

Risk factors for new-onset cat sensitization among adults: A population-based international cohort study

Mario Olivieri, MD,^a Jan-Paul Zock, PhD,^{b,c,d} Simone Accordini, MSc,^e Joachim Heinrich, PhD,^f Deborah Jarvis, MBBS,^g Nino Künzli, MD,^{h,i} Josep M. Antó, MD,^{b,c,d,j} Dan Norbäck, PhD,^k Cecilie Svanes, MD,^l and Giuseppe Verlato, PhD,^e for the Indoor Working Group of the European Community Respiratory Health Survey II Verona, Italy, Barcelona, Spain, Neuherberg, Germany, London, United Kingdom, Basel, Switzerland, Uppsala, Sweden, and Bergen, Norway

Background: Cat exposure during childhood has been shown to increase the risk of developing cat sensitization, while the effect of cat exposure in adulthood has not yet been established.

Objective: To evaluate new-onset sensitization to cat in adulthood in relation to changes in cat keeping.

Methods: A total of 6292 European Community Respiratory Health Survey I (ECRHS I) participants aged 20 to 44 years from 28 European centers, who were not sensitized to cat, were reevaluated 9 years later in ECRHS II. Present and past cat ownership and total and specific IgE levels were assessed in both surveys. Allergen-specific sensitization was defined as a specific serum IgE level of 0.35 kU/L or more.

Results: A total of 4468 subjects did not have a cat in ECRHS I or ECRHS II, 473 had a cat only at baseline, 651 acquired a cat during the follow-up, and 700 had a cat at both evaluations. Two hundred thirty-one subjects (3.7%) became sensitized to cat. In a 2-level multivariable Poisson regression model, cat acquisition during follow-up was significantly associated with new-onset cat sensitization (relative risk = 1.85, 95% CI 1.23-2.78) when compared with those without a cat at both surveys. Preexisting sensitization to other allergens, a history of asthma, nasal allergies and eczema, and high total IgE level were also significant risk factors for developing cat sensitization, while cat ownership in childhood was a significant protective factor.

Conclusion: Our data support that acquiring a cat in adulthood nearly doubles the risk of developing cat sensitization. Hence, cat avoidance should be considered in adults, especially in those sensitized to other allergens and reporting a history of allergic diseases. (*J Allergy Clin Immunol* 2012;129:420-5.)

Key words: Sensitization, cat allergen, cat ownership, epidemiology, adulthood

Several clinical and epidemiological studies have reported that exposure and sensitization to cats are significantly associated with atopy in both children¹ and adults.² Moreover, cat exposure and sensitization have been proposed as important risk factors for asthma.^{3,4} In a longitudinal study conducted with the European Community Respiratory Health Survey (ECRHS) population, IgE sensitization to cat at baseline was an independent risk factor for new-onset asthma.⁵

In the Western world, a large proportion of households have cats and, in line with this, cat keeping in childhood and adulthood has been reported to be 50% and 22%, respectively, in participants in ECRHS I.⁶ In addition, even people not keeping cats may be at risk for sensitization since cat allergen has also been detected in houses without cats and in public places.^{1,7,8}

Cross-sectional studies have yielded inconsistent results on the association of cat exposure with cat sensitization.⁹ A cross-sectional analysis of participants taking part in the first follow-up of ECRHS¹⁰ found no association between community prevalence of detectable cat-specific IgE and either prevalence of cat ownership or mean community cat allergen levels.

As far as longitudinal studies are concerned, most birth cohort studies have shown that exposure to cat allergen leads to a higher risk of developing cat sensitization in children.¹¹⁻¹⁶ Longitudinal studies in schoolchildren instead found no association or even an inverse association between cat ownership and cat sensitization.^{17,18} In adults, a strong positive association between cat ownership at baseline and incidence of cat sensitization was reported by a Danish study.¹⁹

Moreover, different timing and intensity of allergen exposure have been shown to produce different effects in the life span.²⁰ For instance, analysis of ECRHS I showed that retrospectively reported cat ownership in childhood was associated with lower cat sensitization in adulthood.²¹

The aim of the present study was to evaluate new-onset cat sensitization in a population-based cohort of European adults, as a function of changes in cat keeping. Other potential determinants, such as a history of allergic diseases, previous sensitization to other allergens, and cat exposure in early life,²¹ were also investigated.

