

# Heredity, pet ownership, and confounding control in a population-based birth cohort

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**Background:** The association between pet ownership in childhood and subsequent allergic disease is controversial. Bias related to selection of pet exposure has been suggested as a reason for contradictory study results.

**Objective:** The purpose of this investigation was to elucidate how pet exposure depends on family history of allergic disease, smoking, and socioeconomic factors in a prospective birth cohort.

**Methods:** Parents of 4089 two-month-old children answered a questionnaire that included detailed questions about family history of asthma (maternal, paternal, and sibling), rhinoconjunctivitis, atopic eczema/dermatitis syndrome, pollen and pet allergy, smoking habits, parental occupation, and family pet ownership (cat and dog). Dust samples collected from the mothers' beds were analyzed for *Fel d 1* and *Can f 1* in a subgroup of the cohort.

**Results:** Cats were less frequently kept in families with parental asthma, rhinoconjunctivitis, or pet or pollen allergy (3.5% to 5.8%) than in families without parental allergic disease (10.8% to 11.8%). Dogs were less common in families with (3.3%) than in families without (5.9%) parental atopic eczema/dermatitis syndrome. Families with smoking mothers and those with low socioeconomic index kept cats and dogs more frequently. Cat allergen levels were lower in homes with than in homes without maternal pet allergy, and this tended to hold true even for homes without a cat. Cat ownership decreased from birth to 2 years of age, especially in families with parental history of allergic diseases.

**Conclusion:** There seems to be a selection of pet exposure

based on parental history of allergy, maternal smoking, and socioeconomic factors. This has to be taken into consideration in evaluations of risk associations between pet exposure and allergic disease in childhood. (*J Allergy Clin Immunol* 2003;111:800-6.)

**Key words:** Asthma, cats, dogs, allergens, *Fel d 1*, *Can f 1*, heredity, primary prevention, confounding factors, prospective studies

In recent years, numerous studies have focused on the role of environmental factors in the development of asthma and allergic disease, in which early exposure to pets is a controversial issue. For example, one literature review suggested an increased risk of sensitization in childhood after early pet exposure,<sup>1</sup> whereas another found little consistent association between allergen exposure and asthma prevalence.<sup>2</sup> A recent meta-analysis concluded that pet exposure increased the risk of wheezing in older children,<sup>3</sup> and other recent studies have added contradictory data on the relationship between pet exposure and sensitization or asthma in children, adolescents, and adults.<sup>4-11</sup>

The complexity of the issue might be due in part to differences in study design (cohort, case-control, cross-sectional), definition of exposure (pet ownership or allergen levels), and definition of outcome (sensitization or asthma), as well as differences in selection mechanisms for pet contact. Families with histories of allergic diseases might be less prone to keep pets, and many countries have primary prevention programs that advise families with heredity for allergic diseases not to keep pets. Meanwhile, cat allergen is ubiquitous in society and might induce sensitization in predisposed individuals regardless of pet ownership.<sup>12-14</sup> Taken together, these conditions might lead to distorted study results.

The aim of this report is to assess selection of pet ownership and the importance of controlling for this potential confounder in a population-based birth cohort study with a prospective design.

## MATERIAL AND METHODS

### Study population and questionnaire data

The BAMSE study uses a prospective longitudinal birth-cohort design to assess risk factors for allergic diseases in childhood. Details about the study have been published elsewhere.<sup>15</sup> Briefly, 4089 children born between February 1994 and November 1996 in predefined areas of Stockholm were recruited in a population-based

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*Abbreviations used*

AEDS: Atopic eczema/dermatitis syndrome  
OR: Odds ratio

manner. The first questionnaire, answered when the children were (on average) 2 months old, contained detailed questions regarding all of the following: parental history of allergic diseases; maternal, paternal, and sibling symptoms and doctor's diagnosis of asthma; allergic rhinoconjunctivitis; atopic eczema/dermatitis syndrome (AEDS); and pollen and pet allergy. Information on pet ownership (cat or dog), maternal smoking during pregnancy and after giving birth, and parental socioeconomic index<sup>16</sup> was also reported. When the children were 1 year old and again when they were 2 years old, similar questionnaires were mailed to all parents and information on pet ownership was updated.

