Thorax 2001;56:589-595 589

# Original articles

# Asthma in preschool children: prevalence and risk factors

M M Haby, J K Peat, G B Marks, A J Woolcock, S R Leeder

#### **Abstract**

Background-The prevalence of asthma in children has increased in many countries over recent years. To plan effective interventions to reverse this trend we need a better understanding of the risk factors for asthma in early life. This study was undertaken to measure the prevalence of, and risk factors for, asthma in preschool children.

Methods-Parents of children aged 3-5 years living in two cities (Lismore, n=383; Wagga Wagga, n=591) in New South Wales, Australia were surveyed by questionnaire to ascertain the presence of asthma and various proposed risk factors for asthma in their children. Recent asthma was defined as ever having been diagnosed with asthma and having cough or wheeze in the last 12 months and having used an asthma medication in the last 12 months. Atopy was measured by skin prick tests to six common allergens.

Results—The prevalence of recent asthma was 22% in Lismore and 18% in Wagga Wagga. Factors which increased the risk of recent asthma were: atopy (odds ratio (OR) 2.35, 95% CI 1.49 to 3.72), having a parent with a history of asthma (OR 2.05, 95% CI 1.34 to 3.16), having had a serious respiratory infection in the first 2 years of life (OR 1.93, 95% CI 1.25 to 2.99), and a high dietary intake of polyunsaturated fats (OR 2.03, 95% CI 1.15 to 3.60). Breast feeding (OR 0.41, 95% CI 0.22 to 0.74) and having three or more older siblings (OR 0.16, 95% CI 0.04 to 0.71) decreased the risk of recent asthma.

Conclusions-Of the factors tested, those that have the greatest potential to be modified to reduce the risk of asthma are breast feeding and consumption of polyunsaturated fats.

children

Asthma is a major public health problem in developed countries, especially in children.12 Ultimately we want to prevent asthma, not just

to relieve its symptoms. However, the causes of

asthma and the reasons for its increasing

prevalence in the past few decades are not

(Thorax 2001;56:589-595) Keywords: asthma; prevalence; risk factors; preschool

Centre for Community Child Health, Royal Children's Hospital Melbourne, Parkville, Victoria 3052, Australia M M Haby

Department of Paediatrics and Child Health, University of Sydney, NSW 2006, Australia J K Peat

Institute of Respiratory Medicine, University of Sydney G B Marks A J Woolcock

Faculty of Medicine, University of Sydney S R Leeder

Correspondence to: Dr M M Haby michelle.haby@dhs.vic.gov.au

Received 16 August 2000 Returned to authors 4 December 2000 Revised version received 19 March 2001 Accepted for publication 23 April 2001

known.3 4 At present we can implement prevention strategies for asthma based on currently available evidence of risk factors. Some prevention strategies have been tested, including changes to early diet and/or to house dust mite exposure, but these have not been successful in significantly reducing the incidence of asthma for more than the first year of life.5-8 Clearly, better evidence of possible causal or preventive factors needs to be collected so that better prevention strategies can be developed.

Risk factors for asthma have been studied extensively in school age children but there is little information about younger children. The advantage of studying preschool age children is that information about potential risk factors and their effects is collected closer to the time of disease inception. However, these children are not young enough to make disease misclassification a significant problem—that is, by misclassifying transient early wheeze asthma.9

In this paper we describe the epidemiology of asthma in preschool age children (3–5 years) in two rural Australian cities, one with a humid climate and close to the coast (Lismore) and the other a dry inland city (Wagga Wagga). We also investigate important putative risk factors for asthma, including dietary fatty acid intake,10 number of older siblings,11 breast feeding,12 and atopy,13 which have all been identified as being associated with asthma in older children.

# Methods

STUDY DESIGN, SETTING AND SUBJECTS

The studies were cross sectional in design and were conducted in May and June 1995. Parents completed a questionnaire asking about asthma, respiratory symptoms, and possible risk factors for asthma in their child. Atopy was measured by skin prick tests in the children. Questionnaires were completed before skin prick tests were administered.

The subjects were preschool age children born between 1 July 1989 and 30 June 1992 (aged 3–5 years at the time of testing) living in the cities of Wagga Wagga (dry inland city) or Lismore (humid coastal city), both in New South Wales. These two towns were selected because they have different weather conditions and different dominant allergens (house dust mite in Lismore and rye grass and Alternaria tenuis in Wagga Wagga). Because there is no unique register of preschool age children in

590 Haby, Peat, Marks, et al

Australia, the study base was constructed from three sources in both cities: records of all children immunised through the local council; all children in family day care; and all preschools, day care centres, and playgroups in the cities. Questionnaires were posted directly to parents if the child had been immunised through the local council or was attending family day care. Otherwise, parents received the questionnaire via their child's preschool, child care centre, or playgroup.

