

NAC Manchester Asthma and Allergy Study (^{NAC}MAAS): risk factors for asthma and allergic disorders in adults

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Summary

Background Asthma and atopic disorders are the most common chronic diseases in the developed countries. Knowledge of the risk factors for these disorders may facilitate the development of preventive strategies aimed at reducing prevalence rates.

Objectives To investigate the risk factors for asthma and allergic diseases in a large number of adults who are the parents of children in the National Asthma Campaign Manchester Asthma and Allergy Study.

Methods All pregnant women and their partners attending 'Booking' antenatal clinics were invited to take part in the study. Questionnaire data were collected including the history of asthma and other atopic diseases, pet ownership and smoking habits, and skin prick tests were performed. The prevalence of atopy and the risk factors for asthma and allergic disorders were investigated in all subjects who completed the questionnaire and underwent skin testing. Statistical analysis was carried out using logistic regression. Initially, risk factors were assessed by univariate analysis to see how each potential explanatory variable affected the probability of having allergic disease. Variables were then tested in a forward stepwise multivariate analysis.

Results In 5687 adult subjects there was a very high (48.2%) prevalence of atopy, and 9.7% of subjects had a diagnosis of asthma. In a multivariate regression analysis sensitization to dust mite, cat, dog and mixed grasses were all independently associated with asthma. The odds ratios for current asthma increased with the increasing number of positive skin tests (any two allergens – OR 4.3, 95% CI 3.3–5.5; any three allergens – OR 7.0 95% CI 5.3–9.3; all four allergens – OR 10.4, 95% CI 7.7–14; $P < 0.00001$). Dog ownership (OR 1.31, 95% CI 1.10–1.57; $P = 0.003$) and current smoking (OR 1.36, 95% CI 1.15–1.62; $P = 0.0004$) were significantly and directly associated with 'asthma ever'. Thirteen per cent of participants reported a history of eczema. In the multivariate analysis the strongest independent associate of eczema was sensitization to dog (OR 1.37, 95% CI 1.14–1.63, $P < 0.0001$). Apart from dog, the strength of the association between sensitization to common allergens and eczema appeared to be much lower than in the case of asthma. The prevalence of hay fever was high (20.6%), and in the multivariate analysis the association between sensitization to pollen and hay fever was extremely strong (OR 13.6, 95% CI 11.3–16.3; $P < 0.0001$).

Conclusions The results of the current study emphasize the importance of sensitization to indoor allergens in asthma. However, evidence of a possible direct role of allergen exposure in asthma causation remains unclear.

Keywords: asthma, eczema, hay fever, allergens, skin prick tests

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Introduction

The prevalence and severity of asthma is increasing, especially in children. The cause of this increase has been the subject of many debates and cannot be genetic in origin. It is generally accepted that environmental factors such as motor vehicle pollution and passive smoking can trigger an asthma attack in an established asthmatic patient, but it seems unlikely that they are the cause of increased disease prevalence. Other factors currently receiving much attention are extensive vaccination programmes, which have changed the immunity of a generation with consequently fewer natural infections [1], changes in diet [2] particularly food preservation, the addition of antibiotics to much of the food we eat, and the inappropriate use of broad-spectrum antibiotics to treat illness [3]. At the same time life style changes have created homes that are better insulated and more energy efficient, resulting in a warm and humid environment with low ventilation rates, ideal for house dust mite growth. Many homes now also have cats and dogs living indoors. Sensitization to indoor allergens (house dust mite, cat, dog) has been shown as an important risk factor for asthma [4]. Speculation currently exists as to whether the development of sensitivity to indoor allergens during childhood and the symptoms and severity of asthma in later life may be related to allergen exposure in infancy [5] and even *in utero* [6].

In this publication we report on the risk factors for asthma and allergic diseases in 5687 adults. They are the parents screened for inclusion of their children in the National Asthma Campaign Manchester Asthma and Allergy Study (^{NAC}MAAS), which investigates the relationship between genetic predisposition and environmental exposures in the development of atopy, asthma and other allergic diseases, and whether it is possible to prevent allergic sensitization and the development of asthma and other allergic disorders in children at high risk by the use of environmental control.

