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Prenatal and postnatal exposure to pet ownership and lung function in children: the Seven Northeastern Cities Study

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Abstract

To evaluate the association between prenatal and postnatal exposure to pet ownership and lung function in children, a cross-sectional study named Seven Northeastern Cities (SNEC) study was conducted. In this study, children's lung function including the forced expiratory volume in 1 second (FEV_1), forced vital capacity (FVC), maximal mid-expiratory flow (MMEF), peak expiratory flow (PEF) were measured by spirometers, and pet ownership situations was collected by questionnaire. Analyzed by multiple logistic regression and generalized linear modeling, we found that for all subjects, pet exposure in the first 2 years of life was significantly associated with lung function impairment of FVC<85% predicted (adjusted odds ratio [aOR]=1.28; 95% confidence interval [CI]=1.01, 1.63). For current pet exposure, the increased odds of lung function impairment ranged from 35% (aOR=1.35; 95% CI=1.12, 1.62) for FVC<85% predicted to 57% (aOR=1.57; 95%CI=1.29, 1.93) for FEV_1 <85% predicted. The *in utero* exposure was not related to lung function impairment. Compared with other pets, higher odds were observed among children with dogs. When stratified by gender, girls with current pet exposure were more likely to have lung function impairment than boys. It implies self-reported exposures to pets were negatively associated with lung function among the children under study.

Keywords: Pets, Lung function, Children, Gender difference, Prevention, Exposure

Practical implications Our findings indicate the 'harmful' effects of domestic pets on lung function. Girls may be more susceptible to current pet exposure than boys. These results have relevance for public health and prevention among children.

Introduction

Early life lung function is critical for respiratory health throughout life [1-4]. Among several environmental determinants in early life that may affect early life lung function, rising rates of pet ownership globally have stimulated our interest to perform a study on the impact of household pets. According to a report in 2015, pet ownership increased by 54.2% since 2009 in

China compared to the global pet ownership which increased by 24.0%[5,6]. In such circumstance, the relationships between early pet ownership on asthma and allergies have been extensively studied, its impact on early life lung function has not received the same attention.

Although studies have focused on bronchial hyper-responsiveness (BHR) or specific airway resistance (sRaw) assessed by challenge tests[7-15], few have specifically focused on FEV_1, FVC and their ratio along with PEF. Most of these studies, including cross-sectional and birth cohort study designs, found no associations for living with pets and the risk of respiratory or allergic conditions [11,12,15,16]. However, in a cohort study, Bertelsen et al[17] evaluated 260 children's health status with early life exposure to indoor allergens and endotoxin at 10 years of age. Findings from this investigation suggested positive associations between exposure to cat allergens early in life and the risk of late childhood asthma (aOR=1.20, 95% CI: 1.01-1.43) and BHR (aOR: 1.22, 95% CI: 1.02-1.46) per 10 micro g/g dust increase in cat allergen exposure at 2 years of age. In a prospective birth cohort study, Lowe et al[10] followed 996 children and found no significant longitudinal effect due to owning a cat, a dog, or owning both a cat and a dog in early life. However, they found that the lung function of children who were both dog sensitized and exposed to dog allergen was lower than that of sensitized children without exposure and exposed children without sensitization. Conversely, another prospective birth cohort study, Ownby et al[8] followed 474 children and found a reduction in BHR in boys at 6 to 7 years of age with exposure to 2 or more dogs or cats in the first year of life compared to no dog or cat exposure, and suggested that exposure to dogs and cats may be associated, at least in boys, with a reduced risk of asthma. Recently, the Avon Longitudinal Study of Parents and Children (ALSPAC) which followed 4,706 children from birth to age 7, found pet ownership was not associated with 8 years' lung function, with the exception of positive associations of rodent and bird ownership with better lung function[18]. This study was the only one we identified that mostly focused on the relationship of pet ownership with lung function.

The question of whether pet-keeping influences children's lung function has been fiercely debated over the past 20 years and is still controversial due to lack of consistent evidence. Further research is essential to evaluate the association between pets and lung function. To add to this debate, we used data from the Seven Northeastern Cities (SNEC) Study, a cross-sectional study in China, to investigate associations of pet ownership with the measured lung function of children.

Methods

Study population and overall design

We have conducted this large epidemiologic study across the seven Northeastern cities in China in two waves. Wave 1 was during a period from 2008-2009 and Wave 2 was conducted from 2012-2013. Wave 1 was conducted to assess the relationship of outdoor and indoor air pollution with asthma and asthma-related symptoms in children using among 31,049 children from 25 districts of the seven cities in Northeastern China[19-27]. Wave 2, which occurred in 2012-2013, was conducted to evaluate the effects of air pollution on lung function, blood pressure, and mental health, including attention deficit hyperactivity disorder (ADHD) and sleep disorder[28-33]. While the seven cities were the same, a total of 70,000 new children were randomly selected from 48 kindergartens, 24 elementary school, and 24 middle schools. The present study was based on the data collected in Wave 2 from April 2012 to May 2013. See Supplementary Materials for details. And briefly, a total of 24 urban districts were selected from the seven cities: three districts in Anshan, Benxi, and Dandong, four districts in Dalian and Fushun, two districts in Liaoyang and five districts in Shenyang. To generate a representative sample of all districts, random sampling was used to select one elementary and middle school from each of these 24 districts. Furthermore, within each selected school, one or two classrooms from each grade level were randomly selected as the sample. To participate, students' had to have lived within this district for at least two years prior to the start of the study. We followed all study strictly according to the Sun Yat-sen University’s ethical standards. The Sun Yat-sen University Institutional Human Ethics Committee (Ethics Approval Number: 026) approved all performed human experiments and the approval was consistent with the Declaration Helsinki-Ethical Principles for Medical Research Involving Human Subjects. In addition, prior to data collection, the parent/guardian of each child provided a written informed consent. After the initial data collection, the data analysis was conducted from May 2015 to October 2016.

