

ORIGINAL ARTICLE

Effect of endotoxin and allergens on neonatal lung function and infancy respiratory symptoms and eczema

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Abstract

Background: Exposure to endotoxin and allergens in house dust has been found to be associated with childhood wheeze and asthma. Neonatal lung function is rarely examined in relation to this exposure.

Objectives: To assess the association between exposure to endotoxin, house dust mite and cat allergens and neonatal lung function, and respiratory symptoms and eczema in infancy.

Methods: In the Wheezing Illnesses Study Leidsche Rijn (WHISTLER) birth cohort study, levels of endotoxin, house dust mite allergens, and cat allergen have been measured in dust samples collected in the child's home. Lung function was measured before age 2 months, and respiratory symptoms and eczema were recorded in a daily diary during the first year of life. Associations of lung function (N = 302), respiratory symptoms (N = 361), and eczema (N = 342) with endotoxin and allergen levels have been studied by means of linear and logistic regression, respectively.

Results: Mattress dust endotoxin was associated with a significant increase in neonatal respiratory compliance [adjusted mean difference (95% confidence interval) 2.31 (0.33; 4.29) ml/kPa per interquartile range increase in exposure] and a non-significant decrease in neonatal airway resistance [0.32 (−0.77; 0.14) kPa/l/s]. There were no associations between allergen exposure and neonatal lung function and respiratory symptoms.

Conclusions: Environmental exposure to endotoxin may have an important role in the development of lung function.

The results of studies assessing the relationship between exposure to endotoxin and childhood asthma and related symptoms are inconsistent. A recent meta-analysis of the results of studies on the association of endotoxin exposure with wheeze and asthma in children reported a positive association between endotoxin concentrations and wheeze in infants and toddlers, whereas inverse association between exposure to house dust endotoxin and indicators of asthma were so far mainly reported for older (school aged) children (1).

Likewise, the results of studies assessing the relationship between cat allergen exposure and childhood asthma and related symptoms are inconsistent. Some studies reported (small) positive associations between exposure to cat allergen and wheeze (2) and persistent wheeze in children (3). Other studies did not find associations between cat allergen

exposure and bronchial hypersensitivity and asthma (4, 5) or reported negative associations with wheeze (6–8).

In the 1990s, Sporik et al. (9) reported a positive association between exposure to high levels of mite allergens in early childhood and increased risk of asthma development later in life. Later, several other studies reported positive associations between house dust mite allergen levels and allergic sensitization as well as the development of asthma and airway inflammation in preschool and school children in particular with allergic parents (3, 10). Much less is known about the role of mite allergen exposure and its effects during the early years of life.

Few studies so far have examined the association between exposure to house dust allergens and lung function, focusing on either (asthmatic) adults (11) or children aged 3 yr (12), and studies on house dust allergen exposure and infant respiratory

symptoms are scarce. No study so far has examined neonatal lung function in relation to house dust allergen and endotoxin exposures. However, there is some evidence for an impact of maternal prenatal allergen exposure on fetal responses from studies reporting positive, inverse U-shaped and U-shaped associations between maternal prenatal exposure to cat allergen, house dust mite allergens and endotoxin, respectively, and cord-blood IgE levels (13, 14). We therefore examined the association between neonatal lung function and respiratory symptoms and eczema during the first year of life in relation to exposure to house dust endotoxin, cat, and mite allergens as part of the Wheezing Illnesses Study Leidsche Rijn (WHISTLER) birth cohort study.

Materials and methods

Study design and population

The study is part of the WHISTLER birth cohort study investigating determinants for wheezing illnesses that has been described elsewhere (15). In brief, it is a single-center prospective birth cohort study based on a population sample of currently over 2500 healthy newborns from the Leidsche Rijn, a newly built suburb of the city of Utrecht, the Netherlands. Recruitment of infants in WHISTLER has started in December 2001, and participants were followed for respiratory events. Recruitment was carried out through birth registration records of the city council, which accordingly notified WHISTLER and 'Stichting Thuiszorg', the homecare foundation for the region. Within 14 days, the eligible families were asked to participate by telephone. Infants were excluded from the WHISTLER cohort if the gestational age was <36 wk, or if they had a major congenital abnormality or a neonatal respiratory disease. Initial recruitment for WHISTLER has started with a response rate of 75.6%.

Children in WHISTLER aged between 1 and 2 yr were considered eligible for the present study if their parents agreed to collect house dust samples. Around 70% of the contacted parents agreed to participate in dust sampling.

Dust collection and analysis

Dust samples were collected when the child was between 1 and 2 yr old. Samples were collected from three locations: the child's mattress, bedroom floor, and the living room floor. Sample collection took place in two periods and with different collection techniques, according to standardized similar protocols, which have been described elsewhere (16). Between 2005 and 2006, field workers collected dust samples in 419 households using ALK filters. Between 2007 and 2008, 108 participating parents collected dust samples in their houses using dust sampling socks. A comparison of the two collection methods has been published elsewhere (16). All samples were kept at -20°C until extraction.

Cat allergen (*Fel d1*) and house dust mite allergens *Dermatophagoides pteronyssinus* (*Der p1*) and *Dermatophagoides farinae* (*Der f1*) were measured in all dust samples. Endotoxins were measured in mattress dust only for budgetary reasons. Dust

samples were extracted and analyzed essentially as described earlier (17). In brief, first endotoxin and then the allergens were extracted. All aliquots were kept at -20°C until analysis. Endotoxin was measured using a kinetic chromogenic limulus amoebocyte lysate test. ALK filter extracts and sampling sock extracts were analyzed for allergens with an enzyme immunoassay from Indoor Biotechnologies (Cardiff, UK).

Allergen levels were expressed per gram of dust. Samples with non-detectable amounts of allergens were assigned a value of two-thirds of the lowest detectable value.

Outcome measures

Neonatal lung function, respiratory symptoms and eczema were the outcome variables for this study. Neonatal lung function was measured before the age of 2 months using a heated Lilly-type pneumotachometer (Hans Rudolph, Kansas City, MO, USA) recording passive respiratory mechanics (compliance and resistance). The pneumotachometer was attached to a facemask sealed to the infants face with therapeutic silicone putty. The measurement was taken in supine position during natural sleep, without the use of any sedation. The measurement of passive respiratory mechanics and its validation is published elsewhere (18–20). Intra- and interobserver variations were found to be low (19).

Respiratory symptoms, defined by cough, wheeze, and sputum production, were recorded by the mother on a daily basis in a diary form provided by the WHISTLER team every month. The number of symptomatic days recorded daily in the diaries was added up for the whole year. The 80th percentile was used as cut-off to define 'frequent wheeze', 'frequent cough', and 'frequent sputum production'. This cut-off value corresponded to 7 days of wheeze, 20 days of sputum production, and 94 days of cough. In addition, 'ever wheeze' (defined as >1 day of wheeze during the first year of life), an outcome widely used in other studies, was used as an outcome measure. Likewise, eczema was recorded by the mother in a diary. 'Ever eczema' was defined as >1 month with eczema during the first year of life.

Covariates

Information on covariates such as breastfeeding, smoking, and pet ownership was also collected through the diaries. Information about parental allergies and household characteristics was collected through questionnaires filled in by the mother during baseline examination. Parental education was defined as high if mother or father had achieved a higher vocational level or university level. Parental allergies were defined as allergy to pollen, house dust mite, or pets.

