Cross sectional study of the relation between sibling number and asthma, hay fever, and eczema

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Abstract

***Objectives*—To document the relation between sibling number and atopic disease, and to assess the contribution of possible confounding factors to the protective effect of siblings in relation to asthma and hay fever.**

***Design and subjects*—Cross sectional survey by parental questionnaire in Tasmania, Australia, on 6378 children (92% of those eligible) who reached 7 years of age during 1995.**

***Methods*—Exercise challenge lung function testing was conducted on 428 children. Analyses reported were conducted on singleton births only (n = 6158).**

***Results*—The prevalences of a history of asthma ever, hay fever, and eczema were 27%, 19%, and 22%, respectively. Asthma and hay fever, but not eczema, were inversely related to sibling number, with evidence of a dose–response trend. The mean age at onset for asthma or wheezy breathing decreased as the number of siblings increased. The inverse association between sibling number and asthma or hay fever persisted after adjustment for several confounders, such as parental smoking or breast feeding, but did not persist after adjustment for household size in 1995.**

***Conclusions*—The protective effect of high sibling number could not be separated from household size at age 7, and it appears to be operating after birth and influences the age at onset of asthma symptoms. Further work to increase knowledge of how the protective effect of the presence of siblings works might have important implications for the understanding of the pathogenesis of asthma.**

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The prevalence of childhood asthma has increased in many Western countries. Because of the worldwide increase in the prevalence and morbidity of childhood atopic disease, a major focus of current research is to obtain a better understanding of the pathogenesis of allergic disease and how it might be prevented.[1] The reasons for this increase are unknown, but environmental factors are likely to be important.[2] Environmental factors might also explain why children with no siblings are at higher risk of atopic disease. In 1989, Strachan reported a striking inverse relation between the prevalence of allergic rhinitis at ages 11 and 23 and the number of older siblings in a national sample from the UK of 17 414 children born in 1958.[3] He suggested that this pattern was consistent with the hypothesis that respiratory infections brought about by contact with older siblings in early life might impede the development of allergies.[3] In 1994, a cross sectional survey of 9–11 year old German children found atopic sensitisation, as measured by one positive skin test to six common aeroallergens, decreased linearly with increasing number of siblings.[4] The National Study of Health and Growth in England and Scotland collected data on respiratory symptoms in children aged 5–11 years and parental atopic disease in 1990 and 1991.[5] The study found that children who resided with three or more siblings were less likely to have asthma than only children (adjusted odds ratio (AOR) 0.5; 95% confidence interval (CI), 0.4 to 0.6).[5] Ecological data indicate that there is a higher prevalence of asthma and allergies in populations in which the incidence of respiratory infection is low.[6] This observation raises the possibility that decreasing respiratory infection rates in early life might account for part of the increase in asthma prevalence in many Western countries.[6] This suggestion is consistent with some immunological findings relating to the infant period. Recent work has found that T helper (Th) cell types might be differentially promoted during the infant period. Viral and bacterial infection results in promotion of the Th1 cell lineage, which damps down the Th2 cell lineage. Th2 cells release interleukin 4 (IL-4) and IL-5, which are involved in IgE mediated disease.[7] The purpose of our paper is to examine the relation between the number of siblings and asthma and other atopic diseases, and to assess the contribution of possible confounding factors to the association between number of siblings and asthma and hay fever.