### Dust samples

Dust samples for analysis of indoor levels of the allergens Fel d 1 and Can f 1 were collected from the mother's mattress at the time of the first questionnaire. Collection, storage, extraction, and analyses of allergen concentrations were performed as described earlier, except that mattresses were vacuumed for 2.5 minutes.<sup>17</sup> For statistical analysis, any dust sample with an Fel d 1 level below the detection limit (0.055 µg/g) was assigned a value of 0.054 µg/g, and any sample with a Can f 1 level below the detection limit (0.200 µg/g) was assigned a value of 0.199 µg/g. To evaluate how allergen levels were related to history of allergic disease, a subset of 512 dust samples from the homes of 167 children who had asthma at 2 years of age and the homes of 345 controls was analyzed.

### Statistical analyses

Variables for reported history of asthma, allergic rhinoconjunctivitis, AEDS, and pet and pollen allergy were created for mother, father, and siblings individually and in combination. Reported disease in siblings was used only for comparison with other children with siblings. Reported disease in 2 parents or in 1 parent and 1 sibling was denoted a double family history of allergy; these children were compared with those without double heredity. The prevalence of cat or dog ownership, broken down by heredity, smoking, and socioeconomic index, was calculated along with 95% CIs. Odds ratios (ORs) for heredity and pet ownership were estimated with logistic regression. In a multivariate regression analysis, the outcome cat or dog ownership was adjusted for different hereditary factors, maternal smoking, and socioeconomic index. To illustrate pet ownership over time, parental history of asthma or rhinoconjunctivitis in combination with reported pet or pollen allergy was related to the percentage of cat and dog owners at birth and at 1 and 2 years of age. Data on key variables, such as reported parental allergy, pet ownership, smoking, and socioeconomic factors, had to be complete for the individual to be included; this left 4023 children (98%) for data analysis.

Because of the skewed distribution of allergen levels, a nonparametric test (Mann-Whitney) was performed to compare the groups with and without heredity. Analyses were performed with Stata 7.0. Permission for the study was obtained from the Ethics Committee of Karolinska Institutet. Informed consent was obtained from the parents.

## RESULTS

### Prevalence of pet ownership in relation to family history, smoking, and socioeconomic

In the entire cohort, cat ownership at the median age of 2 months was reported by 10.0% of the families; dog

ownership was reported by 5.2%. Cats were less frequently kept in families with reported parental asthma, rhinoconjunctivitis, or pet or pollen allergy (3.5% to 5.8%) than in families without any parental allergic disease (10.8% to 11.8%). Dog ownership, on the other hand, varied little between the group with and the group without parental history of allergic disease, AEDS being an exception (Table I).

Approximately 50% of the cohort members had older siblings (1952 children). There was no difference in the prevalence of pet ownership between families with 1 child and families with more than 1 child. In those with reported asthma or pet or pollen allergy among siblings, cat ownership was significantly lower (3.2% to 4.3%) than in those without reported allergy (10.2% to 10.5%), whereas dog ownership was more rare only in families with reported AEDS or pet allergy in a sibling (1.6% to 2.1% vs 5.4% to 5.7%). The same pattern was seen in families with double heredity for allergic diseases. Families in which the mother smoked kept pets much more frequently than others, as did families with lower socioeconomic index (Table I).

### Multivariate regression analysis

Table II illustrates the fact that the crude OR was statistically significant for the relationship between cat ownership and all hereditary factors except AEDS, whereas with multivariate regression analysis, cat ownership was negatively associated with maternal pet allergy (OR, 0.26; 95% CI, 0.15-0.48). In addition, paternal pet allergy was negatively associated with cat ownership, though to a lesser extent (OR, 0.58; 95% CI, 0.33-1.03). However, dog ownership was negatively associated only with reported maternal AEDS in both crude and adjusted analyses (Table II). In contrast, dog ownership was strongly associated with paternal asthma (OR, 2.06; 95% CI, 1.19-3.59). After adjustments, cat and dog ownership remained more common in families with smoking mothers and in those with low socioeconomic index.

Fig 1 shows how cat and dog ownership changed over time from birth to 2 years of age.

### Dust samples

The median levels of the cat allergen Fel d 1 were significantly lower in families with (n = 72) than in families without reported maternal pet allergy (n = 439; median [25th-75th percentile], 0.21 µg/g dust [0.06-0.46] vs 0.29 µg/g dust [0.08-2.2]; *P* < .01). Even when families with cat at home were excluded, a trend toward a difference in levels of Fel d 1 remained (*P* = .12; Fig 2). No difference in cat allergen levels was seen in families with reported pet allergy among fathers or siblings. Levels of the dog allergen Can f 1 did not differ between families with (n = 84) and families without (n = 425) reported maternal history of AEDS; data pertaining to those without any dogs at home are presented in Fig 3. Furthermore, there was no difference in the distribution of cat and dog allergen levels between cases and controls (data not shown).

