Published in final edited form as:

Ann Epidemiol. 2004 September ; 14(8): 543–550.

Indoor allergens, asthma, and asthma-related symptoms among adolescents in Wuhan, China

Päivi M. Salo MS^a, Jiang Xia MD^b, C. Anderson Johnson PhD^c, Yan Li MD^d, Edward L. Avol PhD^c, Jie Gong MD^b, and Stephanie J. London MD^a

a National Institute of Environmental Health Sciences, Epidemiology Branch, Natl Inst Health, Dept of Health and Human Services, Research Triangle Park, NC, USA

b Wuhan Public Health and Anti-Epidemic Station, Wuhan, Hubei Province, China

c Department of Preventive Medicine, USC Keck School of Medicine, Los Angeles, CA, USA

d Wuhan Health Bureau, Wuhan, Hubei Province, China

Abstract

Purpose—Information on indoor allergen exposures among non-Western populations, which have lower prevalence of atopic illness, is scant. We examined whether exposures to common indoor allergens were associated with doctor-diagnosed asthma and asthma-related symptoms among Chinese adolescents.

Methods—A cross-sectional study of 4185 ninth grade students was conducted at 22 randomly selected schools in Wuhan, China. Information on respiratory health and exposures to indoor allergens was obtained by a self-administered questionnaire completed in class.

Results—Having animals currently was associated with persistent cough (prevalence odds ratio [POR] = 1.54, 95% confidence interval [CI] 1.21–2.11) and wheeze (POR = 1.41, 95% CI 1.03–1.94). Early-life exposure to animals was also associated with doctor-diagnosed asthma (POR = 1.95, 95% CI 1.35–2.82). Associations with respiratory symptoms strengthened with higher levels of exposure and for exposure in both early childhood and in adolescence. Exposure to cockroaches and having mold/water damage in the home contributed especially to wheezing (POR=2.03, 95% CI 1.41–2.90 for cockroaches; POR = 2.49, 95% CI 1.82–3.40 for mold/water damage).

Conclusions—Indoor allergen exposures were positively associated with asthma diagnosis and persistent respiratory symptoms among Chinese adolescents. Neither early-life nor current exposure to animals was protective for asthma or asthma-related symptoms.

Keywords

Asthma; Allergens; Children; China; Indoor

Selected Abbreviations and Acronyms

POR = prevalence odds ratio; CI = confidence interval; SD = standard deviation; EU = endotoxin unit

INTRODUCTION

The role of indoor allergens in childhood asthma has been investigated in several studies (1–6). Although there is substantial evidence that exposure to inhaled allergens exacerbates asthma in sensitized individuals (1,2), the causal role of indoor allergens in the development of asthma has been challenged (7–10). Recent data suggest that early-life exposure to animals, especially farm animals, can diminish risk of allergic asthma (11).

The most common indoor allergens are generated from animals, molds, house dust mites, and household pests such as cockroaches (2,12). Their contribution to childhood asthma seems to vary in different parts of the world because children with asthma tend to become sensitized to allergens prominent in their living environments (2,4). However, there is little information about how exposures to indoor allergens affect children's respiratory health among non-Western populations, which have lower rates of asthma. China provides a distinct opportunity to examine exposures to indoor allergens in relation to children's respiratory health because the prevalence of asthma and atopic illness has remained very low among Chinese populations on the mainland compared to populations in industrialized countries in the West as well as in Hong Kong (13–15).

We examined whether self-reported exposures to common indoor allergens were associated with doctor-diagnosed asthma and asthma-related symptoms in a cross-sectional study of ninth grade students in the greater metropolitan area of Wuhan, China. To consider the importance of early-life exposure to animals, we ascertained exposure to pets and farm animals during two different periods of childhood: before and after the age of six years.

METHODS

Participants and study procedure

In the spring of 2001, 4,185 ninth grade students at 22 public schools in and around Wuhan, China completed a self-administered questionnaire on respiratory symptoms and home environment. Two schools were randomly selected from each of the 11 administrative units (nine districts and two counties) governed by the city of Wuhan, the capital of Hubei Province (16). The resulting 22 schools included 14 schools from urban, three schools from suburban, and five schools from rural areas. Local study staff informed students about the survey at the participating schools. After obtaining written parental consent, students viewed a video demonstrating wheezing (17) and completed the questionnaire in class with study staff in attendance. The study protocol was approved by the Institutional Review Boards at the Wuhan Public Health and Anti-Epidemic Station and the National Institute of Environmental Health Sciences.