Methods

A cross sectional survey for childhood atopic disease was conducted in Tasmania in 1995. In March 1995, parental questionnaires were distributed through all primary schools, home learning, and distance education organisations in the state to the parents of children reaching the age of 7 in 1995. The questionnaire collected information using 65 questions. These were, in sequence: identification; questions from the 1968 Tasmanian Asthma Survey[8]; the eight core questions on asthma and wheeze from the International Study of Asthma and Allergy in Children (ISAAC) protocol[9]; asthma medication use; hospitalisation for respiratory illness;

Table 1 Cross sectional association between selected child or parental characteristics and asthma or hay fever

Child or parental characteristic	*Prevalence of asthma among those with factor*	*Prevalence of asthma among those without factor*	*OR (95% CI) for asthma*	*Prevalence of hay fever among those with factor*	*Prevalence of hay fever among those without factor*	*OR (95% CI) for hay fever*
History of bronchitis	48.6% (662/1361)	21.1% (976/4626)	3.54 (3.12, 4.02)	31.0% (425/1369)	16.1% (744/4626)	2.35 (2.04, 2.70)
History of pneumonia	53.6% (221/412)	25.4% (1418/5575)	3.39 (2.77, 4.15)	31.0% (129/416)	18.7% (1041/5580)	1.96 (1.58, 2.44)
History of frequent ear infection (more than two per year)	39.5% (590/1494)	23.4% (1052/4497)	2.14 (1.89, 2.42)	28.5% (430/1508)	16.5% (740/4492)	2.02 (1.76, 2.32)
Father in full time employment	26.1% (1086/4163)	29.2% (563/1926)	0.85 (0.64, 0.96)	19.3% (804/4172)	19.7% (379/1926)	0.97 (0.85, 1.12)
Low maternal education (< 12 years)	29.6% (1047/3538)	23.9% (594/2483)	1.34 (1.19, 1.50)	20.4% (721/3540)	18.0% (448/2491)	1.17 (1.02, 1.33)
Maternal active smoking in 1995	31.9% (596/1868)	25.0% (1059/4234)	1.41 (1.25, 1.58)	19.0% (355/1869)	19.7% (835/4243)	0.96 (0.83, 1.10)
Other household resident smoking in 1995	28.5% (515/1810)	26.2% (1065/4068)	1.12 (0.99, 1.27)	18.7% (339/1809)	19.6% 801/4078)	0.94 (0.82, 1.09)
Any breast feeding	26.0% (1219/4692)	31.0% (447/1444)	0.78 (0.69, 0.89)	19.2% (900/4697)	20.1% (291/1448)	0.94 (0.81, 1.09)
Regular child care at age 0	32.3% (181/561)	26.3% (1111/4222)	1.33 (1.10, 1.61)	19.7% (110/559)	19.0% (805/4230)	1.04 (0.83, 1.30)
Regular child care at age 1	29.9% (274/918)	26.0% (1011/3901)	1.22 (1.04, 1.43)	18.8% (172/917)	19.0% (744/3999)	0.98 (0.82, 1.18)
Regular child care at age 2	31.4% (433/1380)	25.6% (943/3680)	1.33 (1.16, 1.52)	19.0% (263/1382)	19.4% (715/3690)	0.98 (0.84, 1.14)
Regular child care at age 3	29.8% (565/1897)	25.6% (859/3358)	1.23 (1.09, 1.40)	20.0% (378/1894)	19.2% (647/3367)	1.05 (0.91, 1.21)
Regular child care at age 4	29% (591/2034)	25.8% (817/3171)	1.18 (1.04, 1.34)	19.3% (392/2033)	19.4% (617/3177)	0.99 (0.86, 1.14)
Male sex	31.2% (970/3111)	23.0% (700/3047)	1.52 (1.36, 1.70)	21.0% (655/3114)	17.7% (540/3052)	1.24 (1.09, 1.41)
Family history of asthma (among grandparents, parents, and siblings)	40.0% (1217/3045)	14.2% (424/2987)	4.02 (3.55, 4.56)	25.5% (778/3051)	13.1% (390/2988)	2.28 (1.99, 2.61)
Mother has a history of asthma or wheezy breathing	46.3% (612/1323)	21.8% (1030/4728)	3.09 (2.72, 3.51)	32.2% (426/1324)	15.7% (742/4735)	2.55 (2.22, 2.93)
Father has a history of asthma or wheezy breathing	44.0% (470/1068)	23.1% (1101/4760)	2.61 (2.27, 3.00)	29.3% (314/1071)	16.8% (803/4767)	2.05 (1.76, 2.38)
Prematurity (< 37 weeks' gestation)	37.2% (152/409)	26.3% (1504/5710)	1.65 (1.34, 2.04)	22.3% (93/418)	19.1% (1093/5710)	1.21 (0.95, 1.54)
Maternal age (per year)	–	–	0.96 (0.95, 0.97)	–	–	1.00 (0.99, 1.02)
Number of residents per household in 1995 (per resident)	–	–	0.89 (0.85, 0.94)	–	–	0.89 (0.85, 0.94)