In Lismore we attempted to study all eligible children from the three sources, and in Wagga Wagga we randomly selected approximately half of the children for study. Because of the overlapping nature of these sources, it was not possible to ascertain the exact size of the study base. After adjusting for overlap between the three sources, the estimated number of parents who received the questionnaire was 1583. There were 974 questionnaire respondents, representing a minimum response rate of 62%. However, 1583 is an overestimate of the number who actually received the questionnaire. We were not given access to the names and addresses of children attending family day care in Wagga Wagga (n=232) so were not able to check for out of date addresses. The response rate of 62% assumes no out of date addresses. However, if all non-responders had out of date addresses the response rate would be 68%. In Lismore 33% of the family day care records were found to be out of date.

Because of resource constraints, a large subsample of children was randomly selected to undergo skin prick testing. For those selected from preschools, day care centres, or playgroups, the unit of selection for skin prick tests was the centre. For those selected from immunisation or family day care records, the unit of selection was the individual child. Skin prick tests were conducted in 650 children, who did not differ significantly from those who did not have skin prick tests with respect to the proportion with recent asthma (20% v 18%,  $\chi^2$ =0.5, p=0.5), proportion ever breast fed  $(87\% \ v \ 86\%, \ \chi^2=0.2, \ p=0.6)$ , and the proportion whose mother smoked during pregnancy (20% v 21%,  $\chi^2$ =0.1, p=0.7).

Ethical approval for the studies was obtained from the University of Sydney human ethics committee and informed consent was obtained from parents before including a child in the study.

#### QUESTIONNAIRE

Details of asthma, respiratory symptoms, and possible risk factors for asthma were collected by a parent completed questionnaire. The questions used in this paper are shown in table 1, together with their repeatability.

Table 1 Ouestions used to measure asthma, symptoms and possible risk factors, with their repeatability

1able 1 Questions used to measure astrma, symptoms and possible risk factors, with their repeatability					
Question	No of responses*	ACC (95% CI)	Kappa (95% CI)		
Asthma ever Has your child ever been diagnosed as having asthma by a doctor or at a hospital?	102	1.00	1.00		
	102	1.00	1.00		
Symptoms	104	0.05 (0.04 0.00)	0.04 (0.50 0.05)		
Has your child ever wheezed? (Wheezing is a whistling noise that comes from the chest)  If yes, was this in the last 12 months?	104 28	0.97 (0.94 to 0.99) 0.94 (0.88 to 1.01)	0.84 (0.73 to 0.95) 0.60 (0.20 to 1.01)		
Has your child ever had wheezing during or after physical activity?	102	0.94 (0.88 to 1.01) 0.98 (0.96 to 1.00)	0.85 (0.71 to 0.99)		
If yes, was this in the last 12 months?	15	1.00	1.00		
Has your child ever had a cough which lasted more than 3 weeks?	103	0.94 (0.91 to 0.98)	0.74 (0.60 to 0.89)		
If yes, was this in the last 12 months?	29	0.90 (0.82 to 0.99)	0.55 (0.20 to 0.90)		
Medications		()	(,		
Has your child ever taken any of the following medicines (medicine includes inhalers, liquids, tablets, nebulisers):					
(a) Ventolin, Bricanyl, Berotec, Respolin	104	0.99 (0.97 to 1.00)	0.94 (0.87 to 1.01)		
In the last 12 months, how often has your child taken this medicine (not at all, <4 times, 4–12 times, >12 times)?	41	0.73 (0.61 to 0.85)	0.52 (0.32 to 0.72)†		
b) Intal, Becotide, Becloforte, Pulmicort	81	0.99 (0.97 to 1.00)	0.93 (0.84 to 1.03)		
In the last 12 months, how often has your child taken this medicine (not at all, <4 times, 4-12 times, >12 times)?	19	0.85 (0.73 to 0.98)	0.63 (0.33 to 0.92)†		
Personal information					
Is your child male or female? (male/female)	104	0.99 (0.98 to 1.00)	0.96 (0.91 to 1.01)		
How many brothers and sisters does he/she have? (number)	104	1.00	1.00†		
Diet					
Was your child breast fed?	104	0.98 (0.96 to 1.00)	0.80 (0.61 to 0.99)		
If yes, for how long was your child exclusively breast fed? (months)	85	· · · · · · · · ·	0.74‡		
Which of the following fats does your child usually have on bread or toast: butter; canola or soy; other e.g.			•		
sunflower, safflower, mixed vegetable?	101	0.90 (0.85 to 0.94)	0.72 (0.60 to 0.83)		
When roasting/frying your child's food which type of fat/oil is most commonly used: butter, lard, dripping; olive					
or canola; other e.g. sunflower, safflower, corn, peanut?	103	0.95 (0.92 to 0.98)	0.79 (0.68 to 0.91)		
Smoking					
Did the child's mother smoke during pregnancy?	103	0.99 (0.98 to 1.00)	0.91 (0.79 to 1.03)		
Did the child's mother smoke during the first 6 months of the child's life?	102	0.99 (0.98 to 1.00)	0.92 (0.80 to 1.03)		
Did the child's father smoke during the first 6 months of the child's life?	103	0.98 (0.96 to 1.00)	0.91 (0.82 to 1.00)		
Respiratory illnesses					
Has your child ever been diagnosed as having any of the following illnesses by a doctor or at a hospital:					
(a) Pneumonia?	104	1.00	1.00		
(b) Bronchiolitis?	102	0.97 (0.95 to 0.99)	0.59 (0.30 to 0.89)		
(c) Whooping cough?	103	1.00 (0.99 to 1.00)	0.80 (0.40 to 1.19)		
(d) Bronchitis?	101 102	0.95 (0.92 to 0.98)	0.66 (0.47 to 0.86)		
(e) Croup? Age at diagnosis (<1 year, 1-<2 years, 2-<3 years, ≥3 years)  √	102	0.97 (0.95 to 0.99)	0.75 (0.56 to 0.94)		
rige at diagnosis (~1 year, 1-~2 years, 2-~) years, >) years,					

