

Original article

Effects of pets on asthma development up to 8 years of age: the PIAMA study

Background: Recall bias may provide discrepant relationships of pet exposure with sensitization and asthma development. We studied prospectively effects of pets at home on development of sensitization, asthma and respiratory symptoms from birth up to age 8 years.

Methods: Event history analysis was performed on annually registered data of 2951 children, participating in the PIAMA birth cohort study.

Results: Children with a cat or dog at home at 3 months of age had a significantly lower prevalence of sensitization to inhalant allergens at age 8, but not of asthma. A cat decreased the risk of house dust mite sensitization at age 8 [odds ratio (OR) = 0.68, 95% confidence interval (CI) 0.49–0.95], a dog of pollen sensitization (OR = 0.49, 95% CI: 0.29–0.83). A cat or dog at home did not significantly affect asthma incidence in each subsequent year. From 2 years of age onwards, the incidence of wheeze (OR = 1.52, 95% CI: 1.12–2.05) and a dry cough at night (OR = 1.28, 95% CI: 1.05–1.57) was higher in children with a dog, whereas removal of a dog increased the risk of developing asthma symptoms. Comparing analyses using prospectively and retrospectively collected data on diagnosed asthma showed important recall bias.

Conclusions: Our prospective study shows a protective effect of early presence of pets at home on sensitization to inhalant allergens, but no prevention of asthma development. Furthermore, children with pets had more frequent transient or intermittent asthma symptoms. Parental report of asthma by recall may provide spurious results of these associations.

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It has been reported that the early presence of pets at home prevents sensitization to common inhalant allergens in schoolchildren (1–4). Studies on the association between pets and asthma have shown inconsistent results and it is yet unclear whether the observed protective effect

Abbreviations: CI, confidence interval; HDM, house dust mite; Ig, immunoglobulin; OR, odds ratio.

of the presence of pets on sensitization to inhalant allergens may prevent the development of asthma (1, 5–9). A meta-analysis of predominantly cross-sectional studies indicated a small positive association (OR = 1.2) between early pet exposure and asthma in populations with a median age of 6 years and older (10). Early pet exposure has not been shown to be associated with asthma in the first years of life in birth cohort-studies

(11, 12). In contrast, results from a follow-up study in schoolchildren suggest that early exposure to pets decreases the risk of asthma development at school age (13).

Short-term relationships between pet exposure *after* the first years of life and the subsequent development of asthma have not been studied so far. Longitudinal analyses over a broad age range are needed to investigate this properly, because the presence of pets in the home may be influenced by avoidance of pet keeping in case a child or its family members have developed asthma symptoms. Furthermore, parents may not recall correctly at older age of the children whether pets were present or whether a doctor diagnosed asthma at a young age. This may lead to recall bias affecting the outcomes of analyses as well.

We studied the effect of the presence of cats and dogs in the home at any age in childhood on the incidence of asthma from birth up to 8 years of life. We used questionnaire data on pet keeping at each year and assessed its association with sensitization and respiratory symptoms in each subsequent year in 2951 children from the PIAMA cohort.

Methods

Study design

The PIAMA birth cohort study consisted of two parts: a placebo controlled intervention study in which the effect of mite impermeable mattress covers was studied and a natural history study in which no intervention took place. In this study, only data from the natural history part of the study are presented.

Details of the study design have been published previously (14). Recruitment took place in 1996–1997. A screening questionnaire was distributed to 10232 pregnant women visiting one of 52 prenatal clinics. Mothers reporting a history of asthma, current hay fever or allergy to pets or house dust mite (HDM) were defined as allergic. Based on this screening, a random selection of 763 allergic women and 5084 nonallergic women were invited to participate in the natural history study; 3291 (472 allergic and 2819 nonallergic) agreed and gave written informed consent. The response rates to the annual questionnaires ranged from 3030 (92%) at age 1 to 2732 (83%) at age 8 years.

The study population consisted of 2951 children with available data on symptoms, presence of pets and potential confounders in the first year of life. Immunoglobulin (Ig)E was measured in 1248 of these children. The study protocol was approved by the medical ethics committees of the participating institutions.

Definitions

Data on symptoms, cats or dogs at home and potential confounders were collected by postal questionnaires during the last trimester of pregnancy, at 3 months of age and yearly around the birthday of the child until 8 years of age.