use of asthma medication; attendance at regular child care; history of respiratory illness; family history (siblings, parents, and grandparents) of atopic and other disease; maternal/paternal history of asthma, wheezy breathing, or hay fever; maternal and paternal education, occupation, and employment; parental and other smoking; whether mother or others smoke in same room as child; duration of breast feeding; age of introduction to solids; some aspects of current diet; history of a cat as family pet; and details of the current home environment. Regular child care was defined as the child attending a child care arrangement with more than two other children at least once a week for three hours or more. For our paper, the term "asthma" refers to any history of asthma (ISAAC question 6), and current asthma is defined as a positive history of asthma (ISAAC question 6) and recent wheeze in the past 12 months (ISAAC question 2).

A total of 6913 forms were sent out. By 31 December 1995, 6378 questionnaires had been filled in by parents and returned (92% of all eligible children). Not all participating parents answered all questions. Most parents answered most questions. The sibling relationship between twins may differ from other sibling relationships, so the children in multiple births were excluded from the analyses reported here. Data on asthma were available for 6158 of the eligible singleton children. However, a lower proportion provided details of regular child care (table 1).

In addition, exercise challenge lung function testing was conducted at 23 randomly selected schools in southern Tasmania on 428 children (92% of eligible children) in a manner described elsewhere.[10] The exercise protocol was based on the work of Haby *et al.*[11] Briefly, the children were instructed to take a maximal breath in and then blow out as hard and as fast as they could in the standing position without a nose clip. After instruction and two practice attempts, each child performed sets of three forced expiratory manoeuvres (FEV_1 measurements) until two readings within 100 ml of one another were obtained in a set. The highest FEV_1 overall, excluding the two practice attempts, was taken as the baseline measurement of FEV_1. The child then ran for six minutes on a 100 m track with a nose clip and heart rate monitor.[10] Following exercise, FEV_1 measurements were made at three, five, and 10 minutes. At each point, three expiratory manoeuvres were performed. The minimum of the maximal values recorded at three, five, and 10 minutes was defined as the postexercise FEV_1. Ethical approval was obtained from the ethics committee (human experimentation), University of Tasmania and the Department of Education, Cultural and Community Development.

STATISTICAL ANALYSIS

Odds ratios (ORs) were estimated by logistic regression analysis[12] using dummy variables for the sibling categories in table 2, with "none" as the baseline group. An assessment of the effect of number of siblings was conducted by using a linear term in the logistic regression model as well as by grouping sibling number into various categories and comparing how they predicted asthma risk in a logistic model. The associations between the factors in table 3 and asthma were first investigated using contingency tables and the Maentel-Haensel χ^2 test.[12] ORs are presented to indicate the direction and strength of the associations. The χ^2 test of association was used to compare the characteristics of "only children" with those of children with siblings. To examine the possible contribution of confounders, multiple logistic regression[12] models that included terms for the exposure and potential confounding variables were used. Tabular and graphical displays suggested that number of siblings might have an influence on the age (in years) of onset of asthma or wheezy breathing. For children with asthma, the mean age of onset of symptoms was calculated for