Questionnaire survey

Administration of the study questionnaire was conducted as follows. First, school teachers were given verbal and written instructions to distribute and collect the questionnaires with envelopes and forms to record questionnaire responses. Teachers were also responsible to explain the questionnaire to parents and obtain the consent to participate. Consenting parents could choose to either attend a parent's night where they filled out the questionnaire voluntarily or take it home and return it in a sealed envelope.

Lung function measurement

The lung function measurements in this study included forced expiratory volume in 1 second (FEV_1), forced vital capacity (FVC), maximal mid-expiratory flow (MMEF), and peak expiratory flow (PEF), which were measured utilizing two portable electronic spirometers (Spirolab, MIR, Italy). Spirolab spirometers are auto-calibrated and evaluated independently. They have sensitivity and specificity values of 97.75%, 73.04% compared to lower limit of normal, respectively for lung function measures [34]. The lung function data were collected based on the American Thoracic Society (ATS) and European Respiratory Society (ERS) standards by two technicians and researchers who were experienced in the use of electronic spirometers. The test requires the children at least 10 years old to exhale for at least six seconds, and the children younger than 10 years old exhale for at least three seconds. The collected data for FVC and FEV_1 were the largest value(s) obtained from any of the three satisfactory curves. Additionally, the first and second largest FVC and FEV_1 values of these three curves should vary by less than 5% from each other.

We used the lung function predicted values, which were obtained from the reference equations identified from our own study[35]. Specifically, a spirometric pattern was regarded as impairments of lung function if FEV_1% <85%, or FVC <85%, or PEF<75%, or MMEF<75% of the predicted value of the respective parameter.

Pet ownership exposures

Pet ownership was assessed by asking if parents/guardians keep any pets in the house, and then questions about pet ownership status was further ascertained, such as species and the number of pets: dog, cat, bird, farm animals (chicken, duck, or goose) or other pets (tortoises, hamsters, gold fishes, lizards, or other pets kept in the home other than cats, dogs, birds and farm animals). Importantly, at the time of the questionnaire, parents were also asked to recall whether they kept pets while their children were *in utero*, during the first 2 years of their children's lives, and whether they currently keep pets. The exposures were subsequently categorized into 3 categories: pet exposure *in utero*; pet exposure in the first 2 years, and current pet exposure.

Assessment of other covariates

A number of covariates were also assessed in the study including body mass index (BMI), socio-demographic factors, and several key health behaviors. We defined overweight and obesity based on the Centers for Disease Control and Prevention (CDC) BMI growth charts, which uses one-month age intervals and is by age and sex. Overweight was defined as BMI between 85th and 95th percentile. We used electronic scales (at 0.1kg) and fixed stadiometers (at 0.1cm) to measure height and weight when participants were without shoes in light garments. Family income per year was categorized into five categories: <5,000 RMB (Chinese Yuan, RenMinBi), 5,000-9,999RMB, 10,000-29,999RMB, 30,000-100,000RMB, or >100,000RMB. Parental education level was categorized into two groups: ≥high school or <high school. Environmental tobacco smoke (ETS) exposure was defined as living with someone who smokes cigarettes daily in the house. The child's asthma status was defined as "yes" if the parent/guardian reported that a doctor had ever diagnosed the child as having asthma. Breastfeeding information was obtained by asking if the mother breastfed the child for at least three months. We obtained domestic fuel information by asking parents/guardians if they use coal for cooking or space heating. House close to main road was dichotomous variable defined by residence's house close to main road. Exercise per week was continuous variable estimated by how many hours per week the child spent on physical activities.

Statistical analysis

We processed the data first for normality by using both Shapiro–Wilks *W*-test and homogeneity by using Bartlett's test for unequal variances. For continuous variables, we calculated mean ± standard deviation (SD); and for categorical variables we calculated relative frequencies. Chi-square tests were performed to calculate the associations between categorical variables. We tested the association of pet ownership status with lung function using generalized linear models. Multiple logistic regression analyses were used to determine whether pet ownership status was associated with risk of impaired lung function after adjustment for potential confounders (i.e., age of the children, BMI, parental education, breast feeding status, income, ETS, home coal use and study districts). We included a covariate in the final model if the estimated effects changed more than 10% when the covariate was brought into the base model. All analyses were conducted using SAS software (Version 9.1; SAS Institute Inc., Cary, NC, USA). All statistical tests were two-tailed and p-values < 0.05 were considered statistically significant.

Results

There were total 7,326 children randomly recruited from 24 elementary school and 24 middle school respectively. As there were 7,109 children both completed the lung function and the questionnaires measurement, the overall response rate was 96%. Further, 279 children (4%) were excluded since they lived less than 2 years in their district. So finally there were 6,740 children from 24 districts of Northeast China included in this study. Characteristics of these children are included in Table 1. The average age of the study population was 11.6 ± 2.1 years (range 7-14 years) and 50.2% (n=3382) was male. We found statistically significant gender differences. Girls were more likely to be breastfed for at least three months (72.6% vs 68.4%), be exposed to pets in the first 2 years (11.6% vs 8.7%), to have current exposure to dogs (10.5% vs 8.5%), and to have ≥2 pets in home (7.2% vs 5.5%). Boys suffered more from asthma (8.1% vs 5.5%). For BMI, 59.4% of boys were considered normal, 16.4% were overweight, and 24.2% were obese. Compared with boys, girls tended to be of normal weight (74.8% vs 59.4%). Additionally, gender differences were also found for lung function and exercise time per week; males had longer exercise time per week and better spirometry status.

