Linkage Study

In 1966, Acheson pioneered one of the most important record linkage projects known as the Oxford Record Linkage Study (ORLS), and defined terms and categories for handling routinely collected data.[408] At the time, Britain had a single health care system that provided almost all medical care for the population, and therefore an opportunity existed to follow the medical record of individuals from birth to death.

This ORLS was designed to test the feasibility and cost of prospectively accumulating information about key health events for a defined population in cumulative personal and family files. Other aims involved developing computer methods of record linkage, studying the applications of the files in medical and operational research, and to promote its extension on a national basis if successful.[409]

The ORLS resulted in many papers being published, and has been influential outside its own region on other linkage projects, especially the Scottish Record Linkage System.[410] As a result, record linkage has since been widely acknowledged as an important epidemiological tool, however although the term has become one of general use[411], there still only a few examples of record linkage systems worldwide.[405]

The data provided by the ORLS enabled a number of notable studies to assess the trends and outcomes of surgical interventions [412-415], prevalence studies of disease processes [416-418], trend studies [419-422], and other common conditions.[423-426] Yet, despite a significant number of papers published over more than forty years, it is generally considered that the study has under-performed, and that it really only scratched the surface of possibility.[427]

Scottish Record Linkage System

Scotland had long held sets of computerised medical records at a national level that were large in time and scope.[410, 428] However, they only contained information about episodes of care, since there was no systematic method to establish which records belonged to the same patient.

The Scottish Record Linkage System (SRLS) resulted from a decision in the mid-1980's to bring an end to existing procedures and to implement a new record linkage system.[410] It was envisaged that a new system would enable linked data to be simply interrogated rather than re-linked for each inquiry, and that existing demands for epidemiological and health services research based on linked data could be satisfied more rapidly. More importantly, it was felt that increasing emphasis on the management and monitoring of health service activity and the quality and outcomes of care would require a facility for the rapid generation and analysis of patient-based data.[410]

The long term goal of the system was that all records held centrally should be brought together into one data set with all records pertaining to each patient grouped together, with facilities for carrying out ad-hoc linkages.[410] For the first three years, the project developed and implemented techniques of record linkage and constructed the linked data sets. This national database linked inpatient data to death certificate information for a population of approximately 5.1 million.[429] Since then, new data are linked in to the database on an annual basis, where data from 1975 to date comprises 18 million records for almost 4 million people, which is used extensively to support clinical audit and effectiveness within the NHS in Scotland.[430]

The SRLS, by virtue of its completeness of data, continues to provide a rich environment for studies that not only can identify disease prevalence [431]and outcome indicators [432, 433] but also can be reliably used to detect differences in quality of care.[429] Another aspect of these data includes the opportunity for assessing the effectiveness and safety of new medicines. New linkage techniques have played a greater role by

providing information on linking drug exposures and outcomes in general practice [434] and making a significant contribution to pharmaco-vigilance and drug safety studies in the entire population of Scotland.[435]

Rochester Epidemiology Project

The Rochester Epidemiology Project (REP) is a unique medical records-linkage system that encompasses the care delivered to residents of Rochester and Olmsted County, Minnesota, and contains patient details since the beginning of the twentieth century.[436] It was envisioned that a population based data resource could be developed by combining the clinical documentation of the Mayo Clinic with that obtained by other community providers, most notably the Olmsted Medical Group and its affiliated Olmsted Community Hospital.[437]

The resulting system now provides a capability for population based studies of disease causes and outcomes that are unique in the United States.[436] By enabling access to details of medical care given to local residents, the 'diagnostic archive', the project is able to provide accurate incidence data for almost any serious condition and to support population based analytical studies of disease causes and outcomes. Hence, epidemiologic studies of a wide range of disorders have been possible [438-442] and have culminated in almost 900 publications since the system was organised in 1966.[436]

Olmsted County is one of the few places in the world where the occurrence and natural history of diseases can be accurately described and analysed in a defined population for a half century or more.[436] In particular, secular trends in morbidity and mortality can be assessed, such as the association between age of onset of disease and age of death.[443] However, there are limits to the REP as a resource for epidemiologists, due to the small size of the local population. The diagnostic archive is too small to provide definitive information about rare but potentially important conditions, and the homogeneity of the population limits the extent to which results based on it can be generalised.[437]

Manitoba Population Health Information System

University-based researchers in Manitoba, Canada, began to use administrative data routinely collected as part of the national health insurance plan to design an integrated database and population-based health information system (POPULIS).[444] The system permits analyses of demographic changes, expenditure patterns, and hospital performance in relation to the population served.[445]

More specifically, POPULIS has provided decision-makers with the capability to make critical comparisons across regions and subregions of residents' health status, socioeconomic risk characteristics and use of hospitals, nursing homes and physicians.[445] The integrated database now facilitates outcomes research across hospitals and counties, utilisation review within single hospitals and longitudinal research on health reforms.[445]

3.4.2 Medical Record Linkage in Australia

The contribution of record linkage studies to public health interventions cannot be underestimated. Moreover, for most populations, information already exists on health status and other factors that influence health at many points during a lifetime.[446]

In Australia, many of the health outcomes of interest to epidemiologists are routinely recorded in administrative databases or are available from medical records. These include the births, deaths and cancer registers, the Health Insurance Commission (HIC), and the Pharmaceutical Benefits Scheme (PBS). The Australian Bureau of Statistics (ABS) also conduct regular health surveys which include individual health data and risk factors, and a five yearly census elicits the changing demographic, social and economic characteristics of individuals.[446] As information exists already for many individuals, the process of record linkage is a viable alternative to collecting data from individuals.

Although there have been numerous studies conducted using the linkage of population-based records to date, there have been relatively few record linkage studies in Australia, compared to North America and Europe. Notably, most of these have used state rather than national data. Examples of state based research using record linkage include work carried out by the Institute for Child Health Research in Western Australia.[447] Links were created from midwives' notification records, birth registrations, death certificates, hospital in-patient morbidity data, and the Western Australian birth defects and cerebral palsy registers.[446] This database continues to be used now in a wide range of studies of perinatal and paediatric outcomes.[447]

As well as stimulating further research, these studies have influenced preventative strategies and the provision of services. Studies derived from this database include maternal and infant outcomes for Aboriginal families [448], the surveillance and documentation of *Haemophilus influenzae type b* disease [449], ascertainment of terminations due to neural tube defects [450], and a description of birth defects in the offspring of women with diabetes.[447] Both preventative and curative evaluations of care have been possible, an example being a study of outcomes in planned home and hospital births.[447] Further, the database has been used as a sampling frame for case-control and cohort studies.[446]

It has become clear that linked medical records have a high potential for successfully investigating disease aetiology and identifying factors influencing health and the utilisation of health services. This can then lead to the sensible planning and allocation of scarce resources. However, there have been two major obstacles to the wide use of record linkage at any national level in Australia: legislation that protects privacy and limits the use of specific databases, and a shortage of linkable databases.[446]

Currently, a properly designed and conducted record linkage study poses a minimal threat to privacy or confidentiality. All details relating to the matching, handling and storage of data must be specified in a research proposal, must conform to the National

Health and Medical Research Council (NHMRC) guidelines and must be approved by the sponsoring institution's ethics committee.[451]

Prior to the WA Data Linkage System, there had been no comprehensive system of linked health records in Australia. There were, however, a few examples of linkage systems used for special research purposes, but these were conducted on an ad-hoc basis only. These included a study of perinatal and paediatric outcomes using the Maternal and Child Health Linked Database [447], the Roadwatch Road Injury Research Database [452], studies of the incidence of myocardial infarction [453] and an evaluation of the patterns of surgical treatment of breast cancer based on linked cancer registry and hospital morbidity records in New South Wales.[454] The only national project conducted in this time was a pilot study of linkage of Health Insurance Commission Medicare records to explore the feasibility of such linkage.[455]

However, record linkage studies have contributed in part to highlighting inadequacies in Australia's health statistics. These inadequacies were explored at a workshop on national health statistics held by the Australian Institute of Health in 1985.[456] Subsequently, as a result from this workshop, significant initiatives resulted in agreements including the National Health Information Agreement, which aimed to improve the quality and availability of national health information.[457]

3.4.3 The WA Data Linkage Project and the WA Data Linkage System

The WA Data Linkage Project is a collaboration between the Information Collection and Management Branch at the Department of Health (Western Australia), the Centre for Health Services Research at the University of Western Australia, the Division of Health Sciences at Curtin University of Technology, and the Telethon Institute for Child Health Research.[458] With funding from the Lotteries Commission, work began in 1995 on the Western Australian Data Linkage System, an ambitious attempt to link the available administrative health data within a single Australian state in a systematic manner.[405]

An ideal location for such a study, Western Australia (WA) is well suited due to its stable population characteristics, isolated geography, concentration of health services in the capital, Perth, and a high level of cooperation between the academic and service sectors.[405]

The WA Department of Health and the Office of the Registrar General of Births, Deaths and Marriages manage a number of population-based health information systems. Legislation defined a compulsory standard format for all data provided, and six core datasets were included in the original WA Data Linkage System.[405] These were birth records, the midwives' notification system, cancer register, hospital morbidity data system, mental health services register and mortality records.

Construction of the WA Data Linkage System was originally commenced in 1995 using two large computers and the Automatch software package.[459] As unique health care identification numbers are not in use in Australia, all linkages were identified using probabilistic matching. This involved processing of the data from the six core datasets through many passes of the Automatch software matching on variables such as the unit medical record number (unique only to metropolitan public hospitals), surname, given name, initial, date of birth, sex and address. Clerical checking of additional information was undertaken for possible matches that fell within a zone between definite matches and definite non-matches.

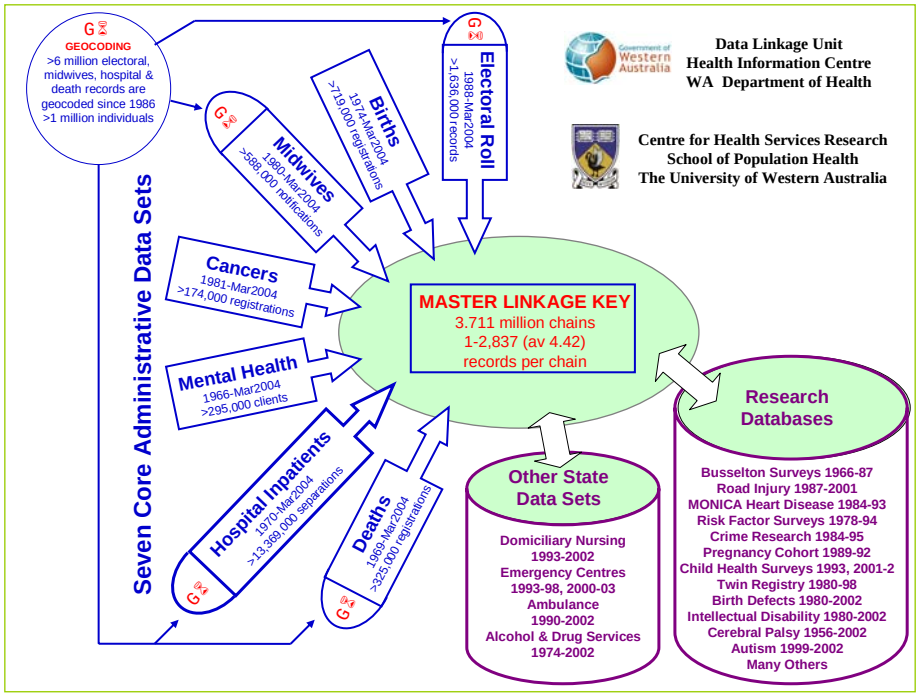
At first, 15 years of all datasets covering the period 1980-1994 were chosen for the initial construction phase, except the cancer registry, which began in 1981.[405] This elicited almost seven million records taking up more than four gigabytes of disk storage. Hospital morbidity and mortality data from 1972-1979 and other health related datasets have since been progressively added to the system, with regular updates of core data added, as files become available.[405]

Other datasets incorporated included a number of substantial and long-standing population based research databases maintained by the School of Population Health at The University of Western Australia. These included the Busselton Health Surveys

from 1966 to 1995, the Roadwatch Road Injury Database, the MONICA Coronary Heart Disease Register and the National Heart Foundation Risk Prevalence Surveys.[405] The relationship of the various databases and the linkage system can be seen in Figure 2 below.

Although it is considered that the data quality in the WA Data Linkage System is generally good, borne out by a scarcity of missing data, one limitation is the absence of primary medical contact data such as general practitioner or physician visits. The Health Insurance Commission (a Commonwealth government organization) holds all data covering contact with physicians, and despite not containing any specific diagnostic information, this data is rarely available in identified form without patient consent. Future projects may include links for the WA Data Linkage System to national datasets, but this data was not available at the time of this study.[405]

Figure 2: WA Data Linkage System, Data Linkage Unit linkage slide and statistics



Source: Prof. CDJ Holman, Chair, WA Data Linkage Management Committee, 2005

At a state level, it is planned to add other datasets in the WA Data Linkage System, including hospital outpatient and laboratory records, public hospital costing data and domiciliary nursing records.[460] The inclusion of the state electoral roll has assisted in the conduct of longitudinal research designs, and the linkage of the WA Ambulance Dataset to the WA Data Linkage System has been pivotal in the description of the epidemiology of pre-hospital care.

The 'chain of links' method developed by the software team allows the record linkages to be reconstituted as they were on any previous date, so data can be continuously updated as new records come to hand.[405] Data output from the WA Data Linkage System has a form in which all records pertain to an individual regardless of the dataset used as the original source, the file structure having variable records per case and a mixed record format. This enables commonly used software packages such as the Statistical Analysis System (SAS) and the Statistical Package for the Social Sciences (SPSS) to be able to read and analyse the files produced.

3.4.4 The St John Ambulance (Western Australia) Dataset

The WA Ambulance Dataset is a computerised record of all cases attended by rural and metropolitan ambulances of the SJA-WA. The resultant dataset includes data from June 1989 to date, some 1.3 million cases. For many of the same reasons that make the WA Data Linkage System unique, the WA Ambulance Dataset is also unique.

Seventy three percent of the 1.8 million population of Western Australia reside in the capital city of Perth, which is home to the state's five teaching hospitals. The SJA-WA, under contract from the Health Department of Western Australia, is the only provider of ambulance services and patient transport in the state, except for some patient transport services from an adjoining suburban light aircraft airport that host operations run by the Royal Flying Doctor Service. These and other factors provide ideal conditions for epidemiological research, including the geographical remoteness of Western Australia, the natural barrier inland Australia affords, a relatively stable population and the absence of border drift with adjoining state ambulance services.

When the SJA receives a call, a priority and dispatch code was generated which was passed to the dispatcher in the Ambulance Operations Centre (AOC). Once the call was dispatched to an ambulance, a unique case number was generated and time critical information was entered from a radio data transfer terminal installed in each vehicle. Recorded live into the system at the AOC, remaining information was completed by ambulance paramedics on a patient care record (PCR) for each attendance. Information recorded on this form included many variables, encompassing aspects of demographic detail, patient history, operational data, assessment and management.[461]

When the call was competed, the information from these records were then transcribed and coded into the SJA administration system. Since 1996, the original PCR has been scanned for permanent record and retrieval (micro-fiche records exist for the period 1989 to 1996). The Western Australian Prehospital Care Research Unit (WAPCRU) was a collaborative initiative of the University of Western Australia and SJA active at the time of the study, and one of its responsibilities was to extract data from this system, where after some file manipulation, merged and prepared data was ready for linkage to the WA Data Linkage System. Although the WAPCRU is now defunct, the prehospital care research role it established, including data extraction from SJA, continues to be undertaken under the auspices of Emergency Medicine at the University of Western Australia.

3.4.5 Methods of Data Linkage

The previously discussed data linkage projects outlined the importance and potential that record linkage has in the areas of public health and related health issues. Yet traditionally, many projects have been implemented in an ad-hoc manner with the researcher empirically deciding the match criteria. This usually involved a large number of passes through the data with little statistical justification for the process and was difficult to repeat if required.[399]

The process of linking involves the selection of potentially linkable records, the matching of these records and then linking them together. *Matching* is the process of comparing pairs of records to determine whether they should be linked, whereas *linking* is the process by which pairs of correctly matched records are brought together in such a way that the may be treated as a single record for one individual.[411]

The most important requirement for correct matching is that there should be the means of uniquely identifying the person or event on every set of records to be matched. Some records may have a unique identifier that largely guarantees identification by means of a single item such as a hospital unit number or form number, in which case matching can be a simple process. Gill and Baldwin described this method as 'all-or-none' matching since the pairs of records compared either match or don't, with no question of partial agreement.[462]

However, it becomes more difficult when the records do not contain unique identifiers, because matching then depends on achieving the closest equivalent to unique identification by using several matching variables. In this case each variable is only a partial identifier, but in combination with other variables provide an accurate enough match for the purposes of the linked data. The use of several identifiers to match records was called 'probability matching' as the aim of the process was to estimate the probability that the records in each pair refer to the same individual or event.[399]

Deterministic Linkage

The 'all-or-none' matching Gill and Baldwin described has since become known as the *deterministic linkage* process.[462] It is based on the availability of a characteristic of a person or event that is fixed, easily recorded and unique, but also readily accessible and available. Unfortunately, few identifiers meet all these conditions, and although personal traits such as fingerprints, voice-prints or gene-prints have been suggested as perfect identifiers in medical care, such traits are not currently practical as identifiers in medical record linkage.[462]

The closest approximation to an ideal matching device would be a series of numbers large enough to encompass all the members of a population. Either a serial, derived or composite number would be assigned to each individual that is unique and stays with him or her for life, and beyond. Serial numbering systems are often used for patient records in medical record systems of hospitals, derived numbers are often used for filing systems in general practice, and composite systems have tended to be restricted to specialist areas, such as the armed forces.[463]

All of these systems are prone to error for various reasons, regardless of the method of recording. The most common type is *transcription* or *substitution* error, where an incorrect character through mis-hearing, mis-reading or mis-keying replaces one or more correct characters.[462] *Transposition* errors occur when adjacent characters are usually transposed adjacently or across an intervening character. The remaining sources of error are *shifting,* when a number is shifted right or left by addition or omission of a zero, and other types or errors and mistakes.[462]

In the UK, the National Health Service (NHS) number is the only assigned number that can realistically be used for large scale deterministic matching of medical records, being a unique, fixed identification number for almost the whole population.[462] The US has a similar pervasive numbering system utilizing the Social Security Number (SSN).[464] Despite their value to deterministic linkage, these types of numbers can still have major drawbacks. Firstly, the chance of errors mentioned previously may cause missed or false matches, and a single miscoded value can cause a link to fail, even if the evidence for a link based on other identifiers is perfect. Secondly the number needs to be generally available on all relevant record information for easy, successful matching.[465]

This type of deterministic linkage can be broken up into two types, *simple deterministic linkage* and *sequential deterministic linkage*.

Simple Deterministic Linkage

This method usually relies on the availability of some unique personal identifier on the birth or death certificate. This system exists in Norway and Israel where the identifier is a number commonly assigned at birth and is part of the civil registration of birth [466] or at the point of immigration into the country.[467] In Norway, the father's personal number is also linked into the file that encompasses approximately 80% of births, whereas the Israel system links the unique numbers for all birth records that belong to the same mother.[467] Matching is simply done on this number.

Sequential Deterministic Linkage

Often, there is a situation where a single identifier is not available on the specific records to be linked. Methods of sequential deterministic linkage have been developed to overcome this, where linkage variables are placed in a hierarchy of decreasing or increasing value [467, 468]. For example, a series of sequential comparisons can be made on files that contain some but not all the data under study, each comparison being a more discriminatory step. In this case, some weighting of variables may occur, but most of the linkages are still based on exact matches, although probabilistic matching may be carried out if the proportion of linked records is lower than expected.[467, 468]

Probabilistic Linkage

Probabilistic linkage methodology addresses the problem of matching two files of individual data under conditions of uncertainty. Newcombe and Kennedy first proposed the concepts of weights based on the probabilities of chance agreement between component value states.[469, 470] Fellegi and Sunter formalized this idea and pioneered the theory of record linkage by presenting an optimal decision procedure to set cut-off threshold weights to decide on acceptable probabilities for matches and non-matches.[471] This probability model was further extended by Jaro, who used an estimation of maximum likelihood model for probability estimation.[399] Multistage by nature, it

required the matching of several variables that define the unique identity of an individual or event.

This new matching technique was implemented in the Automatch Record Linkage System software suite, which was the software used for the linkage process described in this study.[472]

Record linkage in its simplest form involves two files A and B with records that pertain to individual cases, consisting of fields that hold the information to be matched. For a successful match, one or more fields in file A must have an equivalent field in file B, for example if a match is sought on surname, both files must have a field containing surname information.[399] If the number of records in file A is *n*, and file B is *m*, then the number of all possible record pairs is *n x m*.[471]

The objective of the linkage process is to classify each pair into one of two sets, matched record pairs M or unmatched record pairs U. The problem is that for any files of reasonable size, it is not feasible to compare all the possible combinations of record pairs, so a process called *blocking* is used. Blocking is a method to limit the number of pairs being examined by only searching for a match within a subset.[399] By utilizing a multiple-pass strategy, small blocks and an initially restrictive blocking scheme, most of the records will match on the first pass, with subsequent and less restrictive passes having fewer records to match.[399]

Each field contains information that helps to determine whether a record pair matches or not, but some fields, say for example the hospital Unit Medical Record Number (UMRN), provide more reliable information than others, say for example, gender. The more reliable the field, the greater the probability is that a field agrees given that the record pair being examined is a matched pair.[399] Similarly, there is another probability that a field agrees given that the record pair being examined is an unmatched pair, effectively the probability that the field agrees at random.[399]

By *weighting* the fields (a logarithm of the ratio between these two probabilities) a composite weight can be calculated as the sum of all individual weights for all field comparisons.[399] A field disagreement results in a negative weight and an agreement a positive weight, so the higher the score, the greater the agreement. These composite weights result generally in a bimodal distribution, where there is one mode for highly negative weights since most cases are unmatched pairs, and another mode at highly positive weights for the matched cases.[399]

By applying a decision procedure, threshold weights can be computed for acceptable probabilities for false matches and false non-matches, where weights higher than the high threshold weight are considered matched, weights below the low threshold are non-matches, and those between the two are for review.[399] If this review area is wide, then the probability of incorrect assignment is low, but if narrow then this probability increases.[399]

The probabilistic linkage technique has been used extensively in both epidemiological [473-477] and genetic studies.[467, 478, 479] Despite the complexity of the underlying theory, the only real impediments to successful probabilistic linkage of records is adequate computer power and time, and errors and omissions in the identifiers on the original records.[467]

3.4.6 Linkage of the WA Ambulance Dataset and the WA Data Linkage System

In Western Australia, there is no common matching variable such as a unique patient identification number. Only the major teaching hospitals share a similar Unit Medical Record Number (UMRN), but this is not comprehensive or adequate enough for a deterministic linkage process. Successful linkage of the WA Ambulance Dataset with the WA Data Linkage System then must rely on a sympathetic data structure that allows successful matching by a probabilistic process, with common identifiers that will enable linkage of the two datasets.

To preserve the anonymity and confidentiality of patient data and to comply with the various legislative strictures on the distribution of data, all matching is performed at the Data Linkage Unit (DLU) of the WA Department of Health. In the case of the WA Ambulance Dataset, demographic data stripped of all clinical information is submitted to the Health Department for matching with name identified data of two core subsets of the WA Data Linkage System, the Morbidity Data System (hospital data) and the Mortality Data System (death data).

As the linkage to the hospital and death data involves a process of matching common variables from each dataset, the data is subject to a number of checking processes to reduce errors and anomalies in the primary matching variables.[480] These include name standardisation, address cleaning and other variable checking to ensure correct coding such as sex and validation of dates. For linkage of the WA Ambulance Dataset to the WA Data Linkage System, primary matching variables used included surname, given names, date of birth, gender and address.

To overcome the effects of most discrepancies in spelling, surnames are changed into a coded format. The New York State Intelligence Information System (NYSIIS) name compression algorithm is first applied, a process that produces a character code representing the surname.[481] This process performs various tasks such as giving often-confused letter groups commonality like ‘ch’ and ‘gh’ or ‘sh’ and ‘sch’ as well as removing vowels. For example ‘Docherty’ and ‘Dougherty’ would be reduced to the same NYSIIS code.[482] The surnames are also subjected to a process called Soundex, a computer program that allocates the same code to similar sounding non-initial consonants.[410] The resultant NYSIIS and Soundex codes are assigned a differential weight for agreement depending upon their frequency. Table 10 below summarises the fields and codes used for matching.

Table 10: Fields and codes used for matching

Variable Name	Description
sname	surname
nysiis	a 6 character compression code for surname field
soundex	a 6 character phonetic code for surname field
gname*x*	given name fields 1 or 2 (*x* = 1,2)
initial*x*	initials for given name fields 1 or 2 (*x* = 1,2)
dobirth	date of birth
dobyyyy	year from date of birth
dobmm	month from date of birth
dobdd	day from date of birth
sex	gender of patient
addr8	an 8 character compressed address field
pcode	postcode component of address

Source: Data Linkage Unit, Department of Health, Western Australia, 2001.

Given the volume of data involved, it is not feasible to compare every record with every other record. Therefore the data sets are linked using standard blocking on the above matching variables. The Automatch software [459] analyses the data using probabilistic techniques to find links within the data. The computer algorithm in this software calculates a score for each pair of records, which is proportional to the likelihood that they belong to the same person and/or episode of care. The overall score or weight is the sum of scores derived from the comparison of each item of identifying information.[399]

Once the records are linked they are flagged in the data file as linked, using ‘Y’ for 'yes'. Records yet to be linked will be flagged as ‘N’ for 'no' and are selected for linkage in the next run. Each run of linkage can contain up to 8 passes. An extract file containing all links found is built and duplicates are established between links.[459] There are two types of duplicates; those where two or more morbidity chains link to the same ambulance record and those where two or more ambulance records link to the same morbidity chain.

Where two or more ambulance records link to the same morbidity chain, these are likely to be either the same person with more than one ambulance episode or a transfer from one hospital to another, and are included in the linked dataset.[480] Where two or more morbidity chains link to the same ambulance record, these are usually the result of discrepancies in linkage between the current and previous linkage episodes and are discarded after checking.[480]

A separate links file is created that contains a list of the links between the ambulance case records and the hospital episodes of care. This links file connects the two datasets, with anonymity maintained by the encryption of identifying numbers and de-identification of the resultant datasets.[480] The resultant linked file reflects a chain of links, meaning there can be multiple ambulance episodes and hospital admissions recorded in the file for a single patient.

Next, death data is then merged to the linked file so that the death information for a patient is appended to each of the episodes of care for that patient, and not just the episode of care involving their death.[480] This is important for the analysis of outcome data later in the study. The resultant data is in the form of a flat text file of fixed variable format containing, for any particular patient, all ambulance episodes linked to all inpatient hospital episodes with relevant death details where applicable.[480]

Match Type

Once an ambulance record is matched to a chain of links, a secondary process is run where each ambulance record is compared to all of the matched records in the chain to try and identify the specific hospital record that coincided with the ambulance transport.[480] By calculating the difference in days of the hospital admission date and the ambulance attendance date, and checking that hospital codes match, eight different match type levels were determined (Table 11).

The purpose of this matching is to be able to obtain outcome information for each ambulance episode. It is therefore possible to ascertain whether an asthma patient transported by ambulance was actually admitted to hospital and for how long, where and how they were discharged, and other hospital clinical information. Based on clinical knowledge, discussion with SJA staff, and the experience of previous and

current researchers, it was decided that only those cases that had a match type of 1 to 5 were accepted as true links, thus minimizing the inclusion of false matches. By using the ICD diagnostic and procedural codes recorded on hospital inpatient records and comparing these to the problem code on the ambulance patient care record (PCR), it was also possible to derive a measure of sensitivity and specificity of the ambulance paramedic-derived problem codes.

Table 11: Match Type levels derived from matching ambulance records against hospital records in a chain of links.

Match Type	Description
Matches accepted as true links.	
1	Hospital and dates both match.
2	Hospitals do not match, dates match.
3	Hospitals match, ambulance date one day before hospital date.
4	Hospitals do not match, ambulance date one day before hospital date.
5	Hospitals match, ambulance date one day after hospital date.
Matches rejected as false links.	
6	Hospitals do not match, ambulance date one day after hospital date.
7	Ambulance date 2 to 7 days before or after hospital date.
8	Closest hospital record in terms of dates after 7 days (before or after).

Source: Data Linkage Unit, Department of Health, Western Australia, 2001.

Note: Emergency Department presentations are not represented here.

3.4.7 ICD Coding

Data from the Morbidity Data System (the hospital data component of the WA Data Linkage System) can be categorised into four main groups: identifiers, socio-demographic details, administrative information and clinical details.[483] Data items are considered consistent with the definitions published in the Australian National Health Data Dictionary [484], and clinical information is coded according to the International Classification of Diseases (ICD) system. The ICD system is a World Health Organization endorsed system for the classification of morbidity and mortality information for statistical purposes.[485]

For the period of 1990 to 1999, the coding schema used in Australia was ICD-9-CM, with the United States 1990 amendments adopted in 1991, the United States 1992 amendments adopted in 1993, and the Australian Version (First edition) adopted in 1995.[483] Diagnostic codes are presented as a tabular list organized within three broad categories: types of conditions, anatomical groupings and signs, symptoms and ill-defined conditions. The ICD-9-CM system consists of three, four and five digit codes that usually represent increasing levels of specificity.[486] For example, the three-digit code of '493' represents asthma, while the four-digit code '493.0' represents atopic asthma. The fifth-digit sub-classification is used to define whether the asthma is with or without status asthmaticus. Thus an ICD-9-CM code of 493.01 represents atopic asthma with status asthmaticus.

In 1999, the new coding schema of ICD-10-AM was adopted with ICD-10-AM (Second Edition) being adopted in the year 2000.[483] This represented a complete revision of coding conventions which included a change to an alphanumeric coding system, new chapters and some relocation of diseases and conditions.[487] As the hospital data has retained the ICD codes that were entered at the time, data analyses in this study has accounted for both coding schema and treats them specifically as required. Table 12 below shows how the specific codes for asthma in ICD-9-CM were mapped to corresponding codes in ICD-10-AM for the data in the hospital data.[488]

Table 12: Mapping diagnostic codes for asthma across ICD-9 and ICD-1O

ICD-9-CM CODE	ICD-10-AM CODE
493.00 (Extrinsic asthma without status asthmaticus)	J45.0 (Predominantly allergic asthma)
493.10 (Intrinsic asthma without status asthmaticus)	J45.1 (Non-allergic asthma)
493.20 (Chronic obstructive asthma without status asthmaticus)	J45.8 (Other specified chronic obstructive pulmonary disease including asthma
493.90 (Asthma, unspecified without status asthmaticus)	J45.9 (Asthma unspecified including asthmatic bronchitis)
493.01 (Extrinsic asthma with status asthmaticus)	J46 (Status asthmaticus)
493.11 (Intrinsic asthma with status asthmaticus)	J46 (Status asthmaticus)
493.21 (Chronic obstructive asthma with status asthmaticus)	J46 (Status asthmaticus)
493.91 (Asthma, unspecified with status asthmaticus)	J46 (Status asthmaticus)
Note: As 493.2X (chronic obstructive asthma) has no direct match, it has been mapped to ICD10 category J45.8 with other chronic obstructive lung disease.	

Source: Epidemiology Branch, Health Information Centre, Department of Health, Western Australia, 2001.

3.5 DATA VALIDATION

3.5.1 Validation and the Linked Dataset

The linked dataset that has been used for this study is made up of hospital, death and ambulance data. Before analysis could commence it was necessary to review what steps have been taken to validate or ensure data integrity of these three components.

The Morbidity Data System (hospital data) included name, demographic information, dates and times of admission and discharge, ICD-coded hospital in-patient diagnoses and procedures, separation status, and other information.[483] This data originates from every metropolitan and regional hospital in Western Australia, both public and private. In 2002, there were approximately 400,000 public hospital and 250,000 private hospital separations in Western Australia.[489]

On discharge of a patient, each hospital must submit to the Health Department of Western Australia (HDWA) a form describing certain information about their episodes of care. This form, the HA22, is the cornerstone of funding arrangements to care providers, so for this reason it is in all stakeholders' interests that the information be as accurate as possible.[489]

On receipt of the HA22 at the HDWA, a number of checks are performed. The HA22 is examined for logical errors including correct date sequence, invalid postcodes, mental health legal status (if the patient has been in an authorised ward), and other checks between certain items, such as private patients and their private health insurance status.[489]

In addition to the above checks, there is also an audit of clinical coding performed, where a check is made to see if the ICD codes assigned are correct. This auditing process is important for sustaining funding arrangements to the hospitals. Specific information is crosschecked, for example, ensuring morbidity data matches the medical records and that Casemix and Diagnostic Related Group (DRG) information is recorded correctly.[489] However, it is noted that only public hospitals undergo audit about every two years, not all records are audited and the error rate can vary markedly from hospital

to hospital and between individual coding staff. Error rates may be as low as 5% for an experienced coding clerk, or as high as 35% for a novice coding clerk.[489]

The Mortality Data System (death data) included date, time, ICD-coded cause of death, and a text description of all deaths in Western Australia, where the registration of all deaths are compulsory.[490] The doctor who was responsible for the medical care of a person before their death or who examined the body after death, must complete and sign a medical certificate of cause of death within 48 hours.[491] The Western Australian Health Act (1911) imposes stringent guidelines and checks on both doctors completing the medical certificate and funeral directors receiving bodies from the morgue for funereal purposes, helping to minimise errors of detail and identification.[490]

The Registry of Births, Deaths and Marriages must receive a death registration form within 14 days of the date of death.[491] Data is collected and collated on an ongoing basis where it is stored on their internal computer system. Internal embedded checks search the data for duplicates or inconsistencies where possible, but it must be noted there are no formal validation or auditing processes in place to check the data, either prospectively or retrospectively.[490] There are some cases that are flagged pending further attention. Examples include those that are subject to coronial inquiry, traditional aboriginal burials, death and burials in remote areas, burials at sea, and special ethnic funeral arrangements that are outside usual funereal guidelines. Often data for these events may be missing or incomplete.[490]

From the above, it is clear the hospital data and death data components of the WA Data Linkage System have been subjected to a variety of processes before being fit for linkage. It is also clear that the actual process of collecting the data provided inherent obstacles to attempted validation. By virtue of the large and diverse number of sources, wide geographic locations, complexity of disparate computer systems, and the high component of manual intervention required to simply provide existing patient data, it appears that validation would require unacceptably large amounts of time, money and personnel resources.

For these reasons, and the lack of sufficient evidence that increased accuracy will significantly affect performance indicators or outcomes, neither the WA Department of

Health nor the Registry of Births, Deaths and Marriages have indicated any current plans to undertake formal validation programs other than the checks discussed previously.[489, 490] It is noted though, that a number of researchers in WA have validated coding for their individual studies. In the light of this, it was concluded that validation of the hospital and death data would not be possible within the scope of this study, and that the hospital and death data provided to the Data Linkage Unit (DLU) for linkage would be used on an 'as is' basis.

This however has not precluded any validation being performed on the data post-linkage, for the DLU has undertaken a number of data linkage quality measurement and improvement projects. In 1999, an estimate of the quality of the links in the system was made using a weighted sample of pairs of potentially matched records and detailed manual checking of pairs with weights between an upper threshold and lower threshold. At that time, it was found that the level of false positives (mismatches) was 0.11% and the level of false negatives (missed matches) was also 0.11%.[405]

Elsewhere, link quality has been measured against a known standard [492], however there was no appropriate benchmark for the WA system, as it is considered the 'platinum standard' for other linkage systems. Therefore, link quality had to rely on detailed, manual scrutiny of sampled linked chains.

A quality review project in 2001 estimated the level of false positives in a random sample of 5000 hospital admission records for 1990 to be 0.6%.[493] Over the next year, several new datasets were linked to the system, and many doubtful links involving name and address changes over time were resolved. A repeat study in 2002 reviewed another 5000 randomly chosen records from 1990, and found that 0.3% of the chains contained false positives, a substantial improvement in accuracy.[493] Continual feedback from the DLU to the custodians of the hospital and death data regarding editing of data ensures ongoing improvement in accuracy of the core data sets.

For the third (and most important) component of the linked dataset used in this thesis, the WA Ambulance Dataset, there was a simple and effective method of validating the data. As one of the primary objectives of this study was to describe ambulance cases

and episodes of care, validation was achieved by designing a process that compared original data to that described in the database.