ACC = average correct classification.

Data are for 104 repeat questionnaires; possible responses are "yes" or "no" unless indicated after the question.

<sup>\*</sup>For both questionnaires.

<sup>†</sup>Weighted kappa was used.

Statistic used was the intraclass correlation coefficient because data are continuous.

<sup>\$</sup>Repeatability not calculated because there were too few responses (<12) to this question for each of the illnesses.

Asthma in preschool children 591

Children were classified as having recent asthma if they had ever been diagnosed as having asthma *and* had used an asthma medication in the previous 12 months *and* had symptoms of cough or wheeze in the previous 12 months.

The potential risk or protective factors measured are listed in table 3. Polyunsaturated fat intake was defined as high if children usually had polyunsaturated fats on bread or toast and parents usually used polyunsaturated fats when roasting or frying their child's food. Polyunsaturated fat intake was defined as low if mono-unsaturated or saturated fats were usually consumed and medium if a mixture of these fats was used.

### REPEATABILITY OF THE QUESTIONNAIRE

A random sample of 207 children was selected from the 286 Lismore children who underwent skin prick tests to receive a second copy of the questionnaire 2 months after the first. Parents were asked to complete the questionnaire to help in assessing its validity. The questionnaire was completed and returned by the parents of 104 of the children (50%). There were no significant differences in the prevalence of asthma, serious respiratory infections, or asthma medication use between children for whom only the first questionnaire was completed and those for whom both questionnaires were completed.

#### ATOPY

Atopy was measured by skin prick test reactions to six allergens (Hollister-Stier, Miles Inc, Elkhart, IN, USA) applied to the forearm.14 The allergens tested and the allergy units (AU), biological allergen units (BAU) or weight/volume ratio (W/V) were standardised Dermatophagoides pteronyssinus (30 000 AU/ ml), Alternaria tenuis (1:10 W/V), standardised cat pelt (10 000 BAU/ml), perennial rye grass (1:20 W/V), whole cow's milk (1:20 W/V), and whole egg (1:20 W/V). These allergens, together with positive (histamine 10 mg/ml) and negative (glycerol) controls, were applied into a stencil stamped on the forearm with ink and pricked with a lancet (Long point Microlance, Becton-Dickson, Rutherford, NJ, USA). After 15 minutes the weal size was recorded for each allergen as the mean of the largest axis and its perpendicular. Mean values were rounded down to the nearest millimetre. For the small number of children in whom the histamine skin test was negative or the control test positive, these tests were repeated. No child had duplicate negative histamine or duplicate positive glycerol tests. Children were defined as being atopic if they had a skin weal size of  $\geq 2$  mm to one or more of the six allergens tested. This method for measuring atopy has been shown to have good repeatability.<sup>15</sup>

#### ANALYSIS OF DATA

Data were analysed using the statistical package SAS (Version 6.12, SAS Institute Inc, Cary, NC, USA). Prevalence rates (population proportions) are presented with their 95% confidence intervals (95% CI). For all analyses p values of <0.05 were regarded as statistically significant.

