

ORIGINAL ARTICLE

Gender differences in indoor allergen exposure and association with current rhinitis

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Summary

Background Differences between boys and girls in allergic manifestations are well known, and this difference is possibly not attributed to physiological differences alone.

Objective We, therefore, investigated whether boys and girls could be exposed to different allergen levels at home and whether indoor allergen levels could be differently associated with rhinitis in boys and girls at 10 years of age.

Methods Cat, dog and house dust mite (HDM) allergen levels in mattress dust and interview data regarding current allergic disease were available for 797 10-year-old children (360 girls) in The Environment and Childhood Asthma Study in Oslo.

Results Girls had higher concentrations of cat and dog allergens in their mattresses compared with boys, also in homes without cats [geometric mean 95% confidence intervals (95% CI): 0.37 (0.31, 0.44) for girls and 0.26 (0.23, 0.30) µg cat allergen/g dust for boys, $P = 0.002$], and without dogs [girls: 0.74 (0.63, 0.86) and boys: 0.55 (0.48, 0.62) µg dog allergen/g dust, $P = 0.003$]. No difference was observed for HDM allergen (Der p 1) levels. Of the 190 (23.8%) children reporting current rhinitis, 144 (75.8%) were sensitized to at least one allergen. The adjusted odds ratio for current rhinitis increased with 1.20 (95% CI: 1.01, 1.42) per 1 µg/g dust increase in Der p 1 for girls ($P = 0.037$), but not for boys ($P = 0.91$).

Conclusion Girls had higher levels of cat and dog allergens in mattress dust compared with boys, whereas no difference was observed for Der p 1 allergen. Nevertheless, only increasing levels of Der p 1 and not cat and dog allergens significantly increased the risk of current rhinitis in girls, whereas no significant association was observed for boys.

Keywords gender, house dust mite, indoor allergens, pet keeping, rhinitis

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Introduction

Rhinitis is one of the atopic manifestations in children, and is associated with asthma [1, 2] and bronchial hyperresponsiveness (BHR) [3], but may also be present independently of allergic sensitization. Exposure to indoor allergens such as animal dander and house dust mite (HDM) has been reported to increase the risk for both asthma and rhinitis [4]. Indoor allergens may exacerbate symptoms and increase BHR also in non-asthmatic subjects with allergic rhinitis (AR) [4, 5]. Thus, allergen avoidance may reduce symptoms in some allergen-sensitized individuals. The observed inverse association

between pet keeping and sensitization to pet allergens [6] has been attributed to pet avoidance in allergic families [6, 7]. We have reported previously that families of children with doctor-confirmed AR were less likely to acquire cats and dogs during the first 10 years of life [8]. However, to avoid allergen exposure is difficult because pet allergens are ubiquitously present in public areas and passively transferred to homes without pets [9, 10]. Moreover, even low allergen levels may induce symptoms in sensitized patients, as was shown by demonstrating nasal symptoms in patients challenged with concentrations of cat allergen (Fel d 1) comparable with allergen levels in homes without cats [11].

In many populations, exposure to HDM allergens at home is common with a corresponding high population prevalence of HDM sensitization [12]. In other populations, such as many areas of Scandinavia, HDM allergens are rarely found in the mattresses of children's beds [13, 14], and sensitization to cat and dog is more common than sensitization to HDM allergen [15, 16]. However, even low HDM allergen (Der p 1) levels have been associated with allergic sensitization [14, 16], and also with nasal symptoms [17] and asthma exacerbation [18] in patients *without* detectable serum-specific IgE (s-IgE) to HDM.

In pre-puberty, boys are consistently reported to have a higher prevalence of asthma and allergies than girls, whereas *after* puberty, the highest prevalence of asthma and rhinitis is often found among females [19, 20]. However, boys and girls differ not only in physiology but also in their behaviour and interests, which may influence the level of allergen exposure. Differences in risk factors and susceptibility to pet exposure have been reported [21]. Moreover, the families of the children in the present study were more likely to acquire furry pets if the index child was a girl compared with families in which the index child was a boy [8].

It is not clear to what extent gender affects the associations between allergen exposure and allergic disease in school age. Gender-specific differences in environmental exposure have recently been proposed as an important topic in need for more research [22]. The aims of the present study were therefore first to describe the level of exposure to indoor allergens for girls and boys, and secondly to assess whether there was a gender interaction between indoor allergen levels and the association with rhinitis and BHR.