Statistical analysis

Linear regression was used to analyze the association between endotoxin and allergen exposure and the lung function variables compliance and resistance. Logistic regression was used to analyze the associations between endotoxin and allergen exposure and the diary-based outcomes. Endotoxin

concentrations were used as continuous exposure variables in regression analyses after natural-log (ln) transformation. As a substantial percentage of samples had non-detectable house dust mite allergen levels, mite allergen levels were categorized into three categories. Samples with levels below the limit of detection were defined as the reference category, and samples with detectable mite allergen were divided into two groups using the median of the detectable concentrations as a cut-off. Cat allergen concentrations were also divided into three categories. As the percentage of samples with non-detectable cat allergen levels was low, tertiles were used as cut-offs. The following potential confounders were included in the analysis: gender, birth weight, breastfeeding for at least 4 months, presence of older siblings, day-care attendance during the first year of the child's life, parental education, parental allergies, maternal smoking during pregnancy, presence of pets, use of natural gas for cooking, and season of dust collection. In analyses of the lung function variables, we additionally adjusted for the age height, and weight at the lung function measurement. Children with < 10 diaries, without any health and exposure information, and children with incomplete confounder data were excluded from the analyses. A total of 372 children (302 with neonatal lung function measurements and 361 with data on respiratory symptoms during the first year of life) were included in the final analysis. All statistical analyses were performed with the Statistical Analysis System (SAS version 9.2; Cary, NC, USA). Statistical significance was defined by a two-sided α -level of 5%.

Results

Characteristics of the 372 infants that were included in the present analyses and of the entire WHISTLER population are presented in Table 1. Approximately one-third of the study population had pets at home. Cats were the most common pets (26%); 68% of the mothers and 57% of the fathers had a high education, and 57% of the children had at least one allergic parent. Children who were included in the present analysis were significantly more often breastfed and had significantly more often allergic parents and significantly less often mothers who smoked during pregnancy compared to the entire WHISTLER cohort. Distribution of health outcomes is presented in Table 2. The mean respiratory compliance and resistance found in this population is comparable to an earlier analysis of these variables within the total WHISTLER cohort (19). The distribution of the total number of days recorded with symptoms during the whole year was right skewed (data not shown).

Table 3 shows the distribution of the endotoxin and allergen concentrations in the mattress dust samples. For all the allergens, concentrations on the child mattress were found to have the highest values, followed by those on the bedroom floor and the living room floor. The presence of cat allergen was widespread, also in homes without cats. Endotoxin and *Der f1* levels in mattress dust were significantly lower in spring compared to winter. No other statistically significant differences in endotoxin and allergen levels between seasons were found (data not shown).

Table 1 Characteristics of the population included in the analysis (N = 372) and the entire Wheezing Illnesses Study Leidsche Rijn cohort* (N = 1198)

Variable	Population included in analysis		Entire WHISTLER	
	N		N	
Male gender, %	49.2	372	50.1	1198
Birth weight (gr.), mean [s.d.]	3559 [508]	372	3511 [526]	1195
Breastfeeding >4 months, %	47.0	372	41.4	1025
At least one sibling at home, %	47.6	372	50.9	1195
Day-care attendance ever during the first year, %	74.2	372	73.0	984
High parental education, %	77.4	372	83.8	930
Allergic parents (to mite, pets or pollen), %				
Yes	57.0	372	44.0	1198
No	27.2	372	22.5	1198
Unknown	15.9	372	33.5	1198
Smoking by mother during pregnancy, %	4.6	372	7.0	1198
Pet at home (cats included), %	35.2	372	36.1	1198
Use of gas for cooking, %	26.6	372	n.a.	
Season of dust collection				
Winter (Jan-Mar)	29.6	372	n.a.	
Spring (Apr-Jun)	7.8	372	n.a.	
Summer (Jul-Sep)	30.6	372	n.a.	
Autumn (Oct-Dec)	32.0	372	n.a.	

*All children born during the same period, that is, between April 12, 2001 and October 15, 2006. n.a., not available/not applicable.

Table 4 shows crude and adjusted associations between endotoxin concentrations in the child's mattress dust, neonatal lung function, and respiratory symptoms during the first year of life. In crude and adjusted analyses, we found a statistically significant positive association between mattress dust endotoxin and compliance. A marginally statistically significant negative association between mattress dust endotoxin and airway resistance was found in crude, but not in adjusted analyses. There was no association between mattress endotoxin and respiratory symptoms during the first year of life. Table 5 shows adjusted associations between mattress dust levels of *Der p1*, *Der f1*, and *Fel d1*. Crude associations and associations with bedroom floor and living room floor levels are presented in Tables S1–S5 of the online data supplement. After adjustment for confounders, there was no association between mite and cat allergen levels in house dust and the health outcomes studied except for a decrease in frequent wheeze in children with high levels of *Der f1* in living room floor dust. Results for *Fel d1* did not change when we adjusted for 'pets other than cats' instead of 'any pets' (data not shown).

Table 2 Distribution of health outcomes

Variable		Total number
Neonatal lung function		
Respiratory compliance (ml/kPa), mean [range]	43.3 [14.8–86.6]	302
Airway resistance (kPa/l/s), mean [range]	7.5 [3.3–19.5]	302
Age at measurement (days), mean [range]	31.8 [10–63]	302
Length at measurement (cm), mean [range]	54.7 [48.5–60.6]	302
Weight at measurement (g), mean [range]	4396 [2970–5940]	302
Respiratory symptoms during 1st year of life		
Frequent wheeze, %	18.0	361
Ever wheeze, %	42.9	361
Frequent sputum production, %	20.5	361
Frequent cough, %	22.4	361
Eczema during 1st year of life		
Ever eczema, %	31.9	342

Table 3 Distribution of endotoxin and allergen concentrations in dust samples collected in the child's home

	N	GM (GSD)	%<LOD
Endotoxin (EU/mg dust)			
Mattress	367	10.7 (3.7)	0
<i>Der p1</i> (ng/g dust)			
Mattress	356	48.5 (6.7)	43.5
Child's bedroom floor	350	40.2 (3.8)	59.5
Living room floor	352	19.4 (4.8)	68.8
<i>Der f1</i> (ng/g dust)			
Mattress	341	71.0 (10.7)	12.6
Bedroom floor	324	23.5 (12.0)	36.9
Living room floor	331	6.1 (10.4)	52.4
<i>Fel d1</i> (ng/g dust)			
Mattress	350	199.8 (8.7)	3.7
Bedroom floor	329	90.2 (18.0)	18.0
Living room floor	318	61.4 (16.4)	16.9

LOD, limit of detection.

For 14% (50/356) of the participants, parents reported the use of asthma medication during the first year of life. This may have influenced the observed associations of endotoxin and allergen levels with respiratory symptoms. We therefore repeated our analysis without these 50 children. There was still no association between respiratory symptoms and the health outcomes studied (data not shown).

