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Asthma in Australian children

Findings from *Growing Up in Australia*, the Longitudinal Study of Australian Children

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Contents

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Abbreviations

ACAM	Australian Centre for Asthma Monitoring
CI	Confidence interval
FaHCSIA	Australian Government Department of Families, Housing, Community Services and Indigenous Affairs
GP	General practitioner
HR	Hazard ratio
ICS	Inhaled Corticosteroids
ISAAC	International Study of Asthma and Allergies in Childhood
LABA	Long-acting beta agonists
LSAC	Longitudinal Study of Australian Children
LSIC	Longitudinal Study of Indigenous Children
MBS	Medical Benefits Scheme
NHS	National Health Survey
OR	Odds ratio
PAF	Population attributable fraction
PBS	Pharmaceuticals Benefits Scheme
RR	Relative risk or Rate ratio
SABA	Short-acting beta agonists
SEIFA	Socio-Economic Indexes for Areas

Summary

The issues

The prevalence of asthma in Australian children is amongst the highest in the world. Improved understanding of the way asthma and related wheezing illnesses progress through early childhood may have important implications for practice and for policy.

This report presents findings about asthma and wheezing illness in infants (first year of life) and in kindergarten children (fifth year of life) who were followed over two years in the national Longitudinal Study of Australian Children. The report also links the children's data to the use of health services through the records of the Medical Benefits Schedule (MBS) and the Pharmaceutical Benefits Scheme (PBS).

Infants

- Asthma or wheeze during the first three years of life was more common among those who: were boys, had older siblings, attended child care, were born at an early gestational age, and were admitted to Neonatal Intensive Care Unit after birth.
- Asthma or wheeze during this period was also more common in infants whose mothers: had asthma, were relatively young, or smoked during pregnancy.
- Infants who were breastfed had a lower risk of having asthma or wheeze during this time.

Kindergarten children

- Asthma in kindergarten-aged children was more common among those who: were living in remote or very remote areas and had food or other allergies.
- Among kindergarten-age children with wheeze, those who use medications for asthma and those who had more than 3 episodes of wheezing which lasted for a week or more in the preceding year, were more likely than others to still experience wheeze 2 years later.
- Children who had wheeze or asthma in their fifth year, were more likely than other children to be hospitalised, to attend an emergency department, and to visit a general practitioner (GP) over the next two years, and were also more likely to be overweight or obese two years later.
- Parents of children with wheeze or asthma were more likely to report that their child had poorer health or disturbed sleeping patterns.

Conclusions

There are important differences between wheezing illness in infancy and kindergarten-aged children, both in the nature of the disease and in its risk factors. Wheezing illness is a common disorder that contributes to a range of important health problems in kindergarten-age children. Further study of this cohort will expand our knowledge about asthma and related problems in children.

1 Introduction

Asthma is a chronic inflammatory condition of the airways, affecting an estimated 300 million people worldwide (GINA 2004). The common features of asthma are recurrent episodes of wheezing, breathlessness and chest tightness, associated with widespread narrowing of the airways (NAEPP 1997). However, these features are difficult to identify in young children. Parents report that their infant or child has wheezing, noisy breathing and, sometimes, fast breathing (Mellis 2009). A range of entities, such as viral bronchiolitis, bronchitis, or upper respiratory tract infections, may all manifest in similar ways or with overlapping clinical features. Children with wheezing may be labelled with the diagnosis 'asthma', 'wheezing illness' or one of these other illnesses mentioned above. Sometimes the diagnosis of asthma is made in retrospect, when it is clear that the disease is more than transient episodes of wheezing. 'Asthma' is not a precisely defined entity in preschool-age children. In this report we have tended to use the term 'asthma' and 'wheezing illness' interchangeably when referring to younger children. In citing data from other reports, we have adhered to the terms used in those reports.

Prevalence of asthma in Australian children

The International Study of Asthma and Allergies in Childhood (ISAAC) has consistently identified Australia, along with the UK, New Zealand and the Republic of Ireland, as having a relatively high prevalence of asthma in children, by international standards (Lai et al. 2009; Pearce et al. 2007). The National Health Survey (NHS) 2004–05 provides the most recent nationwide data on the prevalence of asthma in Australia. This survey found that asthma is the most common long-term medical condition in children, with prevalence being higher among boys than girls (ABS 2006). It is estimated that 20.8% of children aged 0 to 15 years have ever been diagnosed with asthma, while 11.3% of children within the same age group have a current diagnosis (ACAM 2008). Comparison of results from the 2004–05 NHS with those reported in a similar survey in 2001 shows that the prevalence of childhood asthma appears to have reached a plateau since peaking during the 1980s and early 1990s. The reasons for this remain uncertain.

Risk factors for asthma and its consequences in children

There are many pathways leading to the development of asthma and wheezing illness. Interactions among a range of genetic and environmental risk factors are thought to play an important role. Researchers in this field are attempting to understand the nature of the gene–environment interaction that leads to disease in children, so that they can develop interventions aimed at reducing the prevalence and incidence of asthma. Cohort studies have been conducted to examine putative risk factors for childhood asthma, persistence of the illness and poorer outcomes, such as more frequent use of health-care services. Interventions directed at these risk factors could potentially lead to a reduction in the burden of disease attributed to childhood asthma. There is evidence that inherited attributes,

prenatal and postnatal events, and early childhood exposures may all contribute to the development of asthma and related disorders in children (see Table 1.1).

Table 1.1: Characteristics, behaviours and environmental exposures that have been linked, positively or negatively, to the presence of asthma

Inherent factors	Sex	Dik et al. 2004; Strachan 1985
	Genetics	Bottema et al. 2008; Vercelli 2003
	Family heredity	London et al. 2001; Metsala et al. 2008
	Socioeconomic status	Cesaroni et al. 2003
	Remoteness	Clement et al. 2008
	Aboriginality	Bremner et al. 1998; Valery et al. 2001; Valery et al. 2003; Veale et al. 1996
	Ethnicity and migration	Leung et al. 1994; Netuveli et al. 2005; Wilson et al. 2006
Prenatal and postnatal factors	Maternal smoking	Li et al. 2005; Stein et al. 1999
	Mode of delivery	Metsala et al. 2008; Sears 1997
	Prematurity	Jaakkola et al. 2001; Miller 2001
	Multiple births	McKeever et al. 2001; Toos et al. 2008
	Breastfeeding	Chandra 1997; Dyson et al. 2005; Oddy 2000; Oddy et al. 1999
Early childhood exposures	Bronchiolitis	Jackson et al. 2008
	Reduced physical activity	Lucas & Platts-Mills 2005
	Siblings	Doull 2001; Martinez & Holt 1999; Strachan 2000
	Child care attendance	Von Mutius 2007
	Pet ownership	Hesselmar et al. 1999
Other conditions	Eczema	Burgess et al. 2008
	Food and digestive allergies	Tariq et al. 2000
	Obesity	Sutherland 2008
	Allergic rhinitis	Dik et al. 2004

Note: Inclusion here does not imply a causal relationship has been demonstrated.

Not all children with asthma or wheezing in early childhood have persisting disease. In many children the wheezing is relatively transient. Children with more troublesome asthma in early childhood are more likely to have persistent disease (Jenkins M A et al. 1994; Oswald 1994; Reed 2006; Sears 1994). Other reported risk factors for persistent asthma include early onset of the disease, having a family history of asthma, being allergic, having airway hyperresponsiveness (twitchiness of the airways), increased frequency of respiratory infections and lack of contact with older children (Lewis et al. 1995; Martinez 2002a; Reed 2006; Sears et al. 2003; To et al. 2007). The use of health-care services for asthma may be influenced by access, education, socioeconomic status, country of birth and length of time in Australia (Christakis et al. 2001; Jones et al. 2008). Other risk factors associated with health

care use, particularly hospitalisation, include the severity of asthma, poor asthma management and improper use of asthma medications (Christakis et al. 2001; Rasmussen et al. 2002).

Rationale for this study

The Australian Centre for Asthma Monitoring (ACAM) has previously explored childhood asthma in Australia using data from the National Health Surveys. However, these are cross-sectional surveys with limited data on both risk factors and outcomes and no capacity to link these over time. Further exploration of the issues identified above requires data from a cohort study.

In 2003, the Australian Government Department of Families, Housing, Community Services and Indigenous Affairs (FaHCSIA) in partnership with the Australian Institute of Family Studies and a consortium of leading researchers initiated data collection for the Growing Up in Australia: the Longitudinal Study of Australian Children (LSAC). The study has a broad, multidisciplinary base, involving a broadly representative sample of Australian children, and examines topical issues of policy relevance. It explores family and social issues relevant to children's development, and addresses a range of research questions about family functioning, health, non-parental childcare and education. Data are being collected from two separate cohorts, aged 0–1 year and 4–5 years at recruitment, every two years. In this report ACAM has used these LSAC data to investigate childhood asthma in Australia.

Study aims

This study investigates the incidence, prevalence, risk factors, management and consequences of parent-reported wheeze or asthma among infants and kindergarten-age children in Australia. It aims to answer the following questions:

1. What risk factors are associated with the development of wheeze and asthma among infants in the first three years of life?
2. What risk factors are associated with the development of asthma among children between the fifth and seventh years of life?
3. What risk factors are associated with the persistence of wheeze between the fifth and seventh years of life?
4. What health services and medications are used in relation to childhood asthma?
5. What are the consequences or outcomes of childhood asthma or wheeze?

Definitions of the terms 'parent-reported wheeze' and 'asthma' are provided in *Chapter 2*.

Structure of this report

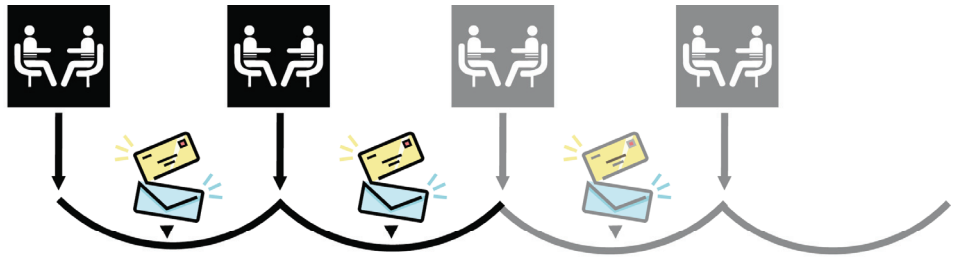
This chapter has introduced the background to this study, the questions posed, the data that were used and the issues taken into account in the analyses; while the second chapter includes a detailed description of the data source and the methods used to analyse the data. The subsequent chapters will address each of the five main study questions described in the study aims.

In *Chapter 3*, risk factors associated with the development of wheeze or asthma in infants are examined. In *Chapter 4*, risk factors associated with the development of asthma in kindergarten-age children are examined. *Chapter 5* presents data on the persistence of wheeze in the kindergarten cohort. Health service utilisation and medication use in relation to childhood asthma is explored in *Chapter 6*. The last study question, investigating outcomes associated with childhood asthma, is addressed in *Chapter 7*. The concluding chapter of this report summarises the main findings across all chapters and considers the limitations as well as the future possibilities for studies using these data.

2 Methods

Data source

This report presents results from ACAM's analysis of data from Growing Up in Australia: the Longitudinal Study of Australian Children. LSAC was initiated and is funded by the Australian Government Department of Families, Community Services and Indigenous Affairs (FaCSIA) and aims to explore a range of research questions about children's development and wellbeing. The study commenced in 2004 with a sample of approximately 10,000 children recruited from the Medicare enrolments database. With the exception of children living in some remote areas of Australia, the sample is broadly representative of Australian children in each of two selected age cohorts: children born between March 2003 and February 2004 and, hence, aged 3–19 months at baseline (infant cohort) and children born between March 1999 and February 2000 and, hence, aged 4 years and 3 months to 5 years and 7 months at baseline (kindergarten cohort). The intention of the study is to reassess the children every two years until 2010, at which time the infant cohort will be 6–7 years of age and the kindergarten cohort will be 10–11 years of age, using a combination of face-to-face interviews and mail-out surveys as shown in Figure 2.1.



Note: Data from baseline and 2 year follow-up have been analysed in this report.

Figure 2.1: Timeline of the Longitudinal Study of Australian Children, indicating face-to-face interviews and mail-out surveys and the age of the cohorts at these times

The primary study informant is the person, such as the child's parent or main care giver, who knows the most about the child, their birth, history and current routines (FaHCSIA: Wake et al. 2008). Typically this has been the child's biological mother (Sanson et al. 2002). In addition, the LSAC cohorts have been linked to the PBS and MBS databases, where consent was given for this linkage (approximately 93% of parents gave permission). This will facilitate the acquisition of data on the child's use of medicines and medical care during the course of the study.

The analysis presented here relates to data on asthma and wheezing, together with relevant data on risk factors and outcomes, that were collected when the infant or child was enrolled (that is, baseline or Wave 1) and at the 2 year follow-up assessment (that is, Wave 2) on both cohorts.

Definitions

Wheeze is a term used throughout this report to describe parent-reported symptoms of wheezing, which was evaluated as a positive response to the question 'Has [child] had an illness with wheezing in the chest which lasted for a week or more in the last 12 months?'.

Asthma is used to describe parent-reported asthma that has 'ever' been clinically diagnosed by a physician and has been evaluated as a positive response to the question 'Has a doctor ever told you that [child] has asthma?'.

Maternal asthma. Information about maternal asthma was not collected as part of the LSAC. In our analysis we have assumed that mothers who reported using either prescribed or 'over-the-counter' medicines for asthma during pregnancy, had asthma.

The use of prescribed medications for asthma during pregnancy was defined as a positive response to the question 'During the pregnancy with [child] did you/child's mother take any medicines or tablets on a doctor's prescription?' and then by marking 'asthma medication' in response to 'What prescribed medicines or tablets were taken?'. Likewise, the use of over-the-counter medication for asthma was evaluated as a positive response to the question 'During the pregnancy with [child], did you/child's mother take any over-the-counter medicines or tablets, like paracetamol or vitamins?' and then by marking 'asthma medications (Ventolin etc.)' in response to 'What over-the-counter medications were used?'.

Study data

At baseline of the LSAC, 5,107 infants and 4,983 4–5 year old children were recruited, representing 57% and 50%, respectively, of those approached to participate (Table 2.1). The main reasons for non-participation at baseline were refusals, or non-contact due to PO Box or families having moved. Children with a name matching that of a child that had died were removed from the sample. A design weight was calculated for each child selected in the survey, to adjust for initial non-response (Soloff et al. 2006). Ninety percent of both cohorts participated in the 2 year follow-up assessment.

Table 2.1: Sample sizes and response rates by cohort and wave

	Infant cohort		Kindergarten cohort	
	Wave 1 (baseline) (0–1 years)	Wave 2 (follow-up) (2–3 years)	Wave 1 (baseline) (4–5 years)	Wave 2 (follow-up) (6–7 years)
Number sent a letter of invitation	8,921	..	9,893	..
Number recruited	5,107	4,606	4,983	4,464
Response rate	57%	90%	50%	90%

.. Not applicable

Note: Response rates for wave 2 (follow-up) are based on the number of participants retained from wave 1 (baseline).

Representativeness of the data

The LSAC sample is broadly representative of the Australian population (FaHCSIA: Wake et al. 2008). However, there are aspects of the LSAC sample design which have introduced bias into the sample. These include a selection design based on geographical representation and voluntary participation.

The Medicare database was used as the sampling frame for LSAC to ensure that the sample chosen was representative of infants and 4–5 year old children in Australia. In the first stage of the design postcodes were selected for inclusion. Some remote postcodes were excluded from the sample due to the small number of children residing in these remote areas and the excessive costs that would have been associated with data collection (Soloff et al. 2005). As a consequence, the sample frame excludes 40% of children living in remote areas (FaHCSIA: Wake et al. 2008; Hunter 2008). Furthermore, the study design explicitly excluded Indigenous communities in remote areas. The under-representation of children, especially Indigenous children, living in remote areas significantly impedes our analysis of associations between remoteness and asthma.