Table 2 describes the proportion of four impaired spirometric measures of lung function (FVC<85% predicted, FEV_1<85% predicted, PEF<75% predicted, and MMEF<75% predicted). Compared with no current pet exposure, the prevalence of four lung function impairments all increased with current pet exposure (FVC<85% predicted, 10.5%; FEV_1<85% predicted, 7.7%; PEF<75% predicted, 6.2% and MMEF<75% predicted, 8.7%), dog and other pets in home, and having 1 or ≥2 pets in home ($p<0.05$). Having a bird in home only showed significant differences for the MMEF<75% predicted measure. For pet exposure in the first 2 years of life, significant differences were only observed for FVC <85% predicted. No significant differences were found for any of the four lung function impairment measures for pet exposure *in utero*.

Multiple logistic regression analysis was conducted to examine the risk of lung function impairment related to pet exposure, as presented in Table 3. Overall, for all subjects, current pet exposure (aOR ranged from 1.35 (95%CI: 1.12, 1.62) to 1.57 (95%CI: 1.29, 1.93)), current exposure to dogs (aOR ranged from 1.70 (95%CI: 1.31, 2.21) to 2.10 (95%CI: 1.58, 2.79)) and other pets (aOR ranged from 1.29 (95%CI: 1.00, 1.66) to 1.49 (95%CI: 1.12, 1.99)), having 1 (aOR ranged from 1.28 (95%CI: 1.04, 1.58) to 1.43 (95%CI: 1.13, 1.80)) or ≥2 pets in home (aOR ranged from 1.51 (95%CI: 1.13, 2.03) to 1.97 (95%CI: 1.45, 2.68)) were associated with increased odds of all four lung function impairments. Current exposure to birds was associated with increased odds of PEF (aOR=1.97, 95%CI: 1.00-3.88) and MMEF (aOR=2.07, 95%CI: 1.17-3.67). While pet exposure in the first 2 years was only associated with increased odds of lung function impairment measured by FVC for all subjects (aOR=1.28, 95%CI: 1.01-1.63). Compared with other pets, higher odds were observed among children with dogs (except for bird exposure for PEF<75% predicted and MMEF<75% predicted). Compared to subjects with 1 pet in home, subjects with ≥2 pets had higher odds of all four lung function impairments. Stratified by gender, girls reporting current pet exposure were more likely to have lung function impairment than boys, especially PEF, the interactions between current pet exposure and gender on PEF impairment were statistically significant (P =

0.0434). Nonsignificant effects were seen for exposure to pets *in utero* or cat and farm animals at home across all measures of impairment for males, females, and all subjects.

Table 4 presents the results of the relationship between pet ownership and lung function tests. Overall, the estimated decreases in mean lung function for pet exposure in the first 2 years of life were 46 mL (95% CI: -89, -3) for FVC, 43 mL (95%C I: -81, -5) for FEV_1, and 149 mL (95% CI: -234, -64) for PEF. For current pet exposure, the estimated decreases in mean lung function ranged from 56 mL (95%CI: -88, -24) for FVC to 131 mL (95%CI: -195, -67) for PEF. The negative associations of exposure to dogs and having 1 or ≥2 pets in the home with all four lung function tests were all significant (β coefficients range from -53 to -199 mL). Bird exposure was only associated with decreased lung function measured by PEF (β= -239, 95%CI: -456, -21), exposure to other pets was associated with decreased lung function as measured by FVC (β= -51, 95% CI: -92, -10), FEV_1 (β= -68, 95% CI: -105, -32) and PEF (β= -102, 95% CI: -184, -21). In contrast, there were no significant relationships found between pet exposure *in utero*, cats or farm animals in home and any lung function parameters. For females, a similar pattern was observed. However, for males, the significant negative effects were only seen from pet exposure in the first 2 years on lung function, as measured by FVC and PEF, and for exposure to dogs on FVC, FEV_1 and PEF. Girls reporting current pet exposure were more likely to have MMEF impairment than boys (-123 (95%CI: -185, -62) VS -8 (95%CI: -80, 65)), the interactions between current pet exposure and gender on MMEF impairment were statistically significant (P = 0.0214).

To clarify the life-time specific exposure to pets and its connection to lung function, a more detailed analysis on pet ownership exposure in different periods were shown in table 5, Figure 1 and Table S5. Compared with children without pet exposure at any time, the children with only current pet exposure were consistently having a reduced FVC, FEV_1, PEF and MMEF.

Considering that asthma status may be a mediator in the relationship between pet exposure and lung function in childhood, we further analyzed the association between pet exposure and lung function impairment, stratified by asthma status [see Supplemental Material, Table S3 and Table S4]. A similar pattern was observed in subjects without asthma as shown in Table S3 and Table S4. Table S3 presents the effects of pet exposures in the postnatal environment compared to prenatal. For subjects with asthma, only a few categories of pet exposure were significantly associated with impaired lung function, as measured by FEV_1 (including current pet exposure, dogs or birds in home and having 1 or ≥2 pets in home).

DISCUSSION

The present study sought to shed light on the association between pet ownership and lung function in children living in 24 districts of Northeast China. To our knowledge, the current paper is the first attempt to determine the association between pet ownership and lung function in Chinese children. Considering it has been debated for over 20 years over whether pet-ownership can impact children's lung function and there has been a lack of consistent evidence to address this study question, we regard it worthwhile to test this hypothesis. We found that exposure to pets at home was associated with reduced lung function and the association appears to be influenced by the type, number of pets, the exposure time, and the gender of the child.

A wide range of original study designs, as well as syntheses of these studies in systematic reviews, have reported the effects of early life exposure to pet ownership (mainly cats and dogs) and the development of asthma and asthma-like symptoms[24, 36-41], bronchial hyper-responsiveness[9,12-14,16,42,43] and specific airway resistance[10]. However, to our knowledge, there is a paucity of data on the effect of prenatal and postnatal exposure of a wide range of pet types on lung function in early childhood. In this study, we found there were no associations between cat ownership and lung function, which was consistent with studies conducted by Collin et al[18] and Nelson et al[9]. However, we did find that dog and other pet ownerships were associated with an increased risk of lung function impairment measured by FVC, FEV_1, PEF and MMEF (aOR ranged from 1.29 (95%CI: 1.00, 1.66)) to 2.10 (95%CI: 1.58, 2.79), Table 3), which differed from the results of the two studies mentioned above. In the present study, we also found that current bird ownership was associated with impairment in lung function as measured by PEF and MMEF (aOR were 1.97 (95%CI: 1.45, 2.68) and 2.07

(95%CI: 1.17, 3.67) respectively, Table 3). In contrast to our findings, Collin et al[18] reported weak evidence of positive associations between bird ownership and lung function (FEV_1 and FVC) at age 8 years, though the author declared these may most plausibly be ascribed to chance.