Materials and methods

Subjects

The present study reports results from the 10-year follow-up of the birth cohort 'The Environment and Childhood Asthma Study' (ECA) initiated in Oslo in 1992–1993. In total, 1019 (84%) of 1215 invited children participated in the 10-year follow-up study. In addition to clinical examination of the child and parental structured interview, which have been described previously in detail [23], the parents were also asked to collect dust from the children's mattresses. One hundred and fifty-four parents did not want to collect a dust sample, 27 did not return the sample and 41 samples could not be analysed due to insufficient amounts of dust. The remaining 797 children with available dust samples were included in the present study.

The 797 children with a mean age of 10.6 years (min.: 8.8, max.: 12.3) had less often cats at home (18.2% vs. 26.4%, $P=0.007$), less often parents who smoked (37.7% vs. 46.8%, $P=0.015$) and more often parents with a higher

income than the 222 non-included children (no dust sample). They were otherwise comparable with regard to other demographic variables, the prevalence of allergic disease reported for the index children and their parents, dog ownership and reported pet avoidance (see supporting information Table S1 for details).

Written informed consent was obtained from the parents, and the study was approved by the Regional Committee for Ethics in Medical Research and the Norwegian Data Inspectorate and reported to the Norwegian Biobank Registry.

Dust sampling and extraction

The families were instructed not to change the linen on the children's beds the week before sampling of the mattress dust. The dust was collected by the parents themselves after standardized instructions. The mattresses were vacuumed for 4 min with the families own vacuum cleaners equipped with a special dust collector (P-B Miljø A/S, Bjerringbro, Denmark) [24]. The dust sampling containers were returned to the laboratory at the Norwegian Institute of Public Health, where the dust was vacuumed (sieved) through a filter with a pore size of 0.3 µm. The fine fraction of the dust was weighed and extracted in phosphate-buffered saline with 0.02% NaN₃ to a final concentration of 25 mg dust/mL extraction fluid. The suspensions were incubated overnight in an end-over-end roller at room temperature. After centrifugation, the supernatant was harvested and stored at –20 °C until analysis.

Analyses of cat, dog and mite allergens

The concentrations of the major cat (*Felis domesticus* Fel d 1), dog (*Canis familiaris* Can f 1) and HDM (*Dermatophagoides pteronyssinus* Der p 1) allergens were determined by ELISA following the manufacturer's instructions (Indoor Biotechnologies, Clewyd, UK) [25] and as described in detail elsewhere [26]. Results were given as micrograms allergen per gram fine fraction dust. The detection limits of the ELISA were determined according to the standard curve for each run. Values below the detection limit were, for statistical purposes, given values of 2/3 of the detection limits: 0.12 µg/g for Der p 1, 0.03 µg/g for Can f 1 and 0.20 µg/g for Fel d 1. For the dog allergen assay, 57 samples were below the detection limit, 215 samples for cat allergen and 697 for HDM allergen (Der p 1).

Clinical examination at the 10-year follow-up

The examination was performed at least 4 weeks after any respiratory tract infection, and included blood tests, skin prick tests (SPT) for allergic sensitization, lung function by forced flow-volume measurements and BHR measured

by a methacholine challenge test and a treadmill exercise test, performed on separate days.

SPT was performed according to European standards [27] with the following standardized allergen extracts from ALK (Soluprick[®], ALK-Abello, Hørsholm, Denmark): HDM (*D. pteronyssinus* and *Dermatophagoides farinae*), German cockroach, dog, cat and rabbit dander, birch, timothy (grass) and mugwort pollen, moulds (*Cladosporium herbarium* and *Alternaria*), egg white, milk, peanut and codfish. SPT was considered positive with a weal diameter at least 3 mm larger than the negative control (saline).

s-IgE was measured with a radioallergosorbent fluorescence immunoassay (ImmunoCAP[®] system, Phadia, Uppsala, Sweden). Specific IgE was analysed with the same panel of allergens as for SPT, and considered positive when s-IgE ≥ 0.35 kU/L.

Baseline spirometry was performed according to European standards [28] using a Sensor Medics Vmax 20c instrument (SensorMedics Diagnostics, Yorba Linda, CA, USA) before and after methacholine and exercise challenge tests on separate days. According to international guidelines [23], short- and long-acting β -2 receptor agonists were withheld for at least 3 and 18 h, respectively, before investigations.