The Health Insurance Commission (HIC) invited selected families to participate in the study by letter. Families could opt out of the study by either phoning a 1800 number or returning a reply paid form (Soloff et al. 2006). Parents or carers of 31% of infants and 35% of 4–5 year old children declined to participate. This non-participation rate might potentially be a source of selection bias. In fact, mothers who had not completed Year 12 at school and those who spoke a language other than English were more likely refuse to participate in LSAC (Soloff et al. 2006). Non-response was also more common for single-parent families, Indigenous children, families that spoke a language other than English at home, the child's father not having completed Year 12 and the child not having any siblings (FaHCSIA: Wake et al. 2008; Soloff et al. 2006). The effect of this potential selection bias due to non-response was minimised by the use of a data weighting scheme designed to adjust for differences between the sociodemographic structure of the LSAC sample and that of the Australian population.

In summary, the results presented here are broadly representative of Australian infants and children between the ages of 4 and 5 years, except for children living in very remote areas.

Analysis methods

A general description of the analysis methods used in this report is provided here. Further information about analysis methods that are relevant to specific chapters of this report can be found within those chapters.

Incidence

Incidence is defined as the number of new cases (of a disease, condition or event) occurring in a population during a given period.

Incidence rates are calculated as the number of *new* cases in a period of time divided by the total person years at risk during that period.

In this report, incidence rates have been calculated for:

- the incidence of wheeze or asthma by the age of 2–3 years among the infant cohort; and

- the incidence of asthma between ages 5 and 7 years among the child cohort.

For the infant cohort, the total person years at risk at 2 year follow-up was calculated as the sum of the total time of observation for each child, that is, from birth up to age 2–3 years.

For the kindergarten cohort, the total person years at risk at 2 year follow-up was calculated as the sum of the time between baseline and 2 year follow-up, for each child who did not have asthma at the baseline survey.

Tests for association

Logistic regression

Associations between risk factors measured at baseline and outcomes measured at 2 year follow-up were assessed using logistic regression models that accounted for the clustered survey design (Proc Surveylogistic, SAS version 9.1). Univariate analyses were conducted first, to estimate the unadjusted associations. Multivariable logistic regression was then used to identify any independent associations between each risk factor and the outcome.

Odds ratios

Results derived from the logistic regression models were expressed as odds ratios (OR) with 95% confidence intervals. The OR is the ratio of the odds of an outcome, such as the incidence of asthma, in children with a specific risk factor and the odds of that outcome in children without that risk factor.

Rate ratios

The effect of asthma status at baseline in the kindergarten cohort on outcomes during follow-up was estimated as a rate ratio.

For a particular outcome, the rate ratio (RR) was calculated as:

$$RR = P_e / P_{ue}$$

where P_e is the proportion of children with the outcome at age 6–7 years among children with wheeze or ever diagnosed asthma at age 4–5 years; and

P_{ue} is the proportion of children with the outcome at age 6–7 years among children with no wheeze or ever diagnosed asthma at age 4–5 years.

The P_e and P_{ue} were estimated using Proc Surveymeans, SAS version 9.1, to account for the clustered survey design.

The 95% confidence intervals (95% CI) for the rate ratios were calculated as:

$$95\%\ CI = RR^{(1 \pm 1.96/\chi)}$$

where $\chi = (P_e - P_{ue}) / \sqrt{se(P_e)^2 + se(P_{ue})^2}$ (Parkin et al. 1992).

Population attributable fraction

To quantify the impact of having wheeze or ever diagnosed asthma at age 4–5 years on outcomes measured at age 6–7 years, we calculated the population attributable fraction (PAF) for each outcome. PAF can be described as the reduction in the proportion of the

population who would experience a particular outcome (for example, hospitalisation) if no children had the risk factor, in this case wheeze or ever diagnosed asthma at baseline.

For a particular outcome, the PAF% was calculated as:

$$PAF\% = (P_e \times (RR - 1)/(P_e \times (RR - 1) + 1)) \times 100$$

where P_e is the prevalence of wheeze or ever diagnosed asthma at age 4–5 years and RR is the rate ratio for the association between having wheeze or ever diagnosed asthma at baseline and experiencing the outcome during follow-up.

3 Risk factors for the development of wheeze or asthma among infants in the first three years of life

Asthma in the first three years of life is different from asthma in later childhood (Le Souëf 2000; Young et al. 2000). Martinez and colleagues (1995) described this difference in terms of three distinct phenotypes of wheeze in infants, namely: transient early wheeze, viral induced wheeze (or non-atopic wheeze) and genuine atopic asthma. The last of these is the condition most likely to continue into mid-childhood and beyond.

In the 2004–05 NHS the prevalence of current asthma was lowest in 0–1 year olds (6.6%) but increased to 19.8% in 2–4 year old children (ACAM 2008). This implies that between the first year of life and subsequent years of childhood there is a high incidence of asthma. However, an alternative explanation for some of the increased prevalence is that doctors are more willing to apply the diagnostic label of asthma to wheezing illness in later years.

The Tucson Children's Respiratory Study, a large longitudinal assessment of the natural history of asthma conducted in the US, reported that a majority of infants who wheeze in the first 3 years of life experience what Martinez and colleagues (1995) termed 'transient early wheeze', often virus-induced, preceded by poor lung function at birth; and these infants are not at an increased risk of developing asthma in later childhood (Le Souëf 2002; Martinez et al. 1995; Young et al. 2000). There is evidence that being male, maternal asthma, maternal smoking during pregnancy, young maternal age, early gestation and low birthweight may be associated with impaired lung function during the first few years of life (Dezateux et al. 1999; Martinez et al. 1995; Taussig et al. 2003; Young et al. 2000). Furthermore, among infants with a genetic predisposition to asthma, alterations in airway physiology may increase the propensity to wheeze (Dezateux et al. 1999). These findings suggest that respiratory symptoms in infancy are associated with genetic and *in utero* factors that influence airway physiology rather than asthma *per se* (Dezateux et al. 1999; Le Souëf 2000). However, there is still a substantial minority of children who experience wheeze during lower respiratory infection in early life and continue to wheeze during later childhood.

Researchers in this field are looking for factors that differentiate a transient respiratory condition from a predisposition to asthma in wheezing infants. Identifying these conditions with different prognoses in infancy might allow the development of targeted interventions, to prevent the development of asthma in later childhood.

Methods

Two year follow-up data from the LSAC infant cohort were used to investigate risk factors for the development of wheeze or asthma during infancy (the first three years of life).

It is inherently challenging to diagnose asthma among infants. The nature of the disease is often intermittent and common symptoms of asthma, such as wheezing, coughing and shortness of breath, are not specific for the condition and can often be associated with other common illnesses (GINA 2004; Poulos et al. 2005). The identification of wheeze as being the most important symptom in diagnosing current asthma in young children has led to the

inclusion of self-report based questions in population surveys like the LSAC, which asks parents whether their child has experienced wheeze in the last 12 months (GINA 2004). Self-report of wheeze has been shown to have good specificity and sensitivity when compared with clinical diagnosis of asthma (Jenkins M A et al. 1996; Keller & Lowenstein 2002), although this may not be the case for parent-report of wheeze in children.

We have used a cumulative measure of the incidence of asthma among LSAC participants by including all subjects who meet one or more of the following three criteria:

- parent-report of illness with wheeze at baseline,
- parent-report of illness with wheeze at 2 year follow-up, or
- asthma diagnosed at 2 year follow-up.

Data on potential risk factors were ascertained in the baseline survey.

The LSAC did not collect data on parental history of asthma or atopic disease. In our analysis we have defined the maternal use of asthma medication during pregnancy, as a proxy measure of maternal asthma (see *Chapter 2*).

Results

The overall cumulative incidence of wheeze or asthma among infants was 16.9 per 100 person-years (Table 3.1). The incidence of wheeze (15.4%) was more than double the incidence of asthma (6.4%).

Table 3.1: Incidence of wheeze or asthma by the age of 2–3 years, infant cohort

	Number of children at risk	Number of cases	Person-years	Incidence per 100 person-years
Asthma [(a)]	4,580	628[(a)]	10,480	6.4 (5.9–6.9)
Wheezing [(b)]	4,595	1,537[(b)]	10,515	15.4 (14.7–16.1)
Asthma or wheezing [(c)]	4,584	1,691[(c)]	10,490	16.9 (16.1–17.6)

Note: Incidence per 100 persons-years is weighted to the Australian population aged 0–1 years at end March 2004.

(a) Yes to the question 'Has a doctor ever told you that child has asthma?' at age 2–3 years (2 year follow-up/Wave 2).

(b) Yes to the question 'Has child had an illness with wheezing in the chest which lasted for a week or more in the last 12 months?' at ages 0–1 year (baseline/Wave 1) or 2–3 years (2 year follow-up/Wave 2).

(c) Yes to the questions 'Has child had an illness with wheezing in the chest which lasted for a week or more in the last 12 months?' at ages 0–1 year (baseline/Wave 1) or 2–3 years (2 year follow-up/Wave 2) or 'Has a doctor ever told you that child has asthma?' at age 2–3 years (2 year follow-up/Wave 2).

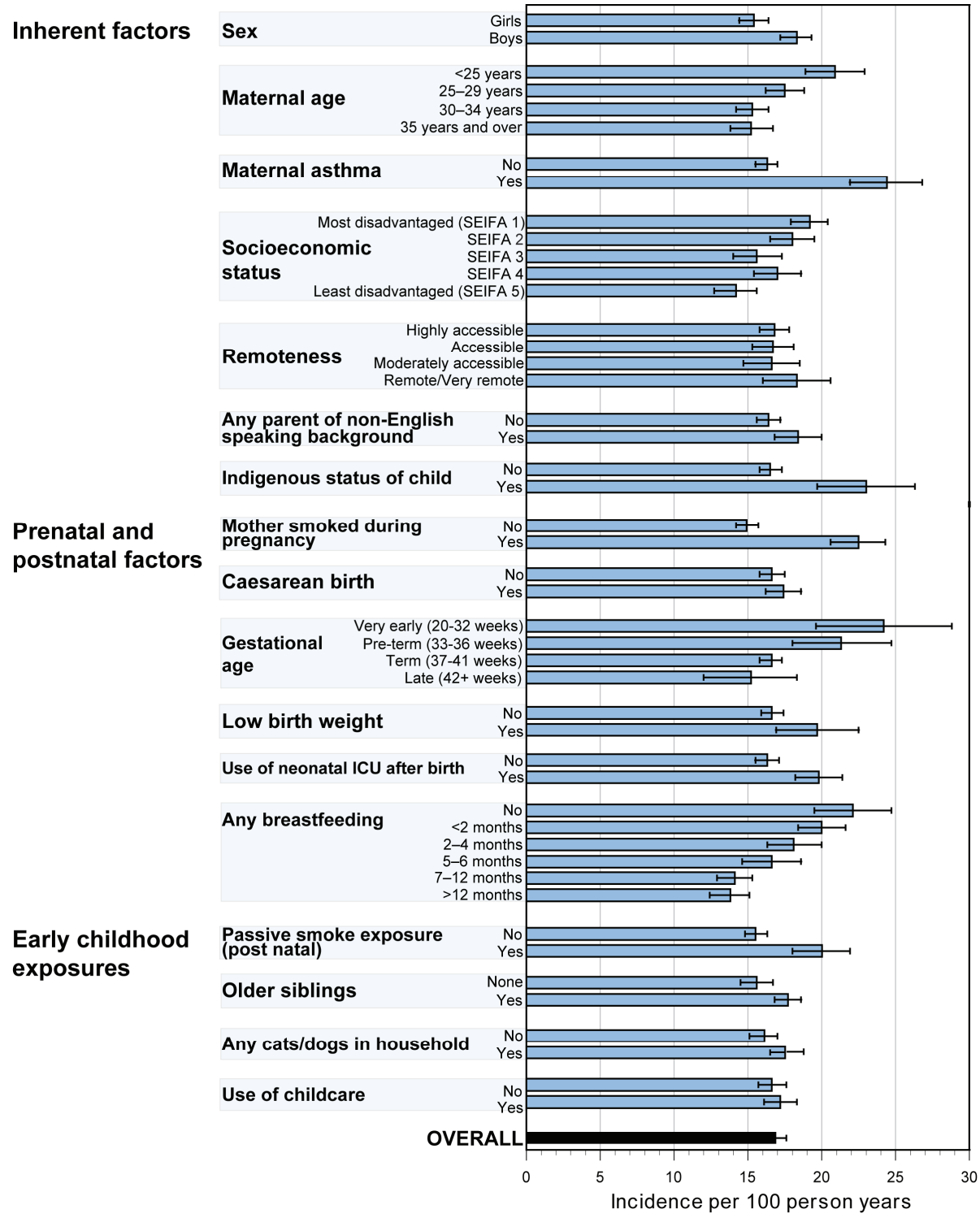
The incidence of parent-reported wheeze or asthma (Figure 3.1) was highest for infants who were:

- of Aboriginal or Torres Strait Islander origin
- born prematurely
- never breastfed
- exposed to passive cigarette smoke at baseline;

and infants whose mothers:

- were younger

- had asthma (use of asthma medication during pregnancy was used as a marker of maternal asthma)
- smoked during pregnancy.



Note: Error bars indicate 95% confidence interval.

Figure 3.1: Incidence of parent-reported wheeze or asthma over 2 year follow-up, by baseline risk factors, infant cohort

Table 3.2: Baseline risk factors for wheeze or asthma by 2 year follow-up in the infant cohort (univariate analysis, n=4,584)

Baseline risk factor	Number of cases (%)	Odds ratio	95% CI	Overall p-value
INHERENT FACTORS				
Sex (n=4,584)				<0.0001
Girls	760 (33.9)	1.00		
Boys	931 (39.7)	1.32	1.15–1.50	
Maternal age (n=4,569)				<0.0001
<25 years	308 (46.4)	1.82	1.43–2.31	
25–29 years	464 (38.9)	1.28	1.06–1.55	
30–34 years	593 (34.1)	1.02	0.85–1.22	
35 years and over	320 (33.0)	1.00		
Maternal asthma[(a)] (n=4,561)				<0.0001
No	1,506 (35.5)	1.00		
Yes	173 (53.6)	2.13	1.69–2.69	
Socioeconomic status[(b)] (n=4,584)				<0.0001
Most disadvantaged (SEIFA 1)	365 (41.3)	1.69	1.39–2.05	
SEIFA 2	333 (39.5)	1.45	1.18–1.78	
SEIFA 3	328 (34.9)	1.16	0.93–1.46	
SEIFA 4	373 (37.3)	1.34	1.08–1.66	
Least disadvantaged (SEIFA 5)	292 (31.8)	1.00		
Remoteness of residence[(c)] (n=4,531)				0.8746
Highly accessible	940 (37.3)	1.00		
Accessible	386 (36.2)	0.98	0.83–1.16	
Moderately accessible	270 (36.0)	0.99	0.80–1.22	
Remote/Very remote	71 (36.4)	1.10	0.85–1.43	
Any parent of non-English-speaking background (n=4,435)				0.0105
No	1,264 (36.1)	1.00		
Yes	377 (40.5)	1.24	1.05–1.46	
Indigenous status of child (n=4,584)				0.0001
No	1,601 (36.4)	1.00		
Yes	90 (50.0)	1.79	1.33–2.42	
PRENATAL AND POSTNATAL FACTORS				
Mother smoked during pregnancy (n=4,571)				<0.0001
No	1,105 (33.3)	1.00		
Yes	315 (50.2)	2.08	1.74–2.49	
Caesarean birth (n=4,583)				0.2789
No	1,171 (36.5)	1.00		
Yes	520 (37.8)	1.08	0.94–1.24	