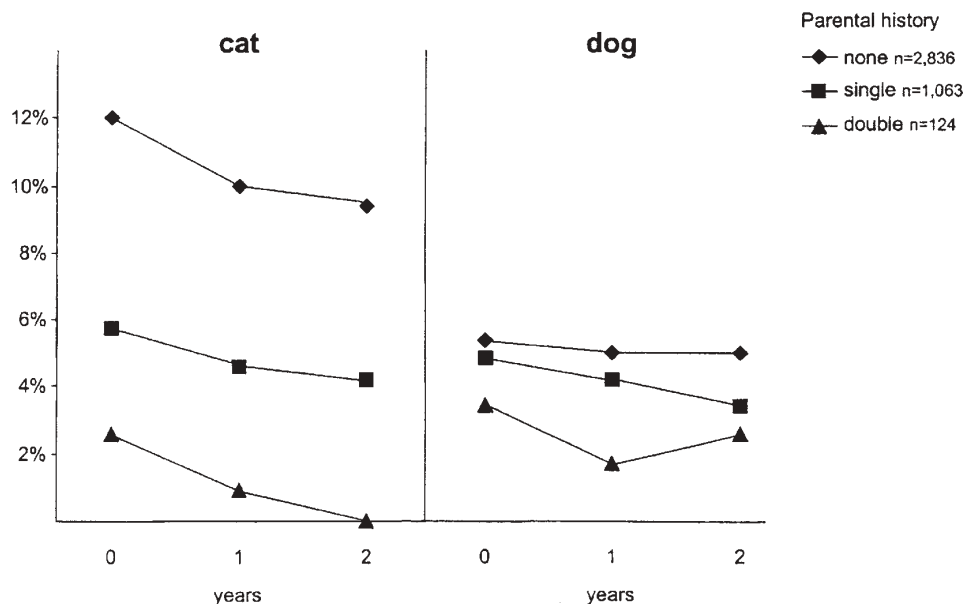


FIG 1. Cat and dog ownership over time, from birth to 1 year and 2 years of age in families with no, single, or double parental history of allergic disease (asthma or rhinoconjunctivitis combined with pet or pollen allergy).

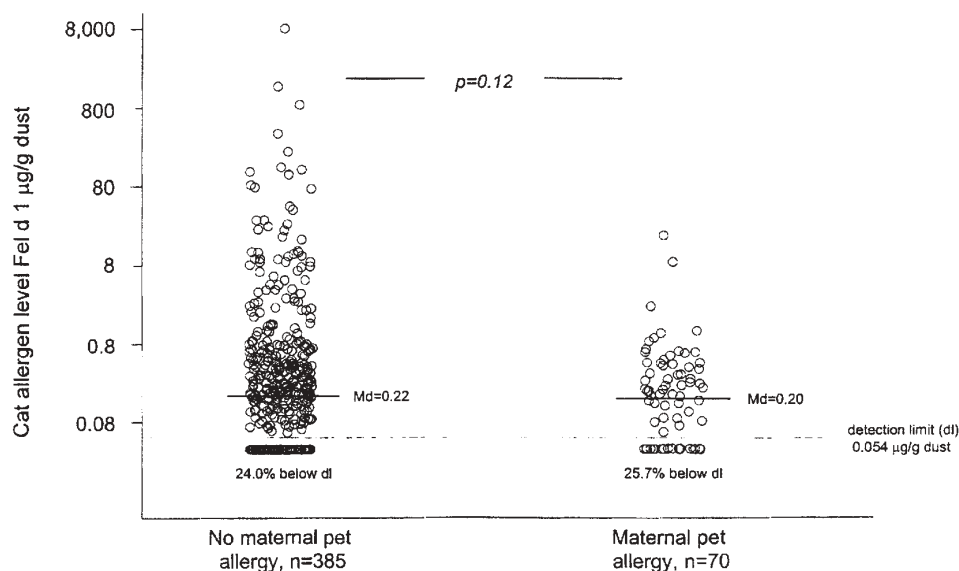
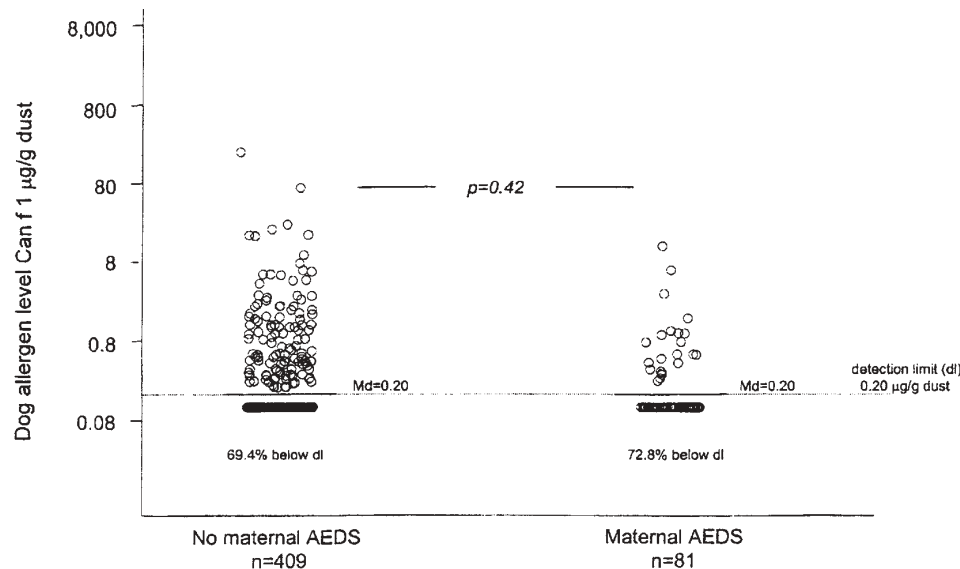