From ^athe Unit of Occupational Medicine, University Hospital of Verona, Verona; ^bthe Centre for Research in Environmental Epidemiology (CREAL), Barcelona; ^cHospital del Mar Research Institute (IMIM), Barcelona; ^dCentro de Investigación Biomédica en Red de Epidemiología y Salud Pública (CIBERESP), Barcelona; ^ethe Unit of Epidemiology and Medical Statistics, University of Verona, Verona; ^fthe Institute of Epidemiology, GSF-National Research Center for Environment and Health, Neuherberg; ^gthe Respiratory Epidemiology and Public Health Group, Imperial College, London; ^hthe Swiss Tropical and Public Health Institute, Basel; ⁱthe University of Basel, Basel; ^jthe Department of Health and Experimental Sciences, Universitat Pompeu Fabra, Barcelona; ^kthe Department of Medical Science/Occupational and Environmental Medicine, Uppsala University, Uppsala; and ^lthe Department of Thoracic Medicine, Institute of Medicine, University of Bergen, Bergen.

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Corresponding author: Giuseppe Verlato, PhD, Sezione di Epidemiologia & Statistica Medica, Università di Verona, C/o Istituti Biologici II, Strada Le Grazie 8, 37134 Verona, Italy. E-mail: giuseppe.verlato@univr.it.

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Abbreviations used

ECRHS: European Community Respiratory Health Survey
RR: Relative risk

METHODS

Study design

ECRHS is an international multicenter study of asthma. The first survey (ECRHS I)²² was carried out in 1991-1993 on random community-based samples of adults aged 20 to 44 years. Each participant was sent a brief questionnaire (stage 1) and, from those who responded, a 20% random sample was invited to undergo a more detailed clinical examination (stage 2). In addition, a sample (called "symptomatic sample" in the article) consisting of subjects, not already included in the random sample, who reported asthma-like symptoms in the last 12 months, or who were using asthma medication in stage 1, was also studied. Subjects from the random and from the "symptomatic" samples were examined by using the same methods. ECRHS II²³ was a follow-up study of all the participants in stage 2 of ECRHS I, performed between 1999 and 2002 (the full protocol can be found at www.ecrhs.org). In both studies, subjects answered a standardized questionnaire administered by trained interviewers and they underwent blood tests. The present study includes data from 28 centers that took part in ECRHS II. Ethical approval was obtained for each center from the appropriate institutional or regional ethics committee, and written consent was obtained from each participant.

A total of 18,356 subjects participated in the clinical stage of ECRHS I; in 14,138 of these, cat-specific IgE level was measured. In 7,318 subjects, cat-specific IgE level was also measured at follow-up. Of these, 828 were not included in this analysis as they were sensitized to cat at ECRHS I, and a further 198 because they lacked information on cat ownership. This left 6,292 subjects for the analysis. The average follow-up of these subjects was 8.6 ± 1.1 years (mean $\pm$ SD).

Pet keeping

Information on current adult pet keeping was obtained from interview data in ECRHS I and II. At both surveys, the subjects were asked "Do you keep a cat?" According to this question, changes in cat ownership were classified as follows: *no cat* (without a cat at both surveys), *cat removal* (cat keeping at baseline but not at follow-up), *cat continuation* (keeping a cat at both ECRHS I and ECRHS II), and *cat acquisition* (cat keeping at follow-up in a subject who did not have a cat at baseline). In addition, subjects keeping a cat at ECRHS I and/or ECRHS II were asked whether their cat was allowed in their bedroom. Information on childhood pet keeping was obtained retrospectively through a face-to-face interview in ECRHS II. The subject was asked the following questions: "Was there a cat in your home during your first year of life? When you were aged 1 to 4 years? When you were aged 5 to 15 years?"

In addition, in ECRHS II, subjects were asked whether they experienced cough/whistle/chest tightness/shortness of breath/runny, stuffy nose, sneeze/itchy, or watering eyes when they were near animals.

Assessment of serum IgE

Total serum IgE and IgE levels specific to house dust mite, timothy grass, cat, and *Cladosporium* were measured centrally at Pharmacia Uppsala for ECRHS I and at King's College London for ECRHS II, using the Pharmacia CAP system (Uppsala, Sweden); the Cohen's kappa coefficient between the 2 laboratories as regards cat sensitization was 0.87.²⁴ Specific IgE values of 0.35 kIU/L or more were considered positive.