Methods

Between October 1995 and July 1997 all pregnant women and their partners attending 'Booking' antenatal clinic at Wythenshawe and Stepping Hill Hospitals were given a detailed information sheet and invitation to take part in the study by reception staff. The study was then further explained in a personal interview with one of the researchers before informed consent was obtained. If fathers were not present at the antenatal clinic they were sent information and an invitation to attend open access evening clinics.

Participants were asked to complete a questionnaire giving basic demographic data and a history of atopic

disorders, pet ownership and smoking habits. The questions were derived from the American Thoracic Society-DLD-78 questionnaire, and included: Has a doctor ever told you that you have asthma/eczema/hay fever? Do you have asthma/eczema/hay fever now? Do you take any asthma medication? Skin prick testing was carried out in the antenatal clinic or by invitation to an 'open access' evening clinic.

Skin prick testing

Skin tests were performed by the prick method on the volar surface of the forearm. The test sites were at least 3 cm apart and were not placed within 5 cm from the wrist and 3 cm from elbow. Skin tests were performed with standardized allergen preparations (Bayer Corporation, Elkhart, IN, USA). The extracts of the four most common inhalant allergens were used (*D. pteronyssinus*, cat, dog, mixed grasses) with negative and positive (Histamine dihydrochloride 10 mg/mL) controls. One drop of test solution was applied and the lancet was pressed at 90° to the skin surface through a drop of test solution. The same pressure was applied every time and a separate lancet for each allergen and control solution was used. The test solutions were then carefully blotted off. Test sites were inspected and the size of reaction recorded as the mean of the longest and the midpoint orthogonal diameters after 15 min. Weal diameter at least 3 mm greater than the negative control was regarded as a positive response.

Statistical analysis

The prevalence of atopy and the risk factors for asthma and other allergic disorders were investigated in all subjects who completed the questionnaire and underwent skin prick testing. The potential for dependence between the allergic conditions data for each woman and her partner was assessed using Kappa coefficient and the data were modelled for the sexes both individually and together to check for consistency.

Statistical analysis was carried out using logistic regression. Initially, risk factors were assessed by univariate analysis (i.e. analysis performed without adjusting for any of the covariates), to see how each potential explanatory variable (e.g. sensitization to house dust mites, cat, dog, and pollen, smoking, pet ownership, etc.) affected the probability of having allergic disease. Variables were then tested in a forward stepwise multivariate analysis combining the relevant variables to control for the effect of each explanatory variable on the other variables studied. The size of the effect of each of the risk factors was measured using the odds ratios (OR) and 95% confidence intervals (CI). The data were analysed using the Statistical Package for Social Sciences (SPSS) version 8.0.

Results

A total of 5890 pregnant females attending 654 antenatal clinics at the two study hospitals were invited to take part, of whom 1306 declined the invitation. Two hundred and seventy out of 1306 participants who declined the invitation to participate in the study completed the questionnaires. A further 1060 failed to meet the entry criteria for inclusion of their unborn child in the study (e.g. > 16 weeks pregnant at 'booking' appointment, < 18 years of age). Three thousand five hundred and twenty-four (3524) pregnant women and 2163 of their partners completed the questionnaire and were skin prick tested, giving a total sample of 5687 adult participants (mean age 29.6 years, range 18–45 years). Kappa coefficient revealed no dependence between the allergic conditions data for women and their partners, indicating that there was no association between the couples (asthma: $\kappa = 0.034$, $P = 0.22$; eczema: $\kappa = 0.036$, $P = 0.20$; hay fever: $\kappa = 0.034$, $P = 0.22$).

