DOCKETED

Docket Number:	19-BSTD-03
Project Title:	2022 Energy Code Pre-Rulemaking
TN #:	235291
Document Title:	Southern California Gas Company Comments - Comments on Sept 30, 2020, IAQ Workshop
Description:	N/A
Filer:	System
Organization:	Southern California Gas Company
Submitter Role:	Public
Submission Date:	10/16/2020 5:14:30 PM
Docketed Date:	10/19/2020

Comment Received From: Southern California Gas Company
Submitted On: 10/16/2020
Docket Number: 19-BSTD-03

Comments on Sept 30, 2020, IAQ Workshop

Additional Health studies referenced by Ramboll and SoCalGas, part 1

Additional submitted attachment is included below.

Kile *et al. Environmental Health* 2014, **13**:71
http://www.ehjournal.net/content/13/1/71

ENVIRONMENTAL HEALTH

RESEARCH Open Access

A cross-sectional study of the association between ventilation of gas stoves and chronic respiratory illness in U.S. children enrolled in NHANESIII

Molly L Kile[1*], Eric S Coker[1], Ellen Smit[1], Daniel Sudakin[2], John Molitor[1] and Anna K Harding[1]

Abstract

Background: Gas stoves emit pollutants that are respiratory irritants. U.S. children under age 6 who live in homes where gas stoves are used for cooking or heating have an increased risk of asthma, wheeze and reduced lung function. Yet few studies have examined whether using ventilation when operating gas stoves is associated with a decrease in the prevalence of respiratory illnesses in this population.

Methods: The Third National Health and Nutrition Examination Survey was used to identify U.S. children aged 2–16 years with information on respiratory outcomes (asthma, wheeze, and bronchitis) who lived in homes where gas stoves were used in the previous 12 months and whose parents provided information on ventilation. Logistic regression models evaluated the association between prevalent respiratory outcomes and ventilation in homes that used gas stoves for cooking and/or heating. Linear regression models assessed the association between spirometry measurements and ventilation use in children aged 8–16 years.

Results: The adjusted odds of asthma (Odds Ratio [OR] = 0.64; 95% confidence intervals [CI]: 0.43, 0.97), wheeze (OR = 0.60, 95% CI: 0.42, 0.86), and bronchitis (OR = 0.60, 95% CI: 0.37, 0.95) were lower among children whose parents reported using ventilation compared to children whose parents reported not using ventilation when operating gas stoves. One-second forced expiratory volume (FEV_1) and FEV_1/FVC ratio was also higher in girls who lived in households that used gas stoves with ventilation compared to households that used gas stoves without ventilation.

Conclusions: In homes that used gas stoves, children whose parents reported using ventilation when operating their stove had higher lung function and lower odds of asthma, wheeze, and bronchitis compared to homes that never used ventilation or did not have ventilation available after adjusting for other risk factors. Additional research on the efficacy of ventilation as an intervention for ameliorating respiratory symptoms in children with asthma is warranted.

Keywords: Asthma, Wheeze, Bronchitis, Gas stoves, Ventilation, Spirometry, NHANES, Children

---

* Correspondence: Molly.Kile@oregonstate.edu
[1]College of Public Health and Human Sciences, Oregon State University, 15 Milam, Corvallis, OR 97331, USA
Full list of author information is available at the end of the article

Background

Asthma is the most common chronic childhood disease and is characterized by recurrent airway obstruction, bronchial hyper-responsiveness, and airway inflammation [1]. It is also the leading cause of childhood hospitalizations and school absenteeism [2]. There is considerable evidence that air pollution - specifically coarse and fine particulate matter, ozone, sulfur dioxides, and nitrogen oxides - is associated with increased rates of asthma, asthma morbidity, respiratory illness and diminished lung function in children [3-8].

In the indoor environment, gas stoves are a common source of air pollution, including combustion-related particulate matter and nitrogen oxides [9-16]. While gas stoves are primarily used for cooking, approximately 7.7 million U.S. households (9.3%) reported using their gas stove or oven for heat at least once during the previous year [17]. There is considerable evidence from epidemiological studies in developed countries that gas stoves used for cooking and/or heat are associated with an increased risk of asthma and respiratory symptoms in children [9,18-33]. Although other studies that have examined the relationship between gas stoves or nitrogen dioxide levels in homes do not observe significant associations with asthma symptoms in childhood [34-36].

Housing characteristics have been shown to influence indoor air pollution levels. For instance, indoor air concentrations of nitrogen dioxide can be higher than ambient levels if there are unvented combustion appliances in the home, such as gas stoves [37]. Ventilation has also been shown to reduce the concentration of other indoor air pollutants such as formaldehyde and volatile organic compounds [38]. There are many different types of household ventilation systems, some of which are automatic, and some of which require point-of-use operation such as kitchen stove vent hoods. While several studies have examined the role of ventilation on indoor air pollutants and indoor air pollution on children's chronic respiratory illnesses, little is known about the role of behavior related to point-of-use ventilation and how this behavior might influence children's respiratory health [39-41]. Subsequently, we theorized that if gas stoves in homes and their emissions are related to asthma and its symptoms in children, then using ventilation when operating gas stoves should reduce indoor air pollution levels and benefit children's respiratory health outcomes. Specifically, we hypothesized that using ventilation when operating gas stoves should be associated with a lower prevalence of chronic respiratory illnesses in children.

Methods

Study population

The Third National Health and Nutrition Examination Survey (NHANES III) is a nationally representative cross-sectional survey of the civilian non-institutionalized U.S. population conducted by the National Center for Health Statistics from 1988–1994. Participants were administered standardized interviews in their homes and underwent physical examinations and laboratory testing in mobile examination centers [42]. NHANES III includes data on children's respiratory health, spirometry data and residential characteristics, which provide a unique opportunity to assess the relationship between parental habits when using gas stoves and respiratory illnesses in U.S. children.

To focus on the association between respiratory illnesses in children and parental use of ventilation in homes that had gas stoves in their kitchens, the current analysis was restricted to children aged 2–16 years (n = 12,570) whose parents: *i)* reported that a gas stove was used in the past twelve months in their child's primary residence (yes); *ii)* provided information on the presence of ventilation near the gas stove (yes/no) and their use of ventilation (never, rarely, sometimes, or always); *iii)* provided information on their child's respiratory health (doctor-diagnosed asthma [yes/no], doctor-diagnosed bronchitis [yes/no], and chest wheeze [yes/no]); and *iv)* reported their child's body mass index, parental history of asthma or hay fever (yes/no), presence of a pet in the household (yes/no), and history of smoking cigarettes indoors (yes/no). Twelve respondents did not answer the question about ventilation. Fewer participants consented to the examination portion of the survey where measurements were taken to compute body mass index. This resulted in data on 7,378, 7,380, and 7,378 children who resided in a home that had a gas stove in the kitchen and who provided information on asthma, wheeze, and chronic bronchitis respectively. Additionally, spirometry measurements were measured only in a subset of children ≥ 8 years old (N = 2,400). Details on deriving the sample size are provided in Additional file 1: Figure S1. Missing data was assumed to be completely at random.

NHANES III was approved by the National Center for Health Statistics Institutional Review Board. Participants who were 12 to 17 years old and their parents provided informed consent; participants who were 7 to 11 years old provided assent and their parents provided consent; and, parents provided informed consent for those <7 years old.

Behaviors when using gas stoves and ventilation characterization

Parents were asked, "Is there a gas stove or oven used to cook in this house (yes/no)." Only parents who answered "yes" were asked the follow up question about ventilation. Due to this skip pattern design in the NHANES III questionnaire, the analytical sample was restricted to children whose parents answered "yes" to the gas stove question. Children were classified as living in households that used gas stoves for heat (yes/no) based on their parent's response to the question, "Was this gas stove or oven used to heat the house over the past 12 months (yes/no)".

Ventilation was characterized based on parent's response to, "Is there an exhaust fan near this stove that sends fumes outside the home (yes/no)" and, "How often is this exhaust fan used (never, rarely, sometimes, or always)." We classified children as living in a household that did not use ventilation if parents stated that there was no exhaust fan or that they never used the exhaust fan. We classified children as living in a household that used ventilation if parents reported that they rarely, sometimes or always used the exhaust fan.

Respiratory health outcomes

For children aged 2–16 years of age, dichotomous respiratory health outcomes were available including parent-reported: *i)* doctor-diagnosed asthma, *ii)* chest wheeze or whistling in past 12 months, and *iii)* doctor-diagnosed chronic bronchitis.

Lung function tests were performed at the mobile examination centers on children between 8–16 years of age following spirometry protocols issued by the American Thoracic Society [43].

Sociodemographic factors and covariates

Selected characteristics were assessed for their relationship to respiratory outcomes and parental behaviors regarding gas stoves. These included age group, sex, race-ethnicity, parental education, parental history of asthma or hay fever, body mass index percentile for age cut-offs following the U.S. Centers for Disease and Prevention recommended guidelines [44], poverty income ratio, household income < \$20,000, cigarette smoking indoors, heating with a gas stove, the presence of pets in the household (only cats, dogs and birds), type of residence (rural versus urban) and US census region.

Statistical approach

To account for the complex sampling design, data were analyzed using appropriate NHANES sample weights using the "svy" command in Stata version 12.1 (StataCorp, College Station, TX). The weighted proportions of participants with respiratory health outcomes and 95% confidence intervals were calculated for children residing in four different settings in homes: (1) where parents reported using ventilation when operating gas stoves for cooking or heating; (2) where parents reported not using ventilation when operating a gas stove for cooking or heating; (3) where parents reported using ventilation when operating gas stoves for cooking only; and, (4) where parents reported not using ventilation when operating gas stoves for cooking only. Chi-squared tests assessed the association between prevalent respiratory health outcomes and ventilation use. Covariates were included in the models if they were associated with a respiratory health outcome at $\alpha < 0.20$. Additionally, household income below \$20,000, which had the least amount of missing data, was included in each model because prior research has demonstrated a strong association between income and reported ventilation use.

Multivariate linear regression models assessed the association between percent of predicted spirometry measurements (one-second forced expiratory volume [FEV_1], forced vital capacity [FVC], and FEV_1/FVC ratio) and gas stoves in all children aged 8–16 years. These models were also stratified by sex. Reference population spirometry values were calculated using NHANES III race and sex specific estimating equations that accounted for age and height for FEV_1 and FVC, as derived by Hankinson et al. [45] and Collen et al. [46]. Percent-predicted values were calculated by taking the ratio of observed spirometry measurements over predicted values and multiplying by 100%. Model covariates accounted for environmental and host factors such as indoor cigarette smoking, the presence of pets in the home, household income < \$20,000, using a gas stove for heating purposes, and asthma status.