Other IgE sensitization at baseline was defined as specific IgE to house dust mite (*Dermatophagoides pteronyssinus*), timothy grass, and/or *Cladosporium herbarum* at ECRHS I.

Statistical analysis

The significance of the association between new-onset cat sensitization and potential risk factors (sex, smoking habits, allergic diseases, other IgE

sensitization, cat ownership in childhood, changes in cat ownership) was evaluated by using the Fisher exact test. The same test was used to evaluate the influence of new-onset cat sensitization on symptoms when exposed to animals.

The relationship between developing cat sensitization and changes in cat ownership was further investigated by a 2-level²⁵ Poisson regression model²⁶ with level-1 units (subjects) nested into level-2 units (ECRHS centers). The model had new-onset cat sensitization as the dependent variable, a random intercept term at level 2, and changes in cat ownership (no cat, cat removal, cat acquisition, cat continuation) as fixed effect. Also, the following potential confounders were taken into account: type of sample (symptomatic vs random), gender, age, follow-up duration, smoking habits (nonsmoker, ex-smoker, current smoker), allergic diseases (asthma ever, nasal allergies, eczema), other IgE sensitization, total IgE level, keeping cat in childhood, and center-specific prevalence of cat ownership. The significance of the interaction between changes in cat ownership and each potential confounder was also tested. The relative risk (RR) for continuous variables (age and total IgE) was computed for an increase in the value of 1 SD. The significance of model fit was evaluated by using the likelihood ratio test.

RESULTS

Baseline characteristics of the cohort under study are presented in Table I. The mean age was 34.5 ± 7.1 years (mean $\pm$ SD), and the male to female ratio was close to 1.

Four thousand four hundred sixty-eight subjects (71.0%) had a cat neither in ECRHS I nor in ECRHS II, 473 (7.5%) had a cat only at baseline, 700 (11.1%) had a cat at both evaluations, and 651 (10.3%) had a cat only at follow-up. The cat was allowed in the bedroom by most of the people who kept a cat at both surveys (660 of 700 = 94.3%) or acquired a new cat during the follow-up (602 of 651 = 92.5%), and by two thirds of those who got rid of the cat (303 of 473 = 64.1%).

As shown in Table II, 231 subjects (3.7%) became sensitized to cat during the follow-up. The cumulative incidence of cat sensitization was about 3- to 4-fold higher in individuals who either reported a history of allergic diseases (asthma, nasal allergies) or were sensitized to allergens other than cat at baseline. A lower increase was observed in subjects reporting eczema. The cumulative incidence of cat sensitization was also affected by changes in cat ownership, being the lowest among subjects without a cat at both surveys and the highest among subjects who acquired a cat during the follow-up. New-onset cat sensitization was not significantly affected by sex, age, and smoking habits. Having had a cat in childhood, compared with those without a cat in childhood, had a significant protective effect on new-onset cat sensitization.

Factors that were significantly associated with new-onset cat sensitization in univariable analysis remained significant predictors in the multivariable analysis also (Table II). In the 2-level Poisson regression model, controlling for relevant confounders, acquiring a cat during the follow-up was associated with a nearly 2-fold increase in the risk of new-onset cat sensitization (RR = 1.85, 95% CI 1.23-2.78, in those who acquired a cat vs those without a cat at both surveys) (Table II). Also, atopic diseases (asthma ever, nasal allergies, and eczema), IgE sensitization to other allergens, and serum total IgE level ($P < .001$) were significant risk factors for incident cat sensitization, while cat ownership in childhood was a significant protective factor. Sex, age, smoking habits, prevalence of cat ownership ($P = .730$), type of sample ($P = .083$), and duration of follow-up ($P = .469$) were not independent predictors of new-onset cat sensitization.

Interestingly, allowing the cat in the bedroom was a prerequisite for new-onset cat sensitization among those who kept a cat at

TABLE I. Baseline characteristics of the study population of ECRHS II participants who were not sensitized to cat at ECRHS I (N = 6292)