Discussion

In this study, we found inverse associations between mattress dust endotoxin and neonatal lung function (increasing

Table 4 Crude and adjusted associations *between endotoxin concentrations in the child's mattress dust, neonatal lung function, and respiratory symptoms and eczema during the first year of life

	Crude		Adjusted†	
	Beta	95% CI	Beta	95% CI
Lung function (N = 298)				
Compliance	2.44	0.45; 4.42	2.31	0.33; 4.29
Resistance	−0.31	−0.74; 0.13	−0.32	−0.77; 0.14
	OR	95% CI	OR	95% CI
Respiratory symptoms (N = 356)				
Frequent wheeze	0.93	0.61; 1.41	0.90	0.57; 1.41
Ever wheeze	1.00	0.73; 1.39	1.03	0.73; 1.46
Frequent sputum production	0.73	0.49; 1.09	0.71	0.46; 1.09
Frequent cough	1.17	0.80; 1.72	1.05	0.69; 1.60
Ever eczema (N = 340)				
	0.88	0.62; 1.25	0.75	0.48; 1.17

*Associations are presented for an interquartile range increase in ln-transformed endotoxin concentrations, which corresponds to a 7.7-fold increase on the original scale. †Adjusted for gender, birth weight, breastfeeding, presence of siblings, day-care attendance, parental education, parental allergies, maternal smoking during pregnancy, pets at home, gas cooking, and season of dust collection. Lung function was additionally adjusted for age, height, and weight at lung function measurements.

compliance and decreasing resistance with increasing exposure). There were no associations between cat and house dust mite allergen exposure and the health outcomes studied.

The population of this study was similar to the WHISTLER cohort it was recruited from with regard to gender, birth weight, siblings, day-care attendance, parental education, and pets at home. The relatively high level of parental education could possibly have led to avoidance measures taken by the parents in reducing dust exposure. Breastfeeding and parental allergies were more frequent in the study population; maternal smoking during pregnancy was less frequent in the study population compared to the WHISTLER cohort it was recruited from. This may limit the generalizability of the results to the rest of the population. In our study population, half of the children had at least one allergic parent. It has been shown that children of allergic parents might be less exposed to environmental risk factors (21).

A potential limitation of this study is that exposure was measured 1–12 months after the recording of the outcome measures of lung function and respiratory symptoms. However, several studies with repeated allergen measurements found that allergen levels were relatively stable over such time periods (22, 23). Moreover, there is some evidence that a single endotoxin measurement is a valid estimate of exposure for longer time periods (23–25).

Another limitation of this study may be the lack of data on allergic sensitization as it has been suggested that exposure to endotoxin is inversely associated with atopic wheeze and asthma, but not with non-atopic wheeze and asthma (26), and we were not able to distinguish atopic from non-atopic wheeze.

Table 5 Adjusted *associations between *Der p1*, *Der f1*, and *Fel d1* concentrations in the child's mattress dust and neonatal lung function and respiratory symptoms during the first year of life

	Medium vs. low†		High vs. low†	
	Beta	95% CI	Beta	95% CI
<i>Der p1</i>				
Lung function (N = 289)				
Compliance	2.31	−0.71; 5.34	0.52	−2.62; 3.65
Resistance	−0.12	−0.82; 0.58	−0.12	−0.84; 0.61
	OR	95% CI	OR	95% CI
Respiratory symptoms (N = 347)				
Frequent wheeze	1.33	0.66; 2.65	1.18	0.57; 2.45
Ever wheeze	0.97	0.56; 1.67	0.90	0.52; 1.56
Frequent sputum production	0.58	0.28; 1.19	1.09	0.57; 2.08
Frequent cough	0.57	0.29; 1.11	0.61	0.31; 1.20
Ever eczema (N = 328)	0.63	0.34; 1.17	0.73	0.40; 1.32
	Beta	95% CI	Beta	95% CI
<i>Der f1</i>				
Lung function (N = 273)				
Compliance	−3.12	−7.31; 1.07	−2.57	−6.92; 1.77
Resistance	0.85	−0.12; 1.81	0.34	−0.66; 1.34
	OR	95% CI	OR	95% CI
Respiratory symptoms (N = 331)				
Frequent wheeze	0.98	0.40; 2.42	1.10	0.42; 2.88
Ever wheeze	0.98	0.48; 2.02	1.06	0.50; 2.26
Frequent sputum production	0.71	0.30; 1.67	0.78	0.32; 1.91
Frequent cough	1.21	0.51; 2.88	1.06	0.42; 2.67
Ever eczema (N = 316)	0.50	0.23; 1.09	0.72	0.32; 1.62
	Beta	95% CI	Beta	95% CI
<i>Fel d1</i>				
Lung function (N = 283)				
Compliance	−0.60	−3.82; 2.63	−0.35	−4.08; 3.38
Resistance	−0.07	−0.81; 0.68	0.22	−0.64; 1.08
	OR	95% CI	OR	95% CI
Respiratory symptoms (N = 341)				
Frequent wheeze	0.54	0.26; 1.11	0.57	0.24; 1.34
Ever wheeze	0.69	0.40; 1.21	0.65	0.34; 1.24
Frequent sputum production	1.46	0.73; 2.92	0.98	0.42; 2.28
Frequent cough	1.08	0.55; 2.16	1.25	0.55; 2.86
Ever eczema (N = 322)	1.00	0.55; 1.84	1.09	0.52; 2.27

*Adjusted for gender, birth weight, breastfeeding, presence of siblings, day-care attendance, parental education, parental allergies, maternal smoking during pregnancy, pets at home, gas cooking, and season of dust collection. Lung function was additionally adjusted for age, height, and weight at lung function measurements. †Low, medium, and high exposure are defined as <LOD, LOD − 155.7 ng/g, and >155.7 ng/g for *Der p1*; <LOD, LOD − 121.0 ng/g, and >121.0 ng/g for *Der f1*; <67.3 ng/g; 67.3–389.9 ng/g; and >389.9 ng/g for *Fel d1*.

To the best of our knowledge, no study so far has examined the association between house dust allergen and endotoxin exposure and neonatal lung function. One study (12) examined lung function in children aged 3 yr in relation to allergen exposure. The authors found significant deficits in lung function in sensitized but not in non-sensitized children exposed to sensitizing allergens. In the present study, we were not able to investigate potential interactions between exposure and allergic sensitization because no information was available on allergic sensitization of the children.

Our findings of an inverse association between neonatal lung function and mattress dust endotoxin levels are interesting in view of the findings of other studies that investigated the association between endotoxin exposure and asthma and related symptoms in children. A recent meta-analysis of the results of 19 studies on the association of endotoxin exposure with wheeze and asthma in children reported a positive association between endotoxin concentrations per gram of dust sampled and wheeze in infants and toddlers [combined OR (95% CI) 1.48 (1.10–1.98)], whereas inverse association between exposure to house dust endotoxin and indicators of

asthma were so far mainly reported for older (school aged) children [combined OR (95% CI) 0.82 (0.67–0.97)] living in rural and non-rural environments (1). Differences in endotoxin levels between our study and the other studies on early life symptoms may explain part of this disagreement. However, given the fact that endotoxin levels in the present study were comparable to those in a study from New Zealand (27), lower than those in two American studies (28, 29), and higher than those in a German study (30), this is not very likely. Differences in outcome assessment may also explain part of the disagreement. In most of the other studies, annual or biannual retrospective questionnaires were used to define wheezing. Only in one study from Boston (28), wheeze has been recorded repeatedly during the first year of life (at age 1 and 2 months and every other month thereafter) similar to what has been done in our study. Finally, the characteristics of the study population and the selection criteria were different for the different studies; for example, in the Boston cohort (28), only infants of allergic parents were recruited. Another possible explanation for the inconsistency of our findings with the findings of other studies may be that house dust composition differs between countries. Microbial agents other than the ones measured in the present study, for instance, extracellular polysaccharides, fungal $\beta(1,3)$ -glucans, and muramic acid, which have been found to be associated with asthma (31) and (atopic) wheeze (31, 32), may mediate immunologic effects similar to the effect of endotoxin. Nevertheless, if confirmed by other studies, a potential inverse association between neonatal lung function and mattress dust endotoxin may have far-reaching consequences as low lung function at birth has been shown to be a major risk factor for low lung function in later life (33, 34).