The methacholine challenge test was measured as PD₂₀ methacholine according to international guidelines [29], by the inhalation of doubling doses of methacholine, nebulized by the Spira nebuliser (Spira Respiratory Care Center Ltd, Hämeenlinna, Finland). The response was reported as the dose of methacholine that caused a fall in forced expiratory volume in 1 s (FEV₁) of 20% from the (post-saline) baseline value (PD₂₀ methacholine). A standardized exercise test [30] was performed on the second day by a 6–8-min treadmill run at a 95% estimated maximum pulse level with 5.5% inclination. The exercise test was considered positive for exercise-induced bronchoconstriction with a fall in FEV₁ > 10% of baseline FEV₁ measured 3–20 min after running had ceased.

Parental structured interview

The parental structured interview included central ISAAC questions related to airway symptoms of the child, including rhinitis. Children with confirmed symptoms of rhinitis during the last 12 months were asked additional questions related to rhinitis, including perceived triggers of rhinitis (furry pets, pollens, temperature changes, physical activity or unknown), in which seasons the symptoms occurred (all year, spring/summer or autumn/winter) and the impact the rhinitis symptoms had on daily life activities (none, some, moderate or severe). Pet exposure was assessed based upon the following questions: 'Do you currently keep a dog?' and 'Is the child in regular contact with a dog?' and the same questions were asked in relation to cats. Concurrent information regarding pet ownership

during the first 2 years of life was retrieved from questionnaires [26].

Definitions

Current rhinitis was defined by the presence of at least one of the following symptoms during the last 12 months (without a cold): runny nose, blocked nose or sneezing. *Current conjunctivitis* required a report of itchy/runny eyes within the last 12 months.

Rhinitis with allergic sensitization was defined by current rhinitis combined with at least one positive SPT and/or s-IgE to any of the *inhalant seasonal* (pollen or moulds) or *perennial* (HDM, cat, dog, rabbit or cockroach) allergens.

BHR was defined by the methacholine dose-response slope (DRS) (a higher DRS indicating more BHR) calculated from each individual as percent decline in FEV₁ after the final dose of methacholine divided by the cumulative dose of methacholine inhaled [31].

Asthma was defined by the presence of at least two of the three criteria: asthma symptoms, doctor's diagnosis of asthma and the use of asthma medication. *Current asthma* was defined as asthma plus at least one of the following criteria: asthma symptoms or the use of asthma medication within the last 12 months and a positive exercise challenge test at the 10-year follow-up visit [23].

Statistical analyses

Categorical variables were compared using Pearson's χ^2 -test. One-way ANOVA was used to compare allergen concentrations [log transformed and presented as geometric mean (GM) and 95% confidence intervals (95% CI)]. Two-way ANOVA was used when adjusting for pet keeping. The presence or absence of pets at home usually results in bimodally distributed allergen concentrations. Hence, the differences in allergen mean concentration between boys and girls were analysed separately for children *with* and *without* pet ownership. Associations between the indoor allergen exposure levels and *current rhinitis*, *impact on daily life activities* and *rhinitis with unknown triggers* were analysed by multivariate logistic regression models. For the children included in the present study, BHR, asthma and allergic sensitization were important phenotypes and co-morbidities of rhinitis [32], and pet avoidance was found to be associated with rhinitis [8]. These variables were, together with gender, included as covariates in the multivariate models. More severe BHR has also been associated with indoor allergen exposure [5], and a separate linear regression model was therefore used for DRS. For DRS, there was a violation of the normality and homoscedasticity assumptions, even for log-transformed values. Consequently, a robust regression was performed using Huiber's method [33]. The result of the regression

analysis was back-transformed for DRS. The final model for unknown rhinitis triggers was ascertained with the Akaike information criterion [34]. The criterion for linearity for the logistic regression model and the condition for normally distributed residuals of the dependent variables in the linear regression model were both fulfilled. Cat, dog and HDM allergens were, therefore, used as continuous variables without log-transformation in the logistic and linear regression models. All models were formally tested for confounding and interaction. According to Hosmer and Lemeshow [35], only statistically significant interactions were included in the models. The results were reported as stratified analyses only when the final multivariate model included a significant interaction term. P -values ≤ 0.05 were considered significant. Statistical analyses were performed with Statistical Package for Social Sciences (SPSS version 14.0, SPSS Inc., Chicago, IL, USA). For the robust regression, Number Cruncher Statistical System (NCSS version 2007, Kaysville, UT, USA) was applied.

Results

Current rhinitis was found in 190/797 (23.8%) of the 10-year-old children. Boys had significantly more often current asthma, rhinitis and wheeze as well as BHR compared with the girls (Table 1). Also, the boys were significantly more often sensitized to perennial, seasonal and food allergens than the girls (Table 1).