Results

Population characteristics and prevalence rates of respiratory illnesses for children residing in homes that used a gas stove are presented in Table 1. Overall, the unadjusted prevalence of wheeze (14.2% vs. 19.3%, p-value = 0.01, N = 7,380) and bronchitis (3.2% vs. 5.0%, p-value = 0.02, N = 7,378) were lower among children residing in households that reported using ventilation when operating their gas stoves compared to households that did not use ventilation when operating their gas stove. The unadjusted prevalence of asthma (8.1% vs. 11.1%, p-value = 0.11, N = 7,378) was not significantly different between households by ventilation status. The unadjusted prevalence of asthma (8.86% vs. 13.54%, p = 0.04) and wheeze (15.7% vs. 23.26%, p = 0.003), but not bronchitis (3.94% vs. 4.48%, p = 0.62), was lower among children residing in households that reported not using a gas stove for heat compared to households that used a gas stove for heat. In unadjusted models, asthma prevalence was also associated with gender, BMI, parental history of asthma or hay fever, household income < \$20,000, and age group. The unadjusted prevalence of chronic bronchitis was associated with age, race-ethnicity, parental history of asthma or hay fever, indoor cigarette smoke, household income < \$20,000, and census region. The unadjusted prevalence of wheeze was associated with age, parental history of asthma or hay fever, the presence of a pet with fur or a bird in the home, indoor cigarette smoke, race-ethnicity, household

Table 1 Mean percent prevalence with 95% confidence intervals of asthma, wheeze, and bronchitis among children aged 2–16 living in homes with gas stoves by different stove use habits[1]

	Ever diagnosed with asthma (N = 7,390)			**Wheeze in past 12 months (N = 7,392)**			**Ever diagnosed with chronic bronchitis (N = 7,390)**		
Variable	**No. cases**	**Prevalence (95% CI)**	***P-value*[2]**	**No. cases**	**Prevalence (95% CI)**	***P-value*[2]**	**No. cases**	**Prevalence (95% CI)**	***P-value*[2]**
Total cases	572	9.48 (8.87, 11.30)		1,422	16.58 (14.88, 18.28)		329	4.05 (3.08, 5.03)	
Vent used w/gas stove		*n = 7,378*			*n = 7,380*			*n = 7,378*	
Yes	260	8.07 (6.11, 10.59)	*0.11*	643	14.20 (11.79, 17.01)	*0.01*	134	3.17 (2.20, 4.53)	*0.02*
No	310	11.09 (8.42, 14.47)		776	19.30 (16.90, 21.95)		194	5.08 (3.85, 6.67)	
Gas stove used for heating		*n = 7,346*			*N = 7,348*			*n = 7,346*	
Yes	117	13.54 (9.46, 19.03)	*0.04*	278	23.26 (18.35, 29.03)	*0.003*	74	4.48 (2.73, 7.25)	*0.62*
No	447	8.86 (7.16, 10.92)		1,133	15.70 (14.05, 17.52)		251	3.94 (3.03, 5.09)	
Vent and Stove Use		*n = 7,334*			*n = 7,336*			*n = 7,334*	
Vent not used and stove used for cooking and heating	78	13.63 (8.59, 20.97)	*0.13*	197	25.07 (18.58, 32.91)	*0.003*	60	5.43 (3.51, 8.33)	*0.10*
Vent used and stove used for cooking and heating	39	13.40 (7.41, 23.03)		81	20.14 (13.84, 28.38)		14	2.82 (1.09, 7.08)	
Vent not used and stove only used for cooking	224	10.36 (7.48, 14.18)		*568*	18.13 (15.59, 20.99)		130	4.87 (3.52, 6.72)	
Vent used and stove only used for cooking	221	7.67 (5.63, 10.35)		*562*	13.76 (11.32, 16.63)		120	3.20 (2.19, 4.65)	

[1] Unweighted sample sizes and weighted proportions (prevalence).
[2] P-values obtained from χ2 test.

income < $20,000, and BMI. Parental education and urban versus rural residence were not associated with any health outcomes (data not shown).

Multivariate logistic regression models were used to evaluate the odds of chronic respiratory illnesses in children who lived in homes where gas stoves were ventilated and only used for cooking while adjusting for other confounders (Table 2: Model 1). After adjusting for confounders, children who lived in homes where parents reported that they used ventilation were less likely to be diagnosed with asthma (aOR = 0.64, 95% CI: 0.43, 0.97), diagnosed with chronic bronchitis (aOR = 0.60, 95% CI: 0.37, 0.95), or report wheeze (aOR = 0.60, 95% CI: 0.42, 0.86). When parental habits regarding using a gas stove for heating were included as an additional covariate (Table 3: Model 2), only wheeze (aOR = 0.62, 95% CI: 0.44-0.89) and chronic bronchitis (aOR = 0.61, 95% CI: 0.38-0.98) remained significantly associated with vented gas stoves after adjusting for other confounders (p = 0.01 and p = 0.04, respectively). In homes where parents reported using gas stoves only for cooking and not heating, children were significantly less likely to have a diagnosis of

Table 2 Adjusted Odds ratios and 95% confidence intervals for the association between respiratory illnesses in children aged 2–16 years who live in households that use gas stove with ventilation compared to households that use gas stoves without ventilation (Model 1)

	Ever diagnosed with asthma[a] (N = 5,745)		**Wheeze in past 12 months[b] (N = 5,744)**		**Ever diagnosed with bronchitis[c] (N = 7,255)**	
Ventilation of gas stove	**No. cases**	**OR (95% CI)**	**No. cases**	**OR (95% CI)**	**No. cases**	**OR (95% CI)**
No	*269*	1 Ref.	*561*	1 Ref.	*188*	1 Ref.
Yes	*224*	0.64 (0.43, 0.97)*	*458*	0.60 (0.42, 0.86)*	*128*	0.60 (0.37, 0.95)*

*P-value <0.05.
[a] Adjusted for age group, sex, parental history of asthma or hay fever, and furry or feathery pets in the house, household income < $20,000, and BMI percentiles for age.
[b] Adjusted for age group, parental history of asthma or hay fever, furry or feathery pets in the house, indoor tobacco smoke, race-ethnicity, household income < $20,000, and BMI percentile for age.
[c] Adjusted for age group, parental history of asthma or hay fever, indoor tobacco smoke, race-ethnicity, household income < $20,000, and census region.

Table 3 Adjusted Odds ratios and 95% confidence intervals for the association between respiratory illnesses in children aged 2–16 years and gas stove use habits (Model 2)

	Ever diagnosed with asthma[a] (N = 5,646)		Wheeze in past 12 months[b] (N = 5,647)		Ever diagnosed with bronchitis[c] (N = 7,114)	
	No. cases	OR (95% CI)	*No. cases*	OR (95% CI)	*No. cases*	OR (95% CI)
Gas stove used with ventilation						
No	*263*	1 Ref.	*555*	1 Ref.	*184*	1 Ref.
Yes	*224*	0.68 (0.45, 1.04)	*458*	0.62 (0.44, 0.89)*	*128*	0.61 (0.38, 0.98)*
Gas stove used for heating						
Yes	*382*	1 Ref.	*795*	1 Ref.	*239*	1 Ref.
No	*105*	0.56 (0.34, 0.94)*	*218*	0.57 (0.38, 0.85)*	*73*	1.12 (0.66, 1.92)

*P-value <0.05.

[a] Adjusted for gas stove used for heating, age group, sex, parental history of asthma or hay fever, and pets in the house, household income < $20,000, and BMI.

[b] Adjusted for gas stove used for heating, age group, parental history of asthma or hay fever, pets in the house, indoor tobacco smoke, race-ethnicity, household income < $20,000, and BMI.

[c] Adjusted for gas stove used for heating, age group, parental history of asthma or hay fever, indoor tobacco smoke, race-ethnicity, household income < $20,000, and census region.

asthma (aOR = 0.56, 95% CI: 0.34-0.94) and wheeze (aOR = 0.57, 95% CI: 0.38-0.85), compared to children in homes that used a gas stove for cooking and heating after adjusting for other confounders. The odds of chronic bronchitis, however, was not significantly different for households that used a gas stove only for cooking compared to households that used a gas stove for cooking and heating (aOR = 1.12, 95% CI: 0.66-1.92) after adjusting for other confounders.

Table 4 examined the potential for joint effects of ventilation practices and using the gas stove for heating on respiratory illness in children. Compared to children living in homes where parents reported not using ventilation and who also used the gas stove for heat, using ventilation lowered the odds of asthma in children by 14%; not using the stove for heat lowered the odds by 38%; and using ventilation and not using the stove for heat lowered the odds by 59%. Similar results were found for wheezing. However, no significant association was observed for the joint effect of ventilation and using the gas stove heat on the odds of chronic bronchitis.

The relationship between lung function and behavioral factors related to gas stoves are presented in Table 5. The FEV_1 measurements ranged between 468 mL to 5683 mL with a weighted mean and standard deviation of 2658 mL and 882 mL. The FVC measurements ranged between 864 to 6846 mL with a weighted mean and standard deviation of 3069 mL and 1036 mL. For the FEV_1/FVC ratio, we observed a range between 31.6% and 100% with a weighted mean and standard error of 86.9% and 0.2%. Among children aged 8–16 years who provided spirometry measurements, unadjusted mean FEV_1 and FVC were higher in children who lived in homes where parents used an exhaust vent compared to children who lived in homes where there was no exhaust vent or parents reported not using the exhaust vent when operating their gas stoves (Table 5). Table 6 compares the percent of predicted (or normalized) differences in spirometry measurements among children aged 8–16 years in households that operated gas stoves with ventilation compared to households that operated gas stoves without ventilation. In fully adjusted models, the overall percent-predicted FEV_1 ($p = 0.08$), FVC ($p = 0.20$) and FEV_1/FVC ($p = 0.11$) were modestly higher in children living in homes with vented gas stoves compared to homes without ventilation of gas stoves, although these did not reach statistical significance (Table 6). Although after stratifying by sex, we observed that the percent-

Table 4 Adjusted Odds ratios and 95% confidence intervals for respiratory illnesses in children aged 2–16 years and the joint association between ventilation (yes/no) and gas stove use habits (cooking only/cooking and heating)

	Asthma[a] (N = 5,646)		Wheeze[b] (N = 5,647)		Bronchitis[c] (N = 7,114)	
	No. cases	aOR (95% CI)	*No. cases*	aOR (95% CI)	*No. cases*	aOR (95% CI)
Vent not used and stove used for cooking & heating	*69*	1 Ref.	*156*	1 Ref.	*59*	1 Ref.
Vent used and stove used for cooking & heating	*36*	0.86 (0.34, 2.17)	*62*	0.62 (0.31, 1.20)	*14*	0.49 (0.21, 1.12)
Vent not used and stove used only for cooking	*194*	0.62 (0.32, 1.23)	*399*	0.57 (0.35, 0.92)*	*125*	1.05 (0.61, 1.81)
Vent used and stove used only for cooking	*188*	0.41 (0.23, 0.74)*	*396*	0.35 (0.21, 0.60)*	*114*	0.65 (0.36, 1.19)

*P-value <0.05.