The repeatability of the questionnaire was assessed using the average correct classification rate (ACC) and Cohen's kappa for categorical data. Repeatability was considered to be good when the ACC was >0.80 and kappa was >0.60.<sup>16</sup> Intraclass correlation coefficient (ICC) was used to assess the repeatability of continuous data using the method described by Armitage and Berry.<sup>17</sup> To be useful, it has been suggested that questions should have an ICC of at least 0.6.<sup>18</sup>

 $\chi^2$  tests were used to compare proportions between groups and the Mantel-Haenszel γ<sup>2</sup> test for trend was used to determine if a significant linear trend was present in ordered categorical variables. Homogeneity of the odds ratios for each potential risk factor, between atopic and non-atopic children and between Lismore and Wagga Wagga, was tested by the Breslow-Day test. Logistic regression analyses were conducted to identify independent risk factors for recent asthma. All potential risk factors were included in the initial model—that is, all factors listed in table 3. The risk factors with the lowest Wald  $\chi^2$  value were then excluded, one at a time, until only variables with a p value of <0.05 remained. This is the final model shown in the top section of table 4. The significance of risk factors with three or more levelsthat is, polyunsaturated fats, number of older siblings-were tested by assessing the reduction in the log likelihood statistic (-2Ln(L))

Table 2 Prevalence (%) of asthma, asthma symptoms, and asthma medication use in preschool children in Lismore and Wagga Wagga

	Lismore (n=383)	Wagga Wagga (n=591)
Asthma diagnosed ever	30.0 (25.4 to 34.6)	27.3 (23.7 to 30.9)
Asthma symptoms in last 12 months:	,	· · · · · · · · · · · · · · · · · · ·
Wheeze	30.8 (26.2 to 35.4)	28.8 (25.1 to 32.4)
Cough or wheeze	38.6 (33.8 to 43.5)	37.2 (33.3 to 41.1)
Asthma medication used in last 12 months:		
$\beta_2$ agonist	30.3 (25.7 to 34.9)	24.4 (20.9 to 27.8)*
Corticosteroid or sodium cromoglycate	15.4 (11.8 to 19.0)	12.2 (9.5 to 14.8)
Any asthma medication	30.8 (26.2 to 35.4)	25.4 (21.9 to 28.9)
Recent asthma (diagnosed asthma and recent symptoms and recent medications)	21.7 (17.5 to 25.8)	18.1 (15.0 to 21.2)
Recent untreated asthma (diagnosed asthma and recent symptoms but no recent		
medications)	1.8 (0.5 to 3.1)	3.2 (1.8 to 4.6)
Recent asthma symptoms without diagnosis or recent medications	11.0 (7.9 to 14.1)	12.4 (9.7 to 15.1)
Diagnosed asthma <i>or</i> recent symptoms <i>or</i> recent medications	48.3 (43.3 to 53.3)	45.0 (41.0 to 49.0)
Ever admitted to hospital for asthma	6.3 (4.8 to 7.8)	5.9 (4.4 to 7.4)

<sup>\*</sup>p<0.05 v Lismore ( $\chi^2$  test).

592 Haby, Peat, Marks, et al

Table 3 Risk factors for recent asthma in Australian preschool children

	Prevalence (%) of risk factor in children			
Risk factor	Without recent asthma (n=784)	With recent asthma (n=190)	— Unadjusted odds ratio for recent asthma (95% CI)	
Atopic (n=650)	22.9	36.6	1.94 (1.29 to 2.93)	
Either parent ever had asthma	30.6	52.8	2.53 (1.82 to 3.53)	
Serious respiratory infection in first 2 years of life*	28.4	49.0	2.41 (1.74 to 3.34)	
Breast fed ever	88.3	82.0	0.61 (0.40 to 0.93)	
Polyunsaturated fats				
low (referent category)	51.7	51.4	1.00	
medium	32.8	28.7	0.88 (0.61 to 1.28)	
high	15.5	20.0	1.30 (0.85 to 2.01)	
Number of older siblings				
0 (referent category)	40.9	40.0	1.00	
1	34.1	34.7	1.04 (0.72 to 1.51)	
2	16.7	18.4	1.13 (0.73 to 1.78)	
≥3	8.4	6.8	0.83 (0.45 to 1.62)	
Currently living in Lismore (Wagga Wagga is				
referent category)	38.3	43.7	1.25 (0.91 to 1.73)	
Male (female is referent category)	51.4	59.5	1.39 (1.01 to 1.91)	
Mother smoked during pregnancy	19.8	22.6	1.19 (0.81 to 1.74)	
Either parent smoked in first 6 months of child's life	38.1	45.3	1.34 (0.98 to 1.85)	

Unless otherwise stated, the referent category for each risk factor is absence of the risk factor.

when they were added to the model. Multivariate analyses that included atopy were conducted in the subsample of 650 children who underwent skin prick tests.