Questionnaire data

We assessed children's respiratory health and potential risk factors such as exposures to indoor allergens by questionnaire. We included respiratory health related questions from a standardized questionnaire (ATS-DLD-78-C) translated into Chinese for a previous study in Wuhan and other Chinese cities (18). We focused on asthma-related symptoms during the past 12 months, rather than asthma diagnosis, as our primary outcome measure. We asked whether children had cough almost every day in the absence of colds during the past 12 months and whether they had wheezing over the past 12 months, with and without colds. For the analysis, we combined wheezing with and without colds because only a small number of children (67 subjects) reported wheezing without colds. Additionally, we asked whether a doctor had ever diagnosed children with asthma and/or hay fever.

Current exposure to animals was characterized by questions defining type and number of animals in the child's household. We created a categorical variable indicating whether the child was exposed to dogs, cats, farm animals or other types of animals. We included chickens, ducks, cows and pigs in the farm animal category. Children who did not have any animals were assigned to the reference category. We also asked whether children allowed animals to enter the room where they slept during the past 12 months. To evaluate the importance of early-life exposure to animals, we asked children about their exposures to animals prior to the age of six years. We asked the same questions asked about current animals with reference to the period before age six. We considered subjects exposed to pests if they confirmed seeing vermin (separate questions for cockroaches, mice or rats) in the home during the past 12 months. To assess exposure to dampness and mold growth in the past 12 months we asked whether there were any signs of flooding, water damage or mold growth (any surfaces other than food) in the home.

Statistical analysis

We calculated prevalence odds ratios (PORs with 95% confidence intervals) for each of the three outcome measures (cough without colds in the past 12 months, any wheezing in the past 12 months, and doctor-diagnosed asthma) by unconditional logistic regression (Proc Logistic in SAS System for Windows, Version 8.01). We excluded 39 subjects with missing data on any of the outcome or exposure variables leaving 4,146 subjects for the analysis. The following covariates were assessed as potential confounders: gender, living area (rural, suburban, urban), use of domestic cooking and heating fuels, environmental tobacco smoke, personal smoking, physical activity, and time spent indoors and outdoors. Our multivariate models are adjusted only for child's sex and living area because inclusion of the other variables did not appreciably change the associations. Mutual adjustment of the indoor allergen variables (animals, pests, molds) resulted in less than a 10% change in the prevalence odds ratios. Thus, we present these variables singly.

RESULTS

Characteristics of the study population are presented in Table 1. The mean age of the ninth grade students was 15.2 years (SD 0.6 years). Prevalence of wheezing in the past 12 months, doctor-diagnosed asthma (Table 1), and allergies was rare in this population, consistent with previous studies among Chinese children (13–15). Only 127 subjects (3.1%) reported ever having had doctor-diagnosed asthma. Lifetime prevalence of hay fever was 2%. The majority of the subjects who reported doctor-diagnosed asthma (86.6%) or wheezing in the past 12 months (89.6%) did not report any history of hay fever. Of the ever-diagnosed asthmatics, 22.0% reported wheeze and 10.2% reported persistent cough in the past 12 months. Prevalence of these symptoms was much lower among children who had no asthma diagnosis; only 3.6% reported wheeze and 4.1% reported cough during the past year. Exposures to animals, pests, and mold in the home environment were common among the adolescents (Table 1).

Currently having animals in the household was positively associated with cough and wheeze in the past 12 months, but not with ever-diagnosis of asthma (Table 2). The associations between the respiratory symptoms and animal exposure were stronger among children who allowed animals to enter the room where they slept (POR=1.86, 95% CI 1.31, 2.64 for cough; POR=1.51, 95% CI 1.04, 2.17 for wheeze) than among those who did not. In addition, subjects who had two or more animals were more likely to report persistent symptoms of cough and wheeze than those who had only one animal.

Exposure to animals before the age of six years was associated with both asthma diagnosis and asthma-related respiratory symptoms, especially wheezing (Table 3). For wheeze and cough, there was little difference in the associations by the type of animal(s) (dogs, cats, farm animals,

or other animals) that children were exposed to during early childhood. However, exposure to farm animals in early life was strongly related to ever-diagnosed asthma (POR=2.62, 95% CI 1.66, 4.12). The associations between the respiratory symptoms and early animal exposure were stronger for children who had slept in a room where their animals were allowed to enter.