FIG 2. Levels of the cat allergen Fel d 1 in 455 families without any cats at home, subdivided by maternal pet allergy. Median (*Md*) concentration of cat allergen and percentage of dust samples below the detection limit (*dl*) are indicated.

## DISCUSSION

The main finding of this study is that there is a selection of pet ownership based on family history of allergic disease, maternal smoking, and socioeconomic factors. Maternal pet allergy is the most decisive factor with respect to the keeping of a cat, whereas dog ownership is less common in families with reported maternal AEDS. Our data also suggest that indirect cat exposure, indicated by measurable levels of cat allergen in homes without cats, differs between families with and families without maternal pet allergy.

Children with family histories of allergic disease have increased risks of developing sensitization and asthma, and it is therefore essential to stratify or adjust for family history when interpreting epidemiologic studies of risk factors for allergic diseases.<sup>18,19</sup> Most studies have adjusted for family history—predominantly, history of atopy<sup>4,20</sup>—and some studies have adjusted for history of maternal asthma<sup>9,21</sup> or asthma with hay fever.<sup>22</sup> Our data suggest that other factors, such as parental pet allergy, parental AEDS, or allergic disease in siblings, might need to be taken into consideration for adequate confounding control.



**FIG 3.** Levels of the dog allergen Can f 1 in 490 families without any dogs at home, subdivided by maternal AEDS. Median (*Md*) concentration of dog allergen and percentage of dust samples below the detection limit (*dl*) are indicated.

It has previously been shown that cat allergen is ubiquitous in society and that indirect cat contact worsens asthma in sensitized individuals.<sup>12,14,23</sup> In our study, there tended to be lower levels of the cat allergen Fel d 1 in homes with maternal pet allergy, which suggests avoidance measures in families with allergy. Levels of the dog allergen Can f 1 in homes without any dogs had no clear relation to reported maternal AEDS, perhaps because most families had dog allergen levels below the detection limit. However, dog ownership was less common only in families with reported parental AEDS and in those with reported double pet allergy, which suggests that dog allergen could be less allergenic than cat allergen.

The usefulness of primary prevention measures intended to reduce allergic diseases has been much debated.<sup>24-26</sup> For more than a decade, preventive strategies in Sweden have focused on influencing such risk factors as parental smoking, short duration of breastfeeding, dampness in the house, and, in high-risk families, the keeping of pets. We found families with low socioeconomic status and families with smoking mothers to be more prone to keep pets, which confirms the findings of previous studies<sup>15,27</sup>; this might be due to a lower propensity to follow the prevention program. It has also been discussed whether children at high risk of atopy are born into low-risk environments, and there is reason to believe that this might be another source of residual confounding.<sup>28,29</sup> Nevertheless, these children might later in life be indirectly exposed to high enough levels of pet allergens to induce sensitization or allergic disease.

In epidemiologic research it is always important to assess bias in the interpretation of study results. Apart from recall bias in retrospectively designed studies and

selection bias introduced into studies, information bias and misclassification of exposure or outcome have to be taken into consideration.<sup>30,31</sup> Families that have pets and want to keep them might report wheezing less often than families without pets, and families with atopic constitutions might choose not to report pet ownership if the primary prevention program advises them not to keep pets.