[a] Adjusted for age group, sex, parental history of asthma or hay fever, household income < $20,000, pets in the house, and BMI.

[b] Adjusted for age group, parental history of asthma or hay fever, pets in the house, indoor tobacco smoke, race-ethnicity, household income < $20,000, and BMI.

[c] Adjusted for age group, parental history of asthma or hay fever, indoor tobacco smoke, race-ethnicity, household income < $20,000, and census region.

Table 5 Univariate association between behaviors related to gas stove use and spirometry measurements for FEV_1 (mL), FVC (mL) and FEV_1/FVC Ratio in children aged 8–16 years

	N	Mean FEV_1 (95% CI)	Mean FVC (95% CI)	FEV_1/FVC (95% CI)
All	*2,472*	2658 (2586, 2730)	3069 (2977, 3161)	86.9% (86.5, 87.3)
Vented Gas Stove				
Yes	*1,147*	2742 (2645, 2841)*	3147[†] (3027, 3267)	87.4% (86.8, 88.0)
No	*1,325*	2562 (2457, 2668)	2981 (2850, 3113)	86.4% (85.8, 87.1)
Gas Stove Used for Heating				
Yes	*441*	2569 (2385, 2755)	2963 (2751, 3175)	86.9% (85.9, 87.9)
No	*2,017*	2670 (2595, 2744)	3084 (2989, 3179)	86.9% (86.5, 87.3)

*p-value ≤0.05.
[†]0.05 < p-value ≤ 0.1.

predicted FEV_1 was almost 3% higher in girls ($p = 0.02$) that lived in homes where parents reported using ventilation compared to homes where ventilation was not used. There was no significant association between venting of gas stoves with FVC in girls ($p = 0.13$). The percent-predicted FEV_1/FVC ratio was 1.6% (95%CI: 0.16, 3.0, p-value = 0.03) higher among girls living in homes that reported vent usage compared to girls in homes that reported not using ventilation with gas stoves (Table 6). No associations between spirometry measurements and ventilation were observed in boys. In addition, no association between spirometry and heating with a gas stove were observed overall or in the sex-stratified analysis.

Discussion

The results show that among children who live in households with a gas stove kitchen appliance, the prevalence of respiratory illness was lowest in children when ventilation was used when operating the gas stove and when the gas stove was not used for heat. Our finding support previous analysis of NHANES III by Lanphear et al. [28], which found that using a gas stove for heating increased the likelihood of asthma in children. Our analysis suggests that ventilation is likely an effect modifier of this association. Furthermore, we observed better lung function in children living in households where ventilation was used when operating the gas stove than in households that did not have ventilation or where no ventilation was used. This association with lung function was only significant in girls and it is unclear whether this stems from a greater sensitivity to gas stove emissions or differential behaviors that would result in more frequent exposure to gas stoves. Children's lung function, however, was not associated with parental report of using the gas stove for heat.

While indoor air pollution measurements are not available in NHANESIII, there is considerable evidence that gas stoves emit pollutants that adversely impact respiratory health and lend biological plausibility to our findings. Gas cooking and heating are a major source of nitrogen dioxide in the indoor environment [34-36]. In animal models, dose-dependent effects of nitrogen dioxide include activation of nuclear factors (NF-kB) within airway epithelial cells, resulting in neutrophilic inflammation and increased release of inflammatory cytokines [47]. Other mechanistic studies have consistently described that nitrogen dioxide has adjuvant properties in the development of allergic asthma by promoting eosinophilia, and the production of antigen-specific IgE and IgG antibodies [48]. In epidemiological studies, short- and long-term exposure to nitrogen dioxide has been inversely associated with FEV1 in pediatric populations [49,50]. A recent prospective epidemiological study found a higher

Table 6 Differences in percent of predicted spirometry (observed/predicted*100%) indicators among children aged 8–16 years in households that operated gas stoves with ventilation compared to households that operated gas stoves without ventilation that is stratified by gender (females N = 1,192; males N = 1,186)

		FEV_1 (Crude)	FEV_1 (Adjusted)[a]	FVC (Crude)	FVC (Adjusted)[a]	FEV_1/FVC (Crude)	FEV_1/FVC (Adjusted)[a]
		Difference[b] (95% CI)	Difference[b] (95% CI)	Difference[b] (95% CI)	Difference[b] (95% CI)	Difference[b] (95% CI)	Difference[b] (95% CI)
	N	*2,378*	*2,335*	*2,3378*	*2,335*	*2,378*	*2,335*
All	*1113*	2.75 (0.29, 5.21)*	2.33 (−0.29, 4.95)	2.08 (−0.66, 4.82)	1.75 (−0.95, 4.44)	1.14 (−.03, 2.31)	0.97 (−0.24, 2.17)
Female	*570*	2.86 (0.71, 5.01)*	2.93 (0.57, 5.30)*	1.6 (−0.4, 3.6)	1.76 (−0.51, 4.02)	1.45 (0.05, 2.85)*	1.58 (0.16, 3.00)*
Male	*543*	2.62 (−1.36, 6.61)	1.74 (−1.74, 5.24)	2.24 (−2.47, 6.96)	1.59 (−2.14, 5.32)	0.87 (−0.56, 2.30)	0.43 (−0.94, 1.81)

[a]Adjusted for environmental tobacco smoke, using a gas stove for heating, furry or feathery pets in the home, asthma status and household income < $20,000.
[b]NHANESIII reference spirometry measurements derived from Hankinson et al. [45].
*P-value <0.05.

risk of asthma morbidity among asthmatic children exposed to nitrogen dioxide levels below the US EPA outdoor air standard [51]. Polycyclic aromatic hydrocarbons (PAHs), another pollutant emitted from gas stoves, is also known to augment the allergic response by enhancing the release of inflammatory mediators in the immune system [52,53]. Polycyclic aromatic hydrocarbons are commonly found in association with fine particulate matter ($PM_{2.5}$), which has been inversely associated with FEV_1 in preschool children [54]. A recent case–control study in children found strong associations between environmental exposure to PAHs and multiple asthma-related biomarkers including IgE and inflammatory cytokines [55].

Using an exhaust fan can improve indoor air quality and reduce pollutants generated from gas stoves [9-16,56-58]. Thus, it is plausible that children who live in households that use exhaust fans when operating their gas stoves have better lung function and lower odds of respiratory illnesses. The assessment of the presence or absence of an exhaust fan in homes with gas stoves may be an important environmental factor to consider when taking an exposure history. Physicians, nurses, or health educators could encourage parents to use exhaust fans when operating gas stoves as an additional intervention for improving their children's respiratory health. Further, physicians, nurses and health educators could discourage the use of a gas stove as a household heating source.

It is important to note that this study has several limitations. While the study is generalizable to all U.S. non institutionalized children ages 2–16 years of age, it is cross-sectional and so we cannot comment on the temporal relationship between households with gas stoves, parental use of ventilation, and respiratory illnesses. NHANES III does not measure indoor air pollution levels which also limits our ability to quantitatively evaluate the relationship between gas stove emissions, ventilation practices, and respiratory outcomes. This analysis did not control for ambient air pollution concentrations because this data is not collected in NHANES and while it is possible to link NHANES data to ambient air pollution this would require access to restricted data that was outside the scope of this study. Nor did this survey collect information on the specific type of ventilation system or its effectiveness. Collecting information on the types of ventilation and its effectiveness by quantitatively measuring indoor air pollution in a nationally representative survey, like NHANES, would be very useful for future studies examining the relationship between gas stoves and respiratory health. Additionally, both the exposures and the outcomes in this study relied upon parental recall which may be a source of bias. It is therefore possible that respondents under-reported smoking behaviors which could explain why indoor smoke exposure was not a risk factor for asthma even though exposure to environmental smoke exposure was a risk factor for bronchitis in this sample. However, the consistency of our results between parental-reported respiratory illnesses in children and quantitative lung function measurements provide additional confidence in the association between ventilation practices and children's respiratory health. There were also missing observations, particularly for BMI because fewer people consent to the physiological measurement portion of the survey. However, when we analyze the data without BMI using the larger sample size, the statistical significance of the observed associations did not change in any meaningful way for asthma or wheeze (data not shown). Missing data could lead to selection bias but the consistency in the results (with or without BMI) makes this seem unlikely. Finally, the survey only queried respondents about ventilation if they indicated that they had a gas stove making it impossible to evaluate the effect of ventilation on respiratory outcomes in homes that electric stoves. Moreover, we opted to categorize ventilation usage using an extreme dichotomy (no exhaust fan or never use exhaust fan versus rarely, sometimes and always using exhaust fan) rather than four gradations of ventilation use (never, rarely, sometimes and always) because the division between rarely and sometimes is somewhat ambiguous and only 15 people with asthma and 17 people with bronchitis reported "rarely" using their exhaust fan.

Conclusion

This study observed that using a ventilating exhaust fan when operating a gas stove for cooking or heating was associated with a lower prevalence of asthma and other chronic respiratory symptoms in U.S. children after adjusting for other risk factors. Ensuring that ventilation is installed near gas stoves and that it is used when operating gas stoves is important, as is, only using gas stoves for cooking and not as an auxiliary heat source. The built environment and how people interact with their built environment, such as gas stoves, can change over time and it is important that national surveys continue to ask questions about gas stoves, ventilation, and behaviors related to their use in surveys that also collect information about children's respiratory health. Additionally, while the type of stoves and heating used in households are often considered by health care providers who are evaluating indoor air quality risk factors in pediatric patients, additional questions relating to the presence of an exhaust fan may provide an opportunity for preventive intervention and improved outcomes.

Additional file

Additional file 1: Figure S1. Description of the population selection criteria used to restrict to children aged 2-16 years of age who live in homes with gas stoves and have complete data for the covariates included in the multivariate regression models.

Abbreviations

CI: Confidence interval; FEV_1: Forced expiratory volume in 1 second; FVC: Forced vital capacity; NHANES: National Health and Nutrition Examination Survey; NOx: Nitrogen oxides; OR: Odds ratio; P: p-value; PAH: Polycyclic aromatic hydrocarbons; Pct: Percentile; SES: Socioeconomic status.

Competing interest

The authors declare that they have no competing interests.