The attributable fraction was estimated using the adjusted odds ratio from the final logistic regression model and the proportion of the population exposed.19 Since the odds ratio for breast feeding was less than 1, an attributable fraction was calculated for not being breast fed (odds ratio 2.45). The attributable fraction is the proportion of cases of recent asthma that can be attributed to the risk factor of interest.19 Although the causal inference in this statistic has not been established in this study, it does give an indication of the level of importance of each risk factor in the population because it takes into account both the size of the risk (odds ratio) as well as the prevalence of the risk factor in the population.

### Results

Of the 974 children who participated in the study, 98% were white, 76% were born in their town of current residence, 53% were male, and 38%, 47% and 12% were aged 3, 4 or 5 years,

respectively. The proportion of 5 year old children was lower because some had already started school and were not attending preschools or day care centres.

The repeatability of the questions used in this study is shown in table 1. When the criteria for good repeatability for categorical data of an ACC of >0.80 and kappa of >0.60 were used, most of the questions met this minimum standard with many being well above it.

The prevalence rates for recent asthma, doctor diagnosed asthma, asthma symptoms, and use of asthma medication are shown in table 2. These rates were not significantly different between the two study cities, except for the use of  $\beta_2$  agonists in the previous 12 months which was higher in Lismore than in Wagga Wagga.

Table 3 shows the prevalence of each potential risk factor in children with and without recent asthma and unadjusted odds ratios for the association of each of these variables with the presence of recent asthma. Adjusted odds ratios are shown in table 4. Variables in the top part of the table were significant and were included in the final logistic regression model. Variables in the lower part of the table were not

Table 4 Multiple logistic regression analysis of risk factors for recent asthma in Australian preschool children

Risk factor	Adjusted odds ratio (95% CI) for recent asthma	Adjusted odds ratio (95% GI) for recent asthma (final model without infections)
Significant risk factors (final model)*		
Atopic (n=650)	2.35 (1.49 to 3.72)	2.25 (1.43 to 3.54)
Either parent ever had asthma	2.05 (1.34 to 3.16)	2.17 (1.42 to 3.31)
Serious respiratory infection in first 2 years of life‡	1.93 (1.25 to 2.99)	_
Breast fed ever	0.41 (0.22 to 0.74)	0.44 (0.25 to 0.80)
Polyunsaturated fats (low is referent category)		
medium	1.02 (0.62 to 1.67)	1.03 (0.63 to 1.68)
high	2.03 (1.15 to 3.60)	1.92 (1.09 to 3.38)
Number of older siblings (0 is referent category)		
1	1.21 (0.75 to 1.95)	1.27 (0.79 to 2.03)
2	1.21 (0.65 to 2.23)	1.31 (0.72 to 2.41)
≥3	0.16 (0.04 to 0.71)	0.17 (0.04 to 0.75)
Non-significant risk factors (initial model)†		
Currently living in Lismore (Wagga Wagga is referent category)	1.42 (0.92 to 2.18)	
Male (female is referent category)	1.33 (0.86 to 2.06)	
Mother smoked during pregnancy	0.77 (0.40 to 1.48)	
Either parent smoked in first 6 months of child's life	1.62 (0.95 to 2.75)	

Unless otherwise stated, the referent category for each risk factor is absence of the risk factor. Multivariate analyses were conducted in the 650 children who had skin prick tests.

<sup>\*</sup>Serious respiratory infections included pneumonia, bronchiolitis, whooping cough, bronchitis or croup.

<sup>\*55</sup> and †60 children, respectively, were deleted from this analysis due to missing values for one or more variables.

<sup>‡</sup>Serious respiratory infections included pneumonia, bronchiolitis, whooping cough, bronchitis or croup.

Asthma in preschool children 593

significant. Adjusted odds ratios shown for these variables are from the initial logistic regression model that included all potential risk factors—that is, all factors listed in tables 3 and 4. The relation between each of these potential risk factors and the presence of asthma did not differ between atopic and non-atopic children or between Lismore and Wagga Wagga. Removal from the model of serious respiratory infections in the first 2 years of life changed some parameter estimates by more than 10% (suggestive of confounding) but did not alter the conclusions of the study (table 4).

The attributable fractions for a high dietary intake of polyunsaturated fats and not having been breast fed were 0.17 and 0.16, respectively. Thus, 17% of the cases of recent asthma in this population can be attributed to a high dietary intake of polyunsaturated fats and 16% to not breast feeding.

There was no significant dose response relation between the duration of exclusive breast feeding (adjusted OR=0.94 per month, 95% CI 0.87 to 1.01) or the age at which bottle feeding began (adjusted OR=0.97 per month, 95% CI 0.91 to 1.03) and the risk of asthma. However, children who had ever been breast fed, even for 3 months or less, had a reduced risk of having asthma (adjusted odds ratio 0.43, 95% CI 0.22 to 0.83, compared with children who had never been breast fed).