3.5.2 SJA Data Validation

For each case of ambulance attendance over the twelve-year study period, data from these events have been recorded in an electronic database, which include name identifiers, ambulance service operational data and clinical information.[461] Some data was entered directly via input from mobile radio data transfer terminals installed in each vehicle, the remainder manually entered on the Patient Care Record (PCR) by the ambulance paramedic at the completion of each case.[461]

When the call was completed, the information from these records was transcribed by coding clerks into the Patient Recording System (PRS). This then creates the complete details of that particular case, after the addition of internal administrative parameters such as cost details and expanded clinical and audit variables.[461]

Following data transcription, the PCR was originally rendered to microfiche (until August 1997), but is now scanned electronically for archival purposes. The original paper PCR's were destroyed on a monthly basis 12 months after transcription into the database.[461] The microfiche and electronic images are now the only source of original data after the destruction of the original records, and it is these images that are used for the purposes of validation.

The reason for this validation study is two-fold. Firstly, to achieve the aim of describing the trends of ambulance usage it is necessary to ascertain how accurately data has been transcribed from the PCR to electronic format. As all study components rely on analysis of the electronic data, it is important to know how reliably this data reflects that of its original source. Secondly, for the component of the study that looks at outcome trends, it is necessary to ascertain how accurate are the key matching variables through which linkage to the WA Data Linkage System is achieved.

3.5.3 Method of Validation

The PCR has undergone two major changes since 1990, largely due to expansion of the clinical variables recorded. In September 1994, minor changes to socio-demographic variables were made and more clinical variables were added, whilst in May 1999, clinical variables were further expanded to reflect changes in policy and protocol.[461]

It is important to note that the WA Ambulance Dataset not only stores the information transcribed from the PCR, but also information from the Computer Aided Despatch (CAD) system, and a large number of derived variables including time, costing, and clinical information.[461] As a result, the ensuing dataset has gradually evolved from 157 variables in year 1990 to 286 variables in year 2001. Appendix 4 shows a blank Patient Care Record that is currently used by ambulance paramedics.

For purposes of validation, the variables recorded in the WA Ambulance Dataset are classified as either Type 1 or Type 2 variables. Type 1 variables originate from the CAD system and the Patient Recording System (PRS) and are either entered directly into or derived by the data system. In the PRS, certain measures have been designed to minimize the chance of input errors. Mandatory fields such as time are taken straight from the system clock, and safety checks are designed to only allow legal characters and ranges in certain fields. This way, input will be rejected if it fails entry criteria and rules for that particular field, thus reducing the chance of substitution or transposition errors.[461] An example would be where a field may be left blank, but if a value is entered it can only be of a legal value.

This serves two purposes, the first being that the coding clerk must enter a value from a pre-determined or pre-selected range and secondly, allows auditing of the value entered. An obviously wrong entry can be corrected before data is posted into the system, but a missed wrong entry may cause dependant derived variables to be wrong also. As this is not a transcription issue, there are no errors of this type, but this does not preclude errors of shifting, omission or other causes. It is not possible to validate these variables, as there is no original document with which to perform a comparison.

However, Type 2 variables are transcribed from the PCR, and along with the patient demographic information, poses the most likely source of error. To reduce potential error, on input the clinical fields are also subject to the checks and measures described above. However, an error of omission by either coding clerk or ambulance paramedic cannot be prevented in non-mandatory fields. The patient details, address, postcode and date of birth fields are potentially at highest risk for errors. Type 1 and 2 variables are described in Table 13 below.

Table 13: Type 1 and 2 variable descriptions

Variable Description	Type	Variable Description	Type
Case number	1	Pre-Ambulance Care by Bystanders	2
Incident date	1	Pre-Ambulance Care Adequate	2
Incident date	1	Pre-Ambulance Care Inadequate	2
Region	1	Glascow Coma scale	2
Depot	1	ECG	2
Driver	1	Location of Condition	2
Attendant	1	Burns	2
Time call received	1	Trauma Injury	2
Time vehicle departed	1	Fractures	2
Time arrived at scene	1	Bleeding	2
Time departed scene	1	Airway	2
Time at destination	1	Breathing	2
Time cleared	1	Circulation	2
Priority	1	Oxygen	2
Dispatch code	1	Posture	2
Audit	1	Analgesia	2
Trip kilometres	2	Splints	2
Transport from address - postcode	2	IV Infusion	2
Transport to address - postcode	2	Medication	2
Patient address - postcode	2	Defibrillation	2
Patient gender	2	Changes en Route	2
Patient date of birth	2	Doctor at Scene	2
Medic alert number	2	Patient title	2
Problem code	2	Warrant number	1,2
Problem urgency	2	Ambulance Not Required	1,2
Patient mobility	2		

Fortunately, the St John Ambulance is mostly self-funded [396] and as such, demands extremely accurate patient and address information for billing purposes, so great time and care is taken to ensure the most accurate details are obtained.[461] As these are also the key variables upon which the matching and linking process is performed, greater accuracy and less error improve the likelihood of successful linkage.

In addition to correcting patient and address details, some routine checking is done, but there is no ongoing auditing program in place. In practice, two to three percent of cases get checked when errors are suspected or data is incomplete, and if errors are found the data is corrected and overwritten. In the majority of these cases it is usually an error in one of the time variables. Further, monthly statistics are collated, and the summarized results may occasionally outline obvious errors, which can then be examined and corrected if necessary.[461]

From the years 1990 to 2001, there have been 1,085,406 cases of ambulance attendance recorded in the WA Ambulance Dataset. Table 14 shows the numbers of cases per year for the twelve year period under study.

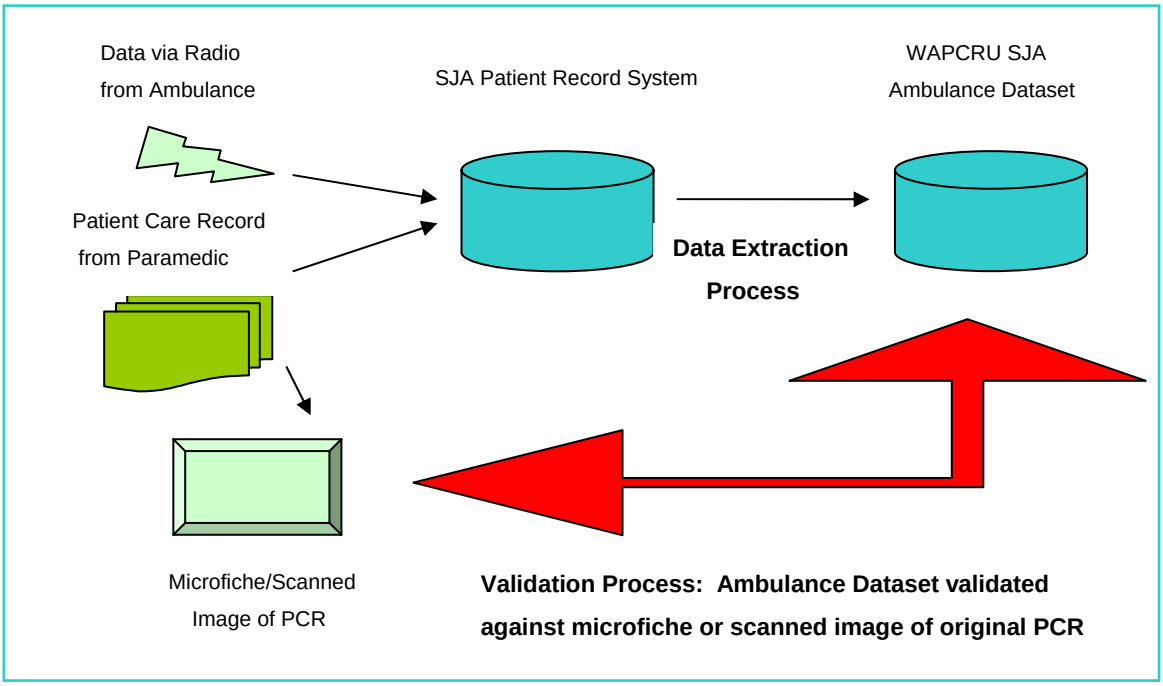
Table 14: Number of ambulance cases per year

Year	No. of Cases
1990	68,337
1991	67,490
1992	73,258
1993	79,121
1994	82,689
1995	82,174
1996	88,989
1997	92,634
1998	98,682
1999	110,074
2000	117,999
2001	123,959
Total No. of Cases:	**1,085,406**

Using the random case selection function of SPSS [494], a sample set of 200 cases were selected from each of the first eleven years for the purposes of validation. Data for the year 2001 was excluded from validation, because at the time there was incomplete data for that year. Although subsequent analyses in this study use complete 2001 data, it was decided that the eleven-year period would be adequate for validation purposes. The process of validation was a very manual process and required a heavy investment in time and resources and considerable inconvenience to SJA personnel. After analysis of the validation results, it became apparent that the additional year of data would elicit little new information, and did not warrant additional time spent on the process.

For each case selected the data contained in the WA Ambulance Dataset was compared with the original information recorded on the PCR. Discrepancies between data items were noted and the proportion of inaccuracies in each data field was determined. A diagram outlining the basic validation process can be seen below in Figure 3.

Figure 3: Validation Process Flowchart



The use of remote radio transmitted data terminals in ambulances did not commence until July 1994.[461] Up to this point the time variables *received, departed, scene, depart scene, destination,* and *cleared* were transcribed from the PCR on the completion of the case. After this date, data was transmitted electronically via radio direct to the CAD system, except on occasions when this system failed. When this happened, the times recorded by the ambulance paramedics on the PCR were used as the official times.

To assess errors in the time variables, an arbitrary error range of plus or minus five minutes was established. Five minutes was selected as this was considered the average amount of deviation that an ambulance paramedic might expect their watch to differ from actual real time. This means that if the recorded time on the PCR deviated from that of the database by more than five minutes, then an error would be generated.

When a case is generated and an ambulance is despatched, a priority and despatch code is generated by the despatch clerk. The ambulance paramedic records problem code and problem urgency on the PCR after attending the patient. However, over time these codes have changed, and as the database only reflects data in current form, there were discrepancies between the information recorded on the PCR and that of the database. This is not an error condition but reflects the result of conversion to a more recent coding scheme. Appendix 5 shows how these codes have changed over time.

To differentiate between errors that arise from incorrect data and those that arise from conversion or adaptation from previous coding schema, it was decided to divide errors into hard errors and soft errors. Hard errors are those that either occur in a key matching variable, or are wrong in any other variable that cannot be explained by conversion from a previous coding scheme. An example would be an error in the surname of a patient or a clinical code that has either been omitted in the database but recorded on the PCR or vice versa.

Soft errors are those that may occur due to differences in previous coding schema, the lack of a comparable field or occur in non-key matching variables. Examples would be where just the year of birth was recorded prior to 1994, a problem code is converted from a previous schema or where partial information exists on the PCR but not the database, such as a stand down or case cancelled.

Of the 2200 cases examined in the validation subset, 2146 (97.5%) could be validated against the original PCR image, either electronic or microfiche. For the remainder, 33 microfiche PCR's were missing or indecipherable, and for electronic images, 1 PCR was different to that indexed, 16 PCR's were not indexed, and 4 PCR's were indexed but not found.

Table 15 shows the number of hard and soft errors that occurred for each of the 59 variables audited in the validation process. Some of these variables have undergone various life cycles and conversions over time. The figures show the number of hard and soft errors after correction when explanation by means of conversion, substitution, or adaptation to a new schema has been taken into account.

Table 15: Hard and Soft Errors for Validation Variables (valid %)

Variable	Total Errors	Hard Errors	% Hard Errors	Soft Errors	% Soft Errors	Variable	Total Errors	Hard Errors	% Hard Errors	Soft Errors	% Soft Errors
Case Number	1	1	0.05								
Incident Date	7	3	0.33	4	0.19	Call Priority	31			31	1.44
Region	0					Dispatch Code	62			62	2.89
Depot	81			81	3.77	Mobility	181			181	8.43
Driver	40			40	1.86	Medic Alert Num.	1			1	0.05
Attendant	44			44	2.05	Problem Code	73			73	3.40
Call Received	34			34	1.58	Problem Urgency	58			58	2.70
Time Departed	66			66	3.08	Pre-Ambulance Care 1	12	12	0.56		
Arrive at Scene	44			44	2.05	Pre-Ambulance Care 2	17	16	0.75	1	0.05
Depart Scene	49			49	2.28	GCS	36	36	1.68		
Destination	48			48	2.24	ECG	18	18	0.84		
Clear Call	93			93	4.33	Location	18	18	0.84		
Distance Travelled	13			13	0.61	Burns	0				
From Hospital	2	1	0.05	1	0.05	Trauma Injury	6	6	0.28		
From Address 1	15	3	0.14	12	0.56	Fractures	3	3	0.14		
From Address 2	13	1	0.05	12	0.56	Bleeding	16	16	0.75		
From Postcode	3	1	0.05	2	0.09	Airway	3	3	0.14		
To Hospital	4	2	0.09	2	0.09	Breathing	1	1	0.05		
To Address 1	2	1	0.05	1	0.05	Circulation	0				
To Address 2	2	1	0.05	1	0.05	Oxygen	8	8	0.37		
To Postcode	2	1	0.05	1	0.05	Posture	14	14	0.65		
Title	8	4	0.19	4	0.19	Analgesia	4	4	0.19		
Surname	10	5	0.23	5	0.23	Splints	10	10	0.47		
First Name/Initial	14	6	0.28	8	0.37	I/V Infusion	12	12	0.56		
Patient Address 1	22	20	0.93	2	0.09	Medications	5	5	0.23		
Patient Address 2	12	10	0.47	2	0.09	Defibrillation	1	1	0.05		
Patient Postcode	12	10	0.47	2	0.09	Changes en Route	15	15	0.70		
Gender	8	4	0.19	4	0.19	Doctor at Scene	6	4	0.19	2	0.09
Date of Birth	19	18	0.84	1	0.05	Audit	1	1	0.05		
Warrant Number	25			25	1.16	Amb. Not Required	75	9	0.42	66	3.08

Certain of these variables require comment to explain the context of their error conditions. For example, the variable *incident date* exhibits only 7 soft errors, of which all but one are obvious mistakes in either day, month or year fields. This had been corrected in the CAD system on input in earlier years, and automatically by the system in real time in recent years with the written date on the PCR being ignored. Although successful record linking is not contingent on this field for patient identification purposes, once a link is established the probability of a case match to a hospital episode is based in part on the difference in days from the ambulance case to the hospital episode. An accurate incident date will improve the likelihood of case matching.

Other variables such as *depot*, *driver*, and *attendant* exhibit high rates of soft errors. However, due to a long history of change in depot numbers, the movement and renumbering of volunteer ambulance paramedics, and their irrelevance to the aims of this study, correction was not attempted for these variables.

An example where corrections were possible and appropriate was the presence of soft errors in variables *pre-ambulance care 1* and *pre-ambulance care 2*. As of January 1999, the field value of these two variables were changed from field 3 and 4 to field 2 and 3 in the CAD system, but the WAPCRU data extraction process continued to use the old field values. This caused a shifting error of data from the original field 4 to new field 2 and the omission of data in new field 3. The process of this validation study revealed this error, which has now been adjusted. However, the original data supplied by the CAD system was correct and remains unaltered, whereas the extracted data from the WAPCRU system was adjusted to correct the anomaly.

Further, the variable *priority* had two life cycles prior to WAPCRU extraction. The first cycle involves a coding scheme used by the communications centre with a range of possible variables from 1 to 9. This was then converted to a range of 1 to 5 when transferred to the patient recording system. Similarly, variables *dispatch code* and *problem code* had undergone a major change in 1994, and another minor change in 1999.

For example, prior to October 1994, the only two variables on the PCR reporting the dispatch and transport processes are *priority* and *ambulance code,* information

generated by the communications centre. New variables, *problem code* and *problem urgency,* were added after this time to describe the actual clinical state and transport priority to destinations as encountered by the ambulance paramedics. If the variable *ambulance code* was considered the equivalent to the variable *dispatch code,* conversion to a current coding scheme would generate a large number of soft errors. However, as communication centre staff have assessed and entered the current values for *problem code* and *dispatch code* independently and not as a result of conversion at the time of input, these values have been accepted as correct and not flagged as soft errors.

Finally, a brief summary of the 7 matching variables that were critical in the context of successful linkage with the hospital and death data is outlined below. Table 16 shows these key variables, their associated errors, and a breakdown of the cause of error.

Table 16: Key matching variables, their associated errors, and a breakdown of the cause of error.

Variable	Total Errors	Hard Errors	Cause of Errors	Soft Errors	Cause of Errors
Surname	10	5	3 Spelt Wrong 1 Missing DB 1 Unknown	5	4 ANR/Stood Down 1 Assist
First Name/Initial	14	6	4 Missing DB 2 Wrong	8	8 ANR/Stood Down
Patient Address 1	22	20	8 No. Wrong 5 Missing DB 3 Missing PCR 4 Wrong	2	2 Misspelled
Patient Address 2	12	10	4 Missing DB 4 Wrong 2 Missing PCR	2	2 ANR/Stood Down
Patient Postcode	12	10	4 Missing DB 4 Wrong 2 Missing PCR	2	2 ANR/Stood Down
Gender	8	4	2 Missing DB 1 Missing PCR 1 Unknown	4	4 ANR/Stood Down
Date of Birth	19	18	12 Wrong 4 Missing DB 2 Missing PCR	1	1 ANR/Stood Down

Legend:

Missing DB	Missing from Ambulance Database
Missing PCR	Missing from Patient Care Record
No. Wrong	House or Unit Number Wrong
ANR/Stood Down	Ambulance Not Required or Stood Down
Assist	Second Ambulance to Assist

For the variable *surname*, the most important hard errors are those that are wrong or missing from the database. Misspelled surnames will likely survive the linkage process due to the Soundex and Nysiis name checking algorithms [481], but those absent or entirely wrong will be rejected. Similarly, this is true for the address variables *patient address 1* and *patient address 2,* as these will be processed using the *addr8* algorithm, which tolerates some variation.[480]

Although those fields that are reported missing from the PCR have generated a hard error, the information that is entered into the database may have been acquired subsequent to the closing of the call. It is not possible to ascertain the accuracy or source of this information, but matching will still occur on this data.

For those cases where an ambulance was not required (ANR), these are considered soft errors because on matching they will be rejected, as the case will not have generated an admission record in the Morbidity Data System.

Prior to October 1994 the date of birth was only coded as year of birth. For example, a date of birth of say 02.07.08 would be coded as 01.01.1908, despite the original PCR holding correct date of birth data. In the case of the variable *date of birth,* these conversions have not been considered soft errors as matching strategies can utilise the year variable independent to month and day variables. Although subsequent passes in the record linking process would normally match on month and day variables, pre-1994 data submitted for linkage containing only the year of birth data will simply have the effect of reducing the overall probability of optimal linkage based on the key variable *date of birth*.

3.5.4 Results of Validation

The linked database used for analysis in this study was comprised of morbidity (hospital), mortality (death), and ambulance data components. For reasons described previously, no attempts were made to validate the morbidity and mortality data. The ambulance data was not only the most critical component, but also the most accessible and readily validated.

Of the 2200 cases examined, 97.5% could be validated against the original PCR image. For the 59 variables audited in the validation process, the percentage of valid hard errors ranged from 0% to 1.68%, and the percentage of valid soft errors ranged from 0% to 8.43%. In the 7 key variables that linkage was performed on, the percentage of valid hard errors ranged from 0.19% to 0.93%, and the percentage of valid soft errors ranged from 0.05% to 0.37%.

Given these exceptional low error rates, it can be concluded that the data provided by the St John Ambulance for linkage is valid, reflects a high degree of accuracy, and can be utilised for linkage studies with a high degree of confidence.

3.6 COMORBIDITY

3.6.1 Introduction

Comorbidity can been defined as a clinical condition that exists before a patient's admission to the hospital, is not related to the principal reason for the hospitalisation, and is likely to be a significant factor influencing mortality and resource use in the hospital.[495] It has become accepted amongst both researchers and clinicians that patient outcomes may be influenced by the presence of pre-existing ailments known as comorbidities. As early as 1970, it was noted that the failure to classify and analyse comorbid diseases led to many difficulties in medical statistics [496], and early investigators often employed restrictive eligibility criteria to eliminate patients who had comorbidities.[497] Doing this may have increased certainty that an observed difference was attributable to the index disease or treatment, and not to the confounding influence of comorbid disease, but generally reduced sample size and power and was usually at the cost of external generalization.[497, 498]

It has also been acknowledged that measuring comorbidity is important in correcting for bias and predicting study outcome, and comorbidity scores are increasingly being used to reduce potential confounding in epidemiological studies.[499] This is particularly relevant for an observational analytical study such as this one, where there is no opportunity to randomise cases to a particular intervention group to reduce the risk of bias. There have been a number of efforts to quantify measures of comorbidity to adjust for potential confounding by pre-existing ailments on outcome [500-503] and to date, there are as many as thirteen different methods identified to assess comorbidity.[504]

The aim of this chapter is to explore the selection of the most appropriate comorbid index and create a comorbidity index suitable for modelling to determine if comorbidity affects the outcomes of those patients with asthma who are transported by ambulance.

3.6.2 The Charlson Index and Comorbidity

Various surrogate measures have been suggested as a proxy for comorbidity such as age or hospital length of stay. Age is the simplest comorbidity score, and is used widely in epidemiology to control for confounding. However, despite being recorded accurately and ubiquitously in large administrative databases, it is a relatively poor index of comorbidity and does not perform well as a true measure of risk.[499]

Comorbidity has now been studied for the last thirty years, and various strategies have been used to deal with comorbidity, resulting in the development of comorbidity scoring systems useful for both patient classification in clinical research and prognostication in medical care.[500, 505-508] These include the creation of binary indicators for groups of comorbid conditions, stratification based on the absence or presence of comorbidity and grouping comorbid conditions into an index that elicits a single score for multiple comorbidities.[495]

The creation and use of a single valid variable that includes many concurrent comorbid conditions increases statistical efficiency in multivariate modelling, avoiding the necessity of modelling each individual comorbidity separately, and potentially increases the comparability of findings from disparate studies.[499]

Among the different scoring systems developed, the Charlson index has proven to be relatively easy to construct, and versions for use with administrative databases based on the International Classification of Diseases (ICD) are readily available. It is also the most widely used measure of comorbidity reported in the literature [509] and the most extensively studied comorbidity index for predicting mortality.[504]

The Charlson index was generated from the adjusted relative risks of mortality in a cohort of medical patients used as a training population, with these relative risks used as weights for different comorbid conditions and then validated on a separate cohort of breast cancer patients as a test population.[495] Comorbid conditions which had a relative risk for one-year mortality above 1.2 were identified and included in the index, and weights were assigned for each condition, then summed to create a single index for each patient.[500] A higher Charlson index score was associated with a greater comorbid

burden and subsequently shown to be associated with a stepwise increase in observed mortality. It was suggested that this method could be used to prospectively classify comorbid conditions which might alter the risk of mortality in longitudinal studies.[500]

With the use of both ICD 9 and ICD 10 codes in many administrative datasets, the Charlson index has been adapted for both ICD 9 and ICD 10 coding schema. Two different versions of the Charlson index have become popular amongst investigators, with the method chosen by Deyo, et. al.[510] tending to adhere to a strict interpretation of the original Charlson comorbidity definition, and the Dartmouth-Manitoba adaptation [511, 512] aiming for a more conceptual mapping of codes to comorbid conditions.

However, both methods are able to distinguish between diagnoses more likely related to chronic comorbid conditions and those likely to complications associated with the index admission [510, 512], and have been shown to be effective as a measure of comorbidity in a variety of clinical populations such as patients with lumbar spine surgery in the United States [510], patients with ischaemic heart disease in Canada [513] and patients who underwent bypass surgery in all Massachusetts hospitals.[514] As there is a dearth of information on the effect of comorbidity on asthma outcomes, it would seem imperative to test an adaptation of the Charlson index for this purpose.

Although other adaptations of the Charlson index have been described [513, 514], the Dartmouth-Manitoba adaptation [511, 512] was chosen as the preferred method for this analysis. Reasons for this choice include the international popularity of the method, a history of extensive use by the Centre for Health Services Research (CHSR) at The University of Western Australia (UWA), and the ready utility of replication across different studies. Table 17 below shows the diagnostic categories and assigned ICD codes in the Dartmouth-Manitoba adaptation [511, 512] of the Charlson comorbidity index. Procedure codes are also included in this adaptation of the index, but for brevity they have been excluded from the table, however, a complete table including all ICD disease and procedure codes can be found in Appendix 6.

Table 17: Charlson comorbidity categories, ICD9 & 10, diseases only.

Diagnostic category	Weight [500]	Dartmouth-Manitoba ICD-9-CM & ICD-10-AM codes.[512]
Myocardial Infarction	1	410.xx, 412, I21.x, I25.2
Congestive heart failure	1	402.01, 402.11, 402.91, 425.x, 428.x, 429.3, 404.01, 404.03, 404.11, 404.13, 404.91, 404.93, I11., I42., I50., I13., I11., I43., I11.0, I13.0, I13.2, I42.x, I43.x, I50.x, I51.7'
Peripheral vascular disease	1	440.x, 441.x, 442.x, 443.1-443.9, 447.1, 785.4, I70.x, I71, I71.x, I72, I72.x, I73.x, I77.1
Cerebrovascular disease	1	362.34,430-436, 437-437.1, 437.9, 438,781 4, 784.3, 997.0, G45.x, H34.0, I60.x, I61.x, I62.x, I63.x, I64, I65.x, I66.x, G45., R47.0,
Dementia	1	290 x, 331-331.2, F00.x, F01.x, F02.0, F02.1, F02.3, F02.4, F02.8, F03, G30.x, G31.0, G31.1
Chronic pulmonary disease	1	415 0, 416.8-416.9, 491.x-494, 496, I26., I26.0, I27., I27.0, I27.8, I27.9, J41.x, J42, J43.x, J44.x, J45.x, J46, J47
Rheumatologic disease	1	710 x, 714.x, M05, M05.0x, M05.1x, M05.2x, M05.3x, M05.8x, M05.9x, M06, M06.0x, M06.1x, M06.2x, M06.4x, M06.8x, M06.9x, M08, M08.0x, M08.2x, M08.4x, M12.0x, M32.x, M33, M34.x, M35.x
Peptic ulcer disease	1	531 xx-534.xx, K25.x, K26.x, K27.x, K28.x
Mild liver disease	1	571 2, 571.5-571.6, 571.8-571.9, K70, K70.2, K70.3, K72, K72.1, K73, K73.0, K73.1, K73.8, K73.9, K74.x, 'K76, K76.0
Diabetes (mild to moderate)	1	250 Ox-250.3x, E10., E10.0x, E10.10, E10.11-E10.16, E10.9x, E10.65, E11.00-E11.02, E11.10-E11.16, E11.65, E11.9x, E12, E12.0, E12.1x, E12.9x, E13.00-E13.02, E13, E13.10-E13.16, E13.65, E13.9x, E14, E14.00, E14.01, E14.02, E14.10-E14.16, E14.9, E14.90, E14.91
Diabetes with chronic complications	2	250.4x-250.9x. E10.20-'E10.23, E10.29, E10.30-'E10.36, E10.39, E10.40-E10.43, E10.49, E10.50-E10.53, E10.59, E10.60-E10.64, E10.69, E10.70, E10.71, E10.73, E10.8, E11.20-E11.23, E11.29, E11.30-E11.36, E11.39, E11.40-E11.43, E11.49, E11.50-E11.53, E11.59, E11.60-E11.64, E11.69, E11.70-E11.73, E11.8, E11.8x, E12.2x, E12.3x, E12.4x, E12.5x, E12.6x, E12.7x, E12.8x, E13.20-E13.23, E13.29, E13.30-E13.36, E13.39, E13.40-E13.43, E13.49, E13.50-E13.53, E13.59, E13.60-E13.64, E13.69, E13.70-E13.73, E13.8, E13.81, E14.20-E14.23, E14.29, E14.30, E14.31-E14.36, E14.39, E14.40-E14.43, E14.49, E14.50-14.53, E14.59, E14.60-E14.64, E14.69, E14.70-E14.73, E14.8, E14.80, E14.81
Hemiplegia or paraplegia	2	342 x, 344.x, G81, G81.0, G81.1, G81.9, G82.x, 'G82.0x, G82.1x, G82.2x, G82.3x, G82.4x, G82.5x, G83.x, S14.7x
Renal Disease	2	585 586, V42.0, V45.1, V56.x, N18, N18.x, N19, Z49.1, Z49.2, Z94.0, Z99.2
Any malignancy, including lymphoma and leukaemia	2	140.x- 171.x, 1 74.x- 1 95.x, 200.xx-208.x, 273 0, 273.3, V1O.46, C00., C00.x, C01., C02.x, C03., C03.x, C04., C04.x, C05., C05.x, C06., C06.x, C07., C08., C08.x, C09., C09.x, C10., C10.x, C11., C11.x, C12., C13., C13.x, C14., C14.x, C15., C15.x, C16., C16.x, C17., C17.x, C18., C18.x, C19., C20., C21., C21.x, C22., C22.x, C23., C24., C24.x, C25., C25.x, C26., C26.x, C30., C30.x, C30.1, C31., C31.x, C32., C32.x, C33., C34., C34.x, C37., C38., C38.x, C39., C39.x, C40., C40.x, C41., C41.0, C41.0x, C41.x, C43., C43.x, C44., C44.x, C45., C45.x, C46., C46.x, C47., C47.x, C48., C48.x, C49., C49.x, C50., C50.x, C51., C51.x, C52., C53., C53.x, C54., C54.x, C55., C56., C57., C57.x, C58., C60., C60.x, C61., C62., C62.x, C63., C63.x, C64., C65., C66., C67., C67.x, C68., C68.x, C69., C69.x, C70., C70.x, C71., C71.x, C72., C72.x, C73., C74., C74.0, C74.x, C75., C75.x, C76., C76.x, C81., C81.x, C82., C82.x, C83., C83.x, C84., C84.x, C85., C85.x, C88., C88.x, C90., C90.x, C91., C91.x, C92., C92.x, C93., C93.x, C94., C94.x, C95., C95.x, C96.0, C96.x, D89.0,
Moderate/severe liver disease	3	572.2-572.4, 456.0-456.2x, I85., I85.x, I98., I98.2, I98.x, K72, K72.x, K75.0, K75.1, K76.6, K76.7, K72.,
Metastatic solid tumour	6	196.x-199.x, C77., C77.x, C78., C78.x, C79., C79.x, C80., C97
AIDS	6	042.x-044.x, B20, B20., B21, B21., B22, 'B22., B23, B23., B23.x, B24, B24.'

3.6.3 Comorbidity Methods

The administrative hospital data provided by the Morbidity Data System for this study contains up to 19 ICD discharge diagnostic codes, the first being a mandatory field describing the principal discharge diagnosis.[483] When two or more equally treated conditions exist at the time of admission, the condition requiring the most resources is selected as principal diagnosis.[515] Further diagnoses are recorded for any other conditions that may affect patient care, including clinical evaluation, treatments, diagnostic procedures, extended length of stays, or increased nursing care and monitoring.[515]

One limitation is that complications that arise during a hospital stay are recognised as being distinct from a comorbid condition, but are often hard to define and unable to be distinguished in the hospital data. SPSS syntax, based on the Dartmouth-Manitoba adaptation [512] as developed by the CHSR, was used to generate a Charlson comorbidity index for each episode of interest, in this study's case, the patient's index admission (defined below).

Recent work conducted by the CHSR had shown that there was potential for overestimation of the comorbid effect if analysis included comorbid conditions that related to hospital admissions that occurred more than twelve months prior to the episode of interest.[516] This was particularly true for those conditions that may have been completely resolved with treatment. As a result, it has become standard practice to only include comorbid conditions identified where the admission date is within the twelve-month period prior to the episode of interest.[516]

It is noted, however, that the association between the duration of comorbid conditions and the outcome of an ambulance-transported episode of asthma has yet to be determined. Hence, the effect of applying longer time periods than twelve months to the inclusion of comorbid conditions is also unknown. However, previous studies have shown little or no significant effect of extending the qualifying period. For example a study involving the effect of comorbidity on cardiac arrest survival analysed the comorbid effect based on varying numbers of years of hospital records (1, 2, 5, and 10

years) and found little difference in the performance of the model of cardiac arrest survival irrespective of the number of years of hospital records used.[517]

In the light of this, and for purposes of comparability across research studies, the candidate has elected to use the twelve month period as recommended by the CHSR for the calculation of the comorbidity index, created as follows. All discharge diagnostic codes from hospital morbidity episodes associated with an asthma ambulance transport were coded according to the 17 diagnostic categories of the Charlson Index (comorb1 to comorb17), the value 1 denoting the presence of a comorbid condition. As the study spanned the transition from ICD9 to ICD10 coding regimes [485], the syntax was adjusted to cover both ICD9 and ICD10 codes.

The last hospital admission that linked to an ambulance transport for asthma for any particular patient was deemed to be the index admission for that patient, and any prior hospital morbidity record with a separation date within twelve months of the index admission was considered eligible for the inclusion of comorbid conditions. If the time between the last hospital admission and the index admission was greater than twelve months, the comorbidity index was set to zero.

Once syntax was run, the data comprised a series of episodes reflecting the previous twelve months comorbidity up to and including the index record for each patient, with a 0/1 flag attached to each qualified comorbid condition. The data was then aggregated by patient for the 17 diagnostic categories (comorb1 to comorb17), eliciting a single line of the sum of all instances for each category.

These were then recoded to a dichotomous 0/1 variable to indicate the presence or absence of a comorbid diagnostic category, on which syntax was run to calculate the Charlson index. This resulted in an overall Charlson index calculated for the entire period of study from 1991 to 2001 for comparison, and a variable that could be used for modelling purposes.

3.7 SOCIOECONOMIC FACTORS

3.7.1 Introduction

Previous research has highlighted that some ethnic minorities of low socio-economic status (SES) in the United States are disproportionately represented in the trends of increasing asthma prevalence, morbidity, and mortality.[166, 167] However, in Chinese, African and other indigenous populations the prevalence of asthma is between 0.5% and 12% compared to countries such as Australia and New Zealand, where the prevalence is much higher at approximately 20-25%.[168] However, there is little in the published literature to either explain these differences or address the question of how SES specifically relates to asthma outcomes. There have been a number of major publications in Australia that have used census-based indices to show associations between area-defined socio-economic disadvantage and health status.[518]

This chapter explores the effects that SES may have on the incidence and outcome of those patients with asthma that are transported by ambulance throughout the period of the study. The SEIFA index will be used to represent the SES of the patients in this study, being a summary measure of SES derived from the five-year Australian Population Census data.[519]

3.7.2 SEIFA

The Australian Bureau of Statistics conducted the first Australian Census of Population and Housing in 1911. It was followed by others in 1921, 1933, 1947 and 1954. Since 1961, a population census has been conducted every five years to obtain a wide range of economic and social information about the Australian population.[520]

Socio-Economic Indexes for Areas (SEIFA) are indices of summary measures derived from census data and provide a method of determining the level of social and economic well being in that region to allow ranking of regions or areas. The indices are compiled at the level of the census Collection District (CD) in which a person lives, are produced from principal components analyses of selected census-based socio-economic variables,

and have been standardised to have a mean of 1000 and a standard deviation of 100 across all the CD's of Australia.[519, 521] A Collection District (CD) is the smallest geographical area usually made up of approximately 250 dwellings, which would be equivalent to a small group of suburban blocks in an urban area. A Postal Area (POA) is a census specific hierarchy comprised of those whole CD's that best fit within the boundaries of an Australian Post postcode [521], and can be considered the equivalent of a postcode. Data collected for this study spans three census periods over twelve years, and it is the postal area geographical group (POA) that this study will be most concerned with.

The three census period data each produced the following indices:

- Urban Index of Relative Socio-Economic Advantage (1991, 1996)
- Rural Index of Relative Socio-Economic Advantage (1991, 1996)
- Index of Advantage/Disadvantage (2001)
- Index of Relative Socio-Economic Disadvantage (All)
- Index of Economic Resources (All)
- Index of Education and Occupation (All)

Each index summarized different dimensions of the socio-economic condition of areas, and has been shown to be useful constructs in describing relationships with various dimensions of health status.[247, 522] The Index of Relative Socio-Economic Disadvantage (IRSD) is the SEIFA index most frequently used in health analysis, summarizing particular attributes including low income, low educational attainment, high unemployment and jobs in relatively unskilled occupations.[238]

Frequent use of these indices have been made in the field of public health research and the academic public health research literature, especially the IRSD.[523-527] Major publications from the New South Wales Health Department [528], the NSW Cancer Council [522], the Australian Institute of Health and Welfare [247, 529] and the National Centre for Epidemiology and Population Health and the Australian Bureau of Statistics [530], have all used the IRSD to show associations between area-defined socio-economic

disadvantage and health status. Widespread use of standard indexes by researchers also carries the advantage of research comparability.[518]

However, the use of these indices has two principal limitations.[518, 531] Firstly, the indices are created by analysis of census-based socio-economic variables which are then standardised and collapsed down into a summary variable. This makes them imprecise instruments, for although they may be able to report broad descriptive associations, e.g. confirming that a particular health status is related to SES, if a causative pathway were being explored, they would lack specificity to guide aetiological investigations and health promotion activities.[518] The second limitation is that the scores produced by principal components analysis (which underpins the summary variables) are not totally unambiguous indicators.[518] This means that although areas sharing the same SEIFA score may share similar constituent profiles, there will be cases where the scores mask significant socio-economic differences between areas.[531]

However, despite these limitations, the SEIFA indices are considered entirely appropriate indicators for this study, as the intent is to establish and report on any summary association between the use of ambulance services by patients with asthma and SES, and the influence of SES on outcome. As the linked data used in this study does not include information that make up the individual components of the SEIFA indices (e.g. income, qualifications, labour force status/occupation), the use of the summary variable provides the best opportunity to examine SES effects.