Cat and dog allergen levels in mattress dust

The highest cat (Fel d 1) and dog (Can f 1) allergen levels were found in homes of current cat owners (18.2%) and dog owners (14.3%); GM (95% CI): 37.9 (26.3, 54.7) and 32.2 (26.1, 44.8) μg allergen/g dust, respectively (Fig. 1). In mattresses of children who owned cats (38/640, 5.9%) or dogs previously (41/672, 6.1%), the cat and dog allergen concentrations were significantly higher than for those who had never kept pets (Fig. 1). Cat and dog allergen concentrations were also significantly higher in the mattresses of children with regular contact with cats or dogs outside their home compared with children with no ownership or regular contact with these animals (both $P < 0.001$) (Fig. 1).

Girls tended to report cat ownership (21.1%) more often than boys (15.9%), $P = 0.06$, but girls and boys who did not keep cats at home, did not differ in reports on regular contact with cats *outside* home ($P = 0.4$) (Table 1). Boys and girls reported similar dog ownership (13.4% and 15.4%, respectively, $P = 0.4$), and contact with dogs outside home ($P = 0.9$). Nevertheless, the levels of both cat and dog allergens in mattress dust were significantly higher for girls compared with boys (Table 1). Girls compared with boys had significantly higher concentra-

tions of cat ($P = 0.003$) and dog ($P = 0.002$) allergens in their mattress dust if they did not have cats or dogs, respectively, at home (Table 1), as well as if they did have cats at home ($P = 0.001$). The dog allergen levels were on the other hand similar among boys and girls with dogs at home ($P = 0.34$).

Allergic sensitization and allergen exposure

The children sensitized to at least one inhalant allergen had significantly lower concentrations of cat allergen in mattress dust: GM (95% CI): 0.99 (0.77, 1.26) μg /g dust compared with non-sensitized children: 1.54 (1.27, 1.87), $P = 0.006$ ($P = 0.16$ adjusted for cat ownership). A significant difference was also found between dog allergen concentrations in mattress dust of sensitized children: GM (95% CI): 0.41 (0.32, 0.53) μg /g dust and non-sensitized children: 0.75 (0.62, 0.91), $P < 0.001$ ($P < 0.001$ adjusted for dog ownership) (Table 2).

HDM allergen (Der p 1) concentrations in the mattress dust samples were, in general, low and 87.7% of the samples had levels below the detection limit of the assay. Nevertheless, the Der p 1 allergen concentration in mattress dust of children sensitized to Der p (8.8%) was significantly higher than for children without Der p sensitization: GM (95% CI): 0.21 (0.16, 0.28) and 0.16 (0.15, 0.17) μg /g dust, respectively, $P = 0.004$.

Allergen exposure, current rhinitis and bronchial hyperresponsiveness

Among girls and boys with current rhinitis, boys were more often sensitized to inhalant allergens (83.9%) than girls (62.5%) ($P = 0.001$). However, there was no difference in the frequency of reporting conjunctivitis symptoms, which types of triggers that were related to their symptoms or the impact that the symptoms had on their daily life activities (all $P \geq 0.4$).

Children *with* current rhinitis had significantly less often pets at home and lower pet allergen concentrations compared with children *without* rhinitis [cat allergen: GM (95% CI): 0.97 (0.72, 1.29) and 1.46 (1.22, 1.74) μg /g dust, respectively, $P = 0.023$, and for dog allergen: 0.40 (0.30, 0.52) and 0.70 (0.58, 0.84) μg /g dust, respectively, $P = 0.002$] (Table 2).

In a multivariate logistic regression model for current rhinitis, gender interacted with asthma ($P = 0.020$) and HDM allergen exposure ($P = 0.049$). The adjusted odds ratio for current rhinitis in girls increased with 1.20 (95% CI: 1.01, 1.42) per 1 μg /g dust increase in Der p 1 allergen concentrations, $P = 0.037$, whereas no association was observed for boys ($P = 0.91$) (Table 3). Neither cat nor dog allergen concentrations were significantly associated with current rhinitis symptoms in the multivariate model.