Endotoxins are cell-wall components of the outer membrane of gram-negative bacteria. They are considered to be a marker for the hygienic level (35, 36). The inverse association between neonatal lung function and endotoxin levels could be a further support of the so-called hygiene hypothesis, suggesting that hygiene standards in modern societies may be partly responsible for the increase in atopic disease (37). However, it is too early to draw definitive conclusions from our findings for the development of asthma and allergies. Further study is needed when the children are older.

The exact mechanisms behind the association between endotoxin exposure and neonatal lung function are not clear. It has been hypothesized that the development of an atopic immune response starts during fetal life (38). Allergen-specific T cells have been detected at birth, suggesting that prenatal allergen exposure affects the development of the immune system (39, 40). Moreover, there is some evidence for an impact of maternal prenatal allergen exposure on fetal responses from studies reporting associations between maternal prenatal exposure to cat allergen, house dust mite allergens and endotoxin, and cord-blood IgE levels (13, 14). The presence of allergens in amniotic fluid has been proposed as a possible mechanism (39–41).

Studies on the effects of house dust mite allergens on respiratory symptoms during the first years of life are scarce. During the last decade, however, several prospective studies

published on the association between exposure to house dust mite allergens and asthma and allergies in preschool and schoolchildren. None of these studies reported a direct association between house dust mite allergen exposure and symptoms of asthma. In the AMICS study, there was no association between *Der p1* levels in living room floor dust at age 3 months and wheeze and asthma until age 6 yr (42). In the CAS study, there was no association between *Der p1* and *Der f1* levels and asthma and bronchial hyper-responsiveness at the age of 6–7 yr (43). In another study, no association was found between house dust mite allergen exposure and wheeze (5). In the MAS study, no direct association was found between house dust mite exposure and asthma, wheeze, and bronchial hyper-responsiveness at the age of 5 yr (44). Similar results were reported from the CAPPS study, where no association was found between house dust mite exposure and asthma at age 7 yr (45). In the PIAMA study, a temporary positive association between house dust mite allergen exposure at the age of 3 months and later asthma symptoms was found for children with the highest exposure to house dust mite allergens (46). The lack of an association between house dust mite allergen exposure and respiratory symptoms in the present study is thus in agreement with the findings of other prospective studies. House dust mite levels in the present study were much lower than levels reported from previous Dutch studies and slightly lower than those found in the 1996–98 period in the Dutch PIAMA study (47).

Likewise, studies on the effects of cat allergens on respiratory symptoms during the first years of life are scarce. Findings of prospective cohort studies on the association between cat allergen exposure and symptoms of asthma are not consistent. The AMICS and PIAMA studies reported (small) positive associations between cat allergen exposure and asthma-related symptoms such as wheeze (2) and persistent wheeze (3) in children aged up to 4 yr. In the AMICS study, the small effect of cat allergen exposure on wheeze was found to vary with age (2) with no effect for the first year of life, which is in agreement with the findings of the present study. No association was found between cat allergen exposure and the development of asthma until age 7 yr in the prospective MAS study (4). Another study reported a decreased risk of wheeze at age 5 yr among children with high levels of *Fel d1* exposure (5).

We conclude from our results that environmental exposure to endotoxin may have an important role in the development of lung function.

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Supporting Information

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

Table S1. Crude associations between *Der p1* concentrations in the child's mattress, bedroom floor and living room floor dust and neonatal lung function and respiratory symptoms during the first year of life.

Table S2. Crude associations between *Der f1* concentrations in the child's mattress, bedroom floor and living room floor dust and neonatal lung function and respiratory symptoms during the first year of life.

Table S3. Crude associations between *Fel d1* concentrations in the child's mattress, bedroom floor and living room

floor dust and neonatal lung function and respiratory symptoms during the first year of life.

Table S4. Adjusted *associations between *Der p1* and *Der f1* concentrations in the child's bedroom floor and living room floor dust and neonatal lung function and respiratory symptoms during the first year of life.

Table S5. Adjusted *associations between *Fel d1* concentrations in the child's bedroom floor and living room floor dust and neonatal lung function and respiratory symptoms during the first year of life.

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**Endotoxin and allergens, neonatal lung function and infancy respiratory
symptoms and eczema**

Online Supplement

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Table 1. Crude associations between *Der p 1* concentrations in the child's mattress, bedroom floor and living room floor dust and neonatal lung function and respiratory symptoms during the first year of life.

			Medium vs low*		High vs low*	
Mattress						
Lung function (N=289)		beta	(95% CI)	beta	(95% CI)	
Compliance		0.43	(-2.72;3.58)	-0.06	(-3.31;3.18)	
Resistance		-0.04	(-0.71;0.63)	0.07	(-0.62;0.76)	
Respiratory (N=347)	symptoms	OR	(95% CI)	OR	(95% CI)	
Frequent wheeze		1.21	(0.63;2.31)	0.93	(0.47;1.84)	
Ever wheeze		0.93	(0.56;1.54)	0.80	(0.48;1.34)	
Frequent sputum production		0.54	(0.27;1.07)	1.01	(0.55;1.84)	
Frequent cough		0.55	(0.30;1.03)	0.52	(0.28;0.98)	
Eczema ever (N = 328)		0.67	(0.38; 1.20)	0.80	(0.46; 1.39)	
Bedroom floor						
Lung function (N=285)		beta	(95% CI)	beta	(95% CI)	
Compliance		-3.31	(-6.58;-0.04)	-1.89	(-5.22;1.44)	
Resistance		-0.07	(-0.77;0.64)	0.13	(-0.59;0.85)	
Respiratory (N=339)	symptoms	OR	(95% CI)	OR	(95% CI)	
Frequent wheeze		0.87	(0.43;1.78)	0.62	(0.28;1.36)	
Ever wheeze		0.61	(0.35;1.07)	0.57	(0.32;1.01)	
Frequent sputum production		0.85	(0.43;1.70)	0.77	(0.38;1.57)	
Frequent cough		0.71	(0.35;1.44)	1.02	(0.53;1.95)	
Eczema ever (N = 321)		0.58	(0.30; 1.12)	0.53	(0.28; 1.00)	
Living room floor						
Lung function (N=286)		beta	(95% CI)	beta	(95% CI)	
Compliance		0.41	(-3.22;4.03)	-0.50	(-4.30;3.29)	
Resistance		-0.21	(-0.95;0.53)	0.41	(-0.37;1.18)	
Respiratory (N=343)	symptoms	OR	(95% CI)	OR	(95% CI)	
Frequent wheeze		1.34	(0.62;2.92)	2.28	(1.13;4.57)	
Ever wheeze		0.80	(0.43;1.48)	1.10	(0.60;1.99)	
Frequent sputum production		1.12	(0.55;2.30)	0.78	(0.36;1.72)	
Frequent cough		1.38	(0.69;2.74)	1.38	(0.69;2.74)	
Eczema ever (N = 325)		0.97	(0.50; 1.87)	0.85	(0.43; 1.68)	

*low, medium and high exposure are defined as < LOD, LOD – 155.7 ng/g, and >155.7 ng/g for mattress; < LOD, LOD – 147.9 ng/g, and >147.9 ng/g for bedroom floor; < LOD, LOD –171.7 ng/g, and >171.7 ng/g for living room floor

Table 2. Crude associations between *Der f* 1 concentrations in the child's mattress, bedroom floor and living room floor dust and neonatal lung function and respiratory symptoms during the first year of life.