Prevalence of atopy, asthma, allergic disorders and pet ownership

Analysis of questionnaire data on those subjects who agreed to take part and were skin prick tested is presented in Table 1. The prevalence of physician-diagnosed asthma, other allergic diseases, pet ownership and smoking is shown in all subjects and by sex. Eight hundred and seventy-eight subjects (15.4%) reported asthma ever, 554 (9.7%) were diagnosed as 'having current asthma' by their family practitioner, and 572 (10.1%) were prescribed asthma medication. The proportion of participants reporting asthma ever, current asthma, eczema and other allergies was significantly higher amongst females compared to males ($P < 0.001$). No difference between sexes was found for hay fever. A significantly higher proportion of women than men were prescribed anti-asthma treatment (OR 1.5, 95% CI 1.26–1.78; $P < 0.001$). Pet ownership was very common in this sample, with 40.7% of the subjects keeping pets (cat and/or dog) in their homes. Cat ownership was more common than dog ownership (Table 1). Of 959 subjects with skin test positive to cats, 212 (22.1%) lived in a home with a cat. Similarly, 17.1% of the dog-sensitized individuals (95/557) lived in a home with a dog. Of 239 subjects with a current physician-diagnosed asthma who were skin test positive to cats, 19.7% (47) lived in a home with a cat. The proportion of dog-sensitized participants with current physician-diagnosed asthma who lived in a home with a dog was 22.6% (36/159). Approximately a quarter of participants were current smokers, and the proportion of smokers was significantly higher in men compared to women (OR 1.46, 95% CI 1.33–1.59; $P < 0.001$).

The prevalence of asthma, eczema, hay fever and pet ownership in 270 out of 1306 participants who declined the invitation to participate in the study, but completed the questionnaires, was the same as in those taking part (asthma ever: 15.0%, $P = 0.93$; current asthma 10.5%, $P = 0.67$; prescribed asthma medication 9.0%, $P = 0.67$; history of eczema 13.1%, $P = 0.46$; history of hay fever 19.5%, $P = 0.7$; cat ownership 28.5%, $P = 0.22$; dog ownership 21.0%, $P = 1.0$).

Sensitivity to common inhalant allergens assessed by skin testing

The prevalence of sensitization to four common inhalant allergens and the combination of sensitization to different allergens in all subjects and by sex are presented in Table 2. Overall, 2743 subjects (48.2%) were atopic (i.e. sensitized to at least one of the allergens). House dust mite was the most common sensitizer (34.1%), closely followed by mixed grasses (34%). Sensitivity to cat was significantly more common than sensitivity to dogs (16.9% vs. 9.8%).

In total, 1265 women were skin test positive to either dust mite, cat or dog, and 213 were sensitized to all three indoor allergens. Forty-six per cent (46%) of the multiple-sensitized women reported a history of asthma, compared to 21% of those sensitized to dust mite only, 27% in a group sensitive to cat alone and 19% in those sensitized to dog only. Of 1098 females with positive skin tests to grasses, 311 were sensitized to this outdoor allergen only. In this group sensitive to pollen only, 52% reported having hay fever and 16% gave a history of asthma.

Analysis of the skin test data in men gave remarkably similar results. One hundred and thirty-seven (137) men were skin test positive to all three indoor allergens (dust mite, cat and dog), and 44% of these reported having asthma. Men mono-sensitized to dust mite or cat or dog reported, respectively, a 16%, 12% and 21% history of asthma. Altogether 215 men were sensitized to pollen alone, 50% of whom gave a history of hay fever, with only 6.5% reporting a diagnosis of asthma.

Risk factors for asthma and other atopic disorders

Prevalence of sensitization to four common inhalant allergens in participants with and without a current physician diagnosis of asthma is presented in Table 3. Risk factors for asthma, eczema and hay fever were assessed by logistic regression to see how each potential explanatory variable (e.g. sensitization to house dust mites, cat, dog, and pollen, smoking, pet ownership) affected the probability of being affected.

The univariate analysis of potential risk factors for asthma ever, current asthma, eczema and hay fever is

Table 1. Prevalence of allergic disease, pet ownership and smoking in 5687 participants who agreed to take part and were skin tested

	All subjects (<i>n</i> = 5687)		Females (<i>n</i> = 3524)		Males (<i>n</i> = 2163)	
	Frequency	%	Frequency	%	Frequency	%
<i>Prevalence of allergic diseases</i>						
Asthma ever	878	15.4	587	16.7	291	13.5
Current asthma	554	9.7	394	11.2	160	7.4
Prescribed asthma medication	572	10.1	406	11.5	166	7.7
History of eczema	759	13.3	561	15.9	198	9.2
History of hay fever	1172	20.6	720	20.4	462	20.9
Other allergies	805	14.2	565	16	240	11.1
<i>Pet ownership</i>						
Cat owner	1425	25.1	906	25.7	519	24
Dog owner	1207	21.2	776	22	431	19.9
Cat and dog owner	320	5.6	205	5.8	115	5.3
No pets	3375	59.3	2047	58.1	1328	61.4
<i>Smoking status</i>						
Current smoker	1488	26.2	786	22.3	702	32.5