The risk for asthma associated with a maternal and a paternal history of asthma was similar (adjusted OR=1.95 (95% CI 1.17 to 3.24) for maternal asthma and 2.31 (95% CI 1.41 to 3.77) for paternal asthma).

## Discussion

The prevalence of recent asthma in preschool children in Lismore was 22% and in Wagga Wagga was 18% (table 2). Atopy, having a parent with a history of asthma, having had a serious respiratory infection in the first 2 years of life, and a high dietary intake of polyunsaturated fats were significant risk factors for asthma in this population of preschool age children (table 4). Breast feeding and having three or more older siblings were both protective factors for asthma. Of these, the factors that have the greatest potential to be modified to prevent asthma are breast feeding and consumption of fats. We did not confirm the results from previous studies which suggest that maternal allergic disease is a greater risk factor for childhood asthma than paternal allergic disease.20

Most previous cross sectional studies of early life risk factors for asthma have been conducted in school age children. There is a risk of recall error or bias in such studies because of the relatively remote nature of the antecedent events. In this study we have sought to minimise the risk of recall bias by studying younger preschool age children. This age range was chosen to gain more reliable information on early life risk factors while avoiding the risk of misclassification of transient early wheeze as asthma. The response rate for the study was less than ideal, which raises the possibility that the study may have been subject to selection

bias. However, the observation that the prevalence of recent asthma and atopy did not differ between the three sources from which children were selected is evidence that selection bias is unlikely to be a major problem in this study, especially for measures of association. Prevalence figures for asthma, symptoms, and asthma medication use are more likely to be overestimates than underestimates because of the greater interest in participating in the study for the parents of children with signs or symptoms of asthma.

We have tested the repeatability of the questionnaire and found that the questions used to define recent asthma and risk factors had good repeatability, with ACC values above 0.8 and kappa values above 0.6 for most questions (table 1). We also measured and controlled for atopy, which was a significant risk factor for asthma and enabled us to test for possible effect modification of the relation between other risk factors and asthma. This was important because atopy has previously been shown to be an effect modifier of the relation between breast feeding and asthma.12 Finally, we used a stricter definition for recent asthma than has been used in other studies of asthma in preschool children in order to delineate only the children with clinically important asthma. This definition is also likely to have excluded those children who have transient early wheeze.

The prevalence of recent asthma found in this study is higher than in the only other study of preschool children conducted in Australia (current asthma 10-17%).21 It is also higher than the prevalence of asthma found in studies of preschool children in other countries, including Canada (current wheeze 10.8%),<sup>22</sup> USA (current asthma 3.2-4.3%),23 and England (asthma ever 13.8%).24 These differences occurred despite the stricter definition of recent asthma used in the current study, which required a doctor diagnosis of asthma as well as recent symptoms and recent use of an asthma medication. If all children with recent symptoms were classified as having asthma, the prevalence of asthma would have been 30-40% (table 2). The prevalence of use of an asthma medication in the previous 12 months was also high at 25–30%, mostly because of a high rate of use of  $\beta_2$  agonists rather than preventative medications (sodium cromoglycate and inhaled steroids).

A high level of polyunsaturated fats, defined as the use of polyunsaturated fats on bread and in cooking, was associated with an increased risk of recent asthma and could account for up to 17% of cases in this population. A possible explanation for this finding is that an increased consumption of polyunsaturated fats leads to an increased ratio of omega-6 to omega-3 fatty acids consumed in the diet. It has been hypothesised that the increased consumption of polyunsaturated fats seen in Australia in recent years following campaigns to reduce heart disease could be partly responsible for the increasing prevalence of asthma.<sup>25</sup> Polyunsaturated fats are a rich source of omega-6 fatty acids, such as linoleic acid, which can 594 Haby, Peat, Marks, et al

> increase the synthesis of prostaglandin E2. The net effect is to increase the risk of inflammation, which may increase the risk of asthma.<sup>2</sup> Omega-3 fatty acids have the opposite effect by inhibiting the formation of prostaglandin E, and protecting against inflammation.26 Thus, reduced consumption of omega-3 fatty acids may also increase the risk of asthma due to a loss of protection against inflammation. Certainly, the evidence for an effect of fatty acids on asthma is increasing and, if the relationship is found to be causal, there is potential to modify fatty acid consumption patterns to reduce the incidence of asthma.

