

Dog and cat exposure and respective pet allergy in early childhood

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Abstract

Background: The association of dog and cat exposure in early childhood with the incidence of respective allergies has remained controversial. The aim of the study was to obtain population-based evidence on the association of early exposure to dog or cat, or both, with dog and cat allergies.

Methods: The study population was identified from the nationwide population register comprising all children aged 1–4 yr (N = 4779) born between 2001 and 2005 and living in the province of South Karelia, Finland. Cross-sectional questionnaire data on pet exposure in infancy and physician-diagnosed pet allergies were obtained from 3024 participants and merged with longitudinally accumulated data on sIgE and skin prick tests indicating allergic sensitization abstracted from all patient records in the area.

Results: The adjusted relative incidence of positive test results (with 95% confidence intervals) was 2.69 (1.45–5.02) for dog and 5.03 (2.47–10.2) for cat allergens among children exposed to a respective pet alone compared with children without such exposure. The corresponding adjusted prevalence odds ratios for diagnosed dog and cat allergies were 1.75 (0.77–3.79) and 5.13 (2.30–11.4), respectively. The association between pet exposure and the incidence of positive test results was independent of parents' allergies.

Conclusions: Early exposure to dog and cat at home is associated with a higher incidence of respective pet allergy during the first four years of life. Further evidence from population-based studies with longer follow-up is required to justify any recommendation concerning early pet contacts with a view to preventing pet allergies later in life.

Pet contacts have been suggested to increase the risk of allergic diseases and sensitization or protect against them, and some studies report not having found any association at all (1–10). Children having contacts with furry pet animals reportedly have a lower risk to become sensitized to aeroallergens than children without such contacts (11). However, the role of specific allergen contacts such as pet exposure in the development of respective allergies has remained unclear and contradictory findings have been reported (3–8, 12–18). Exposure to an allergen has been considered as a prerequisite for both the development of sensitization and that of tolerance (17, 19, 20).

Some 50% of children in industrialized countries suffer from allergies which therefore constitute a major public health problem worldwide (2, 21). Keeping cats and dogs is common

in urban families although wide variations exist between countries (10, 22). The entire population is exposed to pet allergens at least to some extent depending on the pet density in the area (7, 12). In Sweden (23), sensitization to pet allergens has increased since the 1990s along with urbanization and decreased exposure to furry animals. However, little information exists on the association between pet exposure and the occurrence of clinical pet allergy in large unselected populations with longitudinal study design (2–4, 12).

This study provides real-life population-based evidence on the association between early exposure to dog and/or cat and the incidence of testing for sensitization to dog and cat allergens and their positive test results as well as the prevalence of diagnosed pet allergies during the first four years of life.

Methods

Study design and setting

The South Karelian Allergy Research Project (SKARP) is a cohort study focusing on the occurrences and risk factors for allergies. The SKARP population was identified from the Finnish Population Register Centre comprising all children born between April 2001 and March 2005 and living in the province of South Karelia (N = 4779) (Fig. 1). The study design includes both a longitudinal and cross-sectional component, as reported elsewhere in detail (24).

In the cross-sectional part, a questionnaire survey was conducted in close cooperation with local child health clinics between March 2005 and September 2006, when the children were 1–4 yr old and had their annual checkups. The parents of 3308 children (69%) returned the questionnaire.

In the longitudinal part, the results of all the tests for allergic (IgE mediated) sensitization were collected from all healthcare units in the area independently of the questionnaire survey. All tests had been ordered by a physician for clinical purposes and performed between April 2001 and September 2006. The test data cover the entire population studied, including the non-participants, too. The test data were individually linked with the questionnaire data using the child's unique personal

identity code (PIC). The linkage was successful in 3262 children from 2802 families.

Ethics and permissions

The protocol was reviewed by the Ethical Committee of the Northern Ostrobothnia Hospital District (95/2003). The data of tests for allergic sensitization were collected with the permission of the Finnish Ministry of Social Affairs and Health. The parents gave permission to use the PIC for the record linkage. None of the authors was involved with the medical care of the study population.

Outcomes

As longitudinal outcomes, we considered the occurrence of the first test and the first positive test result separately for dog and cat allergens. Skin prick test (SPT) and specific immunoglobulin E antibodies (sIgE) were combined into a joint outcome, as both of these methods indicate IgE-mediated immunological response. The cutoff point for a positive result from a sIgE was 0.35 kU/l with RAST-CAP FEIA and Phadiatop Combi and 1.43 standardized units per ml with Magic Lite, the latter of which was used in one child (the result was negative). We used alternatively a higher cutoff point 0.70 kU/l for sIgEs (25). The

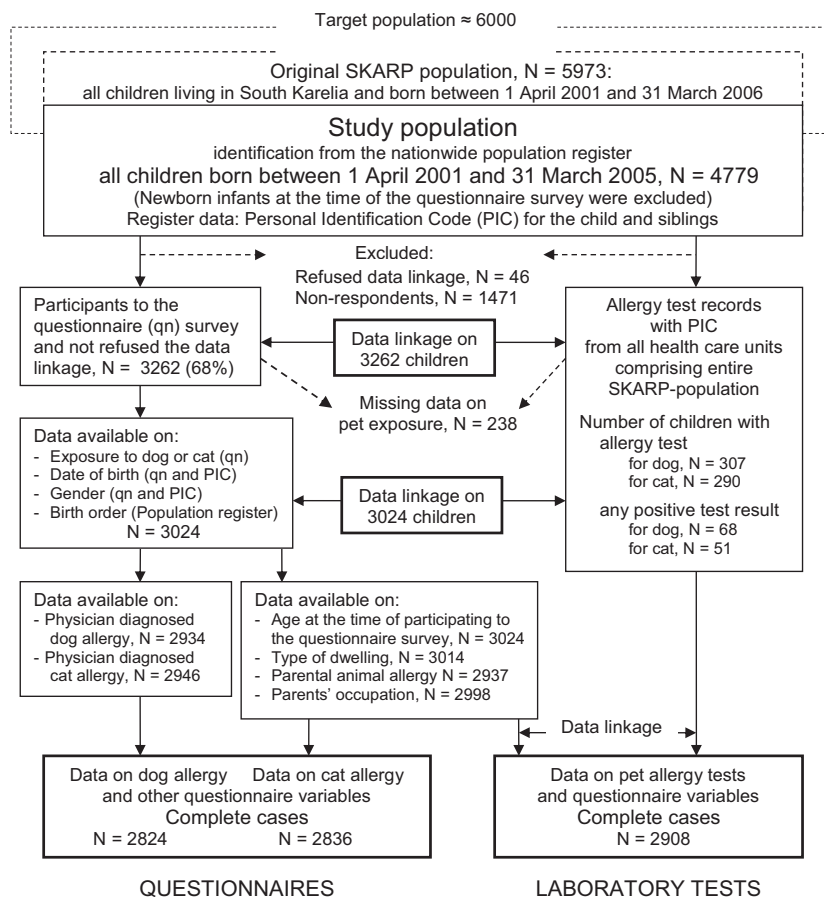


Figure 1 Flow diagram of the South Karelia Allergy Research Project (the SKARP).

cutoff point for SPTs was defined as the mean of two orthogonal diameters of the urticarial weal of 3 mm, applied to both positive and negative controls. Test values equal or above the cutoff point were considered as positive. As a cross-sectional outcome, we used the history of physician-diagnosed pet allergies based on parental responses to the questions shown in Online Supplement. English translations of the entire questionnaires are available at www.oulu.fi/terveystietee/node/29090.