presented in Table 4. Sensitization to each of the four allergens (i.e. house dust mite, cat, dog and pollen) was significantly associated with asthma ever, current asthma and eczema. Unsurprisingly, sensitization to mixed grasses was very strongly associated with hay fever, with sensitization to other allergens also being significant associates of this atopic condition. Being sensitized to more than one allergen considerably increased the magnitude of risk for asthma ever (two allergens – OR 3.9, 95% CI 3.2–4.9; three allergens – OR 6.9, 95% CI 5.4–8.7; all

four allergens OR 9.8, 95% CI 7.6–12.7) and current asthma (any two allergens – OR 4.3, 95% CI 3.3–5.5; any three allergens – OR 7.0 95% CI 5.3–9.3; all four allergens – OR 10.4, 95% CI 7.7–14; $P < 0.00001$).

Sensitization to more than one allergen also increased the risk of eczema, but not to the same extent as the association between multiple sensitization and asthma. Being sensitized to pollen alone in the absence of sensitization to any of the indoor allergens, and male sex, were significantly and inversely associated with asthma. In this analysis,

Table 2. Prevalence of sensitization to four common inhalant allergens in 5687 participants who agreed to take part and were skin tested

	All subjects (<i>n</i> = 5687)		Females (<i>n</i> = 3524)		Males (<i>n</i> = 2163)	
	Frequency	%	Frequency	%	Frequency	%
<i>Sensitization to allergens</i>						
House dust mite	1940	34.1	1078	30.6	862	39.9
Cat	959	16.9	589	16.7	370	17.1
Dog	557	9.8	338	9.6	219	10.1
Pollen	1931	34	1098	31.2	833	38.5
Atopic	2743	48.2	1576	44.7	1167	54
Sensitized to 1 allergen	1175	20.7	687	19.5	488	22.6
Sensitized to 2 allergens	810	14.2	444	12.6	366	16.9
Sensitized to 3 allergens	440	7.7	252	7.2	188	8.7
Sensitized to 4 allergens	318	5.6	193	5.5	125	5.8
Sensitized to pollen only	526	9.2	311	8.8	215	9.9

Table 3. Prevalence of sensitization to four common inhalant allergens in participants with and without a current physician diagnosis of asthma

	Physician-diagnosed asthma (<i>n</i> = 554)		Non asthmatic (<i>n</i> = 5133)	
	Frequency	%	Frequency	%
<i>Sensitization to allergens (skin test positive)</i>				
Dust mite	347	62.64	1593	31.03
Cat	239	43.14	720	14.03
Dog	159	28.70	398	7.75
Pollen	326	58.84	1605	31.27

current smoking was not associated with asthma. Dog ownership was significantly associated with current asthma, but there was a trend for an inverse relationship for cat ownership (OR 0.84, 95% CI 0.68–1.0; $P = 0.08$). We found no association between pet ownership and eczema in the univariate analysis. Current smoking was not found to be associated with asthma or eczema, but it was strongly and inversely associated with hay fever (OR 0.7, 95% CI 0.6–0.8, $P = < 0.0001$).

The finding of a lower prevalence of asthma in pollen-only allergic subjects may be an artefact of the univariate analysis. We therefore compared the prevalence of asthma between pollen-only allergic subjects and non-allergic subjects, and found no significant differences between these two groups (the prevalence of current asthma was 4.3% and 5.9% in non-atopic and pollen only allergic groups, respectively; $P = 0.11$, chi-square test).

The results of multivariate regression analysis are presented in Table 5. Sensitization to dust mite, cat, dog and pollen were all independently associated with asthma ever, current asthma and eczema. The association between sensitization to pollen and hay fever was found to be extremely strong (OR 13.6, 95% CI 11.3–16.3, $P = < 0.00001$). In this analysis sensitization to dust mite and current smoking were again found to be inversely associated with hay fever. Being female was a significant associate of asthma and eczema but gender was not an associate of hay fever. The other independent associates of asthma were dog ownership and current smoking.