We considered early-life and current exposures to animals in the same model by classifying children into the following categories: no animals during childhood, animals currently but not before the age of six, animals only before the age of six, and animals currently and before the age of six. Children exposed to animals both in early and later childhood were more likely to have persistent symptoms of cough and wheeze than those who had animals at only one of the two periods (Table 4). Exposure to animals in early life contributed significantly to asthma and wheezing, irrespective of whether subjects were currently exposed to animals or not.

Exposures to pests and mold/water damage in the household in the past 12 months (Table 5) were both positively associated with asthma diagnosis and asthma-related symptoms. The strongest associations were seen for wheeze; exposure to cockroaches (POR=2.03, 95% CI 1.41, 2.90) and reported mold growth and water damage in the home (POR=2.49, 95% CI 1.82, 3.40) increased the odds of wheezing considerably.

DISCUSSION

Both current and early-life exposures to animals had adverse effects on respiratory health in this Chinese population of adolescents with low prevalence of asthma and allergic rhinitis. Associations between asthma-related symptoms and exposure to animals, either in early childhood or later, were stronger when animals were allowed to enter child's bedroom and in the presence of three or more animals, suggesting a greater effect with higher levels of exposure. Exposures to pests, mold or recent water damage in the home were also associated with asthma diagnosis and asthma-related symptoms. The results agree with findings from another recent study of risk factors for asthma among children in China (19). However, our study includes additional data on exposures to farm animals and exposures to animals in early childhood.

The relationship between exposure to animals and allergic respiratory diseases in childhood is controversial. Although sensitization to allergens derived from domestic pets has been associated with asthma prevalence and exacerbation (3), some recent studies suggest that exposure to animals in early life may reduce risk of developing allergic sensitization, asthma and wheezing (11,20–23). In particular, growing up on a farm and exposure to livestock appears to provide protection against development of atopic disease among some Western populations (24–29). It has been proposed that high exposure to microbial products, such as bacterial endotoxin, in the first years of life may mediate this protective effect (11,30,31). In Western populations (32,33), the presence of pets and farm animals may be an important determinant of microbial burden because increasing levels of hygiene have reduced microbial exposures. Conversely, among non-Western populations, protective effects of animals may not necessarily be seen because microbial burden early in life, irrespective of pets, may be high enough to favor Th1-type immunity (30). In this Chinese population, microbial burden, including exposure to endotoxin, is likely to be higher during early childhood than among Western populations. We conducted four-hour measurements of airborne endotoxin levels in four of the participating schools and found that airborne endotoxin levels in these Wuhan schools were much higher (29.86–93.38 EU/m³) than levels found in Western homes (0.02–19.82 EU/m³) (34). Although levels of sanitation have improved in China in recent decades, flush toilets and potable tap water remain uncommon in many areas (35,36). For example, open pits in concrete floors are still the standard toilets in many of the schools in this study in Wuhan. However, mechanisms by which exposure to animals can provide protection against atopic disease such

as asthma are not yet clear. Another recent hypothesis suggests that the protective effect of animals may also be explained by induced tolerance (37).

We did not find that exposure to domestic or farm animals before the age of six years reduced the risk of asthma or asthma-related symptoms in adolescence. In agreement with our findings, exposure to pets has been found to increase risk for asthma and wheezing among older children and adolescents in Western populations (38–40). In a recent prospective study, exposure to pets contributed to the onset of asthma in older children (41). However, that study did not have information on exposure to pets in early life; we found that current exposure to animals was not associated with doctor-diagnosed asthma in the absence of early exposure (Table 4). This might reflect that tendency for children who get pets after the age of six, to be those who have not shown any manifestations of asthma or allergic rhinitis. We also found some evidence for selective removal of pets in asthmatic children. Among subjects who had animals before the age of six, exposure to animals in adolescence was slightly less prevalent among diagnosed asthmatics compared to children with no diagnosis of asthma (57.7% vs. 66.1%). Avoidance of pets in families who have asthmatic or allergic family members has been observed in Western populations (40,42).

Individual response to animal exposures in childhood is likely influenced by genetic susceptibility (43,44). We were not able to examine whether the effect of animal exposure differed by hereditary factors. The low prevalence of atopic disease in this population would not have given us the power to examine the interaction between family history and animal exposures in relation to asthma-related outcomes even if we had collected parental information.