> In this study, having at least three older siblings considerably reduced the risk of recent asthma. Several other studies have also shown an association between number of siblings and decreased risk of allergic diseases including asthma.11 27-30 The suggested explanation for this association is that the greater the number of older siblings, the greater the exposure to infections in early life which may protect against asthma and other allergic diseases.<sup>27 31</sup> However, we did not find a positive relation between number of older siblings and the prevalence of serious respiratory infections. Further, we found that serious respiratory infections significantly increased the risk of recent asthma. The explanation for these conflicting findings could be that the relationship of infections with asthma is dependent upon the timing, type, and/or severity of the infections. For example, it has been suggested that exposure to infections in the first weeks of life may protect against asthma,31 while respiratory infections contracted after this time may be early signs of asthma, misdiagnosed asthma, or a cause of asthma. Also, the protective effect of older siblings was only significant for children with three or more older siblings, which only applied to 8% of children in this study and not to their younger brothers and sisters.

> Breast feeding reduced the risk of recent asthma, which is consistent with findings in other studies that have examined this relationship.12 32 33 In concordance with a US birth cohort study,12 we did not find that the duration of breast feeding was related to the risk of asthma. Together, this evidence suggests that breast feeding in the first days or weeks of life is most important in terms of reducing the risk of asthma, and not breast feeding could account for up to 16% of cases in this population.

> Children who were atopic were 2.5 times more likely to have recent asthma than those who were not atopic, after controlling for other significant risk factors. We expected that atopy would be a significant risk factor for asthma as suggested by previous research.<sup>12</sup> <sup>13</sup> <sup>34</sup> However, the association was weaker than has been found in studies of older children. Only 36% of children with recent asthma were atopic compared with 23% of children without recent asthma whereas, in older children with asthma, up to 90% are atopic. It is not clear whether this weaker association between asthma and atopy in early childhood indicates a lesser role for

atopy in this age group. An alternative explanation is that it reflects the difficulties in establishing both phenotypes—that is, atopy and asthma—in young children. For example, it is possible that the group of children with recent asthma may include some with transient early wheeze and/or some children who are yet to manifest atopy as a positive skin prick test.

The lack of a significant association between recent asthma and maternal smoking in pregnancy or parental smoking in the first 6 months of the child's life was unexpected as an increased risk of asthma with smoking, especially in pregnancy, is commonly reported in the literature. In addition, we expected boys to have a greater risk of asthma than girls, as reported in the literature. However, while there was an indication of an increased risk for boys (table 3), this was not significant when adjusted for other risk factors (table 4).

The findings from this study have extended our knowledge of the early life determinants of asthma. We found that the consumption of fatty acids and the number of older siblings do have a significant association with recent asthma, and that breast feeding is associated with a decreased risk of asthma. These findings provide an important basis for the planning of future trials to prevent the onset of asthma during early childhood.

The authors thank the children and parents who participated in the study; Lismore and Wagga Wagga City Councils; Family Day Care; and the preschools, child care centres and playgroups that helped facilitate the study. They also thank the research assistants who helped in the organisation of the study, data collection, and data management.

All investigators contributed to the design of the study, to the an investigators continued to the design of the study, to the interpretation of the results and to the writing of the paper. Michelle Haby organised and supervised the fieldwork, data entry and management and performed the data analyses.

Funding: Financial support for the studies was provided by the National Health and Medical Research Council (NHMRC), the Community Health and Anti-Tuberculosis Association, and the Institute of Respiratory Medicine. This work was undertaken while Michelle Haby was a PhD candidate, supported by a scholarship from the Public Health Research and Development Committee of the NHMRC.

- 1 Peat JK, Toelle BG, Gray EJ, et al. Prevalence and severity of childhood asthma and allergic sensitisation in seven climatic regions of New South Wales. Med J Aust 1995;163:22-6.
- 2 International Study of Asthma and Allergies in Childhood (ISAAC) Steering Committee. Worldwide variation in prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema: ISAAC. *Lancet* 1998;**351**:1225-
- 3 Robertson CF, Heycock E, Bishop J, et al. Prevalence of asthma in Melbourne schoolchildren: changes over 26 years. BMJ 1991;302:1116-8.
- 4 Peat JK, van den Berg RH, Green WF, et al. Changing prevalence of asthma in Australian children. BMJ 1994; 308:1591–6.
- 5 Hide DW, Matthews S, Tariq S, et al. Allergen avoidance in infancy and allergy at 4 years of age. Allergy 1996;51:89-
- 95.
   6 Lucas A, Brooke OJ, Morley R, et al. Early diet of preterm infants and development of allergic or atopic disease: randomised prospective study. BMJ 1990;300:837–40.
   7 Merrett TG, Burr ML, Butland BK, et al. Infant feeding and
- allergy: 12-month prospective study of 500 babies born into allergic families. *Ann Allergy* 1988;**61**:13–20. Zeiger RS, Heller S, Mellon MH, *et al.* Effect of combined
- maternal and infant food-allergen avoidance on develop-
- ment of atopy in early infancy: a randomized study. J. Allergy Clin Immunol 1989;84:72–89.