It has been suggested that only prospective studies be used to estimate associations between exposure and disease.<sup>32</sup> Our data on pet ownership over time illustrate both the difficulty of interpreting cross-sectional studies on risk associations to allergic disease and the risk of distorted study results. As to whether the observed decrease in cat ownership is due to preventive measures or to the fact that the index child or a sibling has developed symptoms of allergic disease, we can only speculate. The data also indicate that the number of children with parents having histories of allergic disease, especially those with double heredity, might be too small to reach sufficient statistical power for the assessment of any relations between exposure and disease. Thus, considering the selection of pet ownership in a population, it is possible that even prospective studies would have to be randomized on the basis of heredity for allergic disease to find true relationships between exposure and disease. From an ethical point of view such studies might be difficult to justify.

In conclusion, selection of pet ownership needs to be taken into consideration in the interpretation of epidemiologic studies.

We gratefully acknowledge the children and parents of the BAMSE cohort, without whose invaluable assistance this study would not have been possible.

**TABLE I.** Cat and dog ownership in relation to parental history of allergic disease, maternal smoking, and socioeconomic index

	N	Cat ownership			Dog ownership		
		n	Percent	95% CI	n	Percent	95% CI
Parental history							
Asthma							
Yes	642	34	5.3	3.6-7.0	40	6.2	4.4-8.1
No	3381	366	10.8	9.8-11.9	171	5.0	4.3-5.8
Rhinoconjunctivitis							
Yes	1234	72	5.8	4.5-7.1	55	4.4	3.3-5.6
No	2789	328	11.8	10.6-13.0	156	5.6	4.7-6.4
AEDS							
Yes	1042	84	8.1	6.4-9.7	34	3.3	2.2-4.3
No	2981	316	10.6	9.5-11.7	177	5.9	5.1-6.8
Pet allergy							
Yes	882	31	3.5	2.3-4.7	36	4.1	2.8-5.4
No	3141	369	11.7	10.6-12.9	175	5.6	4.8-6.4
Pollen allergy							
Yes	1139	61	5.4	4.0-6.7	48	4.2	3.0-5.4
No	2884	339	11.8	10.6-12.9	163	5.6	4.8-6.5
Sibling history							
Asthma							
Yes	170	6	3.5	0.8-6.3	5	2.9	0.4-5.5
No	1782	187	10.5	9.1-11.9	95	5.3	4.3-6.4
Rhinoconjunctivitis							
Yes	98	7	7.1	2.0-12.2	6	6.1	1.4-10.9
No	1854	186	10.0	8.7-11.4	94	5.1	4.1-6.1
AEDS							
Yes	326	24	7.4	4.5-10.2	7	2.1	0.6-3.7
No	1626	169	10.4	8.9-11.9	93	5.7	4.6-6.8
Pet allergy							
Yes	123	4	3.2	0.1-6.4	2	1.6	-0.6-3.9
No	1829	189	10.3	8.9-11.7	98	5.4	4.3-6.4
Pollen allergy							
Yes	115	5	4.3	0.6-8.1	5	4.3	0.6-8.1
No	1837	188	10.2	8.8-11.6	95	5.2	4.2-6.2
Double history*							
Asthma							
Yes	88	2	2.3	-0.8-5.4	2	2.3	-0.8-5.4
No	3279	360	11.0	9.9-12.4	167	5.1	4.3-5.8
Rhinoconjunctivitis							
Yes	185	9	4.9	1.8-8.0	6	3.2	0.7-5.8
No	2739	323	11.8	10.6-13.0	153	5.6	4.7-6.4
AEDS							
Yes	205	12	5.8	2.6-9.1	3	1.5	-0.2-3.1
No	2788	302	10.8	9.7-12.0	172	6.2	5.3-7.1
Pet allergy							
Yes	99	2	2.0	-0.8-4.8	2	2.0	-0.8-4.8
No	3062	365	11.9	10.8-13.1	99	5.7	4.9-6.5
Pollen allergy							
Yes	144	4	2.8	0.1-5.5	5	3.5	0.5-6.5
No	2843	335	11.9	10.7-13.1	160	5.7	4.8-6.5
Maternal smoking							
Yes	543	102	18.8	15.4-22.1	50	9.2	6.8-11.6
No	3480	298	8.6	7.6-9.5	161	4.6	3.9-5.3
Socioeconomic index							
Blue collar	722	104	14.4	11.9-17.2	59	8.2	6.3-10.4
White collar	1714	190	11.1	9.6-12.7	112	6.5	5.4-7.8
Management/self-employed	1572	106	6.7	5.6-8.1	40	2.5	1.8-3.4

AEDS, Atopic eczema/dermatitis syndrome.