Explanatory variables

Gender, birth order, place of residence, type of dwelling, parents' occupations, and animal allergy in biological parents and dog and/or cat exposure at home during the first year of life (*early exposure*) were used as explanatory variables, data sources of which are shown in Fig. 1 and categorizations described in Online Supplement.

Statistical methods

The cumulative incidences of the first test and the first positive result were described by the Kaplan–Meier method, using the survival package (function `survfit`) in the R environment release 3.0.2 (www.r-project.org). The outcome event was either the first test for allergic sensitization performed or the first positive test, as appropriate. The risk time was defined as a period between the child's date of birth and the date of the event if such an event occurred. For children without any pertinent event, the risk time ended on the closing date of data collection (September 30, 2006). In addition, the incidence rate ratios (RR) of the first test and of the first positive result were

estimated, adjusting for gender, birth order, type of dwelling, parental occupation (health care or other), and parental animal allergies, by fitting a Cox regression model (function `coxph` of R) that included all these covariates together with the main exposure variable.

The cross-sectional outcomes (physician-diagnosed dog and cat allergy) referred to their lifetime occurrence by the age of the child at the time their parents answered the questionnaire. These were examined by a logistic regression model (function `glm` of R). The prevalence odds ratios (OR) for the diagnosed pet allergy were calculated from the fitted model, adjusted for the same variables as in the Cox model above plus the child's age when the parents returned the questionnaire.

The proportion of children with a positive result out of all tested children was calculated. Among the tested subpopulation, the ORs for a positive test result were also obtained by logistic regression including the same variables as the Cox models.

Results

Information on early exposure to dog and cat was available for 93% (N = 3024) of the participants (Fig. 1). Altogether, 47% of children had early exposure to pets (dog and/or cat) (Table 1). Pet-keeping was relatively common despite parental animal allergies being quite prevalent, too.

The incidence of testing for sensitization to dog or cat allergens and their positive test results showed little variation between the participants and non-participants of the questionnaire survey (Fig. S1). Out of all children tested for cat or dog allergen, 9% (27/290) and 10% (31/307), respectively, had been

Table 1 Distribution of children according to exposure to dog and/or cat at home before the age of 1 yr, classified by selected explanatory factors.

	N (%)	Dog and/or cat at home (%)				Total
		Neither dog nor cat	Dog only	Cat only	Dog and cat	
Gender						
Boy	1536 (51)	53	25	14	9	100
Girl	1488 (49)	53	25	13	10	100
Birth order						
Not firstborn	1592 (53)	57	22	12	9	100
Firstborn	1432 (47)	47	28	16	9	100
Parents' occupation in health care						
Neither	2315 (78)	52	24	14	10	100
Either	683 (22)	56	27	10	7	100
Type of dwelling						
Block	560 (19)	60	19	15	5	100
Row house or semi-detached house	478 (16)	58	23	12	7	100
Detached house	1776 (59)	52	27	12	9	100
Farmhouse	200 (7)	29	24	20	28	100
Parental animal allergies						
Neither parent	2013 (69)	47	28	15	10	100
Either parent	924 (31)	64	19	10	7	100
Total	3024 (100)	53	25	13	9	100

tested solely for the respective allergen. Altogether, 2% of children with dog and/or cat exposure had been tested for the allergic sensitization to respective pet only. Independently of dog or cat exposure, almost 90% of children tested for sensitization to pet allergens were also reported at least some allergic symptoms. Among them, atopic eczema had been perceived at some time by parents or diagnosed by a physician in 63% (200/318), allergic urticaria in 31% (95/307), pollen allergy/hay fever in 29% (92/315), allergic conjunctivitis in 14% (45/312), and/or symptoms or diagnosis of asthma in 48% (155/320).

Risk factors for testing for sensitization to pet allergens and positive test results

By the age of 4 yr, the cumulative incidence of the first test for allergic sensitization to both dog and cat allergens (11%) and that of a positive result (2%) in these tests were higher among boys than girls, among firstborn than others, in children whose either parent had a healthcare occupation and in offspring of parent(s) with a diagnosed animal allergy (Tables 2 and 3). The associations were similar in kind for the prevalence of diagnosed dog and cat allergy as they were for the cumulative incidences of positive tests.

The incidences of testing for dog or cat allergy were higher (RR 1.25; 95% CI 0.93–1.68 and RR 1.95; 1.40–2.72, respectively) among children with than without early exposure to respective pet at home (Tables 2 and 3). The incidence of positive test for dog was nearly threefold higher (RR 2.69; 95% CI 1.45–5.02) and that for cat fivefold higher (RR 5.03; 95% CI 2.47–10.2) among the exposed vs. non-exposed to respective pets (Tables 2 and 3). The lifetime prevalence of cat allergy diagnoses was five times higher (OR 5.13; 95% CI 2.30–11.4) among children exposed to a cat only. Also, the prevalence of dog allergy was higher (OR 1.75; 95% CI 0.77–3.79) among children exposed to a dog alone than among non-exposed ones, albeit the association was more equivocal regarding diagnosed dog than cat allergy.

Independently of allergic family history, the incidence of a positive test for either dog or cat allergens was higher and started to rise earlier in children exposed to respective pet allergens at home compared with non-exposed ones (Fig. 2).

The analyses were repeated using SPT and sIgE separately as outcomes. The association between pet exposure and positive results remained virtually unchanged, although with smaller numbers the statistical precision was weaker (Table S1).

Proportion of positive tests among children tested for sensitization to pet allergens

The proportion of children with a positive result out of all tested children was much higher among children exposed to dog (30%; 31/102) and cat (29%; 25/85) than those unexposed to the respective pet (16%; 29/182 and 11%; 20/187) (calculated from Tables 2 and 3). Among the subpopulation of tested subjects, the ORs for the positive test results were higher

among children with than without early exposure for respective pet. In most pet exposure classes, the RRs were more than twofold higher for positive tests than for respective testing for allergic sensitization (Tables 2 and 3).