  Martinez FD, Wright AL, Taussig LM, et al. Asthma and wheezing in the first six years of life. N Engl J Med 1995;332:133–8.
- 10 Peat JK, Tovey E, Gray EJ, et al. Asthma severity and morbidity in a population sample of Sydney schoolchildren Part II: Importance of house dust mite allergens. Aust NZ J Med 1994;24:270–6.
- 11 Rona RJ, Duran-Tauleria E, Chinn S. Family size, atopic disorders in parents, asthma in children, and ethnicity. J Allergy Clin Immunol 1997;99:454-60.

Asthma in preschool children 595

- 12 Wright AL, Holberg CJ, Taussig LM, et al. Relationship of infant feeding to recurrent wheezing at age 6 years. Arch Pediatr Adolesc Med 1995;149:758-63.
  13 Peat JK, Woolcock AJ. Sensitivity to common allergens: relation to respiratory symptoms and bronchial hyperresponsiveness in children from three different climatic and proceedings. Proceedings of Australia Clim. Eng. Marca: 1001.111673.
- responsiveness in ciniaren from three different climate areas of Australia. Clim Exp Allergy 1991;21:573–81.

  14 Pepys J. Skin testing. Br J Hosp Med 1975;14:412–7.

  15 Haby MM, Marks GB, Peat JK, et al. Day care attendance before the age of two protects against atopy in preschool age children. Pediatr Pulmonol 2000;30:377–84.

  16 Altman DG. Practical statistics for medical research. London:
- Chapman and Hall, 1992.

  17 Armitage P, Berry G. Statistical methods in medical research.

  3rd ed. Oxford: Blackwell Sciences, 1994.
- 18 Chinn S. Repeatability and method comparison. *Thorax* 1991;46:454–6.
- Kleinbaum DG, Kupper LL, Morgenstern H. Epidemiological research: principles and quantitative methods. New York: Van Nostrand Reinhold, 1982.
   Moffatt MF, Cookson WOCM. Maternal effects in atopic disease. Clin Exp Allergy 1998;28(Suppl 1):56-61.
   Australian Bureau of Statistics. 1989-90 National health sur-
- vey. Lifestyle and health. Catalogue No. 4364.0 1991. 22 Kirshner B, Gold M, Zimmerman B. Comparison between
- the prevalence and treatment of wheezing and coughing in Brampton and Mississauga children. J Clin Epidemiol
- 1990;43:765–71.
   Schwartz J, Gold D, Dockery DW, et al. Predictors of asthma and persistent wheeze in a national sample of children in the United States. Association with social class, perinatal events, and race. Am Rev Respir Dis 1990;142: 555–62.

- 24 Luyt DK, Burton PR, Simpson H. Epidemiological study of wheeze, doctor diagnosed asthma, and cough in preschool children in Leicestershire. BMJ 1993;306:1386-90.
- Hodge L, Peat JK, Salome C. Increased consumption of polyunsaturated oils may be a cause of increased prevalence of childhood asthma. Aust NZ J Med 1994;24:727.
- 26 Black PN, Sharpe S. Dietary fat and asthma: is there a connection? *Eur Respir J* 1997;10:6–12.
- Strachan DP. Hay fever, hygiene, and household size. BMJ 1989;299:1259-60.
- von Mutius E, Martinez FD, Fritzsch C, et al. Skin test reactivity and number of siblings. BMJ 1994;308:692-5
- Jarvis D, Chinn S, Luczynska C, et al. The association of family size with atopy and atopic disease. Clin Exp Allergy 1997;27:240-5.
- 30 Ponsonby A-L, Couper D, Dwyer T, et al. Cross sectional study of the relation between sibling number and asthma, hay fever, and eczema. Arch Dis Child 1998;79:328–33. Martinez FD. Role of viral infections in the inception of
- asthma and allergies during childhood: could they be pro-
- tective? *Thorax* 1994;**49**:1189–91. Lewis S, Richards D, Bynner J, *et al.* Prospective study of risk factors for early and persistent wheezing in childhood.
- Eur Respir J 1995;8:349–56.
  Oddy WH, Holt PG, Sly PD, et al. Association between breast feeding and asthma in 6 year old children: findings of
- a prospective birth cohort study. *BMJ* 1999;319:815–9. Sears MR, Herbison GP, Holdaway MD, *et al.* The relative risks of sensitivity to grass pollen, house dust mite and cat dander in the development of childhood asthma. Clin Exp Allergy 1989;19:419-24.