Commonly, SEIFA data has been used to group survey respondents into quintiles of a particular index. Comparisons can then be made between respondents living in areas based on SEIFA quintiles across a range of health-related characteristics.[238]

3.7.3 SEIFA Methods

To be able to estimate the effect SES has on the asthma patient utilization of ambulance services and outcomes, the home address for each of the cases was geocoded to derive the 1991, 1996 and 2001 census Collector's District (CD). Unfortunately, not all patient addresses could be successfully geocoded to a CD, with information missing in 5.9% of cases for 1991 and 1996 and 14.3% in 2001. However, although a larger statistical area, postcode information was present in the majority of cases, and where missing, most could be resolved to a known postcode manually. In view of the potential of missing CD information to reduce validity of results, and the completeness of postcode information, it was decided to use postcode information and not CD information for analysis.

In the ambulance data, two addresses were recorded, one being the patient's home address, the other being where the patient was attended. The postcode of the patient's home address was mapped to the appropriate ABS postal area (*home_poa*), and then the postcode of the address of actual ambulance attendance for that case was also mapped to the appropriate ABS postal area (POA) for comparative purposes (*from_poa*).

Where a CD resided over two postcodes, the postal area was deemed to be that where the majority of the CD resided geographically.[238] This meant that there may be small discrepancies between the total population of a particular postcode and its postal area, however all SEIFA IRSD indices for postal areas were a derived measure based on attributes of the individual CD's within that area. Therefore, as this study compares the IRSD for postal areas which are based on CD attributes, it is considered both reasonable and appropriate to use the postal area IRSD as a surrogate measure of disadvantage for postcodes.

As this study encompassed three census periods, SES indices were calculated for each census period using three different census denominators, to elicit an SES index that was applicable to any period of the study. For example, the calculation of the SES quintiles

for home and attended postal areas in 1991 used the 1991 census population data for those postal areas at that time.

In practical terms this meant a more accurate representation of SES for that time, thus any discussion that involved the early years of the study could be examined in terms of the 1991 census data, the middle years of the study in terms of 1996 census data, and the final years in terms of 2001 census data. This way, any particular episode of care for a patient over the time of the study would be examined in terms of the relevant census SES period.

The steps taken to derive the five quintiles of SES based on the SEIFA Index of Relative Socio-economic Disadvantage (IRSD) were based on a method used previously by the School of Population Health of the University of Western Australia [517], and were as follows:

- Population numbers of residents were obtained for each of the postal areas in Western Australia from the ABS Census data of 1991, 1996 and 2001. Gender information for postal areas was only available for the 1996 and 2001 census periods.
- For each one of the three census periods, the Western Australian population was sorted by SEIFA IRSD in descending order for postal areas. This meant that the highest IRSD index indicated the highest SES.
- The data was then categorized in to five quintiles, each representing approximately 20% of the cumulative population (1 = highest SES, 5=lowest SES) for each of the census periods.
- The number of asthma cases transported by ambulance was then aggregated for each postal area that comprised each quintile, resulting in a crude rate of asthma cases for each quintile of SES for each census period.

- The age standardised rate of asthma cases for each quintile were then calculated for postal areas (both *home_poa* and *from_poa*), and age-stratified (both five and ten year strata) rates were also calculated using the standard Australian 2001 population (Appendix 7).
- Poisson regression analysis was then used to describe differences in crude, gender, age standardised and age stratified rates for the 5 quintiles of SES, as described by the SEIFA IRSD for each census period (Appendix 8).

Poisson regression analysis for the last step described above was performed using the SAS GENMOD procedure. This was because the data in the linked file was correlated data, where approximately 25 percent of the patients have presented more than once with an episode of asthma over the period of the study. As a result, overdispersion would occur, with the potential to lead to an underestimation of variance-terms and confidence intervals and make results look more significant.[532, 533] However, in Poisson analysis, overdispersion can be taken into account by estimating a dispersion parameter, and the SAS GENMOD procedure was chosen to perform the Poisson regression analysis because a dispersion parameter could be estimated to readily correct for overdispersion. In this case the appropriate parameter chosen was a deviance scale estimated by the deviance divided by its degrees of freedom.[534]

3.8 STATISTICAL MODELLING

3.8.1 Introduction

Regression methods have become an integral component of any data analysis concerned with describing the relationship between a dependent (outcome) variable and one or more independent (predictor) variables.[535] Ever since Cornfield, et. al. [536] first used multiple logistic functions to estimate the risk of developing coronary heart disease from a knowledge of systolic blood pressure and serum cholesterol, the logistic regression model has become the standard analysis, especially for outcome data in health services research.[535] In the area of health sciences, the discrete outcome is commonly a dichotomous (binary) variable such as disease/no disease or death/no death, and it is within this discipline that logistic regression techniques have particularly grown in popularity.[537]

The goal of logistic regression analysis is the same as that of any model-building technique used in statistics, and that is to 'find the best and most parsimonious, yet biologically reasonable model to describe the relationship between an outcome (dependent or response variable) and a set of independent (predictor or explanatory) variables'.[535]

Logistic regression allows the prediction of a discrete outcome from a mixed set of variables that may be continuous, discrete, or dichotomous.[537] Logistic regression is quite flexible and differs from other regression techniques in the underlying assumptions and the methods for checking whether or not data fit the assumptions of the model.[538] For example, unlike discriminant-function analysis, logistic regression has fewer assumptions about the distribution of the predictor variables, i.e. the predictors do not have to be normally distributed, linearly related, or of equal variance within each group.

3.8.2 The Logistic Regression Model

The simple linear regression equation $\hat{y} = \alpha + \beta\chi$ describes a linear relationship between χ and y in which, for each unit increase in χ, the estimated value of y increases on the average by β units and in which $\hat{y} = \alpha$ when $\chi = 0$.[537] In epidemiological investigation, the values of χ and y are derived from a cohort or samples of individuals or cases. When the dependent is a dichotomy, simple linear regression cannot be used as a suitable modelling method and binary logistic regression needs to be employed. Multinomial logistic regression exists to handle the case where dependents have more classes than two.

The logistic regression model estimates the probability of an event occurring (P) given the explanatory variables $\chi_1, \chi_2, \ldots, \chi_p$, such that [537]:

$$P = \frac{e^{\alpha + \beta 0 + \beta 1\chi 1 + \beta 2\chi 2 + \ldots + \beta p\chi p}}{1 + e^{\alpha + \beta 0 + \beta 1\chi 1 + \beta 2\chi 2 + \ldots + \beta p\chi p}}$$

which can be shown alternatively:

$$P = \frac{1}{1 + e^{-(\alpha + \beta 0 + \beta 1\chi 1 + \beta 2\chi 2 + \ldots + \beta p\chi p)}}$$

The estimated probability of the event not occurring is 1 – P:

$$1 - P = \frac{e^{-(\alpha + \beta 0 + \beta 1\chi 1 + \beta 2\chi 2 + \ldots + \beta p\chi p)}}{1 + e^{-(\alpha + \beta 0 + \beta 1\chi 1 + \beta 2\chi 2 + \ldots + \beta p\chi p)}}$$

The odds of an event are obtained by dividing the probability of an event by the probability of no event [539]:

$$\frac{P}{1 - P} = \frac{1}{e^{-(\alpha + \beta 0 + \beta 1\chi 1 + \beta 2\chi 2 + \ldots + \beta p\chi p)}}$$

$$= e^{\alpha + \beta 0 + \beta 1\chi 1 + \beta 2\chi 2 + \ldots + \beta p\chi p}$$

The underlying basis of the logistic regression model is the natural logarithm of the odds of the outcome, known as the log odds or logit transformation of P:

$$\log (P / 1 - P) = \alpha + \beta 0 + \beta 1\chi 1 + \beta 2\chi 2 + \ldots + \beta p\chi p$$

The relative odds of an event (odds ratio) is a comparison of those for whom $\chi 1$ is present ($\chi 1 = 1$) with those for whom $\chi 1$ is absent ($\chi 1 = 0$), calculated as below:

$$OR = \frac{e^{\alpha + \beta 0 + \beta 1 + \beta 2\chi 2 + \ldots + \beta p\chi p}}{e^{\alpha + \beta 0 + 0 + \beta 2\chi 2 + \ldots + \beta p\chi p}}$$

$$= e^{\beta 1}$$

Logistic regression applies maximum likelihood estimation after transforming the dependent into a logit variable (the natural log of the odds of the dependent occurring or not). Logistic regression calculates changes in the log odds of the outcome (dependent), not changes in the outcome itself. In this way, the logistic regression coefficients resulting are those that most closely agree with the observed data.[535]

As the logistic model for the probability of outcome elicits values that are always between zero and one, this has important implications for the interpretation of the coefficients. The coefficients obtained indicate the magnitude of the increase or decrease in the log odds produced by one unit of change in the value of the predictor

variable, and thus indicate the effect of an individual variable on the log odds of the outcome with all remaining variables held constant.[540]

One of the outcomes of interest in this study is death by the asthma patient after being transported to hospital by ambulance, and one of the specific goals of the logistic regression modelling in this study is to identify those patient and treatment characteristics that predict the probability of survival. Death is measured as a dichotomous outcome (yes/no) at three time periods relative to discharge from hospital, namely at discharge (died in hospital), at one month from discharge and at one year from discharge. These time periods have been chosen because of their of extensive use by the Centre for Health Services Research (CHSR) at The University of Western Australia (UWA), and the ready utility of replication and comparability across different studies.

3.8.3 Model Development

There remains lively discussion amongst researchers as to the best strategy in developing a model. The traditional and well-accepted approach to model development is to strive for the most parsimonious model based on statistical significance of the coefficients [537], but there is also a line of thinking that all scientifically relevant variables should be included in the model, to optimally control for confounding.[541] However, criticism has been levelled at this strategy for the potential of 'overfitting' the model, resulting in numerically unstable estimates characterised by unrealistically large estimated coefficients and/or estimated standard errors.[535]

For the purposes of this study, the candidate has elected for a strategy that borrowed a little from both ends of the spectrum. Those predictors that have been identified in previous research to be associated with the outcome, along with relevant predictors that have been shown to have a univariate association with the outcome have been included. Predictors that may have an association with the outcome but make no theoretical or clinical sense have been excluded. As a result, the predictor (independent) variables age, gender, cumulative length of stay, comorbidity index score, total number of admissions, and ventilation history have been selected for modelling purposes with

death and readmission being outcomes of interest. The death outcome is analysed at three levels; death at discharge, death within thirty days from discharge, and death within thirty days to one year after discharge, and the readmission outcome is analysed at two levels; readmission within seven days from discharge, and readmission within thirty days of discharge.

There are three major types of logistic regression: direct or standard, where all predictors enter the equation simultaneously; sequential, where the researcher can specify the order of entry of predictors into the model; and stepwise, where the inclusion and removal of predictors from the equation are based solely on statistical criteria.[537] The SPSS LOGISTIC REGRESSION procedure allows the use of all three of these techniques to specify and control the method of entry of variables into the model. Stepwise methods have been criticised for their ability to generate biologically implausible models from the injudicious inclusion of variables [535], but this can be readily mitigated by including only in the model those reasonable variables that make clinical sense in the context of the outcome, and using the stepwise procedure cautiously in the development of a robust model.

3.8.4 Assumptions and Limitations of Logistic Regression

Logistic regression is able to analyse a mix of all types of predictors, e.g. continuous, discrete and dichotomous), and although the outcome variable does have to be discrete, a continuous variable can be converted to a discrete one when there is reason to do so. The technique has the useful property of producing predicted values that are probabilities between 0 and 1.[537] There are, however, certain limitations that must be addressed, and these will be discussed below.

Linearity in the Logit

Logistic regression does not assume linearity of relationship between the predictors and the outcome, does not require normally distributed variables and does not assume homoscedasticity.[537] It does, however assume that observations are independent and that the logit of the outcome variable is linearly related to the predictor variables. To test this, the logistical transformation (logit) of the predicted probabilities of the different outcome variables were plotted against each predictor variable and examined

graphically for linearity.[535] All of the predictor variables displayed a linear relationship to the logit of the outcome, so it is concluded that the assumption of linearity for the model has not been violated.

Ratio of Cases to Variables

It was also necessary to check that the number of cases available for analysis was adequate for the purposes of regression analysis. Tabachnick and Fidell [537] suggest a formula for calculating sample sizes requirements, taking into account the number of predictor variables that may be used. For this study, where stepwise regression techniques were used, the formula was such: $N > 50 + 40m$ (where m = number of predictor variables). This calculation suggests a minimum number of 450 cases if up to ten independent variables were used in the development of a regression model. The study cohort included 15,671 ambulance cases linked to 9,766 hospital separations, and elicited 3,471 index admissions available for analysis, which was considered more than adequate in size for purposes of regression analysis.

Multicollinearity

Multicollinearity exists when there is a relationship among the independent variables and they are highly correlated (say for example, $r = 0.9$ and above).[537] Regression techniques elicit inaccurate results in the presence of multicollinearity, so it was necessary to check for high inter-correlations amongst the predictor variables chosen for the regression model. There is no formal way to test for multicollinearity in the logistic regression procedure of SPSS, but this test can be legitimately performed as part of collinearity diagnostics under the SPSS multiple regression statistics procedure.[537]

All predictor variables chosen for analysis in the logistic regression model were tested for collinearity by fitting them to an SPSS multiple regression model, and examining the results. Analysis of the Collinearity Statistics section of results in the Coefficients Table of the multiple regression output, elicits two values of interest, Tolerance and VIF. Tolerance is an indicator of how much of the variability of the specific predictor is not explained by the other predictor variables in the model and is calculated using the formula $1- R^2$ for each variable, where R^2 is a measure of how much of the variance in the dependent variable is explained by the model. Tolerance values that are very low

(less than 0.1) indicate that a variable has high correlation with other variables in the model, suggesting the possibility of multicollinearity.

The other value, VIF (Variance inflation factor), is the inverse of the Tolerance value (1 divided by Tolerance), and VIF values above 10 would indicate the presence of multicollinearity.[541] For all combinations of included predictors and for all outcome variables, the Tolerance value was at least 0.758, with a VIF never exceeding 1.320, suggesting that there is no evidence to support the presence of any inter-correlating variables.[541]

Outliers

One or more cases may be very poorly predicted by the model, and a case that actually is in one category of outcome may show a high probability for being in another category. If there are enough cases like this, the model has poor fit.[537] Outliers can be detected by a number of methods including the analysis of standardised residuals and Cook's distance, both calculated as an option in the SPSS logistic regression procedure.[537]

The residual is the difference between the observed probability of an event and the predicted probability of the event, as calculated by the model [542], and the standardised residual is the residual divided by an estimated of its standard deviation. Standardised residuals greater than 2 are the extreme 5% of cases and greater than 3 are the extreme 1% of values, suggesting potential outliers.[538] Cook's distance is a measure of influence of a case, and offers information about how much deleting a case will affect the residual for that case as well as the residuals of the other cases.[542] If the value of Cook's distance is greater than one, this suggests a case of heavy influence and it should be investigated.[538]

Both of these diagnostic tests were run against all possible combinations of predictor variables fitted to the logistic regression model for all survival outcomes. Some cases were identified where the standard residuals were greater than 2 in most of the models, suggesting outliers, but there were only three cases that exceeded the Cook's distance threshold value of one. These cases were examined closely, and there was no evidence to suggest that these were not legitimate cases. In the light of this, and the fact that

other analysis shows adequate model fit (see section 3.8.5), it was considered that although these cases may well be considered outliers, they should remain in the data for analysis.

Independence of errors

Logistic regression assumes that responses of different cases are independent of each other, i.e. it is assumed that each response comes from a different, unrelated, case. If the levels of the outcome variables are formed by any time period in which measurements are taken (e.g. before and after some treatment), have been matched on a 1 to 1 basis (e.g. a matched case-control study) or are the result of a repeated-measures design, then logistic regression procedures may be inappropriate because of correlated errors.[537]

For this study, each episode of care has been carefully recorded with many variables describing a range of demographic, geographic, treatment and clinical data, with the primary outcome under study being death. As there may be multiple episodes recorded over time for a single patient, it must be assumed there is a lack of independence between each episode of care for that particular patient. Some variables may remain constant (cluster-level covariates) over the period of the study, e.g. gender and socioeconomic status, whereas others may change from one episode to another (cluster-specific covariates), e.g. age, urgency, response time and treatment. The date also changes in a systematic way and can been used to model temporal effects, but the issue of correlated data and the subsequent lack of independence needed to be addressed.

For the outcome of survival, the index admission was defined as the last admission for asthma by a particular patient. Survival was defined by death relative to the time of discharge from this index admission, categorised into the three periods of interest; at discharge, within thirty days of discharge or within one year of discharge. The data was sorted longitudinally by date and time, and variables of interest were chosen from the episodes of care of a patient up to and/or including the index admission.

As the outcomes of survival were relative to the index admission, it was then appropriate to reduce the multivariate responses from each patient (cluster) into a univariate response without major loss of information.[543] This involved calculating

accumulated data from previous episodes of care for a patient and then copying the results onto the index admission record, e.g. Charlson comorbidity index, cumulative length of stay, ventilation history and total number of admissions.

This method resulted in one episode of care per patient in the study which included all the necessary covariates for logistic regression. Summarizing the data effectively collapsed multiple response information from cluster-specific episodes for a patient into one response per cluster, whilst retaining characteristics of the cluster.[543] This created a true between-subjects strategy, removed any potential violation of independence from the model due to correlated data, and allowed standard SPSS logistic regression analysis to be performed for all of the survival outcomes.

3.8.5 Goodness of Fit

The term 'goodness of fit' relates to how well the logistic regression model developed actually describes the outcome variable of interest.[537] Logistic regression has two types of inferential tests: the tests of models and tests of individual predictors. It is noted that there are not only numerous possible comparisons among models (e.g. between the constant-only model and the full model, or between a chosen model and the perfect model, etc.), but also several tests to evaluate goodness of fit.[537] As no single test is universally preferred, to test for goodness of fit for both the model and predictors, the candidate has elected to use those tests that have been used regularly by other researchers and available in the SPSS software.[537]

The first step in this analysis was to check if the predictors as a group contribute to prediction of the outcome. There are a number of methods to achieve this, and two of these methods, described below, were used for this purpose.

Constant-Only Model versus Full Model

This is done by a comparison of the constant-only model with a model that has the constant plus all predictors.[537] If no improvement is found when all predictors are added, the predictors are unrelated to the outcome.

Often called the likelihood ratio test [534], this comparison uses the log-likelihood technique, where the probabilities associated with the predicted and actual outcomes for each case are summed. The change in likelihood values is used to determine the effect on the fit of the model as predictor variables are added and deleted from the model.[542] In general, as predictors are added/deleted, log-likelihood decreases/increases. When one model contains all the predictor variables, and the other model contains only the constant, the difference in their log-likelihoods is calculated to create a statistic that is distributed as chi square.[537]

This is calculated as the difference between the minus twice the log of the likelihood (-2LL) of the model with predictors and the model without. This obtains a quantity whose distribution is known and hence can be used for hypothesis testing.[535] The degrees of freedom (df) are the difference between degrees in freedom for the bigger and smaller models, where the full model has 1 df for each predictor and one for the constant, and the constant-only model has 1 df.[537]

For each of the models under analysis the -2LL for constant-only and all predictors included were calculated and chi-square statistics reported (See Appendix 9). It can be seen that for all models, the significance level for the chi-square statistic was $P < 0.000$, leading to rejection of the null hypothesis that the coefficients for the variables entered into the model are zero, and leading to the conclusion that the predictor variables are associated with the outcome.

Deciles-of-risk

The Hosmer-Lemeshow goodness-of-fit test evaluates deciles-of-risk by creating ordered groups of cases and then comparing the number actually in each group with the number predicted into each group by the logistic regression model. Cases are sorted by their estimated probability on the outcome variable and then divided into ten groups. The cases are then divided into two groups on the outcome variable to form a 2 x 10 matrix of observed frequencies, and then expected frequencies for each of the 20 cells are obtained from the model. If the logistic regression model fit is good, most of the cases with outcome 1 will be in the higher deciles of risk and most with outcome 0 will be in the lower deciles of risk. If the model fit is not good, then the cases are roughly evenly spread among the deciles of risk for both outcomes 1 and 0.[537]

The contingency tables for the Hosmer and Lemeshow test are displayed along with results of the test in the formal output of SPSS analysis. Examination of these contingency tables confirmed that for all models, most of cases with outcome 1 were in the higher deciles-of-risk. Goodness-of-fit was formally evaluated using the Hosmer-Lemeshow statistic where a good model produced a non-significant chi-square. Again, for each of the models under analysis, the chi-square statistic ranged from 3.016 to14.431 on 8 df and significance level ranged from 0.933 to not less than 0.071 (Appendix 9). Thus the null hypothesis of no difference between the observed and predicted values for this model was not rejected, suggesting that the model fitted the data reasonably well.[541]

3.8.6 The Logistic GEE Model

The second outcome of interest in this study was that of readmission. Two readmission outcomes were defined as an admission for asthma that followed a previous admission for asthma by the same patient within either seven days (readm7) or thirty days (readm30). As the calculation of readmission variables involved time-dependent longitudinal data for each patient (cluster), the use of normal logistic regression was not used, due to a potential lack of independence within the cluster of episodes of care for a patient.

For analysis of clustered data, the logistic generalized estimating equation (GEE) model has become a widely used method.[544] The GEE model developed from quasi-likelihood methods that were introduced to the generalised linear model (GLM) approach by Wedderburn [545] and Nelder and Wedderburn [546] during the early seventies. This work has been developed and extended by others [547, 548], and has since been used widely in cross-sectional analyses.[549] Liang and Zeger [550] proposed an extension of the GLM for the analysis of correlated data in the context of repeated observations over time, and in doing so spawned the current development and growth of the various GEE models available today.[551]

Just as the maximum likelihood theory underpins the foundation for GLM, quasi-likelihood theory underpins that for GEE models. For a dichotomous outcome, the logit

(log odds) function is used as a link function, and the logistic model for correlated data looks almost identical to the standard logistic model, seen below.[552]

$$\log (P / 1 - P) \quad = \quad \beta 0 + \beta 1 \chi 1 + \beta 2 \chi 2 + \ldots + \beta p \chi p$$

The difference is in the underlying assumptions of the model, including the presence of correlations, and the way in which the parameters are estimated. There are several advantages for using the GEE approach for estimating models with correlated data. In general, with longitudinal data, independent variables may or may not vary within a cluster. A time-dependent variable can vary in value, whereas a time-independent variable does not, and the values of the outcome variable, in general, will vary within a cluster. A correlated analysis attempts to account for the variation of the outcome from both within and between clusters.[552]

Further, as the researcher can specify the nature of the working correlation structure, the models allows for the explicit inclusion of knowledge, based on theoretical considerations and assumptions about within-cluster interdependencies. At the same time, the parameter estimates obtained through the application of these models are very robust to misspecification of those correlations, which is important as the researcher's understanding of those relationships may often be imperfect at best.[551]

Numerous simulation studies have shown that although accurately modelling of the correlation structure of the data improves the efficiency of the GEE estimates, this robustness means that good estimates of the regression parameters can still be obtained even when the researcher is unsure of the exact nature of the correlation among the covariates.[550, 553]

Another advantage of GEE modelling is that results can be reported and interpreted in the same way as simple logistic regression. Odds ratio estimates, confidence intervals, and Wald test statistics are obtained using the GEE model output in the same manner (i.e. with the same formulas) as output from a standard logistic regression.[554, 555] The difference between the GEE and standard logistic regression models are the underlying assumptions and how their variances are estimated [552], for example, the GEE model is not based on full-information maximum likelihood.

This means that likelihood-ratio tests for model fit and block significance used in standard logistic regression are not available. However, GEE models are fully amenable to other asymptotically identical tests such as score and Wald tests, and most statistical packages which implement GEE models also provide procedures for conducting such tests.[551]

3.8.7 Model Choice for Readmission Outcome

It has become a common practice in the analysis of correlated patient data that if the majority of the patients in the cohort have more than one record, then it is recommended to use a GEE population-averaged model.[556] The choice of a specific correlation structure is defined within the model to best describe what the researcher knows about the data.[556]

There is a large and rapidly expanding literature dealing with methods for the analysis of correlated data and established models for correlated binary data are now readily available in many of the major software packages.[535] As the SPSS program did not have the capability to adjust for correlated data, the software package STATA [557] was used for GEE modelling purposes.

For health data, common choices include either an exchangeable correlation structure where the order of observations within a cluster is arbitrary, or an autoregressive correlated structure where there are repeated responses over time within a given cluster. If there was not a majority of patients with more than one record, it has also become accepted that a standard logistic regression model may be used with a robust standard error as long as the data could be defined by some cluster-specific variable.[535]

In this study, there were 5,961 individual patient clusters, of which 4,389 (73.6%) only had one admission during the period of the study. However, the remaining 1,572 patients accounted for 5,377 admissions (min: 1, max: 50: mean: 3.4), which was 55.1% of total admissions. At face value, it appeared that a standard logistic regression model with robust standard error would be adequate for analysis, but in the absence of a clear definition of ‘majority’ and a dearth of clear guidelines for the selection of the best

model [535, 544, 552], the candidate chose to compare and contrast both methods, with a view to obtaining the best model.

Variables were selected for modelling purposes via the same process as described for the survival outcomes previously. For the readmission outcome at seven days (readm7) the predictor (independent) variables age, gender, urgency and ventilation for asthma were selected, and for the readmission outcome at thirty days (readm30) the predictor (independent) variables age, gender, and ventilation for asthma were selected for modelling purposes.

For the analysis of the readmission outcomes, the software package STATA was used as it was capable of estimating both logistic and GEE models for binary outcomes and allowed a variety of correlation structures that could be considered when performing a correlated analysis. These correlation structures were as follows: independent, exchangeable, AR1 autoregressive, stationary *m* dependent, unstructured and fixed. In addition, robust standard errors were available and could be clustered by observation, time-point, or other user-specified variables.[558]

Autoregressive (AR1) correlation structure

The assumption behind the use of the exchangeable correlation structure is that any two responses within a cluster have the same correlation (ρ).[552] However, for purposes of analysis the candidate has chosen the autoregressive correlation structure, as it is based on the assumption that the correlation between responses depends on the interval of time between responses. As an example, two admissions for an asthma patient only days apart are considered to be more highly correlated than two admissions for that same patient that occur years apart.

AR1 is a special case of autoregressive correlation structure, and is widely used because it assumes only one correlation parameter and software packages readily accommodate it.[535] The AR1 assumption is that the correlation between any two responses from the same subject equals a baseline correlation (ρ) raised to a power equal to the absolute difference between the times of the responses, seen below [552]:

AR1 Assumption: Y at t_1 and t_2:

$$\rho_{t1,t2} = \rho^{|t1 - t2|}$$

As with the exchangeable correlation structure, the AR1 structure has just one correlation parameter, but in contrast to the exchangeable assumption, the order of responses within a cluster is not arbitrary, as the time interval is also taken into account.[552] Therefore, the AR1 structure is considered by the candidate to be a more intuitively appropriate approach for analysis of the readmission outcomes.

Goodness of Fit for Logistic GEE Model

Goodness of fit tests were conducted by running the STATA 'lfit' and 'lfit, group(10)' commands after previously estimating the logistic model. The routine *lfit* presents a Pearson chi-square goodness-of-fit test for the logistic model (observed versus expected frequencies of y=1, using cells defined by the covariate (x-variable) patterns). The routine *lfit, group(10)* invokes the Hosmer & Lemeshow deciles-of-risk test (discussed earlier) which groups the data in deciles of estimated probabilities and performs the test with 10 approximately equal-size groups.

For the seven-day readmission outcome *lfit* elicited a $\chi2$ (1052) = 1280.18, significant at p <0.000, and *lfit, group(10)* elicited a $\chi2$ (8) = 3.95, not significant at p = 0.862. The generalised Wald test statistic elicited a $\chi2$ (4) = 93.77, significant at p < 0.000 for the LR model and $\chi2$ (4) = 97.35, significant at p < 0.000 for the GEE model, suggesting a good fit to both of the models. For the thirty-day readmission outcome, modelling revealed only one significant predictor variable, and as such there was inadequate information for the *lfit* and *lfit, group(10)* analyses. However the generalised Wald test statistic, at $\chi2$ (1) = 14.43, significant at p <0.000 for the LR model, and $\chi2$ (1) = 9.62, and significant at p =0.019 for the GEE model, suggested this predictor is reliably associated with the outcome for both models.[537]

3.8.8 Summary

The primary statistical modelling techniques used in the analysis of the linked data for this thesis were logistic regression and general estimating equation (GEE). They allowed the estimation of the effects on the outcome by adjusting for independent and aggregate effects of predictor variables. The coefficients have then been used to estimate the magnitude of the relationship between the outcome and a predictor, whilst adjusting for other confounders, and the calculation of respective odds ratios.

Logistic regression model for survival outcome.

Tests for assumptions of the logistic model showed that there were no obvious violations, and following successful checks for linearity of the predictors to the logit of outcome, all continuous variables were entered into the model for the outcome of survival, with gender being entered as a categorical variable. Both model and predictor variable goodness-of-fit tests revealed that the model fitted the data well. The model was developed by the candidate using a combination of direct entry, step-wise and sequential methods to enter variables and/or interactions of interest into the model.

Variables chosen for examination included those that showed significant univariate association with the outcome, or were identified as relevant by previous research evidence. As a result the variables age, gender, Charlson comorbidity index, cumulative length of stay, ventilation history (6 variables) and total number of admissions were selected for modelling for the primary outcome of survival.

GEE model for readmission outcome.

Both logistic and population-averaged GEE models with a robust standard error were used for analysis of the readmission outcomes. For both models, a cluster variable (*ptseq*) was defined to identify individual patients. As the GEE model is a generalisation of quasi-likelihood estimation, the joint distribution of the data did not need to be specified however, in the presence of clustered patient data, an autoregressive correlation structure (AR1) was chosen to describe how the responses within clusters were related to each other. The cluster variable (*ptseq*) and a time-dependent variable (*t_seq*) were used to define when an episode of care occurred for a patient over the period of the study, for the purposes of the autoregressive process. An assumption was made of independence between patients (clusters).

The models were developed by the candidate using a combination of direct entry methods to enter variables and/or interactions of interest into the model. Variables chosen for examination included those that showed significant univariate association with the outcome, or were identified as relevant by previous research evidence. As a result the variables age, gender, ventilation for asthma, invasive ventilation, problem urgency (ATS) and season (season2) were selected for modelling for the outcomes of readmission within seven days of a previous hospital asthma admission.

The variables chosen to model the outcome of readmission within thirty days of a previous hospital asthma admission were age, gender, ventilation for asthma, both invasive and non-invasive ventilation and season (season2). Results from both of the modelling methods are reported as odds ratios with 95% confidence intervals and P values. Goodness-of-fit tests suggested that both models fit the data well.

Both methods resulted in comparable results, with the identification of the same variables of significance. Similar odds ratios and confidence intervals were obtained, although the GEE model tended to slightly underestimate the odds ratios with narrower confidence intervals in comparison to the LR model. This was the same for both of the readmission variables. Based on these results, and in the light of the theoretical rationale behind the nomination of a correlation structure for these data, the candidate has chosen to select the GEE model as the preferred method for analysis of the readmission outcomes.

4.0 RESULTS

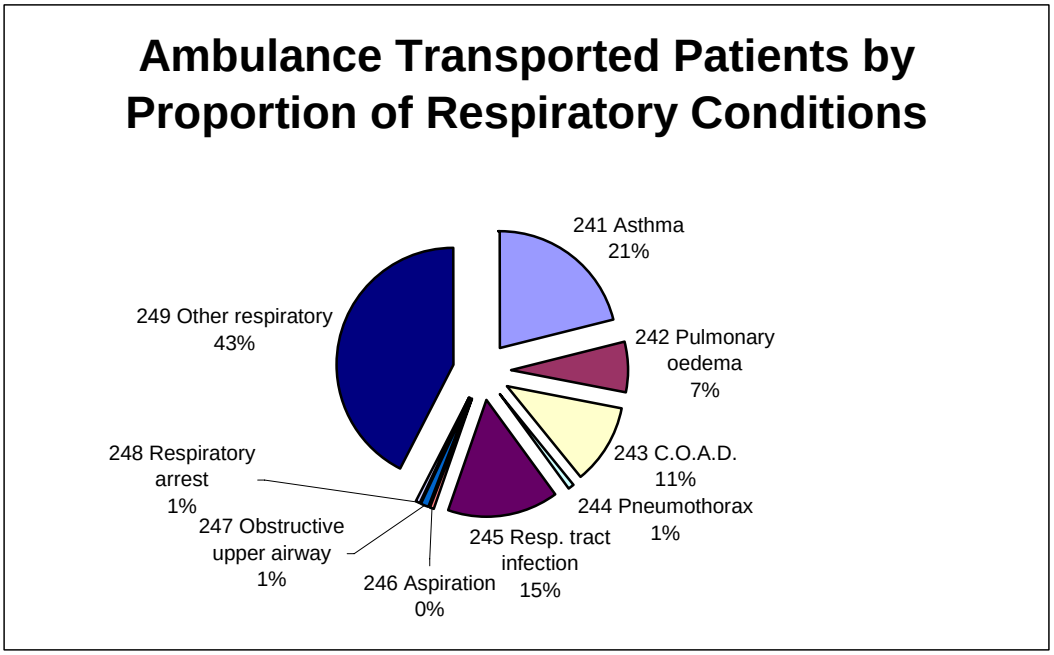
Wherever mentioned in this thesis, the level at which results are considered significant will be $p < 0.05$.

4.1 DESCRIPTIVE RESULTS

4.1.1 All Cases

There were 1,085,406 cases transported by ambulance over the twelve-year study period. For all transports by ambulance paramedics, there were 74,659 (6.9%) cases coded as a respiratory condition (ambulance problem codes 241-249). Of this respiratory group there were 15,671 metropolitan cases coded as asthma (ambulance problem code 241), which was 21% of respiratory cases and 1.4% of all cases (Figure 4).

Figure 4: Ambulance Transported Patients by Proportion of Respiratory Conditions, 1990-2001.



The number of cases transported for respiratory conditions has risen over time from 5.3% in 1990 to 6.6% in 2001 of all cases, peaking at 8.3% in 1997. Asthma cases, however, fell from 31.8% in 1990 to 14.8% in 2001 of respiratory cases, and 1.7% to 1.0% of all cases over the same time period (see Table 18).

Table 18: Comparison of Ambulance Transported Asthma Cases as a percentage of Respiratory and All Cases transports by year 1990-2001.

