



Asthma and asthma related symptoms in 23,326 Chinese children in relation to indoor and outdoor environmental factors: The Seven Northeastern Cities (SNEC) Study

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HIGHLIGHTS

- We studied air pollution and respiratory health in 23,326 Chinese children.
- Home renovation, carpet, and pet were associated with increased ORs of asthma.
- Close to main road, smokestack/factory was associated with increased ORs of asthma.
- Ventilation device use was associated with decreased ORs of asthma.
- PM₁₀, SO₂, NO₂, and O₃ were associated with increased ORs of asthma.

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ABSTRACT

Background: Both the levels and patterns of outdoor and indoor air pollutants have changed dramatically during the last decade in China. However, few studies have evaluated the effects of the present air pollution on the health of Chinese children. This study examines the association between outdoor and indoor air pollution and respiratory diseases among children living in Liaoning, a heavy industrial province of China.

Methods: A cross-sectional study of 23,326 Chinese children aged 6 to 13 years was conducted in 25 districts of 7 cities in Northeast China during 2009. Three-year (2006–2008) average concentrations of particles with an aerodynamic diameter of $\leq 10 \mu\text{m}$ (PM₁₀), sulfur dioxide (SO₂), nitrogen dioxides (NO₂), and ozone (O₃) were calculated from monitoring stations in each of the 25 districts. We used two-level logistic regression models to examine the effects of yearly variations in exposure to each pollutant, controlling for important covariates.

Results: The prevalence of respiratory symptoms was higher for those dwelling close to a busy road, those living near smokestacks or factories, those living with smokers, those living in one-story houses typically with small yards, and those with home renovation, bedroom carpet or pets. Ventilation device use was associated with decreased odds of asthma in children. The adjusted odds ratio for diagnosed asthma was 1.34 (95% confidence interval [CI], 1.24–1.45) per 31 $\mu\text{g}/\text{m}^3$ increase in PM₁₀, 1.23 (95%CI, 1.14–1.32) per 21 $\mu\text{g}/\text{m}^3$ increase in SO₂, 1.25 (95%CI, 1.16–1.36) per 10 $\mu\text{g}/\text{m}^3$ increase in NO₂, and 1.31 (95%CI, 1.21–1.41) per 23 $\mu\text{g}/\text{m}^3$ increase in O₃, respectively.

Conclusion: Outdoor and indoor air pollution was associated with an increased likelihood of respiratory morbidity among Chinese children.

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1. Introduction

Asthma is a chronic inflammatory lung disease characterized by recurrent episodes of breathlessness, wheezing, coughing, and chest tightness. Asthma is the most common respiratory diseases in young children, affecting up to 30% of children (Pearce et al., 2007). Although recent studies indicated that it has plateaued or may even be declining in many developed countries, in developing countries including China, the prevalence of asthma has started to increase in the most recent decade (Montefort et al., 2011; Pearce et al., 2007). Research suggests that

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this increase cannot be explained by genetic factors and improvements in diagnostic methods alone, environmental factors including outdoor and indoor air pollution may play an important role in increasing the asthma epidemic (Dong et al., 2011; Heinrich, 2011; McConnell et al., 2006; Peters et al., 1999; Zhang et al., 2002). Although numerous epidemiologic studies have examined the links between air pollution and respiratory diseases in children, the results of these studies are not consistent (Almqvist et al., 2010; Behrens et al., 2005; Brunekreef et al., 2012; Bufford and Gern 2007; Fuertes et al., 2013; Gruzieva et al., 2013; McConnell et al., 2006; Peters et al., 1999; Zhang et al., 2002). For example, evidence shows that indoor air pollution such as pets exposure in home (Behrens et al., 2005; Brunekreef et al., 2012; Lombardi et al., 2010) and ambient air pollution (Peters et al., 1999; Zhang et al., 2002) all exacerbate respiratory diseases in children, whereas, several studies have reported that those exposed to pets had a lower prevalence of allergic rhinitis and asthma in childhood (Almqvist et al., 2010; Bufford and Gern 2007; Horak et al., 2002). Furthermore, two recent large cross-sectional European studies found no clear association between incidence of asthma and traffic-related ambient air pollutants among more than 10,000 children (Fuertes et al., 2013; Gruzieva et al., 2014). Some of the inconsistencies in reported associations between air pollution and respiratory health may be due to differences in air pollutant sources and composition between different regions (Kim et al., 2008; Kim et al., 2005).

With the rapid development of economic and urbanization in China, the levels and patterns of outdoor and indoor air pollutants have changed dramatically. The levels of inhalable particles (less than 10 μm in diameter [PM_{10}]) and sulfur dioxide (SO_2) in many cities are higher than the national standard and WHO guidelines, although they have declined gradually in recent years (Dong et al., 2013; Zhang et al., 2002). Concurrently, with the rapid increase in motor vehicle ownership, the composition of urban air pollution has shifted from coal smoke to a mix of coal smoke and motor vehicle emission and the levels have stayed high since the 2000s. Meanwhile, the levels of

indoor coal smoke pollution have decreased rapidly as more people have moved to new houses with gas or electric power. New building materials, household pets, and tobacco smoke exposure have also affected the types and levels of indoor air pollution. However, few studies have evaluated the health effects of the changing and mixing air pollution in China in the past decade. To evaluate the associations between air pollution and children's respiratory symptoms and illnesses, we conducted a cross-sectional survey in seven cities in Liaoning province, an industrial area of Northeastern of China.