Table 1. Characteristics and allergen levels in mattress dust (reported as µg allergen/g dust) of all included children and differences between boys and girls (percent or otherwise stated)

	All children (n = 797)	Girls (n = 360)	Boys (n = 437)	P-value (girls vs. boys)
Age [mean (min, max)]	10.6 (8.8, 12.3)	10.6 (8.8, 12.3)	10.6 (9.0, 12.3)	0.99
Current asthma	15.0	10.6	18.7	0.002
Current wheeze	13.6	9.8	16.8	0.004
Current rhinitis	23.8	20.1	27.1	0.021
DRS [GM (95% CI)]	1.37 (1.22–1.54)	1.12 (0.95–1.33)	1.61 (1.36–1.90)	0.003
Sensitization to at least one allergen	34.0	25.3	41.2	<0.001
Food allergens*	16.6	11.7	20.5	0.001
Seasonal allergens†	27.9	19.5	34.8	<0.001
Perennial allergens‡	23.7	16.4	29.7	<0.001
House dust mite allergens§	9.0	6.7	11.1	0.04
Cat allergen	12.8	8.6	16.2	0.001
Dog allergen	13.7	8.1	18.3	<0.001
Pet ownership and allergen exposure				
Dog ownership	14.3	15.4	13.4	0.4
Regular contact with dogs outside home	11.4	11.5	11.3	0.9
Dog allergen, all homes [GM (95% CI)]	0.61 (0.53, 0.72)	0.78 (0.62, 0.98)	0.50 (0.41, 0.62)	0.006
Dog allergen, homes without dogs [GM (95% CI)]¶	0.31 (0.27, 0.34)	0.37 (0.31, 0.44)	0.26 (0.23, 0.30)	0.002¶
Cat ownership	18.2	21.1	15.9	0.06
Regular contact with cats outside home	7.5	8.4	6.7	0.4
Cat allergen, all homes [GM (95% CI)]	1.32 (1.14, 1.54)	1.93 (1.50, 2.47)	0.97 (0.81, 1.17)	<0.001
Cat allergen in homes without cats [GM (95% CI)]**	0.62 (0.56, 0.69)	0.74 (0.63, 0.86)	0.55 (0.48, 0.62)	0.003¶
House dust mite allergen, Der p 1 [GM (95% CI)]	0.16 (0.15, 0.17)	0.16 (0.15, 0.17)	0.16 (0.15, 0.18)	0.6
Reported pet avoidance	33.7	31.4	35.6	0.2

*Egg white, milk, peanut and/or codfish.

†Pollens and/or moulds.

‡HDM, cat, dog, rabbit and/or cockroach.

§Der p and/or Der f.

¶Homes without dog, all (n = 671), girls (n = 297), boys (n = 374).

¶P < 0.001 for cat and P = 0.001 for dog allergen levels after adjustment for pet contact and ownership.

**Homes without cats, all (n = 640), girls (n = 276), boys (n = 364).

DRS, dose-response slope; GM, geometric mean; 95% CI, 95% confidence interval.

In a multivariate linear regression model with BHR (DRS) as the dependent variable, allergic sensitization interacted with dog allergen levels ($P = 0.004$). DRS decreased with 0.99 [regression coefficient (b) (95% CI: 0.98, 1.00), $P = 0.004$] per 1 µg/g dust increase in dog allergen concentrations, for children *with* allergic sensitization (Table 4). The association was not significant for children without allergic sensitization ($P = 0.25$).

HDM, cat and dog allergen concentrations in mattress dust were not associated with the impact that the rhinitis symptoms had on daily life activities (none/some vs. moderate/severe) (results not shown).

Cat and dog allergen exposure in relation to reported triggers of rhinitis

Children reporting at least one perceived rhinitis trigger ($n = 149$) reported mostly symptoms related to allergen exposure (97.3%), most often pollen (62.0%) or both pollen *and* furry pets (28.3%). Only a few of these children reported symptoms related to furry pets only (7.0%).

Children with unknown triggers ($n = 41$) were more likely to have symptoms throughout the year (55.6%) compared with those with perceived rhinitis triggers (24.6%), $P < 0.001$. The children with unknown triggers were also less likely to be sensitized for an allergen (34.1%) compared with those with perceived rhinitis triggers (87.2%), $P < 0.001$.

The children with unknown triggers of rhinitis had significantly higher concentrations of dog allergen in their mattress dust [GM (95% CI): 0.67 (0.37, 1.22) µg/g dust] compared with the children with perceived rhinitis triggers [0.34 (0.25, 0.46)], $P = 0.050$ (two-way ANOVA with adjustment for dog ownership). However, in the multivariate logistic regression model with indoor allergen levels, allergic sensitization and reported pet avoidance as explanatory variables, only Der p 1 allergen levels in interaction with pet avoidance were significant determinants of rhinitis with unknown triggers. The adjusted odds ratio for rhinitis with unknown triggers increased with 2.52 (95% CI: 1.26, 5.03) per 1 µg/g dust increase in Der p 1 allergen concentrations ($P = 0.01$) for the children *with* a reported pet avoidance, whereas no association was

observed for children *without* a reported pet avoidance ($P = 0.82$).