Authors' contributions

MLK: Coordinated data analysis and interpretation, drafted the manuscript, and approved the final manuscript as submitted. ESC: Conducted the data analysis, contributed to the drafting of the manuscript, and approved the final manuscript as submitted. ES: Supervised the data analysis, critically reviewed the manuscript, and approved the final manuscript as submitted. DS: Contributed to data interpretation, contributed to manuscript draft, and approved the final manuscript as submitted. JM: Contributed to the review and interpretation of the statistical results and approved the final manuscript as submitted. AKH: Conceptualized the study design, contributed to drafting of manuscript, and approved the final manuscript as submitted.

Acknowledgements

This work was supported by grants from the US National Institute of Environmental Health Sciences NIEHS Grant P42 ES016465 and P30 ES000210.

Author details

[1]College of Public Health and Human Sciences, Oregon State University, 15 Milam, Corvallis, OR 97331, USA. [2]Environmental and Molecular Toxicology, College of Agricultural Sciences, Oregon State University, Corvallis, OR 97331, USA.

Received: 24 April 2014 Accepted: 25 August 2014
Published: 2 September 2014

References

1. Bloom B, Cohen RA, Freeman G: **Summary health statistics for U.S. children: National Health Interview Survey, 2010. National Center for Health Statistics.** *Vital Health Stat* 2011, **10**(250).
2. Herzog R, Cunningham-Rundles S: **Pediatric asthma: natural history, assessment, and treatment.** *Mt Sinai J Med* 2011, **78:**645–660.
3. Friedman MS, Powell KE, Hutwagner L, Graham LM, Teague WG: **Impact of changes in transportation and commuting behaviors during the 1996 Summer Olympic Games in Atlanta on air quality and childhood asthma.** *J Am Med Assoc* 2001, **285:**897–905.
4. Infanterivard C: **Childhood asthma and indoor environmental risk factors.** *Am J Epidemiol* 1993, **137:**834–844.
5. Peters JM, Avol E, Navidi W, London SJ, Gauderman WJ, Lurmann F, Linn WS, Margolis H, Rappaport E, Gong H, Thomas DC: **A study of twelve southern California communities with differing levels and types of air pollution - I. Prevalence of respiratory morbidity.** *Am J Respir Crit Care Med* 1999, **159:**760–767.
6. Peters JM, Avol E, Gauderman WJ, Linn WS, Navidi W, London SJ, Margolis H, Rappaport E, Vora H, Gong H, Thomas DC: **A study of twelve southern California communities with differing levels and types of air pollution - II. Effects on pulmonary function.** *Am J Respir Crit Care Med* 1999, **159:**768–775.
7. Schwartz J: **Air pollution and children's health.** *Pediatrics* 2004, **113:**1037–1043.
8. Shima M, Adachi M: **Effect of outdoor and indoor nitrogen dioxide on respiratory symptoms in schoolchildren.** *Int J Epidemiol* 2000, **29:**862–870.
9. Belanger K, Gent JF, Triche EW, Bracken MB, Leaderer BP: **Association of indoor nitrogen dioxide exposure with respiratory symptoms in children with asthma.** *Am J Respir Crit Care Med* 2006, **173:**297–303.
10. Bhangar S, Mullen NA, Hering SV, Kreisberg NM, Nazaroff WW: **Ultrafine particle concentrations and exposures in seven residences in northern California.** *Indoor Air* 2011, **21:**132–144.
11. Brown KW, Sarnat JA, Suh HH, Coull BA, Koutrakis P: **Factors influencing relationships between personal and ambient concentrations of gaseous and particulate pollutants.** *Sci Total Environ* 2009, **407:**3754–3765.
12. Hansel NN, Breysse PN, McCormack MC, Matsui EC, Curtin-Brosnan J, Williams DL, Moore JL, Cuhran JL, Diette GB: **A longitudinal study of indoor nitrogen dioxide levels and respiratory symptoms in inner-city children with asthma.** *Environ Health Perspect* 2008, **116:**1428–1432.
13. Institute of Medicine: *Clearing the Air: Asthma and Indoor Air Exposures.* Washington, DC: The National Academies Press; 2000.
14. Nitschke M, Smith BJ, Pilotto LS, Pisaniello DL, Abramson MJ, Ruffin RE: **Respiratory health effects of nitrogen dioxide exposure and current guidelines.** *Int J Environ Health Res* 1999, **9:**39–53.
15. Piechocki-Minguy A, Plaisance H, Schadkowski C, Sagnier I, Saison JY, Galloo JC, Guillermo R: **A case study of personal exposure to nitrogen dioxide using a new high sensitive diffusive sampler.** *Sci Total Environ* 2006, **366:**55–64.
16. Wallace L, Ott W: **Personal exposure to ultrafine particles.** *J Expo Sci Environ Epidemiol* 2011, **21:**20–30.
17. CDC, Prevention CfDCa: **Use of unvented residential heating appliances – United States, 1988–1994.** In *Morbidity and Mortality Weekly Report. vol. 46.* Atlanta, GA: CDC; 1997:1221–1224.
18. Behrens T, Maziak W, Weiland SK, Rzehak P, Siebert E, Keil U: **Symptoms of asthma and the home environment. The ISAAC I and III cross-sectional surveys in Munster, Germany.** *Int Arch Allergy Immunol* 2005, **137:**53–61.
19. Belanger K, Beckett W, Triche E, Bracken MB, Holford T, Ren P, McSharry JE, Gold DR, Platts-Mills TAE, Leaderer BP: **Symptoms of wheeze and persistent cough in the first year of life: associations with indoor allergens, air contaminants, and maternal history of asthma.** *Am J Epidemiol* 2003, **158:**195–202.
20. Berkey CS, Ware JH, Dockery DW, Ferris BG, Speizer FE: **Indoor air-pollution and pulmonary-function growth in preadolescent children.** *Am J Epidemiol* 1986, **123:**250–260.
21. Chapman RS, Hadden WC, Perlin SA: **Influences of asthma and household environment on lung function in children and adolescents - The Third National Health and Nutrition Examination Survey.** *Am J Epidemiol* 2003, **158:**175–189.
22. Corbo GM, Forastiere F, Agabiti N, Dell'Orco V, Pistelli R, Aebischer ML, Valente S, Perucci CA: **Effect of gas cooking on lung function in adolescents: modifying role of sex and immunoglobulin E.** *Thorax* 2001, **56:**536–540.
23. Cuijpers CEJ, Swaen GMH, Wesseling G, Sturmans F, Wouters EFM: **Adverse effects of the indoor environment on respiratory health in primary school children.** *Environ Res* 1995, **68:**11–23.
24. de Bilderling G, Chauhan AJ, Jeffs JAR, Withers N, Johnston SL, Holgate ST, Clough JB: **Gas cooking and smoking habits and the risk of childhood and adolescent wheeze.** *Am J Epidemiol* 2005, **162:**513–522.
25. Garrett MH, Hooper MA, Hooper BM, Abramson MJ: **Respiratory symptoms in children and indoor exposure to nitrogen dioxide and gas stoves.** *Am J Respir Crit Care Med* 1998, **158:**891–895.
26. Holscher B, Heinrich J, Jacob B, Ritz B, Wichmann HE: **Gas cooking, respiratory health and white blood cell counts in children.** *Int J Hyg Environ Health* 2000, **203:**29–37.
27. Jarvis D, Chinn S, Luczynska C, Burney P: **Association of respiratory symptoms and lung function in young adults with use of domestic gas appliances.** *Lancet* 1996, **347:**426–431.
28. Lanphear BP, Aligne CA, Auinger P, Weitzman M, Byrd RS: **Residential exposures associated with asthma in US children.** *Pediatrics* 2001, **107:**505–511.
29. Moshammer H, Fletcher T, Heinrich J, Hoek G, Hruba F, Pattenden S, Rudnai P, Slachtova H, Speizer FE, Zlotkowska R, Neuberger M: **Gas cooking is associated with small reductions in lung function in children.** *Eur Resp J* 2010, **36:**249–254.
30. Pershagen G, Rylander E, Norberg S, Eriksson M, Nordvall SL: **Air pollution involving nitrogen dioxide exposure and wheezing bronchitis in children.** *Int J Epidemiol* 1995, **24:**1147–1153.
31. Smith BJ, Nitschke M, Pilotto LS, Ruffin RE, Pisaniello DL, Willson KJ: **Health effects of daily indoor nitrogen dioxide exposure in people with asthma.** *Eur Resp J* 2000, **16:**879–885.