The presence of household pests was associated with both asthma diagnosis and asthma-related symptoms among these Chinese adolescents. Pests, especially cockroaches, are sources of aeroallergens (1). Many studies have demonstrated that exposure and sensitization to cockroach allergens are associated with asthma and acute asthma exacerbations in areas where infestation is common (2). In our data, exposure to cockroaches contributed substantially to wheezing in the past year.

Dampness and mold growth in the home environment have been associated with adverse respiratory effects, particularly among children (45,46). Several molds are known to be allergenic and contain biologically active molecules (45), such as mycotoxins and (1→3)- β -D-glucans, which can induce adverse respiratory health effects (47,48). Self-reported mold growth in homes has been associated not only with subjective symptoms but also with peak flow variability, which is an objective respiratory outcome measure (49). Our results agree with existing data; we found that reported mold and water damage in child's home was a strong risk factor for persistent respiratory symptoms. Wuhan has been subject to flooding in recent years, which may have enhanced mold growth in homes. Although water damage and visible mold growth may also correlate with dust mite exposure, published data suggests that dust mites do not explain the association between residential fungal contamination and respiratory symptoms (50,51). In addition, a recent study proposed that sensitization to molds and dust mites may contribute independently to asthma among Chinese asthmatics (52).

A limitation of our study was that our outcome measures were based on questionnaire responses alone. However, large epidemiological studies of asthma often rely on reports on recent symptom history and physician's diagnosis of asthma because these self-reported measures are cost efficient, practical and their repeatability is generally good (53–55). In particular, self-completed written questionnaires have been the principal instrument for obtaining prevalence information about this age group (e.g. ISAAC studies) (14). Adolescents may report their own symptoms and health status more accurately than their parents; some studies suggest that Chinese parents may deny or underreport child's symptoms or illnesses (13,56). We recognize

that self-reported asthma diagnosis may reflect differences in diagnostic practices across populations (53,57). In contrast, respiratory symptoms, including symptoms of wheeze and cough, should be reported consistently across populations (57). Both of them are cardinal symptoms of asthma, although indoor allergen exposure could be associated with cough via mechanisms other than those that are specific to asthma. To improve the quality of our self-reported outcomes, we included audiovisual presentation of wheezing symptoms (17). In our analysis, we evaluated both diagnosed asthma and asthma-related symptoms in the past 12 months to reduce potential bias introduced by behavioral modification due to diagnosis or differential access to health care.

Questionnaires have limited ability to quantify exposures; some exposures will be misclassified based on questionnaire measures of exposure alone. For example, homes without pets may have detectable levels of animal allergens. However, levels of these allergens are usually much higher in homes of pet owners (58,59). Elevated levels of fungi and atypical mycoflora in indoor environments most often result from water or moisture damage that enables excessive mold growth (60,61). Inspection for visible signs of water damage and mold growth is an essential part of mycological investigations in buildings (62,63). Because health hazards of indoor air pollutants are not widely known among Chinese children (64), serious differential misclassification either of the exposures or outcomes is unlikely. Therefore, our effect estimates (PORs) may be underestimated (65,66).

In cross-sectional studies, the temporal relationship between exposure(s) and outcome(s) can be difficult to determine. The hypothesis that early exposure to animals may protect against asthma and allergies has generally focused on exposures before the age of two. However, we thought that children would not be able to recall this period accurately. Thus, we asked them whether they had pets or farm animals before the age of six. We believe that children can remember animals they had at the age of 4 to 6 years, although the possibility of recall bias cannot be excluded. We are not able to ascertain whether animals reported before the age of six were acquired after two years of age or whether animals were removed during early years of life because of symptoms or diagnosis of asthma. However, if animals were selectively removed, the observed associations would be underestimated.

The major strength of this study is that the public school system ensured a large and representative sample of rural, suburban, and urban populations in the Wuhan area. Our study is one of the few studies that have examined exposures to indoor allergens in relation to children's respiratory health in mainland China (13,15,19,52).

In conclusion, self-reported exposures to indoor allergens derived from animals, pests, and mold in the home contributed independently to asthma-related symptoms of cough and wheeze in this cohort of Chinese adolescents. Although prevalence of childhood allergic respiratory diseases such as asthma has remained much lower in China than in industrialized Western populations, common indoor allergens appear to be risk factors for asthma and asthma-related symptoms in older children in both populations. Early exposure to animals, pets or farm animals, did not protect against asthma or persistent asthma-like symptoms in this Chinese population.