			Medium vs low*		High vs low*	
Mattress						
Lung function (N=273)			beta	(95% CI)	beta	(95% CI)
Compliance			-	(-3.27; 7.68;1.13)	-2.13	(-6.56;2.29)
Resistance			0.70	(-0.25;1.64)	0.37	(-0.58;1.32)
Respiratory symptoms (N=331)			OR	(95% CI)	OR	(95% CI)
Frequent wheeze			0.79	(0.34;1.86)	0.76	(0.32;1.78)
Ever wheeze			0.87	(0.44;1.72)	0.85	(0.43;1.68)
Frequent sputum production			0.67	(0.30;1.50)	0.77	(0.35;1.69)
Frequent cough			1.02	(0.46;2.28)	0.91	(0.40;2.04)
Eczema ever (N = 316)			0.47	(0.22; 0.97)	0.80	(0.39; 1.63)
Bedroom floor						
Lung function (N=265)			beta	(95% CI)	beta	(95% CI)
Compliance			-	(-2.02; 5.23;1.18)	-2.44	(-5.68;0.80)
Resistance			-	(-1.55;-0.89; 0.22)	-0.10	(-0.77;0.57)
Respiratory symptoms (N=314)			OR	(95% CI)	OR	(95% CI)
Frequent wheeze			0.65	(0.32;1.30)	0.79	(0.40;1.56)
Ever wheeze			0.69	(0.40;1.18)	0.91	(0.53;1.57)
Frequent sputum production			0.83	(0.44;1.59)	0.77	(0.40;1.49)
Frequent cough			0.77	(0.41;1.45)	0.81	(0.43;1.54)
Eczema ever (N = 296)			0.99	(0.55; 1.79)	1.11	(0.62; 1.99)
Living room floor						
Lung function (N=268)			beta	(95% CI)	beta	(95% CI)
Compliance			-	(-0.98; 4.22;2.25)	1.92	(-1.37;5.20)
Resistance			-	(-0.45; 1.14;0.23)	-0.12	(-0.82;0.58)
Respiratory symptoms (N=321)			OR	(95% CI)	OR	(95% CI)
Frequent wheeze			0.66	(0.32;1.35)	0.41	(0.18;0.92)
Ever wheeze			1.18	(0.68;2.03)	0.70	(0.40;1.23)
Frequent sputum production			0.78	(0.39;1.57)	0.84	(0.42;1.67)
Frequent cough			1.05	(0.55;2.02)	1.20	(0.64;2.26)
Eczema ever (N = 306)			0.96	(0.53; 1.74)	0.88	(0.49; 1.60)

*low, medium and high exposure are defined as < LOD, LOD – 121.0 ng/g, and >121.0 ng/g for mattress; < LOD, LOD – 85.7 ng/g, and > 85.7 ng/g for bedroom floor; < LOD, LOD – 59.2 ng/g, and > 59.2 ng/g for living room floor

Table 3. Crude associations between *Fel d 1* concentrations in the child's mattress, bedroom floor and living room floor dust and neonatal lung function and respiratory symptoms during the first year of life.

		Medium vs low*		High vs low*	
Mattress					
Lung function (N=283)		beta	(95% CI)	beta	(95% CI)
Compliance		-	(- 0.09; 3.40;3.21)	-0.29	(-3.47;2.89)
Resistance		0.06	(- 0.66;0.77)	0.31	(-0.37;0.99)
Respiratory (N=341)	symptoms	OR	(95% CI)	OR	(95% CI)
Frequent wheeze		0.55	(0.28;1.09)	0.57	(0.29;1.11)
Ever wheeze		0.67	(0.39;1.13)	0.63	(0.37;1.07)
Frequent sputum production		1.55	(0.80;2.99)	1.20	(0.61;2.35)
Frequent cough		0.99	(0.53;1.87)	1.05	(0.56;1.96)
Eczema ever (N = 322)		1.04	(0.59; 1.84)	0.83	(0.47; 1.47)
Bedroom floor					
Lung function (N=270)		beta	(95% CI)	beta	(95% CI)
Compliance		-	(- 0.04; 3.39;3.31)	-0.63	(-3.87;2.61)
Resistance		0.06	(- 0.64;0.77)	0.08	(-0.61;0.76)
Respiratory (N=319)	symptoms	OR	(95% CI)	OR	(95% CI)
Frequent wheeze		0.91	(0.46;1.79)	0.44	(0.20;0.97)
Ever wheeze		0.70	(0.41;1.21)	0.56	(0.32;0.97)
Frequent sputum production		1.37	(0.70;2.69)	0.94	(0.46;1.90)
Frequent cough		0.56	(0.29;1.08)	0.86	(0.47;1.60)
Eczema ever (N = 304)		1.35	(0.75; 2.42)	0.95	(0.52; 1.75)
Living room floor					
Lung function (N=256)		beta	(95% CI)	beta	(95% CI)
Compliance		1.17	(- 2.23;4.57)	0.15	(-3.12;3.41)
Resistance		-	(- 0.05; 0.76;0.67)	0.45	(-0.24;1.14)
Respiratory (N=311)	symptoms	OR	(95% CI)	OR	(95% CI)
Frequent wheeze		0.72	(0.35;1.47)	0.84	(0.42;1.68)
Ever wheeze		1.04	(0.60;1.80)	0.80	(0.46;1.39)
Frequent sputum production		0.79	(0.40;1.55)	0.96	(0.49;1.85)
Frequent cough		0.84	(0.44;1.63)	1.18	(0.63;2.23)
Eczema ever (N = 294)		1.85	(1.02; 3.34)	0.82	(0.44; 1.54)

*low, medium and high exposure are defined as < 68.0 ng/g; 68.0-389.9 ng/g; and > 389.9 ng/g for mattress; < 36.2 ng/g; 36.2-304.7 ng/g; and > 304.7 ng/g for bedroom floor; < 18.2 ng/g; 18.2-145.6 ng/g; and > 145.6 ng/g for living room floor

Table 4. Adjusted *associations between *Der p1* and *Der f 1* concentrations in the child's bedroom floor and living room floor dust and neonatal lung function and respiratory symptoms during the first year of life.