Discussion

In the present study, girls had higher levels of cat and dog allergens in mattress dust compared with boys, a differ-

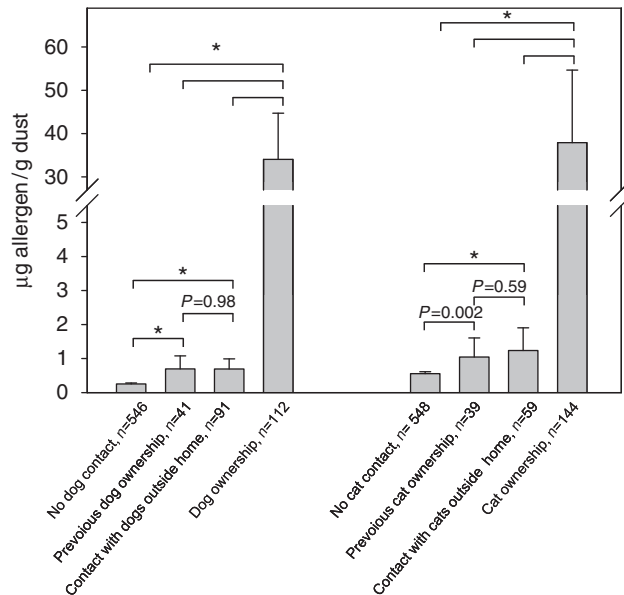


Fig. 1. Differences in dog allergen levels [geometric mean (bars) with 95% confidence interval] between children with no dog contact or ownership ever, previous dog ownership, contact with dogs outside home and current dog ownership; same for cat allergens. * $P < 0.001$.

ence that could not be explained by pet ownership alone. Children with rhinitis were less likely to keep pets and had lower levels of pet allergens in the mattresses than children without rhinitis. Although the HDM allergen, Der p 1, was detectable only in 12% of the dust samples, increasing Der p 1 levels were found to increase the risk of current rhinitis, but in girls only. Also, Der p 1 levels were associated with rhinitis in children who were unaware of their rhinitis trigger.

Higher cat and dog allergen levels in mattresses of girls compared with boys, also after adjustment for pet ownership have to our knowledge not been reported previously. In line with our previous study [8], a recent Swedish study reported more cat keeping among girls than boys [21], with a significant association between cat keeping and risk for current wheeze in girls only. These findings as well as those reported in the present paper may be due to a greater inclination among girls to be with and cuddle pets. Although not tested in the present study, a higher allergen level could be related to the tendency for girls to decorate their room with plush animals, fluffy pillows and carpets, which may act as reservoirs for the allergens, as suggested by others [36, 37]. Carpets on the bedroom floor were, in the present study, more often reported for girls than for boys (13.2% vs. 9.3%, respectively, $P = 0.08$). However, allergen reservoirs increase the amount of dust, and it is uncertain how this affects the allergen concentration in dust samples. Nevertheless, associations between allergic sensitization in young children and soft toys in their bed have been reported by others [38], albeit without describing allergen levels or gender-related differences.

Table 2. Association between cat and dog ownership and allergen levels for children with and without allergic sensitization and current rhinitis

		Cat ownership			Cat allergen		
		<i>n</i>	%	<i>P</i> -value	[GM (95% CI)]	<i>P</i> -value	<i>P</i> -value*
Inhalant sensitization [†]	No	523	20.5	0.02	1.54 (1.27, 1.87)	0.006	0.164
	Yes	269	13.8		0.99 (0.77, 1.26)		
Cat sensitization	No	690	19.0	0.1	1.34 (1.14, 1.58)	0.6	0.4
	Yes	102	12.7		1.18 (0.75, 1.86)		
Current rhinitis	No	21.3	21.3	<0.001	1.46 (1.22, 1.74)	0.023	0.4
	Yes	8.4	8.4		0.97 (0.72, 1.29)		
		Dog ownership			Dog allergen		
		<i>n</i>	%	<i>P</i> -value	[GM (95% CI)]	<i>P</i> -value	<i>P</i> -value*
Inhalant sensitization [†]	No	523	15.9	0.07	0.75 (0.62, 0.91)	<0.001	<0.001
	Yes	269	11.2		0.41 (0.32, 0.53)		
Dog sensitization	No	681	15.1	0.1	0.68 (0.57, 0.80)	0.001	0.002
	Yes	109	9.2		0.32 (0.22, 0.47)		
Current rhinitis	No	601	16.0	0.02	0.70 (0.58, 0.84)	0.002	0.068
	Yes	190	8.9		0.40 (0.30, 0.52)		

*Adjusted for cat or dog ownership.