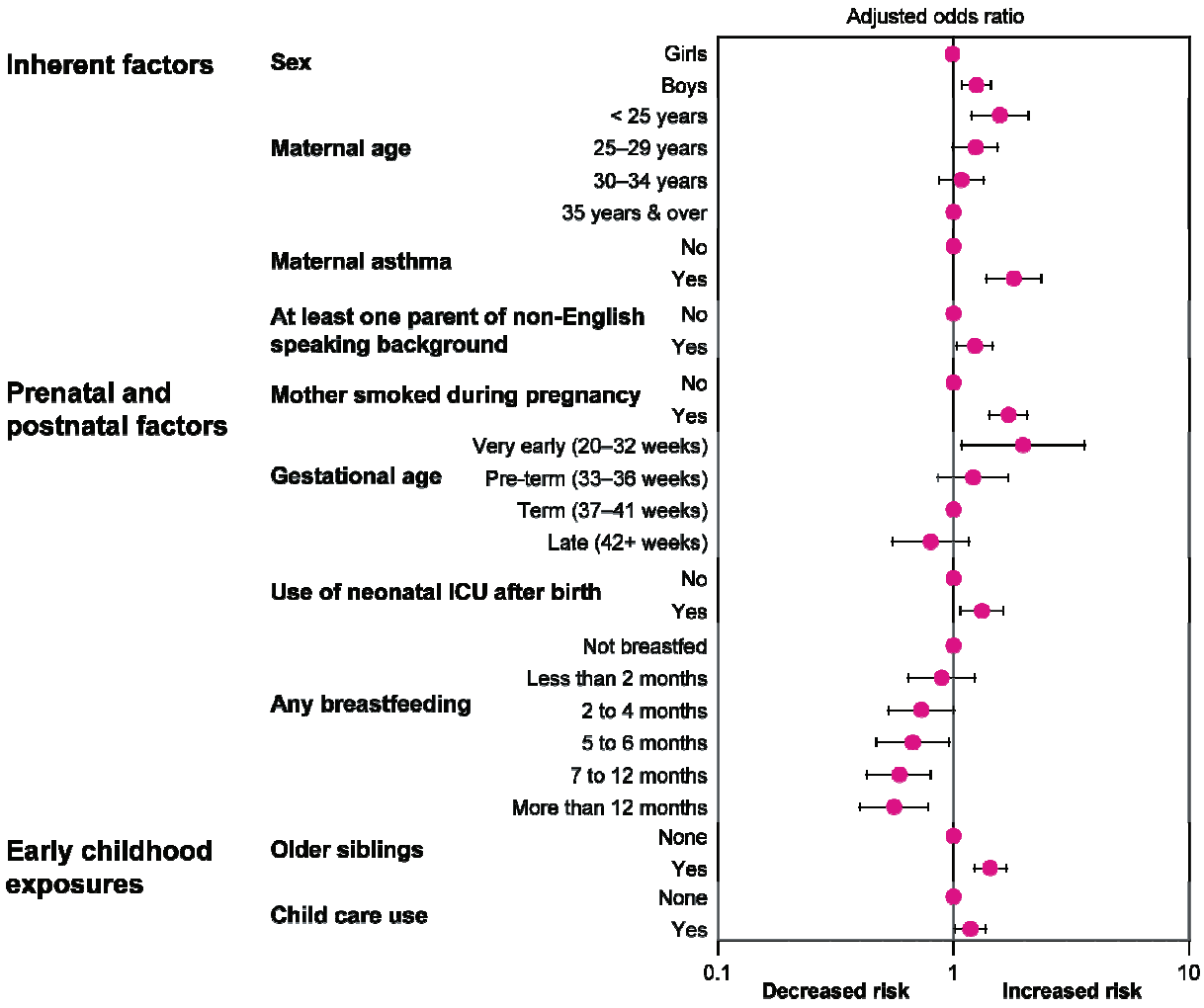
(continued)

Table 3.2 (continued): Baseline risk factors for wheeze or asthma by 2 year follow-up in the infant cohort (univariate analysis, n=4,584)

Baseline risk factor	Number of cases (%)	Odds ratio	95% CI	Overall p-value
PRENATAL AND POSTNATAL FACTORS (CONTINUED)				
Gestational age (n=4,577)				0.0004
Very early (20–32 weeks)	42 (59.2)	2.18	1.37–3.46	
Pre-term (33–36 weeks)	103 (46.8)	1.58	1.15–2.18	
Term (37–41 weeks)	1,477 (36.2)	1.00		
Late (42+ weeks)	68 (32.9)	0.88	0.65–1.21	
Child's birthweight (n=4,558)				0.0235
Not low birth weight	1,572 (36.3)	1.00		
Low birth weight	103 (46.0)	1.38	1.04–1.83	
Use of Neonatal Intensive Care Unit after birth (n=4,580)				<0.0001
No	1,360 (35.6)	1.00		
Yes	330 (43.5)	1.39	1.19–1.63	
Any breastfeeding (n=4,578)				<0.0001
Not breastfed	173 (49.1)	1.00		
Less than 2 months	413 (45.3)	0.81	0.61–1.08	
2 to 4 months	247 (41.0)	0.67	0.51–0.88	
5 to 6 months	176 (37.8)	0.59	0.44–0.80	
7 to 12 months	377 (30.1)	0.45	0.35–0.58	
More than 12 months	303 (30.5)	0.43	0.32–0.58	
EARLY CHILDHOOD EXPOSURES				
Passive smoke exposure (postnatal) (n=4,044)				<0.0001
No	1,200 (34.6)	1.00		
Yes	251 (43.7)	1.52	1.25–1.84	
Presence of older siblings (n=4,584)				0.0015
None	646 (34.3)	1.00		
Yes	1,045 (38.7)	1.23	1.08–1.39	
Pets (cats or dogs) in household (n=4,573)				0.0495
No	733 (35.8)	1.00		
Yes	954(37.8)	1.14	1.0–1.31	
Use of child care (n=4,584)				0.0342
No	979 (35.1)	1.00		
Yes	712 (39.7)	1.15	1.01–1.31	

(a) Maternal use of medication for asthma during pregnancy was used as a proxy for maternal asthma.
(b) Residential postcodes classified according to the Socioeconomic Indexes for Areas (SEIFA) Index of relative disadvantage.
(c) Residential postcodes classified according to the Accessibility/Remoteness Index of Australia (ARIA).

Being male, maternal asthma, younger maternal age, having older siblings, maternal smoking during pregnancy, early gestational age, admission to a Neonatal Intensive Care Unit (NICU), absence of breastfeeding and child care attendance were found to be independently associated with an increased risk of onset of wheeze or asthma during the two years after the first year of life (Figure 3.2; Table A.2).



Note: See also Table A.2.

Figure 3.2: Independent baseline risk factors for wheeze or asthma by 2 year follow-up in the infant cohort (n=4,584)

Discussion

This analysis found that being male, maternal asthma, young maternal age, maternal smoking during pregnancy, early gestational age, admission to a Neonatal Intensive Care Unit (NICU), having older siblings and attending child care were independently associated with a greater risk of developing asthma during infancy. Breastfeeding was associated with a lower incidence of asthma at this age.

Our results are consistent with the well-documented finding that boys have a higher prevalence of asthma than girls. The literature further suggests that this pattern reverses after puberty (Strachan 1985). Boys have smaller airways than girls relative to lung volume which results in greater airway resistance, making boys more susceptible to wheezing illness (Doershuk et al. 1974; Mandhane et al. 2005; Pagtakhan et al. 1984; Thurlbeck 1982; Xuan et al. 2000).

A family history of asthma or atopic disease is a strong predictor of the development of childhood asthma (Duffy 1997). A Finnish study of all children born between 1996 and 2004 who had been diagnosed with asthma by 2006 and had purchased inhaled corticosteroids (ICS) or montelukast at least once, found maternal asthma to be the strongest predictor of childhood asthma (Metsala et al. 2008). Similarly, the Children's Health Study conducted in Southern California found that maternal asthma was associated with an increase in the risk of early-onset persistent asthma, early-onset transient asthma and late-onset asthma (London et al. 2001). In LSAC there are no explicit data on family history of asthma or allergic diseases. However, data on mothers' use of asthma medication during pregnancy was recorded in this survey and this is likely to be a good indicator for the presence of maternal asthma. In this study, maternal asthma identified in this way was associated with almost a twofold increase in the risk of wheezing or asthma by 2 year follow-up in the infant birth cohort. Hence, our findings are in agreement with the current literature.

There is some evidence that young maternal age may be a predictor of asthma and asthma symptoms in infants. The European Community Respiratory Health Survey found that a maternal age at delivery of between 13 and 19 years was associated with higher prevalence of wheeze and asthma, even after controlling for number of pregnancies, prenatal maternal smoking and socioeconomic status, factors commonly associated with early childbirth and childhood asthma (Laerum et al. 2007). Evidence of a dose–response effect was reported in a Canadian study in which the risk of developing asthma increased as maternal age decreased (Infante-Rivard 1995). However, young maternal age is also associated with low birthweight and pre-term delivery, conditions which have been shown to be linked to reduced lung function (Metsala et al. 2008; Seidman et al. 1991). The LSAC data allowed us to disentangle the effects of maternal age, low birthweight and pre-term delivery on the development of wheeze or asthma in infants. We found that younger maternal age was an independent predictor of the development of wheeze or asthma. There are studies which have found similar results but to our knowledge this is the first report which has adjusted for birthweight and pre-term delivery in a representative Australian birth cohort.

The occurrence of wheeze in infants usually coincides with a respiratory viral infection (Lewis et al. 1995). The Tucson Children's Study found that recurrent wheeze was more common in infants aged between 2 and 3 years who had been taken to day care in the first 6 months of life or who had two or more older siblings. However, at age 6 years these infants were less likely to wheeze than infants who had not had these exposures (Martinez 2002b). This suggests that high level exposure to infections in infancy may result in higher rates of wheeze, induced by respiratory tract infection at that time, but that this is protective against asthma in later childhood. We found both child care attendance and the presence of older siblings to be independent risk factors of wheeze or asthma in this infant cohort.

Maternal smoking during pregnancy was a statistically significant risk factor for the development of wheeze or asthma in infants. The Tucson Children's Study (Stein et al. 1999) and South Californian Children's Health Study had similar findings. The Norwegian Mother and Child Cohort Study (MoBa) went further and assessed infant exposure to parental cigarette smoke during and after pregnancy as risk factors for wheezing illness in order to differentiate these highly correlated factors (Haberg et al. 2007). Prenatal exposure to maternal smoking resulted in higher relative risks than postnatal exposure when all confounders were controlled for. Similarly, we found that after adjusting for maternal smoking during pregnancy the effect of postnatal passive smoke exposure was reduced to a level below significance. Studies have shown that foetal exposure to maternal smoking during pregnancy adversely affects infant lung function growth, and results in structural and

functional changes in the developing lung, which results in smaller airways at birth and an increased propensity to develop wheeze during infancy (Stock & Dezateux 2003).

In contrast to other studies (Mallen et al. 2008), we found that admission to NICU independently predicted the development of wheeze or asthma during the first three years of life. The most common reasons for admission to NICU are prematurity, operative birth, low birthweight and the use of instruments such as forceps during the birth process (AIHW: Laws & Hilder 2008; Tracy et al. 2007). Each of these reasons for admission to NICU has been shown to have an impact on respiratory health (Chan et al. 1989a; Chan et al. 1989b; Lewis et al. 1995; Metsala et al. 2008). It is possible that the statistically significant association between admission to NICU and the development of wheeze or asthma observed in the LSAC actually represents the aggregated effects of prematurity, mode of delivery and birthweight, which were not found to be significant on their own.

Premature birth is defined as being born at or prior to 37 weeks gestation and has been associated with acute health issues including poorer respiratory health (Khalil et al. 1995). A recent meta-analysis of 19 relevant studies estimated that prematurity could account for up to a 36% increased risk of asthma compared with babies born at term (Jaakkola et al. 2001). We found that a gestational age of earlier than 32 weeks doubled the risk of developing wheeze or asthma in infants. This finding is supported by the results of studies conducted in Finland (Metsala et al. 2008), the United Kingdom (Rona et al. 1993) and the United States (Miller J E 2001). A cross-sectional study in Munich, Germany, found that the increased risk of asthma and asthma-like symptoms associated with prematurity was mainly due to the use of mechanical ventilatory support after birth (von Mutius et al. 1993). This finding would be consistent with our observation that the risk of acquiring asthma was not related to prematurity, independent of the effect of admission to NICU.

Exclusive breastfeeding of infants from birth to six months is recommended for short- and long-term health benefits, including a reduction in respiratory infections (Kramer & Kakuma 2004; NHMRC 2003). To date, findings on the effect of breastfeeding on the development of asthma are inconsistent. Some studies have associated breastfeeding with a reduction in the incidence of childhood asthma (Chandra 1997; McVeagh 2002; Oddy 2000; Oddy et al. 1999; Saarinen & Kajosaari 1995), while a number suggest breastfeeding is ineffective in reducing asthma (Mihrshahi et al. 2007; Wright & Holberg 2000) and others have even indicated that breastfeeding could potentially be a risk factor (Duncan & Sears 2008; Sears et al. 2002). Some of the observed differences are explained by different ages at which wheeze or asthma outcomes were assessed. Those studies assessing wheeze before age five years have tended to demonstrate a protective effect, whereas those examining the impact of breastfeeding on asthma in school-age children or later have not shown this beneficial effect. Data from the LSAC suggests a strong protective effect of breastfeeding on wheezing in infancy, which increases with increasing breastfeeding duration. In fact, our results indicate that any duration of breastfeeding can protect infants from developing wheeze or asthma. We found that after adjusting for all other factors, the dose-response effect remained statistically significant ($p = 0.0008$). These results reflect those of the Canadian National Longitudinal Survey of Children and Youth which illustrated that the protective effect of breastfeeding was higher as duration of breastfeeding increased (Dell & To 2001).

Our findings on risk factors for the onset of parent-reported wheeze or asthma in the first three years of life were generally consistent with published data on this subject. They support the claim that the majority of children developing asthma during infancy are not atopic. Rather, wheezing during the first years of life is commonly associated with reduced lung function, which can be influenced by sex, smoke exposure, respiratory tract infections

and various obstetric factors. Although maternal use of asthma medication during pregnancy may be indicative of maternal asthma or even atopic disease, we cannot assess the real significance of this factor in contributing to asthma until further data are collected from this cohort. Analysis of future waves of data collected from this cohort will enable us to revisit the risk factors associated with wheeze or asthma, and hopefully assist us to differentiate those associated with a transient respiratory condition from those associated with a predisposition to asthma.

4 Risk factors for the development of asthma during childhood

Childhood asthma is the result of an interaction between genetics and environmental exposures. The incidence of asthma during later childhood is commonly associated with a family history of atopy. Often eczema, which is also associated with atopy, precedes the development of asthma. Other factors which have been shown to be linked to childhood asthma include pet ownership, number of siblings, attendance at day care, tobacco smoke exposure, socioeconomic status, remoteness of residence and Indigenous status.

Among Australian children aged 0–17 years, the prevalence of current asthma in 2004–05 was highest in 5–11 year olds (26.1%) according to the NHS. The majority of children (76%) who have visited a general practitioner for asthma are classified as having an infrequent episodic pattern of the condition (ACAM 2008). Infrequent episodic asthma is characterised by brief, mild exacerbations occurring less than every three to four weeks and having a total absence of symptoms between exacerbations. Children with this pattern of asthma are not required to take medication daily and manage their condition by inhalation of a beta-agonist aerosol, such as Ventolin™ (salbutamol) or Bricanyl™ (terbutaline), to relieve symptoms. Despite the sporadic nature of the disease, it has an adverse effect on the child's quality of life. In 2003, asthma accounted for 17.6% of all disability-adjusted life years (DALYs) lost for males and 17% of all DALYs lost for females between the ages of 0 and 14 years (Begg et al. 2007), which reflects the high prevalence and disabling nature of asthma in children.

Methods

Two year follow-up data from the LSAC kindergarten cohort were used to investigate risk factors for the development of asthma during childhood. For this analysis the cohort was limited to children aged 4–5 years whose parents reported that their child had never been diagnosed with asthma. Those children whose parents reported that they had subsequently been diagnosed with asthma by age 6–7 years were considered to be incident cases of asthma over the 2 year time period. Information on potential risk factors for asthma was ascertained from data collected at baseline survey (age 4–5 years).

Results

One-fifth (21%) of children had been diagnosed with asthma by the age of 4–5 years. Among the remaining 79% of children with no ever diagnosed asthma, the overall incidence of asthma over the two year interval from the fifth to the seventh year of life was 4.1 per 100 person-years (Table 4.1).