To compare our results with previous studies, we analysed 'diagnosed asthma', defined as asthma ever diagnosed by a doctor and asthma in the last 12 months. In addition, we used a definition based on symptoms or the use of preventive medication. For this

definition, 'asthma' was defined as at least one attack of wheeze or dyspnoea and/or the prescription of inhaled corticosteroids in the last 12 months. A child was defined as having asthma at ages 3, 4, 5, 6 or 7, if wheezing, dyspnoea or steroid use was reported for that year and the child had asthma at age 8.

Specific IgE to mite (*Dermatophagoides pteronyssinus*), cat (*Fel d1*), dog (*Can f1*), grass (*Dactylis glomerata*), Birch (*Betula verrucosa*) and mould (*Alternaria alternata*) was measured by radioallergo-sorbent test. Sensitization was defined as IgE ≥ 0.35 IU/ml.

Data analysis

First, the association between pets at home and the prevalence of asthma and sensitization at age 8 was studied by logistic regression analysis. For these analyses, only the effect of the presence of cats and dogs at 3 months of age was studied to avoid reverse causation bias as a result of avoidance of pets after the development of symptoms in the child.

Secondly, the longitudinal relationship between pet exposure at any age and incidence of asthma and asthmatic symptoms in the subsequent year was studied by event history analysis using a discrete time hazard model (15). The conditional probability of developing symptoms in each discrete time period of 1 year, given that the child did not have symptoms in any earlier time period, i.e. hazard, was related to the presence of pets at the beginning of the particular year. We tested whether the effect of pet exposure on the hazard was identical in every year of life by including interaction terms of age with pet exposure into the regression model.

Odds ratios (OR) and 95% confidence intervals (CI) were calculated from logistic regression analysis, adjusted for a positive history of allergy to pets, HDM or pollen in the parents and a positive history of asthma in the parents or siblings to account for possible bias caused by selective avoidance of pets at home in families with a positive history. Further adjustment was made for gender, duration of (exclusive or partial) breast feeding (never, 1–12 weeks or > 12 weeks), the presence of older siblings, daycare attendance in the first year of life, smoking in the home at least once a week in the child's first year of life, region of birth, parental education level (low, intermediate, high) and the presence and type of intervention. The presence of a cat and dog was included into the models as separate variables.

Results

Study population

At 3 months of age 34% of the children had a cat and 16% had a dog at home. Children with a cat or dog were more likely to have parents with a low education level and were more frequently exposed to cigarette smoke at home than children without cats and dogs (Table 1). In addition, they were breastfed for a shorter period and children with a dog less frequently went to daycare. Children with a cat at home had less frequently older siblings or a parent with allergy to pets. Children with a dog had less frequently a father allergic to other allergens than pets. Maternal asthma was less frequently found in children with a cat, but more frequently in children with a dog.

Children with IgE measurements available were less likely to have a cat or dog at home and more frequently

Table 1. Characteristics of the study population by the presence of cats and dogs at 3 months and the availability of IgE at age 8 ($n = 2951$)

	Cat			Dog			IgE availability age 8		
	No	Yes	<i>P</i> -value	No	Yes	<i>P</i> -value	No	Yes	<i>P</i> -value
Number	1940	1011		2484	467		1703	1248	
Gender (% boys)	51.0	53.6	0.18	51.9	51.8	0.89	51.9	51.8	0.97
Cat at 3 months	0	100		33.9	36.0	0.40	37.5	29.8	<0.01
Dog at 3 months	15.4	16.6	0.40	0	100		17.0	14.3	0.05
Avoidance cat*	22.1	0		14.5	13.3	0.49	13.3	15.8	0.06
Avoidance dog*	11.1	1.6	<0.01	9.5	0		7.2	8.9	0.12
Asthma mother	3.8	1.7	<0.01	2.7	4.7	0.02	2.6	3.6	0.13
Asthma father	7.7	6.5	0.25	7.1	8.4	0.33	6.9	7.9	0.31
Allergy mother									
Yes, not to pets	6.4	6.5	0.89	6.2	7.7	0.22	5.3	7.9	<0.01
Yes, to pets	8.8	3.4	<0.01	6.7	8.4	0.19	6.0	8.2	0.03
Allergy father									
Yes, not to pets	14.5	16.0	0.28	15.6	12.0	0.04	15.4	14.5	0.48
Yes, to pets	16.2	7.9	<0.01	13.2	13.9	0.69	13.0	13.9	0.49
Asthma siblings	4.1	1.8	<0.01	3.5	2.4	0.22	2.9	3.8	0.15
Siblings at home at 3 months	53.6	45.6	<0.01	51.5	47.3	0.10	49.3	52.9	0.06
Daycare first year	24.0	24.1	0.92	25.4	16.9	<0.01	23.2	25.2	0.22
ETS at 3 months	21.5	28.6	<0.01	22.3	33.0	<0.01	24.7	22.9	0.26
Breast feeding									
1–12 weeks	31.3	37.4	<0.01	32.2	39.4	<0.01	35.0	31.2	0.03
> 12 weeks	51.5	44.0	<0.01	51.1	37.5	<0.01	46.0	52.9	<0.01
Mother education†									
Low	22.5	23.5	0.53	20.7	34.3	<0.01	24.1	21.2	0.07
High	36.0	32.4	0.05	38.2	16.7	<0.01	33.9	36.0	0.25
Father education†									
Low	24.1	28.0	0.02	22.9	39.0	<0.01	27.1	23.1	0.01
High	43.3	33.1	<0.01	43.3	21.4	<0.01	38.3	41.9	0.05