	Der p1				Der f1				
	Medium vs low†		High vs low†		Medium vs low‡		High vs low‡		
Bedroom floor									
Lung function (N=285 for Der p1, 265 for Der f1)	beta	(95% CI)	beta	(95% CI)	beta	(95% CI)	beta	(95% CI)	
Compliance	-1.55	(-4.72;1.61)	-0.82	(-4.01;2.37)	-2.05	(-5.05;0.94)	-1.15	(-4.28;1.97)	
Resistance	-0.06	(-0.79;0.67)	0.05	(-0.69;0.78)	-0.78	(-1.46;-0.09)	-0.10	(-0.81;0.62)	
Respiratory symptoms (N=339 for Der p1, 314 for Der f1)	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)	
Frequent wheeze	0.87	(0.41;1.85)	0.73	(0.33;1.64)	0.61	(0.29;1.28)	0.93	(0.45;1.95)	
Ever wheeze	0.58	(0.32;1.04)	0.58	(0.32;1.05)	0.74	(0.42;1.30)	1.09	(0.61;1.94)	
Frequent sputum production	0.81	(0.39;1.67)	0.78	(0.38;1.62)	0.94	(0.47;1.86)	0.92	(0.45;1.88)	
Frequent cough	0.59	(0.28;1.25)	1.08	(0.54;2.16)	0.83	(0.42;1.65)	0.94	(0.47;1.87)	
Eczema ever (N = 321 for Der p1, 295 for Der f1)	0.60	(0.30; 1.20)	0.51	(0.26; 1.00)	0.98	(0.53; 1.83)	0.93	(0.50; 1.75)	
Living room floor									
Lung function (N=286 for Der p1, 268 for Der f1)	beta	(95% CI)	beta	(95% CI)	beta	(95% CI)	beta	(95% CI)	
Compliance	0.67	(-2.89;4.22)	0.84	(-2.78;4.45)	-0.80	(-3.85;2.25)	2.65	(-0.52;5.82)	
Resistance	-0.07	(-0.84;0.71)	0.18	(-0.61;0.97)	-0.47	(-1.16;0.22)	-0.27	(-0.99;0.45)	
Respiratory symptoms (N=343 for Der p1, 321 for Der f1)	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)	
Frequent wheeze	1.19	(0.52;2.69)	1.95	(0.93;4.08)	0.69	(0.32;1.48)	0.40	(0.17;0.95)	
Ever wheeze	0.78	(0.40;1.49)	1.02	(0.54;1.91)	1.18	(0.66;2.09)	0.75	(0.41;1.34)	
Frequent sputum production	1.21	(0.56;2.60)	0.79	(0.35;1.80)	0.77	(0.37;1.62)	0.98	(0.46;2.05)	
Frequent cough	1.29	(0.61;2.71)	1.49	(0.70;3.16)	1.10	(0.55;2.22)	1.41	(0.70;2.85)	
Eczema ever (N = 325 for Der p1, 306 for Der p1)	0.88	(0.43; 1.80)	0.64	(0.31; 1.31)	0.91	(0.48; 1.72)	0.80	(0.42; 1.51)	

*adjusted for gender, birth weight, breastfeeding, presence of siblings, day-care attendance, parental education, parental allergies, maternal smoking during pregnancy, pets at home, gas cooking, and season of dust collection. Lung function was additionally adjusted for age at lung function measurements.

†low, medium and high exposure are defined as < LOD, LOD – 147.9 ng/g, and >147.9 ng/g for bedroom floor; < LOD, LOD –171.7 ng/g, and >171.7 ng/g for living room floor

‡low, medium and high exposure are defined as < LOD, LOD – 85.7 ng/g, and > 85.7 ng/g for bedroom floor; < LOD, LOD – 59.2 ng/g, and > 59.2 ng/g for living room floor

Table 5. Adjusted *associations between *Fel d 1* concentrations in the child's bedroom floor and living room floor dust and neonatal lung function and respiratory symptoms during the first year of life.

		Medium vs low†		High vs low†	
Bedroom floor					
Lung function (N=270)		beta	(95% CI)	beta	(95% CI)
Compliance		0.89	(-2.33;4.11)	0.62	(-3.11;4.36)
Resistance		0.15	(-0.59;0.88)	0.29	(-0.56;1.14)
Respiratory	symptoms	OR	(95% CI)	OR	(95% CI)
(N=319)					
Frequent wheeze		0.84	(0.40;1.77)	0.56	(0.20;1.53)
Ever wheeze		0.74	(0.41;1.33)	0.63	(0.31;1.28)
Frequent sputum production		1.68	(0.81;3.46)	0.98	(0.40;2.44)
Frequent cough		0.52	(0.25;1.07)	1.03	(0.44;2.42)
Eczema ever (N = 304)		1.58	(0.83; 3.02)	1.35	(0.61; 2.98)
Living room floor					
Lung function (N=256)		beta	(95% CI)	beta	(95% CI)
Compliance		1.56	(-1.76;4.89)	0.75	(-2.81;4.30)
Resistance		-0.14	(-0.87;0.58)	0.64	(-0.13;1.42)
Respiratory	symptoms	OR	(95% CI)	OR	(95% CI)
(N=311)					
Frequent wheeze		0.70	(0.33;1.50)	1.10	(0.47;2.59)
Ever wheeze		1.13	(0.63;2.03)	0.83	(0.43;1.62)
Frequent sputum production		0.78	(0.38;1.59)	0.92	(0.41;2.08)
Frequent cough		0.89	(0.43;1.84)	1.25	(0.55;2.86)
Eczema ever (N = 294)		1.85	(0.98; 3.48)	0.91	(0.43; 1.96)

*adjusted for gender, birth weight, breastfeeding, presence of siblings, day-care attendance, parental education, parental allergies, maternal smoking during pregnancy, ETS exposure at home, pets at home, gas cooking, and season of dust collection. Lung function was additionally adjusted for age at lung function measurements.

†low, medium and high exposure are defined as < 36.2 ng/g; 36.2-304.7 ng/g; and > 304.7 ng/g for bedroom floor; < 18.2 ng/g; 18.2-145.6 ng/g; and > 145.6 ng/g for living room floor

**Endotoxin and allergens, neonatal lung function and infancy respiratory
symptoms and eczema**

Online Supplement

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Table 1. Crude associations between *Der p* 1 concentrations in the child's mattress, bedroom floor and living room floor dust and neonatal lung function and respiratory symptoms during the first year of life.

	Medium vs low ¹		High vs low ¹	
Mattress				
Lung function (N=289)	beta	(95% CI)	beta	(95% CI)
Compliance	0.43	(-2.72;3.58)	-0.06	(-3.31;3.18)
Resistance	-0.04	(-0.71;0.63)	0.07	(-0.62;0.76)
Respiratory symptoms (N=347)	OR	(95% CI)	OR	(95% CI)
Frequent wheeze	1.21	(0.63;2.31)	0.93	(0.47;1.84)
Ever wheeze	0.93	(0.56;1.54)	0.80	(0.48;1.34)
Frequent sputum production	0.54	(0.27;1.07)	1.01	(0.55;1.84)
Frequent cough	0.55	(0.30;1.03)	0.52	(0.28;0.98)
<u>Eczema ever (N = 328)</u>	<u>0.67</u>	<u>(0.38; 1.20)</u>	<u>0.80</u>	<u>(0.46; 1.39)</u>
Bedroom floor				
Lung function (N=285)	beta	(95% CI)	beta	(95% CI)
Compliance	-3.31	(-6.58;-0.04)	-1.89	(-5.22;1.44)
Resistance	-0.07	(-0.77;0.64)	0.13	(-0.59;0.85)
Respiratory symptoms (N=339)	OR	(95% CI)	OR	(95% CI)
Frequent wheeze	0.87	(0.43;1.78)	0.62	(0.28;1.36)
Ever wheeze	0.61	(0.35;1.07)	0.57	(0.32;1.01)
Frequent sputum production	0.85	(0.43;1.70)	0.77	(0.38;1.57)
Frequent cough	0.71	(0.35;1.44)	1.02	(0.53;1.95)
<u>Eczema ever (N = 321)</u>	<u>0.58</u>	<u>(0.30; 1.12)</u>	<u>0.53</u>	<u>(0.28; 1.00)</u>
Living room floor				
Lung function (N=286)	beta	(95% CI)	beta	(95% CI)
Compliance	0.41	(-3.22;4.03)	-0.50	(-4.30;3.29)
Resistance	-0.21	(-0.95;0.53)	0.41	(-0.37;1.18)
Respiratory symptoms (N=343)	OR	(95% CI)	OR	(95% CI)
Frequent wheeze	1.34	(0.62;2.92)	2.28	(1.13;4.57)
Ever wheeze	0.80	(0.43;1.48)	1.10	(0.60;1.99)
Frequent sputum production	1.12	(0.55;2.30)	0.78	(0.36;1.72)
Frequent cough	1.38	(0.69;2.74)	1.38	(0.69;2.74)
<u>Eczema ever (N = 325)</u>	<u>0.97</u>	<u>(0.50; 1.87)</u>	<u>0.85</u>	<u>(0.43; 1.68)</u>