Table 4.1: Incidence of asthma at age 6–7 years, kindergarten cohort

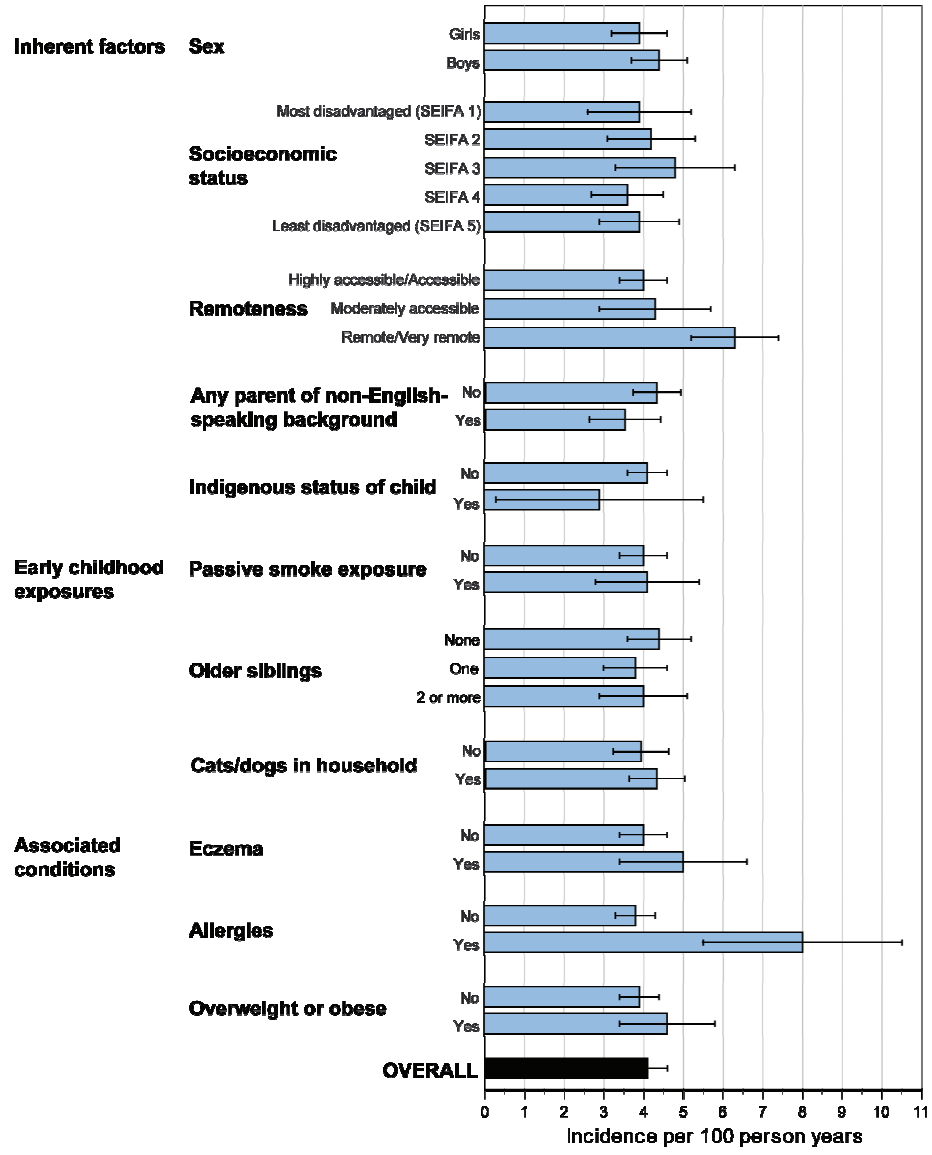
	Number of children at risk	Number of new cases[(a)]	Person-years	Incidence per 100 person-years[(b)]
Boys	1,700	155	3,536	4.4 (3.6–5.1)
Girls	1,818	140	3,785	3.9 (3.2–4.5)
Total	**3,518**	**295**	**7,321**	**4.1 (3.6–4.6)**

(a) 'Yes' to the question 'Has a doctor ever told you that child has asthma?' at 2 year follow-up but 'No' to the same question at baseline.

(b) Weighted to the Australian population aged 4 years as at March 2004.

Note: Numbers in parentheses indicate 95% confidence interval.

The incidence of asthma between the fifth and seventh years of life was highest among children whose parents reported they had 'food or other allergies' and those who lived in *Remote* or *Very remote* areas (Figure 4.1).



Note: Error bars indicate 95% confidence interval.

Figure 4.1: Incidence of asthma over 2 year follow-up among children in the kindergarten cohort, by various baseline risk factors

Associations between baseline risk factors and the incidence of asthma over the following two years were statistically significant for allergies and remoteness (Table 4.2) even after adjusting for all other factors (Figure 4.2). These characteristics remained as significant risk factors for the incidence of asthma even after adjusting for the presence of wheeze (not diagnosed as asthma) at 4–5 years (data not shown).

Table 4.2: Unadjusted odds ratios for the association of the incidence of asthma with the significant baseline risk factors, kindergarten cohort

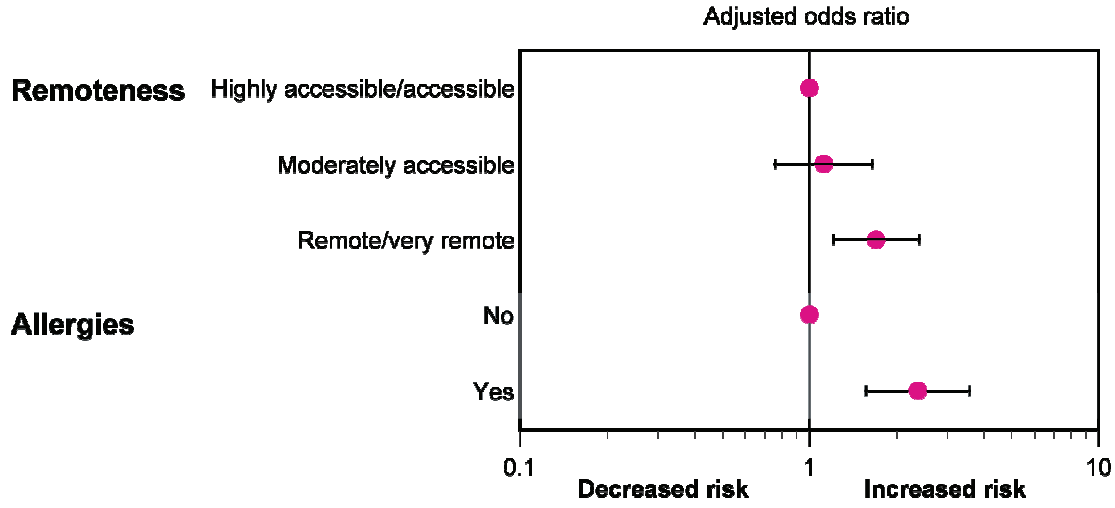
Baseline risk factor	No. children	No. cases	Odds ratio[(a)]	95% CI	p-value
INHERENT FACTORS					
Sex (n=3,518)					0.2815
Girls	1,818	140	1.00		
Boys	1,700	155	1.15	0.89–1.47	
SEIFA Index of relative socioeconomic disadvantage (n=3,518)					0.6620
SEIFA 1 (most disadvantaged)	698	56	1.02	0.65–1.61	
SEIFA 2	667	58	1.10	0.74–1.64	
SEIFA 3	702	67	1.26	0.82–1.94	
SEIFA 4	725	55	0.92	0.62–1.37	
SEIFA 5 (least disadvantaged)	726	59	1.00		
Remoteness of residence (n=3,486)					0.0078
Highly accessible/accessible	2,752	223	1.00		
Moderately accessible	592	51	1.11	0.75–1.62	
Remote/very remote	142	15	1.65	1.20–2.26	
Any parent of non-English speaking background (n=3,391)					0.1321
No	2,441	211	1.00		
Yes	950	67	0.80	0.60–1.07	
Indigenous status of child (n=3,516)					0.4228
Not Indigenous	3,407	289	1.00		
Indigenous	109	6	0.68	0.26–1.76	
EARLY CHILDHOOD EXPOSURES					
Passive smoke exposure (n=3,059)					0.8631
No	2,620	216	1.00		
Yes	439	37	1.03	0.71–1.51	
Older siblings (n=3,518)					0.5523
None	1,487	138	1.00		
1 older sibling	1,228	94	0.85	0.64–1.15	
2+ older siblings	803	63	0.89	0.62–1.27	
Cats or dogs in household (n=3,511)					0.3889
No	1,593	124	1.00		
Yes	1,918	169	1.12	0.86–1.47	

(continued)

Table 4.2 (continued): Unadjusted odds ratios for the association of the incidence of asthma with the significant baseline risk factors, kindergarten cohort

Baseline risk factor	No. children	No. cases	Odds ratio[(a)]	95% CI	p-value
OTHER CONDITIONS					
Eczema (n=3,518)					0.2108
No	3,121	254	1.00		
Yes	397	41	1.28	0.87–1.88	
Allergies (n=3,518)					<0.0001
No	3,278	256	1.00		
Yes	240	39	2.30	1.53–3.47	
Overweight/obese (n=3,490)					0.2366
No	2,803	225	1.00		
Yes	687	65	1.20	0.89–1.64	

(a) Weighted to the Australian population aged 4 years as at March 2004.



Note: See also Table A.4.

Figure 4.2: Independent baseline risk factors for wheeze or asthma by 2 year follow-up in the kindergarten cohort (n=3,518)

Discussion

We used follow-up data from the LSAC to determine the incidence of new asthma diagnoses between the fifth and the seventh years of life, and found that only allergies and remoteness of residence were independently associated with incidence over this period.

Our finding that children living in a *Remote* to *Very remote* area are at a substantially increased risk of developing asthma between the ages of 5 and 7 years should be treated with some caution. It should be noted that only a small number of children included in the cohort were from a *Remote* or *Very remote* area. Furthermore, this segment of the population was relatively under-represented in the cohort and may not be representative of all children

living in these areas. Hence, selection bias needs to be considered as one potential explanation for this finding.

Longitudinal studies have identified a strong relationship between allergy and the subsequent onset of asthma (Kotaniemi-Syrjanen et al. 2003; Tariq et al. 2000; Wahn 2000). In the kindergarten cohort of the LSAC, allergy was evaluated as a positive response to the question 'Does child have any of these ongoing problems?' and then by marking 'Food or other allergies'. This is comparable to the infant cohort in which parents were asked to report specifically on whether their infant had a food or digestive allergy by responding to the question 'Does child have any of these ongoing problems?' and then by marking 'Food or digestive allergies'. Therefore, children reported to have an allergy in the kindergarten cohort may be sensitive to a wide range of things including foods, but also grass, bee stings and other allergens. Our findings support a strong association between allergy and asthma in kindergarten-aged children. Children reported to have an allergy were twice as likely to develop asthma as children who were not reported as having an allergy. Evidence that allergy precedes the development of asthma during childhood is well documented and is often described as the 'atopic march' (Almqvist et al. 2007; Cantani 1999; Schroeder et al. 2009). Although we do not have objective evidence of the presence or absence of atopy, our finding that parent-reported food or other allergies at baseline was associated with a higher incidence of asthma over the 2 year follow-up period is consistent with these previous findings.

Eczema, an inflammatory condition of the skin that is most common in young children, often precedes the onset of asthma (Illi et al. 2004). The Tasmanian Longitudinal Health Study found that children with eczema were more likely to have asthma after the age of seven years (RR 1.98 95%; CI 1.63–2.40) (Burgess et al. 2008). This trend was consistent through preadolescence (Hazard Ratio (HR) 1.70; 95% CI 1.05–2.75), adolescence (HR 2.14; 95% CI 1.33–3.46) and adult life (HR 1.63; 95% CI 1.28–2.09). A recently published systematic review of the literature (van der Hulst et al. 2007) found that the presence of eczema doubled the risk of developing childhood asthma (OR 2.14; 95% CI 1.07–2.75). Eczema was not found to be an independent predictor of the development of asthma in kindergarten-age children in the LSAC cohort. There are two possible explanations for this. One is that eczema was associated with the onset of asthma before kindergarten-age, but not after this age. Another possibility is that parent-report of 'food or other allergies', which was associated with the onset of asthma, explains most of the effect that would otherwise be attributed to eczema.

Exposure to infection early in childhood is thought to reduce the risk of developing asthma (Doull 2001; Martinez & Holt 1999; Strachan 2000). Children exposed to other children, including siblings, are at greater risk of acquiring respiratory and other infections. The size of families has decreased significantly in developed countries (Hoffman 1975). In particular, the average household size in Australia has decreased steadily since the early 1960s (ABS 2008). The decrease in household size has largely been a result of families having fewer children. It has been hypothesised that the increased prevalence of asthma in developed countries is due to the loss of the protection provided by having a higher number of siblings in the household (Strachan 1997). However, a number of studies indicate that the decrease in family size does not sufficiently explain the dramatic increase in prevalence (Butland et al. 1997; Wickens et al. 1999). These studies were limited by their failure to take into consideration the effect of older siblings on the development of asthma. The hygiene hypothesis implies that the lower one's birth order, the more exposure they have to infections and bacteria from their older siblings and the less risk they have of developing asthma. There is empirical evidence to support this: the greater number of older siblings a child has the less likely they are to develop asthma (Seidman et al. 1991). However, we failed

to find a statistically significant association between the number of older siblings and the onset of asthma between ages five and seven years. It may be that the influence of this factor is manifest at any earlier age. If so, this should become apparent with further follow-up of the infant cohort.

Similarly, we did not find an association between pet ownership and the development of asthma. Pet allergy is strongly associated with the presence of asthma and thus it was formerly assumed that pet ownership increased the risk of pet allergy and consequently asthma (Simpson & Custovic 2003). However, most recent studies have shown the opposite, that is, ownership of certain pets, especially during infancy, can actually serve as a protective factor against childhood asthma (Hesselmar et al. 1999; Pohlabeln et al. 2007; Waser et al. 2005). A recent meta-analysis found no overall evidence that pet ownership is a protective factor for asthma in children. However, cat ownership was found to be associated with reduced risk of asthma (OR 0.72; 95% CI 0.55–0.93) (Takkouche et al. 2008). Evidently, the relationship between asthma and exposure to animals is complex.

Our analysis of 2 year follow-up data from the kindergarten cohort of the LSAC indicates that atopy may be the strongest predictor of the onset of asthma at this age.

5 Risk factors for the persistence of wheeze during childhood

Asthma has a variable natural history, with onset and remission occurring at any age. Longitudinal studies suggest that the pattern of asthma through childhood is a strong predictor of persistence (Martinez 2002a, 2002b). The Melbourne Epidemiological Study of Childhood Asthma found that the majority of 7 year olds who had persistent or severe asthma, continued to have asthma or experience wheezing at age 42 years (Robertson 2002). Remission only occurred in 29% of children with persistent asthma and 11% with severe asthma. Similarly, To and colleagues' (2007) Canadian study concluded that markers of severity predict the persistence of childhood asthma. They found that hospitalisation for asthma within 12 months of diagnosis tripled the risk of persistent asthma by age 12 years while at least 4 physician visits doubled the risk of persistent asthma at follow up. Hence, the pattern of asthma severity during childhood appears to be a reliable predictor of asthma outcomes.

Among children, the pattern of asthma is currently classified as infrequent intermittent, frequent intermittent, mild persistent, moderate persistent or severe persistent. Before 2006, a three level classification was used: persistent, frequent episodic and infrequent episodic. The majority of children with asthma in Australia had infrequent episodic asthma (76%), followed by frequent episodic asthma (18.6%), while just over 5% of children had persistent asthma, according to data from a random sample of GP consultations in 2006 (ACAM 2008; AIHW: Britt & Miller 2007). According to the studies described above, children with more severe symptoms may be more likely to experience the persistence of asthma during childhood. The ability to predict the persistence of asthma from the severity of symptoms would assist in reducing morbidity and mortality associated with childhood asthma.

Methods

Two year follow-up data from the LSAC kindergarten cohort were used to investigate risk factors for the persistence of wheeze during childhood. For this analysis the cohort was limited to children whose parents reported they had experienced wheeze in the preceding 12 months at baseline (age 4–5 years). Those whose parents reported that they had wheeze within the preceding 12 months at 2 year follow-up (age 6–7 years) were considered to have persistent wheeze during this time period. Others were considered to be in remission from wheeze. Information on potential risk factors for persistence and remission was ascertained from data collected at baseline survey (age 4–5 years).

Results

Overall, 44.3% of children with reported wheeze at baseline had persistent wheeze at age 6–7 years (Table 5.1). The proportion of children with persistent wheeze did not differ between boys and girls ($p = 0.74$).