ETS, environmental tobacco smoke.

*Avoidance of pets at home due to allergy of family member(s).

†Education level: low = primary, lower vocational and lower general; intermediate = senior high school and intermediate vocational; high = higher vocational and university.

had an allergic mother than children of whom IgE was not obtained (Table 1). In addition, they were breastfed for a longer period and their fathers had a higher education level.

Association between pets at 3 months and sensitization to inhalant allergens at age 8

Table 2 shows that children with a cat at home at 3 months of age were less frequently sensitized to HDM

at age 8 than children without a cat (OR = 0.68, 95% CI: 0.49–0.95, $P = 0.02$). A dog at home was inversely associated with sensitization to inhalant allergens (OR = 0.62, 95% CI: 0.42–0.91, $P = 0.02$), especially with sensitization to pollen at age 8 (birch or *D. glomerata*).

The possibility of effect modification was assessed for gender and family history of asthma or allergy. No significant interaction was observed, although the inverse association between dog exposure and sensitization was

Table 2. Association between pets at home at 3 months of age and sensitization to indoor and pollen allergens at age 8 from logistic regression analysis, adjusted for confounders ($n = 1248$)

IgE ≥ 0.35	Cat					Dog				
	No (%)	Yes (%)	OR*	95% CI	<i>P</i> -value	No (%)	Yes (%)	OR*	95% CI	<i>P</i> -value
HDM	22.6	16.7	0.68	0.49–0.95	0.02	21.6	16.3	0.66	0.42–1.03	0.06
Cat	6.6	7.0	1.01	0.61–1.69	0.96	7.2	3.9	0.49	0.22–1.13	0.09
Dog	2.9	4.6	1.68	0.84–3.36	0.34	3.5	2.8	0.62	0.23–1.66	0.34
Pollen	17.0	16.1	0.90	0.64–1.29	0.57	17.7	10.7	0.49	0.29–0.83	<0.01
Any allergen	31.0	26.3	0.78	0.58–1.04	0.09	30.7	23.0	0.62	0.42–0.91	0.02

HDM, house dust mite. Bold values are significant ($P < 0.05$).

*Adjusted for other pet, gender, maternal allergy, paternal allergy, maternal asthma, paternal asthma, asthma of siblings, duration of breastfeeding and contact with other children at home, daycare attendance, exposure to smoke at home, parental education level and region.

Table 3. Association between pets at home at 3 months of age and the prevalence of (characteristics of) asthma at age 8 from logistic regression analyses, adjusted for confounders ($n = 2628$)

	Cat					Dog				
	No (%)	Yes (%)	OR*	95% CI	P-value	No (%)	Yes (%)	OR*	95% CI	P-value
Asthma	11.8	11.6	1.08	0.82–1.41	0.59	12.0	10.3	0.75	0.52–1.07	0.11
Diagnosed asthma	2.8	3.4	1.28	0.79–2.10	0.32	3.2	2.1	0.59	0.27–1.25	0.17
Wheeze	5.5	5.8	1.16	0.80–1.67	0.44	5.7	4.8	0.77	0.46–1.28	0.32
Dry cough at night	13.0	12.2	1.00	0.77–1.29	0.99	12.2	15.6	1.23	0.90–1.68	0.20
Dyspnoea	7.6	7.2	1.03	0.74–1.43	0.87	7.6	6.9	0.82	0.53–1.26	0.36
Inhaled steroids	5.7	6.0	1.10	0.76–1.58	0.63	5.8	5.7	0.85	0.52–1.37	0.50

*Adjusted for other pet, gender, maternal allergy, paternal allergy, maternal asthma, paternal asthma, asthma of siblings, duration of breastfeeding and contact with other children at home, daycare attendance, exposure to smoke at home, parental education level, region and type of intervention.

significant in girls only (OR = 0.46, 95% CI: 0.24–0.87, $P = 0.02$) and not in boys (OR = 0.73, 95% CI: 0.43–1.23, $P = 0.24$).