\*Double denotes heredity in 2 parents and/or 1 parent and 1 sibling.

**TABLE II.** Odds ratios for cat and dog ownership in relation to background factors

			Odds ratio		
Factor	N	n	Crude	Adjusted*	Adjusted†
Cat ownership					
Maternal history					
Asthma	370	21	0.52 (0.33-0.82)	0.91 (0.55-1.50)	0.89 (0.54-1.47)
Rhinoconjunctivitis	712	46	0.58 (0.42-0.80)	1.22 (0.75-1.98)	1.15 (0.71-1.87)
AEDS	673	57	0.82 (0.61-1.09)	1.00 (0.74-1.37)	1.07 (0.78-1.47)
Pet allergy	506	15	0.25 (0.15-0.42)	0.28 (0.16-0.51)	0.26 (0.15-0.48)
Pollen allergy	605	34	0.50 (0.35-0.72)	0.71 (0.41-1.22)	0.76 (0.44-1.30)
Paternal history					
Asthma	310	15	0.44 (0.26-0.75)	0.73 (0.41-1.31)	0.70 (0.39-1.26)
Rhinoconjunctivitis	678	33	0.42 (0.29-0.60)	0.82 (0.44-1.52)	0.84 (0.45-1.57)
AEDS	474	34	0.67 (0.47-0.97)	0.88 (0.60-1.28)	0.85 (0.58-1.25)
Pet allergy	448	18	0.35 (0.22-0.57)	0.60 (0.34-1.07)	0.58 (0.33-1.03)
Pollen allergy	651	30	0.39 (0.27-0.57)	0.62 (0.33-1.17)	0.66 (0.35-1.25)
Maternal smoking	563	104	2.43 (1.91-3.10)	—	2.29 (1.77-2.95)
Socioeconomic index					
Blue collar	722	104	1.00	—	1.00
White collar	1714	190	0.73 (0.56-0.94)	—	0.81 (0.62-1.05)
Management/self-employed	1572	106	0.43 (0.33-0.58)	—	0.49 (0.36-0.66)
			Odds ratio		
Factor	N	n	Crude	Adjusted*	Adjusted†
Dog ownership					
Maternal history					
Asthma	370	21	1.06 (0.67-1.68)	1.34 (0.77-2.31)	1.30 (0.75-2.24)
Rhinoconjunctivitis	712	30	0.73 (0.49-1.09)	0.72 (0.38-1.37)	0.71 (0.37-1.35)
AEDS	673	22	0.55 (0.35-0.86)	0.53 (0.33-0.86)	0.54 (0.33-0.88)
Pet allergy	506	21	0.73 (0.46-1.16)	0.79 (0.44-1.43)	0.77 (0.42-1.41)
Pollen allergy	605	29	0.86 (0.58-1.29)	1.36 (0.71-2.63)	1.46 (0.76-2.82)
Paternal history					
Asthma	310	21	1.34 (0.84-2.14)	2.09 (1.21-3.61)	2.06 (1.19-3.59)
Rhinoconjunctivitis	678	28	0.74 (0.49-1.11)	1.29 (0.64-2.59)	1.35 (0.67-2.73)
AEDS	474	16	0.60 (0.36-1.00)	0.63 (0.37-1.08)	0.63 (0.37-1.08)
Pet allergy	448	17	0.69 (0.41-1.14)	0.66 (0.35-1.27)	0.65 (0.34-1.24)
Pollen allergy	651	23	0.62 (0.40-0.96)	0.55 (0.26-1.14)	0.56 (0.27-1.17)
Maternal smoking	563	55	2.20 (1.60-3.03)	—	1.86 (1.33-2.61)
Socioeconomic index					
Blue collar	722	59	1.00	—	1.00
White collar	1714	112	0.78 (0.56-1.09)	—	0.87 (0.62-1.21)
Management/self-employed	1572	40	0.29 (0.19-0.44)	—	0.34 (0.22-0.51)

AEDS, Atopic eczema/dermatitis syndrome.

\*Adjusted for other hereditary variables in this Table.

†Adjusted for other hereditary variables in this Table, maternal smoking, and socioeconomic index.

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