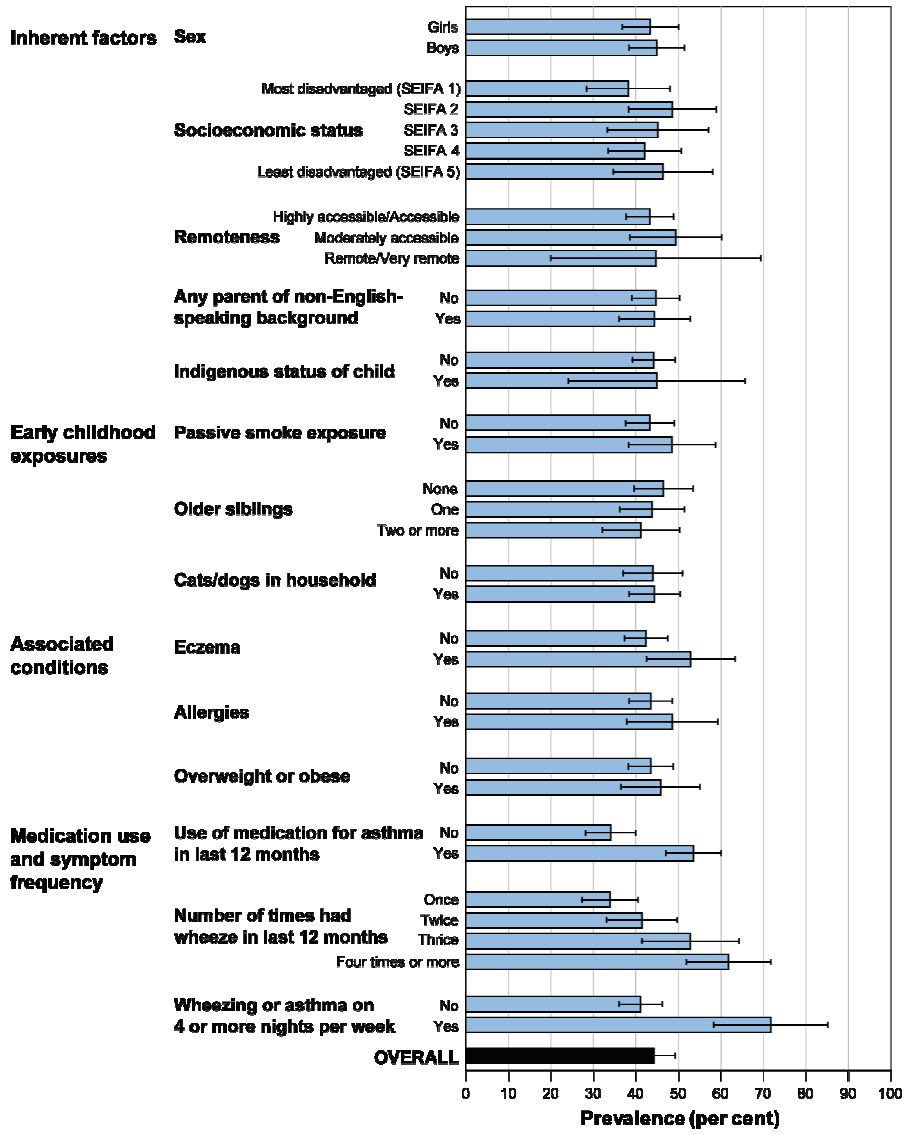
Table 5.1: Prevalence of persistence of wheezing at 2 year follow-up among children with wheeze at baseline, kindergarten cohort

	Number of children with wheeze at baseline	Number of persistent cases[(a)]	Proportion (per cent) with persistent wheeze (95% CI)[(b)]
Boys	371	162	44.9 (38.4–51.4)
Girls	271	113	43.4 (36.8–50.1)
Total	**642**	**275**	**44.3 (39.4–49.2)**

(a) 'Yes' to the question 'In the last 12 months, has child had an illness with wheezing in the chest which lasted for one week or more?'

(b) Weighted to the Australian population aged 4 years as at March 2004.

Persistence of wheeze at age 6–7 years was most common for children who reported disturbed sleep due to wheezing, use of medication for asthma, wheeze on greater than three occasions and eczema, in the 12 months preceding assessment at baseline (Figure 5.1).



Note: Error bars indicate 95% confidence interval.

Figure 5.1 Proportion of children with persistent wheeze among those aged 6–7 years with wheeze at baseline, by baseline risk factors, kindergarten cohort

Among children with wheeze at baseline, those with wheezing or asthma on 4 or more nights a week, those who had used medication for asthma in the last 12 months and those with greater than three occurrences of wheeze in the preceding 12 months were more likely to have persistence of wheeze at follow-up (Table 5.2).

Table 5.2: Risk factors for persistence of wheezing at age 6–7 years among those with wheeze at baseline, kindergarten cohort (univariate analysis)

Baseline risk factor	Number of children	Number of cases	Odds ratio[(a)]	95% CI	p-value
SYMPTOM FREQUENCY AND MEDICATION USE					
Wheezing or asthma on 4 or more nights a week (n=642)					0.0002
No	583	235	1.00		
Yes	59	40	3.62	1.82–7.20	
Use of medication for asthma in the last 12 months (n=638)					< 0.0001
No	303	96	1.00		
Yes	335	176	2.22	1.58–3.14	
Number of times had wheeze in the last 12 months (n=629)					< 0.0001
Once	238	75	1.00		
Twice	184	73	1.38	0.93–2.04	
Three times	96	52	2.18	1.27–3.74	
Four times or more	111	68	3.15	1.91–5.19	
INHERENT FACTORS					
Sex (n=642)					0.7433
Girls	271	113	1.00		
Boys	371	162	1.06	0.74–1.51	
Index of relative socioeconomic disadvantage (n=642)					0.6246
SEIFA 1 (most disadvantaged)	120	44	0.72	0.38–1.34	
SEIFA 2	143	66	1.09	0.58–2.04	
SEIFA 3	139	61	0.95	0.49–1.87	
SEIFA 4	121	50	0.84	0.47–1.51	
SEIFA 5 (least disadvantaged)	119	54	1.00		
Remoteness of residence (n=634)					0.6171
Highly accessible/accessible	496	210	1.00		
Moderately accessible	110	51	1.28	0.79–2.07	
Remote/very remote	28	11	1.06	0.38–2.93	
Any parent of non-English speaking background (n=620)					0.9522
No	467	204	1.00		
Yes	153	64	0.99	0.67–1.46	
Indigenous status of child (n=642)					0.9496
Not Indigenous	616	263	1.00		
Indigenous	26	12	1.03	0.44–2.41	

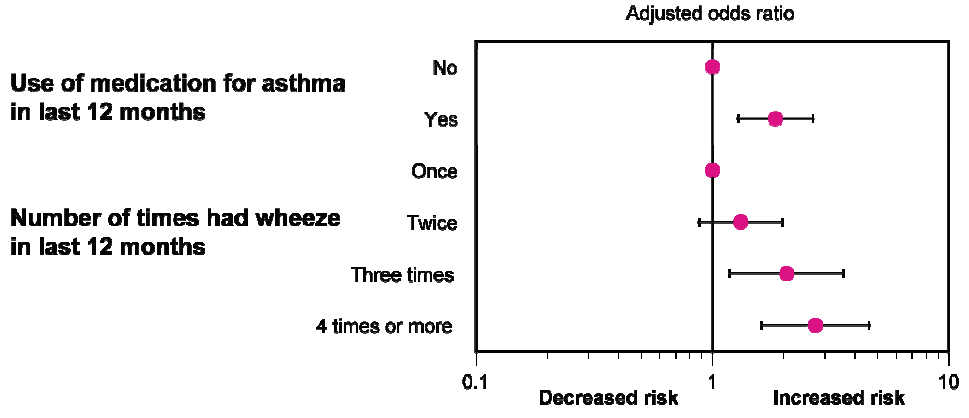
(continued)

Table 5.2 (continued): Risk factors for persistence of wheezing at age 6–7 years among those with wheeze at baseline, kindergarten cohort (univariate analysis)

Baseline risk factor	Number of children	Number of cases	Odds ratio[(a)]	95% CI	p-value
EARLY CHILDHOOD EXPOSURES					
Passive smoke exposure (n=562)					0.8476
No	486	209	1.00		
Yes	76	31	1.05	0.64–1.73	
Older siblings (n=642)					0.6112
None	263	120	1.00		
1 older sibling	240	99	0.90	0.60–1.34	
2+ older siblings	139	56	0.81	0.53–1.24	
Cats or dogs in household (n=642)					0.9289
No	259	111	1.00		
Yes	383	164	1.02	0.72–1.43	
OTHER CONDITIONS					
Eczema (n=642)					0.0598
No	517	213	1.00		
Yes	125	62	1.53	0.98–2.37	
Allergies (n=642)					0.3693
No	549	228	1.00		
Yes	93	47	1.23	0.79–1.92	
Overweight/obese (n=639)					0.3799
No	461	194	1.00		
Yes	101	46	1.23	0.77–1.97	

(a) Weighted to the Australian population aged 4 years as at March 2004.

Use of medication for asthma in the last 12 months and having more than three occurrences of wheeze in the 12 months preceding the baseline assessment were both independent risk factors for the persistence of wheeze at follow-up (Figure 5.2; Table A.6).



Note: See also Table A.6.

Figure 5.2: Independent baseline risk factors for persistence of wheeze by 2 year follow-up in the kindergarten cohort (n=3,518)

Discussion

We found that markers of severity at baseline were indicative of the persistence of wheeze at 2 year follow-up (age 6–7 years).

Several studies have attempted to chart the natural progression of asthma from childhood to adult life in order to examine the risk factors associated with the persistence of wheeze and asthma. The Dunedin Multidisciplinary Health and Development Study is a longitudinal study of 1,037 children born in Dunedin, New Zealand (Sears et al. 2003). Children were followed up from age 9–26 years. Evaluation at 26 years found that over one-quarter (26.9%) of the cohort had experienced either persistent wheezing from 9 years (14.5%) or had relapsed (12.4%). Predictors for persistence and relapse included sensitisation to house dust mites and cat allergen, airway hyperresponsiveness and lower lung function. An earlier age of onset was also found to be a risk factor for relapse. Similarly, an Australian study showed that the presence of atopy, airway hyperresponsiveness, and airflow obstruction at age 8 to 10 years were all independent predictors of the presence of symptoms of asthma at age 23 to 25 years (Toelle et al. 2004; Xuan et al. 2002). In summary, these studies demonstrate that, among primary school-age children with asthma, early onset of the disease, the presence of allergy (atopy), and objective evidence of abnormal airway function (either low lung function or airway hyperresponsiveness) foreshadow persistence of the condition into adult life. LSAC data extend these findings to an earlier period of life. They show that, in kindergarten-age children, the presence of symptoms severe enough to require use of treatment for asthma and the occurrence of more frequent episodes predict persistence of the symptoms over a 2 year period.

Markers of disease severity and of atopy are associated with a greater risk of having asthma and asthma-like symptoms persisting into late childhood. Although there are no established preventive interventions at present, when such interventions are available, allergic children with more severe and frequent symptoms will be the main target for implementation.

6 Use of health services and medication for asthma

Children with asthma use health services for a variety of reasons. These include visiting a general practitioner (GP) for routine review or the prescription of asthma medications, or, in the most extreme cases, admission to an emergency department for urgent management of exacerbations or hospitalisation.

Children under the age of 14 years are more likely than adults to visit a GP for asthma care (ACAM 2008). Of all GP encounters, the proportion of those related to asthma is largest among children aged between 5 and 14 years than at any other age.

Among children aged 0–14 years who visited a GP for their asthma between 2004 and 2007, 39% were prescribed inhaled corticosteroids (ICS) either alone or in combination with long-acting beta agonists (ACAM 2008). Few children were prescribed oral corticosteroids, which are used for management of severe exacerbations, and even fewer were prescribed the non-steroid preventers: leukotriene receptor antagonists or cromones.

Children have high rates of hospitalisation for asthma compared with adults (ACAM 2008), and those who live in areas of greater socioeconomic disadvantage have higher rates than those living in other areas. However, over recent years the number of children receiving hospital care for asthma and the duration of hospital stays for asthma care have decreased. Between 1993–94 and 2006–07 there was a 42% reduction in the rate of hospital admissions for asthma among children, and between 1998–99 and 2006–07 the average length of stay decreased by 24%.

Severe and poorly controlled asthma has important consequences for the child and the health-care system. Children with severe and inadequately controlled asthma are more likely to use emergency medical care or require hospital admission, compared with those who use an asthma action plan and properly administer medications.

The identification of factors associated with health service use in children would assist in the improvement of asthma management plans and, potentially, ease the burden on emergency departments and hospitals.

Methods

Two year follow-up data from the LSAC infant and kindergarten cohorts were used to examine the use of health services for asthma. Data on asthma medications dispensed to members of both cohorts, between the baseline and the 2 year follow-up surveys, were obtained from the PBS database.

Parent-report of medications used for asthma in the last 12 months was also examined using the follow-up survey. Data on hospitalisations for asthma among the kindergarten cohort were obtained from the parent-completed questionnaire at the follow-up survey. There were no data on hospitalisations for asthma in the infant cohort.

Results

Infants

Asthma medication use at 2 year follow-up

In their third year of life, 11.5% of the entire infant cohort and 30.0% of those with parent-reported wheeze or asthma had used asthma medications in the last 12 months (Table 6.1). Among infants who had wheeze or ever diagnosed asthma at age 2–3 years, 10% had used preventer medications (ICS, cromones and/or leukotriene receptor antagonists) at least once during the 2 year period between baseline and follow-up.

Table 6.1: Prevalence[(a)] of asthma medication use at age 2–3 years, infant cohort

	Infants with parent-reported wheeze or asthma at age 2–3 years		All children	
Type of asthma medication and source of information	**Number of children**	**Prevalence per 100 children at risk[(a)] (95% CI)**	**Number of children**	**Prevalence per 100 children at risk[(a)] (95% CI)**
Number of children at risk	1,691		4,606	
Information collected from PBS linked data for medications[(b)] dispensed between baseline and 2 year follow-up				
Any ICS	140	8.7 (7.1–10.2)	156	3.7 (3.1–4.4)
ICS alone	76	5.4 (4.1–6.8)	82	2.2 (1.7–2.8)
ICS in combination with long-acting beta agonists (LABA)	72	3.9 (2.9–4.9)	83	1.8 (1.3–2.2)
Cromones	2	0.1 (0.0–0.4)	5	0.1 (0.0–0.3)
Leukotriene Receptor Antagonists	30	1.6 (1.0–2.1)	31	0.6 (0.4–0.9)
Any of the above medications	167	10.1 (8.5–11.8)	187	4.4 (3.7–5.1)
Information collected at 2 year follow-up from questionnaire				
Medication for asthma in last 12 months	501	30.0 (28.0–32.1)	501	11.5 (10.5–12.6)

(a) Weighted to the Australian population aged 0–1 years as at March 2004.

(b) Does not include over-the-counter items and items that cost less than the general patient copayment, in particular short-acting beta agonists (such as Ventolin) and Prednisone.

Kindergarten cohort

Asthma medication use at 2 year follow-up

In their seventh year of life, 15.5% of the entire kindergarten cohort and 43.5% of those who had parent-reported wheeze or asthma at age 4–5 years had used medication for asthma in the last 12 months, as reported by a parent (Table 6.2). Twenty-two per cent of those who had wheeze or asthma at age 4–5 years had used preventer medications (inhaled corticosteroids, leukotriene receptor antagonists, or cromones) at least once during the 2 year period between baseline and the follow-up.

Table 6.2: Prevalence[a] of asthma medication use at age 6–7 years, kindergarten cohort

Type of asthma medication and source of information	Children with parent-reported wheeze or asthma at baseline: Number of children	Children with parent-reported wheeze or asthma at baseline: Prevalence per 100 children at risk[a] (95% CI)	All children: Number of children	All children: Prevalence per 100 children at risk[a] (95% CI)
Number of children at risk	1,202		4,464	
Information collected from PBS linked data for medications[b] dispensed between baseline and 2 year follow-up				
Any inhaled corticosteroids (ICS)	234	19.3 (17.0–21.7)	319	7.2 (6.4–8.0)
ICS alone	98	8.4 (6.6–10.2)	122	2.8 (2.3–3.4)
ICS in combination with long-acting beta agonists (LABA)	157	12.5 (10.6–14.4)	219	4.8 (4.2–5.5)
Cromones	7	0.4 (0.1–0.8)	13	0.3 (0.1–0.4)
Leukotriene Receptor Antagonists	56	4.4 (3.1–5.7)	69	1.5 (1.1–1.9)
Any of the above medications	268	22.2 (19.5–24.8)	370	8.3 (7.5–9.2)
Information collected at 2 year follow-up from questionnaire				
Medication for asthma in last 12 months	524	43.5 (40.1–46.8)	685	15.5 (14.1–16.8)

(a) Weighted to the Australian population aged 4 years as at March 2004.