	No.	Percent
Sample		
Random	5413	86
Symptomatic	879	14
Sex		
Male	3098	49.2
Female	3194	50.8
Age at baseline (y)		
<30.9	2098	33.3
30.9-38.8	2096	33.3
≥38.9	2098	33.3
Smoking habits		
Never smoker	2727	43.4
Ex-smoker	1354	21.5
Current smoker	2208	35.1
Ever asthma	620	9.9
Allergic rhinitis	1630	26.0
Eczema	2549	40.6
Sensitization to house dust mite, grass, or <i>Cladosporium</i>	1594	25.3
Sensitization to <i>Dermatophagoides pteronyssinus</i>	917	14.6
Sensitization to timothy grass	943	15.0
Sensitization to <i>Cladosporium herbarum</i>	134	2.1
Keeping a cat under 16 y		
No	3120	55
Yes	2552	45

both surveys or acquired a cat during the follow-up: indeed none of the subjects who did not allow the cat in the bedroom (n = 89) became sensitized to cat, while new-onset cat sensitization was recorded in nearly 5% (61 of 1262) of participants allowing the cat in the bedroom ($P = .030$). The power of the study was insufficient to also evaluate the variable "allowing the cat in the bedroom" in multivariable analysis, as the Poisson regression model did not converge when adding this variable.

The effect of cat acquisition on incident cat sensitization was more pronounced in individuals with preexisting sensitization to other allergens. Among subjects not sensitized to other allergens at baseline, the cumulative incidence of cat sensitization increased from 2.0% in subjects without a cat at both surveys to 2.5% in those acquiring a cat, whereas in subjects already sensitized, the cumulative incidence increased from 7.2% to 13.8%. However, the effects of baseline sensitization to other allergens and cat acquisition were simply additive, as no significant interaction emerged in the Poisson regression model ($P = .501$). Likewise, the interaction between changes in cat ownership and any other variable was not significant.

Sensitization to each of the tested allergens at baseline was significantly associated with new-onset cat sensitization in univariable analysis: the cumulative incidence of cat sensitization was 2.7%, 2.7%, and 3.6% in people not sensitized to house dust mite, timothy grass, and *Cladosporium*, respectively, and increased to 9.5%, 9.2%, and 9.0% in those sensitized ($P < .01$). In the multivariable 2-level Poisson regression model, preexisting sensitization to house dust mite turned out to be the most important risk factor for new-onset cat sensitization among the 3 allergens considered (RR = 2.12, 95% CI 1.56-2.92), followed by sensitization to timothy grass (RR = 1.52, 95% CI 1.17-1.98),

while sensitization to mould apparently lost its influence (RR = 1.36, 95% CI 0.73-2.54). This latter observation may be explained by the low prevalence of sensitization to *Cladosporium* (n = 134, 2.1%) and the low power to detect effects.

Subjects who had become sensitized to cat reported more symptoms, especially oculonasal, when exposed to animals than did subjects who did not develop cat-specific IgE ($P < .001$) (Table III).

DISCUSSION

The findings from this study show that new-onset cat sensitization is not negligible in adulthood. Acquiring a cat in adulthood nearly doubles the risk of onset of specific sensitization to cat, and this effect seems to be more pronounced when the cat is allowed in the bedroom. Subjects who became sensitized to cat reported more symptoms, especially oculonasal, when exposed to animals than did subjects who did not develop cat-specific IgE. Preexisting sensitization to other allergens (especially house dust mite), a history of asthma, nasal allergies and eczema, and high total IgE level are also independent risk factors, while having had a cat during childhood protects against new-onset cat sensitization during adulthood.

The cumulative incidence of new-onset cat sensitization was higher in the present study (3.7%) than in the Copenhagen Allergy Study (1.5%).¹⁹ It should be noted, however, that baseline prevalence of cat ownership was also higher in ECRHS I (18.6%) than in the Danish study (13%).

In the present study, the risk of incident cat sensitization was nearly doubled in those acquiring a cat. Interestingly, this effect was confined to those allowing the cat in the bedroom, suggesting that high doses of cat allergen are required to induce cat sensitization. Unfortunately, the study had limited power to fully evaluate this in multivariable analysis. Of note, the hypothesis that the presence of cats in the bedroom could play an important role in cat sensitization had already been put forward in a pediatric population.²⁷

To our knowledge, this is the first study to prospectively investigate new-onset cat sensitization after acquiring a cat at individual level. The Copenhagen Allergy Study¹⁹ addressed new-onset cat sensitization in adulthood as a function of cat ownership, but considered cat ownership at baseline rather than its changes during the follow-up. The study found that the incidence of cat sensitization was 8-fold higher in subjects having a cat at baseline. An Australian study²⁰ reported that the risk of being sensitized to cat at 28 years was halved in those having a cat when younger than 18 years compared with those who had never owned a cat, and more than doubled in those having a cat after that age; however, these findings were not significant maybe for the limited number of subjects (n = 224). Interestingly, ignoring information on cat keeping at follow-up, our study showed no significant association of new-onset cat sensitization with having a cat at baseline (RR = 1.26, CI 0.93-1.71; $P = .239$). This discrepancy underlines that evaluating risk factors only at baseline without taking into account their changes during the follow-up could be misleading.