2. Material and methods

2.1. Study city selection and subject recruitment

The Seven Northeastern Cities study is a cross-sectional study of respiratory health effects of exposure to ambient air pollutants. In order to maximize the inter- and intra-city gradients of the pollutants of interest and minimize the correlation between district-specific ambient pollutants, in April 2009, we selected seven cities (Shenyang, Dalian, Anshan, Fushun, Benxi, Liaoyang, Yingkou) from Liaoning province based on air pollution measurements between 2006 and 2008. Locations of the study cities are shown in Fig. 1. There are five districts in Shenyang, four districts in Dalian and Fushun, and three districts in Anshan, Benxi, Liaoyang and Yingkou, respectively. Each district has only one municipal air monitoring station that generated air pollution data continuously. An elementary school within 1 km of the air monitoring sites was randomly selected from each district, resulting in a total of 25 elementary schools. The participants' home is within one mile from the monitoring stations as well as from the school or kindergarten. Our entry criterion was "the subject should have lived at that place for at least 3 years". The procedures followed were in full accordance with ethical standards of the responsible committee on human experimentation of the China Medical University, and with the principles outlined in the Helsinki Declaration. Endorsed consent forms were obtained from the parents or guardians of the children before their participation in this study.

2.2. Assessment of ambient air pollution exposure

Concentrations of ambient PM_{10} , SO_2 , nitrogen oxides (NO_2), and ozone (O_3) in 2006–2008 were obtained from municipal air pollution monitoring stations. PM_{10} , SO_2 , NO_2 , and O_3 measurements at the municipal monitoring stations strictly followed the standard methods set by the State Environmental Protection Administration of China (1992). The most advanced ambient air automatic monitoring system was used to collect air pollution data across the study cities following the standardized procedures (Dong et al., 2013; Zhang et al., 2002). These standardized procedures were adopted from those of the US Environmental Protection Agency and have been accepted by both US and China sides. Concentrations of each pollutant are measured continuously and reported hourly- PM_{10} by beta-attenuation, SO_2 by ultraviolet fluorescence, NO_2 by chemiluminescence, and O_3 by ultraviolet photometry. Daily 24-hour averages of PM_{10} , SO_2 , and NO_2 ; and daily 8-hour averages (10:00 AM–6:00 PM) of O_3 were calculated based on data from days for which at least 75% of the valid 1-hour values were available. Yearly mean concentrations were calculated from the arithmetic means of all valid daily mean concentrations within the year. Yearly mean concentrations were reported for each monitor only when at least 75% of daily observations for that year were available. The 3-year (2006–2008) average concentrations for each pollutant were reported for each monitor.

2.3. Questionnaire survey

We included respiratory health related questions from the Epidemiologic Standardization Project Questionnaire of the American Thoracic Society (ATS-DLD-78-A) (Ferris, 1978), which has been well validated in previous studies (Dong et al., 2011; Hwang and Lee, 2010;



Fig. 1. Locations of the study cities in Liaoning Province, northeast of China.

Table 1
Housing characteristics and environmental factor exposure in Chinese children ($N = 23,326$).

House characteristics	Definition	Prevalence
House type		
dan-yuan-lou-fang	An apartment unit in a multistory, multiunit building	89.4%
ping-fang	A one-story house typically with a small yard	8.0%
others	Refers to dormitory or any other unspecified house type	2.6%
Having smokestack or factory around house	There was pollution source such as factory and smokestack around the house (<100 m)	20.6%
Home coal use	The use of coal in a household for cooking or space heating	7.7%
Ventilation device use	The use in a household of any of the following ventilation devices: exhaust fan, chimney, or fume hood (typically above a cookstove)	81.4%
House pets	Refers to the feeding in a household of the following pets: dog, cat, bird, chicken, duck, or goose	17.1%
Home renovation	Conducted any of the following renovations in home within the recent 2 years. The choices were installation of linoleum floor, painting, new furniture, wall covering, and suspended ceiling.	33.7%
Early-life exposure: ETS exposure when child was younger than 2 years	Between the times this child was born and he or she turned 2 years old, there some smokers in regular contact with the child including regular visitors, for example, grandparents or baby-sitters.	23.7%
Father smoking	Paternal smoking while living in the home with their children	39.2%
Mother smoking	Maternal smoking while living in the home with their children	0.9%
Parental atopy	A history of maternal or paternal asthma, hay fever, allergic eczema, or allergic conjunctivitis.	4.8%

McConnell et al., 2006; Peters et al., 1999; Salo et al., 2004; Zhang et al., 2002). This questionnaire (ATS) has also been translated into Chinese for previous studies in other Chinese cities (Dong et al., 2011; Hwang and Lee, 2010; Zhang et al., 2002). The questionnaire included detailed questions on date of birth, sex, birth weight, breast-feeding, number of years lived in each residence, types and characteristics of dwelling, method of cooking and heating, location of kitchen, types of home ventilation devices (if any), history and current status of children's respiratory illnesses and symptoms, parental education levels, smoking status of parents and other household members, and parental respiratory health histories. Local study staff informed students about the survey at the participating schools. After signing the written parental consent, parents were invited to a parents' night with the attendance of study staff where teachers explained the study and the conditions of consent. Parents who wished to complete the questionnaire at home returned it (via their child) to the teacher in an envelope. All questionnaire responses were recorded electronically in a database according to a standardized code and file structure. Definitions of housing characteristics and environmental tobacco smoke (ETS) exposure in children were shown in Table 1. The information about "distance from house to main road" and "with a smokestack near home" was gathered from the questionnaire by the following questions: "How long is the distance from the child's house to main traffic road: 1) <20 m, 2) 20–100 m, 3) >100 m", and the question "How long is the distance from the child's house to the smokestack: 1) <20 m, 2) 20–100 m, 3) >100 m, and 4) no smokestack near the home". Here, main road refers to have two or more multi-lane roadways separated by a median. Smokestack, namely a large chimney, refers to the supporting structure for discharging smoke from heating boiler which is used to supply heat by burning coal for the most people living in apartment building during winter time.