Table 2 Variation in atopic disease by sibling number

Siblings	*Asthma prevalence*	*OR (95% CI) for asthma*	*Current asthma prevalence*	*OR (95% CI) for current asthma*	*Hay fever prevalence*	*OR (95% CI) for hay fever*	*Eczema prevalence*	*OR (95% CI) for eczema*
None	34.6% (124/358)	1.00 (reference)	24.4% (87/356)	1.00 (reference)	22.9% (82/358)	1.00 (reference)	23.3% (84/361)	1.00 (reference)
1	28.8% (700/2427)	0.76 (0.60, 0.97)	17.9% (431/2406)	0.67 (0.52, 0.88)	22.0% (536/2433)	0.95 (0.73, 1.24)	22.5% (550/2440)	0.96 (0.74, 1.25)
2	24.9% (479/1925)	0.63 (0.49, 0.80)	14.8% (283/1918)	0.54 (0.41, 0.70)	17.2% (330/1923)	0.70 (0.53, 0.92)	21.2% (409/1920)	0.89 (0.68, 1.16)
3	26.5% (228/862)	0.68 (0.52, 0.88)	17.1% (147/859)	0.64 (0.47, 0.86)	17.7% (153/865)	0.72 (0.53, 0.98)	21.6% (187/867)	0.91 (0.68, 1.22)
4	24.3% (66/272)	0.61 (0.43, 0.86)	15.5% (42/271)	0.57 (0.38, 0.85)	15.6% (43/275)	0.62 (0.41, 0.94)	18.6% (51/274)	0.75 (0.51, 1.11)
≥5	25.8% (34/132)	0.65 (0.42, 1.02)	17.4% (23/132)	0.65 (0.39, 1.09)	20.5% (27/132)	0.87 (0.53, 1.41)	19.5% (26/133)	0.80 (0.49, 1.31)

each particular number of siblings. A weighted regression model was fitted to these means, with the weights being the number of children on whom each mean was based.

The respiratory response to exercise was calculated as the postexercise FEV_1, expressed as a percentage of the baseline FEV_1, and is described in detail elsewhere.[10] The distribution of the percentage drop in FEV_1 was markedly skewed, with a small number of children experiencing a very large drop in FEV_1. To reduce the influence of these extreme values, medians rather then means are presented and the Wilcoxon 2 sample test[12] was used when comparing two groups. All analyses were performed using SAS version 6.09.[13]

Results

PREVALENCE

The prevalence of asthma was 27% (1670 of 6158) and current asthma was 17% (1040 of 6124). The prevalences of histories of eczema and hay fever were 22% (1332 of 6183) and 19% (1195 of 6166), respectively. The prevalence of recent wheeze was 22%. The prevalences of asthma and current asthma were significantly higher among "only children", with ORs of 1.44 (95% CI, 1.15 to 1.81) and 1.61 (95% CI, 1.25 to 2.08), respectively, but not for eczema (OR, 1.09; 95% CI, 0.84 to 1.40) or hay fever (OR, 1.22; 95% CI, 0.95 to 1.58).

"ONLY CHILDREN" AND EXERCISE INDUCED BRONCHIAL HYPERRESPONSIVENESS

The postexercise drop in FEV_1 was larger for children with current asthma (n = 60; median drop, 11.6%) than those with no current asthma (n = 340; median drop, 7.7%) (Wilcoxon 2 sample test, p = 0.0068). However, the drop in FEV_1 did not differ for sibling number. The median drop by sibling number was: no siblings, 8.8%; one sibling, 7.7%; two siblings, 7.5%, three or more siblings, 9.1%; (Kruskal-Wallis test, p = 0.84).