Association between pets at 3 months and asthma at age 8

The presence of a cat or dog at home at 3 months of age was not significantly associated with the presence of asthma or asthma symptoms at age 8 (Table 3). No significant effect modification was found for gender and family history of asthma or allergy.

Association between presence of pets at any age and the incidence of asthma symptoms in the subsequent year

No association was found between a cat or dog at home at any age and the incidence of asthma in the next year (Table 4; Fig. 1). The incidence of wheeze and a dry cough at night after the age of 2 years was higher in children who had a dog at home at the beginning of the

Table 4. Association between pets at home at any age and the incidence of (characteristics of) asthma in the subsequent year from event history analysis, adjusted for confounders ($n = 2948$)

	Cat			Dog		
	OR*	95% CI	P-value	OR*	95% CI	P-value
Asthma	1.04	0.78–1.38	0.81	0.93	0.65–1.34	0.70
Diagnosed asthma	0.89	0.70–1.13	0.34	1.04	0.77–1.39	0.81
Wheeze						
First 2 years	1.05	0.89–1.25	0.56	1.00	0.80–1.24	0.98
3–8th year	1.05	0.80–1.37	0.73	1.52	1.12–2.05	<0.01
Dry cough at night						
First 2 years	1.08	0.91–1.28	0.41	0.92	0.73–1.15	0.44
3–8th year	0.98	0.83–1.16	0.82	1.28	1.05–1.57	<0.01
Dyspnoea	0.94	0.79–1.11	0.46	1.11	0.91–1.36	0.32
Inhaled steroids	0.90	0.71–1.13	0.37	0.88	0.67–1.18	0.40

Bold values are significant ($P < 0.05$). *Adjusted for the other pet, gender, maternal allergy, paternal allergy, maternal asthma, paternal asthma, asthma of siblings, duration of breastfeeding, contact with other children at home, daycare attendance, exposure to smoke at home, parental education level and region.

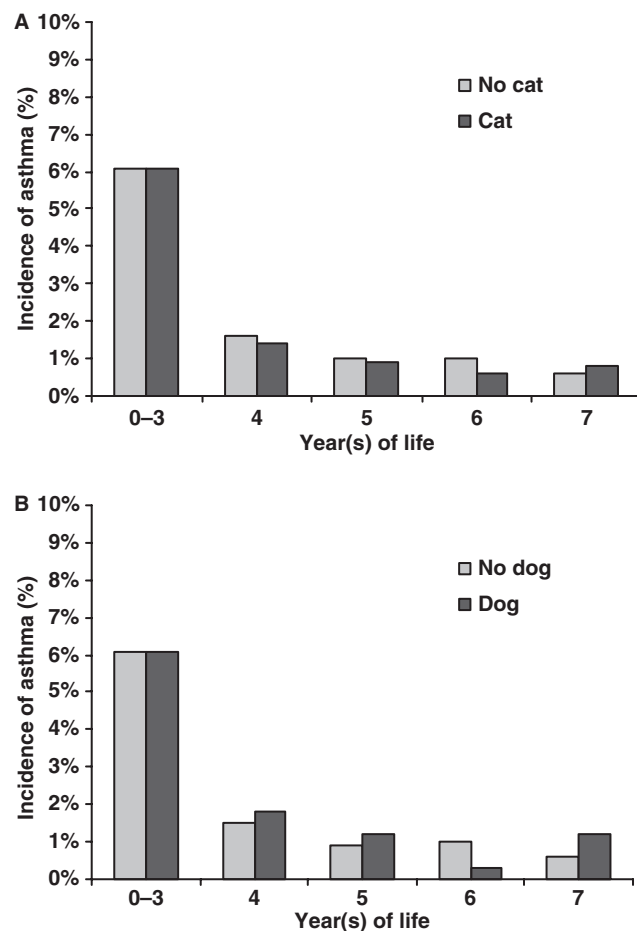


Figure 1. Incidence of asthma in different age-periods by the presence of a cat at home (A) or a dog at home (B) at the beginning of the period. Differences were not statistically significant.

year under study (OR_{wheeze} = 1.52, 95% CI: 1.12–2.05, $P < 0.01$; OR_{cough} = 1.28, 95% CI: 1.05–1.57, $P < 0.01$ respectively), whereas a dog did not increase the incidence of these symptoms in the first 2 years of life (Table 4). The differences in associations between the age period before and after 2 years of age were significant.