The contradictory results regarding the relationships between pet exposure and lung function are difficult to interpret. In western countries different findings may be due to geographic variation and genetic heterogeneity.[44-46] The different associations found between cat, dog and other animals with lung function, may be caused by different levels of endotoxin. Thorne and colleagues [47] found that house dust endotoxin concentrations were associated with many factors, including dog but not cat ownership. Many other studies also found that homes with dogs have significantly more airborne endotoxin.[48-52] Airborne endotoxins have been found to decrease lung function and augment an inflammatory reaction in vivo.[53-55] However, there is also evidence to show that exposure to airborne endotoxin, especially in infancy, may protect against allergy or asthma.[56-58] Therefore, different levels of endotoxins due to the cultural customs [24,59,60] and the cleanliness of the home[61] may contribute to the differences in the findings across countries and different animals. In China, compared with western countries like the UK, pets (especially dogs) may track more endotoxin-laden soil from the environment into the home. More than 20% of families reported washing their pets no more than once a month in a market research study in China[62], therefore the recoverable allergen from hair and dander might be high[63].

We also observed the following factors to affect the lung function of the children in this study. First, number of pets: having 2 or more pets at home was associated with an increased risk of lung function impairment which may warrant further research. Second, exposure time: no significant differences were seen from exposure to pets *in utero*, but current exposure to pets consistently had a negative impact on lung function. However, this might suggest a more acute effect on lung function for current exposure and negative effects of high levels of exposures to allergens and endotoxins as mentioned before. Third, the gender of the child: The observed associations of pet exposure with increased odds of lung function impairment were more significant in females (Tables 3 and 4). The reason may be lung function continues to change during development until the mid-20s, the teenaged children in this study have greater airway reactivity but the lung function growth rate was gender-different.[64-66] The reason may also be related to hormonal differences, with reported links between insulin, adiponectin, leptin or other sex hormones and lung function.[67-69] More detailed gender based studies of pet exposure and lung function may improve our understanding of the complex association of hormones or gender-based behavioral differences with lung function.

There were also some significant findings for FEV_1 in asthmatic children with current pet exposure, having dogs and birds in home, and having 1 or ≥2 pets in home. These significant effects of postnatal pet exposure tend to be larger in asthmatics than their non-asthmatic counterparts [Table S3 and Table S4]. The number of asthmatic children in our study was small (N=460), especially when further categorized by exposure prevalence (see Supplemental Material, Table S1 and Table S2). However, as shown in previous studies[70,71], our findings indicate that living with pets may aggravate symptoms of airway inflammation in asthmatics. Given this consistency with previous research, our findings of increased odds of lung function impairment in asthmatic children in this study were reasonable or convergent with prior evidence.

Some of the mechanisms by which our findings can be explained include: It has been shown that sensitization and inflammation may occur by inhalation of animal-derived home aeroallergens, especially from cats (fel d1) and dogs (can f1)[7,43,72-76]. Traditionally, pet ownership in early life affecting sensitization and allergic lung inflammation has been attributed to the classical IgE-associated inflammation response[77-79]. Experimental studies also have suggested that dog and cat allergens can activate respiratory epithelial cells to release proinflammatory cytokines and chemokines and expression of ICAM-1 by adjuvant-like protease-independent mechanisms[74,80]. Furthermore, recent studies have shown aeroallergen exposure in animal models of pulmonary disease invoked group 2 innate lymphoid cells (ILC2s). ILC2s have been found to play a crucial role in the evolution of type 2 inflammation and in the initiation of the adaptive Th2 response[73,77,81,82]. In addition to pet allergens, animal-derived home endotoxins may be another potential mechanism for the 'harmful' effects of pets, since the pro-inflammatory properties of endotoxin can trigger immune cell activation and cytokine release[83,84]. The manifold effects of endotoxin exposures on human health may be determined based on the dosage and many other factors such as the timing of exposure and the interaction with domestic environmental factors[85-91], which we do not have further data on in this study and need further examination.

There are several limitations in this study. First, the main limitation of our study, as with any cross-sectional questionnaire survey, relates to its inability to assess the temporal direction of associations between pet ownership and lung function impairment, and renders any causal inference impossible. Although we have attempted to reduce the selection and information bias as much as possible, the risk of bias was not eliminated due to the inability to monitor every survey interaction. Moreover, in the current study, the prevalence of overweight and obesity were 15.9% and 17.1% for 7-14 year children, respectively. This prevalence was similar to the results reported from the study from the same area[92], but higher than the prevalence in European [93]. Second, due to the funding and resource limitations, our pet ownership measures were based on questionnaire responses alone. We were unable to measure the individual amount of pet related allergen, which may be able to say more about the actual impact on lung development. Third, our data set did not include other factors which might mediate or modify the observed associations. For example, number of siblings, dampness in the home, whether the individual or parent is allergic or not, time spent outdoors, whether pets were kept indoors or outdoors, frequency and type of contact between children and pets, etc. Developing better exposure variables should be a focus in future studies. Additionally, a small number of children exposed to pets *in utero* in our study (n=370) might have caused the model to be underpowered. Finally, longitudinal studies are needed to determine whether the reduced lung function we observed is a predictor of future onset of respiratory diseases such as asthma.