RELATION BETWEEN NUMBER OF SIBLINGS AND ATOPIC DISEASE

Asthma and hay fever were inversely associated with number of siblings (table 2). After taking into account whether the child had siblings or not, there were significant trends of decreasing prevalences of asthma (p = 0.032) and hay fever (p = 0.0011) with increasing numbers of siblings. Further investigation suggested that the trend was non-linear, with no further protective effect for three or more siblings. For current asthma, the linear trend for a protective effect of increasing number of siblings (beyond the first) was not significant (p = 0.2748), but the effect of two or more siblings was more protective than when a cut off point of one or more siblings was used. No dose–response relation between number of siblings and eczema was observed. For children without asthma, sibling number was not related (p = 0.9322) to the likelihood of having a history of wheezy breathing.

CONTRIBUTION OF OLDER SIBLINGS COMPARED TO YOUNGER SIBLINGS AND INTERBIRTH INTERVAL

The prevalence of asthma differed (p = 0.008) depending on whether the child had no siblings (34.6%), younger siblings only (27.1%), older siblings (27.4%), or both older and younger siblings (25.7%). The prevalence of asthma decreased significantly (p = 0.029) with an increasing number of older siblings (OR, 0.94; 95% CI, 0.89 to 0.99 for each sibling) but not with an increasing number of younger siblings (p = 0.11), although the magnitude of the protective effect was similar (OR, 0.94; 95% CI, 0.88 to 1.01). For hay fever, the number of older siblings had a greater protective effect (OR, 0.90; 95% CI, 0.84 to 0.96) than the

Table 3 Relation between sibling number and mean age at onset of asthma or wheezy breathing for children with asthma

	Mean age at onset of asthma or wheezy breathing in years				
	All children	*Youngest children of sibship*	*Oldest children of sibship*	*Positive family history of asthma*	*No family history of asthma*
Only child	2.40 (n = 115)	–	–	2.11 (n = 70)	2.80 (n = 40)
Children with 1 sibling	2.26 (n = 655)	2.07 (n = 316)	2.43 (n = 339)	2.19 (n = 461)	2.48 (n = 179)
Children with 2 siblings	2.20 (n = 441)	2.23 (n = 156)	2.35 (n = 115)	2.11 (n = 329)	2.46 (n = 110)
Children with 3 siblings	2.16 (n = 207)	2.18 (n = 62)	2.12 (n = 26)	2.01 (n = 162)	2.79 (n = 42)
Children with 4 siblings	1.90 (n = 60)	1.61 (n = 18)	1.50 (n = 2)	1.80 (n = 49)	2.10 (n = 10)
Children with ⩾ 5 siblings	1.72 (n = 29)	2.00 (n = 11)	–	1.74 (n = 27)	1.50 (n = 2)
p value of test for linear trend*	0.0093	0.90	0.11	0.0178	0.59

*There was no evidence to suggest that a non-linear model would have provided a substantially better fit.

Table 4 Effect of number of siblings and interbirth interval for children who are the youngest or oldest in the sibship

Variable	*OR (95% CI) for history of asthma*	*OR (95% CI) for history of hay fever*
For youngest children (n = 2306)		
Number of older siblings 1	1.00 (reference)	1.00 (reference)
Number of older siblings ⩾ 2	0.82 (0.68, 0.99)	0.75 (0.60, 0.92)
Gap to next sibling		
Interbirth interval 0–2 year*	1.00 (reference)	1.00 (reference)
Interbirth interval 3–5 years*	1.09 (0.89, 1.34)	1.39 (1.10, 1.74)
Interbirth interval 6–8 years*	1.26 (0.71, 2.23)	1.44 (0.98, 2.11)
Interbirth interval ⩾ 9 years*	1.02 (0.66, 1.56)	1.45 (0.92, 2.30)
Number of residents in 1995 (per one resident increase) (n = 2287)	0.90 (0.82, 0.99)	0.84 (0.75, 0.93)
For oldest children (n = 1858)		
Number of younger siblings 1	1.00 (reference)	1.00 (reference)
Number of younger siblings ⩾ 2	0.82 (0.66, 1.02)	0.84 (0.67, 1.07)
Gap to next sibling		
Interbirth interval 0–2 years†	1.00 (reference)	1.00 (reference)
Interbirth interval 3–5 years†	0.80 (0.63, 1.00)	0.92 (0.72, 1.19)
Interbirth interval 6–8 years†	1.02 (0.68, 1.54)	1.00 (0.64, 1.56)
Number of residents in 1995 (per one resident increase) (n = 1845)	0.80 (0.69, 0.92)	0.86 (0.75, 1.00)