2.4. Definitions of respiratory symptoms and illnesses

The following specific respiratory symptoms and illnesses were determined from questionnaire responses: *a) Persistent cough*: the answers to several cough-related questions which indicate that the study child has cough on most days (4 or more days per week) for at least 3 months a year either with or without cold during the last 12 months. *b) Persistent phlegm*: the answers to several phlegm-related questions which indicate that the study child has been seem congested or brought up phlegm, sputum, or mucus from the chest on most days (4 or more days per week) for at least 3 months a year either with or without cold during the last 12 months. *c) Doctor diagnosed asthma*: a yes answer to the question "Has a doctor ever diagnosed asthma in your child?" *d) Current asthma*: for those children who have been diagnosed with asthma, a "yes" answer to the question, "Has this child

experienced an asthma attack in the past two years?" or a yes answer to the question "Does this child take medicine or treatment for asthma or asthmatic bronchitis?". *e) Current wheeze*: a yes answer to the question "Does this child's chest ever sound wheezy or whistling, including times when he or she had a cold?" and a yes answer to the question "Has this child had 2 or more such episodes in last 12 months?"

2.5. Statistical methods

The data was analyzed using SAS software (version 9.1; SAS Institute, Cary, N.C., USA). We studied the relationship between district-specific ambient levels of pollutants and prevalence rates of the following questionnaire-based morbidity end points: persistent cough, persistent phlegm, doctor diagnosed asthma, current asthma, and current wheeze. We estimated odds ratios in a two-stage hierarchical model using logistic and ecologic model analyses. The models assume two sources of variation: the variation among subjects in the first stage, part of which could be explained by the individual confounders, and the variation of air pollution among districts in the second stage, part of which could be explained by variables measured at the municipal level. In the analyses we specify that 1) the outcome variable follows the Bernoulli distribution; 2) intercept terms are random at the municipal level; and 3) all the explanatory variables have fixed effects. A logistic regression model was fitted in the first stage for the risk of asthma and asthma related symptoms as a function of site-specific intercepts, j , where $\alpha_j = 1, \dots, 25$, and personal covariates. The adjusted site-specific intercepts and prevalence rates are related by $P_j = e^{\alpha_j} / (1 + e^{\alpha_j})$. In the second stage, these intercept terms representing the logit of the site-specific prevalence rates (P_j ; $j = 1, \dots, 25$), adjusted for personal covariates, were regressed on each site-specific ambient pollutant level by using a linear "ecologic" regression, i.e., $\text{logit } \alpha_j = \alpha + U_j + \beta Z_j$, where U_j denotes the random departure from the predicated prevalence α_j on the logit scale for site j ; Z_j denotes the ambient pollution level for site j . Thus, β can be interpreted as the log odds ratio (per interquartile changes) for each pollutant, adjusted for personal characteristics. The results from the models are presented as odds ratios (ORs), along with their 95% confidence intervals (CIs). The goodness of fit was assessed by likelihood ratio tests (LR) to determine whether a variable contributed significantly to the model. First, we fitted a full model with a complete set of covariates. To elaborate sources of confounding, we fitted models with different combinations of covariates and compared the effect from models with and without the covariate of interest. A covariate was retained in the final model if it was associated with a p -value less than 0.15. A two-tailed probability value of ≤ 0.05 was considered to be statistically significant. Analyses were performed on all subjects, as well as on male and female subjects separately.

Table 2

Distribution of 3-year average air pollutant concentrations ($\mu\text{g}/\text{m}^3$) between 25 districts in seven cities of Liaoning Province 2006–2008.

	PM ₁₀	SO ₂	NO ₂	O ₃
Mean $\pm$ SD	124.2 $\pm$ 24.1	50.3 $\pm$ 16.8	36.7 $\pm$ 7.6	54.8 $\pm$ 16.1
Min	79	20	21	34
5%	87	23	24	36
25%	106	41	32	42
50%	128	50	36	49
75%	137	62	42	65
95%	159	78	47	87
Max	171	80	51	89
Interquartile range ^a	31	21	10	23
National standard ^b	100	60	40	160
% of >NS	76	32	36	0
WHO guideline ^c	20	20	40	100
% of >WHO	100	96	36	0

Abbreviations: PM₁₀, particles with aerodynamic diameter 10 μm or less; SO₂, sulfur dioxide; NO₂, nitrogen dioxide; O₃, ozone.

^a Range from 25th to 75th percentile of district-specific concentrations.

^b China national ambient air quality standard.

^c WHO air quality guidelines, 2005.