In conclusion, we found that self-reported exposures to pets contributed independently to lung function in children. There were no effects of cat ownership, but 'harmful' effects of dog and bird ownership on lung function. Whether exposure to pets has a causal effect on the development of lung function impairment remains to be elucidated.

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Figure Legends:

Figure 1 Estimated absolute changes (95%CI) in lung function in relation to pet ownership exposure in children by the period status, with the reference catalog of children without pet exposure any time. Estimates are adjusted for age, gender, BMI, ETS exposure, parental education, breast feeding status, income, home coal use.

Table 1. Characteristics of children in 25 districts in northeast of China, stratified by gender

Variables	Males (3382)	Females (3358)	Total (6740)
Age (years), Mean(SD)	11.6 ± 2.1	11.5 ± 2.0	11.6 ± 2.1
Body Mass Index category[a]			
Normal weight	2008 (59.37)	2510 (74.75)	4518 (67.03)
Overweight	555 (16.41)	513 (15.28)	1068 (15.85)
Obesity	819 (24.22)	335 (9.98)	1154 (17.12)
[b]ETS exposure: No	1759(52.01)	1700(50.63)	3459 (51.32)
Father	1050 (31.05)	1072 (31.92)	2122 (31.48)
Mother	300 (8.87)	308 (9.17)	608 (9.02)
Other	273 (8.07)	278 (8.28)	551 (8.18)
Parental Education >high school	2101 (62.12)	2110 (62.84)	4211 (62.48)
Breast Feeding	2312 (68.36)	2439 (72.63) [a]	4751 (70.49)
Family income per year			
<5,000RMB[c]	375 (11.09)	383 (11.41)	758 (11.25)

5,000-9,999RMB[c]	431 (12.74)	445 (13.25)	876 (13.00)
10,000-29,999RMB[c]	1197 (35.39)	1197 (35.65)	2394 (35.52)
30,000-100,000RMB[c]	1250 (36.96)	1187 (35.35)	2437 (36.16)
>100,000RMB[c]	129 (3.81)	146 (4.35)	275 (4.08)
Home coal use	357 (10.56)	319 (9.50)	676 (10.03)
House close to main road	1558 (46.07)	1569 (46.72)	3127 (46.39)
House pet exposure			
Pet exposure *in utero*	168(4.97)	202(6.02)	370(5.49)
Pet exposure in the first 2 years	295(8.72)	390(11.61)[a]	685(10.16)
Current pet exposure	694(20.52)	741(22.07)	1435(21.29)
Cat	69(2.50)	79(2.93)	148(2.71)
Dog	249(8.48)	306(10.47)[a]	555(9.47)
Bird	48(1.75)	42(1.58)	90(1.67)
Farm animals	51(1.86)	53(1.99)	104(1.92)
Other pets	386(12.56)	376(12.56)	762(12.56)
Number of pets in home[a]			
1	509(15.05)	499(14.86)	1008(14.96)
>2	185(5.47)	242(7.21)	427(6.33)
Doctor diagnosed asthma	275 (8.13)	185 (5.51)[a]	460 (6.82)
Exercise time per week (hour), Mean (SD)	7.85 ±7.62	7.35±7.87[a]	7.60 ±7.75
Lung Functions			
FVC(mL), Mean (SD)	2818±844	2432±594[a]	2626±755
FEV_1(mL/s), Mean (SD)	2628±775	2296±567[a]	2464±699
PEF(mL/s), Mean (SD)	5164±1534	4389±1160[a]	4778±1415
MMEF(mL/s), Mean (SD)	3491±1153	3208±909[a]	3350±1049

[a]The difference between males and females is significant at the 0.05 level, using Chi square for categorical variables and t test for continuous variables. [b]ETS: Environmental Tobacco Smoke. [c]RMB, Chinese Yuan, RenMinBi.

Table 2. Lung function impairment in relation to prenatal and postnatal exposure to pet ownership in children (N=6740)

Pets exposure	No.	FVC<85%		FEV_1<85%		PEF< 75%		MMEF< 75%	
		n	(%)	n	(%)	n	(%)	n	(%)
Pet exposure *in utero*									
No	6370	710	11.15	547	8.59	435	6.22	601	9.43
Yes	370	49	13.24	31	8.38	23	6.83	33	8.92
Pet exposure in the first 2 years of life									
No	6055	660	10.90	510	8.42	407	6.72	569	9.40
Yes	685	99	14.45[a]	68	9.93	51	7.45	65	9.49
Current pet exposure									
No	5305	558	10.52	406	7.65	330	6.22	459	8.65
Yes	1435	201	14.01[a]	172	11.99[a]	128	8.92[a]	175	12.20[a]
Type of animals in home[b]									
Cat	148	15	10.14	17	11.49	10	6.76	15	10.14
Dog	555	94	16.94[a]	83	14.95[a]	57	10.27[a]	74	13.33[a]
Bird	90	9	10.00	12	13.33	10	11.11	15	16.67[a]
Farm animals	104	7	6.73	11	10.58	7	6.73	12	11.54
Other pets	762	100	13.12[a]	85	11.15[a]	66	8.66[a]	87	11.42[a]
Number of pets in home[b]									

1	1008	136	13.49 [a]	112	11.11[a]	80	7.94[a]	115	11.41[a]
≥2	427	65	15.22 [a]	60	14.05[a]	48	11.24[a]	60	14.05[a]

[a]The difference between category is significant at the 0.05 level, using Chi square for categorical variables.

[b]Compared to subjects with no current pet exposure.