Cross-reactivity between dog and cat exposure and allergies

The occurrence of positive tests for allergic sensitization to dog allergens and that of diagnosed dog allergy were twofold higher among children exposed to either dog or cat alone and threefold higher among those exposed to both of these pets compared to non-exposed children (Table 2). The pattern appeared different for the occurrences of positive tests for allergic sensitization to cat allergens and cat allergy (Table 3). The relative occurrence of these outcomes was even lower among children with early exposure to dog alone than with no pet exposure, but the error margins for the pertinent estimates were wide.

Discussion

Main findings

We found fairly strong population-based evidence that early exposure to dog or cat is associated with a higher risk of positive test results for respective pet allergens and with a diagnosis of pet allergy. The occurrence of both positive tests for sensitization to pet allergens (assessed by SPT and sIgE in serum) and physician's diagnosis of pet allergy were two- to threefold higher for dog and four- to fivefold higher for cat among children with than those without early exposure to the respective pet. Additionally, the association between early pet exposure and respective pet allergy was independent of parental animal allergies.

Strengths and limitations

The main strength of the present work is the real-life longitudinal database of children followed up in a well-defined geographical area, whose questionnaire data were individually linked with all tests for allergic sensitization performed on them. The SKARP is one of the largest studies ever conducted on unselected populations addressing the association between pet exposure and sensitization to respective pet allergens during the first four years of life (2–4, 12). Our data also included the exact dates of tests for allergic sensitization, which enabled us to display the postnatal cumulative incidences of these outcomes separately for dog and cat exposure. The participants of the questionnaire survey represent reasonably well the entire target population and their test data were comprehensively collected in the area (24). A sensitivity analysis (Online Supplement, Tables S2 and S3) showed that missing data on pet exposure caused most likely only negligible bias, because incomplete answering or participation to the questionnaire survey was probably independent of pet exposure.

In Finland, tests for allergic sensitization are always ordered by a physician for diagnostic purposes. Small

Table 2 Cumulative incidences (%; from Kaplan–Meier analyses) up to 4 yr of age and model-adjusted rate ratios (RR)* of the first allergy test and of the first positive result for *dog allergen*† among the participants, the proportion of subjects with a positive test result (PPT) among tested children with odds ratios (OR)‡, and the lifetime prevalence (%) of physician-diagnosed *dog allergy* and model-adjusted odds ratios (OR)§ according to selected explanatory factors. (N, group size; n, number of cases; 95% CI, 95% confidence interval)

	First test			First positive test†				PPT			Physician diagnosed		
	N	% (n)	RR (95% CI)*	% (n)	RR (95% CI)*	%	OR (95% CI)‡	N	% (n)	OR (95% CI)§	N	% (n)	OR (95% CI)§
Gender													
Girl	1599	9.4 (132)	1	1.6 (24)	1	18	1	1524	1.4 (21)	1			
Boy	1663	12.9 (175)	1.22 (0.96, 1.55)	3.0 (44)	1.71 (1.00, 2.92)	25	1.39 (0.74, 2.63)	1564	1.8 (28)	1.17 (0.63, 2.20)			
Birth order													
Firstborn	1530	12.8 (162)	1	3.2 (42)	1	26	1	1462	2.0 (29)	1			
Not firstborn	1732	9.8 (145)	0.77 (0.60, 0.98)	1.5 (26)	0.72 (0.42, 1.21)	18	0.81 (0.43, 1.51)	1626	1.2 (20)	0.89 (0.47, 1.67)			
Type of dwelling													
Block	608	11.9 (54)	1	2.8 (16)	1	30	1	577	2.4 (14)	1			
Row house or semi-detached house	513	10.6 (42)	0.95 (0.62, 1.47)	1.6 (5)	0.34 (0.11, 1.06)	12	0.31 (0.08, 1.03)	502	0.8 (4)	0.46 (0.13, 1.41)			
Detached house	1841	11.5 (189)	1.10 (0.79, 1.53)	2.5 (44)	0.82 (0.43, 1.55)	23	0.82 (0.38, 1.83)	1788	1.6 (29)	0.67 (0.32, 1.50)			
Farmhouse	208	9.4 (16)	0.74 (0.40, 1.39)	1.2 (2)	0.17 (0.02, 1.34)	13	0.18 (0.01, 1.16)	201	1.0 (2)	0.43 (0.06, 1.72)			
Missing	92	7.7 (6)		– (1)				20	– (0)				
Parents' occupation in health care													
Neither parent	2427	10.8 (213)	1	2.0 (42)	1	20	1	2356	1.4 (34)	1			
Either parent	737	12.9 (88)	1.39 (1.07, 1.81)	3.4 (25)	2.08 (1.23, 3.53)	28	1.57 (0.82, 2.97)	708	2.1 (15)	1.52 (0.75, 2.92)			
Missing	98	7.4 (6)		– (1)				24	– (0)				
Parental animal allergies¶													
Neither parent	2118	8.8 (159)	1	1.7 (36)	1	23	1	2056	1.0 (20)	1			
Either parent	978	16.2 (129)	1.85 (1.45, 2.36)	3.8 (30)	1.71 (1.01, 2.91)	23	1.06 (0.56, 2.01)	945	2.9 (27)	2.83 (1.51, 5.33)			
Missing	166	12.3 (19)		0.6 (2)				85	2.3 (2)				
Pet exposure													
No	1595	10.5 (146)	1	1.1 (20)	1	14	1	1540	1.2 (18)	1			
Dog only	747	12.5 (72)	1.25 (0.93, 1.68)	3.4 (22)	2.69 (1.45, 5.02)	31	2.64 (1.26, 5.58)	728	1.5 (11)	1.75 (0.77, 3.79)			
Cat only	408	10.7 (36)	1.17 (0.80, 1.71)	2.6 (9)	2.10 (0.94, 4.65)	25	2.11 (0.79, 5.39)	399	1.8 (7)	2.09 (0.79, 4.99)			
Dog and cat	274	13.3 (30)	1.55 (1.03, 2.33)	4.7 (9)	3.32 (1.45, 7.63)	30	2.70 (0.96, 7.23)	267	3.0 (8)	3.29 (1.23, 7.96)			
Missing	238	10.0 (23)		3.8 (8)				154	3.2 (5)				
Total	3262	11.2 (307)		2.3 (68)		22		3088	1.6 (49)				

*From a Cox model (among complete cases, N = 2908) adjusting for parental animal allergy, gender, birth order, type of dwelling, parents' occupation, and pet exposure.