3. Results

3.1. Air pollution levels

Table 2 summarizes the distribution of the annual mean air pollutants concentrations in the 25 monitoring stations in the year 2006–2008. Percentages of concentrations that exceeded the National

Standard of China (State Environmental Protection Administration, 1996) and WHO Air Quality Guidelines (WHO, 2005) ranged from 72% to 100% of PM₁₀ measurements, 32% to 96% of SO₂, and 36% of NO₂. There are wide variations between districts gradients for PM₁₀ (79–171 $\mu\text{g}/\text{m}^3$), SO₂ (20–80 $\mu\text{g}/\text{m}^3$), and O₃ (34–89 $\mu\text{g}/\text{m}^3$). The correlations of NO₂ with O₃ (0.66) and SO₂ (0.52) tended to be relatively low across the 25 districts, with a higher correlation between PM₁₀ and SO₂ (0.78), and between PM₁₀ and O₃ (0.74).

3.2. Characteristics of subjects

Of a total of 25,271 children, 23,326 returned the medical questionnaire (92.3%). Participation rates varied across districts from 87.9% to 95.3% but did not correlate with either pollution levels or disease prevalence. The children included in the analyses were between 6 to 13 years old, with a mean of 9.5 years (SD 1.9 years). 11,739 children were male. Most children (77.4%) had been breast-fed. The prevalent rates of persistent cough, persistent phlegm, doctor-diagnosed asthma, current asthma, and current wheeze of children were 8.5%, 4.3%, 6.3%, 1.9%, and 5.1%, respectively. The prevalence of asthma and asthma-related symptoms in male were significantly higher than that in female ($p < 0.05$).

3.3. Health effects

Table 3 presents multivariate relationships between the risk of respiratory morbidity and potentially relevant personal or residential characteristics in the first-stage logistic regression. Parental atopic diseases, male, home renovation within the last 2 years, humidifier use at

Table 3

Adjusted odds ratios for housing and personal characteristics association with respiratory morbidity in children, China.

Characteristics	Persistent cough	Persistent phlegm	Diagnosed asthma	Current asthma	Current wheeze
Age (ref: age $\leq$ 7 years old)					
8	0.90 (0.78–1.04)*	0.99 (0.81–1.20)	0.94 (0.80–1.11)	1.00 (0.76–1.30)	0.95 (0.79–1.13)
9	0.82 (0.69–0.97) [†]	0.73 (0.57–0.93) [‡]	0.68 (0.56–0.83) [‡]	0.54 (0.37–0.78) [‡]	0.86 (0.70–1.06)
10	0.89 (0.75–1.05)	1.05 (0.84–1.31)	0.71 (0.58–0.86) [‡]	0.73 (0.52–1.03)*	0.85 (0.69–1.06)
11	0.74 (0.62–0.88) [‡]	0.72 (0.57–0.91) [‡]	0.71 (0.58–0.85) [‡]	0.64 (0.45–0.92) [†]	0.88 (0.70–1.09)
$\geq$ 12	0.58 (0.46–0.72) [‡]	0.68 (0.50–0.91) [‡]	0.58 (0.45–0.75) [‡]	0.53 (0.33–0.84) [‡]	0.69 (0.52–0.92) [†]
Male (ref: female)	1.11 (1.01–1.22) [†]	1.22 (1.07–1.38) [‡]	1.39 (1.25–1.55) [‡]	1.41 (1.16–1.71) [‡]	1.24 (1.10–1.39) [‡]
Height (per inch)	1.00 (0.99–1.00)*	1.00 (0.99–1.01)	1.00 (0.99–1.01)	0.99 (0.98–0.99) [‡]	0.99 (0.98–0.99) [‡]
BIM (kg/m ²)	1.02 (1.01–1.03) [‡]	1.03 (1.01–1.04) [‡]	1.02 (1.01–1.03) [‡]	1.02 (1.00–1.03)*	1.01 (1.00–1.02) [†]
Breast feeding (yes vs. no)	0.78 (0.70–0.87) [‡]	0.69 (0.60–0.80) [‡]	0.78 (0.69–0.89) [‡]	0.80 (0.64–0.99) [†]	0.81 (0.71–0.93) [‡]
Number rooms $\geq$ 3 (ref: <3)	1.03 (0.94–1.14)	1.17 (1.02–1.34) [†]	1.07 (0.95–1.20)	0.88 (0.72–1.07)	0.99 (0.88–1.12)
Distance from house to main road (ref: the distance $\geq$ 100 m)					
<20 m	1.37 (1.21–1.56) [‡]	1.17 (0.98–1.39)*	1.20 (1.04–1.38) [†]	1.21 (0.94–1.56)*	1.24 (1.05–1.45) [‡]
20–100 m	1.17 (1.05–1.30) [‡]	1.01 (0.87–1.17)	1.12 (0.99–1.27)*	1.04 (0.84–1.30)	1.09 (0.95–1.25)
Having smokestack or factory around house (Yes vs no)	1.10 (0.98–1.23)*	1.01 (0.86–1.18)	1.14 (1.00–1.29)*	1.13 (0.90–1.41)	1.15 (1.00–1.33)*
House type (ref: dan-yuan-lou-fang)					
ping-fang	0.82 (0.65–1.04)*	1.31 (0.97–1.76)*	1.22 (0.94–1.57)*	1.23 (0.78–1.97)	1.05 (0.78–1.41)
Other (dorm, etc.)	1.61 (1.24–2.09) [‡]	1.91 (1.38–2.64) [‡]	0.86 (0.59–1.27)	1.03 (0.53–2.01)	1.37 (0.93–2.02)*
Home coal use (Ref: no coal use)	1.00 (0.80–1.26)	0.69 (0.50–0.94) [†]	0.98 (0.76–1.27)	0.79 (0.49–1.30)	1.04 (0.78–1.40)
Bedroom carpet use (ref: no use)	1.40 (1.02–1.94) [†]	1.20 (0.78–1.85)	1.38 (0.96–1.99)*	1.94 (1.13–3.35) [†]	1.47 (0.98–2.20)*
House pets (ref: no pet in home)	1.73 (1.55–1.93) [‡]	2.04 (1.77–2.35) [‡]	1.44 (1.26–1.64) [‡]	1.06 (0.83–1.36)	1.22 (1.05–1.41) [†]
Home renovation (yes vs. no)	1.42 (1.28–1.57) [‡]	1.71 (1.49–1.96) [‡]	1.42 (1.26–1.59) [‡]	1.41 (1.15–1.73) [‡]	1.29 (1.14–1.47) [‡]
Ventilation device use (yes vs. no)	0.79 (0.69–0.90) [‡]	0.80 (0.67–0.96) [†]	0.93 (0.80–1.09)	0.87 (0.66–1.15)	1.00 (0.84–1.20)
Question respondent (Ref: other than mother)					
Parents' education level (Ref: above junior high school)	0.91 (0.78–1.07)	0.86 (0.69–1.06)	1.20 (0.98–1.47)*	1.17 (0.82–1.70)	1.14 (0.91–1.44)
Father smoking (Ref: father nonsmoking)	0.90 (0.81–1.00)*	0.87 (0.76–1.00)*	0.90 (0.80–1.02)*	1.02 (0.82–1.28)	1.15 (1.00–1.32)*
Mother smoking (Ref: mother nonsmoking)	1.15 (1.04–1.27) [‡]	1.19 (1.03–1.37) [†]	1.14 (1.02–1.28) [†]	1.17 (0.95–1.45)*	1.32 (1.16–1.51) [‡]
Passive smoking before 2 years old (Yes vs. no)	1.80 (1.25–2.58) [‡]	1.76 (1.11–2.79) [†]	1.03 (0.63–1.67)	0.76 (0.28–2.07)	1.26 (0.77–2.08)
Parental atopy	1.33 (1.19–1.49) [‡]	1.27 (1.09–1.48) [‡]	1.58 (1.40–1.79) [‡]	1.64 (1.32–2.04) [‡]	1.61 (1.41–1.85) [‡]
	1.56 (1.30–1.88) [‡]	1.92 (1.52–2.41) [‡]	2.14 (1.78–2.58) [‡]	2.52 (1.88–3.38) [‡]	2.45 (2.02–2.97) [‡]