Acknowledgements

This study was supported by the National Cancer Institute/National Institute of Drug Abuse Transdisciplinary Tobacco Use research Center grant (1 P50 CA84735-01) awarded to the University of Southern California and the project Z01 ES 49019 of the Division of Intramural Research, National Institute of Environmental Health Sciences.

We thank the Wuhan Education Committee and the Wuhan Public Health and Anti-Epidemic Station for assistance with data collection and entry.

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Table 1

Characteristics of the study population of 4146 ninth grade students at 22 schools in greater Wuhan, China

Characteristic	N	%
Demographics		
Gender		
Male	2139	51.6
Female	2007	48.4
Living area		
Urban	2401	57.9
Suburban	1117	26.9
Rural	628	15.2
Asthma and asthma related symptoms		
Doctor-diagnosed asthma	127	3.1
Persistent cough without colds in the past 12 months	176	4.3
Any wheezing in the past 12 months	174	4.2
Wheezing with colds	148	3.6
Wheezing without colds	67	1.6
Exposures		
Animals currently		
No animals	2151	51.9
Any animals	1995	48.1
Dogs	883	21.3
Cats	823	19.9
Farm animals	633	15.3
Other animals	852	20.6
Animals before the age of 6 ^a	2122	51.4
Pests in the past 12 months	2349	56.7
Mold/water damage in the past 12 months	965	23.3

^aNumbers exclude 17 subjects who did not complete exposure data before the age of 6 years.

Table 2
Asthma-related symptoms and diagnosed asthma in relation to current animal exposure

Current exposure to animals	Cough without colds in the past 12 months				Wheeze in the past 12 months				Doctor-diagnosed asthma - ever			
	No N ^a	Yes N ^a	POR ^b	(95% CI)	No N ^a	Yes N ^a	POR ^b	(95% CI)	No N ^a	Yes N ^a	POR ^b	(95% CI)
Total	3970	176			3972	174			4019	127		
Animals in child's household												
No	2073	78	1.00		2072	79	1.00		2080	71	1.00	
Yes	1897	98	1.54	(1.12, 2.11)	1900	95	1.41	(1.03, 1.94)	1939	56	1.10	(0.76, 1.58)
Animals enter child's bedroom^c												
No	918	36	1.19	(0.79, 1.79)	912	42	1.31	(0.88, 1.93)	926	28	1.19	(0.75, 1.86)
Yes	979	62	1.86	(1.31, 2.64)	988	53	1.51	(1.04, 2.17)	1013	28	1.02	(0.65, 1.61)
Type of animals^c												
Dogs	839	44	1.53	(1.04, 2.25)	832	51	1.70	(1.18, 2.46)	863	20	0.85	(0.51, 1.40)
Cats	772	51	2.09	(1.43, 3.06)	783	40	1.48	(0.99, 2.23)	802	21	1.11	(0.67, 1.84)
Farm animals	609	31	2.13	(1.27, 3.57)	611	29	1.59	(0.94, 2.69)	627	13	1.66	(0.86, 3.22)
Other animals	805	47	1.65	(1.13, 2.39)	807	45	1.52	(1.04, 2.22)	828	24	0.97	(0.60, 1.55)
Number of animals^c												
1	975	49	1.42	(0.98, 2.05)	983	41	1.14	(0.77, 1.68)	990	34	1.12	(0.74, 1.71)
2	424	22	1.57	(0.96, 2.56)	419	27	1.85	(1.17, 2.92)	433	13	1.13	(0.62, 2.08)
3 or more	498	27	1.92	(1.17, 3.15)	498	27	1.76	(1.07, 2.88)	516	9	0.97	(0.47, 2.01)

^aTotal number of children in each group.

^bPrevalence odds ratios (POR) adjusted for living area (urban, suburban, rural) and gender.

^cAll PORs are computed relative to subjects with no animals.