[†]Any inhalant allergen. Significant variables are highlighted with bold text.

GM, geometric mean; 95% CI, 95% confidence interval.

Table 3. Variables associated with current rhinitis

Variables associated with current rhinitis	Boys (<i>n</i> = 467)		Girls (<i>n</i> = 360)	
	aOR (95% CI)	<i>P</i> -value	aOR (95% CI)	<i>P</i> -value
Allergic sensitization	13.36 (7.46, 23.92)	<0.001	8.70 (4.69, 16.13)	<0.001
Current asthma	2.76 (1.46, 5.22)	0.006	0.66 (0.26, 1.67)	0.38
HDM allergen (1 µg/g dust)	1.00 (0.94, 1.06)	0.91	1.20 (1.01, 1.42)	0.037
Reported pet avoidance	2.15 (1.24, 3.72)	0.002	8.70 (4.69, 16.13)	<0.001

Because of significant gender interaction with asthma ($P = 0.020$) and HDM allergen concentrations ($P = 0.049$), the results were reported separately for boys and girls.

aOR, odds ratio adjusted for the variables in the table. Cat and dog allergen concentrations were initially included in model, but were not significant determinants of current rhinitis in the final multivariate model.

Table 4. Robust linear regression analyses of determinants of DRS

Variables associated with increased DRS*	No allergic sensitization			Allergic sensitization		
	<i>b</i>	95% CI	<i>P</i> -value	<i>b</i>	SE	<i>P</i> -value
Intercept	0.12			0.55		
Dog allergen (1 µg/g dust)	1.00	(1.00, 1.00)	0.25	0.99	(0.98, 1.00)	0.004
Current asthma	1.26	(1.03, 1.53)	0.02	2.06	(1.58, 2.68)	<0.001
Current rhinitis	1.15	(0.94, 1.41)	0.18	1.26	(1.00, 1.59)	0.055
Reported pet avoidance	1.12	(0.97, 1.29)	0.12	1.19	(0.94, 1.50)	0.15

Because of significant interaction between allergic sensitization and dog allergen levels ($P = 0.004$), results were reported separately according to allergic sensitization (to any inhalant allergen).

*A higher DRS indicates more BHR.

b, regression coefficient; gender, HDM and cat allergen exposure were not significant determinants for DRS; DRS, dose-response slope; BHR, bronchial hyperresponsiveness; 95% CI, 95% confidence interval.

Children with regular contact with pets or who were previous pet owners had higher allergen levels in their mattress dust compared with children who had never kept pets, which is consistent with earlier reports [39–41]. These findings illustrate the importance of allergen contamination on the clothes of individuals without pets at home [36] and the difficulty in reducing the allergen load even after removing furry pets [42]. In areas where HDM infestation is uncommon, such as in Scandinavian countries, the allergen load is often dominated by allergens from cats and dogs [10, 13, 16]. However, few children who develop allergic sensitization against cat and dog allergens have kept cats and dogs at home [26, 43]. It has therefore been hypothesized that the indirect exposure at home due to transfer of allergens from clothes can cause the development of allergic sensitization, or alternatively these children become sensitized to cat and dog allergens due to allergen exposure in schools and day-care centres [9, 10, 44]. The presence of pet allergens in homes without pets and even more the presence of HDM allergen may render the patients unable to relate the allergen exposure to their symptoms. Thus, the higher dog allergen levels in mattress dust of children with unknown triggers of rhinitis

could possibly be the cause of their symptoms. This is also compatible with the finding that these children often had rhinitis symptoms throughout the year.

The children with current rhinitis at 10 years of age had lower pet allergen levels in their mattress dust compared with children without rhinitis, and increasing dog allergen levels were associated with reduced DRS (less BHR). Because BHR is also associated with rhinitis [3] in the present cohort [32], this may be related to less acquisition of pets in homes with children suffering from rhinitis, although *removal* of pets due to AR is variable [8].