Discussion

This study of adult participants sought to investigate the risk factors associated with asthma, hay fever and eczema in a large sample of 5687 adults who completed questionnaires and were skin prick tested. The questionnaire identified 9.7% of subjects with current physician diagnosis of asthma, with a 48.2% prevalence of atopic sensitization. Although the possibility of selection bias

cannot be completely excluded (e.g. atopic women may be more interested and likely to agree to be skin tested; partners of atopic women could have greater incentive to follow on and attend open-access clinics for skin testing), we believe that this did not have a major influence on the results. Our response rate was high at 78%. Furthermore, 270 out of 1306 participants declined the invitation to participate in the study, but completed the questionnaire, and the prevalence of asthma, eczema, hay fever and pet ownership was the same as in those taking part.

In accordance with a number of previous studies in adults and children [7–10], the current study demonstrated that sensitization to indoor allergens was strongly associated with asthma. In a multivariate regression analysis sensitization to dust mite, cat, dog and mixed grasses were all independently associated with asthma ever and current asthma. It could be expected that, in keeping with the data from other areas of the world with a humid climate (e.g. Australia [11,12], New Zealand [13,14] and USA [15]), dust mite allergy should be important in the north-west of England. However, although sensitization to dust mites was the strongest independent associate of asthma, the strength of the association was almost equal for sensitization to cats. The odds ratios for asthma substantially increased with the increasing number of positive skin tests, suggesting the positive association between the degree of atopy (assessed by the number of positive skin tests) and disease.

Sensitization to the mainly outdoor grass pollen allergens appeared to be of much less importance in asthma than sensitization to indoor allergens. Furthermore, in the univariate analysis a strong inverse association was found between asthma and sensitization to grass pollen only (i.e. in the absence of sensitization to indoor allergens). A similar protective effect of sensitization to grass pollen on asthma has been reported by Charpin *et al.* in France [16,17]. However, this finding is probably an artefact of the univariate analysis, as no difference in the prevalence of asthma was found between pollen-only allergic subjects and non-allergic subjects. The multivariate analysis suggests that

Table 4. Univariate analysis of potential risk factors for asthma ever, current asthma, eczema and hay fever

	Odds ratio and 95% confidence interval			
	Asthma ever	Current asthma	Eczema	Hay fever
<i>Sensitization to allergens</i>				
House dust mite	3.49* (3.01–4.04)	3.73* (3.11–4.47)	1.75* (1.5–2.05)	2.52* (2.21–2.87)
Cat	4.51* (3.85–5.29)	4.65* (3.86–5.6)	1.9* (1.59–2.28)	4.849* (4.18–5.63)
Dog	4.56* (3.78–5.51)	4.79* (3.88–5.91)	2.48* (2.01–3.05)	4.56* (3.81–5.47)
Pollen	3.29* (2.83–3.81)	3.14* (2.63–3.76)	1.94* (1.66–2.26)	14.31* (12.19–16.79)
Any 2	3.94* (3.2–4.86)	4.28* (3.3–5.54)	1.97* (1.58–2.46)	11.77* (9.47–14.64)
Any 3	6.87* (5.42–8.71)	7.01* (5.28–9.3)	2.29* (1.76–2.99)	18.89* (14.72–24.25)
All 4	9.83* (7.58–12.74)	10.41* (7.74–13.99)	3.44* (2.61–4.54)	19.87* (15.09–26.16)
Mite and Cat	7.12* (5.88–8.62)	7.6* (6.06–9.54)	2.26* (1.83–2.78)	5.49* (4.6–6.56)
Mite and Dog	7.71* (6.17–9.63)	8.33* (6.45–10.75)	3.01* (2.37–3.82)	5.56* (4.5–6.87)
Dog and Cat	6.37* (5.15–7.86)	6.72* (5.31–8.5)	2.7* (2.14–3.4)	6.06* (4.93–7.43)
Mite and Cat and Dog	9.2* (7.21–11.72)	10.19* (7.74–13.15)	3.16* (2.44–4.1)	7.09* (5.62–8.96)
Pollen only	0.67● (0.51–0.89)	0.56◆ (0.38–0.81)	1.17 (0.9–1.5)	4.89 (4.06–5.89)
<i>Pet ownership</i>				
Dog owner	1.27● (1.07–1.5)	1.28◆ (1.04–1.56)	0.93 (0.77–1.12)	0.9 (0.77–1.06)
Cat owner	0.86 (0.72–1.02)	0.84 (0.68–1.0)	0.84 (0.97–1.01)	0.86 (0.74–1)
Smoking status	1.14 (0.97–1.34)	0.96 (0.79–1.17)	0.9 (0.75–1.07)	0.68* (0.58–0.79)
<i>Sex</i>				
Female	1.29◆ (1.1–1.5)	1.58* (1.3–1.91)	1.88* (1.58–2.23)	0.97 (0.85–1.11)

* $P = < 0.0001$. ● $P = 0.001–0.0001$. ◆ $P = 0.05–0.001$.

pollen allergy is associated with an increased risk of asthma, but is a lesser risk than indoor allergens.