Table 3
Asthma-related symptoms and diagnosed asthma in relation to animal exposure before the age of six

Exposure to animals before the age of 6	Cough without colds in the past 12 months				Wheeze in the past 12 months				Doctor-diagnosed asthma - ever			
	No N ^a	Yes N ^a	POR ^b	(95% CI)	No N ^a	Yes N ^a	POR ^b	(95% CI)	No N ^a	Yes N ^a	POR ^b	(95% CI)
Total	3954	175			3956	173			4003	126		
Animals in child's household												
No	1933	74	1.00		1945	62	1.00		1959	48	1.00	
Yes	2021	101	1.42	(1.04, 1.94)	2011	111	1.85	(1.34, 2.55)	2044	78	1.95	(1.35, 2.82)
Animals enter child's bedroom ^c												
No	1135	48	1.21	(0.83, 1.76)	1129	54	1.60	(1.10, 2.34)	1134	49	2.24	(1.49, 3.37)
Yes	882	53	1.69	(1.17, 2.45)	878	57	2.17	(1.49, 3.15)	906	29	1.61	(1.00, 2.58)
Type of animals ^c												
Dogs	1093	58	1.56	(1.09, 2.24)	1084	67	2.10	(1.46, 3.01)	1119	32	1.54	(0.97, 2.44)
Cats	1037	59	1.64	(1.15, 2.35)	1035	61	2.00	(1.38, 2.89)	1068	28	1.38	(0.86, 2.22)
Farm animals	913	48	1.66	(1.11, 2.47)	914	47	1.83	(1.21, 2.76)	925	36	2.62	(1.66, 4.12)
Other animals	801	43	1.40	(0.95, 2.05)	793	51	2.04	(1.39, 2.98)	808	36	1.85	(1.19, 2.88)
Number of animals ^c												
1	815	39	1.33	(0.89, 1.98)	808	46	1.85	(1.25, 2.73)	814	40	2.27	(1.48, 3.49)
2	434	17	1.09	(0.64, 1.88)	431	20	1.53	(0.91, 2.56)	431	20	2.21	(1.29, 3.79)
3 or more	772	45	1.77	(1.19, 2.63)	772	45	2.05	(1.36, 3.10)	799	18	1.33	(0.76, 2.32)

^aTotal number of children in each group.

^bPrevalence odds ratios (POR) adjusted for living area (urban, suburban, rural) and gender.

^cAll PORs are computed relative to subjects with no animals.

Asthma-related symptoms and diagnosed asthma in relation to animal exposure during early childhood and adolescence

Table 4

Animal exposure	Cough without colds in the past 12 months				Wheeze in the past 12 months				Doctor-diagnosed asthma - ever			
	No		Yes		No		Yes		No		Yes	
	N ^a	POR ^b	N ^a	(95% CI)	N ^a	POR ^b	N ^a	(95% CI)	N ^a	POR ^b	N ^a	(95% CI)
Total ^c	3950		174		3951		173		3998		126	
Time period												
< age of 6												
No	1364	1.00	49		1372	1.00	41		1376	1.00	37	
Yes	568	1.25	24	(0.76, 2.06)	571	1.29	21	(0.76, 2.21)	581	0.80	11	(0.41, 1.59)
No	696	1.16	28	(0.72, 1.86)	687	1.84	37	(1.17, 2.90)	691	1.90	33	(1.18, 3.07)
Yes	1322	1.82	73	(1.24, 2.68)	1321	2.11	74	(1.41, 3.16)	1350	1.81	45	(1.15, 2.84)

^aTotal number of children in each group.

^bPrevalence odds ratios (POR) adjusted for living area (urban, suburban, rural) and gender.

^cAnalyses include 4124 subjects who had information on both current exposures to animals and animal exposures before the age of 6.

Asthma-related symptoms and diagnosed asthma in relation to exposure to pests and mold/water damage in child's household in the past 12 months

Table 5

Exposure	Cough without colds in the past 12 months				Wheeze in the past 12 months				Doctor-diagnosed asthma - ever			
	No N ^a	Yes N ^a	POR ^b	(95% CI)	No N ^a	Yes N ^a	POR ^b	(95% CI)	No N ^a	Yes N ^a	POR ^b	(95% CI)
Total	3970	176			3972	174			4019	127		
Pests												
No	1732	65	1.00		1739	58	1.00		1748	49	1.00	
Any pests	2238	111	1.45	(1.05, 2.00)	2233	116	1.66	(1.20, 2.31)	2271	78	1.54	(1.07, 2.23)
Cockroaches	1021	58	1.50	(1.05, 2.16)	1011	68	2.03	(1.41, 2.90)	1029	50	1.74	(1.16, 2.61)
Mold or water damage												
No	3059	122	1.00		3079	102	1.00		3090	91	1.00	
Yes	911	54	1.55	(1.12, 2.16)	893	72	2.49	(1.82, 3.40)	929	36	1.42	(0.96, 2.12)

^aTotal number of children in each group.

^bPrevalence odds ratios (POR) adjusted for living area (urban, suburban, rural) and gender.