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¹ low, medium and high exposure are defined as < LOD, LOD – 155.7 ng/g, and >155.7 ng/g for mattress; < LOD, LOD – 147.9 ng/g, and >147.9 ng/g for bedroom floor; < LOD, LOD –171.7 ng/g, and >171.7 ng/g for living room floor

Table 2. Crude associations between *Der f* 1 concentrations in the child's mattress, bedroom floor and living room floor dust and neonatal lung function and respiratory symptoms during the first year of life.

	Medium vs low ¹		High vs low ¹	
Mattress				
Lung function (N=273)	beta	(95% CI)	beta	(95% CI)
Compliance	-3.27	(-7.68;1.13)	-2.13	(-6.56;2.29)
Resistance	0.70	(-0.25;1.64)	0.37	(-0.58;1.32)
Respiratory symptoms (N=331)	OR	(95% CI)	OR	(95% CI)
Frequent wheeze	0.79	(0.34;1.86)	0.76	(0.32;1.78)
Ever wheeze	0.87	(0.44;1.72)	0.85	(0.43;1.68)
Frequent sputum production	0.67	(0.30;1.50)	0.77	(0.35;1.69)
Frequent cough	1.02	(0.46;2.28)	0.91	(0.40;2.04)
<u>Eczema ever (N = 316)</u>	<u>0.47</u>	<u>(0.22; 0.97)</u>	<u>0.80</u>	<u>(0.39; 1.63)</u>
Bedroom floor				
Lung function (N=265)	beta	(95% CI)	beta	(95% CI)
Compliance	-2.02	(-5.23;1.18)	-2.44	(-5.68;0.80)
Resistance	-0.89	(-1.55;-0.22)	-0.10	(-0.77;0.57)
Respiratory symptoms (N=314)	OR	(95% CI)	OR	(95% CI)
Frequent wheeze	0.65	(0.32;1.30)	0.79	(0.40;1.56)
Ever wheeze	0.69	(0.40;1.18)	0.91	(0.53;1.57)
Frequent sputum production	0.83	(0.44;1.59)	0.77	(0.40;1.49)
Frequent cough	0.77	(0.41;1.45)	0.81	(0.43;1.54)
<u>Eczema ever (N = 296)</u>	<u>0.99</u>	<u>(0.55; 1.79)</u>	<u>1.11</u>	<u>(0.62; 1.99)</u>
Living room floor				
Lung function (N=268)	beta	(95% CI)	beta	(95% CI)
Compliance	-0.98	(-4.22;2.25)	1.92	(-1.37;5.20)
Resistance	-0.45	(-1.14;0.23)	-0.12	(-0.82;0.58)
Respiratory symptoms (N=321)	OR	(95% CI)	OR	(95% CI)
Frequent wheeze	0.66	(0.32;1.35)	0.41	(0.18;0.92)
Ever wheeze	1.18	(0.68;2.03)	0.70	(0.40;1.23)
Frequent sputum production	0.78	(0.39;1.57)	0.84	(0.42;1.67)
Frequent cough	1.05	(0.55;2.02)	1.20	(0.64;2.26)
<u>Eczema ever (N = 306)</u>	<u>0.96</u>	<u>(0.53; 1.74)</u>	<u>0.88</u>	<u>(0.49; 1.60)</u>

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¹ low, medium and high exposure are defined as < LOD, LOD – 121.0 ng/g, and >121.0 ng/g for mattress; < LOD, LOD – 85.7 ng/g, and > 85.7 ng/g for bedroom floor; < LOD, LOD – 59.2 ng/g, and > 59.2 ng/g for living room floor

Table 3. Crude associations between *Fel d 1* concentrations in the child's mattress, bedroom floor and living room floor dust and neonatal lung function and respiratory symptoms during the first year of life.

	Medium vs low ¹		High vs low ¹	
Mattress				
Lung function (N=283)	beta	(95% CI)	beta	(95% CI)
Compliance	-0.09	(-3.40;3.21)	-0.29	(-3.47;2.89)
Resistance	0.06	(-0.66;0.77)	0.31	(-0.37;0.99)
Respiratory symptoms (N=341)	OR	(95% CI)	OR	(95% CI)
Frequent wheeze	0.55	(0.28;1.09)	0.57	(0.29;1.11)
Ever wheeze	0.67	(0.39;1.13)	0.63	(0.37;1.07)
Frequent sputum production	1.55	(0.80;2.99)	1.20	(0.61;2.35)
Frequent cough	0.99	(0.53;1.87)	1.05	(0.56;1.96)
<u>Eczema ever (N = 322)</u>	<u>1.04</u>	<u>(0.59; 1.84)</u>	<u>0.83</u>	<u>(0.47; 1.47)</u>
Bedroom floor				
Lung function (N=270)	beta	(95% CI)	beta	(95% CI)
Compliance	-0.04	(-3.39;3.31)	-0.63	(-3.87;2.61)
Resistance	0.06	(-0.64;0.77)	0.08	(-0.61;0.76)
Respiratory symptoms (N=319)	OR	(95% CI)	OR	(95% CI)
Frequent wheeze	0.91	(0.46;1.79)	0.44	(0.20;0.97)
Ever wheeze	0.70	(0.41;1.21)	0.56	(0.32;0.97)
Frequent sputum production	1.37	(0.70;2.69)	0.94	(0.46;1.90)
Frequent cough	0.56	(0.29;1.08)	0.86	(0.47;1.60)
<u>Eczema ever (N = 304)</u>	<u>1.35</u>	<u>(0.75; 2.42)</u>	<u>0.95</u>	<u>(0.52; 1.75)</u>
Living room floor				
Lung function (N=256)	beta	(95% CI)	beta	(95% CI)
Compliance	1.17	(-2.23;4.57)	0.15	(-3.12;3.41)
Resistance	-0.05	(-0.76;0.67)	0.45	(-0.24;1.14)
Respiratory symptoms (N=311)	OR	(95% CI)	OR	(95% CI)
Frequent wheeze	0.72	(0.35;1.47)	0.84	(0.42;1.68)
Ever wheeze	1.04	(0.60;1.80)	0.80	(0.46;1.39)
Frequent sputum production	0.79	(0.40;1.55)	0.96	(0.49;1.85)
Frequent cough	0.84	(0.44;1.63)	1.18	(0.63;2.23)
<u>Eczema ever (N = 294)</u>	<u>1.85</u>	<u>(1.02; 3.34)</u>	<u>0.82</u>	<u>(0.44; 1.54)</u>

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¹ low, medium and high exposure are defined as < 68.0 ng/g; 68.0-389.9 ng/g; and > 389.9 ng/g for mattress; < 36.2 ng/g; 36.2-304.7 ng/g; and > 304.7 ng/g for bedroom floor; < 18.2 ng/g; 18.2-145.6 ng/g; and > 145.6 ng/g for living room floor

Table 4. Adjusted ¹ associations between *Der p1* and *Der f1* concentrations in the child's bedroom floor and living room floor dust and neonatal lung function and respiratory symptoms during the first year of life.