*Adjusted for number of older siblings; †adjusted for number of younger siblings.

number of younger siblings (OR, 1.00; 95% CI, 0.92 to 1.08). To investigate the separate effects of older and younger siblings further, we examined the relation between sibling number, resident number, and interbirth interval for asthma and hay fever for children who were the eldest or youngest in the sibship (table 4). For youngest children, having two siblings rather than one was associated with a significantly lower OR for asthma and hay fever, and a short interbirth interval to next older sibling was associated with a lower rate of hay fever. For oldest children, there was a non-significant tendency of lower asthma and hay fever rates for increasing number of younger siblings and a short interbirth interval to next sibling was not associated with a significantly lower prevalence of asthma or hay fever. Resident number was inversely associated with asthma and hay fever for both samples (table 4).

RELATION BETWEEN NUMBER OF SIBLINGS AND AGE OF ONSET OF ASTHMA OR WHEEZY BREATHING

The mean age at onset for asthma or wheezy breathing decreased as the number of siblings increased (table 3). The age at onset distribution of asthma or wheezy breathing in completed years for children with asthma was: 0, 19.2%; 1, 23.3%; 2, 17.9%; 3, 14.1%; 4, 11.1%; 5, 10.8%; and 6, 3.6%. The trend of decreasing mean age at onset with increasing number of siblings was not evident if those with a family history of asthma were excluded (table 3). Children with asthma and recent wheeze had a similar age at onset to those with no history of recent wheeze.

FURTHER INVESTIGATIONS OF THE ASSOCIATION BETWEEN PRESENCE OF SIBLINGS AND ASTHMA

First, the characteristics of only children were compared with those of children with siblings. "Only children" were more likely to be in regular child care during any of the first 5 years of life ($p < 0.0001$) and to have a mother of younger age ($p < 0.0001$), a mother who smoked ($p < 0.001$), or had a lower education level (< year 12) ($p = 0.023$). "Only children" were less likely to have a father in full time employment ($p = 0.002$) or to have been breast fed ($p = 0.001$). They were less likely to have a family history of asthma ($p = 0.003$), but this partially reflects the fact that family history includes any positive results among siblings and, hence, there is more likely to be a positive family history of asthma for children in larger sibgroups. "Only children" were less likely to have a high number of residents in the household ($p < 0.001$).

Secondly, the association between various child and family characteristics and hay fever or asthma was examined to allow the identification of potentially confounding factors (table 1) then, the relation between sibling number and asthma or hay fever was examined after individual adjustment for the potential confounders listed in table 1. Adjustment for family history of asthma increased the inverse association between sibling number and asthma. Adjustment for maternal age partially reduced the associations. Adjustment for household resident number removed the relation between sibling number and asthma: no siblings adjusted OR (AOR), 1.00 (baseline); one sibling AOR, 0.89 (95% CI, 0.69 to 1.14); two siblings AOR, 0.84 (95% CI, 0.63 to 1.12); and three or more siblings AOR, 1.05 (95% CI, 0.74 to 1.48). Adjustment for household resident number also removed the inverse association between sibling number and hay fever. Adjustment for regular child care at age 0, 1, 2, or 3, type of home heating, or the other potential confounders in table 1 did not alter the ORs for sibling number and asthma or hay fever by 10% or more.