32. Volkmer RE, Ruffin RE, Wigg NR, Davies N: **The prevalence of respiratory symptoms in South-Australian preschool children: 2. Factors associated with indoor air quality.** *J Paediatr Child Health* 1995, **31**:116–120.
33. Wong TW, Yu TS, Liu HJ, Wong AHS: **Household gas cooking: a risk factor for respiratory illnesses in preschool children.** *Arch Dis Child* 2004, **89**:631–636.
34. Maier WC, Arrighi HM, Morray B, Llewellyn C, Redding GJ: **Indoor risk factors for asthma and wheezing among Seattle school children.** *Environ Health Perspect* 1997, **105**:208–214.
35. Moran SE, Strachan DP, Johnston IDA, Anderson HR: **Effects of exposure to gas cooking in childhood and adulthood on respiratory symptoms, allergic sensitization and lung function in young British adults.** *Clin Exp Allergy* 1999, **29**:1033–1041.
36. Samet JM, Lambert WE, Skipper BJ, Cushing AH, Hunt WC, Young SA, McLaren LC, Schwab M, Spengler JD: **Nitrogen-dioxide and respiratory illness in infants.** *Am Rev Respir Dis* 1993, **148**:1258–1265.
37. Levy JI, Lee K, Spengler JD, Yanagisawa Y: **Impact of residential nitrogen dioxide exposure on personal exposure: an international study.** *J Air Waste Manage* 1998, **48**:553–560.
38. Langer S, Beko G: **Indoor air quality in the Swedish housing stock and its dependence on building characteristics.** *Build Environ* 2013, **69**:44–54.
39. Zhou Y, Zou Y, Li X, Chen S, Zhao Z, He F, Zou W, Luo Q, Li W, Pan Y, Deng XL, Wang XP, Qiu R, Liu SL, Zheng JP, Zhong NS, Ran PX: **Lung function and incidence of chronic obstructive pulmonary disease after improved cooking fuels and kitchen ventilation: a 9-year prospective cohort study.** *PLoS Med* 2014, **11**:e1001621.
40. Oie L, Nafstad P, Botten G, Magnus P, Jaakkola JK: **Ventilation in homes and bronchial obstruction in young children.** *Epidemiology* 1999, **10**:294–299.
41. Bornehag CG, Sundell J, Hagerhed-Engman L, Sigsgaard T: **Association between ventilation rates in 390 Swedish homes and allergic symptoms in children.** *Indoor air* 2005, **15**:275–280.
42. **National Health and Nutrition Examination Survey (NHANES).** [http://www.cdc.gov/nchs/nhanes/nh3data.htm]
43. Society AT: **Standardization of spirometry- 1987 Update.** *Am Rev Respir Dis* 1987, **136**:1285–1298.
44. Centers for Disease Prevention and Control (CDC): **Using the WHO growth charts to assess growth in the United States among children ages birth to 2 years.** [http://www.cdc.gov/nccdphp/dnpao/growthcharts/who/index.htm?s_cid=govD_dnpao_153]
45. Hankinson JL, Odencrantz JR, Fedan KB: **Spirometric reference values from a sample of the general U.S. population.** *Am J Resp Crit Care* 1999, **159**:179–187.
46. Collen J, Greenburg D, Holley A, King CS, Hnatiuk O: **Discordance in spirometric interpretations using three commonly used reference equations vs national health and nutrition examination study III.** *Chest* 2008, **134**:1009–1016.
47. Ather JL, Alcorn JF, Brown AL, Guala AS, Suratt BT, Janssen-Heininger YMW, Poynter ME: **Distinct functions of airway epithelial nuclear factor-kappa b activity regulate nitrogen dioxide-induced acute lung injury.** *Am J Respir Cell Mol* 2010, **43**:443–451.
48. Poynter ME: **Airway epithelial regulation of allergic sensitization in asthma.** *Pulm Pharmacol Ther* 2012, **25**:438–446.
49. Moshammer H, Hutter HP, Hauck H, Neuberger M: **Low levels of air pollution induce changes of lung function in a panel of schoolchildren.** *Europ Respir J* 2006, **27**:1138–1143.
50. Rojas-Martinez R, Perez-Padilla R, Olaiz-Fernandez G, Mendoza-Alvarado L, Moreno-Macias H, Fortoul T, McDonnell W, Loomis D, Romieu I: **Lung function growth in children with long-term exposure to air pollutants in Mexico City.** *Am J Resp Crit Care* 2007, **176**:377–384.
51. Belanger K, Holford TR, Gent JF, Hill ME, Kezik JM, Leaderer BP: **Household levels of nitrogen dioxide and pediatric asthma severity.** *Epidemiology* 2013, **24**:320–330.
52. Lubitz S, Schober W, Pusch G, Effner R, Klopp N, Behrendt H, Buters JT: **Polycyclic aromatic hydrocarbons from diesel emissions exert proallergic effects in birch pollen allergic individuals through enhanced mediator release from basophils.** *Environ Toxicol* 2010, **25**:188–197.
53. Schober W, Lubitz S, Belloni B, Gebauer G, Lintelmann J, Matuschek G, Weichenmeier I, Eberlein-Konig B, Buters J, Behrendt H: **Environmental polycyclic aromatic hydrocarbons (PAHs) enhance allergic inflammation by acting on human basophils.** *Inhal Toxicol* 2007, **19**(Suppl 1):151–156.
54. Jedrychowski WA, Perera FP, Maugeri U, Mrozek-Budzyn D, Mroz E, Klimaszewska-Rembiasz M, Flak E, Edwards S, Spengler J, Jacek R, Sowa A: **Intrauterine exposure to polycyclic aromatic hydrocarbons, fine particulate matter and early wheeze. Prospective birth cohort study in 4-year olds.** *Pediat Allergy and Immu* 2010, **21**(Pt 2):e723–e732.
55. Al-Daghri NM, Alokail MS, Abd-Alrahman SH, Draz HM, Yakout SM, Clerici M: **Polycyclic aromatic hydrocarbon exposure and pediatric asthma in children: a case–control study.** *Environ Health* 2013, **12**:1.
56. Rim D, Wallace L, Nabinger S, Persily A: **Reduction of exposure to ultrafine particles by kitchen exhaust hoods: the effects of exhaust flow rates, particle size, and burner position.** *Science Total Environ* 2012, **432**:350–356.
57. Singer BC, Delp WW, Price PN, Apte MG: **Performance of installed cooking exhaust devices.** *Indoor Air* 2012, **22**:224–234.
58. Zhang Q, Gangupomu RH, Ramirez D, Zhu Y: **Measurement of ultrafine particles and other air pollutants emitted by cooking activities.** *Int J Environ Res Publ Health* 2010, **7**:1744–1759.

doi:10.1186/1476-069X-13-71
Cite this article as: Kile *et al.*: A cross-sectional study of the association between ventilation of gas stoves and chronic respiratory illness in U.S. children enrolled in NHANESIII. *Environmental Health* 2014 **13**:71.

Cooking fuels and prevalence of asthma: a global analysis of phase three of the International Study of Asthma and Allergies in Childhood (ISAAC)

*Gary W K Wong, Bert Brunekreef, Philippa Ellwood, H Ross Anderson, M Innes Asher, Julian Crane, Christopher K W Lai, for the ISAAC Phase Three Study Group**

Lancet Respir Med 2013; 1: 386–94

http://dx.doi.org/10.1016/S2213-2600(13)70073-0

This online publication has been corrected. The corrected version first appeared at thelancet.com/respiratory on July 8, 2013

See **Comment** page 351

*Members listed in the appendix

Department of Paediatrics and School of Public Health (Prof G W K Wong MD), **and Department of Medicine and Therapeutics** (Prof C K W Lai DM), **Chinese University of Hong Kong, Prince of Wales Hospital, Hong Kong SAR, China; Institute for Risk Assessment Sciences and Julius Centre for Health Sciences and Primary Care, University Medical Centre Universiteit Utrecht, Utrecht, Netherlands** (Prof B Brunekreef PhD); **Department of Paediatrics: Child and Youth Health, University of Auckland, Auckland, New Zealand** (P Ellwood MPH, Prof M I Asher MBChB); **MRC-HPA Centre for Environment and Health, Division of Public Health Sciences and Education, St George's, University of London, London, UK** (Prof H R Anderson MD); **and Wellington Asthma Research Group, Department of Medicine, University of Otago, Wellington, New Zealand** (Prof J Crane MBBS)

Correspondence to:
Prof Gary WK Wong, Department of Paediatrics, Prince of Wales Hospital, Chinese University of Hong Kong, Shatin, Hong Kong, China
wingkinwong@cuhk.edu.hk

See **Online** for appendix

Summary

Background Indoor air pollution from a range of household cooking fuels has been implicated in the development and exacerbation of respiratory diseases. In both rich and poor countries, the effects of cooking fuels on asthma and allergies in childhood are unclear. We investigated the association between asthma and the use of a range of cooking fuels around the world.

Methods For phase three of the International Study of Asthma and Allergies in Childhood (ISAAC), written questionnaires were self-completed at school by secondary school students aged 13–14 years, 244 734 (78%) of whom were then shown a video questionnaire on wheezing symptoms. Parents of children aged 6–7 years completed the written questionnaire at home. We investigated the association between types of cooking fuels and symptoms of asthma using logistic regression. Adjustments were made for sex, region of the world, language, gross national income, maternal education, parental smoking, and six other subject-specific covariates. The ISAAC study is now closed, but researchers can continue to use the instruments for further research.

Findings Data were collected between 1999 and 2004. 512 707 primary and secondary school children from 108 centres in 47 countries were included in the analysis. The use of an open fire for cooking was associated with an increased risk of symptoms of asthma and reported asthma in both children aged 6–7 years (odds ratio [OR] for wheeze in the past year, 1·78, 95% CI 1·51–2·10) and those aged 13–14 years (OR 1·20, 95% CI 1·06–1·37). In the final multivariate analyses, ORs for wheeze in the past year and the use of solely an open fire for cooking were 2·17 (95% CI 1·64–2·87) for children aged 6–7 years and 1·35 (1·11–1·64) for children aged 13–14 years. Odds ratios for wheeze in the past year and the use of open fire in combination with other fuels for cooking were 1·51 (1·25–1·81 for children aged 6–7 years and 1·35 (1·15–1·58) for those aged 13–14 years. In both age groups, we detected no evidence of an association between the use of gas as a cooking fuel and either asthma symptoms or asthma diagnosis.

Interpretation The use of open fires for cooking is associated with an increased risk of symptoms of asthma and of asthma diagnosis in children. Because a large percentage of the world population uses open fires for cooking, this method of cooking might be an important modifiable risk factor if the association is proven to be causal.

Funding BUPA Foundation, the Auckland Medical Research Foundation, the Health Research Council of New Zealand, the Asthma and Respiratory Foundation of New Zealand, the Child Health Research Foundation, the Hawke's Bay Medical Research Foundation, the Waikato Medical Research Foundation, Glaxo Wellcome New Zealand, the NZ Lottery Board, Astra Zeneca New Zealand, Hong Kong Research Grant Council, Glaxo Wellcome International Medical Affairs.

Introduction

Despite much research, little is known about the cause of asthma. The international study of asthma and allergies in childhood (ISAAC) has documented a wide variation in asthma prevalence across the world and has also detected evidence of a continuing increase, especially in low-income and middle-income countries.[1,2] The possible role of air pollution in the development of respiratory diseases is a major focus of research. Several studies have investigated the association between indoor air pollution and asthma and chronic obstructive pulmonary disorder (COPD).[3,4] In high-income countries, the use of gas appliances for cooking has been implicated as a cause of respiratory symptoms, particularly in women.[5] The use of gas as cooking fuel has also been implicated as one of the factors that might explain the higher asthma prevalence in Chinese children in Hong Kong compared with children in other Chinese cities.[6] However, results from the European community respiratory health survey of more than 10 000 respondents did not show any relation between the use of gas for cooking and obstructive respiratory symptoms.[7]

Exposures to domestic fire burning of coal and biomass such as wood, animal dung, and crop residues for cooking or heating are widespread, especially in rural areas of poor countries. According to WHO, at least half the world's population live in households in which solid fuels or biomass are the primary fuel for cooking, heating, or both.[8,9] In resource-poor countries, cooking with biomass is typically done on unvented stoves without any form of ventilation system.[10] In India, biomass burning has been shown to be associated with increased respiratory symptoms in children.[11] A nationwide study in India showed that exposure to the combustion of biomass and solid fuels was associated with an increased risk of asthma in women.[12] A study of 508 adults in the USA also showed a positive association between asthma and exposure to cooking indoors with wood and coal.[13] WHO estimated that indoor air pollution from the burning of biomass causes almost 2 million deaths annually.[8] Because the burning of biomass fuel or the use of gas for cooking are potentially modifiable factors, the study of their relation with asthma and wheezing illnesses in children is important.