In the present study, the risk of new-onset cat sensitization was also slightly increased, although not significantly, in subjects who had a cat at baseline but not at the end of follow-up. This pattern could be due to reverse causation: new-onset cat sensitization during the follow-up was probably the cause rather than the effect of getting rid of a cat or not replacing a previous cat.²⁸

TABLE II. Determinants of new-onset cat sensitization

	New-onset cat sensitization: no. (%)	Crude RR (95% CI)*	Adjusted RR (95% CI)†	P value‡
All	231 (3.7%)	—	—	—
Sex				.510
Male	127 (4.1%)	1	1	
Female	104 (3.3%)	0.81 (0.60-1.08)	0.91 (0.69-1.20)	
Tertiles of age (y)				.653
<30.9	87 (4.1%)	1	1	
30.9-38.8	73 (3.5%)	0.78 (0.54-1.15)	0.85 (0.59-1.23)	
>38.8	71 (3.4%)	0.80 (0.63-1.02)	0.94 (0.74-1.19)	
Smoking habits				.886
Never smoker	109 (4.0%)	1	1	
Ex-smoker	48 (3.6%)	0.85 (0.60-1.21)	1.01 (0.71-1.42)	
Current smoker	74 (3.4%)	0.94 (0.70-1.25)	0.93 (0.70-1.23)	
Ever asthma				.044
No	174 (3.1%)	1	1	
Yes	57 (9.2%)	2.76 (2.09-3.65)	1.49 (1.05-2.12)	
Nasal allergies				.002
No	111 (2.4%)	1	1	
Yes	119 (7.3%)	2.78 (2.18-3.55)	1.66 (1.20-2.30)	
Eczema				.048
No	111 (3.0%)	1	1	
Yes	120 (4.7%)	1.54 (1.13-2.09)	1.34 (1.00-1.80)	
Baseline sensitization to other allergens‡				<.001
Not sensitized	98 (2.1%)	1	1	
Sensitized	133 (8.3%)	3.77 (2.82-5.03)	2.31 (1.74-3.07)	
Keeping a cat under 16 y				.001
No	135 (4.3%)	1	1	
Yes	66 (2.6%)	0.60 (0.47-0.76)	0.59 (0.47-0.75)	
Cat ownership				.017
No cat	148 (3.3%)	1	1	
Cat removal	22 (4.7%)	1.31 (0.84-2.03)	1.54 (0.99-2.38)	
Cat continuation	26 (3.7%)	1.01 (0.70-1.45)	1.32 (0.90-1.93)	
Cat acquisition	35 (5.4%)	1.70 (1.09-2.64)	1.85 (1.23-2.78)	

*Crude RR (95% CI) was estimated by a 2-level Poisson regression model, where center was the group variable, considering one variable at a time.

†Adjusted RR (95% CI) and P values were estimated by a 2-level Poisson regression model, where center was the group variable, adjusting for all variables included in this column plus sample, duration of follow-up, community prevalence of cat ownership, and total IgE.

‡House dust mite, grass, or *Cladosporium*.**TABLE III.** Symptoms when exposed to animals as a function of new-onset cat sensitization

	Not sensitized to cat (n = 5882)	Newly sensitized to cat (n = 206)	P value
Cough	187 (3.3)	27 (13.1)	<.001
Wheeze	114 (2.0)	28 (13.6)	<.001
Chest tightness	149 (2.6)	29 (14.1)	<.001
Shortness of breath	145 (2.6)	26 (12.6)	<.001
Runny/stuffy nose or sneeze	449 (7.9)	66 (32.0)	<.001
Itchy or watering eyes	371 (6.5)	70 (34.0)	<.001
All symptoms	577 (10.2)	81 (39.3)	<.001

Numbers are cases, while prevalence is reported in parentheses.