These associations were observed in children with a positive family history only ($OR_{\text{wheeze}} = 1.89$, 95% CI: 1.23–2.90, $P < 0.01$; $OR_{\text{cough}} = 1.47$, 95% CI: 1.07–2.01, $P < 0.01$). Besides, a dog was associated with wheeze in boys only ($OR = 1.65$, 95% CI: 1.10–2.48, $P = 0.02$) and with a dry cough in girls only ($OR = 1.41$, 95% CI: 1.07–1.87, $P = 0.02$).

Association between removal of pets and the incidence of asthma

We studied whether removal of a cat or dog from the home in children without previous asthma symptoms influenced the development of asthma. Removal of a dog was associated with a higher incidence of wheeze ($OR = 2.59$, 95% CI: 1.06–6.32, $P = 0.04$) and prescription of inhaled corticosteroids ($OR = 3.03$, 95% CI: 1.03–8.95, $P = 0.05$) in the year after removal of the dog compared with the incidence in children who never had a dog. No significant relationships were found between removal of a cat and the incidence of asthma or symptoms of asthma.

Association between pets and parental reported 'doctor's diagnosis of asthma ever' at age 8

When we compared the information on the cumulative incidence of a doctor's diagnosis of asthma obtained from the annual registration (prospective data) with the answer to the question 'Has a doctor ever diagnosed asthma' as reported by the parents at age 8 (retrospective data), we found substantial disagreement between both outcomes. At age 8, 40% of the children with a doctor's diagnosis of asthma according to the prospective data were reported not to have had this diagnosis retrospectively.

When we analysed the data with 'a doctor's diagnosis of asthma ever' as reported by the parents retrospectively as outcome, we found a significant positive association with the early presence of a dog ($OR = 1.47$, 95% CI: 1.04–2.09, $P = 0.03$). However, when using the prospective data, this association was smaller and not significant ($OR = 1.28$, 95% CI: 0.94–1.75, $P = 0.11$). The early presence of a cat was not associated with the retrospective 'doctor's diagnosis of asthma ever' ($OR = 1.14$, 95% CI: 0.85–1.53, $P = 0.39$).

Discussion

This prospective study shows that pet exposure in early life may prevent allergic sensitization at age 8. However, exposure to pets at any age in childhood does not affect the development of asthma up to 8 years of age. We found that exposure to dogs *after* the first 2 years increased the risk of transient or intermittent symptoms of wheeze or a dry cough. Furthermore, there was an increased risk of wheeze and prescription of inhaled steroids after a dog was removed from the home.

We did not confirm the positive association between early pet exposure and 'a diagnosis of asthma ever' as reported in a previously published meta-analysis (10). A reason for this discrepancy may be that our prospective study is less prone to bias than retrospective studies. An important strength of our study is that we analysed annually registered data on the occurrence of symptoms and a doctor's diagnosis of asthma up to age 8, instead of relying on the recall and interpretation of parents afterwards. Our results are important by providing suggestive evidence that recall bias affects the outcome of cross-sectional studies when investigating whether pet exposure is important for asthma development.

Another important strength of our study is that our longitudinal data made it possible to study the effect of pet exposure on asthma development with appropriate temporality. To study this association properly, it is important that pet exposure precedes the development of symptoms to avoid reverse causation bias. By studying short-term effects of pets on the development of asthma, we found that exposure to dogs may cause respiratory symptoms *after* the first 2 years of life.

A third strength of our study is that the extensive data on the history of asthma and allergy of all family members provided the possibility to control for bias caused by selective avoidance. Furthermore, we observed that the parents overstated the extent to which they avoided pets at home because of allergy of one of the family members. Almost half of the families with allergy or asthma reported to avoid cats at home for this reason. However, the frequency of cat keeping was not that much lower in these families compared with families with a negative history (29% vs 37%). Importantly, families with a negative history according to our definition rarely reported avoidance, indicating that our definition was highly sensitive towards detection of family cases with asthma or allergy. We decided not to exclude the group with self-reported avoidance from the analyses, because this would imply the selective exclusion of a large group of high risk children without pets, which could have introduced bias.