†Skin prick test to dog allergens with cutoff point ≥ 3 mm or specific immunoglobulin E (IgE) antibodies to dog with cutoff point ≥ 0.35 kU/l. Using a higher cutoff point for sIgE (≥ 0.70 kU/l), the RR for the first positive test for dog allergen was 3.00 (1.54–5.83), 2.49 (1.10–5.67), and 2.95 (1.15–7.57) among those exposed to dog alone, cat alone and both pets, respectively, compared to non-exposed children.

‡From a logistic regression model (among subpopulation of tested subjects) adjusting for the same variables as in the Cox models.

§From a logistic regression model (among complete cases, N = 2824) adjusting for the same variables as in the Cox models plus the child's age when the parents filled the questionnaire.

¶Based on the parents' reports, the child's biological mother and/or father had physician-diagnosed animal dust allergy.

Table 3 Cumulative incidences (%; from Kaplan–Meier analyses) up to 4 yr of age and model-adjusted rate ratios (RR)* of the first allergy test and of the first positive result for *cat allergens*† among the participants, the proportion of subjects with a positive test result (PPT) among tested children with odds ratios (OR)‡, and the lifetime prevalence (%) of physician-diagnosed *cat allergy* and model-adjusted odds ratios (OR)§ according to selected explanatory factors. (N, group size; n, number of cases; 95% CI, 95% confidence interval)

	First test			First positive test†				Physician diagnosed		
	N	% (n)	RR (95% CI)*	% (n)	RR (95% CI)*	PPT %	OR (95% CI)‡	N	% (n)	OR (95% CI)§
Gender										
Girl	1599	9.1 (126)	1	1.6 (18)	1	14	1	1531	1.1 (17)	1
Boy	1663	12.1 (164)	1.20 (0.94, 1.54)	2.5 (33)	1.60 (0.86, 2.96)	20	1.53 (0.77, 3.14)	1569	1.7 (27)	1.37 (0.70, 2.74)
Birth order										
Firstborn	1530	12.0 (162)	1	2.6 (29)	1	20	1	1471	1.8 (26)	1
Not firstborn	1732	9.5 (145)	0.86 (0.67, 1.10)	1.5 (22)	1.07 (0.59, 1.96)	15	1.03 (0.52, 2.06)	1629	1.1 (18)	0.99 (0.50, 1.94)
Type of dwelling										
Block	608	11.8 (53)	1	2.5 (13)	1	25	1	582	2.2 (13)	1
Row house or semi-detached house	513	10.3 (42)	0.92 (0.59, 1.42)	2.0 (7)	0.90 (0.34, 2.38)	17	1.09 (0.34, 3.44)	503	1.0 (5)	0.76 (0.23, 2.26)
Detached house	1841	10.9 (177)	1.00 (0.72, 1.39)	2.1 (30)	0.77 (0.37, 1.62)	17	0.95 (0.40, 2.40)	1794	1.4 (25)	0.71 (0.32, 1.67)
Farmhouse	208	7.9 (13)	0.56 (0.29, 1.09)	– (0)	0.00 (0.00, ∞)	0	0.00 (0.00, ∞)	201	0.5 (1)	0.23 (0.01, 1.29)
Missing	92	5.7 (5)		2.3 (1)				20	– (0)	
Parents' occupation in health care										
Neither parent	2427	10.2 (201)	1	2.0 (36)	1	18	1	2364	1.5 (35)	1
Either parent	737	12.6 (83)	1.41 (1.08, 1.85)	2.2 (14)	1.35 (0.69, 2.64)	17	0.91 (0.41, 1.93)	712	1.3 (9)	0.80 (0.32, 1.77)
Missing	98	6.5 (6)		2.3 (1)				24	– (0)	
Parental animal allergies¶										
Neither parent	2118	8.2 (149)	1	1.7 (27)	1	18	1	2063	0.8 (17)	1
Either parent	978	15.8 (122)	1.87 (1.46, 2.41)	2.9 (22)	1.60 (0.87, 2.98)	18	0.88 (0.43, 1.77)	950	2.6 (25)	3.18 (1.63, 6.31)
Missing	166	12.1 (19)		1.8 (2)				87	2.3 (2)	
Pet exposure										
No	1595	10.0 (138)	1	1.3 (16)	1	12	1	1546	1.0 (15)	1
Dog only	747	9.2 (49)	0.87 (0.62, 1.22)	0.8 (4)	0.64 (0.21, 1.94)	8	0.63 (0.17, 1.90)	731	0.4 (3)	0.62 (0.14, 1.94)
Cat only	408	15.0 (53)	1.95 (1.40, 2.72)	4.3 (16)	5.03 (2.47, 10.25)	30	3.26 (1.41, 7.55)	402	3.2 (13)	5.13 (2.30, 11.42)
Dog and cat	274	14.7 (32)	1.85 (1.24, 2.76)	4.9 (9)	4.36 (1.85, 10.28)	28	2.89 (1.03, 7.81)	267	3.0 (8)	4.34 (1.59, 10.87)
Missing	238	7.6 (18)		3.9 (6)				154	3.2 (5)	
Total	3262	10.7 (290)		2.0 (51)		18		3100	1.4 (44)	

*From a Cox model (among complete cases, N = 2908) adjusting for parental animal allergy, gender, birth order, type of dwelling, parents' occupation, and pet exposure.

†Skin prick test to cat allergens with cutoff point ≥ 3 mm or specific immunoglobulin E antibodies to cat with cutoff point ≥ 0.35 kU/l.

‡From a logistic regression model (among subpopulation of tested subjects) adjusting for the same variables as in the Cox models.

§From a logistic regression model (among complete cases, N = 2836) adjusting for the same variables as in the Cox models plus the child's age when the parents filled the questionnaire.

¶Based on the parents' reports, the child's biological mother and/or father had physician-diagnosed animal dust allergy.

children who need treatment for their allergic symptoms are likely to be tested for suspected allergens. Children may also be tested for allergic sensitization to make the decision to

remove the pet from the home, albeit allergic diseases rarely lead to the removal of the pet or avoiding pet-keeping (26, 27). Children may also be tested in advance, before the pet is