Although the relationship between exposure to environmental tobacco smoke and asthma has received less scientific interest in adults than in children, some evidence is emerging linking tobacco smoke with increased asthma severity and worse health status in adults with established disease [18]. In the current study, smoking was associated with a history of asthma symptoms, but not with a current diagnosis of asthma. The apparent lack of relationship between smoking and physician-diagnosed asthma may be

influenced by a tendency of family practitioners to diagnose smokers with wheeze as having chronic bronchitis rather than asthma [19].

The finding of the current study that a larger proportion of participants were prescribed asthma medication than were diagnosed as current asthmatics could indirectly support this view (particularly as the study participants were young adults amongst whom the diagnosis of COPD is extremely rare). Another indirect indicator that this may be the case is the finding in a recent study by Bodner *et al.* who have demonstrated that current smoking was

Table 5 Multivariate logistic regression analysis of asthma ever, current asthma, eczema and hay fever.

	Odds Ratio and 95% Confidence Interval			
	Asthma ever	Current asthma	Eczema	Hay fever
<i>Sensitization to allergens</i>				
House dust mite	2.05* (1.72–2.44)	2.27* (1.83–2.81)	1.37● (1.14–1.63)	0.68* (0.57–0.81)
Cat	2.04 * (1.65–2.52)	2.02* (1.58–2.59)	NS	1.5* (1.26–1.89)
Dog	1.73* (1.37–2.19)	1.84* (1.42–2.4)	1.73* (1.38–2.19)	1.37◆ (1.09–1.73)
Pollen	1.71* (1.43–2.05)	1.48● (1.18–1.84)	1.57* (1.31–1.88)	13.62* (11.34–16.35)
<i>Pet ownership</i>				
Dog owner	1.31◆ (1.1–1.57)	1.37◆ (1.1–1.69)	NS	NS
<i>Smoking status</i>				
Smoker	1.37● (1.15–1.62)	NS	NS	0.78◆ (0.65–0.93)
<i>Sex</i>				
Female	1.53* (1.3–1.8)	1.82* (1.49–2.22)	2.04* (1.71–2.43)	NS

* $P = < 0.0001$. ● $P = 0.001–0.0001$. ◆ $P = 0.05–0.001$. NS = not significant.

associated with adult onset wheeze, but not with physician-diagnosed adult-onset asthma [19]. This study has also reported that atopy was associated with adult onset wheeze independently of smoking, which is consistent with a body of evidence suggesting that underlying atopy is of major importance.

Another independent associate of asthma was female gender, which is consistent with studies showing female preponderance in adult asthma, compared to a larger proportion of males in childhood asthma.

Dog ownership was strongly associated with asthma in the multivariate analysis. Dog sensitization and exposure have recently been associated with severe asthma [20]. It is possible that these patients with severe chronic inflammation in the airways and mainly late-phase asthmatic reaction fail to recognize early symptoms due to acute exposure to dog allergens. As a consequence, these patients may not perceive their dog as a cause of their disease (this was observed in a recent study of brittle asthmatics in Birmingham, where half of patients with very severe asthma were dog-sensitized dog owners [20]). There was a trend for the inverse association between asthma and cat ownership. Data for cat ownership could be explained by the active avoidance of cats amongst symptomatic individuals who recognize temporal association between exposure to cats and symptoms. However, as this study has not investigated the temporal sequence of events, we

cannot comment whether the trend for the inverse association between cat ownership and asthma is due to selective avoidance. It is difficult to collect the information on temporal sequence of events in a cross-sectional study, as a recall bias may occur.