Items with asterisks are included in the final adjustment model for this measurement. These items are adjusted for each other; remaining variables are adjusted only for the footnoted items, as well as for districts.

* $p < 0.15$; [†] $p < 0.05$; [‡] $p < 0.01$.

Table 4
Adjusted odds ratios of respiratory illness on 2006–2008 ambient air pollutants.^a

Symptom	Pollutant	All subjects		Males		Females	
		OR ^b	95%CI	OR ^b	95%CI	OR ^b	95%CI
Persistent cough	PM ₁₀	1.17	1.09–1.25	1.19	1.09–1.31	1.14	1.03–1.25
	SO ₂	1.06	1.00–1.13	1.08	0.99–1.18	1.03	0.94–1.13
	NO ₂	1.22	1.14–1.31	1.29	1.18–1.42	1.15	1.04–1.27
	O ₃	1.12	1.04–1.20	1.17	1.06–1.29	1.06	0.96–1.17
Persistent phlegm	PM ₁₀	1.15	1.05–1.26	1.13	1.00–1.28	1.18	1.03–1.35
	SO ₂	1.11	1.02–1.20	1.13	1.01–1.27	1.08	0.95–1.23
	NO ₂	1.22	1.11–1.34	1.26	1.11–1.43	1.17	1.01–1.34
	O ₃	1.18	1.08–1.30	1.22	1.07–1.38	1.15	0.99–1.32
Doctor-diagnosed asthma	PM ₁₀	1.34	1.24–1.45	1.32	1.19–1.46	1.38	1.23–1.56
	SO ₂	1.23	1.14–1.32	1.20	1.09–1.32	1.27	1.13–1.41
	NO ₂	1.25	1.16–1.36	1.30	1.17–1.45	1.19	1.06–1.34
	O ₃	1.31	1.21–1.41	1.32	1.19–1.47	1.29	1.14–1.45
Current asthma	PM ₁₀	1.49	1.29–1.72	1.39	1.16–1.68	1.64	1.31–2.05
	SO ₂	1.31	1.16–1.49	1.21	1.03–1.43	1.48	1.22–1.80
	NO ₂	1.22	1.06–1.40	1.25	1.04–1.50	1.18	0.95–1.47
	O ₃	1.25	1.09–1.44	1.25	1.04–1.50	1.26	1.01–1.56
Current wheeze	PM ₁₀	1.16	1.07–1.27	1.13	1.01–1.27	1.20	1.06–1.36
	SO ₂	1.02	0.94–1.10	1.00	0.90–1.11	1.04	0.93–1.17
	NO ₂	0.92	0.84–1.01	0.93	0.83–1.05	0.91	0.80–1.04
	O ₃	1.02	0.93–1.12	1.05	0.93–1.19	0.98	0.86–1.12

^a Single pollutant models adjusted for personal and environmental factors. Models for all subjects are adjusted for the variables with asterisks in Table 3.