After adjustment for family history of asthma, maternal age, breast feeding, and maternal and other adult resident smoking, the sibling effect for asthma was as follows: no siblings AOR, 1.00 (reference); one sibling AOR, 0.73 (95% CI, 0.56 to 0.95); two siblings AOR, 0.58 (95% CI, 0.44 to 0.76); three or more siblings AOR, 0.55 (95% CI, 0.41 to 0.73). With further adjustment for family history of hay fever, the sibling effect for hay fever was: no siblings AOR, 1.00 (reference); one sibling AOR, 0.90 (95% CI, 0.67 to 1.21); two siblings AOR, 0.61 (95% CI, 0.45 to 0.82); three or more siblings AOR, 0.55 (95% CI, 0.40 to 0.76). Again, the further addition of resident number removed the association between sibship size and asthma or hay fever. In this final model, resident number remained significantly and negatively related to asthma or hay fever.

RELATION BETWEEN REGULAR CHILD CARE AND ASTHMA AND ATOPIC DISEASE

Any regular child care during the first 5 years of life was associated with an increased likelihood of asthma (unadjusted OR (UOR), 1.23; 95% CI, 1.07 to 1.41). The number of years of child care was also positively associated with asthma (UOR, 1.07; 95% CI, 1.02 to 1.11 for each year). The relation between child care and asthma did not differ by age of child care commencement. No relation was seen for any

regular child care or number of child care years and hay fever or eczema. Participation in regular child care in any individual year of the first 5 years of life was associated with an increased likelihood of asthma (table 1). After adjustment for all the variables listed in table 1, apart from the child care variables, children in regular child care during any year of the first 5 years of life were still significantly ($p < 0.05$ in each case) more likely to have asthma, with ORs of 1.20 to 1.35. Adjustment for sibling number did not remove the positive association between regular child care at ages 0, 1, 2, 3, or 4 and asthma. Among children with no siblings (n = 244), there was no significant relation between participating in regular child care at ages 0, 1, 2, or 3 and asthma. However, "only children" attending regular child care at age 4 were less likely to have current asthma (OR, 0.22; 95% CI, 0.05 to 0.95) or hay fever (OR, 0.12; 95% CI, 0.02 to 0.65) than "only children" who did not. Children who participated in regular child care during the first year of life were significantly more likely to have a history of frequent ear infections (more than two a year) (OR, 1.38; 95% CI, 1.13 to 1.69), but not bronchitis (OR, 1.19; 95% CI, 0.97 to 1.45), or pneumonia (OR, 1.19; 95% CI, 0.86 to 1.66).

Discussion

In our study, a protective effect of increasing sibling number was found for asthma and hay fever, but not for eczema. Interestingly, although an overall dose response trend was found for the negative association between sibling number and asthma and hay fever, the dose response effect was not constant and no further protective effect was found for three or more siblings. The protective effect of increasing sibling number has now been documented across the spectrum of childhood atopic disease: hay fever,[3 14 15] allergic sensitisation to common allergens,[3 4 14 15] eczema,[16] and asthma.[5] A recent cohort follow up of New Zealand children found no relation between number of siblings and asthma.[17]

In our study, "only children" were more likely to have other characteristics (for example, born to a mother who smokes) that were associated with increased asthma prevalence. However, after adjustment for these factors, the inverse association between large sibship size and asthma or hay fever remained, indicating that the sibling effect was independent of family history of asthma, maternal age, breast feeding, maternal smoking, and participation in child care. However, an increasing number of household residents was protective for asthma or hay fever and, after this was taken into account, there was no independent increase in risk of being an only child. This suggests the adverse effect of being an only child is not independent of the adverse effect of a low number of residents in the home at age 7. This might reflect the fact that sibling number is a determinant of household size and therefore closely related to it, so it is difficult to separate the effects.