Year	All Cases	Respiratory (241-249)	% All Cases	Asthma (Metro)	% Resp Cases	% All Cases
1990	68,337	3,626	5.3	**1,154**	31.8	1.7
1991	67,490	3,727	5.5	**1,125**	30.2	1.7
1992	73,258	4,325	5.9	**1,190**	27.5	1.6
1993	79,121	4,544	5.7	**1,187**	26.1	1.5
1994	82,689	5,401	6.5	**1,321**	24.5	1.6
1995	82,174	6,497	7.9	**1,398**	21.5	1.7
1996	88,989	7,006	7.9	**1,477**	21.1	1.7
1997	92,634	7,727	8.3	**1,576**	20.4	1.7
1998	98,682	7,600	7.7	**1,434**	18.9	1.5
1999	110,074	8,051	7.3	**1,382**	17.2	1.3
2000	117,999	8,027	6.8	**1,220**	15.2	1.0
2001	123,959	8,128	6.6	**1,207**	14.8	1.0
Total	**1,085,406**	**74,659**		**15,671**		

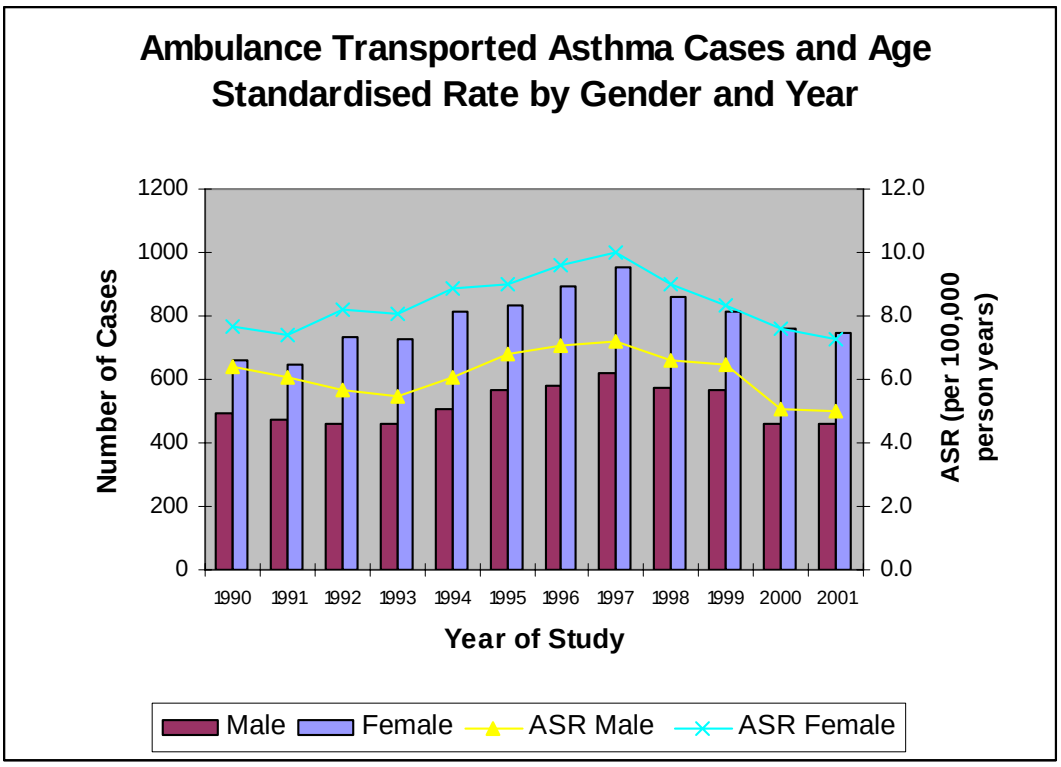
4.1.2 Demographic Variables

Gender and Age.

There was a significant difference in gender for ambulance transported asthma cases overall, with 9453 (60.3%) female cases, 6211 (39.6%) male cases, and 7 (0.04%) unknown cases ($\chi^2_{(1)} = 671$, $p = 0.000$), however there was no significant difference for gender between each of the years of study ($\chi^2_{(11)} = 14.5$, $p = 0.20$). The trend of gender difference is seen in Figure 4 below where female cases consistently exceed male cases by between 19 to 24 percent for each year of the study.

The rate of cases for males and females for each year were directly standardised, using the male and female populations of the 2001 Australian population as standard for metropolitan Perth between 1990 and 2001. Analysis of trends showed a significant yearly difference in age standardised rates for males ($\chi^2_{(11)} = 4.7$, $p = 0.029$) with a rate ratio = 0.992 (95% CI: 0.985, 0.999). This meant there was an average yearly decrease in the age standardised rate for males of 0.8 percent (Figure 5).

Figure 5: Ambulance transported asthma cases and age standardised rate by gender and year.



Note: Direct Standardisation using Australian 2001 Population

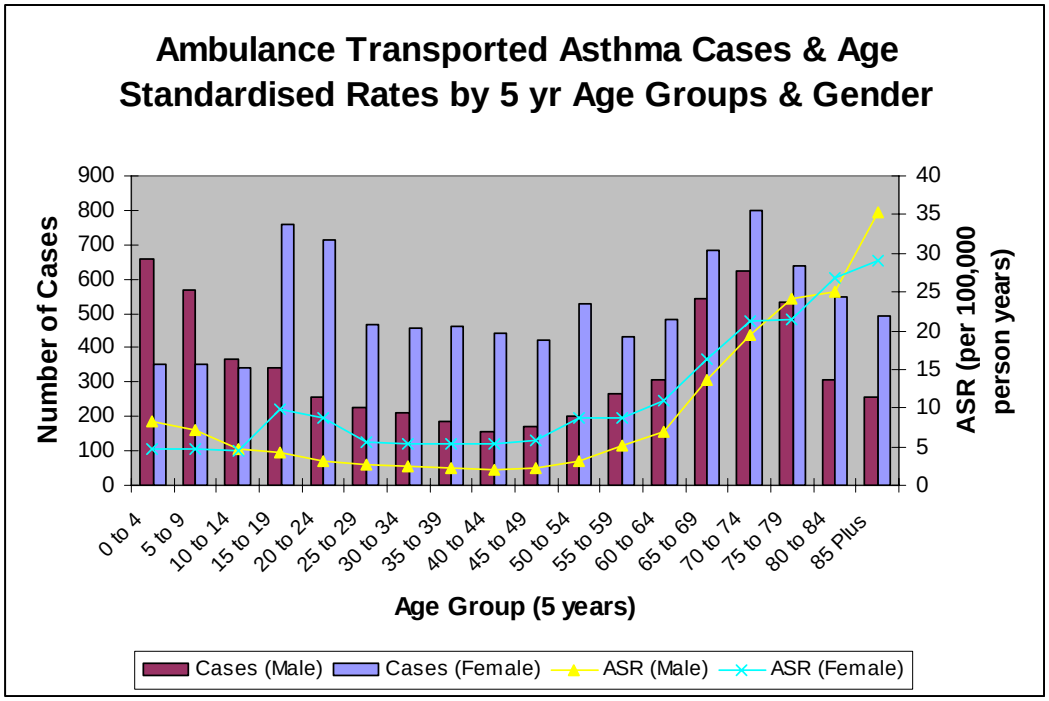
There was also a significant difference in ambulance transported asthma cases between 5-year age groups over the entire study period ($\chi^2_{(17)} = 1134$, $p = 0.000$), with increased numbers of asthma cases in the early childhood, early adult, and elderly age groups (Figure 5). The three age groups with the greatest percentage increase over the study period were 50 to 54 years (93%), 70 to 74 years (56%) and the 85+ years (166%) groups. Despite being the smallest representative age group at the beginning of the study, the 85+ years group had almost trebled in size by the end of the study. A table

outlining the percentage change for all 5 year age groups over the study period can be found in Appendix 10.

The rate of cases for males and females for each 5 year age group were also directly standardised, using the male and female populations of the 2001 Australian population as standard for metropolitan Perth between 1990 and 2001. The age standardised rate for asthma transports increased steadily for the elderly over time. For all cases, the average percentage change in the age standardised rate between age groups from 0 to 49 years was -4.4%, and from 50 to 85+ years was 60.8%. The rate for the eldest group (85+ years) is 4.7 times that of the youngest age group (0 to 4 years).

Figure 6 below shows the age standardised rates for both males and females, compared to the number of cases in each age group. The male age standardised rate exceeded the female age standardised rate in the under-15 years age groups, but did not exceed the female age standardised rate again until the 75 to 79 years group. The sudden increase in female cases in the 15 to 19 years age group can be seen clearly. This phenomena is consistent with results reported in Australia and internationally [6], and discussed previously in this thesis. In the three oldest age groups, the male age-standardised rate again began to exceed the female age-standardised rate.

Figure 6: Ambulance Transported Asthma Cases and Age Standardised Rate by 5 Year Age Groups 1990-2001.



Note: Direct Standardisation using Australian 2001 Population

4.1.3 Ambulance and Temporal Variables

Priority Code.

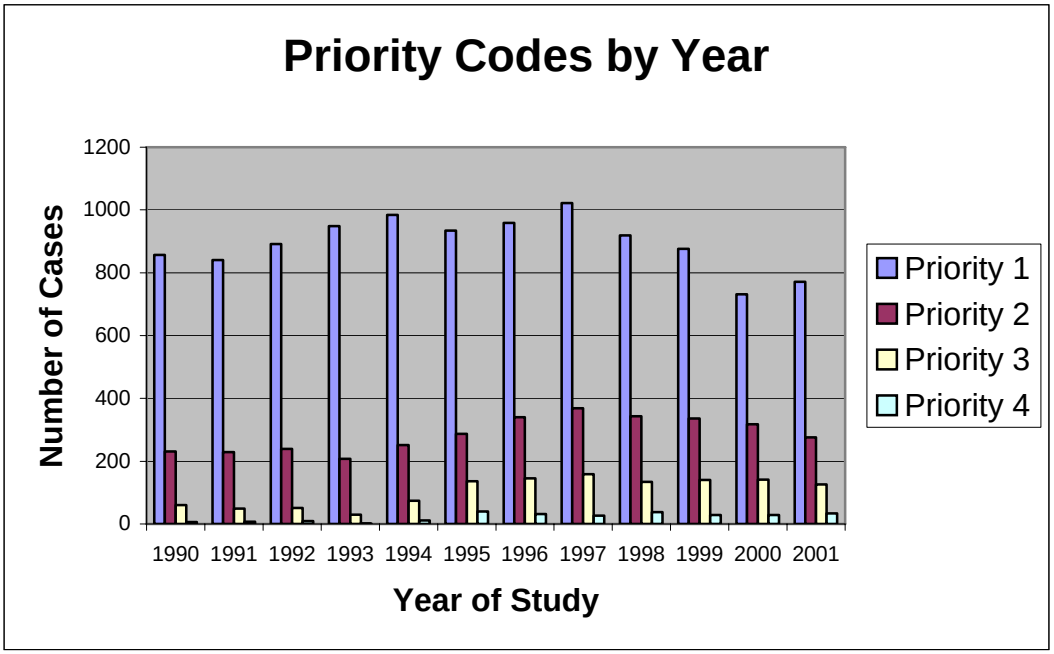
Each ambulance is dispatched with a *priority code*, generated by the communications centre to describe the urgency with which the ambulance should attend the patient. For all asthma cases, ambulances were dispatched *priority code 1* in 68.5 percent of cases (Table 19).

Table 19: Priority Codes for All Cases.

Priority	Frequency (%)
1	10732 (68.5)
2	3428 (21.9)
3	1249 (8.0)
4	262 (1.7)
Total	**15671 (100.0)**

Over time, the proportion of priority 1 transports decreased by 10.4 % and priority 2 transports increased by 2.9%, whereas priority 3 and 4 transports both remained relatively steady from 1995 on (Figure 7).

Figure 7: Priority Codes for All Ambulance Transported Asthma Cases by Year



Priority		1 N (%)	2 N (%)	3 N (%)	4 N (%)	Total
Year	**1990**	857 (74.3)	231 (20.0)	60 (5.2)	6 (0.5)	1154
	1991	840 (74.7)	229 (20.4)	49 (4.4)	7 (0.6)	1125
	1992	891 (74.9)	239 (20.1)	51 (4.3)	9 (0.8)	1190
	1993	948 (79.9)	208 (17.5)	30 (2.5)	1 (0.1)	1187
	1994	984 (74.5)	252 (19.1)	74 (5.6)	11 (0.8)	1321
	1995	934 (66.8)	287 (20.5)	137 (9.8)	40 (2.9)	1398
	1996	959 (64.9)	340 (23.0)	146 (9.9)	32 (2.2)	1477
	1997	1022 (64.8)	369 (23.4)	159 (10.1)	26 (1.6)	1576
	1998	919 (64.1)	343 (23.9)	134 (9.3)	38 (2.6)	1434
	1999	876 (63.4)	336 (24.3)	141 (10.2)	29 (2.1)	1382
	2000	731 (59.9)	318 (26.1)	142 (11.6)	29 (2.4)	1220
	2001	771 (63.9)	276 (22.9)	126 (10.4)	34 (2.8)	1207
Total		**10732 (68.5)**	**3428 (21.9)**	**1249 (8.0)**	**262 (1.7)**	**15671**

Dispatch Code.

Each ambulance case is assigned a *dispatch code* to indicate the most likely group of conditions the ambulance paramedics are likely to encounter. On attendance, the ambulance paramedics decide the *problem code* and *problem urgency* that describes the actual clinical state and severity of the patient. By definition, all cases in this study were assigned the problem code of 241 (asthma) by the ambulance paramedics. Table 20 below shows the dispatch codes for which problem code 241(asthma) was subsequently assigned. Of this group, 95.9% were dispatched as respiratory conditions (code 24), reflecting a high degree of recognition by call centre staff, given the limited amount of information available when a call is received.

Table 20: Dispatch Codes for All Ambulance Transported Asthma Cases

Dispatch Code	Frequency (%)
Respiratory	15028 (95.9)
Cardiac	291 (1.9)
Neurological	123 (0.8)
Illness	54 (0.3)
Trauma	37 (0.2)
Abdominal	32 (0.2)
Urology	17 (0.1)
Geriatric/debility	12 (0.1)
Drug/alcohol induced	11 (0.1)
Unable to code	11 (0.1)
Obstetric/gynaecological	9 (0.1)
Musculoskeletal	9 (0.1)
Endocrine/metabolic	8 (0.1)
Malignancy	7 (0.0)
Allergy	4 (0.0)
Poisoning	4 (0.0)
Environmental	3 (0.0)
Standby	3 (0.0)
Ear/nose/throat	2 (0.0)
Infectious	2 (0.0)
Psychosocial	2 (0.0)
Electrocution	1 (0.0)
Hypothermia	1 (0.0)
Total	**15671 (100.0)**

Problem Urgency (Australasian Triage Score).

After the ambulance paramedics assess the patient clinically, the *problem urgency* is recorded. Problem urgency approximately equates to the Australasian Triage Score (ATS) [397] that is designed for use in pre-hospital and hospital-based emergency services throughout Australia and New Zealand.[461]

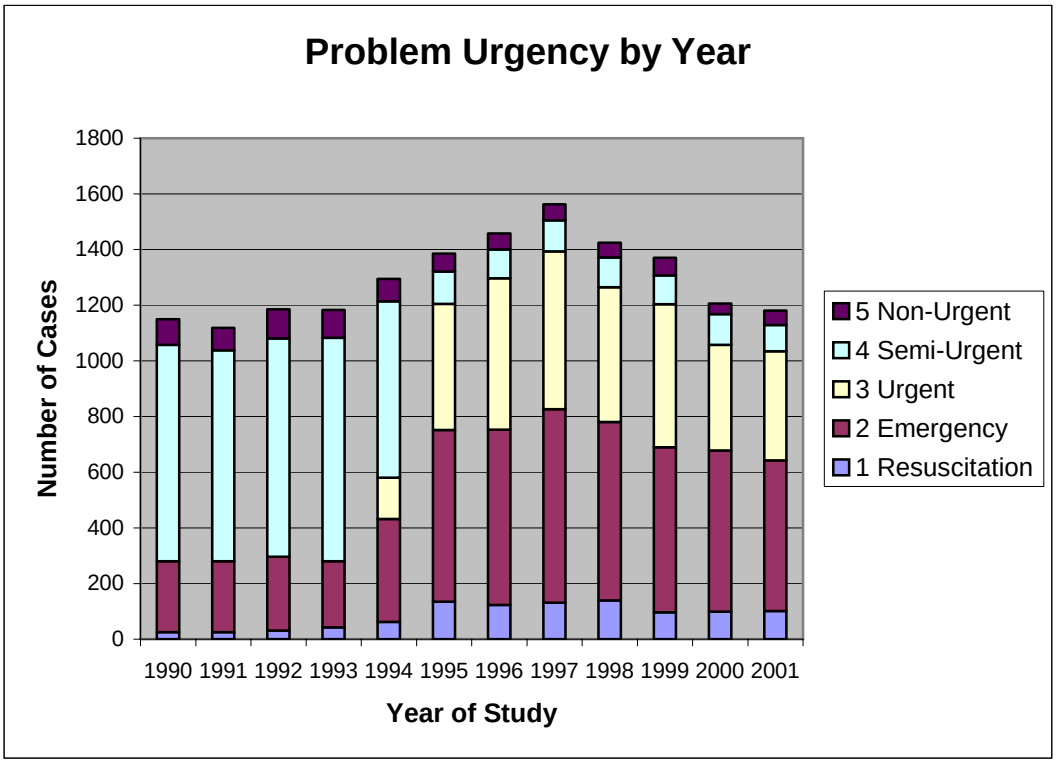
Of the 68.5% of all calls that were dispatched with priority code 1, 6.4% of cases were assessed with problem urgency code 1 and 36.3% of cases problem urgency code 2 (Table 21).

Table 21: Problem Urgency for All Ambulance Transported Asthma Cases

Problem Urgency (ATS)	Frequency (%)
1 (ATS1) Resuscitation – immediate	1010 (6.4)
2 (ATS2) Emergency - within 10 mins	5681 (36.3)
3 (ATS3) Urgent - within 30 mins	3479 (22.2)
4 (ATS4) Semi-urgent - within 60 mins	4504 (28.7)
5 (ATS5) Non-urgent - within 120 mins	839 (5.4)
Total	15513 (99.0)
Missing	158 (1.0)
Total	**15671 (100.0)**

For the first four years of the study, there was little change in the proportions of problem urgency except for problem urgency 1, which increased from 2.2% to 3.6%. Changes to coding practices of problem urgency were made in 1994, meaning there was effectively no problem urgency 3 prior to 1994. From 1995 on, the proportion of problem urgency has varied little (Figure 8).

Figure 8: Problem Urgency by Years



Problem urgency		1 N (%)	2 N (%)	3 N (%)	4 N (%)	5 N (%)	Total N
Years	**1990**	25 (2.2)	255 (22.2)	N/A*	778 (67.7)	91 (7.9)	1149
	1991	25 (2.2)	255 (22.8)	N/A*	758 (67.8)	80 (7.2)	1118
	1992	31 (2.6)	265 (22.4)	N/A*	784 (66.1)	105 (8.9)	1185
	1993	43 (3.6)	237 (20.0)	N/A*	803 (67.9)	100 (8.5)	1183
	1994	62 (4.8)	370 (28.6)	149 (11.5)	633 (48.9)	80 (6.2)	1294
	1995	135 (9.7)	617 (44.6)	453 (32.7)	116 (8.4)	64 (4.6)	1385
	1996	123 (8.4)	630 (43.2)	543 (37.3)	104 (7.1)	57 (3.9)	1457
	1997	131 (8.4)	696 (44.6)	566 (36.2)	112 (7.2)	57 (3.6)	1562
	1998	139 (9.8)	641 (45.0)	484 (34.0)	107 (7.5)	53 (3.7)	1424
	1999	96 (7.0)	594 (43.4)	513 (37.4)	104 (7.6)	63 (4.6)	1370
	2000	99 (8.2)	579 (48.0)	379 (31.4)	111 (9.2)	38 (3.2)	1206
	2001	101 (8.6)	542 (45.9)	392 (33.2)	94 (8.0)	51 (4.3)	1180
Total		**1010 (6.5)**	**5681 (36.6)**	**3479 (22.4)**	**4504 (29.0)**	**839 (5.4)**	**15513**

* N/A - Not Applicable; there was no problem urgency code 3 for 1990 to 1993

Hour of Day.

Test of trend showed a significant difference in the time of day that asthma cases called for an ambulance for the study period ($\chi^2_{(23)}$ =508, p=0.000), with cases peaking mid morning and late evening. The proportion of cases varied with hour of day between each year of the study ($\chi^2_{(253)}$ =312, p=0.007). When hour of day was collapsed into time intervals for modelling purposes, significant differences remained in the

proportions between six-hour intervals and year of study ($\chi^2_{(33)}$ =62.5, p=0.001) and twelve-hour intervals ($\chi^2_{(11)}$ =38, p=0.000) and year of study. Table 22 below shows the circadian pattern of ambulance transported patients with asthma for hour of day and year of study

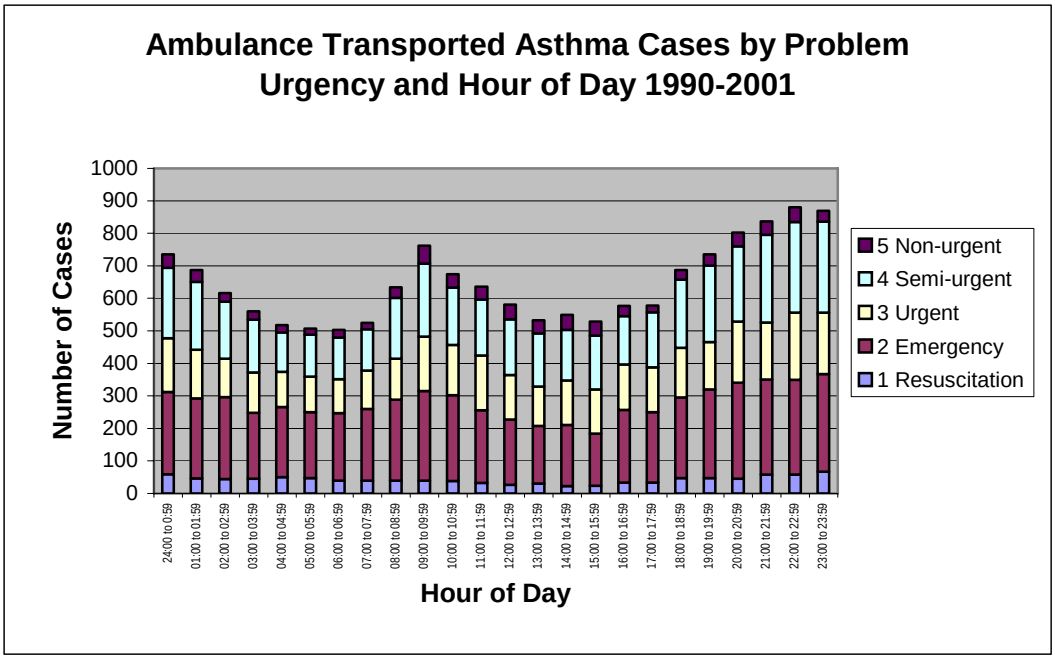
Table 22: Number of ambulance transported asthma cases by year, six-hour and twelve-hour time interval.

Time Period (hour of day)		06:00 to 11:59	12:00 to- 17:59	18:00 to 23:59	24:00 to 05:59	18:00 to 05:59	06:00 to 17:59	Total
Year of Study	1990	263 (22.9%)	235 (20.3%)	358 (31.0%)	298 (25.8%)	656 (56.8%)	498 (43.2%)	1154
	1991	226 (20.1%)	242 (21.5%)	388 (34.5%)	269 (23.9%)	657 (58.4%)	468 (41.6%)	1125
	1992	265 (22.3%)	251 (21.1%)	392 (32.9%)	282 (23.7%)	674 (56.6%)	516 (43.4%)	1190
	1993	274 (23.1%)	259 (21.8%)	383 (32.3%)	271 (22.8%)	654 (55.1%)	533 (44.9%)	1187
	1994	304 (23.0%)	258 (19.5%)	441 (33.4%)	318 (24.1%)	759 (57.5%)	562 (42.5%)	1321
	1995	331 (23.7%)	327 (23.4%)	412 (29.5%)	328 (23.4%)	740 (52.9%)	658 (47.1%)	1398
	1996	376 (25.5%)	309 (20.9%)	452 (30.6%)	340 (23.0%)	792 (53.6%)	685 (46.4%)	1477
	1997	402 (25.5%)	316 (20.1%)	454 (28.8%)	404 (25.6%)	858 (54.4%)	718 (45.6%)	1576
	1998	346 (24.1%)	315 (22.0%)	459 (32.0%)	314 (21.9%)	773 (53.9%)	661 (46.1%)	1434
	1999	334 (24.2%)	309 (22.4%)	425 (30.7%)	314 (22.7%)	739 (53.5%)	643 (46.5%)	1382
	2000	334 (27.4%)	289 (23.7%)	346 (28.3%)	251 (20.6%)	597 (48.9%)	623 (51.1%)	1220
	2001	309 (25.6%)	274 (22.7%)	344 (28.5%)	280 (23.2%)	624 (51.7%)	583 (48.3%)	1207
Total		3764	3384	4854	3669	8523	7148	15671

Note: Shaded areas are where number of cases peak.

When stratified by problem urgency, test of trend showed a significant difference in the proportions of problem urgency and hour of day ($\chi^2_{(92)}$ =182, p=0.000). The highest proportion of ambulance transported asthma cases for problem urgency 1 were between the hours of 03:00 and 07:00 in the morning, and for problem urgency 2, between the hours of 02:00 and 08:00 in the morning, both periods of time where the number of cases transported overall were lowest (Figure 9, shaded).

Figure 9: Ambulance Transported Asthma Cases by Problem Urgency and Hour of Day 1990-2001



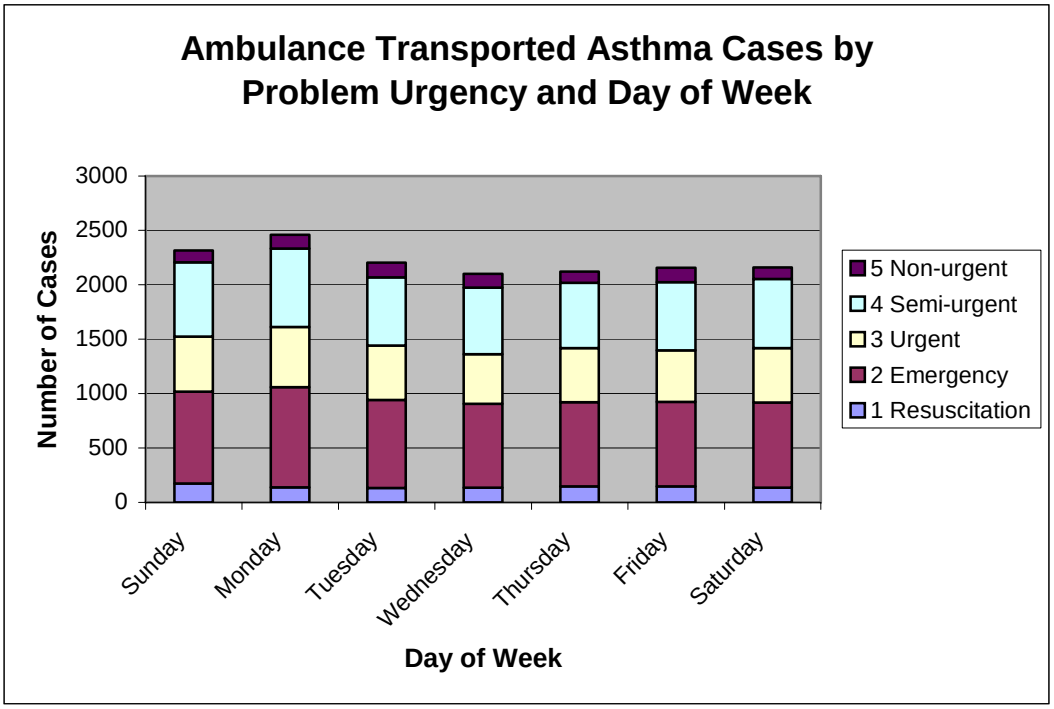
Problem urgency		1 N (%)	2 N (%)	3 N (%)	4 N (%)	5 N (%)	Total N
Hour of Day	24:00 to 00:59	59 (8.0)	253 (34.4)	165 (22.4)	217 (29.5)	41 (5.6)	735
	01:00 to 01:59	46 (6.7)	246 (35.8)	150 (21.8)	209 (30.4)	36 (5.2)	687
	02:00 to 02:59	44 (7.1)	252 (40.9)	118 (19.2)	176 (28.6)	26 (4.2)	616
	03:00 to 03:59	45 (8.0)	203 (36.3)	124 (22.1)	162 (28.9)	26 (4.6)	560
	04:00 to 04:59	50 (9.7)	216 (41.7)	108 (20.8)	121 (23.4)	23 (4.4)	518
	05:00 to 05:59	47 (9.3)	203 (40.0)	109 (21.5)	129 (25.4)	19 (3.7)	507
	06:00 to 06:59	39 (7.8)	208 (41.4)	104 (20.7)	128 (25.4)	24 (4.8)	503
	07:00 to 07:59	39 (7.4)	221 (42.1)	118 (22.5)	127 (24.2)	20 (3.8)	525
	08:00 to 08:59	39 (6.2)	249 (39.3)	126 (19.9)	187 (29.5)	33 (5.2)	634
	09:00 to 09:59	39 (5.1)	276 (36.2)	167 (21.9)	225 (29.5)	55 (7.2)	762
	10:00 to 10:59	38 (5.6)	264 (39.2)	155 (23.0)	176 (26.1)	41 (6.1)	674
	11:00 to 11:59	32 (5.0)	224 (35.2)	168 (26.4)	172 (27.0)	40 (6.3)	636
	12:00 to 12:59	27 (4.6)	200 (34.4)	137 (23.6)	171 (29.4)	46 (7.9)	581
	13:00 to 13:59	31 (5.8)	177 (33.3)	121 (22.7)	163 (30.6)	40 (7.5)	532
	14:00 to 14:59	23 (4.2)	188 (34.2)	136 (24.8)	156 (28.4)	46 (8.4)	549
	15:00 to 15:59	24 (4.5)	160 (30.2)	136 (25.7)	165 (31.2)	44 (8.3)	529
	16:00 to 16:59	33 (5.7)	224 (38.8)	140 (24.3)	148 (25.6)	32 (5.5)	577
	17:00 to 17:59	33 (5.7)	217 (37.5)	138 (23.9)	169 (29.2)	21 (3.6)	578
	18:00 to 18:59	47 (6.8)	248 (36.1)	153 (22.3)	209 (30.4)	30 (4.4)	687
	19:00 to 19:59	47 (6.4)	273 (37.1)	146 (19.9)	235 (32.0)	34 (4.6)	735
	20:00 to 20:59	45 (5.6)	296 (36.9)	188 (23.4)	231 (28.8)	42 (5.2)	802
	21:00 to 21:59	58 (6.9)	292 (34.9)	176 (21.0)	269 (32.1)	42 (5.0)	837
	22:00 to 22:59	58 (6.6)	291 (33.1)	207 (23.5)	279 (31.7)	45 (5.1)	880
	23:00 to 23:59	67 (7.7)	300 (34.5)	189 (21.7)	280 (32.2)	33 (3.8)	869
Total		**1010**	**5681**	**3479**	**4504**	**839**	**15513**

Note: Shaded areas are where proportion of cases peaked

Day of Week.

There is a significant difference in the proportion of cases over the days of the week for the study period ($\chi^2_{(6)}$ =45, p=0.000). This can be seen below in Figure 10 where cases increase over the week from Wednesday and peak on Monday. There was no significant trend of difference for either day of week between the years of the study ($\chi^2_{(66)}$ =63, p=0.58), or for problem urgency and day of week ($\chi^2_{(24)}$ =24, p=0.47).

Figure 10: Ambulance Transported Asthma Cases by Day of Week

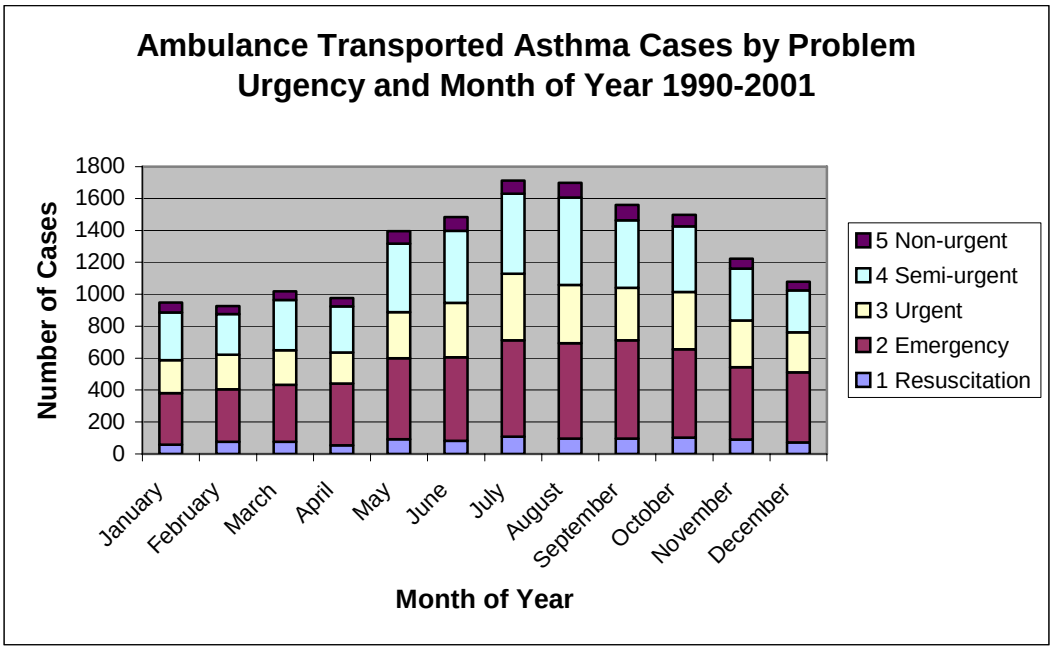


Problem urgency		1 N (%)	2 N (%)	3 N (%)	4 N (%)	5 N (%)	Total N
Day of Week	Sunday	173 (7.5)	844 (36.5)	506 (21.9)	684 (29.5)	107 (4.6)	2314
	Monday	139 (5.6)	921 (37.5)	553 (22.5)	720 (29.3)	125 (5.1)	2458
	Tuesday	131 (5.9)	811 (36.8)	499 (22.7)	626 (28.4)	136 (6.2)	2203
	Wednesday	136 (6.5)	771 (36.7)	456 (21.7)	610 (29.1)	127 (6.0)	2100
	Thursday	147 (6.9)	775 (36.5)	495 (23.3)	600 (28.3)	105 (5.0)	2122
	Friday	148 (6.9)	777 (36.1)	471 (21.9)	628 (29.1)	133 (6.2)	2157
	Saturday	136 (6.3)	782 (36.2)	499 (23.1)	636 (29.5)	106 (4.9)	2159
Total		**1010**	**5681**	**3479**	**4504**	**839**	**15513**

Month of Year

There was a significant difference in the total number of cases over the months of the year for the study period ($\chi^2_{(11)} = 770$, p=0.000). This is shown in Figure 11 below where cases peak in the winter month of July, and are lowest in the summer month of February. There was also a significant trend of difference between problem urgency and month of year ($\chi^2_{(44)} = 77$, p=0.002). The highest proportion of calls occurred in February for problem urgency 1 and in December for problem urgency 2, both summer months.

Figure 11: Ambulance Transported Asthma Cases by Month of Year, 1990-2001



Problem urgency		1 N (%)	2 N (%)	3 N (%)	4 N (%)	5 N (%)	Total
Month of Year	January	58 (6.1)	323 (34.1)	207 (21.8)	297 (31.3)	63 (6.6)	948
	February	77 (8.3)	328 (35.4)	216 (23.3)	255 (27.5)	50 (5.4)	926
	March	77 (7.6)	355 (34.9)	218 (21.4)	314 (30.8)	54 (5.3)	1018
	April	55 (5.6)	386 (39.5)	195 (20.0)	288 (29.5)	52 (5.3)	976
	May	93 (6.7)	506 (36.3)	289 (20.7)	429 (30.8)	78 (5.6)	1395
	June	83 (5.6)	523 (35.2)	341 (23.0)	451 (30.4)	86 (5.8)	1484
	July	109 (6.4)	603 (35.2)	416 (24.3)	502 (29.3)	81 (4.7)	1711
	August	97 (5.7)	597 (35.2)	365 (21.5)	546 (32.2)	92 (5.4)	1697
	September	96 (6.2)	616 (39.5)	328 (21.0)	424 (27.2)	95 (6.1)	1559
	October	102 (6.8)	553 (36.9)	360 (24.0)	411 (27.4)	72 (4.8)	1498
	November	91 (7.4)	452 (37.0)	293 (24.0)	325 (26.6)	61 (5.0)	1222
	December	72 (6.7)	439 (40.7)	251 (23.3)	262 (24.3)	55 (5.1)	1079
Total		**1010**	**5681**	**3479**	**4504**	**839**	**15513**

Note: Shaded areas are where proportion of cases peaked

Hospital Discharge Diagnosis.

Although the Morbidity Data System can record up to 19 discharge diagnoses, for each hospital separation principal discharge diagnosis is always recorded along with any other relevant comorbidity. The principal discharge diagnosis is the principal reason for hospitalisation. Of the ten most common principal discharge diagnoses for ambulance transported asthma cases, asthma accounted for 57.0% (Table 23).

Table 23: Principal discharge diagnoses for ambulance transported asthma cases, 1990-2001.

Principal Discharge Diagnosis	N	%
asthma	5569	57.0
chronic obstructive pulmonary disease	1138	11.7
heart failure	488	5.0
emphysema	262	2.7
chronic bronchitis	240	2.5
unspecified pneumonia	178	1.8
other diseases of respiratory system	148	1.5
acute laryngitis	70	0.7
acute upper respiratory tract infection	55	0.6
pneumococcal pneumonia	49	0.5

Although individual episode of care data was not available for those patients that were admitted to hospital for asthma but not transported by ambulance, all hospital separations recorded by the Morbidity Data System that had a principal discharge diagnosis of asthma and all non-asthma hospital separations was available in summary form for the period of the study. Using these data and the principal discharge diagnosis of asthma as the 'gold standard', a 'true positive' case was defined where the ambulance problem code identifying asthma matched the hospital principal discharge diagnosis of asthma. From this, the sensitivity, specificity and positive predictive value of the ambulance indicator of problem code was then determined (Table 24).