Sensitization to inhalant allergens is considered an important risk factor for the development of asthma (16). Despite the observed preventive effect of pet exposure on allergic sensitization, we could not show a protective effect of pets on the development of asthma in the first 8 years of life. This does not fully rule out that a protective effect can occur later in childhood. A further follow-up of our cohort may clarify whether we can confirm the results of a previous study (13).

How could we explain the effects of dog exposure on transient or mild symptoms of asthma? Although both cat and dog ownership has been associated with microbial exposure, the association has generally been stronger and more consistent for dogs (17, 18). Microbial exposure early in life may, on one hand, protect against the development of atopy later in life by modulating immune

responses, but may, on the other hand, induce an inflammatory response and provoke respiratory symptoms such as wheeze and cough. For instance, endotoxin exposure is known to decrease the risk of atopy, but is also reported to be associated with wheezing symptoms in children (19). Parents may respond to these symptoms by reducing or avoiding exposure to dogs, which may explain why we did not find an association between dogs and persistent symptoms of wheeze.

Interestingly, we found that removal of the dog increased the risk of wheeze and treatment with inhaled corticosteroids in children who never had symptoms before. Positive associations between past ownership of pets and asthma have been reported before; however, they were generally attributed to selective removal of pets *after* the development of symptoms (3, 5). Although our method of analysis makes this explanation very unlikely, we cannot fully exclude that other biases have played a role. It is still conceivable that parents or doctors tend to trivialize and underreport asthmatic symptoms until they observe that the symptoms are persistent after removal of the dog.

A number of limitations in our study have to be considered. One limitation that is present in virtually all studies in early childhood is that there is no firm and clear definition of asthma. We validated our definition in a subgroup of 1132 children who were medically examined at age 8. Indeed, asthma was significantly associated with bronchial hyperresponsiveness to methacholine, the level of forced expiratory volume in 1 s and exhaled NO (data not shown). Especially, in early childhood, when transient symptoms of wheeze or dyspnoea are common, symptoms may be caused by viral infections and not asthma *per se*. This may explain why we did not observe an association between dog exposure and asthmatic symptoms in the first 2 years. It is also compatible with our definition of asthma, i.e. the occurrence of symptoms from birth until 7 years of age when these symptoms were still present at age 8. By doing so, we excluded children with transient respiratory symptoms from the definition of asthma.

Another limitation is that IgE measurements were only available from 1248 children. We have examined which factors were associated with the likelihood of having IgE

measurements. We found that children with pets were less frequently tested for IgE, especially when they had no asthma (41% vs 49%). As we found asthma to be associated with an increased prevalence of sensitization to inhalant allergens, we would expect the inverse association between pet exposure and sensitization to become more negative if there would have been no bias.

Interestingly, we found that 40% of the parents, who reported a doctor's diagnosis of asthma in the prospective data, said retrospectively that a doctor never gave an asthma diagnosis to their child. Even of greater importance is the observation that 'a doctor's diagnosis of asthma ever' as reported by the parents at age 8 was associated with dog exposure, but this was not found using the prospective data. In adults, questions on a doctor's diagnosis of asthma have shown to be biased by disease severity, that is, the false negatives are among those with mild disease (20). If parents tend to underreport mild asthma in their child and dog exposure is related to more severe persistent asthma, this may explain the observed biased association. Another explanation may be that transient asthma symptoms are interpreted and recalled as asthma more frequently when parents had a dog at the time of diagnosis, which may, for example, happen when the disappearance of symptoms is seen as a successful consequence of avoidance of dog exposure. Thus, our discrepant findings caused by bias in questionnaire data underline the need for prospective data to investigate whether common exposures influence the development of asthma. Similarly, retrospective information on early pet exposure may be unreliable and an important source of recall bias. Unfortunately, we have no data available to evaluate this.

In conclusion, our prospective study shows a protective effect of early presence of pets at home on sensitization to inhalant allergens. However, we found no effect of pet exposure on the subsequent development of asthma in the first 8 years of life, although the presence of dogs provokes transient or intermittent respiratory symptoms. Importantly, we show that objective longitudinal data collection is needed to perform this type of studies, as recall bias on a doctor's diagnosis of asthma may give spurious results.

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