For youngest children, the presence of two or more older siblings was associated with lower asthma and hay fever prevalence. A short birth interval to next older sibling was also associated with reduced hay fever rates, as reported recently by Strachan *et al*.[14] For oldest children, the presence of two or more siblings was associated with a lower odds of asthma and hay fever of borderline significance. Thus, the influence of older siblings appeared to be more important than that of younger siblings. However, the findings of a significant protective effect of increasing resident number in 1995 among the oldest child sample, and the finding that the magnitude of the OR reduction was similar for younger and older siblings for asthma, indicates that the protective effect of increasing sibling number might not be acting solely in the first few months after birth.

Exercise induced bronchial hyperresponsiveness was found more commonly in children classified as having current asthma by the parental questionnaire criteria in this study, as in our previous study.[10] However, "only children" were not found to have more exercise induced bronchial hyper responsiveness. This is not surprising, given that exercise induced bronchial hyper-responsiveness has a relatively low sensitivity and a high specificity for current asthma by questionnaire,[10] and that the magnitude of the OR between "only child" status and asthma is less than 2.

The prevalences of recent wheeze and asthma in this sample (22% and 27%, respectively) were lower than those reported in 1992[18] for children aged 8–10 in Belmont (28% and 38%, respectively) and Wagga Wagga (23% and 30%, respectively), even though the children sampled in the latter two New South Wales towns were older and the criterion of asthma diagnosed by a doctor was used, rather than parental report of "asthma ever", as in this study and the recent ISAAC studies. The difference in prevalence might be a result of chance, or different environmental influences. One exposure that might differ is mite allergen density. A recent study of the mite allergen density of infant bedroom floors (n = 72) in southern Tasmanian homes found the geometric mean density for the mite allergen, Der P1, was 2.04 μg/g,[19] which is considerably lower than the mite allergen density reported in a New South Wales study using similar methodology (geometric mean, 22.5 μg/g).[20]

An earlier Australian study[21] found that asthma was more common among children in child care, but a more recent study[22] of school age children (aged 5 years) found that those who attended child care before school experienced half as many asthma episodes during the first winter terms. Increased likelihood of upper respiratory infection,[23] thick nasal discharge,[21] febrile illness,[24] and otitis media have been reported for children attending regular child care before age 5. Here, regular child care during any of the first 5 years of life was associated with a higher risk of asthma, even after adjustment for the possible confounders listed in table 1. Given that children who participate in child care are at increased risk of infection, this observation is not consistent with the theory that viral and bacterial

infection during early life might hamper the development of allergies. However, the data here were based on parental recall, some parents did not provide child care data and an accurate examination of child care participation throughout early life is not possible. An important stage of infant immune development might be from 3–18 months of age. IL-4, a key cytokine in the regulation of IgE antibody formation[7] has recently been found to peak at 6–9 months of age and to predict allergic disease during the first 18 months of life.[25] The observation that "only children" with asthma were less likely to be in regular child care than "only children" without asthma at age 4 might reflect the parental response to asthma in these children, as most had developed asthma before this age.

Our study found that age of onset of asthma or wheezy breathing for children with asthma increased as sibling number decreased. This effect was seen particularly among those with a family history of asthma and was not present among children without such a family history. One possibility is that this reflects reporting bias (that is, the more children in the family, the more likely parents and medical contacts are to classify a child as having asthma at a younger age). However, this might not be the explanation because the effect was not present among youngest children, the group where reporting bias would be expected to be most likely to occur. If this finding is replicated in other studies and found not to be caused by bias or chance, then it could provide a useful insight into how the protective effect of sibling number is operating. For example, the age at onset of asthma has been found previously to be younger among children with asthma who are mite sensitised than children who are not[26] and among children born to smokers.[27]

In summary, a protective effect of increasing sibling number was identified for asthma and hay fever. This effect could not be explained by potential confounding by associated family characteristics such as parental smoking or infant feeding pattern. The protective effect was not independent of household size and appears to be operating for more than a short time after birth. Prospective epidemiological studies are required to obtain clearer insights into the mechanism of the protective effect of sibling number for childhood asthma and atopic disease.

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