Table 24: Sensitivity and specificity for ambulance and hospital admitted asthma cases.

		Hospital Asthma		
		Yes	No	
SJA	Yes	5,569	4,197	9,766
Asthma	No	2,334	538,982	541,316
		7,903	543,179	

Sensitivity = (5,569 / 7,903) x 100% = **70.47%**

Specificity = (538,982 / 543,179) x 100% = **99.23%**

Positive Predictive Value = (5,569 / 9,766) x 100% = **57.02%**

Source of Referral

From1993 to 1999, the source of referral was recorded for each episode of care in the hospital database. As all ambulance transported asthma cases to hospital were admitted via the emergency department, the source of referral could be used to estimate the proportion of ambulance transported asthma cases to total hospital asthma admissions.

Table 25 below summarizes all the hospital separations recorded by the Morbidity Data System that had a principal discharge diagnosis of asthma for the period of the study. Both the number of emergency admissions and ambulance transported hospital asthma admissions increased during 1993 to1999 despite an overall decrease in total admissions for asthma. The proportion of ambulance transported hospital asthma admissions to total emergency admissions has not substantially changed over the period, remaining at approximately 30%.

Table 25: Source of Referral and Transport for all patients admitted with principal discharge diagnosis of asthma.

Source of Referral	Separation Year							Total
	1993	1994	1995	1996	1997	1998	1999	
Other/Unknown	1340	87	38	48	46	35	57	1651
Private medical practice	1537	1601	1256	1136	1278	1184	1214	9206
Nursing home	1	3	2	2	2	3	0	13
Community Health Service	56	43	84	68	64	51	46	412
Inter-hospital transfer	41	61	51	55	74	62	52	396
Outpatient department	457	432	388	255	250	105	91	1978
Emergency *	3809	4551	4715	4548	5144	4698	4524	31989
Waiting list	1	6	237	327	256	62	30	919
Psychiatric facility	0	1	5	0	0	0	0	6
Statistical admission/change	0	0	0	1	17	26	3	47
Total	**7242**	**6785**	**6776**	**6440**	**7131**	**6226**	**6017**	**46617**
Emergency (ED) Admissions	3809	4551	4715	4548	5144	4698	4524	31989
SJA Asthma Admissions	1183	1294	1385	1457	1562	1424	1370	9675
Proportion SJA to ED (%)	**31.1**	**28.4**	**29.4**	**32.0**	**30.4**	**30.3**	**30.3**	**30.2**

Source: Health Information Centre, Health Department, WA, 2004

Length of Stay.

Over the period of the study, for those patients that were transported by ambulance for asthma and admitted, the mean length of stay was 5.8 days (median 4.0) with a standard deviation of 7.3 days (Table 26).

Table 26: Statistics for Length of Stay, 1990-2001.

Length of Stay (Days)	
Number of Ambulance Asthma Cases Admitted	9766
Mean	5.8
Median	4.0
Std. Deviation	7.3
Minimum	1.0
Maximum	154.0

Although the number of ambulance transported asthma cases being admitted varied considerably from year to year, there is little variation in the mean and median length of stay for those cases (see table 27).

Table 27: Ambulance transported asthma cases admitted to hospital, length of stay (days) by year.

Length of Stay (Days)						
Years	**N**	**Mean**	**Std. Dev.**	**95% CI**	**Median**	**95th %'tile**
1990	699	**5.4**	6.4	(4.9, 5.9)	3	18
1991	657	**6.4**	8.5	(5.7, 7.0)	4	22
1992	643	**6.4**	9.3	(5.7, 7.2)	4	20
1993	625	**5.7**	6.6	(5.2, 6.2)	4	16.7
1994	726	**6.1**	9.1	(5.4, 6.8)	4	19
1995	922	**6.1**	8.1	(5.6, 6.6)	4	18
1996	916	**5.9**	6.7	(5.4, 6.3)	4	16
1997	1055	**5.6**	6.9	(5.2, 6.0)	4	18
1998	1012	**5.6**	7.2	(5.2, 6.1)	3	18
1999	874	**5.5**	5.9	(5.2, 5.9)	4	16
2000	834	**5.6**	6.5	(5.1, 6.0)	3	18
2001	803	**5.1**	6.4	(4.7, 5.6)	3	16

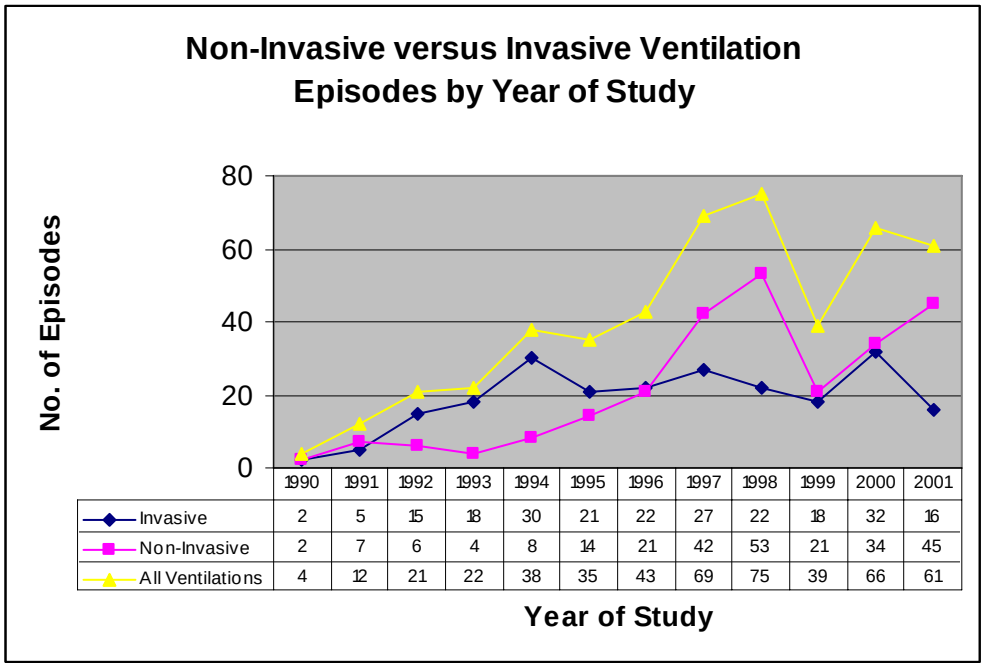
Mechanical Ventilation

The Hospital Morbidity Data System may also record up to nine ICD codes for procedures that have been performed during an admission episode. Non-invasive and invasive mechanical ventilation procedures have separate ICD procedure codes, and so were able to be differentiated on analysis.

Throughout the period of the study, the number of all episodes which included a ventilation procedure has increased. This is consistent with Australian Institute of Health and Welfare figures which have reported a trend of increased proportion of hospitalisations for asthma requiring mechanical ventilation over the period 1998-99 to 2000-01. However, they do not differentiate between non-invasive and invasive procedures.[6]

Figure 12 below shows the number of episodes which included procedures of non-invasive and invasive ventilation. The low incidences of ventilation episodes in the early years of the study may well be a true reflection of procedures performed, but may also be due to incomplete or inconsistent coding or some other form of recording bias.

Figure 12: Non-Invasive versus Invasive Ventilation Episodes by Year of Study.



	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001
Invasive	2	5	15	18	30	21	22	27	22	18	32	16
Non-Invasive	2	7	6	4	8	14	21	42	53	21	34	45
All Ventilations	4	12	21	22	38	35	43	69	75	39	66	61

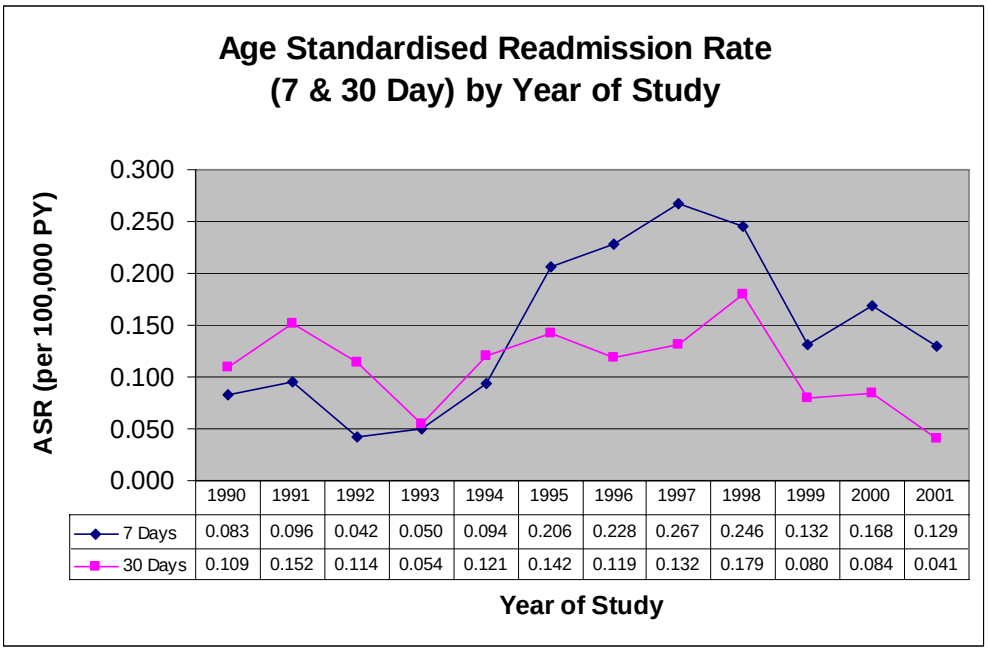
From the period of 1993 on, it is seen that the incidence of non-invasive ventilation episodes tended to increase over time whilst the incidence of invasive ventilation appeared to have reached a plateau.

Readmission

Readmission was defined as a hospital asthma admission within seven days of a previous hospital asthma admission, or within seven and thirty days of a previous hospital asthma admission. These two time periods were chosen due to their common use as readmission variables by the Centre for Health Services Research (University of Western Australia) and in other studies, thus ensuring comparability of results between researchers.

Crude readmission rates were directly standardised to the 2001 Australian population and reported as age standardised rates (ASR), per 100,000 person years (Figure 13). The seven day readmission rate has generally increased over the time of the study, with a noticeable peak in 1997. The thirty day readmission rate did not display an increasing trend, and although a peak was reported in 1998, the rate decreased over the time of the study.

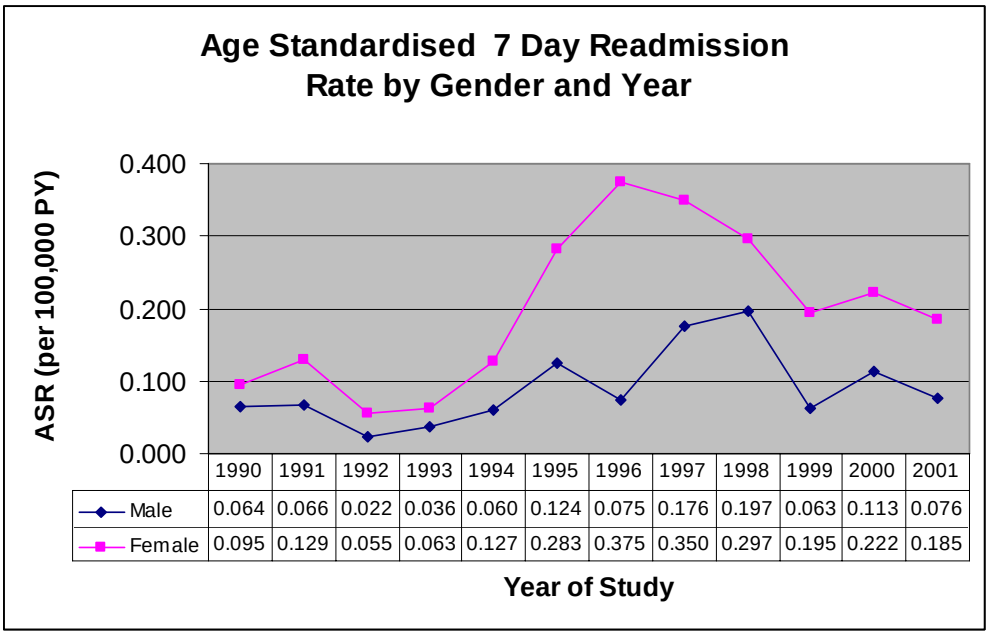
Figure 13: Age standardised readmission rate (7 and 30 day) by year of study.



	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001
7 Days	0.083	0.096	0.042	0.050	0.094	0.206	0.228	0.267	0.246	0.132	0.168	0.129
30 Days	0.109	0.152	0.114	0.054	0.121	0.142	0.119	0.132	0.179	0.080	0.084	0.041

When the seven day readmission rate is stratified by gender, it is seen that the previously noted increasing trend in the ASR was largely attributable to females. The rate for females consistently exceeded that for males for each year of the study. Furthermore, over the period of the study the rate has changed little for males, whereas the rate for females has nearly doubled (Figure 14).

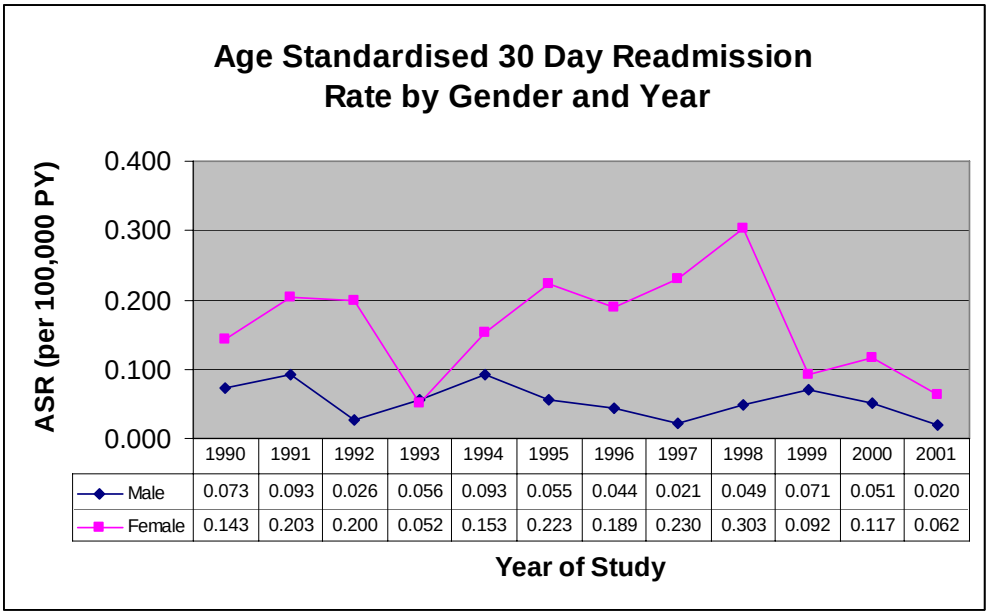
Figure 14: Age standardised 7 day readmission rate by gender and year of study.



	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001
Male	0.064	0.066	0.022	0.036	0.060	0.124	0.075	0.176	0.197	0.063	0.113	0.076
Female	0.095	0.129	0.055	0.063	0.127	0.283	0.375	0.350	0.297	0.195	0.222	0.185

When the thirty day readmission rate is stratified by gender, it is seen that both genders contribute to the previously noted decreasing trend in the ASR. The rate for females consistently exceeded that for males for each year of the study except for 1993. The ASR for females doubled the ASR for males at the beginning of the study, and tripled the ASR for males at the end of the study; with an even wider differential between the rates for the majority of the study years (Figure 15).

Figure 15: Age standardised 30 day readmission rate by gender and year of study.



4.1.4 Socioeconomic Factors

As the period of the study included three census periods, the crude and age standardised rate (ASR) of cases across the socioeconomic (SES) quintiles for each of the census populations was calculated. The ASR for both 5 and 10 year age groups were found to be similar (Appendix 7), so only ten year age group rates have been reported below.

By using the ABS-derived Index of Relative Socio-Economic Disadvantage as a measure of socio-economic status, an inverse association was found between the incidence of ambulance attended asthma cases and socio-economic status. Both crude and age-standardised rates of ambulance attended asthma cases were lowest in the 20% of the population with the highest SEIFA index and highest in the 20% of the population with the lowest SEIFA index. This association remained the same whether the postal area where the case resides or the postal area in which the ambulance attended was used. In view of similar results elicited from both groups (Appendix 8), and as data was more complete for the postal area in which the ambulance attended, results from this group only have been reported below.

There was an increasingly higher crude and age standardised rate of ambulance transported asthma in SES quintile 2 to 5 compared to the highest SES quintile 1 for the postal area where the ambulance attended the case (Table 28). This demonstrates an association between socio-economic status and the incidence of ambulance transported asthma cases. For both crude and age standardised rates, the rate of ambulance transport for asthma is lowest in areas of highest socioeconomic status, and highest in areas of lowest socioeconomic status.

Table 28: Poisson regression comparing the crude and age standardised rates of ambulance transported asthma cases by quintile of SES, postal area where ambulance attended case.

Census Period	SES Quintile	Popn(N)	Crude Rate	Rate Ratio	95% CI	ASR (10yr)	Rate Ratio	95% CI
1991	1 (High SES)	189,393	114.4	1.00		124.6	1.00	
	2	237,825	156.1	1.09	(1.02-1.17)	166.5	1.34	(1.32-1.36)
	3	268,858	244.9	1.51	(1.41-1.61)	265.9	2.13	(2.11-2.17)
	4	236,881	263.3	1.84	(1.73-1.96)	284.4	2.29	(2.26-2.33)
	5 (Low SES)	244,998	433.0	2.94	(2.77-3.11)	473.0	3.81	(3.75-3.86)
1996	1 (High SES)	255,617	139.9	1.00		148.3	1.00	
	2	252,992	178.1	1.27	(1.20-1.35)	187.7	1.27	(1.25-1.29)
	3	264,973	203.2	1.39	(1.31-1.48)	213.4	1.45	(1.42-1.47)
	4	263,287	262.9	1.82	(1.72-1.93)	277.8	1.88	(1.86-1.91)
	5 (Low SES)	261,761	360.7	2.51	(2.38-2.65)	382.3	2.58	(2.55-2.62)
2001	1 (High SES)	267,831	137.2	1.00		141.1	1.00	
	2	291,655	170.7	1.14	(1.08-2.21)	174.6	1.24	(1.22-1.26)
	3	278,834	184.2	1.29	(1.22-1.37)	189.5	1.34	(1.32-1.36)
	4	257,180	216.9	1.65	(1.56-1.74)	221.8	1.57	(1.55-1.60)
	5 (Low SES)	307,639	353.5	2.25	(2.13-2.36)	362.9	2.57	(2.53-2.60)

4.2 OUTCOMES

4.2.1 Survival.

In this study, where a death record for a patient exists, it has been linked to each episode of care for that patient, not just the episode that may have coincided with their death. This allows the calculation of the interval in days from any episode of care to death. Three survival outcome categories were defined this way: death at discharge, death within thirty days from discharge, and death within thirty days to one year after the last discharge for asthma.

Of the 15,671 asthma cases transported by ambulance, 1,877 individual patients linked to a death record and 632 patients (33.7%) of those who died had at least one admission where the principal discharge diagnosis was asthma. Of these, 47 either had a hospital discharge separation code of death (912) or death coincided with the last day of their admission, 33 were discharged alive but died within thirty days, and 145 survived more than thirty days but died within one year of their last discharge (Table 29).

Table 29: Summary of survival outcome for patients with any asthma admission (principal discharge diagnosis = asthma).

	N	Denominator	%
Population served (Metro, Census 2001)	1,323,392		
Ambulance cases transported during study	1,085,406		
Cases transported as respiratory	74,659	1,085,406	6.9%
Cases transported as asthma (metro)	**15,671**	**74,659**	**21.0%**
Individual patients represented by cases	**5,961**		
No. Patient deaths	1,877		
Death with no hospital asthma admission	1,245	1,877	66.3%
Death with any hospital asthma admission	**632**	**1,877**	**33.7%**
Death at discharge	**47**	632	7.4%
Death within thirty days	**33**	632	5.2%
Death within one year	**145**	632	22.9%

In the WA Data Linkage System, the cause of death is recorded in two ways. Firstly, the primary cause of death code is recorded as a text field, which includes the primary cause of death as well as other comorbid conditions and contributing causes. Then, on a

yearly basis, the Australian Bureau of Statistics codes the deaths to ICD9 or ICD10 codes, which are then appended to the death record and integrated into the Mortality Data System at the WA Department of Health. Often, the primary cause of death may not reflect accurately the clinical history of a patient, and additional information recorded in the text field is helpful in establishing a clearer aetiology.

For example, primary cause of death may be acute myocardial infarction, but the contributing cause may be a long history of asthma and chronic airway obstruction. For all three death outcomes examined in this study the two most common causes of death were asthma and chronic airway obstruction, which are also two of the most commonly recorded comorbid conditions for deaths associated with respiratory function, especially in the elderly.

Of the 47 deaths that occurred on discharge (in hospital), asthma was the cause of death in 14 cases and chronic airway obstruction in 18 cases. At 30 days, asthma was the cause of death in 9 cases and chronic airway obstruction in 8 cases, and at one year, asthma was the cause of death in 16 cases and chronic airway obstruction in 34 cases. The proportion of deaths for these two conditions decreased from 68.1% for death on discharge, to 51.5% for death within thirty days of discharge, and 34.5% for death within one year of discharge.

4.2.2 Survival Model Results.

Logistic regression modelling was performed to identify those factors which are predictive of survival, using death status as outcome variables in the models. Firstly, univariate analysis was performed on all predictor variables selected for analysis (Appendix 11). The variables problem urgency (ATS) and socioeconomic status (SES) were not significant in any of the univariate models, despite being modelled both as continuous or categorical variables. Further, neither of the 7 day or 30 day readmission variables reached significance in univariate modelling.

The variable gender, whilst not significant in two out of three of the univariate models for survival, was included in the multivariate model. This was due to the significant differences in age-specific rates described earlier, and significance in the univariate

model for the outcome of death within one year of discharge. Each of the predictor variables were modelled as continuous variables except for gender which was coded as a categorical variable: 0 for male and 1 for female.

4.2.3 Model 1: Predictors for Survival at Discharge

The aim of this analysis was to identify possible factors which predicted death at discharge. The variables age, gender, comorbidity, cumulative length of stay, and total number of previous ventilation episodes were fitted to the multivariate logistic regression model (Table 30).

Age, previous comorbid conditions, cumulative length of stay and total number of previous ventilations were all associated with an excess risk of death on discharge. Despite there being a significant gender difference in age-specific rates, there was not a significant association with gender for death on discharge in the multivariate model.

Each additional year of age at the index admission increased the odds of death by 1.046 (95% CI: 1.028-1.064), and for every increase by 1 of the patient comorbidity index there was an increased likelihood of death on discharge with an odds ratio of 1.363 (95% CI: 1.079-1.721). For each additional day a patient has stayed in hospital in the previous twelve months, the odds of death on discharge increased by 1.028 (95% CI: 1.010-1.046). Those with a history of ventilation for any reason prior to the index admission were found to have nearly double the likelihood of death for each additional episode of ventilation, indicated by an odds ratio of 1.962 (95% CI: 1.224-3.146). All clinically appropriate combinations of interactions failed to reach significance in the multivariate model.

Table 30: Factors predictive of death at discharge from hospital, total ventilation episodes for all admissions.

Death at Discharge			
Predictor	**P Value**	**Odds Ratio**	**95% CI**
age	0.000	1.046	1.028-1.064
comorbidity	0.009	1.363	1.079-1.721
cumulative length of stay	0.002	1.028	1.010-1.046
total no. of previous ventilation episodes	0.005	1.962	1.224-3.146

As noted previously, low incidences of recorded ventilation episodes in the early years of the study may well reflect the true number of procedures performed or some problem with incomplete or inconsistent recording. As this cannot be ascertained, caution need to be exercised in the interpretation of results concerned with ventilation, however it is considered reasonable to continue with the inclusion of the ventilation variables in the model in view of the reported strong association with the outcome.

To examine the influence of ventilation, the same model was fitted again, but this time the focus was on total ventilation episodes that were for hospital asthma admissions only, a subset of the previous tested variable of total number of previous ventilation episodes. An asthma admission was defined as any hospital admission where the principal discharge diagnosis indicated asthma. Results were similar, with all previous associations remaining significant with similar p-values and odds ratios. The odds ratio for total ventilation for hospital asthma admissions only and death on discharge was 2.560 (95% CI: 1.528-4.288), shown in Table 31.

Table 31: Factors predictive of death at discharge from hospital with total ventilation episodes for asthma admissions only.

Death at Discharge			
Predictor	**P Value**	**Odds Ratio**	**95% CI**
age	0.000	1.046	1.028-1.065
comorbidity	0.003	1.416	1.122-1.789
cumulative length of stay	0.008	1.025	1.007-1.044
total no. of previous ventilation episodes	0.000	2.560	1.529-4.288

To further explore the strong association of ventilation history and death on discharge, ventilation events were examined more closely. Four additional variables were created to differentiate between invasive and non-invasive ventilation, and whether the ventilation was for a hospital asthma admission only or for any hospital admission. These variables were total number of non-invasive ventilation episodes for asthma admissions only, total number of non-invasive ventilation episodes for any admission, total number of invasive ventilation episodes for asthma admissions only, and total

number of invasive ventilation episodes for any admission. All four variables were significant at the univariate level for death on discharge.

Each of these variables were entered separately into a multivariate model with the three variables, age, comorbidity index, and cumulative length of stay. Four separate models were fitted with only one each of the ventilation variables. Results shown in Table 32 below show odds ratios only for the ventilation variables as the odds ratios for the three other variables varied little across all four models and will be reported in the final model.

Table 32: Ventilation factors predictive of death on discharge from hospital (entered separately into multivariate model).

Death at Discharge			
Predictor	**P Value**	**Odds Ratio**	**95% CI**
age, cum. length of stay, comorbidity **with:** total number of non-invasive ventilation episodes for asthma admissions only	**0.023**	2.286	1.121-4.663
or: total number of non-invasive ventilation episodes for any admission	**0.009**	2.462	1.250-4.846

Neither total number of invasive ventilation episodes for asthma admissions only nor total number of invasive ventilation episodes for any admission reached significance, and was rejected by the model. However, both total number of non-invasive ventilation episodes for asthma admissions only (OR = 2.286, 95%CI: 1.121, 4.663) and total number of non-invasive ventilation episodes for any admission (OR = 2.462, 95% CI: 1.250, 4.846) were strongly associated with increased risk of death on discharge with similar odds ratios.

As the total number of non-invasive ventilation episodes for any admission variable is a superset of the total number of non-invasive ventilation episodes for asthma admissions only variable, and has a greater association with the likelihood of death, this was chosen as the preferred variable to be fitted to the final model (Table 33). There were no significant interactions in the final model.

Table 33: Factors predictive of death on discharge from hospital.

Death at Discharge			
Predictor	**P Value**	**Odds Ratio**	**95% CI**
age	0.000	1.043	1.026-1.061
comorbidity	0.010	1.360	1.075-1.720
cumulative length of stay	0.000	1.035	1.018-1.051
total number of non-invasive ventilation episodes for any admission	0.009	2.462	1.250-4.864

In summary, there was an increased likelihood of death on discharge if patients were older, had previous comorbid conditions, have stayed in hospital longer in the previous twelve months and required non-invasive ventilation for any reason. The fitted model suggested that each additional year of age at the index admission increased the odds of death by 1.043 (95% CI: 1.026, 1.061). Each increase of one unit in the comorbidity index (OR = 1.360, 95% CI: 1.075, 1.720), each additional day spent in hospital in the previous twelve months (OR=1.035, 95% CI: 1.018, 1.051), and each additional non-invasive ventilation event for any reason (OR = 2.462, 95% CI: 1.250, 4.864) all increased the likelihood of death on discharge. R-square values suggest that between 2.6 and 19.3 percent of the variability is explained by this set of variables, with the model correctly classifying 98.6% of cases overall.

4.2.4 Model 2: Predictors for Survival at Thirty Days

This goal of this portion of the analysis was to identify those factors that predict death which has occurred soon after discharge. The time period of thirty days after discharge was chosen due to its common use as a survival outcome in other studies, and to ensure comparability of results between studies. Once again, the variables age, gender, comorbidity and cumulative length of stay were selected to fit to the model, all of which had a significant univariate association. Neither of the invasive ventilation variables reached significance in the univariate model, whereas both variables for non-invasive ventilation for asthma and any admissions did. For reasons explained earlier, both the non-invasive ventilation variables were also independently fitted to the model.

When entered into the multivariate model, age, previous comorbid conditions (OR = 1.465, 95% CI: 1.136-1.889), and cumulative length of stay (OR = 1.032, 95% CI: 1.013-1.051) showed significant association with death within thirty days of discharge (Table 34). Neither gender nor non-invasive ventilation reached significance of association. All combinations of interactions failed to reach significance in the multivariate model.

Table 34: Factors predictive of death within thirty days from discharge (entered into multivariate model).

Died Within Thirty Days of Discharge			
Predictor	**P Value**	**Odds Ratio**	**95% CI**
age	0.000	1.046	1.025-1.068
comorbidity	0.003	1.465	1.136-1.889
cumulative length of stay	0.001	1.032	1.013-1.051

Each additional year of age at the index admission increased the odds of death at thirty days by 1.046 (95% CI: 1.025-1.068). Each increase of one unit in the comorbidity index (OR 1.465, 95% CI: 1.136, 1.889) and each additional day spent in hospital in the previous twelve months (OR=1.032, 95% CI: 1.013, 1.051) all increased the likelihood of death at thirty days. R-square values suggest that between 2.0 and 19.4 percent of the variability is explained by this set of variables, with the model correctly classifying 99.0% of cases overall.

4.2.5 Model 3: Predictors for Survival at One Year

This goal of this portion of the analysis was to identify factors that predict death which has occurred between thirty days and one year of discharge. This time period was also chosen due to the common use of one-year survival in other outcome studies, and to ensure comparability of results between studies. For this model, the variables age, gender, comorbidity, cumulative length of stay, total number of admissions and total number of asthma admissions were selected to fit to the model, all of which had a significant univariate association.

When entered into the multivariate model age, previous comorbid conditions and cumulative length of stay showed significant association with death between thirty days and one year of discharge (Table 35). Neither gender, total number of admissions nor total number of asthma admissions reached significance of association. All combinations of interactions also failed to reach significance in the multivariate model.

Table 35: Factors predictive of death within thirty days from discharge (entered into multivariate model).

Died Within Thirty Days and One Year of Discharge			
Predictor	**P Value**	**Odds Ratio**	**95% CI**
age	0.000	1.057	1.046-1.069
comorbidity	0.000	1.365	1.172-1.589
cumulative length of stay	0.006	1.019	1.005-1.032

Each additional year of age at the index admission increased the odds of death within one year by 1.057 (95% CI: 1.046-1.069). Each increase by one unit in the comorbidity index (OR = 1.365, (95% CI: 1.172-1.589) and each additional day spent in hospital in the previous twelve months (OR=1.019, 95% CI: 1.005-1.032) all increased the likelihood of death within one year. R-square values suggest that between 7.5 and 25.6 percent of the variability is explained by this set of variables, with the model correctly classifying 95.8% of cases overall.

4.2.6 Readmission Models Results

The readmission outcomes were defined as a hospital asthma admission within seven days of a previous hospital asthma admission or within seven and thirty days of a previous hospital asthma admission. The observance of repeated asthma admissions for a patient represented a cluster of correlated observations, and hence required a cluster-specific estimation model.

Firstly, univariate analysis was performed on all predictor variables of interest. Variables chosen for examination included those that showed significant univariate association with the outcomes, were identified as relevant by previous research evidence, or chosen specifically by the candidate. As a result the variables age, gender, triage score, ventilation for asthma admission and invasive ventilation for any admission were selected for modelling the outcomes of readmission.

The variable time-of-day (tod1) was collapsed into quartiles to reflect morning, afternoon, evening and night categories. Although only one of the categories (tod1(2): 12:00 to 18:00 hours) reached significance at p =0.05 level in the seven day readmission outcome, it was included in multivariate analysis in light of other time-of-day categories just failing to reach significance and the significant temporal trends reported earlier in the descriptive results. For the same reasons, the months of the year were collapsed into two different variables, firstly six-monthly seasons of 'wet' and 'dry' (season2), and then further into the usual three-monthly seasons of the year: summer, autumn, winter and spring (season4). However, only the six-monthly seasonal variable reached significance at the univariate level (Appendix 12).

Each of the predictor variables were modelled as continuous variables, except for the categorical variables time-of-day (tod1) and season (season), in STATA using both the logistic routine with robust standard error and the GEE routine with autoregressive AR1 correlation structure (both clustered on patient). Results from both of the modelling methods are reported as odds ratios with 95% confidence intervals and P values.

4.2.7 Model 4: Predictors for Readmission at Seven Days

This purpose of this portion of the analysis was to identify those factors that predict readmission which has occurred up to seven days after discharge from a previous admission for asthma. Based on univariate analysis and manual choice by the candidate, the variables age, gender, ventilation for asthma admission, invasive ventilation for any admission, problem urgency and season were selected to fit to the model. Neither of the other ventilation variables reached significance in the univariate model, nor the three-month seasonal variable (season4).

When entered into the multivariate GEE model, age, gender, ventilation for asthma, and problem urgency showed significant association with readmission within seven days of discharge from a previous admission for asthma (Table 36). Invasive ventilation for any admission and diurnal season (season2) both failed to reach significance of association, as did all combinations of interactions.

Table 36: Factors predictive of readmission within seven days of a previous asthma admission (entered into multivariate model).

Readmission within 7 Days (GEE Model)			
Predictor	**P Value**	**Odds Ratio**	**95% CI**
age	0.000	0.980	0.975-0.985
gender	0.010	1.461	1.094-1.950
ventilation for asthma admission	0.005	1.871	1.209-2.897
problem urgency (ATS)	0.000	0.697	0.610-0.795

Each additional year of age proffered a modest decrease in the odds of readmission with an odds ratio of 0.980 (95% CI: 0.975-0.985). There was a clear influence of gender, with being female increasing the odds of readmission at 7 days (OR = 1.461 (95% CI: 1.094-1.950). Being ventilated for asthma also increased the odds of readmission (OR = 1.871 (95% CI: 1.209-2.897). Each decrease of 1 in urgency (equating to an increase of 1 in the triage score) decreased the likelihood of readmission with an odds ratio of 0.697 (95% CI: 0.610-0.795).

4.2.8 Model 5: Predictors for Readmission at Thirty Days

This purpose of this portion of the analysis was to identify factors that predict the second of the readmission outcomes, namely admissions which have occurred between seven and thirty days after discharge from a previous admission for asthma. Predictors chosen for modelling were those that were significant or close to significant in univariate analysis and those of interest that were manually chosen by the candidate. These variables were age, gender, ventilation for asthma admission, both invasive and non-invasive ventilation and season (season2).

When entered into the multivariate model, only gender showed significant association with readmission at thirty days (Table 37). Being female increased the odds of readmission by 1.842 (95% CI: 1.252-2.710) in the GEE Model. The variables age, ventilation, season and all combinations of interactions failed to reach significance in the multivariate model.

Table 37: Factors predictive of readmission within thirty days of a previous asthma admission (entered into multivariate model).

	Readmission within 30 Days (GEE Model)		
Predictor	**Odds Ratio**	**95% CI**	**P Value**
gender	1.842	1.252-2.710	0.002

4.3 SUMMARY OF RESULTS

This chapter has explored both demographic and temporal characteristics of patients transported by ambulance for asthma and modelling techniques have been used to identify predictors for the outcomes of survival and readmission. The following summarizes the results that have been reported in this chapter.

- There were 15,671 asthma cases transported in the metropolitan area of Perth, WA, during the study period, comprising 21% of all respiratory cases and 1.4% of all cases. The proportion of respiratory cases increased over the period of study, whilst the proportion of asthma cases over the same period was approximately halved.

- There was a significant difference in representation of gender, with 60.3% of cases being female. Female cases exceeded male cases for all years of the study by between 19 and 24 percent. Trend analysis of age standardised asthma rates show a significant yearly difference for males but not for females.

- There were an increased number of asthma cases in the early childhood, early adult and elderly age groups. Despite being one of the smallest representative age groups, the number of cases in the 85+ years age group trebled over the study period.

- The age standardised rate for asthma steadily increased for the elderly. Trend analysis of the age standardised rate for asthma showed no significant yearly change for each age group, however by comparison, the rate for the 85+ years age group is approximately six times that of the youngest age group.

- The most common despatch code was respiratory conditions (code 24, 95.9%), and the most common priority code used to despatch ambulances to site was priority 1 (68.5%), however only 42.7% were assessed by ambulance paramedics with a problem urgency code (ATS) of 1 (immediate resuscitation) and 2 (emergency). The proportion of problem urgency codes 1, 2 and 3 increased over the time of the study.