The onset of IgE sensitization to cat was associated with a higher prevalence of oculonasal symptoms, which rose from 6% to 8% in not sensitized subjects to 32% to 34% in those newly sensitized. Similarly, in the Copenhagen Allergy Study, the incidence of allergic rhinitis to animals was increased 3-fold in those owing a cat at baseline¹⁹; moreover, in the Normative Ageing Study, sensitization to cat allergen was associated with asthma and new-onset airway hyperresponsiveness in 60-year-old

veterans.⁴ Accordingly, in a previous analysis of the ECRHS data, cat sensitization at baseline (ECRHS I) turned out to be an independent risk factor of new-onset asthma in ECRHS II.⁵

In the present survey, both total and specific IgE levels to common aeroallergens were independent risk factors, suggesting that an immunologic predisposition could be an important determinant of new-onset sensitization. Also, Linneberg et al¹⁹ found that sensitization at baseline to allergens other than cat increased the risk of developing sensitization to cat in a dose-dependent manner.

In agreement with the present investigation, several studies^{20,21,29} have shown that cat ownership during childhood protects against cat sensitization in adulthood. Indeed, the 2010 revision of the Allergic Rhinitis and Its Impact on Asthma guidelines “suggest no special avoidance of pets at home” also because only low-quality evidence is available.³⁰ Hence, the effect of exposure to high doses of cat allergens seemed to be different at different ages. While cat ownership in childhood turned out to be a protective factor against the incidence of cat sensitization during adulthood, cat acquisition at later ages was a risk factor for new-onset cat sensitization but only if the cat was allowed in the bedroom.

Some limitations should be acknowledged in the present study. First of all, temporal changes in cat ownership and in cat

sensitization were assessed by only 2 measures. Moreover, information on pet keeping in childhood was retrospectively reported by adults, and so it could have been affected by a recall bias. However, a good agreement was found between ECRHS I and ECRHS II in reporting childhood pets: Cohen's kappa coefficient was 0.714 for cat.³¹ Finally, IgE levels were centrally assessed in both ECRHS I and ECRHS II by using the same method, but at 2 laboratories (Uppsala and London); however, an excellent agreement was found between the 2 laboratories as regards cat sensitization, Cohen's kappa coefficient being 0.87.²⁴

On the other hand, ECRHS has several strengths. First of all, this survey is a community-based multicenter study that managed to achieve a large sample size. All questionnaires and measurement protocols were standardized, and IgE levels were assessed at a central laboratory. Moreover, results were substantially the same when the cutoff for IgE sensitization was increased from 0.35 to 0.70 kU/L: the RR of new-onset cat sensitization in those acquiring a cat was 2.16 (95% CI 1.33-2.51) as compared with those without a cat at both surveys.

In conclusion, acquiring a cat increases the risk of cat sensitization in adulthood, particularly when the cat is allowed in the bedroom. Having had a cat during childhood seems to protect against new-onset cat sensitization in adulthood. Parents are frequently concerned about acquiring a cat, because they are afraid of increasing the risk of allergies in their children. According to the last revision of the Allergic Rhinitis and its Impact on Asthma guidelines, clinicians and parents should also consider other sensitized family members when balancing the pros and cons of acquiring a cat.³⁰ Our results support this and indicate that adults should consider their own risk for developing allergies when they acquire a cat.

Coordinating Center. Project Leader: P. Burney; Statistician: S. Chinn; Principal Investigator: D. Jarvis; Project Coordinator: J. Knox; Principal Investigator: C. Luczynska; Assistant Statistician: J. Potts; Data Manager: S. Arinze.

Steering Committee for ECRHS II. U. Ackermann-Lieblich (Switzerland); J.M. Antó (Spain); P. Burney (UK); I. Cerveri (Italy); S. Chinn (UK); R. de Marco (Italy); T. Gislason (Iceland); J. Heinrich (Germany); C. Janson (Sweden); D. Jarvis (UK); J. Knox (UK); N. Künzli (Switzerland); B. Leynaert (France); C. Luczynska (UK); F. Neukirch (France); J. Schouten (The Netherlands); J. Sunyer (Spain); C. Svanes (Norway); P. Vermeire (Belgium); M. Wjst (Germany).

Key messages

- Acquiring a cat nearly doubles the risk of developing cat sensitization in adulthood. The risk is higher in subjects reporting preexisting allergic diseases, already sensitized to other allergens, or with high total IgE levels.
- Cat avoidance should be considered in adults, especially in those sensitized to other allergens and reporting a history of allergic diseases.

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