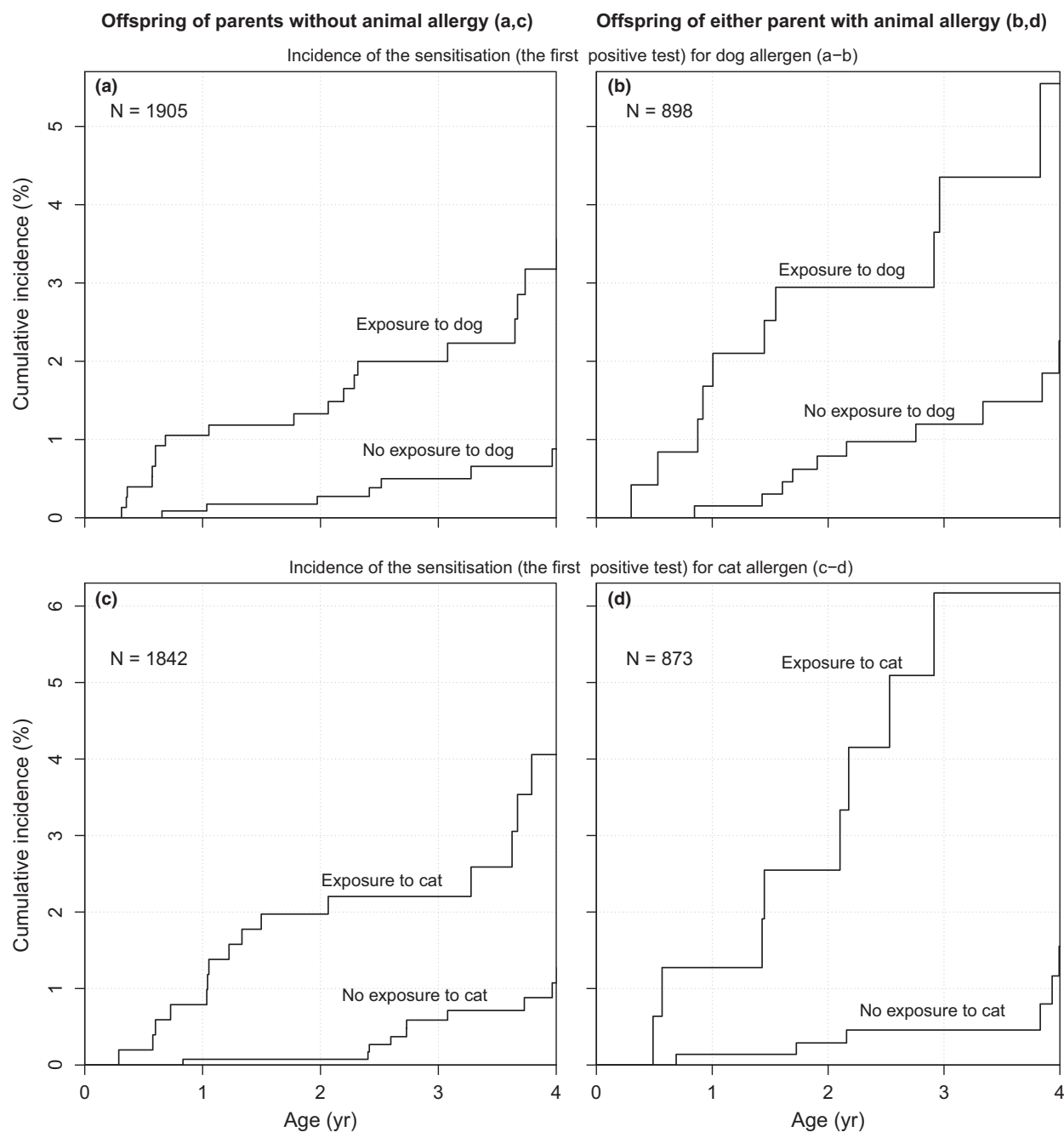


Figure 2 Kaplan–Meier curves of positive tests for dog (a–b) and cat (c–d) allergens in offspring of parents with (right plots) and without (left plots) animal allergy by early pet exposure at home.

taken, to make sure that keeping it will be safe. Nevertheless, tests for allergic sensitization had rarely been performed selectively for a single pet allergen only. Additionally, the proportion of children with a positive test result out of all tested subjects was much higher among children exposed to the respective pet than among non-exposed ones, which provides further support for association between pet exposure and the incidence of pet allergy.

Our results based on a real-life setting reflect reasonably well the occurrence of suspected clinical pet allergy in the area concerned. Obviously, the occurrence of sensitization to pet allergens would have been higher than that coming up from our findings, if we had tested the entire population for these allergens. While a positive test for allergic sensitization alone is not equivalent to clinical allergy, practically all children tested were also reported to have hypersensitivity symptoms of

obvious clinical relevance. However, our results should be interpreted with caution as we cannot confirm that allergic symptoms preceded the tests and in small children the agreement between clinical pet allergy and the results of the tests for sensitization to pet allergens is unknown (28).

Heterogeneity of our test data probably caused some misclassification of the outcome but hardly introduced any major bias to the results. The tests were performed in several laboratories with varying practices, and in most cases, only either SPT or sIgE test was performed depending on availability of test methods in the healthcare unit concerned. Therefore, we may have misclassified some cases with real sensitization for pet allergens (28). The misclassification is obviously independent of pet exposure, however, and therefore most likely attenuated our estimates of the relative rates toward 1. Even when we used higher cutoff points for the sIgEs, our findings remained stable or even strengthened.

The weaknesses of our study include the rough estimates of animal exposures, that is, the lack of information on the number of animals, duration of exposure, and measurements on the true exposure to animal dust. However, an infant is inevitably exposed to high concentrations of pet allergens through the respiratory tract and skin, since during the first year of life he/she crawls and creeps at the same level of indoor air where the pets are living. Parental allergies were also based on questionnaire data, which is the only feasible method to obtain this information in large population studies.

Our conclusions are limited by the short follow-up time. Follow-up of the entire population up to 4 yr or longer would have yielded more cases, narrower confidence intervals, and more information beyond the age of 4 yr. Moreover, our results cannot be distorted by any essential recall bias or a large number of dropouts often seen in prospective studies with long follow-up times, because the children were 1–4 yr at the time of the questionnaire survey. As none of the authors worked as a physician in the area, the results were not distorted by this reason either.

Comparison with other studies

The variations in study design, populations, definition of outcomes, duration or timing of exposure, concentrations of environmental animal exposure, and the age of subjects studied make different studies poorly comparable (2–4, 10, 12). In our unselected population, early exposure to dog or cat was more common than in other European cohort studies on average (47% vs. 24%) (10). Our results corroborate the previous evidence of a positive association between early cat exposure and sensitization to cat at the age of 4 yr (13, 15). On the contrary, a lower prevalence of cat sensitization at the age of 18 yr was reported among children exposed than non-exposed

to cat in infancy (8). However, protective effects of early cat exposure, if any exist, may emerge beyond the first 4 yr of life (8, 16); hence, avoiding early exposure might only postpone the emergence of pet allergies to some later point. No consensus exists whether dog-keeping provides protection against dog allergy (4, 10–12). Chen et al. showed that early dog exposure might protect from inhalant sensitization, but the association between early dog exposure and allergy could not be confirmed (11). Our results—although with wide error margins—were in fact concordant with a possibility that dogs could even protect from sensitization to cat allergens (5, 6). Potential underlying mechanisms could be competitive concentrations or cross-reactivity between dog- and/or cat (or other mammalian)-specific allergens (29, 30). The different effect of cat and dog exposure may also be explained by various lifestyle factors associated with the pet exposure (11).