	Der p1				Der f1			
	Medium vs low ²		High vs low ²		Medium vs low ³		High vs low ³	
Bedroom floor								
Lung function (N=285 for Der p1, 265 for Der f1)	beta	(95% CI)	beta	(95% CI)	beta	(95% CI)	beta	(95% CI)
Compliance	-1.55	(-4.72;1.61)	-0.82	(-4.01;2.37)	-2.05	(-5.05;0.94)	-1.15	(-4.28;1.97)
Resistance	-0.06	(-0.79;0.67)	0.05	(-0.69;0.78)	-0.78	(-1.46;-0.09)	-0.10	(-0.81;0.62)
Respiratory symptoms (N=339 for Der p1, 314 for Der f1)	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)
Frequent wheeze	0.87	(0.41;1.85)	0.73	(0.33;1.64)	0.61	(0.29;1.28)	0.93	(0.45;1.95)
Ever wheeze	0.58	(0.32;1.04)	0.58	(0.32;1.05)	0.74	(0.42;1.30)	1.09	(0.61;1.94)
Frequent sputum production	0.81	(0.39;1.67)	0.78	(0.38;1.62)	0.94	(0.47;1.86)	0.92	(0.45;1.88)
Frequent cough	0.59	(0.28;1.25)	1.08	(0.54;2.16)	0.83	(0.42;1.65)	0.94	(0.47;1.87)
Eczema ever (N = 321 for Der p1, 295 for Der f1)	0.60	(0.30; 1.20)	0.51	(0.26; 1.00)	0.98	(0.53; 1.83)	0.93	(0.50; 1.75)★
Living room floor								
Lung function (N=286 for Der p1, 268 for Der f1)	beta	(95% CI)	beta	(95% CI)	beta	(95% CI)	beta	(95% CI)
Compliance	0.67	(-2.89;4.22)	0.84	(-2.78;4.45)	-0.80	(-3.85;2.25)	2.65	(-0.52;5.82)
Resistance	-0.07	(-0.84;0.71)	0.18	(-0.61;0.97)	-0.47	(-1.16;0.22)	-0.27	(-0.99;0.45)
Respiratory symptoms (N=343 for Der p1, 321 for Der f1)	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)
Frequent wheeze	1.19	(0.52;2.69)	1.95	(0.93;4.08)	0.69	(0.32;1.48)	0.40	(0.17;0.95)
Ever wheeze	0.78	(0.40;1.49)	1.02	(0.54;1.91)	1.18	(0.66;2.09)	0.75	(0.41;1.34)
Frequent sputum production	1.21	(0.56;2.60)	0.79	(0.35;1.80)	0.77	(0.37;1.62)	0.98	(0.46;2.05)
Frequent cough	1.29	(0.61;2.71)	1.49	(0.70;3.16)	1.10	(0.55;2.22)	1.41	(0.70;2.85)
Eczema ever (N = 325 for Der p1, 306 for Der p1)	0.88	(0.43; 1.80)	0.64	(0.31; 1.31)	0.91	(0.48; 1.72)	0.80	(0.42; 1.51)★

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¹ adjusted for gender, birth weight, breastfeeding, presence of siblings, day-care attendance, parental education, parental allergies, maternal smoking during pregnancy, pets at home, gas cooking, and season of dust collection. Lung function was additionally adjusted for age at lung function measurements.

² low, medium and high exposure are defined as < LOD, LOD – 147.9 ng/g, and >147.9 ng/g for bedroom floor; < LOD, LOD – 171.7 ng/g, and >171.7 ng/g for living room floor

³ low, medium and high exposure are defined as < LOD, LOD – 85.7 ng/g, and > 85.7 ng/g for bedroom floor; < LOD, LOD – 59.2 ng/g, and > 59.2 ng/g for living room floor

Table 5. Adjusted ¹ associations between *Fel d 1* concentrations in the child's bedroom floor and living room floor dust and neonatal lung function and respiratory symptoms during the first year of life.

	Medium vs low ²		High vs low ²	
Bedroom floor				
Lung function (N=270)	beta	(95% CI)	beta	(95% CI)
Compliance	0.89	(-2.33;4.11)	0.62	(-3.11;4.36)
Resistance	0.15	(-0.59;0.88)	0.29	(-0.56;1.14)
Respiratory symptoms (N=319)	OR	(95% CI)	OR	(95% CI)
Frequent wheeze	0.84	(0.40;1.77)	0.56	(0.20;1.53)
Ever wheeze	0.74	(0.41;1.33)	0.63	(0.31;1.28)
Frequent sputum production	1.68	(0.81;3.46)	0.98	(0.40;2.44)
Frequent cough	0.52	(0.25;1.07)	1.03	(0.44;2.42)
<u>Eczema ever (N = 304)</u>	<u>1.58</u>	<u>(0.83; 3.02)</u>	<u>1.35</u>	<u>(0.61; 2.98)</u>
Living room floor				
Lung function (N=256)	beta	(95% CI)	beta	(95% CI)
Compliance	1.56	(-1.76;4.89)	0.75	(-2.81;4.30)
Resistance	-0.14	(-0.87;0.58)	0.64	(-0.13;1.42)
Respiratory symptoms (N=311)	OR	(95% CI)	OR	(95% CI)
Frequent wheeze	0.70	(0.33;1.50)	1.10	(0.47;2.59)
Ever wheeze	1.13	(0.63;2.03)	0.83	(0.43;1.62)
Frequent sputum production	0.78	(0.38;1.59)	0.92	(0.41;2.08)
Frequent cough	0.89	(0.43;1.84)	1.25	(0.55;2.86)
<u>Eczema ever (N = 294)</u>	<u>1.85</u>	<u>(0.98; 3.48)</u>	<u>0.91</u>	<u>(0.43; 1.96)</u>

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¹ adjusted for gender, birth weight, breastfeeding, presence of siblings, day-care attendance, parental education, parental allergies, maternal smoking during pregnancy, ETS exposure at home, pets at home, gas cooking, and season of dust collection. Lung function was additionally adjusted for age at lung function measurements.

² low, medium and high exposure are defined as < 36.2 ng/g; 36.2-304.7 ng/g; and > 304.7 ng/g for bedroom floor; < 18.2 ng/g; 18.2-145.6 ng/g; and > 145.6 ng/g for living room floor