Many studies of the association between cooking fuel and asthma have been of low statistical power. Furthermore, estimation of the individual exposure presents a major challenge because the proximity to the sources of exposure, the duration of exposure, and accurate assessment of ventilation are not easily quantifiable in large studies. The existing evidence about the association between household air pollution from biomass burning and asthma is conflicting, with more consistent positive associations in children than in adults.[14–18] We investigated the relation between asthma and the use of a range of cooking fuels in study centres around the world. Using standardised methods, phase one of ISAAC documented large variations in asthma prevalence across the world. Phase two included objective measurements including skin-prick test and bronchial challenge test, providing further support of the importance of environmental factors in the development of asthma. The results reported here are based on a detailed environmental questionnaire administered to children in 47 countries to test different cause hypotheses of asthma as part of the phase three ISAAC study.

Methods

Study design

ISAAC phase three is an expansion using the same study design of the first phase of ISAAC, findings from which showed a wide variation in the prevalence of childhood asthma and related atopic disorders across the world.[1,2,19] The details of the study protocol are available elsewhere.[2,19] Briefly, written questionnaires were self-completed at school by secondary school students aged 13–14 years who were then, in most centres, shown a video questionnaire on wheezing symptoms. 244 734 (78%) adolescents completed a video questionnaire on wheezing symptoms. Parents of children aged 6–7 years completed the written questionnaire at home. School children in these two targeted age groups were randomly selected by individual centres from within a defined geographical area. Studies were done with local ethics approval and the method of consent was determined by local ethics committees.[20] The ISAAC International Data Centre in Auckland, New Zealand, assessed the submitted data for adherence to the standardised ISAAC protocol. In this Article, we focus on "current wheeze" (in response to the question "Have you (has your child) had wheezing or whistling in the chest in the past 12 months?"), "asthma ever" ("Have you (has your child) ever had asthma?"), symptoms of "rhinoconjunctivitis" ("In the past 12 months, have you (has your child) had a problem with sneezing, or a runny, or blocked nose when you (he/she) did not have a cold or the flu?" and "In the past 12 months, has this nose problem been accompanied by itchy-watery eyes?"), and symptoms of "eczema" ("Have you (has your child) had this itchy rash at any time in the past 12 months?" and "Has this itchy rash at any time affected any of the following places: the folds of the elbows, behind the knees, in front of the ankles, under the buttocks, or around the neck, ears or eyes?"). These questions related to eczema were preceded by the question "Have you (has your child) ever had an itchy rash coming and going for at least 6 months?"; if

For the **core and environmental questionnaires** see http://isaac.auckland.ac.nz/

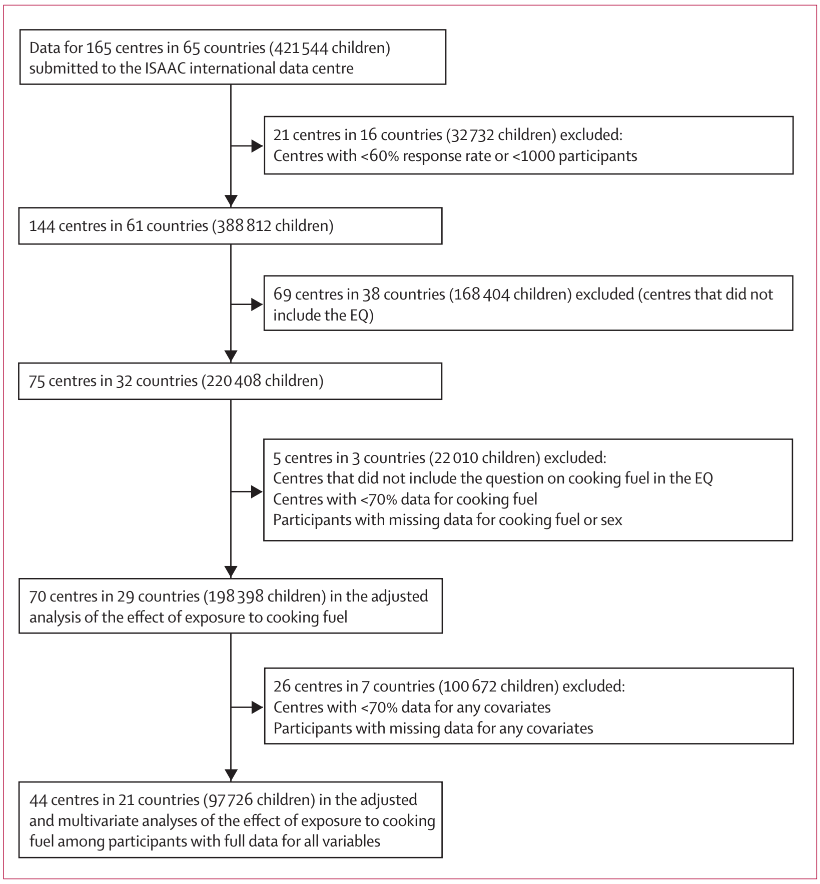

***Figure 1:* Trial profile for children aged 6–7 years**
EQ=environmental questionnaire.

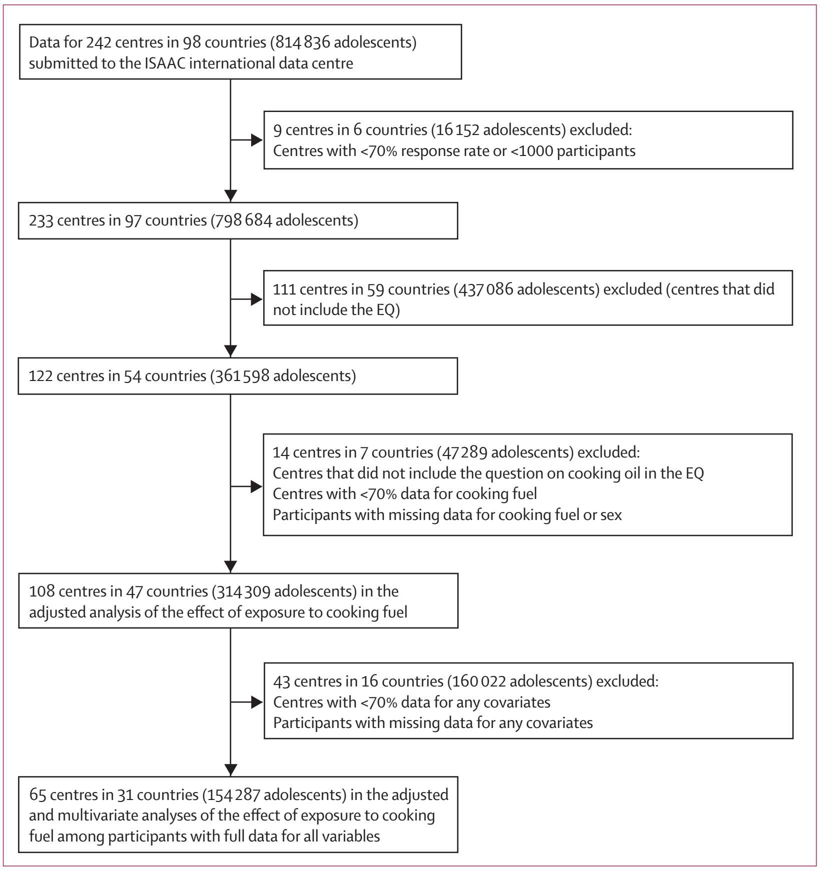

Figure 2: **Trial profile for children aged 13–14 years**
EQ=environmental questionnaire.

the answer to this question was negative, the following questions about eczema were not asked. We analysed "symptoms of severe asthma", defined as children with current wheeze who, according to the written questionnaire, in the past 12 months had four or more attacks of wheeze, or one or more nights of sleep disturbance from wheeze per week, or wheeze that was severe enough to limit the child's speech to only one or two words at a time between breaths. Previous ISAAC analyses showed that a combination of these characteristics of more severe wheezing episodes was more closely associated with asthma mortality and hospital admissions than current wheeze alone.[21] Additionally, children aged 13–14 years were asked to respond to a video questionnaire showing various symptoms of wheeze in children of similar age, and a positive response to the question relating to a scene showing a young person wheezing at rest ("Has your breathing ever been like this in the past 12 months?") was defined as "current wheeze–video".[22]

In ISAAC phase three, an optional environmental questionnaire (dependent on the resources available at each centre) was administered in addition to the core symptom questionnaire to assess several specific cause hypotheses.[19] One of the questions in the environmental questionnaire that we analysed in the present study was "What fuel is usually used for cooking in your house?" The four answers to choose from were "electricity", "gas", "open fires", and "other" (if respondents chose other, they had to specify which fuel they used). Respondents could choose more than one category. For this analysis, we used "electricity" as the reference group, and compared it with the other categories, including "gas", "open fires only", "open fire in combination with other fuel", "multiple non-fire fuel", and "other fuel only". The group of "other fuel" is small but heterogeneous, including the use of microwave, solar power, kerosene, liquid petroleum gas, and methane.

Statistical analysis

We calculated odds ratios (ORs) using generalised linear mixed models for a binomial distribution and logit link and with the centres modelled as a random effect. In the initial analyses of associations between outcomes and use of different types of cooking fuel, all children from centres with submission of cooking fuel data were included with adjustment for sex, region of the world, language, and gross national income. Regions of the world were Africa, Asia-Pacific, Eastern Mediterranean, Latin America, North America, northern and eastern Europe, Oceania, the Indian subcontinent, and western Europe. The written questionnaire was translated from English, according to the standardised ISAAC phase three protocol, into local languages: including Arabic, Chinese, English, Hindi, Indonesian, Portuguese, and Spanish.[24] Centres were allocated to four categories of socioeconomic status based on their country's gross national income per person: low, lower-middle, upper-middle, and high, as categorised by World Bank gross national income data.[25] To define affluent and non-affluent status, we combined the lower three categories as the non-affluent countries and the top category as the affluent countries. In the final models, we did multivariate analyses, adjusting for other covariates in the environmental questionnaire, including maternal education, maternal and paternal smoking, television watching, exercise, siblings (older and younger), consumption of fast food, frequency of truck traffic, and paracetamol use. We included these factors because they were known to be associated with respiratory symptoms or have been shown by our previous studies to be associated with wheeze and asthma.[26,27] We tested the effect modification by sex and by affluence by comparing the log-transformed ORs for boys and girls, and for affluent and non-affluent study centres. The log-odds-ratio for interaction was derived as the difference between the stratum-specific log-odds-ratios, and its variance was estimated as the sum of the variances of each of the stratum-specific log-odds-ratios. For the children aged

13–14 years, data for 242 centres in 98 countries with 814 836 participants were submitted to the ISAAC International Data Centre for data analyses. For children aged 6–7 years, data for 165 centres in 65 countries with 421 544 participants were submitted. Adherence to the ISAAC protocol was assessed, and centres with serious deviations from protocol (<70% response rate for the adolescents and <60% for the children, and centres with <1000 participants for both age groups) were excluded from the worldwide data analyses.[19,23] For inclusion in the final analysis, centres needed 70% or more of participants with data for the use of cooking fuels and all covariates. SAS version 9.1 was used for all analyses.