Conclusions

According to our population-based results, early exposure to dog and cat at home is strongly associated with respective pet allergy and IgE-mediated sensitization to respective pet allergens during the first four years of life. Further evidence from population-based studies with longer follow-up is required to justify any recommendation concerning early pet contacts with a view to preventing pet allergies later in life.

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Conflict of interest

None declared.

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Table S1. Cumulative incidences (%), from Kaplan–Meier analyses up to 4 yr of age and model-adjusted rate ratios (RR)^a of the first positive result for dog and cat allergens in SPT^b and sIgE tests^c among the participants according to selected explanatory factors.

Table S2. Sensitivity analysis for the incidence rate ratios (RR) of positive dog allergy test by selected risk factors based models fitted for all participants, in which the missing values were substituted by the (a) minimum RR assumption and the (b) maximum RR assumption.

Table S3. Sensitivity analysis for the incidence rate ratios (RR) of positive cat allergy test by selected risk factors based models fitted for all participants, in which the missing values were substituted by the (a) minimum RR assumption and the (b) maximum RR assumption.

Figure S1. Kaplan–Meier-curves of testing for sensitisation to pet allergens (a–c) and their positive test results (d–f) among the participants (N = 3262, black solid line) and non-participants (N = 1471, grey dashed line) of the SKARP study.

Online Supplement. Description of variables and Sensitivity analysis.

Table S1 Cumulative incidences (% from Kaplan-Meier analyses) up to four years of age and model-adjusted rate ratios (RR)^a of the first positive result for dog and cat allergens in SPT^b and sIgE tests^c among the participants according to selected explanatory factors. (N=group size, n= number of cases, 95% CI = 95% confidence interval)

		SPT ^b					sIgE ^c			
		DOG			CAT		DOG		CAT ^b	
		N	% (n)	RR (95%CI) ^a	% (n)	RR (95%CI) ^a	% (n)	RR (95%CI) ^a	% (n)	RR (95%CI) ^a
Gender										
	Girl	1599	0.7 (8)	1	1.2 (13)	1	0.9 (18)	1	0.4 (5)	1
	Boy	1663	1.9 (28)	3.26 (1.40, 7.58)	1.6 (22)	1.33 (0.64, 2.77)	1.3 (19)	1.00 (0.51, 1.99)	1.0 (14)	3.07 (0.99, 9.45)
Birth order										
	Firstborn	1530	1.5 (17)	1	1.8 (18)	1	1.8 (28)	1	0.9 (12)	1
	Not firstborn	1732	1.1 (19)	1.38 (0.67, 2.86)	1.1 (17)	1.43 (0.68, 2.98)	0.4 (9)	0.36 (0.17, 0.79)	0.5 (7)	0.74 (0.27, 1.99)
Type of dwelling										
	Block	608	1.6 (9)	1	2.0 (10)	1	1.4 (8)	1	0.7 (4)	1
	Row-house or semi	513	0.8 (3)	0.35 (0.07, 1.71)	0.9 (4)	0.65 (0.20, 2.16)	0.7 (2)	0.31 (0.06, 1.51)	1.1 (3)	1.21 (0.24, 6.02)
	Detached house	1841	1.4 (23)	0.78 (0.33, 1.87)	1.4 (20)	0.63 (0.27, 1.48)	1.3 (25)	0.92 (0.39, 2.16)	0.6 (12)	1.10 (0.30, 4.03)
	Farmhouse	208	0.7 (1)	0.36 (0.04, 3.04)	– (0)	0.00 (0.00, ∞)	0.5 (1)	0.00 (0.00, ∞)	– (0)	0.00 (0.00, ∞)
	Missing	92	– (0)		2.3 (1)		– (1)		– (0)	
Parents' occupation in health care										
	Neither parent	2427	1.4 (25)	1	1.5 (28)	1	0.8 (20)	1	0.6 (11)	1
	Either parent	737	1.3 (11)	1.55 (0.72, 3.31)	0.9 (6)	0.70 (0.27, 1.83)	2.2 (16)	2.71 (1.36, 5.41)	1.2 (8)	2.60 (0.98, 6.90)
	Missing	98	– (0)		– (1)		– (1)		– (0)	
Parental animal allergies ^d										
	Neither parent	2118	1.0 (20)	1	1.3 (20)	1	0.9 (21)	1	0.6 (10)	1
	Either parent	978	2.2 (15)	1.35 (0.64, 2.86)	1.7 (13)	1.25 (0.58, 2.70)	1.7 (15)	1.65 (0.82, 3.36)	1.2 (9)	1.84 (0.69, 4.94)
	Missing	166	0.6 (1)		0.6 (2)		– (1)		– (0)	
Pet exposure										
	No	1595	0.8 (12)	1	0.9 (12)	1	0.3 (9)	1	0.4 (5)	1
	Dog only	747	1.6 (9)	1.91 (0.79, 4.63)	0.4 (2)	0.44 (0.10, 1.98)	2.0 (15)	3.66 (1.57, 8.53)	0.4 (2)	0.94 (0.18, 4.96)
	Cat only	408	2.1 (7)	2.76 (1.07, 7.14)	3.1 (11)	4.43 (1.92, 10.23)	1.0 (3)	1.46 (0.39, 5.45)	1.7 (6)	5.92 (1.75, 19.99)
	Dog and cat	274	1.8 (4)	1.95 (0.54, 7.02)	3.3 (6)	3.48 (1.22, 9.98)	3.4 (6)	5.40 (1.90, 15.35)	2.0 (4)	7.18 (1.88, 27.41)
	Missing	238	2.3 (4)		2.9 (4)		2.5 (4)		1.0 (2)	
Total		3262	1.3 (36)		1.4 (35)		1.1 (37)		0.7 (19)	

a From a Cox model (among complete cases, N=2908) adjusting for parental animal allergy, gender, birth order, type of dwelling, parents' occupation and pet exposure.

b Skin prick test with cut-off point ≥ 3 mm

c Specific Immunoglobulin E (IgE) antibodies with cut-off point ≥ 0.35 kU/l.

d Basing on the parents' reports, the child's biological mother and/or father had physician-diagnosed animal dust allergy

Table S2. Sensitivity analysis for the incidence rate ratios (RR) of positive dog allergy test by selected risk factors based models fitted for all participants, in which the missing values were substituted by the (a) minimum RR assumption and the (b) maximum RR assumption.