(b) Does not include over-the-counter items and items that cost less than the general patient copayment, in particular short-acting beta-agonists (such as Ventolin) and Prednisone.

Hospitalisation for asthma at 2 year follow-up

Among children who had parent-reported wheeze or asthma at age 4–5 years, 2.2% (95% CI 1.3–3.2) had been admitted to hospital for asthma in the 12 months preceding the 2 year follow-up assessment (data not shown).

Frequent asthma symptoms and medication use

Of the 1,202 children who had parent-reported wheeze or asthma at age 4–5 years, 11% had frequent symptoms at age 6–7 years (Table 6.3). As expected, children with frequent symptoms at 2 year follow-up had higher rates of asthma medication use than those with infrequent or no symptoms (Table 6.4).

Table 6.3: Asthma symptoms at age 6–7 years among children with parent-reported wheeze or asthma at age 4–5 years, kindergarten cohort

Frequency of asthma symptoms[a]	Number of children	Per cent (95% CI)
Infrequent or no symptoms	1,082	89.2 (87.2–91.1)
Frequent symptoms	120	10.8 (8.9–12.8)
Total	**1,202**	**100.0**

(a) Frequency of asthma symptoms defined by number of times in last 12 months that child had wheezing that lasted for at least 1 week: 0–2 times = Infrequent or no symptoms; 3+ times = Frequent symptoms.

Table 6.4: Prevalence[a] of asthma medication use at age 6–7 years by frequency of symptoms among children with parent-reported wheeze or asthma at age 4–5 years, kindergarten cohort

	Infrequent or no symptoms		Frequent symptoms	
Type of asthma medication and source of information	Number of children	Prevalence per 100 children at risk[a] (95% CI)	Number of children	Prevalence per 100 children at risk[a] (95% CI)
Number of children at risk	1,082		120	
Information collected from PBS linked data for medications[b] dispensed between baseline and 2 year follow-up				
Any inhaled corticosteroids (ICS)	179	16.2 (13.7–18.6)	55	45.1 (36.1–54.1)
ICS alone	75	6.9 (5.2–8.6)	23	20.5 (12.8–28.2)
ICS in combination with long-acting beta agonists (LABA)	119	10.4 (8.5–12.3)	38	29.9 (21.0–38.7)
Cromones	5	0.3 (0.0–0.7)	2	1.3 (0.0–3.1)
Leukotriene Receptor Antagonists	44	4.0 (2.6–5.4)	12	8.0 (2.9–13.1)
Any of the above medications	208	19.0 (16.2–21.8)	60	48.1 (38.7–57.5)
Information collected at 2 year follow-up from questionnaire				
Medication for asthma in last 12 months	426	38.8 (35.4–42.2)	98	81.8 (74.7–88.9)

(a) Weighted to the Australian population aged 4 years as at March 2004.

(b) Does not include over-the-counter items and items that cost less than the general patient copayment, in particular short-acting beta agonists (such as Ventolin) and Prednisone.

Frequent asthma symptoms and hospitalisation for asthma

Among children with parent-reported wheeze or asthma at age 4–5 years, those who had frequent symptoms at the follow-up assessment were more likely to have been hospitalised for asthma in the preceding 12 months (10.6% (95% CI 4.5–16.7)) than those with infrequent or no symptoms at the follow-up assessment (1.2% (95% CI 0.5–1.9)) (data not shown).

Discussion

Questionnaire data from parents showed that only 30% of infants with wheeze or asthma at age 2–3 years had used any medication for their condition in the last 12 months. This is consistent with the findings of others (Beimfohr et al. 2001). It seems likely that in many cases the symptoms of wheeze among infants and young toddlers did not require treatment. However, there may be some variation in the practice of prescribing asthma medications for children under the age of 6 years (Zuidgeest et al. 2009).

According to information from PBS linked data, most of the medications that were prescribed at this age were not 'preventer' medications. Only 10% of infants with parent-reported wheeze or asthma had filled a script for either ICS (alone or in combination with LABA), cromones or leukotriene receptor antagonists. This is equivalent to approximately one-third of children whose parents reported medication use via questionnaire. These findings reflect the fact that most wheezing illness in infants does not require treatment with this class of medications. Among infants, inhaled bronchodilators are recommended for short-term treatment of virus-associated episodic wheeze (Eigen 2008). The National Asthma Council (NAC) recommends the prescription of short-acting beta agonists (SABA) for all children with symptomatic asthma as a reliever therapy (NAC 2006). Although we cannot directly measure SABA use with the PBS dataset (because most of it is purchased over-the-

counter), our findings suggest that up to two-thirds of medication use reported by parents were SABAs.

Among children in the kindergarten cohort with wheeze or asthma at 4–5 years, parents reported that 43.5% had taken asthma medication in the 12 months preceding 2 year follow-up. It is possible that some of the children with initial parent-reported wheeze or asthma had become asymptomatic or had gone into remission by follow-up. Alternatively, some parents may have forgotten about medication used to treat asthma symptoms during the early part of the 12 months preceding follow-up. The PBS data analysis revealed that 22% of those with parent-reported wheeze or asthma at baseline used ICS, cromones or leukotriene receptor antagonists, at least once during the follow-up period. This is equivalent to approximately 50% of children with parent-reported medication use. Since bronchodilators, such as Ventolin, are the only other commonly used medication for asthma, it is likely that most of the remaining 50% of children were using bronchodilator alone. Another possibility is that some of the parent-reported data represents over-the-counter medication used for asthma, PBS listed items that are privately funded and items that cost less than the general patient copayment.

A comparison of the infant and kindergarten cohort demonstrates that there is a reduction in the use of SABA without 'preventer' medications between infancy and the kindergarten age. This is consistent with current asthma guidelines, which recommend that young children do not require long-term preventive medication and that a stepwise approach to drug therapy should be implemented in symptomatic children (NAC 2006). Infants are more likely to be prescribed SABA alone to deal with exacerbations, which are usually related to a viral respiratory tract infection, while older children are more likely to be prescribed preventer medications in response to the natural progression of their illness.

At 2 year follow-up, 161 children from the kindergarten cohort who were asymptomatic at baseline (4.9%) had taken asthma medication in the previous 12 months (data not shown). A majority of these cases will have been new asthma cases, although some may have been prescribed this medication for viral respiratory tract infections.

Nearly half of the hospitalisations for asthma within the kindergarten cohort occurred in children who had not reported symptoms or been diagnosed with asthma at the time of the baseline survey (data not shown). In other words, in these children hospitalisation occurred at, or soon after, the time of initial diagnosis. This early childhood period represents a time of relatively high incidence rates for asthma. These data imply that hospitalisation often occurs early in the course of the illness.

Nearly 20% of children with frequent asthma symptoms were reported not to be taking medications for asthma, and over half were not taking preventer medications. We would expect that all such children with frequent symptoms would have been receiving asthma medication. It is possible that either medication use or frequency of symptoms was incorrectly reported for these children. However, it is also possible that this apparent under-treatment may have contributed to the fact that 10.6% of those reporting frequent symptoms at 2 year follow-up also reported that their child had been hospitalised for asthma during the same period. In summary, we have found evidence to suggest that asthma and asthma symptoms are under-treated among a small group of children with frequent symptoms. This may have led to poorer outcomes, including higher rates of hospitalisation.

7 Outcomes for children with wheeze or asthma

Children with asthma experience poorer health outcomes than other children. As discussed in *Chapter 5*, children with asthma are more likely to be hospitalised or visit an emergency department. However, asthma may also affect a child's quality of life. Sleeping patterns (Strunk et al. 2002), absenteeism (van Gent et al. 2007b), weight (Bender et al. 2007; van Gent et al. 2007a) and height (Falliers et al. 1963; Helms 2001) have been shown to be adversely affected by asthma.

In this chapter we have quantified the impact of parent-reported wheeze or asthma in 4–5 year old children on health outcomes over the ensuing two years.

Methods

Two year follow-up data from the LSAC kindergarten cohort were used to examine health outcomes. At baseline, the kindergarten cohort was classified as having or not having parent-reported wheeze or asthma. Outcomes were ascertained at the 2 year follow-up. Rate ratios and PAF were estimated, as described in *Chapter 1*. The PAF represents the proportion of cases of an adverse health outcome that would be avoided if none of the cohort had the risk factor; in this case wheeze or asthma at baseline.

The estimation of PAF requires information on the proportion of the population exposed to the risk factor. In this case, that is the prevalence of wheeze or ever diagnosed asthma at baseline, and the relative risk (or rate ratio) (RR) for the association between the exposure and the health outcome.

Results

The prevalence of wheeze or ever diagnosed asthma among 4–5 year olds was 28% (Table 7.1).

Table 7.1: Prevalence of wheeze or ever diagnosed asthma at 4–5 years, kindergarten cohort

	Number of children	Per cent[(a)] (95% CI)
No	3,243	71.8 (70.2–73.4)
Yes	1,202	27.7 (26.2–29.3)
Don't know	19	0.5 (0.3–0.7)
Total	**4,464**	**100.0**

(a) Weighted to the Australian population aged 4 years as at March 2004.

Table 7.2 shows the RR and PAF of wheeze or ever diagnosed asthma for each of the health outcomes. At age 6–7 years, children who had wheeze or ever diagnosed asthma at age 4–5 years were twice as likely as those without to have been hospitalised in the last 12 months; to have had 13 or more GP visits in the last 2 years; and to report fair or poor health status.

Wheeze or asthma at baseline accounted for approximately 25% of each of these outcomes at a population level.

Analysis of the linked MBS data showed that children in the kindergarten cohort visited a GP an average of 6.4 times over the 2 year follow-up period (data not shown). The average number of GP visits among children who had wheeze or ever diagnosed asthma at baseline was significantly higher (8.1 visits; 95% CI 7.7–8.6) than among those with no wheeze or ever diagnosed asthma at baseline (5.7 visits; 95% CI 5.5–6.0).

Table 7.2: Outcomes at age 6–7 years among children with and without parent-reported wheeze or asthma at age 4–5 years, kindergarten cohort

	Children aged 6–7 years who had wheeze or asthma at age 4–5 years		Children aged 6–7 years who did not have wheeze or asthma at age 4–5 years		Relative Risk (RR) of outcome for children aged 6–7 years who had wheeze or asthma at age 4–5 years		Impact on outcome of having wheeze or asthma at age 4–5 years
	Number of children	Per cent of those at risk[a] (1,202)	Number of children	Per cent of those at risk[a] (3,243)	RR[b]	95% CI RR	PAF%[c]
Hospitalisation for any reason in last 12 months	93	8.1	120	3.9	2.09	1.52–2.88	23.2
Emergency department visit in last 12 months	170	13.6	355	10.3	1.33	1.08–1.62	8.3
13 or more GP visits in last 2 years[d]	236	21.4	280	10.1	2.12	1.75–2.57	23.7
Fair or Poor health status	41	4.0	53	1.9	2.18	1.34–3.53	24.6
Child's sleeping pattern is a moderate or large problem for parent	89	7.9	164	5.5	1.44	1.04–1.97	10.8
Absence from school							
1 or more days in last 4 weeks	606	51.3	1,516	47.4	1.08	1.00–1.17	2.2
2 or more days (75% percentile) in last 4 weeks	335	29.2	815	25.8	1.13	1.01–1.27	3.4
4 or more days (90th percentile) in last 4 weeks	135	12.0	307	9.4	1.27	1.03–1.57	7.1
Overweight or obese	260	23.1	562	18.1	1.28	1.09–1.50	7.2
Overweight or obese at age 6–7 years among children who were not overweight or obese at age 4–5 years	67	8.5 (925 children at risk)	148	6.1 (2,620 children at risk)	1.40	1.03–1. 90	9.6
Shorter than median height for age	464	39.7	1,334	41.9	0.95	0.87–1.04	..

(a) Weighted to the Australian population aged 4 years as at March 2004.

(b) Prevalence of outcome among children with wheeze or ever doctor diagnosed asthma at age 4–5 years compared to prevalence among those with no wheeze or ever doctor diagnosed asthma at age 4–5 years.

(c) Based on the 28% prevalence of wheeze or ever doctor diagnosed asthma at age 4–5 years.

(d) Based on MBS linked data.

Note
PAF=Population Attributable Fraction
RR=Relative risk
.. = not applicable.

Discussion

Childhood asthma is common. Children with asthma or asthma symptoms are more likely to have poorer health outcomes, such as being hospitalised, being admitted to an emergency department, visiting a GP more often and reporting poorer health status, than other children. Although the association between asthma and health outcomes is only modest, the high prevalence of the condition means that it is a big contributor, at a population level, to adverse health outcomes in children.

GP visits, hospitalisation and sleep disturbances can lead to increased school absenteeism, resulting in poor grades and decreased physical activity which may affect a child's emotional state, behaviour and weight (Blackman & Gurka 2007; van Gent et al. 2007b).

Children with asthma are more likely than other children to have disturbed sleep. Within a 28-day screening period, 33.7% of children in the Childhood Asthma Management Program (CAMP) experienced one or more nocturnal awakenings due to asthma (Strunk et al. 2002). Awakenings were more common among children with mild to severe asthma. We found that moderate to severe sleep disturbance was 1.44 times more prevalent among children with wheeze or asthma at age 4–5 years, compared to those without wheeze or asthma at the same age. Furthermore, 11% of sleep disturbance was attributed to wheeze or asthma at age 4–5 years. Sleep disturbance is an important cause of poor health outcomes attributable to asthma in children (Martin 1990; Miller B D & Strunk 1989).

Nocturnal asthma is strongly associated with increased absenteeism from school (Diette et al. 2000; Silverstein et al. 2001). Our results show a linear increase in the number of days absent from school at age 6–7 years, as a function of wheeze or ever diagnosed asthma at age 4–5 years. Absenteeism from school has been shown to result in poorer school performance and increased work absenteeism among parents with caring responsibilities (Blackman & Gurka 2007; Schmier et al. 2007).

There are worldwide epidemics of obesity and asthma, especially among children. The similar aetiology of each disorder has led to speculation about a link between them (Tantisira & Weiss 2001; Weiss & Shore 2004). In addition, children with asthma are limited in their ability to participate in daily activities like sports and other physical games, suggesting that asthmatic children may have an increasingly sedentary lifestyle, to prevent exacerbations (Schmier et al. 2007). Cross-sectional studies have demonstrated an association between asthma and obesity, however they are unable to examine the direction of the relationship (Bender et al. 2007; Shaheen et al. 1999; von Mutius et al. 2001). On the other hand, longitudinal studies have been able to demonstrate that obesity may precede the development of asthma (Camargo et al. 1999; Weiss & Shore 2004). Our data lend some support to an association in the opposite direction. In LSAC, wheeze or asthma reported at age 4–5 years was associated with an increased risk of overweight or obesity at age 6–7 years (RR 1.28, 95% CI 1.09–1.50), even if they were not overweight or obese at the time of the baseline survey (RR 1.40, 95% CI 1.03 to 1.90). Hence, there is a link between asthma and obesity in children. The mechanism underlying it is unknown. It may operate in both directions.

There has been concern about the effect of inhaled or oral steroids on growth in children with asthma (Guilbert et al. 2006; Allen et al. 1994). The LSAC did not find evidence of any negative impact of asthma on height. The limitation to our results is that not all children with parent-reported wheeze or asthma at age 4–5 years will have received treatment.

Our results demonstrate that poorer health outcomes at age 6–7 years can be predicted from the experience of asthma or asthma symptoms at age 4–5 years. Although the impact for individual children is relatively small, the impact at population level is substantial, simply because asthma is such a common condition.

8 Conclusions

Summary of findings

- The development of wheeze or asthma in early life is associated with factors that have been linked, directly or indirectly, to reduced airway function. These include exposure to tobacco smoke, being male, child care attendance, presence of older siblings, maternal age, gestational age and admission to NICU.
- Longer duration of breastfeeding within the first 12 months of life is associated with a reduced risk of wheeze or asthma during infancy.
- Parent-reported food or other allergies in early childhood and remoteness of residence are independent risk factors for the development of asthma between the ages of 4–5 years and 6–7 years.
- Children with wheeze at kindergarten age are more likely to have persistence of this symptom over the next two years, if they have more severe symptoms and/or if they have had eczema.
- More kindergarten-aged children than infants are taking preventer medications.
- Nearly 20% of children aged 6–7 years with frequent asthma symptoms were reported not to be taking medications for asthma and over half were not taking preventer medications.
- Having wheeze or asthma at age 4–5 years doubled the risk of hospitalisation or frequent general practice visits *for any cause* and of reporting fair to poor health status over the next 2 years. At a population level, it accounts for over 20% of each of these outcomes in children aged 6–7 years.