- A significant difference existed between the number of cases transported and the hour of the day, with the number of cases peaking mid morning and late evening. There was also a significant difference for problem urgency and hour of the day.

- Monday was the day where the most number of asthma cases were transported, and although there was a significant difference between the days of the week, there was no change in trend over the period of the study.

- There was a significant annual pattern to asthma transports, with cases peaking in July (winter), and at their lowest point in February (summer).

- The sensitivity of the ambulance indicator of problem code to hospital principal discharge diagnosis was determined to be 70.47%, with a specificity of 99.23%. The positive predictive value was 57.02%.

- The ratio of admission of ambulance transported asthma cases to total emergency admissions has not substantially changed over the period, remaining steady at approximately 30%.

- Length of stay varied little over time, with a mean stay of 5.8 days, and a median stay of 4.0 days.

- Seven day readmission rates generally increased over the period of the study with the increase largely attributable to females, their rates consistently exceeding male rates for all years of the study.

- Thirty day readmission rates decreased for both genders over the period of the study, however female rates continued to substantially exceed those of males for most years of the study.

- Both the crude and age-standardised rates of ambulance transport for asthma is lowest in the quintile of highest socioeconomic status and highest in the quintile of lowest socioeconomic status.

- Statistically significant factors associated with survival at discharge were age (OR = 1.043), comorbidity (OR = 1.360), cumulative length of stay (OR = 1.035) and total number of non-invasive ventilations for any admission (OR = 2.462).

- Statistically significant factors associated with survival at thirty days were age (OR = 1.046), comorbidity (OR = 1.465) and cumulative length of stay (OR = 1.032).

- Statistically significant factors associated with survival at one year were age (OR = 1.057), comorbidity (OR = 1.365) and cumulative length of stay (OR = 1.019).

- Statistically significant factors associated with readmission at seven days were age (OR = 0.980), being female (OR = 1.461), ventilation for asthma (OR = 1.871) and urgency (OR = 0.697), whereas the only statistically significant factor associated with readmission at thirty days was being female (OR = 1.842).

5.0 DISCUSSION AND CONCLUSION

The aim of this thesis has been to describe demographic, socio-economic and clinical trends for ambulance transported patients with asthma, their outcomes and how they have changed over time. This has been possible by utilising novel and unique data linkage methods to investigate all metropolitan asthma cases that were transported by ambulance in Perth, Western Australia (WA), over the twelve-year period of 1990 to 2001.

Earlier in this study, several research questions were raised with regard to the ambulance transport of patients with asthma. It is appropriate at this point to restate those questions.

- What were the age and gender characteristics of patients suffering asthma transported by ambulance, and have trends in these characteristics changed over time ?

- What was the sensitivity and specificity of ambulance paramedic-diagnosed asthma cases ?

- Has the priority code and problem urgency of asthma transported patients changed over time ?

- Was there a circadian, weekly or seasonal variation in the number of patients with asthma transported by ambulance, and have these changed over time ?

- What is the outcome, in terms of survival and readmission to hospital? Specifically, was outcome influenced by problem urgency, co-morbidity or socio-economic factors ?

This chapter comprises an overview and discussion of the descriptive results and trends identified and those factors found to be predictive of the outcomes of survival and readmission. Results and determinants identified are, where possible, compared to those findings reported elsewhere in the literature and are discussed below.

5.1 DISCUSSION

This thesis has described a number of studies which have endeavoured to assess various aspects of the treatment for patients with asthma in the prehospital context. However, the focus has tended to be on issues such as therapeutic action taken in the emergency department (ED), attitudes that patients may have about their prehospital treatment or perhaps the effect of education programs on outcomes.

Although of no less importance, these studies are subject to a number of limitations, the most significant being that the there is little consideration given to the role of ambulance transport of patients. If mentioned at all, ambulance paramedic involvement was only described in the context of treatment administered to a patient either on attendance or en-route to hospital. Denominators chosen were mostly the number of cases that had presented to ED for the sample of interest, and were usually for a specific age group only. There may or may not be admission or readmission data associated with results from these studies.

In addition to the limitations described above, a predominance of cross-sectional study design, inconsistent definitions of asthma and small sample sizes limit the ability of these studies to provide evidence of the role played by the ambulance component of prehospital care.

Also, it has been difficult to comprehensively review and compare trends in the use of ambulance services over an extended period, as there has been a dearth of studies using population based data over time. The closest comparable study was a ten-year review of the operation of St John Ambulance services in the capital city of Papua New Guinea (PNG), but despite comprehensively analysing the utilization of the service[559], no additional information was obtained on the prehospital management of patients with asthma. Further, doubts remain about the comparability and generalisability of results from the PNG emergency medical system to that of Western Australia given the demographic, socio-economic and developmental differences between the two populations.

However, those Australian studies reviewed have been useful in highlighting aspects of the continuum of care in subpopulations, such as the effects of asthma on morbidity [155, 254, 322], readmission rates after an initial presentation to ED for asthma [323-327] and other outcome indicators [328-331], but there is a paucity of evidence regarding the role of the ambulance paramedics in this continuum. It is clear that internationally, the area of prehospital ambulance management of patient care in general is little researched, and specifically for Australia in the area of prehospital ambulance management of asthma, research is almost non-existent.

Trends and other specific results are discussed below under subheadings that are structured to relate to the specific research questions that have been raised earlier.

5.1.1 Gender and Age

Throughout the time of this study, the number of female cases (60.3%) with asthma transported by ambulance outnumbered the male cases (39.6%). Across all years of the study, females exceeded male numbers by at least 19%, highlighted by a significant negative yearly trend for the age-standardised rate in men relative to females over the time of the study. This trend cannot be explained simply by the greater longevity enjoyed by females in Australia, as there is not a significant difference for gender between the years of the study. This increased rate of asthma for females is consistent with studies reported elsewhere.[6, 347, 560] Gender differences in the distribution of patients with asthma in Australia are well documented, with asthma in males more common than females in primary school-aged children, and females outnumbering males after the teenage years.[6] This phenomenon has been reflected in the results of this study.

Age differences were seen in the number of patients with asthma transported by ambulance, with increased number of cases in early childhood and early adult age groups, but the majority in the elderly groups. Worthy of note is the almost linear increase in age standardised rates of asthma transports for age groups 60 years and over. Although the 85+ years age group nearly trebled in size over the period of the study, it remained one of the smallest representative age group in number of persons, yet the ASR for this group was nearly five times that of the youngest age group. This trend is

consistent with a recent review of studies with adjusted risk estimates of the effect of age on the incidence of adult asthma described earlier, which found the risk increased with greater age, most significantly in the highest age group[195]. It is recognized that a reported higher incidence with age may be partly explained by misclassification, most likely with chronic obstructive pulmonary disease, however the findings from these studies implied that the incidence of asthma in the elderly has previously been underestimated[195]. As statistical modelling in this thesis has controlled for the effect of comorbidity, the observed increased incidence of asthma in the elderly is worthy of note.

However, literature suggests that children dominate ED attendances for asthma in Australia [153], with one Australian study enumerating that 67% of presentations for acute asthma were for children aged less than 15 years old.[340] In 2000-2001, the AIHW reported over half of all separations for asthma (51%) occurred in children aged 1-14 years, with the highest rate of ED presentations for asthma in children aged 0-4 years.[246]

It can be seen that results reported in this thesis are counter-intuitive to those reported by the AIHW above, and are worthy of further discussion. One possible reason may be that a higher proportion of babies and very young children would be taken directly to ED by parents or relatives, instead of an ambulance being called. Further, as the ambulance service in Perth is not free and operates on a fee-for-service basis, there may be a disincentive for parents of young patients to either access the service for a first presentation or continue to use the service for subsequent presentations.

Age has also been shown to be a predictor for survival at seven days, thirty days and one year post discharge using logistic regression modelling. Every increasing year of age was shown to be associated with an increased risk of death (4.3 to 5.7%) for all survival outcomes, when comorbidity, cumulative length of stay and ventilation history were controlled for. Modelling also found age to be predictive for readmission at seven days after discharge, where it proffered a modest protective effect on the risk of readmission. For each increasing year of age, the risk of readmission within seven days was reduced by 2%, after controlling for gender, ventilation history and urgency.

Possible explanations for this result may be a trend of decreased severity of asthma with age, or that the likelihood of compliance to new or modified treatment increases (even temporarily) after attendance to ED, especially with the recent memory of an acute asthma episode. However, it has been reported that most deaths due to asthma occur in the elderly [248] (often in the presence of comorbid conditions such as chronic airways limitation), so a suggested decrease in severity of asthma with age would be counter-intuitive to reported results. The protective effect is more likely to be associated with treatment modalities in the ED or, as age is not a predictor for readmission at thirty days, this result may simply be artifactual.

However, being female increased the risk of readmission at seven days by 46.1%, and the risk of readmission at thirty days by 84.2%, which is both consistent with current evidence [6, 561] and age standardised rates reported above, and this will be discussed further in the outcomes subheading below.

What these results have shown is that that certain patient-specific factors are predictive of readmission, and it is accepted that these factors may be independent and non-modifiable risk factors, for certainly a patient has no control over their age or gender. However, it is possible that they may also be markers of other, modifiable factors [339], for example readmissions could be related to increasing age because of unreliable or changing compliance with medication regimes, or perhaps absent or inappropriate home care. It has been highlighted that patient compliance with asthma medication continues to be a problem, and that a patient's perception of the adequacy of their treatment may not necessarily align with that of clinician expectations.[336, 562] Therefore, it is conceivable that apparent patient-specific factors may actually reflect a failure to provide or comply with adequate health care. This raises questions of both health delivery and policy that future research could explore.

5.1.2 Trends over Time

This study has shown a number of trends with respect to the transport by ambulance of patients with asthma in the prehospital setting. During the period of this study, there had been a modest increase in the proportion of respiratory cases compared to all cases transported by ambulance in WA. Moreover, even though the absolute number of all

cases transported by ambulance increased each year during this time, the number of asthma cases transported per year changed little, and the proportion of asthma cases relative to all respiratory cases had halved. Also, it is noted that during the period of this study mortality from asthma in Australia had begun to decline [5, 6, 11], and the prevalence and severity of asthma had reportedly increased.[4, 6] These results appear consistent with reported declines in deaths, hospitalisations and GP consultations from asthma in Australia over the past decade.[6]

However, concern remains about the possible escalating prevalence and severity of asthma [563], and this study has explored aspects regarding the role of the ambulance paramedic and emergency medical services in the prehospital care of the patient with asthma. With respect to emergency medical services, this study has demonstrated that for all asthma cases in the study, 95.9% of despatch codes for the calls were for respiratory emergencies, a high level of accuracy by the ambulance operation centre staff who often work on limited information provided by the caller at the time of logging a call.

The majority of these calls (68.5%) were dispatched as priority 1 (lights and sirens), but over the study period there has been a modest decrease (-10.4 %) in the proportion of priority 1 transports. To explore the accuracy of diagnosis, the problem code (as assessed by the ambulance paramedic on arrival at scene) was compared to the hospital principal discharge diagnosis. It would appear that ambulance paramedics are better at identifying patients who do not have asthma (specificity of 99%) than when they do have asthma (sensitivity of 70%), however with a positive predictive value of 57%, they were not particularly discriminatory in classifying those patients with asthma who were eventually admitted to hospital for asthma.

Given that acute asthma exacerbations often occur in the presence of other comorbid conditions such as chronic airways limitation [248], or can be precipitated by other infections such as common colds, sinusitis, and bronchitis [13], it may be difficult for the ambulance paramedic to isolate asthma from other comorbid conditions as the primary diagnosis in the short time available. With approximately 44% of the study cohort over 55 years old, disentangling individual respiratory conditions of a patient would become more difficult with age as the comorbid burden also increased with age.[500]

A demonstrable reversion of airway obstruction would also be diagnostic of asthma [13], however the time associated with measurement of peak expiratory flow pre-treatment, initiation of treatment (e.g. salbutamol via nebuliser) and preparation for transport by the ambulance paramedic often means that post-treatment peak expiratory flow measurement only occurs after admission to ED. Further, an increase in forced expiratory volume (FEV_1) would be diagnostic of asthma [13], but this is usually measured by spirometers which are not standard in SJA ambulances.

The SJA problem urgency code, approximately equating to the Australasian Triage Score (ATS), has changed over time. However it has been explained previously that the study period was actually two separate periods with two different coding schemes, 1990 to 1993 and 1994 to 2001. If the year of 1994 is excluded on the basis of being a transition year from one coding schema to another, it was observed that the proportion of all problem urgency codes have hardly changed at all over time. It is noticed that despite the high percentage of priority one calls (68.5%), only 42.7% of these cases were considered immediate resuscitation (urgency code 1: 6.4%) or emergency (urgency code 2: 36.3%) by ambulance paramedics. This is most likely the result of the ambulance operations centre taking a cautious approach to respiratory emergencies, and despatching ambulances with a priority one status accordingly.

If problem urgency is examined in terms of circadian variation, the pattern of transport was not evenly distributed over a 24-hour period. There was a significant difference for number of cases transported and hour of day ($\chi^2_{(23)} = 508$, $p = 0.000$) with clear peaks in mid-morning and late evening, and problem urgency and hour of day ($\chi^2_{(92)} = 182$, $p = 0.000$).

Interestingly, the period where the greatest proportion of problem urgency 1 cases was recorded was between the hours of 03:00 to 07:00, and problem urgency 2 cases between the hours of 02:00 and 08:00. If problem urgency was considered a surrogate for asthma severity, this suggests that many of the most severe asthma episodes are occurring in the early hours of the morning, a period where the incidence of asthma cases transported overall is lowest. The nocturnal worsening of asthma is common, and has been found to be related to the daytime severity of asthma [564], continuous asthma

severity [565], as well as changes due to endogenous circadian rhythms in the inflammatory process.[566, 567]

However, despite some early studies reporting approximately 75% of respiratory arrests or deaths from asthma occurring between midnight and 08:00 [568, 569], there appears to be little evidence to suggest diurnal variations place patients with asthma in greater risk at night-time [570], or that circadian differences affect ED presentation, choice of therapy or outcomes.[571, 572] Supporting this hypothesis, modelling from this thesis also found no association between the time of day that a case was transported and the likelihood of readmission or death. This may suggest that night-time asthmatics are more insensitive to the symptoms of severe asthma, as reported elsewhere [572], or simply reflect the tendency of patients to wait longer at night before utilizing ambulance services, resulting in more severe circumstances on attendance by ambulance paramedics but unchanged outcomes.

A statistically significant difference was found between the day of the week and the number of asthma cases that were transported by ambulance ($\chi^2_{(6)} = 45$, $p = 0.000$), where case numbers increased over the week from a low on Wednesday to peak on Monday. The fact that there was no significant difference for the day of the week between the years of the study ($\chi^2_{(66)} = 63$, $p = 0.58$) or for problem urgency and day of the week ($\chi^2_{(24)} = 24$, $p = 0.47$) highlights there is no change to this trend.

Suggestions as to why this occurred may include that there is less private transport available on a Monday, i.e. breadwinners use the family car during weekdays for getting to work. In the case of sudden cardiac death (SCD), it has been suggested that for those employed, the stress of changing from weekend leisure activities to work activities on Monday may account for the observed increased incidence of SCD on Mondays.[573] In view of the many triggers outlined earlier that may be implicated in an asthma attack, it is conceivable that there may be similar precipitating factors at work in the case of patients with asthma to explain this phenomenon.

Many factors may contribute to this, including the stress of returning to a workplace on Monday or stale air from air conditioning systems that have been turned off over the weekend. Visiting public places such as shopping centres or day-care centres may also

be enough to precipitate an acute episode of asthma. Nonetheless, modelling revealed no significant association between the day of the week an asthma patient was transported by ambulance and the likelihood of readmission or death.

In New South Wales and Victoria, there has been marked month-to-month variability in ED presentations for asthma, particularly for children. The lowest rate of ED visits for asthma occurred in January, where there was also the least difference in age groups, and large peaks in ED visits occurred in February and May among children less than 15 years. The February peaks coincided with the end of the school holidays and the return to school, with all the inherent risks to respiratory health associated with it [6, 246], such as close proximity to other students and the concomitant exposure to potential infectious agents. Among persons aged 35 and older, fluctuations in ED visits were less variable, but followed a seasonal pattern with peaks evident in the winter months [6], coinciding with the usual increase of respiratory infections during this time. This age-related variability in ED presentation rates for asthma highlights the importance of different environmental factors in triggering exacerbations of asthma at different ages.[6, 574]

This thesis also examined monthly variations in the number of asthma transports, and found that there is not only a significant difference in the number of cases transported and the month of the year ($\chi^2_{(11)} = 770$, $p = 0.0000$), but also between problem urgency and month of year ($\chi^2_{(44)} = 77$, $p = 0.002$). There was an obvious seasonal pattern, with asthma cases peaking in the winter months of July and August, and decreasing to the lowest point in the summer month of February. This seasonal pattern is likely to reflect the impact of the winter increase in respiratory tract infections.

It is noted that the February peak observed in other studies was not present, but this may be associated with the fact that age group results reported and discussed by the candidate previously do not entirely reflect those reported by the AIHW, and are most likely the result of a different age distribution in the cohort rather than any potentially different aetiology of asthma in Western Australia. For modelling purposes, three and six-monthly 'season' variables were derived from the months of the year to test any association with readmission or survival outcomes, but none of the season variables were found to be significant.

This study also examined the ratio of admission of ambulance transported asthma cases admitted compared to the total number of all admissions for asthma admitted on a per year basis. Source-of-referral statistics for all cases admitted with a principal discharge diagnosis of asthma in the Perth metropolitan area, obtained from the Morbidity Data System independently from the linked data, were able to summarise the origin of patient admissions based on referral type.[575] Unfortunately, differences in coding schema rendered data unreliable for the years 1990 to 1992 and 2000 to 2001, however trend information was available for the years 1993 to 1999.

Remarkably, the ratio of those asthma cases admitted via ED that were transported by ambulance versus all asthma cases admitted varied little over the seven year period, remaining steady at approximately 30%. The source-of-referral data showed an overall decrease in total asthma admissions in Perth over the time of the study, which is commensurate with the decrease in hospital admissions for asthma reported nationally over the same period.[6] Therefore, the relative increase in the number of patients with asthma admitted via ED for asthma may be a proxy for the increased prevalence and severity of asthma in Australia that has been reported elsewhere.[217, 224]

The average length of stay in hospital of those patients with asthma transported by ambulance and subsequently admitted decreased from 6.4 days in 1991 to 5.1 days in 2001. This is approximately double that of the national average length of stay in hospital among people admitted with asthma, where over a similar period, the average length of stay in hospital decreased from 2.9 days to 2.2 days, with trends toward shorter stays being observed in all age groups.[6] Reasons for this decrease may include change in asthma severity, improved management practices or simply changes to funding arrangements for hospitals. For example, a large prospective study (n= 11,939) over 8 years in Melbourne, Australia, found that length of stay and bed use for acute asthma at our hospital were significantly reduced since the introduction of casemix funding, without increases in unplanned readmission rates.[325]

Unfortunately, it was not possible to compare the length of stay for ‘ambulance admissions only’ at the national level as the statistics available did not differentiate between emergency admissions and other admissions; however the difference in rate

bears scrutiny. If there were a significant difference to national figures, the reasons for such a disparity in length of stay may be due to differences in severity, prehospital treatment or in-patient treatment modalities, and certainly would suggest a direction for further research.

5.1.3 Socioeconomic Status

Crude and age-standardised incidence rates of ambulance transported asthma cases were found to be associated with socioeconomic status (SES). Whether the home address or the address at which the ambulance attended was used for analysis, the results were very similar. Incidence rate ratios showed a clear increasing trend from highest to lowest SES.

There was also a statistically significant difference between the rate ratios for SES indices over all three census periods, regardless of postcode strategy used. As shown in the results previously, the pattern of incidence is similar in both groups; however the rate of incidence is higher across all but one of the SES quintiles after age-standardisation. The only quintile where the age-standardised rate ratio was lower than the crude rate ratio was for SES quintile 4 in 2001.

According to the AIHW, in 2001 people living in the most socio-economically disadvantaged localities did not have a substantially higher prevalence of asthma compared to those living in less disadvantaged areas.[6] This finding does contrast with observations in some other countries, e.g. in the USA there was a higher prevalence of asthma in children from lower income families.[576, 577] However, in Australia, both the rate of hospitalisation for asthma was higher for people living in socio-economically disadvantaged areas, and among adults aged 35 years and over, the proportion of all ED presentations that were for asthma tended to be greater in people from more disadvantaged areas.[6]

Caution does need to be exercised in the interpretation of these results, for it is noted that the AIHW has based its estimates on the results of the National Health Survey 2001 (which is the only nationally representative, household survey in which the prevalence of asthma was measured), plus other state, territory and locally based surveys with

varied survey methods, age ranges and sample sizes. As such, the data from these surveys cannot be used to reliably compare states or other population subgroups.[6] However, results from this thesis showing a strong association between SES and the incidence of ambulance transport corroborate those of the AIHW, especially for the adult population.

In the light of this strong association, modelling to explore the effect of SES on the outcomes of readmission or survival for the cases transported was performed, and as reported, modelling for all outcomes found that SES failed to show any statistically significant association with readmission or survival, after controlling for other factors known to be associated with outcome. This may mean that there is indeed no effect of SES on outcome, or it may also mean that the estimate of SES in this study lacks adequate sensitivity.

It is accepted that the SEIFA Index of Relative Socio-Economic Disadvantage is commonly used to calculate socio-economic status in health research in Australia [578, 579], but caution has been expressed in its use because by its very nature, it is a composite summary of many indicators of social and demographic variables based on a geographical area.[531] As such, geographical areas with a similar SEIFA score may not necessarily reflect the same social and demographic profiles and may require quite different strategies with regard to health planning.

Nonetheless, whilst no direct association was demonstrated between SES and readmission or survival, this does not preclude SES from being a significant factor in the incidence of ambulance transported asthma cases, and intimates important health service and resource planning implications, addressing such issues as distance from health services, accessibility, availability of alternative forms of care and efficacy of self-management.

5.1.4 Outcomes

The two major outcomes examined in this study were survival and readmission. A third outcome, re-presentation, was identified as one of interest, but a lack of linked data between SJA and ED data precluded this from being examined. A current linkage project is under way in Western Australia to link emergency department data from the major metropolitan hospitals to the WA Data Linkage System, and future research efforts will be able to provide insight into the complete continuum of care for a patient through analysis of linked prehospital, emergency, inpatient and mortality data.

Survival.

Survival was categorised into three variables, where death was flagged for a patient either at discharge, within seven days of discharge or within one year of discharge. It was noted that for all three death categories the two main causes of death were either asthma or chronic airway obstruction; two of the most commonly recorded comorbid conditions for death associated with respiratory function, especially in the elderly.

Modelling using logistic regression was performed and those factors which were predictive of survival were identified.

For all three survival outcomes, age, comorbidity and cumulative length of stay had a significant association. It is reasonable to expect that increased age, an increased burden of disease and more frequent and longer stays in hospital will all contribute to poorer expected survival outcomes.

However, the need for assisted ventilation for patients with severe asthma on admission is also of great interest. The presence of ventilation episodes for a patient can be used as a convenient indicator for the severity of disease. It is known that a life-threatening asthma attack that leads to intensive care unit (ICU) admission, intubation, or both identifies a patient at high risk of subsequent morbidity and mortality.[580] It is also known that intubation during asthma hospitalisations is associated with worse outcomes and higher costs.[581]

In the WA Data Linkage System, there was a data record that flagged the number of days a patient spent in ICU within a hospital, but unfortunately this record was incomplete and often inaccurate, and as this record could not reliably indicate all ICU attendances, it was not considered suitable for purposes of analysis.

Further, as more life support procedures are increasingly being initiated and managed in emergency departments, both ED and ICU records would be required to reliably describe the treatment a patient received. This is not possible within the scope of this study, but further research to explore the role of ED, ICU and advanced airway management in life-threatening asthma on outcomes is indicated.

The ventilation variable described above encompasses both invasive and non-invasive procedures. The role of non-invasive procedures in airway management is evolving, indicated by the increased incidence of non-invasive ventilation procedures in the latter years compared to the early years of this study. Non-invasive ventilation has been shown to be effective in patients with acute respiratory failure due to pulmonary oedema and exacerbations of chronic obstructive pulmonary disease, but its role in an acute asthma attack has remained uncertain. The use of bi-level pressure ventilation (BPV) or bi-level positive airways pressure (BiPAP) in selected patients with a severe asthma attack has been shown to improve lung function, alleviate the attack faster and significantly reduce the need for hospitalisation.[582]

Monitoring trends in the occurrence of invasive and non-invasive ventilation procedures can provide insight into the epidemiology of severe, life-threatening asthma and asthma deaths. This study has shown an increasing use of non-invasive ventilation procedures over time, which could indicate a trend of increasing severity of asthma, which has been reported elsewhere. However, interpreting these trends may be problematic due to the variations in criteria for ventilation across institutions, especially in the light of policies that may indicate the use of non-invasive procedures as a means to averting the need for intubation and more invasive procedures.[6]

Disentangling the use of non-invasive ventilation procedures in severe asthma for reasons of need versus reasons of choice of treatment, and the differentiation of invasive to non-invasive methods in airway support and their effects on morbidity and mortality

are both beyond the scope of this thesis. However, as data linkage structures become more comprehensive, the potential for evaluation of more robust outcomes based on these and other procedures will become possible.

Readmission.

As reported previously, the seven day age standardised readmission rate increased over time, but when differentiated by gender, the increase was largely attributable to females. This differed to the thirty day age standardised readmission rate where the overall rate decreased, especially in the latter years of the study. There was an increasing trend for female readmission rate over the majority of the study, with the rate only decreasing substantially in the last few years of the study. This is in contrast to a generally decreasing trend for males. The female readmission rate was consistently more than double the readmission rate for males for most years of the study. As there was an increasing trend evident in the female readmission rate for the study period up until 1998, it is unknown whether the decrease in rates identified in the last few years of the study were the effect of a cyclical trend or an indication of some new permanent trend.

Factors associated with readmission at seven days were found to be age (OR = 0.980), being female (OR = 1.461), ventilation for asthma (OR = 1.871) and problem urgency (OR = 0.697), whereas the only factor associated with readmission at thirty days was being female (OR = 1.842). The presence of gender as a predictor of readmission is unsurprising considering the proportion of females in the study and results reported by the candidate earlier. These results are confirmed by national data where readmission rates have been reported higher in females than males [6], particularly those aged between 15-64 years.

International data also confirms that gender-specific differences exist with female readmissions outnumbering male readmissions [583], especially in high-risk categories.[560] It has been suggested that mechanisms contributing to gender differences in asthma admissions may include differences in aetiological pathways or pathophysiological response, differences in the ventilatory response to hypercapnia or in the tolerance to airway obstruction, and are deserved of further study.[560]

Problem urgency also showed a significant association with readmission at seven days, where the less urgent the episode, the less risk there is of readmission. The significance of the ventilation for asthma variable indicates that there is an association of episode severity with readmission at seven days, but only for ventilation procedures performed for an asthma episode of care. It is known that in paediatric patients with asthma, risk factors for short-term readmission include a history of previous admission to a neonatal intensive care unit (NICU) [342], and although it is not clarified what interventions were initiated, it is assumed ventilation would be at least one option.

The issue that gender was the only predictor at readmission within thirty days is also not surprising. Gender is identified as a baseline risk for readmission identified in other reported research. Studies in paediatric populations identify being female, previous ICU admissions and history of previous asthma admissions as predictors of readmission [342, 347], and in adult studies being female [347] and at high-risk predict readmission.[560] In the current study readmission had been defined relative to a previous asthma admission, and although ICU status could not be confirmed per se, high-risk status could be estimated in terms of ventilation status and problem urgency as proxies. It could be expected that these variables may be adequate as proxies for factors identified in other research.

However, the lack of significance of ventilation or problem urgency on modelling thirty day readmission invites comment. It may be that without comparable and definitive indicators for ICU and high-risk, and the limitations of clinical data that a retrospective design such as the current study affords, expecting comparability in results may be optimistic. It is also possible that the cohort of patients analysed in this study are a different population with a different aetiological pattern of disease.

Nonetheless, the conclusion that being female is the sole predictor for readmission at thirty days does not appear unreasonable. To put this result into a clinical context, treatment a patient received for asthma in hospital would be to alleviate acute symptoms, stabilise their condition and plan for either new or modified treatment regimes post-discharge. It could be assumed that in the seven days post-discharge period, there may still be other factors that influence the risk of readmission, including recurring triggers and treatments that may have been initiated but are yet to be effective.

It could also be assumed that most treatment regimes initiated or altered in hospital and continued post discharge would have some degree of effect by thirty days. Further, it is known that asthma is often accompanied by other conditions such as respiratory infection and chronic obstructive airways disease, especially in the elderly. These patients are likely to be prescribed additional therapies concurrent to their existing asthma therapy, and these too will be subject to a time lag before becoming effective.

However, by thirty days it could be assumed that any therapy prescribed has had adequate time to become therapeutic and either positively or negatively influences the patient's health. In this scenario, it could be expected that the acute asthma episode that precipitated the initial admission should be adequately under control within thirty days, attenuating the effect of those other factors that may affect readmission and thus reducing the risk of readmission to hospital. At thirty days, the effect of a strong predictor such as gender would also have been attenuated, but may also become the only predictor to continue to exert an influence on outcome.

One caveat to this scenario is noted here, in that re-representation to the emergency department (ED) without admission has not been able to be factored into these results. This means that a patient may have re-presented to ED for deterioration in their condition within seven or thirty days of a previous admission, but was discharged from ED without admission. Pending data linkages with emergency data will enable these gaps in knowledge to be addressed.

Socioeconomic status was not found to be significant for the outcome of readmission, and this is consistent with studies reported elsewhere. A Canadian study also found that SES measured at the neighbourhood level has no significant impact on rehospitalisation for asthma among Canadian adults.[561] Although hospital separation rates are reported to be higher among indigenous Australians than among other Australians across all age groups [6], it was not possible to differentiate these patients on the basis of race or ethnicity with the data available and as such, it was not possible to assess separately the influence of socioeconomic status on readmission for these groups.

5.1.5 Strategies to Improve Outcomes

In Australia, there has been a declining trend in deaths attributed to asthma since 1989, although the death rate due to asthma in Australia is still considered moderately high by international standards.[563] The risk of death from asthma occurs in all age groups and increases with age [6], and despite optimum therapy and management, death sometimes results.[584] A decreasing mortality rate from asthma in Australia is complemented with increasing prevalence and severity.[563] Although there are limited data on the prevalence of asthma with regards to the levels of severity and control in the general community, estimations suggest that in Australia, between one-third to one-half of adults with asthma have moderate or severe disease.[6]

It has been shown from previous discussion that predictors identified to be associated with increased risk of death or readmission could be considered indicators of the burden and severity of asthma as a disease in the population. Although not a point of focus of this study, it nevertheless is considered necessary to briefly outline strategies that are currently undertaken that have potential to reduce the burden of disease caused by asthma and its complications, and in doing so improve outcomes for these patients.

Over the last twenty years, consensus has been reached that written asthma management plans (AMP) and regular use of medications that control the disease and prevent exacerbations are key elements in the effective management of asthma.[6] Further, the role of spirometry as an important tool in the diagnosis, assessment and follow-up of patients with asthma has been recognised for many years.

The AMP enables people with asthma to recognise deterioration in their condition promptly and respond appropriately, by following written instructions to introduce or alter medications depending on changes in symptoms and peak expiratory flow measurements.[6] The aim is to assist the process of early intervention and prevent or reduce the severity of acute asthma episodes. There is evidence that for patients with asthma who use an AMP, outcomes are improved when used in conjunction with training in self-management and regular medical review. These include less need for

hospitalisation, less urgent GP visits, less additional medication and better lung function.[316]

It has also been shown that written AMP's may reduce the risk of death from asthma by 70%.[585] Despite these findings, the majority of people with asthma do not have written AMP's. In recent Australian surveys, the proportion of adults with current asthma who possessed an AMP ranged from 15-22 %.[6] Although there was an apparent increase in the use of AMPs in the early 1990's which coincided with public awareness campaigns launched by the National Asthma Council, this trend has not been sustained.[336, 341, 381]

Spirometry, the measurement of spirometric lung function, is important in the diagnosis, assessment of severity and monitoring changes over time in asthma and other lung disorders. Over the last decade, Medicare claims by providers for reimbursement highlights decreased office-based spirometry and increased laboratory-based lung function testing, especially those under 55 years old. For people aged between 5 and 34 years, spirometry rates are higher for those living in socioeconomically advantaged areas.[6] If this is an issue of inequity of access to health care based on socioeconomic grounds, it cannot be assessed here, but it would certainly merit further investigation.

Inhaled short acting beta agonists and inhaled corticosteroids are the most commonly used medications among people with asthma, with the majority delivered by metered dose inhalers.[6] Most inhaled corticosteroids are delivered in the strongest strength formulation available, which is likely to be unnecessary for all people taking them, however despite this fact, there is evidence that the majority of people with asthma do not use inhaled steroids regularly.[6]

The recent introduction of combination formulation of steroids and long acting beta agonists will reduce the potency of inhaled corticosteroids required.[6] Brief asthma education programs designed to improve inhaler skills and teach patients how to adjust their drug doses according to peak flow measurements and their treatment plans has shown that substantial changes in illness behaviour and the use of health care facilities can be achieved [302], but encouraging the asthma patient to adhere to treatment regimes remains a challenge.

Evidence also suggests that the ED can be an appropriate setting for an intervention that improves outcomes [304], but such programs need to link the patient back to the primary health care provider, such as a GP or physician. However, the barriers to follow-up care and regular use of a primary health care provider still need to be identified so that future interventions can address these issues.[313] It has been shown that paediatric asthma clinical pathways in hospitals can result in decreased length of stay and overall costs without increasing the rate of admission [309], and asthma nurse specialist interventions can reduce not only total hospitalisations and readmissions, but also reduce lost work or school days.[307]

Further, brief self-management programs for patients during a hospital admission can reduce post-discharge morbidity and readmission for adult patients with asthma [306] and readmissions for children.[305] Also, outpatient programs can be used as a vehicle to reduce readmissions for adult asthma.[303] Something as simple as a follow-up visit for patients who have recently been treated in ED for asthma have been shown to be effective in reducing early relapse.[311, 349]

To put all the above into perspective, there is much that could be done at the prehospital, in-patient and post-discharge stages of a patient's care to prevent or reduce the severity of exacerbations of asthma and subsequent consumption of health services. What proportion of these activities could fall to ambulance paramedics remains unknown, as their main activity to date has been the management and treatment of the acute asthma episode. This management may include the administration of oxygen, $beta_2$ agonist nebulisers or adrenaline, and intermittent positive pressure ventilation, but all resulting in transportation of the patient in the quickest and safest way to hospital.

The fact that activities initiated in ED, designed to reduce or prevent relapse or readmission due to asthma, have been shown to have positive effects on patient health outcomes raises the question of how different should the role of prehospital care be in the future. This is not merely a question of speculation, for if evidence suggests health benefits may be gained by changing the prehospital health care paradigm, then surely this is worthy of further attention.

Perhaps changing the scope of the emergency medical system is one solution, where ambulance call centres could function as advice centres, and phone, video and web-based health advice is offered first, with ambulances dispatched only as a last resort. Perhaps all existing patients with asthma must have written AMP's as part of health care contracts with the ambulance and hospital services, and are given drug and treatment advice remotely, with their progress monitored and assessed for effectiveness before a decision for emergency transportation to hospital is made. As it is known that prehospital drug therapies and advanced life support for asthma can be effective in improving patient outcomes [368, 586], it is conceivable that a future model of the management of all but the most severe asthma may focus on treating patients with asthma in the community rather than in tertiary centres, via collaboration with patients, families and the expanded role of ambulance paramedics.

Whatever the future may look like, continual fiscal pressure on health services and delivery provide strong reasons to seek and find efficient and economical solutions to old problems using new innovations and technology. It is important that alternative models of care are explored.

Further, the key to preventing readmissions, reducing comorbidity, and reducing length of stay lays in multi-dimensional and proactive education, and health interventions that encompasses the general public and health professionals alike. Whether the resolve and resources exist or can be found to achieve this remains unknown, but in knowing the cost of asthma to the community, and the health benefits that could be realized with effective management, these factors alone should urge us on.

5.2 STUDY LIMITATIONS

This portion of the discussion seeks to outline those factors that may limit or influence the interpretation of the results presented in this thesis.

Efforts have been expended to produce the best possible linkage outcome for the matching of the datasets used in this study. However, despite best efforts, the quality of the data used for this analysis can only be as good as the quality of the original datasets. By their very nature, large administrative datasets will invariably contain errors and omissions, and the probabilistic method of matching and linking these datasets can guarantee a high level of confidence in the integrity of the data, but never a perfect match. Nonetheless, as estimated error rates in the linkage of data used for this thesis are considered less than 1%, and validation of the WA Ambulance Dataset outlined in this thesis shows ambulance data to be accurate and reliable, there is confidence that the datasets used for this thesis are in good health for the purposes of analysis.