In recent years intriguing and often conflicting data on the effect of pet ownership in early life on the subsequent development of sensitization and atopic disease have been reported. Some studies found that exposure to cats and dogs in early infancy was associated with specific IgE sensitization and allergic disease later in childhood [21], others reported the opposite finding –i.e. a protective effect [22,23].

In the Stage II of the ECRHS, Svanes *et al.* reported a strong protective effect of dog ownership in childhood on adult atopy [24]. A further report from the same study found a significant positive association between current cat ownership and sensitization to cats in subjects without, but not in those with, respiratory symptoms, suggesting selective cat avoidance in those with problems related to pets [25]. However, an inverse association between cat ownership in childhood and sensitization to cats in adulthood was seen in all subjects, irrespective of symptoms [25].

Is it possible to explain the differences between various studies? Cat allergen is ubiquitous, and exposure outside the domestic environment may lead to specific IgE responses. The recent report from the ECRHS has indirectly confirmed

the potential importance of passive exposure, finding a significant correlation between the community prevalence of cat ownership and community prevalence of sensitization to cats, prevalence of respiratory symptoms, physician-diagnosed asthma and current asthma medication in 35 centres from 16 different countries [25]. If cumulative exposure to allergens is important for the development of sensitization (and symptoms), then clear-cut differences regarding pet ownership are likely to be seen only in early life. The cumulative passive exposure of non-pet owners in homes without pets and public places may induce sensitization in later childhood and adolescence, confounding the effect of pet ownership. However, this cannot account for the apparent protective effect of pet ownership seen in some studies. Selection bias may be partly responsible. Alternatively, high levels of exposure may lead to the development of tolerance. Pet ownership in early life may also result in increased microbial exposure, enhancing TH1 immunity [25,26]. Only the long-term prospective studies, avoiding recall biases and with objective measure of exposure, will provide a definitive answer to this important question and enable us to decide about appropriate public health strategies.

In this study population, 13.3% of participants reported a history of eczema, with a considerably higher proportion of females reporting disease than males (15.9% vs. 9.2%). In the multivariate analysis the strongest independent associate of eczema was sensitization to dog. This could suggest that allergy to dog, although less common than sensitization to other inhalant allergens, may be associated with more severe disease, perhaps affecting more than one target organ (e.g. both asthma and eczema; adjusted odds ratios for the association between sensitization to dogs and asthma and eczema were remarkably similar). House dust mite and pollen were also independently and significantly associated with eczema, whilst sensitization to cats lost its significance. Apart from dog, the strength of the association between sensitization to common allergens and eczema appeared to be much lower than in the case of asthma.

The prevalence of hay fever in the current study was high (20.6%), with no gender difference. In the multivariate regression analysis, after controlling for the effect of the other explanatory variables, the association between sensitization to pollen and hay fever was extremely strong, with an odds ratio of 13.6. This expected finding supports the validity of the approach. A surprising finding, however, was the inverse association between sensitization to house dust mite and hay fever. It is possible that individuals with dust mite and pollen allergy are more likely to develop perennial symptoms and asthma. Alternatively, this finding may be an artefact of the analysis, as the prevalence of hay fever in subjects sensitized to mites was 31.1%, compared to 15.2% in those skin test negative to mites. Current

smoking was also significantly and inversely associated with hay fever, possibly because patients with hay fever either stop smoking, or do not start it in the first place. Thus, the observed lower level of hay fever in smokers may be explained by 'healthy smoker bias' (the tendency for those with allergic symptoms not to smoke) [27]. Jarvis *et al.* have recently reported that compared to lifetime non-smokers, current smokers were at increased risk of sensitization to dust mites, but at decreased risk of sensitization to grasses [28], which is in agreement with the results of the current study.

Another intriguing finding was that although prevalence of sensitization to common allergens was higher amongst males, the prevalence of both asthma and eczema was significantly higher in females. It is tempting to speculate that atopic females may be at higher risk of developing a phenotypic expression of atopic disease than males due to some as yet unknown factors (e.g. hormonal, size of the airways, etc.).

The results of the current study emphasize the importance of sensitization to indoor allergens in asthma, eczema and hay fever. There is no direct proof that exposure to indoor allergens is the cause of asthma. However, in an effort to prevent asthma we may have to use the information on risk factors known to be strongly associated with the disease (even though they may not be directly responsible for the increasing prevalence), and indoor allergens appear a reasonable candidate for intervention [29,30].

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