Table 3. Adjusted OR and 95% confidence interval of lung function impairment in relation to prenatal and postnatal exposure to pet ownership in children (N=6740)[a]

	Males		Females		Total		Interaction
	aOR	95%CI	aOR	95%CI	aOR	95%CI	*P* Value
FVC <85% predicted							
Pet exposure *in utero*	1.15	0.71, 1.87	1.13	0.74, 1.74	1.13	0.82, 1.56	0.6828
Pet exposure in the first 2 years	**1.46**	**1.03, 2.08**	1.15	0.83, 1.58	**1.28**	**1.01, 1.63**	0.1889
Current pet exposure	**1.31**	**0.99, 1.72**	**1.37**	**1.07, 1.75**	**1.35**	**1.12, 1.62**	0.9924
Type of animals in home							
Cat	1.21	0.57, 2.54	0.59	0.25, 1.41	0.89	0.51, 1.56	0.1360
Dog	**1.70**	**1.13, 2.54**	**1.73**	**1.22, 2.45**	**1.70**	**1.31, 2.21**	0.5056
Bird	0.80	0.28, 2.28	1.07	0.41, 2.76	0.93	0.46, 1.87	0.7107
Farm animals	0.86	0.32, 2.30	0.33	0.08, 1.43	0.59	0.26, 1.32	0.1949
Other pets	1.38	0.98, 1.95	1.20	0.87, 1.67	**1.30**	**1.03, 1.65**	0.7482
Number of pets in home							
1	1.23	0.90, 1.68	**1.31**	**0.99, 1.75**	**1.28**	**1.04, 1.58**	0.7680
>2	1.53	0.97, 2.40	**1.52**	**1.03, 2.23**	**1.51**	**1.13, 2.03**	0.5876
FEV_1 <85% predicted							
Pet exposure *in utero*	0.96	0.56, 1.66	0.89	0.51, 1.56	0.9	0.61, 1.33	0.5363
Pet exposure in the first 2 years	**1.44**	**0.99, 2.09**	0.92	0.61, 1.39	1.15	0.87, 1.51	**0.0490**
Current pet exposure	1.29	0.96, 1.72	**1.89**	**1.43, 2.51**	**1.57**	**1.29, 1.93**	0.2576
Type of animals in home							
Cat	1.23	0.56, 2.70	1.63	0.77, 3.46	1.41	0.82, 2.42	0.7893
Dog	1.49	0.97, 2.29	**2.69**	**1.85, 3.92**	**2.10**	**1.58, 2.79**	0.2067
Bird	1.44	0.60, 3.47	2.20	0.90, 5.36	1.75	0.94, 3.27	0.6396
Farm animals	1.17	0.46, 2.95	1.44	0.51, 4.06	1.26	0.63, 2.52	0.9543
Other pets	**1.45**	**1.02, 2.06**	**1.51**	**1.03, 2.21**	**1.48**	**1.14, 1.92**	0.9226
Number of pets in home							

1	1.16	0.83, 1.61	**1.73**	**1.24, 2.40**	**1.43**	**1.13, 1.80**	0.2875
>2	**1.71**	**1.08, 2.71**	**2.27**	**1.49, 3.44**	**1.97**	**1.45, 2.68**	0.6881

Table 3. continued

	Males		Females		Total		Interaction
	aOR	95%CI	aOR	95%CI	aOR	95%CI	*P* Value
PEF <75% predicted							
Pet exposure *in utero*	0.59	0.26, 1.38	1.17	0.69, 1.99	0.89	0.57, 1.39	0.2905
Pet exposure in the first 2 years	0.93	0.54, 1.60	1.32	0.90, 1.95	1.13	0.82, 1.54	0.4930
Current pet exposure	1.07	0.73, 1.56	**1.88**	**1.41, 2.49**	**1.52**	**1.21, 1.90**	**0.0434**
Type of animals in home							
Cat	0.94	0.33, 2.72	1.23	0.50, 2.99	1.01	0.51, 2.00	0.9647
Dog	1.41	0.83, 2.42	**2.13**	**1.41, 3.22**	**1.82**	**1.31, 2.52**	0.8044
Bird	1.71	0.60, 4.89	2.18	0.89, 5.39	**1.97**	**1.00, 3.88**	0.7906
Farm animals	1.25	0.41, 3.83	1.17	0.32, 4.21	1.14	0.49, 2.65	0.4898
Other pets	1.02	0.62, 1.68	**1.85**	**1.29, 2.64**	**1.49**	**1.12, 1.99**	**0.0260**
Number of pets in home							
1	0.97	0.62, 1.52	**1.68**	**1.20, 2.35**	**1.37**	**1.05, 1.79**	0.0702
>2	1.36	0.75, 2.46	**2.33**	**1.53, 3.54**	**1.87**	**1.33, 2.63**	0.3058
MMEF <75% predicted							
Pet exposure *in utero*	0.67	0.35, 1.30	1.15	0.72, 1.84	0.94	0.64, 1.36	0.2123
Pet exposure in the first 2 years	0.97	0.63, 1.51	1.04	0.73, 1.50	1.02	0.77, 1.35	0.7863
Current pet exposure	1.18	0.87, 1.59	**1.66**	**1.28, 2.14**	**1.43**	**1.18, 1.74**	0.1056
Type of animals in home							
Cat	0.89	0.35, 2.30	1.61	0.79, 3.29	1.24	0.70, 2.18	0.3668
Dog	1.39	0.88, 2.20	**1.94**	**1.34, 2.82**	**1.72**	**1.29, 2.29**	0.4434
Bird	1.29	0.50, 3.33	**3.05**	**1.46, 6.38**	**2.07**	**1.17, 3.67**	0.1608
Farm animals	1.36	0.50, 3.72	1.89	0.76, 4.70	1.60	0.81, 3.13	0.6522
Other pets	1.13	0.77, 1.66	**1.46**	**1.05, 2.04**	**1.29**	**1.00-1.66**	0.2737
Number of pets in home							
1	1.09	0.77, 1.55	**1.52**	**1.13, 2.05**	**1.31**	**1.05, 1.65**	0.1977
>2	1.44	0.87, 2.39	**2.04**	**1.39, 3.01**	**1.78**	**1.31, 2.41**	0.2979

aOR, adjusted odds ratios; CI, confidence intervals. [a]Models for all subjects are adjusted for age, BMI, ETS exposure, parental education, breast feeding status, income, home coal use. All aOR are compared to the reference category (no pet exposure *in utero*, no pet exposure in the first 2 years, or no current pet exposure). Bold font represents the statistically significant difference at $p < 0.05$.