The choice to use a retrospective design utilising the linked databases afforded a rich opportunity to explore hospital outcomes, comorbidities and other factors over time. The absence of linkage to emergency department records unfortunately prevented the capture of information about what transpired for those 5,905 patients who were transported to hospital by ambulance for asthma but were subsequently discharged. As these cases were not linked to any hospital records, this prevented the assessment of re-presentation as an outcome. The absence of ED data also precluded the assessment of treatment options initiated by ambulance paramedics and continued by ED staff, and subsequent outcomes for all cases. This issue is now being resolved by recent ongoing linkage of emergency department data to the WA Data Linkage System.

Collecting data prospectively for this research project may have elicited better information regarding an episode of care, such as the circumstances surrounding an asthma event, duration of symptoms prior to the attendance of an ambulance, the workload facing the ambulance service at the time calls were received or medical attention received in the emergency department. However, notwithstanding the merits of prospective data collection for patient history and outcomes, the costs and logistical restraints make achieving this at the population level unrealistic. It is considered that

the retrospective design used in this study is the best choice possible to analyse population level data.

Although this study has placed considerable emphasis on the outcome of survival, there exists no mechanism to assess quality of life of the asthma patient, as this is also clearly important. Unfortunately, neither the SJA data nor the Morbidity Data System data provided any reliable information on the neurological, functional or psychosocial status of patients who were discharged.

The study cohort was defined by the criteria of being transported by ambulance for asthma. Selection of cases in this manner precluded a group of 2,334 patients who were transported to hospital by ambulance for other conditions but were later shown to have asthma. Similarly, the cohort of patients who were admitted to hospital for asthma but did not use an ambulance are also absent. Ideally, the study population would have included all patients presenting to the ED with asthma from both ambulance and other sources, those diagnosed with asthma in ED, as well as those 2,334 patients not presenting as asthma but subsequently admitted with asthma.

However, as explained earlier, the absence of ED and non-linked hospital data precluded this, so therefore the exclusion of these groups from analysis may limit to some extent the generalisation of the study results. One limitation is that the prediction of readmission outcome was based only on those admissions associated with ambulance transported asthma cases. Death data was independent of hospital admission data, so death as an outcome was not influenced by this limitation. It could be presumed that the proportion of cases used for predicting readmission were no different from the proportion not identified, but as this is not known, the results of readmission predictors may not be generalised to all patients with asthma.

The use of the Charlson comorbidity index has achieved substantial momentum in recent years as a useful tool for modelling outcomes, allowing flexibility and comparability across research efforts. It is noted, however, that the Charlson index was designed originally for a small adult population with a single specific disease and although its generalisation across other populations has now been readily accepted by researchers [499], certain comorbid conditions may not be relevant for children. As this

study examines all age groups, there may be potential for some residual confounding by comorbidity. Further, it may not always be possible to discern whether a particular diagnostic code refers to a complication or a comorbid condition, so there is potential for codes that may be included in the calculation of the comorbidity index to be actual complications, thus influencing results by exaggerating the association of comorbidity on outcomes.

The SEIFA Index of Relative Socio-Economic Disadvantage (IRSD) used in analysis for this thesis summarizes particular attributes, eg. income, education, and employment status, but does have some limitations as described previously.[518, 531] The IRSD is created by analysing and standardising census-based socio-economic variables, which are then collapsed into a summary variable, making the index less precise.[518] Further, as the scores are produced by principal components analysis, they are not totally unambiguous indicators, meaning that although areas sharing the same SEIFA score may share similar constituent profiles, there will be cases where the scores mask significant socio-economic differences between areas.[518, 531]

With respect to this thesis, the selection of the cohort cases based on ambulance use only may introduce bias, for example, age or socioeconomic status may influence the decision to access ambulance services. However, as it was not possible to disaggregate the individual components of the index score, the candidate was unable to assess the effect of these individual components, and hence could not comment on issues relating to the reason an ambulance may or may not be chosen for transport, for example, the cost of primary care or ownership of a car. Nevertheless, age and socioeconomic status were controlled for in modelling outcomes in the study cohort.

It is acknowledged that any association identified in this study does not automatically imply a causal relationship. However, notwithstanding the limitations identified above, any relationship identified contributes to the body of evidence for both the evaluation and creation of health strategies, more than simply opinion or rhetoric alone.[517]

5.3 CONCLUSION

This study has been able to describe the epidemiology and outcome of asthma cases transported by ambulance in the metropolitan area of Perth, Western Australia, for the period of 1990 to 2001. This has been possible due to a uniquely isolated geography, an ambulance service that operates as a monopoly, and a linked database that has allowed analysis of population-level data.

The St John Ambulance attended 15,671 asthma cases throughout the study, and despite an encouraging decrease in the proportion of asthma cases over time, the proportion of respiratory cases has risen over the same period of time. However, despite these changes, the proportion of ambulance-transported asthma cases compared to all asthma cases admitted to hospital remained the same throughout the study, with mean length of hospital stay varying little over time. Ambulance paramedics correctly diagnosed asthma patients approximately 70% of the time, although the positive predictive value for the ambulance problem code of asthma was only 57%. Age standardised asthma rates highlighted a significantly widening differential between females and males over time, with more than half of attendances being female. The number of asthma cases overall varied with age, with the greatest proportion of cases in the elderly group, and the highest age standardised rate for asthma attendance in the 85+ years group, exceeding the rate of the youngest group six-fold. The elderly age group should be an area of much increased focus for health planning and strategy.

Temporal trends showed clear patterns where ambulance attendances peaked in mid-mornings, late evenings, Mondays and the winter months. However, on modelling, these proved to not have a significant association with the outcomes of survival and readmission. Modelling did identify several factors found to be associated with survival, these being: age, comorbidity, cumulative length of stay and total number of ventilations for any reason. Factors found to be associated with readmission were being female, ventilation for asthma and problem urgency.

Whilst nothing can be done to alter the age of a person, this study confirms the gender differential in asthma admissions that has been reported widely, where female cases of asthma exceed those of males. This highlights the fact that there is still much to learn

about the pathophysiology of asthma, and contributes a little more evidence to the hypothesis that there may be a different aetiology or expression of the disease in females.

The other factors identified, comorbidity, cumulative length of stay and ventilation status could all be considered indicators of the burden and severity of disease in the community. Health planning and policy decisions that seek to improve outcomes of patients with asthma would need to target areas that reduce or ameliorate conditions contributing to increased comorbid conditions and the length and frequency of hospital admissions. Mechanical ventilation, whether invasive or non-invasive, represents a severe, life-threatening event where a patient has inadequate ventilation and decreased oxygenation. Monitoring trends in the use of these procedures provides insight into the epidemiology of severe, life-threatening asthma. It is likely that episodes of mechanical ventilation indicate either more severe disease, or delayed and/or ineffective treatment for exacerbations of asthma. Regardless, the solution to reducing the incidence of ventilation resides in a better understanding of the factors contributing to the severity of asthma, so that patients who may be at greater risk can be pinpointed with appropriate preventative strategies.

Although it has not been a focus of this study, described in the literature of this thesis are many strategies that have potential to reduce the number and severity of exacerbations of asthma, reduce the incidence of admissions and readmissions, and improve the quality of life for asthma sufferers. These may be as simple as avoiding triggers, stopping smoking and taking medication appropriately. Other strategies shown to work take the form of written asthma management plans, education programs on discharge, and follow-up visits either at home, general practitioner or physician, asthma clinics or hospitals. However, it would appear that in the absence of a cure, and despite the presence of known strategies that have been shown to alleviate suffering and improve quality of life, the challenge remains to find better ways to encourage the asthmatic that, according to evidence widely published, seems reluctant to embrace these strategies.

Paradoxically, the more this thesis has explored the role of the ambulance paramedic in the prehospital treatment of asthma patients, the less it appears that opportunity exists

for the ambulance paramedic to influence patient health outcomes in a meaningful way, within the current paradigm of prehospital care. This by no means discounts the valuable extent to which ambulance services contribute to the continuum of care, for they perform essential duties concerned with the management of acute asthma episodes, such as the initiation of emergency treatments and immediate evacuation to hospital, all of which contribute to improving short-term health outcomes. Further, in the scenario of acute severe asthma, timely and appropriate treatment of a patient with asthma by ambulance paramedics can be life-saving.

However, whilst prehospital care by the ambulance paramedic is predominantly focussed on managing the acute episode, it has little to offer in terms of ongoing and long-term clinical management. The current model of 'scoop, run, treat and release' by emergency medical systems in Western Australia is inadequate to address the challenges presented by a complex, incurable, prevalent disease such as asthma. A paradigm shift to proactive and preventive management of asthma would require the increased engagement of patients in self-management, primary care providers to be more interested in existing and new programs, a broadened role in the community for ambulance services, a greater resolve by hospitals to educate and follow up asthma patients in order to reduce relapse and readmission, and the political will by government to support an environment in which it could happen.

In summary, this is the first study in Australia to describe the epidemiology and outcome of ambulance transported patients with asthma in a population-based cohort using linked data. The linking of complete population datasets using probabilistic record linking has afforded a unique insight into the continuum of care for the asthma patient. The recording of comorbid conditions and geo-coded demographic data allowed the creation of comorbidity and socioeconomic indices that have been used to model determinants of outcomes, including readmission and short, medium and long term survival.

Modelling found patients with asthma using an ambulance were more likely to be female, require admission and ventilation, originate from areas of lower socioeconomic status and are more likely to survive. The observed trends appear to be consistent over time. Findings from this study were found to be consistent with results previously

published in the literature. The future addition of emergency department and selected clinical data to the existing stable of linked datasets will eventually provide an exciting and uniquely rich and diverse foundation for future research efforts.

In some respects, this thesis has raised more questions than it has answered, but whilst highlighting limitations with respect to study design and analysis, and issues of comparability between other study designs and populations, it also confirms the enormous potential that linked data analysis at the population level has in epidemiological research. The process described in this thesis has provided a much clearer understanding of the epidemiology of patients with asthma who have been transported by ambulance paramedics in Perth, Western Australia.

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7.0 APPENDICES

Appendix 1: Clinical Measures and Outcomes, Drug Therapies – Summary of the Literature

Author	Date of Review	Topic	Identified Studies	Included Studies	Outcome Indicators	Results Reported As	Results
Edmonds, M.L. Camargo, C.A. et. al.	27 May 2003	Early use inhaled corticosteroids in the emergency department treatment of acute asthma.		6 (352 cases)	Admission rates, PEFR, FEV1	OR, WMD 95% CI	Inhaled steroids reduced admission rates in patients with acute asthma, but it is unclear if there is a benefit of ICS when used in addition to systemic steroids. Insufficient evidence that ICS therapy changes pulmonary function in acute asthma.
Rowe, B.H. Spooner, C.H et. al.	22 Jan 2001	Early emergency department treatment of acute asthma with systemic corticosteroids.		12 (863 cases)	Admission rates	OR 95% CI	Use of systemic corticosteroids within 1 hour of presentation to an ED significantly reduces the need for hospital admission in patients with acute asthma. Benefits are greatest in patients with more severe asthma and those not currently receiving steroids.
Cates, C.J. Rowe, B.H., et. al.	4 Jan 2006	Holding chambers versus nebulisers for beta-agonist treatment of acute asthma.		22 (1520 cases)	Adm. rates, LOS, PEFR, FEV1, Pulse	RR, WMD 95% CI	Metered-dose inhalers with holding chambers produced outcomes that were at least equivalent to nebuliser delivery. Holding chambers may have some advantages compared to nebulisers for children with acute asthma.
Ni, Chroinin M Greenstone, IR Ducharme, FM	18 Oct 2004	Addition of inhaled long-acting beta2-agonists to inhaled steroids as first line therapy for persistent asthma in steroid-naive adults	18	9	FEV1, Exacerbation rates	WMD, RR 95% CI	There is insufficient evidence at present to recommend use of combination therapy rather than inhaled corticosteroids alone as a first-line treatment.
Parameswaran, K. Belda, J., et. al.	19 June 2000	Addition of intravenous aminophylline to beta2-agonists in adults with Asthma	210	27	PEFR, FEV1	WMD, OR 95% CI	No significant effect of aminophylline on airflow outcomes at any time period.
Ducharme, F. Hicks, G., et. al.	14 Jan 2003	Addition of anti-leukotriene agents to inhaled corticosteroids for chronic asthma.	438	13	PEF	WMD, RR 95% CI	Insufficient evidence to support anti-leukotriene agents as add-on therapy, but modest glucocortocoid sparing effect.
Abramson, M.J. Puy, R.M., et. al.	19 Aug 2003	Allergen immunotherapy for asthma.		75	Asthma sympt. & medications	SMD, RR	Immunotherapy reduces asthma symptoms and use of asthma medications and improves bronchial hyper-reactivity.
Ducharme, F. Di Salvio, F	26 Jan 2004	Anti-leukotriene agents compared to inhaled corticosteroids in the management of recurrent and/or chronic asthma in adults and children		27	Exacerbation & withdrawal rates, lung funct., adverse effects	FEV1, RR 95% CI	For most asthma outcomes, ICS at 400mcg/day are more effective than anti-leukotriene agents given in the usual metered doses. Exact dose of equivalence of anti-leukotriene agents is undetermined. Inhaled glucocorticoids should remain the first line monotherapy for persistent asthma
McDonald NJ Bara AI McKean M.	20 Jan 2003	Anticholinergic therapy for chronic asthma in children over two years of age		8	PEFR, FEV1	OR 95% CI	Not enough evidence on the effects of anticholinergic drugs for chronic asthma in children over two years of age.
Dean T, Dewey A, Bara A,	20 Oct 2003	Azathioprine as an oral corticosteroid sparing agent for asthma		2 (23 cases)	FEV_1, FVC, PaO_2 and symptoms.	OR 95% CI	There is a clear lack of evidence to support the use of azathioprine in the treatment of chronic asthma as a steroid sparing-agent. Large, long-term studies with pre-defined steroid reducing protocols are required before recommendations for clinical practice can be made.
Sharek, P.J. Bergman, D.A. Ducharme, F.	26 Juky 1999	Beclomethasone for asthma in children: effects on linear growth.	159	3	Linear growth	MA cm/year 95% CI	Significant decrease in linear growth occurred in childrem treated with beclomethasone compared to placebo or non-steroidal therapy.
Adams, N. Bestall, J., et. al.	10 July 2001	Budesonide for chronic asthma in children and adults.		43 (2801 cases)	FEV1, PEF	WMD, RR	Budesonide use strongly supported in chronic asthma.

Continued overleaf.....

Plotnick, L.H. Ducharme, F.M.	24 July 2000	Combined inhaled anticholinergics and beta2-agonists for initial treatment of acute asthma in children.	40	13	Hospital Admission FEV1	RR, SMD	Single dose not effective, but multiple doses safe, improves lung function, reduces hospital admissions.
Manser, R. Reid, D. Abramson, M	22 Jan 2001	Corticosteroids for severe acute asthma in hospitalized patients.		9 (344 cases)	FEV1, Low/Med/High dose groups	MA (6 trial) WMD 95% CI	No clinical or statistically significant differences detected in comparison groups.
Smith, M. Iqbal, S., et al.	15 Dec 2002	Corticosteroids for hospitalised children with acute asthma.		7 (426 cases)	LOS, Relapse, Symptoms, PEF, FEV1, O_2 given	OR, NNT 95% CI	Systemic corticosteroids produce some improvements for children admitted hospital with acute asthma.
Rowe, B.H. Spooner, C.H et. al.	22 Jan 2001	Corticosteroids for preventing relapse following acute exacerbations of asthma.	169	8	Relapse rates, beta-agonist use, lung funct.	OR, WMD 95% CI	A short course of corticosteroids following assessment for an acute exacerbation of asthma significantly reduces the number of relapses to additional care and decreases beta-agonist use without an apparent increase in side effects.
Adams, N. Bestall, J.M. Jones, P.W.	15 Nov 2001	Fluticasone versus beclomethasone or budesonide for chronic asthma.		43 (>10,000 cases)	FEV1, PEFR, Side effects.	WMD, OR 95% CI	Fluticasone given at half the daily dose of beclomethasone or budesonide leads to small improvements in measures of airway caliber, but it appears to have a higher risk of causing side-effects when given at the same daily dose.
Rodrigo, G. Rodrigo, C., et. al.	27 Nov 2002	Helium-oxygen mixture for nonintubated acute asthma patients.		6 (369 cases)	Spirometric PFT	WMD 95% CI	The existing evidence does not support the administration of helium-oxygen mixture to patients presenting to the ED with moderate to severe acute asthma.
Adams, N. Cates, C.J., et. al.	28 Feb 2002	Holding chambers versus nebulisers for inhaled steroids in chronic asthma.		2 (63 cases)	PEFR	T-test	Budesonide in high dose delivered by the particular nebuliser used in the only double-blinded study included was more effective than that delivered by spacer.
Adams, N. Bestall, J., et. al.	25 Oct 1999	Inhaled beclomethasone at different doses for chronic asthma.		11 (1614 cases)	PEFR, FEV1	WMD 95% CI	Beclomethasone appears to demonstrate a shallow dose response effect in long-term asthma for a small number of efficacy outcomes over a range of daily doses.
Adams, N. Bestall, J., et. al.	24 Jan 2000	Inhaled beclomethasone versus budesonide for chronic asthma.		24 (1174 cases)	FEV1,PEFR Meta-analysis	WMD 95% CI	Limited randomized controlled trial data prevents comparison of relative efficacies of Beclomethasone and Budesonide. Results confounded by different delivery use.
Adams, N. Bestall, J., et. al.	24 Jan 2005	Inhaled beclomethasone versus placebo for chronic asthma.		60 (6542 cases)	FEV1, PEFR Beta2-agonists	WMD, RR 95% CI	This review has quantified the efficacy of CFC-BDP and HFA-BDP in the treatment of chronic asthma and strongly supports its use. There are insufficient data to draw any conclusions concerning dose-response in people with severe asthma.
Jones, A. Peters, J., et. al.	13 Aug 2001	Inhaled beta-agonists for asthma in mechanically ventilated patients.	152	4, None met study criteria			There are no data from RCT's to provide evidence for or against current practices regarding the use of inhaled beta2-agoists in intubated, ventilated asthma patients.
Adams, N. Bestall, J., et. al.	10 Nov 2001	Inhaled budesonide at different doses for chronic asthma.		24 (3907 cases)	FEV1, PEFR Symptoms	RR 95% CI	Budesonide has significant dose/response effects between low & high doses for improved FEV1 in severe asthma, and reduces exacerbations in mod/severe asthma.
Adams, N. Bestall, J., et. al.	25 Jan 2005	Inhaled fluticasone at different doses for chronic asthma.		45 (8193 cases)	PEFR	WMD, OR 95% CI	Effects are dose dependent but relatively small. At dose ratios of 1:2, there are significant differences in favour of the higher dose in morning peak flow across the low dose range.
Adams, N. Bestall, J., et. al	22 May 2001	Inhaled fluticasone proprionate for chronic asthma.		28 (5788 cases)	FEV1, PEFR	WMD, SMD, OR	Doses in the range 100-1000mcg/day are effective. Slight dose-response effect over low to high doses. High doses FP has oral-corticosteroid reducing properties.
Adams NP Bestall JC, et al	20 Apr 2005	Inhaled fluticasone versus placebo for chronic asthma in adults and children.		68 (11104 cases)	FEV1, PEFR, S&S, Beta2-agonists	OR 95% CI	Doses of FP in the range 100-1000 mcg/d are effective. In most patients with mild-moderate asthma improvements with low dose FP are only a little less than those associated with high doseswhen compared with placebo.
Blitz M, Blitz S, et aL	20 July 2005	Inhaled magnesium sulfate in the treatment of acute asthma.		6 (296 cases)	FEV1, PEFR	SMD, RR	Nebulised inhaled magnesium sulfate in addition to β_2-agonist in the treatment of an acute asthma exacerbation, appears to have benefits with respect to improved pulmonary function and is significantly greater in more severe asthma exacerbations.

Continued overleaf.....

Walters, E.H.	17 Dec	Inhaled short acting beta2-agonist use in chronic	800	49	Airway calibre,	FEV1, PEFR	No clinically or statistically significant differences were found in airway calibre

Walters, J.	2002	asthma: regular versus as needed treatment.			rescue meds., asthma sympt.	Puffs/24hrs	measurements. Regular treatment groups required less rescue medication, and had fewer days with asthma symptoms.
Wouden JC, Tasche MJA, et al	21 Jult 2003	Inhaled sodium cromoglycate for asthma in children.		24 (1074 cases)		95% CI	The evidence of the efficacy of sodium cromoglycate over placebo is not proven. Publication bias is likely to have overestimated the beneficial effects of sodium cromoglycate as maintenance therapy in childhood asthma.
Edmonds, M.L. Camargo, C.A. et. al.	16 Apr 2002	Inhaled steroids for acute asthma following emergency department discharge.		10 (909 cases)	Relapse Secondary outcomes.	OR 95% CI	Insufficient evidence that ICS therapy provides additional benefit when used in combination with standard CS therapy upon discharge from ED for acute asthma. Some evidence that high dose ICS alone may be as effective as CS in mild asthma.
Mash, B. Bheekie, A., et. al.	30 May 2002	Inhaled versus oral steroids for adults with chronic asthma.	1285	10			Comment: A daily dose of prednisolone 7.5/10 mg/day appears to be equivalent to moderate-high dose inhaled corticosteroids, with the lowest effective dose given.
Mitra, A. Bassler, D. Ducharme, F.M.	8 Jan 2002	Intravenous aminophylline for acute severe asthma in children over 2 years using inhaled bronchodilators.		35	FEV1 Symptom score LOS, Nebuliser	WMD, RR 95% CI	Addition of intravenous aminophylline should be considered in the treatment of children hospitalised with acute severe asthma with sub-optimal response to initial inhaled bronchodilator therapy. No reduction in LOS or nebulisers was seen.
Travers, A. Jones, A.P., et. al.	22 Jan 2001	Intravenous beta2-agonists for acute asthma in the emergency department.	746	15 (584 cases)	PEFR, Pulse Side Effects	OR, BPM 95% CI	There is no evidence to support the use of IV beta2-agonists in patients with severe acute asthma. These drugs should be given by inhalation.
EH Walters, Walters JAE, Gibson MDP	21 July 2003	Long-acting beta agonists for stable chronic asthma		85	PEFR	WMD 95% CI	Regular use of long acting beta-2 agonist bronchodilator agents in chronic asthma combined with regular preventer medication gives effective asthma control in adults and adolescents
Ram FSF, Cates CJ, Ducharme FM	24 Jan 2005	Long-acting beta2-agonists versus anti-leukotrienes as add-on therapy to inhaled corticosteroids for chronic asthma.	12	8 (5,895 cases)	PEFR, FEV1	WMD, RR 95% CI	In asthmatic adults inadequately controlled on low doses of inhaled steroids, the addition of LABA is superior to LTRA for preventing exacerbations requiring systemic steroids, and for improving lung function, symptoms, and use of rescue beta-2-agonists.
Wilson, A.J. Gibson, P.G. Coughlan, J.	17 Aug 1999	Long acting bet-agonists versus theophylline for maintenance treatment of asthma.		6	FEV1 Adverse events CNS events	RR 95% CI	Salmeterol may be more effective than theophylline in reducing asthma symptoms including night waking and improving lung function. More adverse events occurred in subjects using theophylline when compared to salmeterol.
Richeldi, L. Ferrara, G., et. al.	30 Aug 2001	Macrolides for chronic asthma.	95	5 (357 cases)	Symptoms Eosinophilic markers	SMD WMD 95% CI	Considering the small number of patients studied, there is insufficient evidence to support or refute the use of macrolides in patients with chronic asthma. Further studies are needed to clarify the role of macrolides in subgroups of asthmatics.
Rowe, B.H. Bretzlaff, J.A. et. al.	22 Oct 1999	Magnesium sulfate for treating exacerbations of acute asthma in the emergency department/		7 (665 cases)	PEFR, FEV1 Adm. Rate	WMD OR 95% CI	Current evidence does not support routine use of intravenous magnesium sulfate in all patients with acute asthma presenting to the emergency department. Magnesium sulfate appears to be safe and beneficial in severe acute asthma.
Kelly, K. Spooner, C.H. Rowe, B.H.	11 Dec 2002	Nedocromil sodium (NCS) versus sodium cromoglycate (SCG) for preventing exercise-induced bronchoconstriction (EIB) in asthmatics.	92	8 (117 Cases)	FEV1, Taste Sore Throat	WMD OR 95% CI	No significant differences were evident between the effect of NCS and SCG during the immediate post-exercise period in adults and children with EIB with regards to pulmonary function – specifically maximum percent decrease in FEV1, complete protection, clinical protection, or side effects.
Hayashi, K. Yanagi, M., et. al.	20 Jan 2003	Oxatomide for stable asthma in adults and children.		6	PEFR, FEV1 FVC	OR 95% CI	There is no evidence to show that oxatomide has a significant effect on the control of stable asthma. Improvement in some lung function outcomes were reported.
Ram, F.S.F. Brocklebank, D.M.	30 Nov 2001	Pressurised metered dose inhalers versus all other hand-held inhaler devices to deliver beta2-agonist bronchodilators for non-acute asthma.		84	Dichotomous outcomes.	RR, OR 95% CI	In patients with stable asthma, short-acting beta2-bronchodilators in standard CFC-pMDI's are as effective as any other devices. The effect of HFA-pDMI's on requirement for oral corticosteroid courses to treat acute exacerbations should be confirmed. Effectiveness studies that use an intention-to-treat analysis are required.

Continued overleaf.....

Walters, E.H.	22 July	Regular treatment with long acting beta agonists		31	PEFR	WMD, RR	Long acting inhaled beta agonists have advantages across a wide range of

Walters, J.A.E. Gibson, P.W.	2002	versus daily regular acting agonists in adults and children with stable asthma.			Rescue meds.	95% CI	physiological and clinical outcomes.
Evans, D.J. Cullinan, P. et. al.	1 Feb 2002	Cyclosporin as an oral corticosteroids sparing agent in stable asthma.		3	Steroid dose reduction.	SMD 95% CI	The changes with cyclosporin are small and of questionable clinical significance. Given the side effects of cyclosporin, the evidence available does not recommend use of this drug in the treatment of oral corticosteroids dependent asthma.
Dewey, A. Bara, A., et. al.	20 Jan 2003	Dapsone as an oral corticosteroid sparing agent for asthma.		None			No randomized controlled trials have been published, so there is no reliable evidence to show whether dapsone is beneficial or otherwise.
Evans, D.J. Cullinan, P. et. al.	1 Feb 2002	Gold an oral corticosteroid sparing agent in stable asthma.		3 (376 cases)	Steroid dose Proteinuria Dermatitis/Ecz.	OR 95% CI	The changes seen in the reviewed trials are small and probably of limited clinical significance. Given the side effects of gold and necessity for monitoring, the use of gold as a steroid sparing agent in asthma cannot be recommended.
Davies, H. Olson, L. Gibson, P.	7 Dec 2001	Methotrexate as a steroid sparing agent for asthma in adults.		10 (185 cases)	Steroid dose FEV1 Hepatotoxicity	WMD, OR 95% CI	Methotrexate may have a small sparing effect in adults with asthma who are dependent on oral corticosteroids. However, overall reduction is probably not large enough to reduce steroid-induced adverse effects.
Evans, D.J. Cullinan, P. et. al.	22 Oct 2002	Troleandomycin as an oral corticosteroids sparing agent in stable asthma		3 (112 cases)	Steroid dose Lung function	SMD 95% CI	There is insufficient evidence to support the use of troleandomycin in the treatment of steroid dependent asthma.

PEFR	Peak Expiratory Flow Rate
FEV1	Forced Expiratory Volume (1 second)
WMD	Weighted Mean Difference
OR	Odds Ratio
RR	Risk Ratio
95% CI	95% Confidence Interval
ICS	Inhaled Corticosteroids
MA	Meta-Analysis
LOS	Length of Stay
RCT	Randomised Controlled Trial
SMD	Standardised Mean Difference
BPM	Beats Per Minute
CNS	Central Nervous System
FVC	Forced Vital Capacity
S&S	Signs and Symptoms

Appendix 2: Clinical Measures and Outcomes, Lifestyle Changes, Environmental Changes, and Alternative Therapies – Summary of the Literature

Author	Date of Review	Topic	Identified Studies	Included Studies	Outcome Indicators	Results Reported As	Results
McCarney, RW Brinkhaus, B Lasserson. TJ	21 Jul 2003	Acupuncture for chronic asthma.		11 (324 cases)	FEV1, PEFR	SMD 95% CI	There is not enough evidence to make recommendations about the value of acupuncture in asthma treatment. Further research needs to consider the complexities and different types of acupuncture.
Holloway, E. Ram, F.S.F.	26 Jan 2004	Breathing exercises for asthma.	42	5	PEFR Med. use		No reliable conclusions can be drawn concerning the use of breathing exercises for asthma in clinical practice.
Bara, A.I. Barley, E.A.	18 June 2001	Caffeine for asthma.		6 (55 cases)	FEV1 Mid Expiratory	SMD 95% CI	Caffeine appears to improve airways function modestly in people with asthma for up to four hours. People may need to avoid caffeine for at least four hours prior to lung function testing.
Woods, R.K. Thien, F.C.K. Abramson, M.J.	11 Feb 2002	Dietary marine fatty acids (fish oil) for asthma on adults and children.		9	FEV1, PEFR S&S, Meds, Admissions		There is little evidence to recommend that people with asthma supplement or modify their dietary intake of marine n-3 fatty acids (fish oil) in order to improve their asthma control. Equally, there is no evidence that they are at risk if they do.
Ardern, K.D. Ram, F.S.F	19 Feb 2004	Dietary salt reduction or exclusion for allergic asthma.	56	6	FEV1, PEFR Med use	WMD 95% CI	Based on currently available evidence it is not possible to conclude whether dietary salt reduction has any place in the treatment or management of asthma.
Panton, J. Barley, E.A.	23 Feb 2005	Family therapy for asthma in children.		2 (55 cases)	FEV1, PEFR Med. use		There is some indication that family therapy may be a useful adjunct to medication for children with asthma, but more research is needed.
Campbell, F. Jones, K. Gibson, P.	23 June 2000	Feather versus non-feather bedding for asthma.	126	None			Whilst recent epidemiological studies suggest that feather bedding is associated with less frequent wheeze than man-made fibre fillings, the evidence currently available is insufficient to assess the clinical benefits of feather bedding in asthma.
Gibson, P.G. Henry, R.L. Coughlan, J.L.	12 Sep 2002	Gastro-oesophageal reflux treatment for asthma in adults and children.		12	Lung function S&S, Med use Nocturnal		In asthmatic subjects with gastro-oesophageal reflux, there was no overall improvement in asthma following treatment for gastro-oesophageal reflux. Subgroups of patients may gain benefit, but it is difficult to predict responders.
McCarney RW, Linde K, Lasserson TJ	23 Sep 2003	Homeopathy for chronic asthma.		6 (556 cases)	Symp. severity Lung function		There is not enough evidence to reliably assess the possible role of homeopathy in asthma. As well as randomised trials there is need for observational data to document different methods of homeopathic prescribing and how patients respond.
Gotzsche, P.C. Johansen, H.K. et. al.	3 Aug 2004	House dust mite control measures for asthma.		49 (2733 cases)	Symptom score Med. use PEFR	RR, SMD 95% CI	Chemical and physical methods aimed at reducing exposure to house dust mite allergens cannot be recommended. It is doubtful whether further studies, similar to the ones in our meta-analysis, are worthwhile.
Singh, M. Bara, A. Gibson, P.	28 Sep 2001	Humidity control for chronic asthma.		1	Clinical benefits	Dust mite and Antigen levels	There is a need for studying the health benefits of dehumidification by a double blind randomised controlled trial with adequate sample size measuring clinical outcomes in patients of asthma.
Ram, FSF Wellington, SR Barnes, NC	21 July 2003	Inspiratory muscle training for asthma		5 (76 cases)	PI (max)	WMD 95% CI	Currently there is insufficient evidence to suggest that inspiratory muscle training provides any clinical benefit to patients with asthma.
Hondras, M.A. Linde, K. Jones, A.P.	20 April 2005	Manual therapy for asthma.	473	3 (156 cases)	Lung function		There is not enough evidence to draw a conclusion about the effects of manual therapy by physiotherapists and chiropractors for adults or children with asthma.

Continued overleaf.....

Ram, FSF	20 July	Non-invasive positive pressure ventilation for	11	1	FEV_1, FVC, PEFR		The application of NPPV in patients suffering from status asthmaticus, despite some

Wellington, SR et al	2005	treatment of respiratory failure due to severe acute exacerbations of asthma.		(30 cases)	and respiratory rate		interesting and very promising preliminary results, still remains controversial. Large, prospective, randomised controlled trials are therefore needed to determine the role of NPPV in status asthmaticus.
Ram, F.S.F. Robinson, S.M. Black, P.N.	27 Dec 1999	Physical training for asthma.		8	Lung function Nunber of days wheeze	O2 uptake 95% CI	In people with asthma, physical training can improve cardiopulmonary fitness without changing lung function. It is not known whether improved fitness is translated into improved quality of life.
Sheikh, A. Alves, B. Dhami, S.	6 Apr 2001	Pneumococcal vaccine for asthma.	3	1 (30 cases)	Asthma episodes	per child per year	This review found very limited evidence to support the routine use of pneumococcal vaccine in people with asthma. A randomised trial of vaccine efficacy in children and adults with asthma is needed.
Kilburn, S. Lasserson, T.J. McKean, M.	22 Jan 2001	Pet allergen control measures for allergic asthma in children and adults.	34	2 (57 cases)	Various		The available trials were too small to provide evidence for or against the use of air filtration units to reduce allergen levels in the management of pet-allergic asthma. There are no trials of allergen reducing measures, such as pet washing or removal.
Beamon, S. Falkenbach, A. et. al.	9 Jan 2001	Speleotherapy for asthma.		3 (124 cases)	Lung function		The available evidence does not permit a reliable conclusion as to whether speleo-therapeutic interventions are effective for the treatment of chronic asthma. Randomised controlled trials with long-term follow-up are necessary.
Ardern, K.D/ Ram, F.S.F.	31 May 2001	Tartrazine exclusion for allergic asthma.	18	6	Various		Due to the paucity of available evidence, it is not possible to provide firm conclusions as to the effects of tartrazine on asthma control.
Ram, F.S.F. Rowe, B.H. Kaur, B.	1 Apr 2004	Vitamin C supplement for asthma.	71	16			At present, evidence from randomised controlled trials is insufficient to recommend a specific role for vitamin C in the treatment of asthma. A methodologically strong and large-scale RCT is warranted to address the effectiveness of vitamin C.
Cates, C.J. Jefferson, T.O. et. al.	26 Aug 1999	Vaccines for preventing influenza on people with asthma.		9	Influenza Incidence	Risk difference 95% CI	There is not enough evidence to assess the benefits and risks of influenza vaccination for people with asthma.

Appendix 3: National Health Priority Area asthma indicators proposed by Australian Centre for Asthma Monitoring, 2003

Asthma Indicator
HEALTH STATUS AND OUTCOMES **Prevalence of asthma** Prevalence of ever having doctor diagnosed asthma Prevalence of current asthma Prevalence of recent wheeze Prevalence of airway hyper-responsiveness **Human function and wellbeing** Impact of asthma on quality of life Index of asthma control **Deaths** Death rate for asthma, ages 5–34 years Death rate for asthma, all ages
DETERMINANTS OF HEALTH **Environmental factors** Prevalence of smoking in the household where children with asthma reside Prevalence of occupational asthma **Health behaviours** Prevalence of smoking in people with asthma **Community capacity** Proportion of schools using the Asthma Friendly Schools Program
HEALTH SYSTEM PERFORMANCE Rate of hospital separations for asthma Number of individuals with separations for asthma per 1,000 resident population per year Hospital re-admissions for asthma Hospital patient days for asthma Rate of ED attendance for asthma Rate of asthma-related general practice encounters Rate of Asthma 3+ Visit Plan payments Rate of healthcare visits for acute asthma exacerbations Proportion of people with asthma with an asthma action plan Proportion of people with asthma who use preventers regularly Proportion of people with asthma who have had recent spirometry Costs of asthma

Source:

Review of proposed National Health Priority Area asthma indicators and data sources.