Some limitations of LSAC

Growing Up in Australia is a broad, multidisciplinary study that has been developed to examine the impact of Australia's unique social, economic and cultural environment on the next generation, particularly in regard to issues of policy relevance. While every effort was taken to ensure the methodological strengths of the study data, there are some weaknesses that must be acknowledged in our presentation of the results.

The LSAC used the Medicare register as a sampling frame on the premise that it is the most comprehensive database of Australia's population. This sample design was selected as its major strength is its representativeness of the general population. In theory, every Australian child is on the Medicare register and therefore each child of relevant age would have had an equal chance of being selected for the study. In practice, the LSAC sample excluded infants and children who were living in very remote areas, due to the excessive costs associated with their inclusion (Hunter 2008). As many of the people living in these very remote areas are Aboriginal and Torres Strait Islander Australians, they are under-represented in the LSAC sample. Furthermore, Indigenous communities in remote areas were specifically excluded from the study, and the survey questions and instruments used to collect information for the LSAC may not be sensitive to the unique cultural and social life of Aboriginal and Torres

Strait Islander children (Hunter 2008). These factors mean that LSAC is not a reliable source of health, social and cultural information about remote Indigenous populations. To respond appropriately to the diverse circumstances faced by Aboriginal and Torres Strait Islander children, FaHCSIA has funded a parallel study, Footprints in Time—The Longitudinal Study of Indigenous Children (LSIC). Similar to the LSAC, the LSIC is collecting important information on health, culture, education, housing and family relationships from a truly representative Indigenous sample.

The initial sample from the Medicare enrolments database included 9,259 children aged 0–1 years (infant cohort) and 10,275 children aged 4–5 years (kindergarten cohort). The initial response rates for the infant and kindergarten cohort were 57% and 50%, respectively. The main reasons for non-participation in the baseline surveys were refusal and non-contact because a PO Box address had been supplied or families had changed address. Mothers who had not completed year 12 at school or who spoke a language other than English were more likely to refuse to participate in LSAC (Soloff et al. 2006). Other differences have also been reported (FaHCSIA: Wake et al. 2008). To some extent the resultant selection bias was addressed by weighting to the sociodemographic distribution of the Australian population. However, the effect of other, unmeasured differences between respondents and non-respondents cannot be adjusted for, and the overall low participation rate does increase the risk of uncorrected selection bias.

There is often a large disparity between parents' and general practitioners' interpretation of wheeze and other symptoms related to asthma (Mellis 2009). A major weakness of the LSAC is the dependence on parents as the primary study informants. In particular, the LSAC depends on parent-reported wheeze and parent-reported doctor diagnoses of asthma. Although studies have shown that self-reported wheeze in adults is a valid measure, parent-reported wheeze has serious limitations. Findings from a hospital-based observational study of children aged between 4 months and 15 years showed less than 50% agreement between clinician diagnosed wheeze and parent-report of wheeze (Cane et al. 2000). There are also substantial problems associated with parents reporting on doctor diagnosed asthma. Zuidgeest et al. (2008) surmised that parent-reported doctor diagnosed asthma, taken from questionnaire data, over-estimated asthma compared with GP records. On the other hand, another study indicated that parents under-reported asthma status (Yoo et al. 2007). In the LSAC's kindergarten cohort, we found that 20% of parents, who had indicated that their child had 'ever' been diagnosed with asthma at baseline, did not report 'ever asthma' at 2 year follow-up, indicating poor recall. This has been noted in previous studies (Peat et al. 1992) and may reflect a change in the child's health and the level of parental concern.

A family history of asthma is one of the strongest risk factors for the development of childhood asthma (Kurukulaaratchy et al. 2003; Wahn 2000). Unfortunately, the LSAC did not collect data on parental history of asthma or atopic disease. We were, therefore, unable to analyse the direct impact of family history on the development of wheeze or asthma in offspring and the differential effect of paternal and maternal asthma. In our analysis, we used the maternal use of asthma medication variable as a marker of maternal asthma. However, there are limitations associated with using this variable from which to infer maternal asthma. It is uncertain whether the use of asthma medication during pregnancy was due to a pre-existing long-term condition or whether symptoms were related to the pregnancy. It is also possible that mothers who indicated asthma medication use during pregnancy may have bought over-the-counter medications and have never had a physician diagnose them with asthma.

A further limitation, inherent in all questionnaire-based studies such as LSAC, is the absence of any objective data; in particular, on atopy and lung function. Both of these are central to the diagnosis of asthma and the assessment of severity. In this report, we have cited data from studies that have measured these attributes objectively, in order to supplement the LSAC data where this was appropriate.

Finally, information on medication use derived from the PBS data is not comprehensive. This is because over-the-counter items and items that cost less than the general patient copayment, such as short-acting beta agonists (Ventolin™) and oral steroids (prednisone) are not routinely recorded in the PBS dataset.

Further study

The analysis of baseline and 2 year follow-up data presented in this report has provided insight into many aspects of asthma and the development of asthma in infants and young children. Data collection for Growing up in Australia: the LSAC will continue until 2010 and possibly beyond this time. It will be important to analyse future waves of LSAC data to investigate the rates of remission and persistence for infants who were reported as having developed wheeze or asthma at the 2 year follow-up. This will enable us to differentiate the risk factors associated with transient wheeze from those that indicate a predisposition to chronic asthma. In addition, future waves of data from the kindergarten cohort will help to identify the risk factors associated with asthma that persists into late childhood.

Conclusion

LSAC provides valuable insights into the incidence, natural history, and outcomes of asthma in children. The concurrent follow-up of the two cohorts starting at different ages, will, over time, allow valuable information to be acquired over the full span of childhood. This initial analysis has demonstrated the important differences between wheezing illness in infancy and wheezing illness in kindergarten-aged children, both in the nature of the disease and in the risk factors for the disease. It has also highlighted the importance of wheezing illness, a very common disorder, as a contributor to a range of important adverse health outcomes in the kindergarten-age cohort. Further study of this cohort will expand our knowledge about asthma and related problems in children.

Appendix 1: Statistical tables

Table A.1: Number of infants at risk at start of follow-up and crude cumulative incidence of wheeze or asthma at age 0–1 and 2–3 years, according to different baseline risk factors, infant cohort

Baseline risk factor	n (% of total)[(a)]	Incidence per 100 person-years (95% CI)
Total	**4,584**	**16.9 (16.1–17.6)**
INHERENT FACTORS		
Sex		
Girls	2,240 (48.9)	15.4 (14.4–16.4)
Boys	2,344 (51.1)	18.3 (17.2–19.3)
Maternal age		
<25 years	664 (14.5)	20.9 (18.9–22.9)
25–29 years	1,194 (26.1)	17.5 (16.2–18.8)
30–34 years	1,741 (38.1)	15.3 (14.2–16.4)
35 years and over	970 (21.2)	15.2 (13.8–16.7)
Maternal asthma		
None	4,238 (92.9)	16.3 (15.5–17.0)
Yes	323 (7.1)	24.4 (21.9–26.8)
SEIFA Index of relative socioeconomic disadvantage		
Most disadvantaged	883 (19.3)	19.2 (17.9–20.4)
SEIFA 2	842 (18.4)	18.0 (16.5–19.5)
SEIFA 3	940 (20.5)	15.6 (14.0–17.3)
SEIFA 4	1,001 (21.8)	17.0 (15.4–18.6)
Least disadvantaged	918 (20.0)	14.2 (12.7–15.6)
Remoteness of residence		
Highly accessible	2,520 (55.6)	16.8 (15.8–17.8)
Accessible	1,067 (23.5)	16.7 (15.3–18.1)
Moderately accessible	749 (16.5)	16.6 (14.7–18.5)
Remote/Very remote	195 (4.3)	18.3 (16.0–20.6)
Any parent of non-English-speaking background		
No	3,505 (79.0)	16.4 (15.6–17.2)
Yes	930 (21.0)	18.4 (16.8–20.0)
Indigenous status of child		
No	4,404 (96.1)	16.5 (15.8–17.3)
Yes	180 (3.9)	23.0 (19.7–26.3)

(continued)

Table A.1 (continued): Number of infants at risk at start of follow-up and crude cumulative incidence of wheeze or asthma at age 0–1 and 2–3 years, according to different baseline risk factors, infant cohort

Baseline risk factor	n (% of total)[(a)]	Incidence per 100 person-years
PRENATAL AND POSTNATAL FACTORS		
Mother smoked during pregnancy		
No	3,319 (84.1)	14.9 (14.2–15.7)
Yes	628 (15.9)	22.5 (20.6–24.3)
Caesarean birth		
No	3,207 (70.0)	16.6 (15.8–17.5)
Yes	1,376 (30.0)	17.4 (16.2–18.6)
Gestational age		
Very early (20–32 weeks)	71 (1.6)	24.2 (19.6–28.8)
Pre-term (33–36 weeks)	220 (4.8)	21.3 (18.0–24.7)
Term (37–41 weeks)	4,079 (89.1)	16.6 (15.8–17.3)
Late (42+ weeks)	207 (4.5)	15.2 (12.0–18.3)
Child's birthweight		
Not low birthweight	4,334 (95.1)	16.6 (15.9–17.4)
Low birthweight	224 (4.9)	19.7 (16.9–22.5)
Use of Neonatal Intensive Care Unit after birth		
No	3,822 (83.4)	16.3 (15.5–17.1)
Yes	758 (16.6)	19.8 (18.2–21.4)
Any breastfeeding		
No	352 (7.7)	22.1 (19.5–24.6)
Less than 2 months	912 (19.9)	20.0 (18.4–21.6)
Between 2 and 4 months	602 (13.1)	18.1 (16.3–20.0)
Between 4 and 6 months	466 (10.2)	16.6 (14.6–18.6)
Between 6 and 12 months	1,252 (27.3)	14.1 (12.9–15.3)
More than 12 months	994 (21.7)	13.8 (12.4–15.1)
EARLY CHILDHOOD EXPOSURES		
Passive smoke exposure (postnatal)		
No	3,605 (89.1)	15.5 (14.8–16.3)
Yes	439 (10.9)	21.1 (18.8–23.3)
Older siblings		
None	1,884 (41.1)	15.6 (14.5–16.7)
Yes	2,700 (58.9)	17.7 (16.8–18.6)
Pets (cats or dogs) in household		
No	2,806 (61.4)	16.8 (15.9–17.7)
Yes	1,767 (38.6)	17.0 (15.8–18.1)
Use of child care		
No	2,790 (60.9)	16.6 (15.7–17.6)
Yes	1,794 (39.1)	17.2 (16.1–18.3)

(a) The total of counts for each level of the risk factor does not add up to total n=4,584 due to missing values.

Table A.2: Independent baseline risk factors for wheeze or asthma by 2 year follow-up in the infant cohort (multivariable analysis, n=3,913)

Baseline risk factor	Adjusted odds ratio	95% CI	Overall p-value
INHERENT FACTORS			
Sex			0.0016
Girls	1.00		
Boys	1.25	1.09–1.44	
Maternal age			0.0046
< 25 years	1.57	1.18–2.08	
25–29 years	1.24	0.99–1.54	
30–34 years	1.08	0.87–1.33	
35 years & over	1.00		
Maternal asthma			<0.0001
No	1.00		
Yes	1.80	1.39–2.35	
At least one parent from a non-English speaking background			0.0219
No	1.00		
Yes	1.23	1.03–1.46	
PRENATAL AND POSTNATAL FACTORS			
Mother smoked during pregnancy			<0.0001
No	1.00		
Yes	1.71	1.42–2.06	
Gestational age			0.0787
Very early (20–32 weeks)	1.97	1.08–3.59	
Pre-term (33–36 weeks)	1.21	0.86–1.70	
Term (37–41 weeks)	1.00		
Late (42+ weeks)	0.80	0.55–1.16	
Neonatal Intensive Care Unit after birth			0.0085
No	1.00		
Yes	1.32	1.07–1.63	
Any breastfeeding			<0.0001
Not breastfed	1.00		
Less than 2 months	0.90	0.64–1.23	
2 to 4 months	0.73	0.53–1.00	
5 to 6 months	0.67	0.47–0.96	
7 to 12 months	0.59	0.43–0.80	
More than 12 months	0.56	0.41–0.78	
EARLY CHILDHOOD EXPOSURES			
Presence of older siblings			<0.0001
None	1.00		
Yes	1.43	1.23–1.67	
Use of child care			0.0314
None	1.00		
Yes	1.18	1.02–1.37	

Table A.3: Number of children aged 4–5 years at risk at start of follow-up and crude incidence of asthma at age 6–7 years, according to different baseline risk factors, kindergarten cohort

Baseline risk factor		Number at risk at start of follow-up[(a)]	Incidence per 100 person-years[(b)]
Total		**3,518**	**4.1 (3.6–4.6)**
INHERENT FACTORS			
Sex	Girls	1,818	3.9 (3.2–4.5)
	Boys	1,700	4.4 (3.6–5.1)
Index of relative socioeconomic disadvantage	SEIFA 1 (most disadvantaged)	698	3.9 (2.6–5.2)
	SEIFA 2	667	4.2 (3.2–5.3)
	SEIFA 3	702	4.8 (3.3–6.3)
	SEIFA 4	725	3.6 (2.7–4.5)
	SEIFA 5 (least disadvantaged)	726	3.9 (2.9–5.0)
Remoteness of residence	Highly accessible/accessible	2,752	4.0 (3.4–4.5)
	Moderately accessible	592	4.3 (2.9–5.7)
	Remote/very remote	142	6.3 (5.1–7.4)
Any parent of non-English-speaking background	No	2,441	4.3 (3.7–4.9)
	Yes	950	3.5 (2.6–4.3)
Indigenous status of child	Indigenous	109	2.9 (0.3–5.4)
	Not Indigenous	3,407	4.1 (3.6–4.7)
EARLY CHILDHOOD EXPOSURES			
Passive smoke exposure	No	2,701	4.0 (3.4–4.6)
	Yes	358	3.9 (2.4–5.4)
Number of older siblings	None	1,487	4.4 (3.6–5.2)
	1 older sibling	1,228	3.8 (3.0–4.6)
	2+ older siblings	803	4.0 (2.9–5.0)
Cats or dogs in household	No	1,593	3.9 (3.1–4.6)
	Yes	1,918	4.3 (3.6–5.0)
OTHER CONDITIONS			
Eczema	No	3,121	4.0 (3.4–4.6)
	Yes	397	5.0 (3.4–6.6)
Allergies	No	3,278	3.8 (3.3–4.4)
	Yes	240	8.0 (5.5–10.6)
Overweight/obese	No	2,803	4.6 (3.4–5.8)
	Yes	687	3.9 (3.4–4.4)

(a) The total of counts for each level of the risk factor do not always add up to total n=3,518 due to missing values.

(b) Weighted to the Australian population aged 4 years as at March 2004.

Table A.4: Independent risk factors for new onset asthma during follow-up, kindergarten cohort (n=3,486)

Baseline risk factor	Odds ratio[(a)]	95% CI	p-value
Remoteness of residence			0.0089
Highly accessible/accessible	1.00		
Moderately accessible	1.12	0.76–1.65	
Remote/very remote	1.70	1.21–2.39	
Allergies			<0.0001
No	1.00		
Yes	2.37	1.57–3.59	

(a) Weighted to the Australian population aged 4 years as at March 2004.