Table 4. Estimated Absolute Decrease in Lung Function in Relation to Prenatal and Postnatal Exposure to Pet Ownership in Children (N=6740)[a]

	Males		Females		Total		Interaction
	β	95%CI	β	95%CI	β	95%CI	*P* Value
FVC(mL)							
Pet exposure *in utero*	-73	-163, 17	12	-53, 77	-38	-94, 19	**0.0424**
Pet exposure in the first 2 years	**-76**	**-146, -7**	-18	-66, 31	**-46**	**-89, -3**	0.1426
Current pet exposure	-23	-73, 27	**-76**	**-113, -38**	**-56**	**-88, -24**	0.2701
Type of animals in home							
Cat	-29	-172, 115	18	-85, 120	-26	-115, 63	0.4810
Dog	**-83**	**-164, -2**	**-93**	**-150, -36**	**-93**	**-142, -43**	0.7031
Bird	31	-135, 198	-64	-199, 71	-15	-125, 95	0.5586
Farm animals	97	-73, 267	18	-113, 149	38	-72, 148	0.9138
Other pets	-15	-79, 48	**-71**	**-120, -22**	**-51**	**-92, -10**	0.2638
Number of pets in home							
1	-18	-75, 39	**-78**	**-121, -34**	**-53**	**-90, -16**	0.1438
≥2	-35	-124, 54	**-68**	**-129, -7**	**-60**	**-114, -6**	0.8711
FEV_1(mL/s)							
Pet exposure *in utero*	-54	-133, 24	15	-45, 75	-29	-79, 21	0.0830

Pet exposure in the first 2 years	-59	-119, 2	-22	-67, 23	**-43**	**-81, -5**	0.3992
Current pet exposure	-29	-72, 15	**-95**	**-130, -60**	**-68**	**-96, -39**	0.0707
Type of animals in home							
Cat	-22	-146, 102	-15	-109, 80	-39	-118, 40	0.9479
Dog	**-74**	**-145, -4**	**-113**	**-165, -61**	**-100**	**-144, -55**	0.5360
Bird	40	-104, 184	-110	-234, 15	-32	-130, 66	0.2149
Farm animals	-12	-159, 136	-49	-170, 71	-51	-149, 47	0.9091
Other pets	-33	-87, 22	**-93**	**-138, -48**	**-68**	**-105, -32**	0.2354
Number of pets in home							
1	-28	-77, 21	**-95**	**-135, -55**	**-66**	**-99, -34**	0.0738
≥2	-34	-111, 44	**-93**	**-149, -37**	**-73**	**-121, -25**	0.4774

Table 4. continued

	Males		Females		Total		Interaction
	ß	95%CI	ß	95%CI	ß	95%CI	*P* Value
PEF(mL/s)							
Pet exposure *in utero*	-75	-246, 95	5	-135, 145	-60	-172, 52	0.4455
Pet exposure in the first 2 years	**-173**	**-305, -41**	**-111**	**-215, -6**	**-149**	**-234, -64**	0.8207
Current pet exposure	-53	-149, 42	**-186**	**-267, -105**	**-131**	**-195, -67**	0.0666
Type of animals in home							
Cat	48	-221, 318	-107	-328, 114	-78	-255, 99	0.2392
Dog	**-159**	**-312, -6**	**-200**	**-321, -80**	**-191**	**-289, -92**	0.4422
Bird	-92	-404, 219	**-409**	**-698, -120**	**-239**	**-456, -21**	0.2307
Farm animals	-120	-441, 200	-233	-514, 48	-216	-434, 24	0.5764

Other pets	-32	-152, 87	**-158**	**-263, -52**	**-102**	**-184, -21**	0.2438
Number of pets in home							
1	-53	-161, 54	**-143**	**-237, -49**	**-106**	**-179, -34**	0.2860
>2	-78	-246, 90	**-270**	**-399, -140**	**-199**	**-306, -93**	0.0713
MMEF(mL/s)							
Pet exposure *in utero*	35	-94, 165	-37	-143, 69	-25	-109, 59	0.3267
Pet exposure in the first 2 years	12	-88, 113	-49	-128, 30	-35	-99, 29	0.1174
Current pet exposure	-8	-80, 65	**-123**	**-185, -62**	**-73**	**-121, -25**	**0.0214**
Type of animals in home							
Cat	149	-56, 354	-91	-258,77	-6	-140, 127	**0.0326**
Dog	-34	-151, 83	**-160**	**-252, -68**	**-110**	**-185, -36**	**0.0246**
Bird	9	-229, 246	**-268**	**-488, -48**	-120	-284, 45	0.1229
Farm animals	-136	-380, 108	-193	-406, 20	**-193**	**-357, -29**	0.4405
Other pets	-18	-109, 73	**-80**	**-159, 0**	-51	-113, 10	0.5796
Number of pets in home							
1	-20	-102, 61	**-111**	**-182, -40**	**-72**	**-126, -17**	0.1487
>2	14	-114, 142	**-150**	**-249, -51**	**-84**	**-165, -3**	**0.0216**

β, estimate; CI, confidence intervals. [a]Models for all subjects are adjusted for age, BMI, ETS exposure, parental education, breast feeding status, income, home coal use. Bold font represents the statistically significant difference at $p < 0.05$.