		Model of complete cases N=2908 RR (95%CI)	Model with minimum RR assumptions ^a N=3262 RR (95%CI)	Model with maximum RR assumptions ^b N=3262 RR (95%CI)
Gender				
	Girl	1	1	1
	Boy	1.71 (1.00,2.92)	1.76 (1.07,2.91)	1.75 (1.06,2.88)
Birth order				
	Firstborn	1	1	1
	Not firstborn	0.72 (0.42,1.21)	0.58 (0.35,0.96)	0.55 (0.33,0.90)
Type of dwelling				
	Block	1	1	1
	Row-house or semi	0.34 (0.11,1.06)	0.36 (0.13,0.98)	0.49 (0.18,1.35)
	Detached house	0.82 (0.43,1.55)	0.80 (0.44,1.44)	1.20 (0.66,2.16)
	<i>Farmhouse</i>	0.17 (0.02,1.34)	0.39 (0.11,1.37)	0.45 (0.10,1.95)
Parents' occupation				
	<i>Other</i>	1	1	1
	Health care	2.08 (1.23,3.53)	1.96 (1.19,3.22)	1.56 (0.94,2.57)
Parents' animal allergy				
	<i>Neither</i>	1	1	1
	Mother or Father	1.71 (1.01,2.91)	1.93 (1.18,3.16)	1.93 (1.19,3.15)
Pet exposure				
	<i>No</i>	1	1	1
	Dog only	2.69 (1.45,5.02)	2.13 (1.20,3.78)	2.59 (1.40,4.81)
	Cat only	2.10 (0.94,4.65)	1.63 (0.76,3.48)	2.00 (0.90,4.43)
	Dog and cat	3.32 (1.45,7.63)	2.86 (1.33,6.15)	2.78 (1.43,5.40)

a For each factor included in the model any missing values were substituted by the category having the lowest estimated RR obtained from fitting the model on complete cases only.

b For each factor included in the model any missing values were substituted by the category having the highest estimated RR obtained from fitting the model on complete cases only.

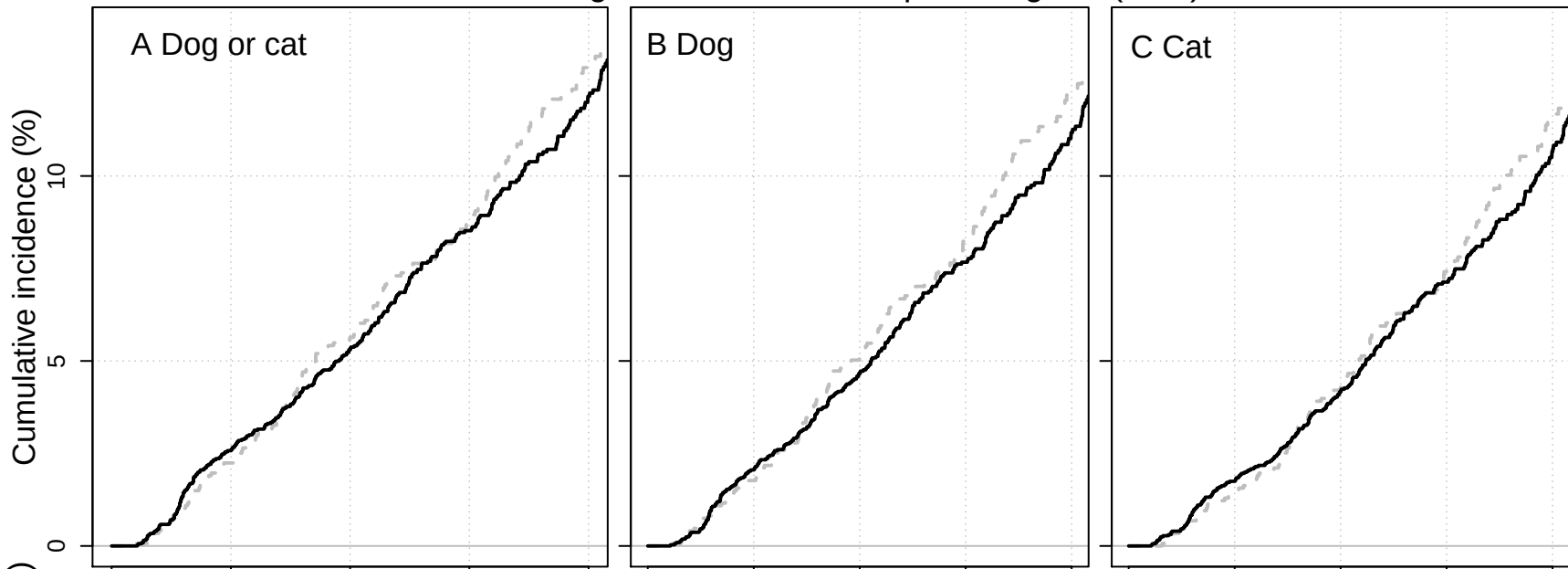
Table S3. Sensitivity analysis for the incidence rate ratios (RR) of positive cat allergy test by selected risk factors based models fitted for all participants, in which the missing values were substituted by the (a) minimum RR assumption and the (b) maximum RR assumption.

		Model of complete cases N=2908 RR (95%CI)	Model with minimum RR assumptions ^a N=3262 RR (95%CI)	Model with maximum RR assumptions ^b N=3262 RR (95%CI)
Gender				
	Girl	1	1	1
	Boy	1.60 (0.86,2.96)	1.70 (0.95,3.03)	1.70 (0.96,3.03)
Birth order				
	Firstborn	1	1	1
	Not firstborn	1.07 (0.59,1.96)	0.81 (0.46,1.43)	0.71 (0.40,1.24)
Type of dwelling				
	Block	1	1	1
	Row-house or semi	0.90 (0.34,2.38)	0.67 (0.27,1.68)	0.89 (0.36,2.24)
	Detached house	0.77 (0.37,1.62)	0.70 (0.36,1.36)	1.08 (0.55,2.11)
	<i>Farmhouse</i>	0.00 (0.00,Inf)	0.13 (0.02,1.00)	0.00 (0.00,Inf)
Parents' occupation				
	<i>Other</i>	1	1	1
	Health care	1.35 (0.69,2.64)	1.37 (0.73,2.54)	1.05 (0.57,1.95)
Parents' animal allergy				
	<i>Neither</i>	1	1	1
	Mother or Father	1.60 (0.87,2.98)	2.02 (1.14,3.58)	1.72 (0.98,3.01)
Pet exposure				
	No	1	1	1
	<i>Dog only</i>	0.64 (0.21,1.94)	1.29 (0.58,2.87)	0.61 (0.20,1.83)
	Cat only	5.03 (2.47,10.25)	4.99 (2.46,10.13)	3.70 (1.92,7.14)
	Dog and cat	4.36 (1.85,10.28)	4.88 (2.13,11.18)	4.63 (2.03,10.57)