Table A.5: Prevalence[(a)] of persistent wheeze at age 6–7 years, according to different baseline risk factors, kindergarten cohort

Baseline risk factor		n[(b)]	Prevalence/100 pop[(b)]
Total		**642**	**44.3 (39.4–49.2)**
SYMPTOMS AND MEDICATION USE			
Disturbed sleep due to wheezing	No	583	41.1 (36.0–46.2)
	Yes	59	71.7 (58.2–85.1)
Use of medication for asthma in the last 12 months	No	303	34.1 (28.1–40.0)
	Yes	335	53.5 (47.0–59.9)
Number of times had wheeze in the last 12 months	Once	238	33.9 (27.4–40.5)
	Twice	184	41.4 (33.1–49.7)
	Thrice	96	52.8 (41.4–64.2)
	Four times or more	111	61.8 (51.9–71.7)
INHERENT FACTORS			
Sex	Girls	271	43.4 (36.8–50.1)
	Boys	371	44.9 (38.4–51.4)
Index of relative socioeconomic disadvantage	SEIFA 1 (most disadvantaged)	120	38.2 (28.4–48.1)
	SEIFA 2	143	48.6 (38.3–58.9)
	SEIFA 3	139	45.2 (33.4–57.1)
	SEIFA 4	121	42.1 (33.5–50.7)
	SEIFA 5 (least disadvantaged)	119	46.4 (34.7–58.2)
Remoteness of residence	Highly accessible/accessible	496	43.3 (37.8–48.9)
	Moderately accessible	110	49.4 (38.5–60.2)
	Remote/very remote	28	44.7 (20.0–69.4)
Non-English-speaking parent	No	467	44.7 (39.1–50.3)
	Yes	153	44.4 (36.0–52.9)
Indigenous status of child	No	616	44.2 (39.3–49.2)
	Yes	26	44.9 (24.1–65.7)

(continued)

Table A.5 (continued): Prevalence[(a)] of persistent wheeze at age 6–7 years, according to different baseline risk factors, kindergarten cohort

Baseline risk factor		n[(b)]	Prevalence/100 pop[(b)]
EARLY CHILDHOOD EXPOSURES			
Passive smoke exposure	No	486	44.1 (38.6–49.6)
	Yes	76	45.3 (34.1–56.6)
Older siblings	None	263	46.5 (39.5–53.4)
	1 older sibling	240	43.8 (36.2–51.3)
	2+ older siblings	139	41.2 (32.1–50.3)
Cats or dogs in household	No	259	44.0 (37.1–51.0)
	Yes	383	44.4 (38.4–50.5)
OTHER CONDITIONS			
Eczema	No	517	42.4 (37.3–47.4)
	Yes	125	52.9 (42.4–63.3)
Allergies	No	549	43.5 (38.4–48.7)
	Yes	93	48.6 (37.9–59.3)
Overweight/obese	No	497	43.5 (38.2–48.8)
	Yes	142	45.8 (36.5–55.1)

(a) Weighted to the Australian population aged 4 years as at March 2004.

(b) The total of counts for each level of the risk factor do not always add up to total (n=642) due to missing values.

Table A.6: Independent risk factors for persistence of wheezing at age 6–7 years among those with wheeze at baseline (multivariate analysis), kindergarten cohort (n=625)

Baseline risk factor	Adjusted odds ratio[(a)]	95% CI	p-value
Use of medication for asthma in the last 12 months			0.0009
No	1.00		
Yes	1.85	1.29–2.67	
Number of times had wheeze in the last 12 months			0.0012
Once	1.00		
Twice	1.32	0.88–1.98	
Three times	2.06	1.18–3.58	
Four times or more	2.73	1.62–4.61	

(a) Weighted to the Australian population aged 4 years as at March 2004.

Table A.7: Variables included in the analyses

		Analysed for:	
Variable	**LSAC description/question**	**Infants**	**Children**
Absence from school	Absenteeism—number of days absent in last 4 weeks: During the previous four weeks of school, how many days has study child been absent? (If school holidays have taken place during the past four weeks, exclude school holidays)	✗	✓
Allergies (Wave 1)	Health status—medical condition: Does child have any of these ongoing problems? Food or other allergies	✗	✓
Allergies (Wave 2)	Health status—medical condition: Does child have any of these ongoing problems? Food or digestive allergies or food intolerance	✓	✓
Any breastfeeding	Health behaviour and risk factors—breastfeeding: How old was child when he/she completely stopped being breastfed? (Include expressed breast milk) (Age in days) Answers categorised into 2 months or less, 3–4 months, 5–6 months, 7–12 months and more than 12 months	✓	✗
Any parent from a non-English speaking background	Family demographics—country of birth: In which country was Parent 1 born? In which country was Parent 2 born? If either parent was born in a country other than Australia, New Zealand, United States of America, Canada, the United Kingdom, Ireland, South Africa and Zimbabwe they are classified as having a non-English speaking background.	✓	✓
Caesarean birth	Health status—birth: What type of birth, or delivery, was it? Caesarean	✓	✗
Cats and/or dogs as pets in the household	Housing—pets: How many cats, dogs or other pets are there in this household? Cats How many cats, dogs or other pets are there in this household? Dogs	✓	✓
Child's sleeping pattern is a moderate or large problem for parent	Health status—sleeping problems: How much is study child's sleeping pattern or habits a problem for you? (1 Not a problem at all; 2 A small problem; 3 A moderate problem; 4 A large problem)	✗	✓
Eczema	Health status—medical condition: Does child have any of these ongoing problems? Eczema	✗	✓
Emergency Department visit in last 12 months	Social capital—services used for Study Child: In the last 12 months, have you used any of these services for the study child? hospital emergency ward	✗	✓

(continued)

Table A.7 (continued): Variables included in the analyses

		Analysed for:	
Variable	**LSAC description/question**	**Infants**	**Children**
Ever-diagnosed asthma	Health status—asthma/wheezing: 'Has a doctor ever told you that Study Child has asthma?'	✓	✓
Fair or poor health status	Health status—general health: In general, how would you say Study Child's current health is? (1 Excellent; 2 Very good; 3 Good; 4 Fair; 5 Poor)	✗	✓
Gestational age	Health status—number of weeks of gestation: After how many weeks of pregnancy was Child born? Was Child born late, on time or early?	✓	✗
Height for age	Health status—physical measurements: Height for age z-score based on CDC growth charts	✗	✓
Hospitalisation for any reason in last 12 months	Health status—had non-injury hospital stays: Not including injuries, in the last 12 months, did Study Child stay in hospital for at least one night for any (other) reason? (Not hospital outpatient or emergency departmental visits)	✗	✓
Indigenous status of the child	Ethnicity—Indigenous status: Is Study Child of Aboriginal or Torres Strait Islander origin?	✓	✓
Low birthweight	Health status—physical measurements at birth: How much did Child weigh at birth? (Grams)	✓	✗
Maternal age	Family demographics—date of birth: What is the Study Child's date of birth? What is biological mother's date of birth? The difference between the infant's date of birth and the biological mother's date of birth	✓	✗
Maternal asthma	Maternal health during pregnancy - type of prescribed medication during pregnancy: What prescribed medicines or tablets were taken? Asthma medication What 'over-the-counter' medications were used? Asthma medications (Ventolin etc.)	✓	✗
Number of GP visits in last 2 years	Count of GP visits in the last 2 years, derived from the MBS linked data	✗	✓
Number of times had wheeze in last 12 months	Health status—asthma/wheezing: In the last 12 months, about how many times did child have wheezing that lasted for a week or more?	✗	✓

(continued)

Table A.7 (continued): Variables included in the analyses

		Analysed for:	
Variable	**LSAC description/question**	**Infants**	**Children**
Overweight or obese	Health status—physical measurements: Categorical representation of BMI, based on cut-offs from Cole et al. (2000, 2007) (1 Underweight III; 2 Underweight II; 3 Underweight I; 4 Normal weight; 5 Overweight; 6 Obese). Cole TJ, Bellizzi MC, Flegal KM, Dietz WH. Establishing a standard definition for child overweight and obesity worldwide: international survey. BMJ 2000; 320 (7244): 1240–3. Cole TJ, Flegal KM, Nicholls D, Jackson AA. Body mass index cut-offs to define thinness in children and adolescents: international survey. BMJ 2007 (7612); 335:194.	✘	✓
Passive smoke exposure	Health behaviour and risk factors—smoking: From Parent 1—Including yourself, how many people who live with you smoke inside the house? From Parent 2—Including yourself, how many people who live with you smoke inside the house? Derived from answers provided by both parents: 0 if both parents answered 0 1or more if either parent answered 1 or more	✓	✓
Presence of older siblings	Family demographics—older siblings: Number of older siblings of Study Child in the household	✓	✓
Remoteness of residence	Neighbourhood status: Remoteness Area Classification	✓	✓
Sex	Family demographics—sex: Is the Study Child male or female?	✓	✓
Smoking during pregnancy	Maternal health during pregnancy—mother smoked cigarettes during pregnancy: During the pregnancy with the Study Child, did you smoke cigarettes?	✓	✘
Socioeconomic disadvantage	Neighbourhood status: SEIFA Disadvantage	✓	✓
Type of asthma medication	Type of asthma medication from the PBS linked data: Inhaled corticosteroids +/- long-acting beta agonists, cromones, leukotriene receptor antagonists	✓	✓
Use of child care	Number of different care arrangements: In total, how many different regular arrangements have you used for Child since birth, including that first arrangement and any current arrangements you have already told me about?	✓	✘

(continued)

Table A.7 (continued): Variables included in the analyses

		Analysed for:	
Variable	**LSAC description/question**	**Infants**	**Children**
Use of medication for asthma in last 12 months	Health status—asthma/wheezing: In the last 12 months has Child taken any medication for asthma?	✓	✓
Use of neonatal intensive care unit after birth	Health status—birth: Did Child have to go into a Neonatal Intensive Care Unit or Special Care Nursery after he/she was born?	✓	✗
Wheeze	Health status—asthma/wheezing: 'In the last 12 months, has Study Child had an illness with wheezing in the chest which lasted for a week or more?'	✓	✓
Wheezing or asthma on four or more nights per week	Health status—sleeping problems: Does Child have any of these problems on 4 or more nights a week, that is, more than half the time? Wheezing or asthma	✗	✓

Glossary

Aboriginal and Torres Strait Islander	A person of Aboriginal and/or Torres Strait Islander descent who identifies as an Aboriginal and/or Torres Strait person and is accepted as such by the community in which he or she lives. Also see *Indigenous*.
Adjusted odds ratio	An odds ratio which is adjusted for the effect of confounding factors. See also *Odds ratio*.
Allergen	Any substance that causes an allergy. It may, for example, be pollen that can trigger hay fever or peanuts that can cause anaphylactic shock.
Asthma	A chronic inflammatory disorder of the airways. In susceptible individuals, this inflammation causes recurrent episodes of wheezing, breathlessness, chest tightness and coughing, particularly at night or in the early morning. These episodes are usually associated with widespread but variable narrowing of the airways that is often reversible, either spontaneously or with treatment. The inflammation also causes increases in existing bronchial hyperresponsiveness ('twitchiness of the airways') to a variety of stimuli.
Asthma action plan	A plan that provides instructions on what to do if your asthma symptoms or peak flow readings worsen. It states your usual treatment and an individualised list of steps to follow, written by your doctor.
Atopic dermatitis	Eczema caused by an allergic reaction.
Atopy or atopic disease	A hereditary tendency to develop sensitivity reactions to allergens (e.g. asthma, hay fever, eczema) (Jenkins C 2005).
Beta-agonist	A bronchodilator drug that relaxes airway muscles, allowing the airways to open up and let more air through. They are called 'beta-agonists' because they activate the beta receptors on the muscles. (Jenkins C 2005). See also *Bronchodilator*.
Bronchodilator	An agent that causes widening of the airways by relaxing the muscles in the airways. See also *Beta-agonist*.
Cohort, and cohort study	Study of the features or incidence of the development of a disease in a group of people (cohort) who have experienced the same event at a specified period in time; for example, 'birth cohort' refers to people born in the same year.
Confidence interval	A statistical term describing a range (interval) of values within which we can be 'confident' that the true value lies. For example, a 95% confidence interval implies that there is 95% confidence that the true value will be included in this interval.

Corticosteroid	A group of drugs similar to the natural corticosteroid hormones produced by the adrenal glands. They have powerful anti-inflammatory properties and are often the treatment of choice for allergic conditions, including asthma.
Disability-adjusted life year	Years of healthy life lost through premature death or living with disability due to illness or injury.
Eczema	Eczema is a general term for skin inflammation (dermatitis). The most common type is atopic dermatitis. See also *Atopic dermatitis* and *Atopy*.
English-speaking background	Includes anyone born in Australia, New Zealand, United Kingdom, Ireland, United States of America, Canada, Zimbabwe or South Africa (Department of Immigration and Multicultural and Indigenous Affairs (DIMIA) English proficiency group 1).
Health Insurance Commission	Administers many health programs on behalf of the Commonwealth Government, including Medicare.
Health risk factor	Any factor which represents a greater risk of a health disorder or other unwanted condition or event. Some risk factors are regarded as causes of disease, others are not necessarily so. An *independent health risk factor* is one which remains a greater risk after taking into account any confounding factors (these are analysed by calculating *adjusted odds ratios*).
Health service use	Use of the available health-care services within the population, including hospitals, emergency departments and general practitioners.
Hyperresponsiveness (airway)	Describes airways that are highly sensitive (or twitchy) and likely to become narrow when exposed to irritants or triggers.
Incidence	The number of new cases (of a disease, condition or event) occurring during a given period. Compare with *Prevalence.*
Indigenous	A person of Aboriginal and/or Torres Strait Islander descent who identifies as an Aboriginal and/or Torres Strait Islander person and is accepted as such by the community with which he or she is associated.
Infant cohort	Children born between March 2003 and February 2004 and, hence, aged 3 to 19 months at baseline of the LSAC. For simplicity, we refer to these as 0–1 year old children throughout the report.
Kindergarten cohort	Children born between March 1999 and February 2000 and, hence, aged 4 years and 3 months to 5 years and 7 months at baseline of the LSAC. For simplicity, we refer to these as 4–5 year old children throughout the report.

Longitudinal study	A study in which the same people are tested as they get older.
Medicare	Australia's universal health-care system, introduced in 1984 to provide eligible Australian residents with affordable, accessible and high quality health care. Medicare was established based on the understanding that all Australians should contribute to the cost of health care according to their ability to pay. It is financed through progressive income tax and an income-related Medicare levy.
Medicare Benefits Scheme	Australia's universal health insurance program which reimburses expenses related to services provided by medical practitioners.
Meta-analysis	A way of 'pooling' data to calculate the sum total of effects of all the studies performed.
Morbidity	Refers to ill health in an individual and to levels of ill health in a population or group.
Mortality	Death.
Natural history	How a disease develops from its beginning to its resolution.
Non-English-speaking background	This term is used to describe people who have settled in Australia but who come from countries where English is not the primary language spoken. Includes people born in all countries not identified as English-speaking-background countries (equivalent to DIMIA English proficiency groups 2 to 4). See also *English-speaking-background.*
Odds ratio	Measures the strength of an association between two variables (usually a risk factor and an outcome). Literally, the ratio of the odds of an outcome in the presence of a risk factor to the odds of that outcome in the absence of that risk factor. An odds ratio of 1 implies that there is no association between the risk factor and the outcome. An odds ratio greater than 1 indicates that those with the risk factor have a greater risk of having the outcome. See also *Adjusted odds ratio*.
Outcome (health outcome)	A health-related change due to a preventive or clinical intervention or service. (The intervention may be single or multiple and the outcome may relate to a person, group or population or be partly or wholly due to the intervention.)
Over-the-counter medication	A medication than can be bought without having to get a doctor's prescription.
p value	The probability that the observed difference or association could have occurred by chance. If that probability is less than 5% (i.e. $p < 0.05$), it is conventionally held that it did not occur by chance and is a true difference or association.

Person-years	The product of the number of years and the number of people within the population who are at risk of a certain condition.
Pharmaceutical Benefits Scheme	A national, government-funded scheme that subsidises the cost of a wide range of pharmaceutical drugs, and that covers all Australians to help them afford standard medications.
Phenotype	The observable characteristics of an individual that have developed as a result of their genetic makeup and environment.
Risk factor	See *Health risk factor*.
SEIFA Index of Relative Socioeconomic Disadvantage	An index of socioeconomic status which provides a summary score for a range of key socioeconomic variables that are related to health status, including household income and resources, education, occupation, fluency in English and Indigenous status.
Statistical significance	An indication from a statistical test that an observed difference or association may be significant, or 'real', because it is unlikely to be due just to chance. A statistical result is often said to be 'significant' if it would occur by chance only once in twenty times or less often. See also *P value*.
Wheeze	Breathing difficulty accompanied by an audible whistling sound.

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List of tables

List of figures