^b OR were scaled to the interquartile range for each pollutant (31 µg/m³ for PM₁₀, 21 µg/m³ for SO₂, 10 µg/m³ for NO₂, and 23 µg/m³ for O₃). Four models are fit for each symptom or condition, one for each pollutant.

home, and ETS exposure in the first 2 years significantly increased the OR for all five symptoms/illnesses. The incidence for some symptoms/illnesses was significantly lower with greater age, breast feeding, and use of a ventilation device in the kitchen.

The overall adjusted prevalence of chest conditions reported on questionnaires was analyzed by district. Prevalence rates varied considerably among districts. To further examine the air quality/respiratory health relationships, we performed ecologic regression analyses on the district intercept terms (log odds ratios) from the individual level models in Table 3. Table 4 includes results based on the 2006–2008 exposure data. As shown in Table 4, PM₁₀, SO₂, NO₂, and O₃ were associated with asthma and related symptoms. And the associations between doctor-diagnosed asthma and the concentrations of PM₁₀ (OR = 1.34; 95%CI, 1.24–1.45), SO₂ (OR = 1.23; 95%CI, 1.14–1.32), NO₂ (OR =

1.25; 95%CI, 1.16–1.36), and O₃ (OR = 1.31; 95%CI, 1.21–1.41) were statistically significant (Fig. 2). The results also showed that outdoor air pollution effects did not differ between males and females, except for significant associations between the prevalence of current asthma and NO₂ (OR = 1.25; 95%CI, 1.04–1.50), persistent phlegm and O₃ (OR = 1.22; 95%CI, 1.07–1.38) in males but not in females.

4. Discussion

In the present study, several indoor environmental factors and ambient air pollutants were associated with increased prevalence of one or more of the studied respiratory diseases and symptoms in Chinese children. Specially, we observed: (1) Bedroom carpet use, pets in the home, home renovation, and passive smoking exposure were associated

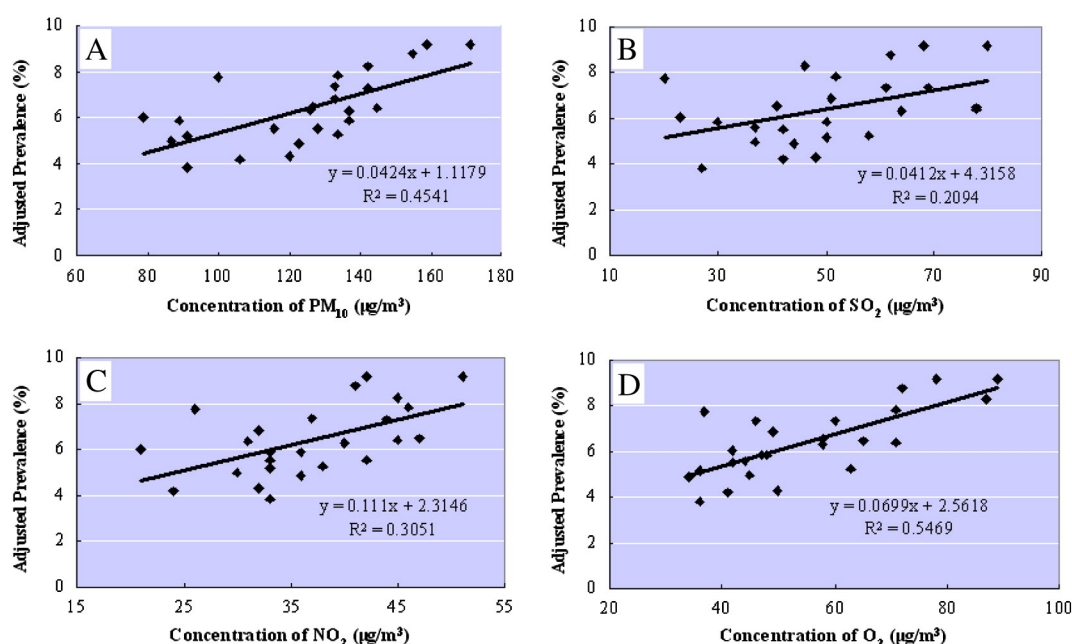


Fig. 2. Correlation between adjusted prevalence of doctor-diagnosed asthma and PM₁₀ (A), SO₂ (B), NO₂ (C), and O₃ (D).

with increased prevalence of asthma and asthma-related symptoms. (2) Living close to a main road, a smokestack or a factory was also positively associated with respiratory diseases and symptoms. (3) Ventilation device use may decrease the prevalence of asthma-related symptoms. (4) Ambient air pollutants were significantly associated with higher prevalence of asthma and asthma-related symptoms in both males and females.