Table 5. Adjusted ORs and 95%CI of lung function impairment in relation to pet ownership exposure in children by the period status (N=6740)

Children	No.	FVC<85%	FEV_1<85%	PEF< 75%	MMEF< 75%
		OR (95%CI)	OR (95%CI)	OR (95%CI)	OR (95%CI)
Without pet exposure any time	4812	1.00	1.00	1.00	1.00
With pet exposure only *in utero*	76	0.34(0.11,1.09)	0.32(0.08,1.32)	1.07(0.42,2.70)	1.06(0.48,2.35)
With pet exposure only in the first 2 years of life	271	**1.45(1.02,2.05)**	1.21(0.79,1.86)	1.08(0.66,1.78)	0.77(0.48,1.25)
With pet exposure only currently	1135	**1.36(1.12,1.67)**	**1.59(1.28,1.98)**	**1.49(1.16,1.90)**	**1.40(1.13,1.73)**
With pet exposure both *in utero* and the first 2 years of life	146	1.09(0.64,1.86)	0.85(0.43,1.70)	0.69(0.30,1.58)	0.91(0.49,1.72)
With pet exposure both *in utero* and currently	32	1.08(0.37,3.12)	0.70(0.16,2.96)	0.46(0.06,3.43)	0.29(0.04,2.17)
With pet exposure both in the first 2 years of life and currently	152	0.94(0.55,1.61)	1.37(0.79,2.35)	**1.89(1.09,3.27)**	**1.78(1.09,2.89)**
With pet exposure in any time	116	**2.23(1.39,3.58)**	**1.88(1.09,3.25)**	1.60(0.82,3.12)	1.41(0.78,2.56)

aOR, adjusted odds ratios; CI, confidence intervals. [a]Models for all subjects are adjusted for age, BMI, ETS exposure, parental education, breast feeding status, income, home coal use. All aOR are compared to the reference category (no pet exposure *in utero*, no pet exposure in the first 2 years, and no current pet exposure). Bold font represents the statistically significant difference at $p< 0.05$.

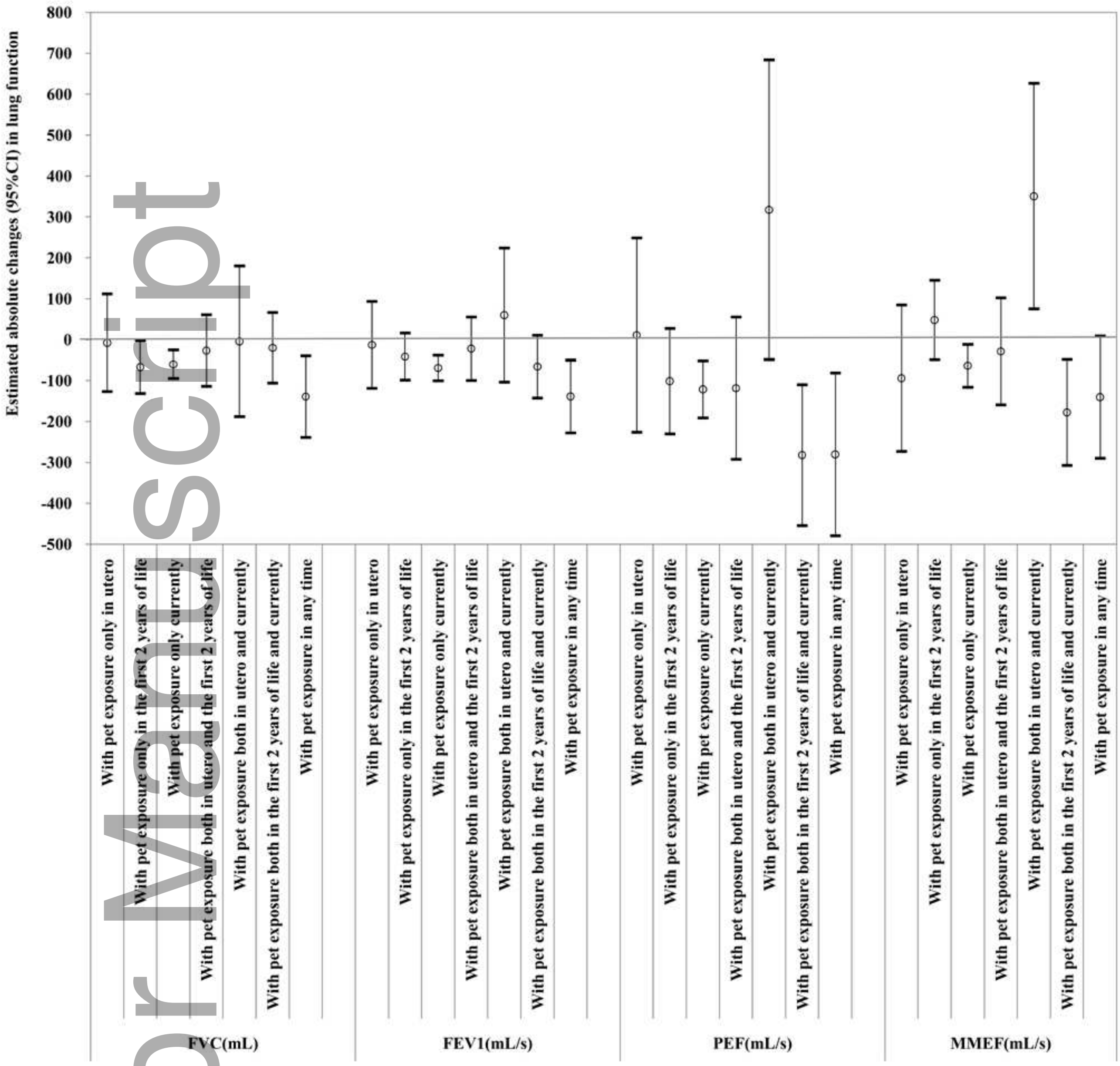

Figure 1 Estimated absolute changes (95%CI) in lung function in relation to pet ownership exposure in children by the period status, with the reference catalog of children without pet exposure any time. Estimates are adjusted for age, gender, BMI, ETS exposure, parental education, breast feeding status, income, home coal use.