Role of the funding source

The study sponsors had no role in the study design, data collection, analysis, data interpretation, writing of the report, or the decision to submit the paper for publication. The authors had the responsibility to write and submit the paper for publication, with the involvement of the ISAAC Phase Three Study Group. The corresponding author had full access to all the data and the final responsibility to submit for publication.

Results

Data were collected between 1999 and 2004. In the initial statistical models, there were 198 398 children aged 6–7 years from 70 centres in 29 countries (figure 1) and 314 309 children aged 13–14 years from 108 centres in 47 countries (figure 2). Tables 1 and 2 show the distribution of the use of different types of fuel for cooking by region for the two age groups (see appendix for the prevalence rates of the various health outcomes in relation to the use of different types of cooking fuel in the two age groups). In the final multivariate analysis, only those children with complete covariate data were included (figures 1 and 2). As shown in tables 1 and 2, the highest percentages for the use of any open fire or open fire only were from Africa, the Indian subcontinent, and the Asia-Pacific region. For the initial and final multivariate analyses in both age groups, we detected statistically significant and consistent associations between the use of an open fire for cooking and current symptoms of wheeze and asthma (tables 3 and 4). In the multivariate analyses for children aged 13–14 years, the "use of open fire only" for cooking was associated with current wheeze as assessed by both the written and video questionnaires (table 4). In children aged 6–7 years, "use of open fire only" for cooking was associated with current wheeze, severe asthma symptoms, and ever reported asthma (table 3). Furthermore, in children aged 13–14 years, the use of open fire only for cooking was associated with ever reported eczema and current symptoms of eczema, and the use of open fire in combination with other fuels for cooking was also associated with ever reported eczema and current symptoms of eczema (table 4). In those aged 6–7 years, the association between the symptom of wheeze or severe asthma with the use of open fires only seemed stronger compared with use of open fire in combination with other fuel (table 3).

Tables 5 and 6 show the association between current wheeze and the use of different types of cooking fuel stratified by sex and country affluence. We did not detect any significant interaction between sex and the use of different fuels in their associations with current wheeze. When stratified by country affluence, the associations with current wheeze were statistically significant for the two age groups for any open fires and open fire only in non-affluent countries only, but tests for interaction between country affluence and use of different fuels in their associations with current wheeze were not significant (appendix).

In both age groups, symptoms of wheeze and ever reported asthma were not associated with the use of gas as a cooking fuel (table 7). Furthermore, none of the associations of these outcomes with gas cooking was statistically significant when stratified according to sex or country affluence in either age group (tables 5 and 6).

	N	Multiple non-fire fuels (%)	Other fuel only (%)	Any open fire (%)	Open fire only (%)	Gas only (%)	Electricity only (%)
Africa	2308	0%	42%	21%	0%	23%	14%
Asia-Pacific	27 022	11%	1%	1%	2%	78%	7%
Eastern Mediterranean	14 977	3%	<0·5%	1%	<0·5%	94%	1%
Indian subcontinent	42 521	4%	9%	3%	4%	79%	1%
Latin America	46 586	3%	<0·5%	1%	1%	91%	5%
North America	3948	1%	0%	<0·5%	0%	67%	32%
Northern and eastern Europe	15 139	5%	<0·5%	1%	3%	65%	26%
Oceania	10 810	7%	<0·5%	<0·5%	1%	9%	82%
Western Europe	35 087	4%	1%	<0·5%	1%	61%	33%
All centres	198 398	5%	3%	1%	2%	74%	15%

Table 1: Global use of different types of fuels for cooking (children aged 6–7 years)

	N	Multiple non-fire fuels (%)	Other fuel only (%)	Any open fire (%)	Fire only (%)	Gas only (%)	Electricity only (%)
Africa	27 563	6%	3%	11%	18%	43%	18%
Asia-Pacific	49 820	8%	4%	3%	3%	71%	12%
Eastern Mediterranean	15 523	4%	1%	2%	<0·5%	91%	3%
Indian subcontinent	41 703	3%	8%	6%	3%	78%	1%
Latin America	79 606	5%	<0·5%	3%	2%	81%	9%
North America	5290	1%	1%	1%	0%	54%	43%
Northern and eastern Europe	26 922	7%	<0·5%	2%	3%	53%	35%
Oceania	19 282	10%	1%	6%	12%	19%	53%
Western Europe	48 600	6%	1%	<0·5%	1%	57%	35%
All centres	314 309	6%	2%	4%	4%	66%	18%

Table 2: Global use of different types of fuels for cooking (children aged 13–14 years)

	Adjusted model		Multivariate analysis	
	Any use of open fire	Use of open fire only	Any use of open fire	Use of open fire only
Current wheeze	1·78 (1·51–2·10)	1·79 (1·52–2·10)	1·51 (1·25–1·81)	2·17 (1·64–2·87)
Current symptoms of severe asthma	1·83 (1·42–2·35)	1·80 (1·40–2·32)	1·33 (1·02–1·73)	1·79 (1·18–2·70)
Asthma ever	1·37 (1·10–1·71)	1·26 (1·06–1·49)	1·32 (1·08–1·61)	1·45 (1·03–2·03)
Current symptoms of rhinoconjunctivitis	1·24 (0·97–1·59)	1·06 (0·86–1·30)	1·02 (0·80–1·30)	1·12 (0·74–1·69)
Hay fever ever	1·16 (0·90–1·49)	1·09 (0·91–1·31)	1·06 (0·84–1·33)	1·20 (0·79–1·82)
Current symptoms of eczema	0·93 (0·73–1·21)	1·14 (0·96–1·35)	1·10 (0·91–1·33)	1·08 (0·75–1·55)
Eczema ever	0·80 (0·64–1·00)	0·97 (0·82–1·15)	0·90 (0·74–1·09)	0·64 (0·45–0·93)

Data are odds ratio (95% CI). The reference category for these estimates is electricity only used for cooking.

Table 3: **Association between any use of open fire and open fire only for cooking and current symptoms of asthma, rhinoconjunctivitis, and eczema (children aged 6–7 years)**

	Adjusted model		Multivariate analysis	
	Any use of open fire	Use of open fire only	Any use of open fire	Use of open fire only
Current wheeze	1·20 (1·06–1·37)	1·19 (1·05–1·35)	1·35 (1·15–1·58)	1·35 (1·11–1·64)
Current wheeze (video)	1·42 (1·18–1·71)	1·37 (1·14–1·64)	1·74 (1·41–2·13)	1·87 (1·46–2·40)
Current symptoms of severe asthma	1·31 (1·12–1·52)	1·29 (1·10–1·50)	1·19 (0·98–1·46)	1·20 (0·93–1·55)
Asthma ever	1·24 (1·10–1·40)	1·23 (1·09–1·39)	1·48 (1·28–1·72)	1·70 (1·43–2·03)
Current symptoms of rhinoconjunctivitis	1·09 (0·96–1·24)	1·07 (0·95–1·21)	1·08 (0·91–1·28)	1·02 (0·83–1·26)
Hay fever ever	1·10 (0·96–1·26)	1·09 (0·95–1·25)	1·15 (0·95–1·40)	1·08 (0·85–1·38)
Current symptoms of eczema	1·35 (1·17–1·56)	1·29 (1·13–1·49)	1·37 (1·13–1·66)	1·33 (1·07–1·66)
Eczema ever	1·23 (1·07–1·42)	1·22 (1·06–1·40)	1·35 (1·12–1·62)	1·42 (1·14–1·76)

Data are odds ratio (95% CI). The reference category for these estimates is electricity only used for cooking.

Table 4: **Association between any use of open fire and open fire only for cooking and current symptoms of asthma, rhinoconjunctivitis, and eczema (children aged 13–14 years)**

Discussion

The findings from this large multicentre survey show that the use of open fires for cooking is associated with symptoms of asthma and ever reported asthma in school children of two age groups: 6–7 years and 13–14 years. The associations were consistent between sexes. Furthermore, the associations were similar using three different validated methods to assess the symptoms of current wheeze or ever reported asthma (self-completed written questionnaire and video questionnaires for children aged 13–14 years and parent-completed questionnaires for children aged 6–7 years).[22,23] When stratified according to country affluence, we found that current wheeze was associated with open-fire cooking in non-affluent countries only.

The potentially detrimental effects of indoor air pollution on the development of respiratory diseases have attracted much attention from the research community. Household air pollution from burning of solid fuels has been shown to be a leading risk factor for global disease burden.[28] The association between acute lower respiratory tract infections and exposure to household burning of biomass has been investigated in several studies and the association has been consistent (panel).[29–31] However, restricted data are available for the relation between burning of biomass and asthma. In epidemiological studies, accurate assessment of exposure can be difficult because the intensity of exposure depends on a range of factors such as proximity to the source of pollution, the duration of exposure, and the ventilation system available in the household. The concentrations of pollution from cooking by open fire with indoor burning of biomass are commonly in the order of hundreds and might be up to several thousand μm/m³ of particulates smaller than 10 μm in diameter (PM_{10}).[32,33] Furthermore, households using biomass fuel in low-income and middle-income countries do not usually have effective ventilation systems to reduce the indoor levels of pollutants. In high-income countries, the effects of gas stoves and other combustion appliances on respiratory symptoms and lung function have been studied extensively. The use of domestic gas appliances has been associated with respiratory symptoms and a diminished respiratory function in children.[34–36] However, the evidence was conflicting as to whether the use of gas cooking is associated with asthma.