February 2004. Australian Centre for Asthma Monitoring, Woolcock Institute of Medical Research

Appendix 4: St John Ambulance (Western Australia) Patient Care Record

SJA PCR here……

Appendix 5: SJA (WA) Problem Codes

SJA (WA) PROBLEM CODES		
PRE 1994	**FROM 18/09/1994**	**FROM 01/05/1999**
TRAUMA	**01 Trauma**	**01 Trauma**
01 Domestic Accident	011 Domestic	011 Domestic
02 Vehicle Accident	012 MVA	012 MVA
03 Sporting Accident	013 Sporting/Recreational	013 Sporting/Recreational
04 Industrial Accident	014 Industrial	014 Industrial
05 Assault	015 Assault	015 Assault
06 Burns Patient	016 Hanging	016 Hanging
07 Collapse	017 Murder	017 Sexual Assault
08 Hanging	018 Suicide	018 Shooting
09 Murder/Suicide	019 Rape	019 Stabbing
10 Rape	020 Shooting	020 Other
11 Shooting	021 Stabbing	
12 Stabbing	022 Other	
13 Other Accident		
SURGICAL	**20 Abdominal**	**20 Abdominal**
14 Abdominal (Acute)	201 Pain	201 Pain
15 GIT Bleed (Known)	202 Haematemesis	202 Haematemesis
16 Gynaecological	203 Melaena	203 Melaena
17 Obstetrical	204 Acute Abdomen	204 Aneurysm
18 Baby Born	205 Aneurysm	205 GIT bleed
19 Other	206 GIT bleed	
CARDIAC	**21 Obstetric/Gynae.**	**21 Obstetric/Gynae.**
21 Arrest	211 Vaginal bleed	211 Vaginal bleed
22 Chest Pain	212 Pre-Eclampsia	212 Pre-Eclampsia
23 Electrocution	213 Ectopic pregnancy	213 Ectopic pregnancy
324 Near Drowning	214 Miscarriage	214 Miscarriage
25 Pulmonary Oedema/CCF	215 Normal labour	215 Normal labour
26 Other	216 Comp. Labour	216 Comp. Labour
	217 Baby bom	217 Baby bom
MEDICAL	218 Neonatal resus.	218 Neonatal resus.
31 Allergy	219 Other	219 Other
32 Asthma		
33 Bites & Stings	**22 Allergy**	**22 Allergy**
34 CVA	221 Anaphylaxis	221 Anaphylaxis
35 Debility/Age	222 Localised	222 Localised
36 Dehydration		
37 Altered Consciousness	**24 Respiratory**	**24 Respiratory**
38 Diabetes/Endocrine	241 Asthma	241 Asthma
39 Disturbed/Abnormal Behav.	242 Pulmonary Oedema	242 Pulmonary Oed.
40 Drug Aoverdose (Inc Alcohol)	243 C.O.A.D.	243 C.O.A.D./C.O.P.D.
41Fits	244 Pneumothorax	244 Pneumothorax
42 Hypothermia	245 Resp.Trac.Inf.	245 Resp.Trac.Inf.
43 Infectious	246 Aspiration	246 Aspiration/Regurgitation
44 Neonatal	247 Obst.upper airway	247 Obst.upper airway
45 Poisoning	248 Resp. Arrest	248 Resp. Arrest
46 Respiratory Distress	249 Other	249 Other (inc.inhalation)
47 C.A.		
48 C.A Terminal	**25 Ear/Nose/Throat**	**25 Ear/Nose/Throat**
49 Other	250 E.N.T.	250 E.N.T.
ROUTINE	**26 Infectious**	**26 Infectious**
51 CAT Scan	261 Significant risk to ambulance personnel	261 Significant risk to AO
52 Cardiac Catheter	262 Septicaemia	262 Septicaemia
53 Day Treatment		263 Localised infection

Continued overleaf.....

SJA (WA) PROBLEM CODES

PRE 1994	FROM 18/09/1994	FROM 01/05/1999
54 Dialysis	263 Localised infection	
55 Hospital Discharge		
56 Radiotherapy	**27 Geriatric/Debility**	**27 Geriatric/Debility**
57 Sporting Fixtures Etc	271 Generalised debility	271 Generalised debility
58 Standing By	272 Transfer	272 Transfer
59 Other		
61 Hoax	**28 Illness**	**28 Illness**
62 Ambulance Not Required	281 Unknown	281 Unspecified
	282 Specified	(requires test expln.)
SUNDRIES	**29 Endocrine/Metabolic**	**29 Endocrine/Metabolic**
71 Bomb Alert	291 Ketoacidosis	291 Ketoacidosis
72 Disaster Exercise	292 Hypoglycaemia	292 Hypoglycaemia
73 Message		
74 Patient Deceased	**30 Musculo/Skeletal**	**30 Musculo/Skeletal**
75 PR Visit	301 Inflammatory/Pain	301 Inflammatory/Pain
76 Other	302 Quad/Para	302 Quad/Para
79 Arrival at Scene	303 Amputee	303 Amputee
80 Depart Scene for		
81 Destination	**31 Neurological**	**31 Neurological**
82 Cleared	311 Altered Consc	311 Altered Consc
83 At Sub Centre	312 C.V.A.	312 C.V.A.
	313 Headaches	313 Headaches
TRANSMISSION CODES	314 Convuls.Febrile	314 Convuls.Febrile
79 Arrived at the scene	315 Convuls.Epilep	315 Convuls.Epilep
80 Mobile	316 Status Epilep.	316 Status Epilep.
81 Arrived destination	317 Syncope	317 Syncope
82 Cleared	318 Unconscious - unknown	318 Unconscious
83 At station	319 Cerebral Bleed	(unknown cause)
84 Police		
85 Fuel	**32 Poisoning**	**32 Poisoning**
86 Fremantle station	321 Ingested	321 Ingested
87 Central station	322 Absorbed	322 Absorbed
88 Belmont HQ	323 Gaseous	323 Gaseous
89 Return to station		
90 Patient deceased	**33 Drug/Alcohol Induced**	**33 Drug/Alcohol Induced**
99 Meal break	331 Mental Illness	332 Overdose (int.s/harm)
	332 Self harm	333 Alcohol intoxication
	333 Intox/Substance abuse	334 Narcotic overdose
	334 Overdose	335 Other substance abuse
	34 Urology	**34 Urology**
	341 Haematuria	341 Haematuria
	342 Retention	342 Retention
	343 Renal Colic	343 Renal Colic
	344 Incontinence	344 Incontinence
		345 Renal Failure (Dialysis)
	35 Environmental	**35 Environmental**
	351 Hypothermia	351 Hypothermia
	352 Hyperthermia	352 Hyperthermia
	353 Barotrauma/Decompr.	353 Barotrauma/Decompr.
	354 Near drowning	354 Near drowning
	355 Electric shock	355 Electric shock
	356 Bums	356 Bums
	357 Bites and Stings	357 Bites and Stings
	36 Malignancy	**36 Malignancy**
	361 Malignancy	361 Malignancy

SJA (WA) PROBLEM CODES		
PRE 1994	**FROM 18/09/1994**	**FROM 01/05/1999**
	37 Psycho/social	**37 Psycho/social**
	371 Psychiatric illness 372 Forms 3 4 5 373 Social problems	371 Psychiatric illness 372 On forms 373 Social problems
	40 Unable	
	401 Unable to Code	
	41 Cardiac	**41 Cardiac**
	411 Chest pain 412 Angina 413 A.M.I 414 C.C.F. 415 Cardio Shock 416 Pacemaker fail 417 Cardiac Dysrythmia 418 Cardiac Arrest 419 Post Cardiac Arrest	411 Chest pain 412 Angina - diagnosed 413 A.M.I. - diagnosed 414 C.C.F. 415 Cardiac Shock 416 Pacemaker fail 417 Cardiac Dysrythmia 418 Cardiac Arrest 419 Post Cardiac Arrest 420 Cath Lab/Procedure
	44 Neo Natal	**44 Neo Natal**
	440 Neo Natal	440 Neo Natal
	50 PR visit	**50 PR visit**
	500 PR visit	500 PR visit
	59 Standby	**59 Standby**
	591 Wait for other ambulance 592 Sporting fixture 593 Dangerous Incident 594 Disaster Exercise	591 Wait for other ambulance 592 Sporting fixture 593 Dangerous Incident 594 Disaster Exercise

Source: Computer Systems Manager, St John Ambulance, Western Australia, 2003

Appendix 6: Charlson comorbidity categories, ICD9 & 10, diseases & procedures.

Diagnostic category	Weight	Dartmouth-Manitoba ICD-9-CM & ICD-10-AM codes
Myocardial Infarction	1	410.xx, 412, I21.x, I25.2
Congestive heart failure	1	402.01, 402.11, 402.91, 425.x, 428.x, 429.3, 404.01, 404.03, 404.11, 404.13, 404.91, 404.93, I11., I42., I50., I13., I11., I43., I11.0, I13.0, I13.2, I42.x, I43.x, I50.x, I51.7'
Peripheral vascular disease	1	440.x, 441.x, 442.x, 443.1-443.9, 447.1, 785.4, (38.13, 38.14, 38.16, 38.18, 38.33, 38.34, 38.36, 38.38, 38.43, 38.44, '38.46, 38.48, 39.22, 39.23, 39.24, 39.25, 39.26, 39.27, 39.28, 39.29), I70.x, I71, I71.x, I72, I72.x, I73.x, I77.1 (32700-02/03/04/07/08/09/10/11, 32708-00/01/02/03, 32712-00/01, 32715-00/01/02/03, 32718-00/01, 32721-00/01, 32724-00/01, 32730-00/01, 32733-00/01, 32739-00, 32742-00, 32745-00, 32748-00, 32751-00/01/02/03, 32754-00/01/02, 32757-00/01, 32763-00-32763-19, 32766-00, 33509-00, 33512-00, 33515-00, 33518-00, 33521-00, 33524-00, 33527-00, 33530-00/01, 33533-00, 33536-00, 33539-00, 33818-00-33818-10, 33821-00-33821-09, 33836-00-33836-03, 33839-00-33839-03, 35515-00, 90210-02, 90211-03-90211-05, 90212-00, 90212-06-90212-09, 90213-02/03, 90229-00, 90211-00/01/02, 90211-06, 90212-01-90212-05, 90212-10)
Cerebrovascular disease	1	362.34,430-436, 437-437.1, 437.9, 438,781 4, 784.3, 997.0, (38.12, 38.42), G45.x, H34.0, I60.x, I61.x, I62.x, I63.x, I64, I65.x, I66.x, G45., R47.0, (32700-00-32700-03, 32700-05-32700-09, 32703-00, 33500-00, 33800-00, 33830-00, 33830-01, 90213-03)
Dementia	1	290 x, 331-331.2, F00.x, F01.x, F02.0, F02.1, F02.3, F02.4, F02.8, F03, G30.x, G31.0, G31.1
Chronic pulmonary disease	1	415 0, 416.8-416.9, 491.x-494, 496, I26., I26.0, I27., I27.0, I27.8, I27.9, J41.x, J42, J43.x, J44.x, J45.x, J46, J47
Rheumatologic disease	1	710 x, 714.x, M05, M05.0x, M05.1x, M05.2x, M05.3x, M05.8x, M05.9x, M06, M06.0x, M06.1x, M06.2x, M06.4x, M06.8x, M06.9x, M08, M08.0x, M08.2x, M08.4x, M12.0x, M32.x, M33, M34.x, M35.x
Peptic ulcer disease	1	531 xx-534.xx, K25.x, K26.x, K27.x, K28.x
Mild liver disease	1	571 2, 571.5-571.6, 571.8-571.9, K70, K70.2, K70.3, K72, K72.1, K73, K73.0, K73.1, K73.8, K73.9, K74.x, 'K76, K76.0
Diabetes (mild to moderate)	1	250 Ox-250.3x, E10., E10.0x, E10.10, E10.11-E10.16, E10.9x, E10.65, E11.00-E11.02, E11.10-E11.16, E11.65, E11.9x, E12, E12.0, E12.1x, E12.9x, E13.00-E13.02, E13, E13.10-E13.16, E13.65, E13.9x, E14, E14.00, E14.01, E14.02, E14.10-E14.16, E14.9, E14.90, E14.91
Diabetes with chronic complications	2	250.4x-250.9x. E10.20-'E10.23, E10.29, E10.30-'E10.36, E10.39, E10.40-E10.43, E10.49, E10.50-E10.53, E10.59, E10.60-E10.64, E10.69, E10.70, E10.71, E10.73, E10.8, E11.20-E11.23, E11.29, E11.30-E11.36, E11.39, E11.40-E11.43, E11.49, E11.50-E11.53, E11.59, E11.60-E11.64, E11.69, E11.70-E11.73, E11.8, E11.8x, E12.2x, E12.3x, E12.4x, E12.5x, E12.6x, E12.7x, E12.8x, E13.20-E13.23, E13.29, E13.30-E13.36, E13.39, E13.40-E13.43, E13.49, E13.50-E13.53, E13.59, E13.60-E13.64, E13.69, E13.70-E13.73, E13.8, E13.81, E14.20-E14.23, E14.29, E14.30, E14.31-E14.36, E14.39, E14.40-E14.43, E14.49, E14.50-14.53, E14.59, E14.60-E14.64, E14.69, E14.70-E14.73, E14.8, E14.80, E14.81 Continued overleaf

Hemiplegia or paraplegia	2	342 x, 344.x, G81, G81.0, G81.1, G81.9, G82.x, 'G82.0x, G82.1x, G82.2x, G82.3x, G82.4x, G82.5x, G83.x, S14.7x
Renal Disease	2	585 586, V42.0, V45.1, V56.x, (39.27, 39.42, 39.93-39.95, 54.98), N18, N18.x, N19, Z49.1, Z49.2, Z94.0, Z99.2, (13100-00-13100-04, 3100-06-13100-08, 34500-00/01, 34509-00/01, 34512-00/01, 34518-00/01)
Any malignancy, including lymphoma and leukaemia	2	140.x- 171.x, 1 74.x- 1 95.x, 200.xx-208.x, 273 0, 273.3, V1O.46, 60.5(P), 62.4-62.41(P), C00., C00.x, C01., C02.x, C03., C03.x, C04., C04.x, C05., C05.x, C06., C06.x, C07., C08., C08.x, C09., C09.x, C10., C10.x, C11., C11.x, C12., C13., C13.x, C14., C14.x, C15., C15.x, C16., C16.x, C17., C17.x, C18., C18.x, C19., C20., C21., C21.x, C22., C22.x, C23., C24., C24.x, C25., C25.x, C26., C26.x, C30., C30.x, C30.1, C31., C31.x, C32., C32.x, C33., C34., C34.x, C37., C38., C38.x, C39., C39.x, C40., C40.x, C41., C41.0, C41.0x, C41.x, C43., C43.x, C44., C44.x, C45., C45.x, C46., C46.x, C47., C47.x, C48., C48.x, C49., C49.x, C50., C50.x, C51., C51.x, C52., C53., C53.x, C54., C54.x, C55., C56., C57., C57.x, C58., C60., C60.x, C61., C62., C62.x, C63., C63.x, C64., C65., C66., C67., C67.x, C68., C68.x, C69., C69.x, C70., C70.x, C71., C71.x, C72., C72.x, C73., C74., C74.0, C74.x, C75., C75.x, C76., C76.x, C81., C81.x, C82., C82.x, C83., C83.x, C84., C84.x, C85., C85.x, C88., C88.x, C90., C90.x, C91., C91.x, C92., C92.x, C93., C93.x, C94., C94.x, C95., C95.x, C96.0, C96.x, D89.0, (30641-01/03, 37209-00, 37210-00, 37211-00)
Moderate or severe liver disease	3	572.2-572.4, 456.0-456.2x, (39.1, 42.91), I85., I85.x, I98., I98.2, I98.x, K72, K72.x, K75.0, K75.1, K76.6, K76.7, K72., (30476-02, 30520-00, 30602-00, 30603-00, 30605-00, 90211-02, 90334-00)
Metastatic solid tumour	6	196.x-199.x, C77., C77.x, C78., C78.x, C79., C79.x, C80., C97
AIDS	6	042.x-044.x, B20, B20., B21, B21., B22, 'B22., B23, B23., B23.x, B24, B24.'

NB: Procedure codes are enclosed in parentheses.

Appendix 7: Poisson regression comparing the crude and age standardised rates (ASR) of ambulance transported asthma cases by quintile of SES, showing population and rate ratios(RR) for 5 and 10 year age groups.

Census Period	SES Quintile	Popn (N)	Crude Rate	Rate Ratio	95% CI	ASR	RR 5 yr	95% CI	RR 10 yr	95% CI
Home_poa (Postal area in which patient resides)										
1991	1 (High)	189,393	111.5	1.00		120.1	1.00		1.00	
	2	237,825	140.4	1.01	0.93-1.08	150.5	1.25	1.23-1.28	1.26	1.24-1.28
	3	268,858	270.9	1.71	1.61-1.82	293.4	2.44	2.41-2.48	2.45	2.41-2.48
	4	236,881	253.9	1.82	1.71-1.94	275.0	2.29	2.25-2.32	2.30	2.26-2.33
	5 (Low)	244,998	396.8	2.76	2.59-2.92	437.2	3.64	3.58-3.69	3.64	3.59-3.70
1996	1 (High)	255,617	129.8	1.00		137.5	1.00		1.00	
	2	252,992	169.6	1.30	1.22-1.38	179.4	1.30	1.28-1.32	1.31	1.29-1.33
	3	264,973	209.1	1.54	1.46-1.34	219.7	1.59	1.57-1.62	1.60	1.58-1.63
	4	263,287	254.1	1.89	1.79-2.01	268.5	1.95	1.92-1.98	1.96	1.93-1.99
	5 (Low)	261,761	349.4	2.61	2.48-2.76	371.5	2.70	2.66-2.74	2.70	2.67-2.74
2001	1 (High)	267,831	124.6	1.00		128.4	1.00		1.00	
	2	291,655	169.7	1.25	1.17-1.32	173.6	1.35	1.33-1.37	1.35	1.33-1.38
	3	278,834	184.5	1.42	1.34-1.51	189.7	1.48	1.45-1.50	1.48	1.45-1.50
	4	257,180	219.0	1.93	1.73-1.94	224.2	1.75	1.72-1.77	1.75	1.72-1.77
	5 (Low)	307,639	336.4	2.34	2.22-2.47	354.6	2.69	2.65-2.73	2.69	2.65-2.73
From_poa (Postal area where ambulance attended patient)										
1991	1 (High)	189,393	114.4	1.00		124.6	1.00		1.00	
	2	237,825	156.1	1.09	1.02-1.17	166.5	1.34	1.31-1.36	1.34	1.32-1.36
j	3	268,858	244.9	1.51	1.41-1.61	265.9	2.13	2.10-2.17	2.13	2.11-2.17
	4	236,881	263.3	1.84	1.73-1.96	284.4	2.28	2.25-2.32	2.29	2.26-2.33
	5 (Low)	244,998	433.0	2.94	2.77-3.11	473.0	3.80	3.74-3.85	3.81	3.75-3.86
1996	1 (High)	255,617	139.9	1.00		148.3	1.00		1.00	
	2	252,992	178.1	1.27	1.20-1.35	187.7	1.26	1.24-1.28	1.27	1.25-1.29
	3	264,973	203.2	1.39	1.31-1.48	213.4	1.44	1.41-1.46	1.45	1.42-1.47
	4	263,287	262.9	1.82	1.72-1.93	277.8	1.87	1.84-1.90	1.88	1.86-1.91
	5 (Low)	261,761	360.7	2.51	2.38-2.65	382.3	2.57	2.54-2.61	2.58	2.55-2.62
2001	1 (High)	267,831	137.2	1.00		141.1	1.00		1.00	
	2	291,655	170.7	1.14	1.08-2.21	174.6	1.24	1.22-1.26	1.24	1.22-1.26
	3	278,834	184.2	1.29	1.22-1.37	189.5	1.34	1.32-1.36	1.34	1.32-1.36
	4	257,180	216.9	1.65	1.56-1.74	221.8	1.57	1.55-1.59	1.57	1.55-1.60
	5 (Low)	307,639	353.5	2.25	2.13-2.36	362.9	2.57	2.53-2.60	2.57	2.53-2.60

Appendix 8: Poisson regression comparing the crude and age standardised rates of ambulance transported asthma cases by quintile of SES, postal area in which case resides and postal area where ambulance attended case.

Census Period	SES Quintile	Popn(N)	Crude Rate	Rate Ratio	95% CI	ASR (10yr)	Rate Ratio	95% CI
Home_poa (Postal Area in which case resides, Metropolitan Only)								
1991	1 (High SES)	189,393	111.5	1.00		120.1	1.00	
	2	237,825	140.4	1.01	(0.93-1.08)	150.5	1.26	(1.24-1.28)
	3	268,858	270.9	1.71	(1.61-1.82)	293.4	2.45	(2.41-2.48)
	4	236,881	253.9	1.82	(1.71-1.94)	275.0	2.30	(2.26-2.33)
	5 (Low SES)	244,998	396.8	2.76	(2.59-2.92)	437.2	3.64	(3.59-3.70)
1996	1 (High SES)	255,617	129.8	1.00		137.5	1.00	
	2	252,992	169.6	1.30	(1.22-1.38)	179.4	1.31	(1.29-1.33)
	3	264,973	209.1	1.54	(1.46-1.34)	219.7	1.60	(1.58-1.63)
	4	263,287	254.1	1.89	(1.79-2.01)	268.5	1.96	(1.93-1.99)
	5 (Low SES)	261,761	349.4	2.61	(2.48-2.76)	371.5	2.70	(2.67-2.74)
2001	1 (High SES)	267,831	124.6	1.00		128.4	1.00	
	2	291,655	169.7	1.25	(1.17-1.32)	173.6	1.35	(1.33-1.38)
	3	278,834	184.5	1.42	(1.34-1.51)	189.7	1.48	(1.45-1.50)
	4	257,180	219.0	1.93	(1.73-1.94)	224.2	1.75	(1.72-1.77)
	5 (Low SES)	307,639	336.4	2.34	(2.22-2.47)	354.6	2.69	(2.65-2.73)
From_poa (Postal area where ambulance attended case, Metropolitan Only)								
1991	1 (High SES)	189,393	114.4	1.00		124.6	1.00	
	2	237,825	156.1	1.09	(1.02-1.17)	166.5	1.34	(1.32-1.36)
	3	268,858	244.9	1.51	(1.41-1.61)	265.9	2.13	(2.11-2.17)
	4	236,881	263.3	1.84	(1.73-1.96)	284.4	2.29	(2.26-2.33)
	5 (Low SES)	244,998	433.0	2.94	(2.77-3.11)	473.0	3.81	(3.75-3.86)
1996	1 (High SES)	255,617	139.9	1.00		148.3	1.00	
	2	252,992	178.1	1.27	(1.20-1.35)	187.7	1.27	(1.25-1.29)
	3	264,973	203.2	1.39	(1.31-1.48)	213.4	1.45	(1.42-1.47)
	4	263,287	262.9	1.82	(1.72-1.93)	277.8	1.88	(1.86-1.91)
	5 (Low SES)	261,761	360.7	2.51	(2.38-2.65)	382.3	2.58	(2.55-2.62)
2001	1 (High SES)	267,831	137.2	1.00		141.1	1.00	
	2	291,655	170.7	1.14	(1.08-2.21)	174.6	1.24	(1.22-1.26)
	3	278,834	184.2	1.29	(1.22-1.37)	189.5	1.34	(1.32-1.36)
	4	257,180	216.9	1.65	(1.56-1.74)	221.8	1.57	(1.55-1.60)
	5 (Low SES)	307,639	353.5	2.25	(2.13-2.36)	362.9	2.57	(2.53-2.60)

Appendix 9: Table showing Goodness-of-Fit results, Constant-Only v's Full Model and Hosmer-Lemeshow Test.

		Constant-Only V's Full Model					Hosmer & Lemeshow Test		
Predictor	Outcome	Constant Only -2LL	Full Model -2LL	Chi Square	df	Sig (P)	Chi Square	df	Sig (P)
age, ch_last_index,	died_1	581.502	476.042	105.460	4	0.000	8.075	8	0.426
cumlos12,	died_30	427.674	350.794	76.880	4	0.000	3.016	8	0.933
tot_vent	died_1y	1392.484	1073.312	319.172	4	0.000	11.497	8	0.175
age, ch_last_index, ,	died_1	581.502	477.191	104.311	4	0.000	9.405	8	0.309
cumlos12,	died_30	427.674	349.907	77.767	4	0.000	4.539	8	0.806
totvent_ni_asthma	died_1y	1392.484	1072.994	319.490	4	0.000	11.330	8	0.184
age, ch_last_index,	died_1	581.502	480.872	100.630	4	0.000	5.863	8	0.663
cumlos12,	died_30	427.674	349.11	78.563	4	0.000	3.673	8	0.885
totvent_i_asthma	died_1y	1392.484	1072.859	319.625	4	0.000	10.780	8	0.214
age, ch_last_index,	died_1	581.502	480.42	101.082	4	0.000	5.485	8	0.705
cumlos12,	died_30	427.674	348.839	78.835	4	0.000	3.658	8	0.887
totvent_i_all	died_1y	1392.484	1073.208	319.276	4	0.000	14.431	8	0.071
age, ch_last_index,	died_1	581.502	475.541	105.961	4	0.000	10.741	8	0.217
cumlos12,	died_30	427.674	349.453	78.221	4	0.000	6.500	8	0.591
totvent_ni_all	died_1y	1392.484	1073.255	319.229	4	0.000	10.911	8	0.207
age, ch_last_index,	died_1	581.502	478.547	102.955	4	0.000	6.383	8	0.604
cumlos12,	died_30	427.674	350.786	76.887	4	0.000	4.120	8	0.846
totadm	died_1y	1392.484	1069.356	323.128	4	0.000	10.903	8	0.207

Appendix 10: No. of ambulance transported asthma cases, by year, percentage change over study period and age standardised rate by 5 year age groups.

Age Group (years)		0 to 4	5 to 9	10 to 14	15 to 19	20 to 24	25 to 29	30 to 34	35 to 39	40 to 44	45 to 49	50 to 54	55 to 59	60 to 64	65 to 69	70 to 74	75 to 79	80 to 84	85+	Total
Year	**1990**	70	86	49	83	94	37	67	36	58	70	29	51	69	94	80	85	61	35	**1154**
	1991	63	75	58	78	86	41	68	56	53	47	47	45	49	88	92	74	54	41	**1115**
	1992	65	67	78	114	88	58	71	45	34	40	46	50	56	93	92	80	67	38	**1182**
	1993	82	70	64	111	103	43	45	52	38	47	51	40	69	100	91	57	79	34	**1176**
	1994	101	78	66	127	94	63	46	62	43	40	75	56	73	88	98	76	66	48	**1300**
	1995	89	86	53	98	97	54	51	71	41	46	78	57	72	129	138	104	67	53	**1384**
	1996	93	80	50	87	89	71	58	64	55	43	88	66	74	122	174	109	70	76	**1469**
	1997	114	93	65	112	85	92	62	65	67	48	63	68	64	132	125	141	95	76	**1567**
	1998	97	80	72	82	68	62	46	41	51	55	72	75	78	110	141	121	93	80	**1424**
	1999	88	66	66	82	62	66	58	51	55	59	60	65	72	91	153	117	82	83	**1376**
	2000	80	73	44	64	46	69	41	52	51	44	64	68	61	90	115	98	63	89	**1212**
	2001	73	68	44	62	57	40	55	52	52	54	56	55	53	89	125	110	59	93	**1197**
Total		1015	922	709	1100	969	696	668	647	598	593	729	696	790	1226	1424	1172	856	746	**15556**
% Change		**4**	**-21**	**-10**	**-25**	**-39**	**8**	**-18**	**44**	**-10**	**-23**	**93**	**8**	**-23**	**-5**	**56**	**29**	**-3**	**166**	**4**
No of Cases (M)		661	568	365	342	255	228	210	185	157	169	202	265	305	541	625	531	308	254	**6171**
No of Cases (F)		354	354	344	758	714	468	458	462	441	424	527	431	485	685	799	641	548	491	**9384**
ASR (M)*		8.3	7.1	4.6	4.2	3.1	2.7	2.4	2.2	1.9	2.3	3.2	5.2	6.9	13.6	19.4	24.1	25	35.4	
ASR (F)*		4.7	4.6	4.5	9.9	8.8	5.5	5.3	5.4	5.4	5.8	8.7	8.8	10.9	16.3	21.2	21.4	26.8	29.1	

* Note: Age Standardisation Rate calculated by direct standardisation to 2001 Australian population.

Appendix 11: Univariate analysis of the relationship of each predictor variable with survival using logistic regression.

Survival	Death at Discharge			Death within 30 Days			Death within One Year		
Predictor	**P**	**Odds Ratio**	**95% CI**	**P**	**Odds Ratio**	**95% CI**	**P**	**Odds Ratio**	**95% CI**
age	**0.000**	**1.053**	**1.036-1.069**	**0.000**	**1.056**	**1.036-1.077**	**0.000**	**1.064**	**1.053-1.075**
gender_n(1)	0.308	1.372	0.747-2.517	0.350	1.415	0.684-2.926	**0.026**	**1.494**	**1.048-2.129**
cumlos12	**0.000**	**1.055**	**1.040-1.070**	**0.000**	**1.052**	**1.036-1.069**	**0.000**	**1.049**	**1.037-1.062**
ch_last	**0.000**	**2.021**	**1.672-2.421**	**0.000**	**2.044**	**1.665-2.509**	**0.000**	**2.087**	**1.816-2.399**
tot_vent	**0.000**	**2.666**	**1.848-3.848**	0.133	1.642	0.860-3.136	0.156	1.340	0.894-2.008
tot_vent_asthma	**0.000**	**2.925**	**1.968-4.347**	0.973	1.021	0.316-3.295	0.892	1.039	0.594-1.821
totvent_ni_asthma	**0.000**	**3.624**	**1.922-6.832**	**0.044**	**2.543**	**1.024-6.291**	0.096	1.729	0.907-3.297
totvent_i_asthma	**0.000**	**2.481**	**1.513-4.068**	0.795	0.759	0.146-4.360	1.000	1.000	0.508-1.968
totvent_ni_all	**0.000**	**3.802**	**2.079-6.954**	**0.008**	**2.919**	**1.321-6.452**	0.146	1.619	0.846-3.098
totvent_i_all	**0.000**	**2.454**	**1.549-3.886**	0.765	0.733	0.143-4.169	0.583	1.170	0.668-2.050
totadm	0.844	0.987	0.868-1.123	0.131	1.055	0.984-1.131	**0.000**	**1.091**	**1.051-1.133**
totadm_asthma	0.817	0.979	0.819-1.171	0.273	1.055	0.958-1.162	**0.035**	**1.059**	**1.004-1.116**
tot_readm7	0.523	1.154	0.743-1.794	0.651	1.135	0.656-1.965	0.395	1.130	0.852-1.498
tot_readm30	0.452	0.501	0.083-3.038	0.126	1.184	0.953-1.470	0.058	1.158	0.995-1.348
n5_home_cumpop91	0.387	1.105	0.881-1.388	0.354	1.140	0.864-1.506	0.609	1.034	0.910-1.175
n5_home_cumpop96	0.862	0.982	0.799-1.206	0.897	0.984	0.767-1.262	0.821	1.014	0.899-1.145
n5_home_cumpop01	0.559	0.942	0.770-1.152	0.452	0.912	0.718-1.159	0.259	0.935	0.831-1.051
n5_metro_cumpop91	0.649	1.051	0.847-1.305	0.440	1.113	0.848-1.462	0.606	1.033	0.912-1.171
n5_metro_cumpop96	0.892	1.014	0.828-1.242	0.965	0.995	0.779-1.269	0.816	1.014	0.902-1.140
n5_metro_cumpop01	0.846	0.981	0.806-1.194	0.451	0.915	0.726-1.153	0.214	0.931	0.832-1.042

Legend:

age	- age of patient at index admission
gender_n	- gender of patient, 0=male, 1=female
cumlos12	- cumulative length of stay for previous 12 months admissions
ch_last	- Charlson comorbidity index
tot_vent	- total no. of ventilation episodes for all admissions
tot_vent_asthma	- total no. of ventilation episodes for asthma admissions only
totvent_ni_asthma	- total no. of ventilation episodes for asthma admissions only, non-invasive
totvent_i_asthma	- total no. of ventilation episodes for asthma admissions only, invasive
totvent_ni_all	- total no. of ventilation episodes for all admissions, non-invasive
totvent_i_all	- total no. of ventilation episodes for all admissions, invasive
totadm	- total no. of admissions
totadm_asthma	- total no. of asthma admissions
tot_readm7	- total no. of readmissions within 7 days of discharge
tot_readm30	- total no. of readmissions within 30 days of discharge
n5_home_cumpop91	- SEIFA quintile for postal area of patient's home address 1991
n5_home_cumpop96	- SEIFA quintile for postal area of patient's home address 1996
n5_home_cumpop01	- SEIFA quintile for postal area of patient's home address 2001
n5_metro_cumpop91	- SEIFA quintile for postal area of ambulance attendance for patient 1991
n5_metro_cumpop96	- SEIFA quintile for postal area of ambulance attendance for patient 1996
n5_metro_cumpop01	- SEIFA quintile for postal area of ambulance attendance for patient 2001

Appendix 12: Univariate analysis of the relationship of each predictor variable with readmission using STATA logistic regression (robust standard error) and GEE model (autoregressive AR1).

Readmission	Within 7 days LR Model			Within 7 days GEE Model			Within 30 Days LR Model			Within 30 Days GEE Model		
Predictor	**Odds Ratio**	**95% CI**	**P**	**Odds Ratio**	**95% CI**	**P**	**Odds Ratio**	**95% CI**	**P**	**Odds Ratio**	**95% CI**	**P**
age	**0.988**	**0.984-0.994**	**0.000**	**0.982**	**0.978-0.987**	**0.000**	0.998	0.992-1.004	0.472	0.994	0.987-1.001	0.073
gender_n	**1.600**	**1.187-2.156**	**0.002**	1.333	0.996-1.783	0.053	**2.188**	**1.461-3.276**	**0.000**	**1.843**	**1.252-2.711**	**0.002**
ventyn	1.309	0.830-2.564	0.247	1.221	0.786-1.898	0.334	0.802	0.415-1.549	0.511	0.878	0.471-1.635	0.681
ventasyn	**3.175**	**2.039-4.943**	**0.000**	**2.515**	**1.632-3.874**	**0.000**	1.888	0.972-3.678	0.061	1.697	0.878-3.278	0.115
vent_ni	0.584	0.241-1.417	0.235	0.552	0.231-1.319	0.181	0.632	0.236-1.693	0.362	0.818	0.348-1.924	0.646
vent_i	**2.154**	**1.306-3.552**	**0.003**	**1.945**	**1.222-3.159**	**0.005**	1.288	0.600-2.762	0.516	1.213	0.548-2.686	0.634
ventboth	1.147	0.166-7.912	0.889	0.957	0.151-6.055	0.963	3.250	0.753-14.025	0.114	3.070	0.788-11.961	0.106
urgency	**0.664**	**0.581-0.758**	**0.000**	**0.697**	**0.611-0.795**	**0.000**	0.942	0.800-1.109	0.473	0.980	0.846-1.136	0.792
tod1(2)	**0.719**	**0.527-0.980**	**0.037**	0.767	0.562-1.047	0.094	1.047	0.686-1.598	0.831	1.204	0.785-1.845	0.395
tod1(3)	0.777	0.579-1.043	0.093	0.789	0.598-1.059	0.115	1.261	0.848-1.875	0.252	1.389	0.942-2.048	0.097
tod1(4)	1.015	0.751-1.371	0.923	1.034	0.762-1.403	0.829	0.818	0.523-1.281	0.380	0.894	0.564-1.418	0.637
season2(2)	**1.285**	**1.008-1.637**	**0.042**	1.203	0.953-1.518	0.120	0.870	0.679-1.115	0.272	0.802	0.631-1.020	0.072
season4(2)	0.984	0.683-1.419	0.931	1.023	0.720-1.454	0.897	0.813	0.498-1.326	0.407	0.777	0.483-1.248	0.296
season4(3)	0.756	0.525-1.090	0.135	0.824	0.579-1.173	0.283	1.103	0.761-1.598	0.604	1.164	0.815-1.661	0.404
season4(4)	0.789	0.540-1.152	0.219	0.864	0.601-1.240	0.427	0.944	0.644-1.384	0.769	1.007	0.694-1.461	0.971

Legend:

age - age of patient at index admission
gender_n - gender of patient, 0=male, 1=female
ventyn - ventilation episode for any reason
ventasyn - ventilation episode for asthma only
vent_ni - ventilation episode for any reason, non-invasive
vent_i - ventilation episode for any reason, invasive
ventboth - ventilation episodes for any reason, both non-invasive and invasive
age - age of patient at index admission

tod1(1) - time of day, 0600 to 1200 hrs (reference category only, not reported in table above)
tod1(2) - time of day, 1200 to 1800 hrs
tod1(3) - time of day, 1800 to 2400 hrs
tod1(4) - time of day, 2400 to 0600 hrs
season2(1) - diurnal season (wet months), June to Nov (reference category only, not reported in table above)
season2(2) - diurnal season (dry Months), Dec to May
season4(1) - quarterly season, Summer, Dec to Feb (reference category only, not reported in table above)
season4(2) - quarterly season, Autumn, Mar to May
season4(3) - quarterly season, Winter, June to Aug
season4(4) - quarterly season, Spring, Sept to Nov