4.1. Effects of household and personal characteristics

We found that certain residential, demographic, and family characteristics were associated with respiratory symptoms and diseases prevalence in school children in Northeast China, independent of outdoor air quality. Children of younger ages had higher prevalence of respiratory morbidities. Males had higher prevalence of respiratory morbidities than females. Breast-feeding was associated with decreased ORs for persistent cough, asthma symptom, and wheeze symptom, suggesting potential favorable effects of breast milk. The age, sex, and breast-feeding effects observed in the present study are consistent with those observed in earlier studies (Gdalevich et al., 2001; Peters et al., 1999; Zhang et al., 2002). In examining the effects of house type, we found that “ping-fang” (one story house) and “other”, compared with *dan-yuan-lou-fang* (apartment), were more likely to be associated with higher prevalence of respiratory morbidity. The reasons for this may be that the environmental health conditions in apartment building are better, for example, in China, water and heat are supplied by district heating systems, and coal or coal gas is used for cooking in concrete apartment building but not in “ping-fang” and “other”. Residential proximity to main roads has been associated with respiratory symptoms (Fuertes et al., 2013; Gruzieva et al., 2013; Perez et al., 2012). As described in Table 3, the prevalence of respiratory morbidity among children was higher with shorter distance from a child's home to an arterial road. Therefore, the traffic air pollution was an important risk factor for respiratory diseases in children. Our results suggested that a smokestack or a factory in the vicinity of the house increased the risk of some respiratory symptoms among children. Study by Căra et al. (2010) and Sultész et al. (2010) also showed similar results. Sultész et al. reported that living not far from an air pollution factory or mine was a significant factor for allergic rhinitis symptoms in 6–12-year-old children (OR = 1.46, 95%CI: 1.18–1.80). The reason may be that a place near a smokestack or a factory has higher concentration of air pollutants.

Indoor air pollution from fuel combustion has long been regarded as an important risk factor for respiratory morbidity and mortality in children (Emmeline and Wall, 2007; Smith et al., 2000). To our surprise, the results showed little association between home coal use and respiratory symptoms. There was even a significantly negative association between coal use and persistent phlegm. An early study in China reported that residential coal use could decrease lung function (Shen et al., 1992). In agreement with our study, Four Chinese Cities Study (Zhang et al., 2002) and Six American Cities Study (Ware et al., 1984) also found a negative association between home coal use and respiratory symptoms of children. However, this finding should be interpreted with care, because there might be large bias in the definition and classification of indoor coal combustion. For example, the investigation of health effects of indoor coal combustion was based on the assumption that other types of fuel were not so ‘dirty’ as coal. Another possible reason is that coal-generated indoor air pollution could be easily diluted by ventilation. Thus, indoor coal use might contribute more to community air pollution levels than to indoor air pollution levels. A third reason might be that children usually stayed out of kitchen when cooking, hence avoided exposure to cooking smoke.

Our findings of significant associations between pet keeping in home and respiratory symptoms are in agreement with other studies. The SIDRIA-2 study in Italy reported that exposure to pets in children in the first year of life was a significant and independent risk factor for

current asthma and asthma related symptoms that appeared at the age of 7 (Lombardi et al., 2010). Results from the International Study of Asthma and Allergy in Childhood (ISAAC) showed a positive association between pet exposure during pregnancy and in the first year of life and asthma, eczema and wheeze in 6- to 7-year-old children (Behrens et al., 2005). Further analysis showed that this positive association was more evident in children in developing countries than in developed countries (Brunekreef et al., 2012). Also, two recent studies showed pet keeping may worsen the relationship between outdoor and indoor air pollution and respiratory symptoms in asthmatic children (Dong et al., 2011; McConnell et al., 2006). In general, inhalation of aeroallergens is considered to increase the risk of asthma development, and sensitization to specific allergens is part of the underlying mechanism. For example, there is strong evidence that occupational exposure to high-molecular-weight allergens increases the risk of asthma (Chan-Yeung and Malo, 1995; Krakowiak et al., 2007). Individuals may become sensitized to specific allergens in the environment and then experience symptoms and signs of asthma when exposed to these allergens. Typically, these reactions can be reproduced in controlled conditions. Our findings of an increased risk of asthma-related symptoms in relation to pet exposure are consistent with this generally accepted theory.

Effects related to home renovation on asthma and asthma symptoms in children were significantly ($p < 0.05$). Recently, the trend for home renovation and decoration has resulted in higher concentrations of formaldehyde and volatile organic compounds, and other chemical pollutants in indoor air (Raw et al., 2004). Substantial evidence indicates that interior surface material use and recent home renovation were associated with an increased risk for developing asthma, asthma-related and other respiratory symptoms (Jaakkola et al., 2004, 2006). The underlying mechanism linking home renovation and respiratory health is unclear. However, some explanations have been hypothesized. Substantial evidence suggests that many renovation materials, including paints, furniture varnish, synthetic carpets, wallpaper, and polyvinyl chloride (PVCs), can emit multiple chemical substances (Bruinen de Bruin et al., 2008; Guo et al., 2009). Some of these chemicals have been shown to have adjuvant effects on T_H2 differentiation and T_H2 cytokine production and have also been shown to provoke the enhancement of mast cell degranulation and eosinophilic infiltration, which influence airway inflammation early on and, therefore, could have an effect on some of the fundamental mechanisms that trigger respiratory symptoms and illness (Bornehag and Nanberg, 2010; Duramad et al., 2007).

The OR for paternal smoking was greater than 1 in all the morbidity outcomes. Some epidemiologic surveys have found that children in early stage tended to be more easily affected by environmental factors (Nafstad et al., 1997; Scholtens et al., 2014). Our study found that passive smoking in the first two years of children's lifetime significantly increased risks for all respiratory morbidities. While some studies reported that maternal smoking had a greater effect on children's respiratory health than paternal smoking because young children tend to stay with their mothers longer than their fathers (Svanes et al., 2004), in the present study, the effect of maternal smoking is actually smaller than that of paternal smoking. Note here also that only 218 (0.9%) mothers reported smoking. In Asia, especially in China, female smoking is less socially acceptable, so the proportion of current women smokers in Chinese cities is lower than in Western countries, where the proportion of maternal smoking has been reported up to 40%, with the proportion of maternal smoking in pregnancy reaching 27% (Svanes et al., 2004). High proportions of women smokers could partly explain the high prevalence of allergic respiratory diseases observed in the Western countries. But it is worth noting the increase in the number of younger and female smokers in recent years in China. Therefore, we should pay due attention to the association between cigarette smoking and children's health, and emphasize the benefit of education for children's health, which will be useful in the prevention of respiratory diseases in children.