The levels of Der p 1 in the present study were low, but are in line with previous reports from Norway [16, 45]. Nevertheless, the children with Der p sensitization had higher Der p 1 levels in mattress dust compared with children without sensitization, as has also been described previously in other Norwegian [16] and Swedish [14] study populations. The association between allergen levels and sensitization was observed regardless of gender, whereas the association between mattress dust levels of Der p 1 and current rhinitis was significant for girls only. The reason why girls, but not boys, should experience rhinitis symptoms due to HDM allergen exposure is

difficult to explain, but one possibility is that the effect of HDM allergen exposure on rhinitis symptoms for boys is masked by the strong association between asthma and rhinitis. A similar explanation may be proposed for the interaction between reported pet avoidance and Der p 1 allergen levels as a determinant for rhinitis with unknown triggers, with the effect of exposure to HDM allergen becoming more apparent [46] when the pet allergen levels are reduced due to active pet avoidance, as reported for the children in the present study [8]. Even if families with reported pet avoidance were likely to make efforts to reduce the overall allergen load (such as regular vacuuming of the mattresses), a reduction of the HDM allergen level has been found to be difficult [47]. Nevertheless, our findings point to the importance of HDM allergen-related symptoms, even for allergen levels that are much lower than those conventionally assumed to be important for disease development.

Strengths and limitations of the present study

A limitation of the present study is the sampling of dust by the parents rather than by fieldworkers as would have been ideal. Despite instructions in standardized procedures, the amount of sampled dust was found to depend on the power of the vacuum cleaners. It was for this reason not feasible to report allergen concentrations in $\mu\text{g}/\text{m}^2$, and $\mu\text{g}/\text{g}$ dust was used. The dust samples were sieved and the allergen concentrations were measured in the fine fraction of the dust. Allergens from cat and dog are found to mainly bind to particles that are part of the fine fraction of the dust [48], and the sieved dust is therefore believed to be representative for the airborne component of the sample. HDM allergens, on the other hand, are more often associated with mite feces that are usually larger particles and less likely to be airborne. However, in a previous study, Der p 1 allergens were found to be evenly distributed in the fine and coarse dust fractions [9], and previous reports from Norway have also reported few mattress dust samples with detectable HDM allergen levels [16, 45]. Therefore, the sieving of the dust samples is unlikely to have substantially reduced the quantity of HDM allergens that could be measured. The results of the multivariate models were reported by stratified analyses only when the formally tested interactions were significant. Thus, the reported results remain similar to the final multivariate models, but more easily available when presented as stratified analyses.

The rhinitis definition was based upon ISAAC questionnaires, but with no clinical examination of the nasal cavity. However, we included objective measures of airways inflammation such as exhaled nitric oxide, consistent with the rhinitis diagnosis in the same population (described in detail elsewhere) [49].

In conclusion, girls had higher concentrations of both cat and dog allergens in their mattresses compared with boys. This was not caused by pet ownership alone, but may be due to behavioural differences between the genders. Even in our population with HDM allergen detected in <13% of samples, exposure to low levels of HDM allergen was found to be associated with current rhinitis in girls and with rhinitis triggered by unknown factors in children with reported pet avoidance.

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Supporting Information

Additional supporting information may be found in the online version of this article:

Table S1. Characteristics of non-included ($n = 222$) and included children ($n = 797$) in the present study characteristics at 10 years of age or otherwise.

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Table S1: Characteristics of non-included (n=222) and included children (n=797) in the present study
Characteristics at 10 years of age or otherwise

	Non-included n=222 (%)	Included n=797 (%)	p-value
Gender (% boys)	51.1	54.8	0.33
First-born child	52.5	47.1	0.15
Parental asthma	14.5	18.9	0.14
Parental rhinoconjunctivitis	47.3	48.4	0.78
<i>Parental education reported at child's birth</i>			
- compulsory	3.8	4.6	
- college	44.3	35.4	
- university	51.9	60.0	0.11*
<i>Type of housing</i>			
- flat	22.4	77.6	
- detached or semi-detached house	22.1	77.9	0.92
<i>Income</i>			
< 350 000 NOK	22.8	13.7	
350 000 -750 000 NOK	49.8	55.8	
> 750 000 NOK	27.4	30.5	0.016*
Parental smoking (at home)	46.8	37.7	0.015
Dog at home	19.1	14.3	0.081
Cat at home	26.4	18.2	0.007
Other furry pets than cat or dog at home	20.9	17.3	0.22
Reported pet avoidance	28.0	33.7	0.11
Rhinitis last 12 months	29.1	23.9	0.12
Current asthma	17.9	15.0	0.31
DRS (GM(95%CI))	1.28 (1.03-1.59)	1.37 (1.22-1.54)	0.60**
Sensitized to any inhalant allergen	35.5	34.0	0.70

* p-value for linear-by-linear association. **ANOVA