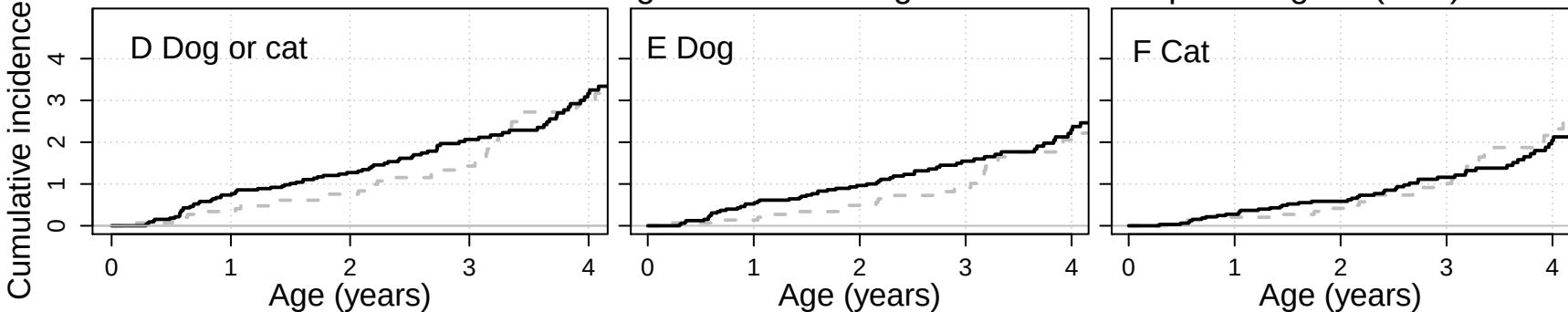
a For each factor included in the model any missing values were substituted by the category having the lowest estimated RR obtained from fitting the model on complete cases only.

b For each factor included in the model any missing values were substituted by the category having the highest estimated RR obtained from fitting the model on complete cases only.

Testing for sensitisation to pet allergens (A–C)



Positive results in SPT or sIgE tests indicating sensitisation to pet allergens (D–F)



Online Supplement

Description of variables

Outcomes

As a cross-sectional outcome, we used the history of physician-diagnosed pet allergies, based on parental responses to the following question: 'Has the child ever been found to have the following allergies, symptoms and/or hypersensitivity reactions, and by whom?' Below this question, the parents were instructed to tick one or more alternatives ('never found', 'perceived by parents', and 'diagnosed by a physician') on the following lines: 'allergy to animal dust, from cats' and 'allergy to animal dust, from dogs'.

Explanatory variables

The date of birth and gender of the child (both are included in the PIC) and the PICs of his/her siblings living in the same household were obtained from the population register. Based on the PICs of the child and siblings, the birth order was classified as 'firstborn' and 'not firstborn'. Firstborn twins were both classified as firstborn. In the questionnaire, the parents were asked: 'Have there ever been animals in the part of the child's home where the family lives?' If they answered 'yes' (other alternatives to be ticked were 'no' and 'not known'), they were instructed to continue by ticking the alternatives 'yes' and 'no' for the age (less than and/or over 1 yr old) when and to which animal (dog, cat, and/or other animal) the child was exposed and non-exposed at home, respectively. In the present paper, we ignored exposure to other animals except dog and cat during the first year of life at home.

The parents were asked to mark: 'In what kind of house does the child live at present?' The alternatives were (a) block of flats, (b) row house or semi-detached house, (c) detached house in a built-up area or population center, (d) detached house in a sparsely populated area, (e) farmhouse without animals, and f) farmhouse with animals in the same yard. The type of dwelling was categorized as follows: (i) block (alternative 'a'), (ii) row house or semi-detached house ('b'), (iii) detached house ('c' or 'd'), and (iv) farmhouse ('e' or 'f').

Further questions asked whether the child's biological mother, father, or both had ever had animal dust allergy. The response alternatives were as follows: (i) physician-diagnosed allergy, (ii) self-perceived allergy, (iii) no allergy ever perceived, and (iv) unknown. Based on the above, the parents were classified to two groups: (i) having an animal allergy if either of the biological parents had been reported physician-diagnosed animal allergy and (ii) not having an animal allergy if neither parents had ever been diagnosed animal allergy.

Parents' occupation was coded as follows: (i) a 'healthcare occupation', if reported in either parent and (ii) an 'other occupation', if the 'health care occupation' was reported in neither and an 'other occupation' in either parent. The questionnaires and their English translations are available at www.oulu.fi/terveystieteet/node/29090.

Parents reported their own perceptions or physician's diagnoses on 'any symptoms of atopic manifestations' (pollen allergy/hay fever, atopic eczema, allergic urticaria, allergic conjunctivitis, symptoms, or diagnosis of asthma). This variable was used to evaluate possible differences of testing practices between children exposed and non-exposed to respective pets.

Sensitivity analysis

Statistical methods

We performed a simple sensitivity analysis to assess, whether the estimation results could have been essentially affected by incomplete responses to the questionnaire. First, a model with the main exposure variables and covariates was fitted and the RRs estimated among complete cases (N=2908), i.e. those subjects with no missing data. Second, for each factor included in the model any missing values were substituted by either (a) the category having the lowest estimated RR (minimum RR assumption), or (b) the category having the highest estimated RR (maximum RR assumption), these lowest and highest RRs being obtained from fitting the above model on complete cases only. Third, for all participants (N=3262) we fitted a model based on minimum RR assumption (a) and another model based on maximum RR assumption (b). See Tables S2 and S3.

Results from sensitivity analyses

According to a lower cut-off point ($\geq 0.35 \text{ kU/l}$) for concentration of dog and cat sIgEs 68 children had IgE-mediated sensitisation for dog and 51 for cat. Respectively, a higher cut-off point ($\geq 0.70 \text{ kU/l}$) yielded IgE-mediated sensitisation for dog in 61 and for cat in 48 children. When a higher cut-off point of sIgE was used, the incidence ratio of the first positive test for dog allergen was higher among those exposed to dog alone (RR 3.00; 95%CI 1.54-5.83) and cat alone (RR 2.49; 95%CI 1.10-5.67) and lower among those exposed to both pets (RR 2.95; 95%CI 1.15-7.57) compared with the results defined by a lower cut-off point of sIgE in Table 2.

The results on the effects of the pet exposure or of any other factors were not essentially affected by incomplete responses to the questionnaire, as the estimated rate ratios based on rather extreme assumptions concerning the missing values were not much different from those obtained from the complete cases only (Tables S2 and S3).