4.2. Effects of ambient air pollution

In the present study, among the 7 selected cities, Shenyang is the capital of the province and the largest and most heavily industrialized city of China, where coal is the primary fuel used for heating and industrial processes in the area, which leads to very high levels of ambient air pollution, especially in winter. Shenyang is also a rapidly developing city; the number of automobiles increased from 300,000 in 2000 to 800,000 in 2009, leading to a high level of traffic related air pollution. Anshan and Benxi are known for their iron and steel industry, while Fushun is known for the world's largest artificial pit—an open-pit coal mine—in operation since about the 12th century, and Liaoyang has a large number of chemical plants. Dalian is located near the coast of the Yellow Sea, and Yingkou lies near Liaodong Bay. These differences in city characteristics contributed to the large gradients in concentrations of ambient air pollutants. The average levels of PM₁₀ and SO₂ were around 6 and 2.5 times higher than WHO recommended limits respectively, substantially extending the upper end of the pollution ranges of previous epidemiological studies conducted in Europe (Fuertes et al., 2013; Hoek et al., 2012) and North America (Peters et al., 1999; Strickland et al., 2010). These wide gradients and 'natural' experiment offered us the opportunity to assess the effect of exposure to ambient air pollution on respiratory health among children within such high pollution range. In agreement with other authors, our results showed that outdoor air pollution exposure (defined over 3 recent years) was associated with the prevalence of respiratory diseases.

Although many epidemiological studies have examined the link between ambient air pollution and allergic diseases in children, the evidence of an association between air pollution and asthma onset and prevalence remains insufficient to infer a causal relationship, and the inconsistent results still do not provide a clear overall picture of health damage. Hoek et al. (2012) reported that long-term exposure to air pollution, characterized by the concentration of PM₁₀, is associated with increased respiratory symptoms. A study from Taiwan found that 8.79-ppb increases of NO₂ were associated with an OR of 1.81 (95%CI, 1.14–2.86) for asthma in children (Hwang and Lee, 2010). Even at relatively low ambient concentrations, ambient air pollution also independently contributed to emergency department visits for pediatric asthma (Strickland et al., 2010). On the other hand, the results of the Four Chinese Cities Study, which was conducted between 1993 and 1996, also showed a significantly increased prevalence of persistent phlegm (OR = 3.21, 95% CI:1.55–6.67) for an interquartile increment of PM₁₀ (87 mg/m³) among children, but did not reveal a relationship between ambient NO₂ or SO₂ levels and the prevalence of respiratory symptoms (Zhang et al., 2002). A study of twelve communities of southern California also did not find any association between ambient air pollutants (PM₁₀, O₃, and NO₂) and respiratory symptoms in children (Peters et al., 1999). Furthermore, the GINIplus and LISAPlus birth cohorts study did not find consistent evidence that ambient air pollution increases the prevalence of childhood asthma, allergic rhinitis or aeroallergen sensitization in later childhood using data from birth cohort participants followed for 10 years in three locations in Germany (Fuertes et al., 2013). Also, two recent large cross-sectional multicenter European studies found no clear association between individually assigned TRAP exposures and asthma or wheeze in approximately 10,000 children (MacIntyre et al., 2014) and allergic sensitization in approximately 7000 children (Gruzjeva et al., 2014). Hoek et al. (2012) summarized that these observed effects' heterogeneity in reported associations between air pollution and respiratory health may be due to differences in study design, study area (air pollution exposure contrasts between communities versus within a community), measured pollutants (particulate matter, sulfur dioxide, nitrogen dioxide and ozone), wording of symptom questions, study population (either population based or high risk), inclusion of potential confounders and statistical methods.

Compared with other studies, especially with the studies conducted in China, our study has several advantages. First, a large number of children (23,326) were selected from 25 districts of seven cities in Northeast China. This reduces the risk of finding spurious associations due to unmeasured confounding factors at the study area level as in single studies. Second, compared to European and American children, the residential mobility of Chinese children is low and the density of elementary schools in China is very high. Monitoring stations located near the schools were also likely to be near the students' homes and thus provided good indicators for both school and home exposure. Nevertheless, the present study has some limitations. Firstly, this is a cross-sectional study design, and the findings cannot be applied to a cause-and-effect relationship between indoor/outdoor air pollution and respiratory diseases. Secondly, due to the nature of the survey questions (yes or no), possible misclassification of the environmental risk factors (Passive smoking) may exist. Third, two-pollutant models were not possible due to the high correlation between pollutants. Lastly, we have been unable to control for weather factors (e.g., temperature or humidity) and the positional relationship between selected schools and background monitor sites (the school is up-wind or down-wind of the monitor sites) in this analysis.

5. Conclusions

In conclusion, this large epidemiologic study of Chinese children confirms that indoor air pollution derived from bedroom carpet, pet exposure in the home, home renovation, early-life exposure of ETS and other risk factors were harmful for respiratory health. Outdoor PM₁₀, SO₂, NO₂ and O₃ concentrations were associated with the prevalence of respiratory symptoms among children.

Conflict of interest

Authors report no conflicts of interest. Authors are alone responsible for the content and writing of the paper

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