About half the world population is exposed to household air pollution from the burning of coal or biomass in open fires, the use of these forms of energy sources have received much attention. The use of biomass fuel has been estimated to be more important than smoking of tobacco as a risk factor for COPD globally.[4] In a meta-analysis done by Kurmi and colleagues, strong associations between the use of solid fuel and COPD (OR 2·80 [95% CI 1·18–4·00]) and chronic bronchitis (2·35 [1·92–2·80]) were seen.[37] Exposure to wood smoke was associated with the greatest risk of development of COPD and chronic bronchitis. In high-income countries, most research studies have focused on the possible effects of the use of gas as cooking fuel. Available data are inconsistent, with some studies showing a positive association between gas cooking and asthma and others showing no association. A multicentre study of children from three Chinese cities showed that exposure to gas cooking was one of the risk factors explaining the higher prevalence of childhood asthma in Hong Kong when compared with children from mainland China.[6] However, the PIAMA birth cohort study did not find any association between gas cooking and any of the respiratory outcomes assessed, including asthma.[38] Furthermore, the results from the European Community Respiratory Health Survey of more than 10 000 adults from 11 countries did not show any association between the use of gas for cooking and obstructive respiratory symptoms.[7] Some of these inconsistencies can be explained by errors in exposure

	Countries (n)	Centres (n)	Children (n)	Multiple non-fire fuels	Other fuel only	Any use of open fire	Open fire only	Gas only
Girls	21	44	48 743	1·31 (1·12–1·54)	0·86 (0·43–1·72)	1·56 (1·19–2·05)	1·93 (1·23–3·02)	0·92 (0·82–1·03)
Boys	21	44	48 983	1·09 (0·94–1·27)	1·10 (0·64–1·90)	1·45 (1·13–1·87)	2·35 (1·64–3·37)	0·99 (0·89–1·09)
Affluent countries	6	19	42 047	1·22 (1·07–1·40)	0·84 (0·45–1·57)	1·27 (0·90–1·79)	1·55 (0·78–3·11)	1·01 (0·92–1·10)
Non-affluent countries	15	25	55 679	1·10 (0·90–1·34)	1·12 (0·61–2·04)	1·49 (1·18–1·88)	2·11 (1·53–2·90)	0·88 (0·76–1·01)

Data are odds ratio (95% CI), unless otherwise stated. The reference category for these estimates is electricity only used for cooking.

Table 5: **Association between cooking fuels and current wheeze by sex or country affluence (children aged 6–7 years)**

	Countries (n)	Centres (n)	Children (n)	Multiple non-fire fuels	Other fuel only	Any use of open fire	Open fire only	Gas only
Girls	31	65	78 550	1·25 (1·06–1·48)	0·72 (0·49–1·06)	1·31 (1·05–1·64)	1·36 (1·04–1·78)	0·98 (0·89–1·09)
Boys	31	65	75 737	1·06 (0·89–1·27)	0·98 (0·70–1·38)	1·39 (1·11–1·74)	1·36 (1·03–1·78)	1·00 (0·90–1·12)
Affluent countries	5	17	43 344	1·08 (0·90–1·31)	1·04 (0·70–1·56)	0·98 (0·61–1·56)	0·75 (0·32–1·75)	1·00 (0·90–1·11)
Non-affluent countries	26	48	110 943	1·18 (1·01–1·39)	0·74 (0·53–1·04)	1·38 (1·16–1·65)	1·39 (1·13–1·71)	0·98 (0·88–1·09)

Data are odds ratio (95% CI), unless otherwise stated. The reference category for these estimates is electricity only used for cooking.

Table 6: **Association between cooking fuels and current wheeze by sex and country affluence (children aged 13–14 years)**

	Adjusted model		Multivariate analysis	
	6–7 years	13–14 years	6–7 years	13–14 years
Current wheeze	0·98 (0·92–1·04)	0·99 (0·94–1·04)	0·96 (0·89–1·03)	0·99 (0·92–1·07)
Current symptoms of severe asthma	1·01 (0·92–1·10)	0·97 (0·91–1·03)	0·97 (0·87–1·09)	0·97 (0·89–1·07)
Asthma ever	0·95 (0·89–1·01)	0·98 (0·93–1·02)	0·94 (0·88–1·02)	0·99 (0·93–1·05)
Current symptoms of rhinoconjunctivitis	1·04 (0·97–1·01)	0·96 (0·91–1·01)	1·00 (0·92–1·09)	0·99 (0·92–1·06)
Hay fever ever	1·02 (0·95– 1·09)	0·96 (0·91–1·01)	1·00 (0·92–1·09)	0·99 (0·92–1·07)
Current symptoms of eczema	0·97 (0·91–1·03)	1·00 (0·94–1·06)	0·94 (0·87–1·02)	1·00 (0·92–1·09)
Eczema ever	0·91 (0·86–0·96)	0·99 (0·93–1·04)	0·93 (0·88–0·99)	1·01 (0·93–1·09)

Data are odds ratio (95% CI), unless otherwise stated. The reference category for these estimates is electricity only used for cooking.

Table 7: **Association between use of gas only for cooking and current symptoms of asthma, rhinoconjunctivitis, and eczema, by age group**

assessment or differences in the toxicity of the pollutant mixtures. The type and efficiency of the ventilation systems could also have affected the relation between gas cooking and respiratory symptoms.

In poor countries, the use of open fire associated with use of biomass burning for cooking is far more common than the use of gas or electricity. Indoor air pollution from biomass burning has been associated with a variety of respiratory illnesses such as respiratory tract infection, asthma, and bronchitis.[39] In a study from Kentucky, USA, adults reported to have used coal or wood indoors for cooking for more than 6 months had an increased risk of asthma (OR 2·3 [1·1–5·0]).[13] A study of 1058 children aged 4–6 years from Guatemala showed that exposure to open fires for cooking was associated with symptom of wheeze (OR 3·4 [1·3–8·5]).[18] A study of 755 children from rural villages in India reported that the use of biomass burning was associated with doctor-diagnosed asthma (OR 4·27 [3·00–4·90]).[40] In addition to many studies showing the association of indoor air pollution and respiratory symptoms, findings from several studies have suggested an association between traffic-related air pollution and symptoms of eczema.[26,41] Our results also showed that there was a consistent association between use of open fire for cooking and reported eczema diagnosis and symptoms of eczema in the older age group, but there was a weak protective effect of the use of open fire only on eczema diagnosis in the younger age group (table 3, multivariate analysis). Two studies have shown a positive association between eczema and the levels of indoor air pollutants such as PM_{10}, nitrogen dioxide and carbon monoxide.[42,43] The normal skin barrier is impaired in patients with eczema. This defect of skin barrier function might enhance the penetration of environmental pollutants or allergens into the skin, resulting in inflammatory responses and persistent symptoms of eczema. Chronic exposure to pollutants could also disrupt the normal skin barrier resulting in increased sensitivity to chemicals or allergens. Further studies are needed to clarify these associations between environmental pollution and eczema, and to expose the possible underlying mechanisms.

The large sample size, the use of standardised methods of assessment, and validated instruments are the strengths of this study. Findings from four validation studies have substantiated the assocation between current wheeze and asthma-related bronchial hyper-responsiveness or confirmation of asthma by physician assessment.[44–47] Our results are consistent with those of other studies in finding that the use of an open fire for cooking was associated with wheeze symptom and reported asthma in both age groups.

Panel: Research in context

Systematic review

We searched PubMed for reports published before March 18, 2013, with the following combinations of the search terms “cooking fuel” and “asthma”, and “biomass fuels” and “asthma”. We identified 40 and 29 reports, respectively. Most of these reports were review articles or studies of the possible effects of gas cooking in rich countries. There were only seven studies investigating the effects of biomass burning and asthma. Among them, only two studies investigated the association in children and both studies were from poor countries. The results of these studies were inconsistent as to whether exposure to biomass burning was associated with asthma or not.

Interpretation

We report a positive association between cooking with open fires and the symptoms and diagnosis of asthma in childhood in both affluent and non-affluent countries. No association was seen with the use of gas. Because cooking with open fires with biomass or coal is very common, especially in non-affluent countries, more detailed studies are urgently needed to establish whether the relation is causal and to assess intervention strategies.

Although not statistically significantly different, the younger age-group seemed to have higher ORs for current wheeze for the exclusive use of open fires as compared with the use of an open fire in combination with other fuels. When stratified according to country affluence, associations tended to be seen only in non-affluent countries. Many factors might affect the health effects of air pollution generated from open fire cooking. These would include the frequency of use of open fire cooking, the type of housing, and the availability and efficiency of kitchen ventilation systems. Most households using open fires for cooking in less affluent countries are usually not equipped with an efficient ventilation system.[10] By comparison with the situation in less affluent countries, kitchen ventilation is likely to be better in homes in affluent countries and this factor could partly explain the discrepancy in the effect of the use of open fire for cooking between affluent and non-affluent countries. A randomised controlled study of 552 women from rural Mexico showed that the use of an improved biomass stove with lower levels of pollution was associated with a reduction of respiratory symptoms and of lung function decline.[48] A major limitation of our study is that we do not have information related to the frequency of open fire cooking and information about kitchen ventilation that would allow us to test these hypotheses. Our environmental questionnaire did not enquire about information related to exposure during pregnancy such that we could not test if exposure factors during pregnancy were associated with various health outcomes in question. The absence of information about the use of asthma drugs is another limitation. Our results would have been strengthened if we could show the association of asthma drug use and exposure to open fire cooking. Furthermore, family history of allergies is a potential confounder but adjustment for parental allergies in our regression models did not change our results.

There are several factors that could affect the validity of our results. In particular, selection bias and recall bias could have led to a spurious positive association between the exposure of open fire cooking and asthma symptoms. We think this is unlikely to explain the present findings because there is coherence between the initial analyses using all available children and the final analyses in selected children adjusted for important covariates, and the results are consistent across the two age groups using three different methods to identify asthma. By contrast with parents of the younger children, children aged 13–14 years are unlikely to be aware of the potential relation between the exposure and asthma symptoms making recall bias less likely. With regards to possible misclassification of exposure, this problem would bias our results towards the null hypothesis. The negative findings from children exposed to open fire cooking in affluent countries might be explained by the lack of statistical power owing to the small sample size. Determination of whether current asthma symptoms were related to the acute exposure or long term exposure could be of interest, but our risk factor questionnaire did not obtain information about the types of cooking fuel used in early life or when the mother was pregnant with the child. The use of multiple non-fire fuels was associated with wheeze in girls in both age groups, and in the younger children in affluent countries (tables 5 and 6). This category of fuel refers to the use of different combinations including gas, electricity, microwave, and even solar energy. Because many of these fuels are thought to be clean sources of energy, the reason for this association is not clear. However, families who can afford the use of multiple types of fuels might have a higher socioeconomic status and if these were more likely to report symptoms or a diagnosis of asthma, a possibility of residual confounding by socioeconomic status could exists that would not be accounted for by the inclusion maternal education in our statistical model.

If the association between open fire cooking and asthma is causal, this factor might be a major modifiable risk factor of asthma in children worldwide. However, more detailed investigations are needed to confirm and quantify this association, understand the underlying mechanisms, and assess intervention strategies. Our results provide further evidence that public policies and measures to reduce indoor air pollution from burning of biomass will translate into significant health benefits especially in developing countries.

Contributors

All authors participated in the development, design, data collection, analysis, and interpretation of this work. GWKW wrote the first draft and all authors contributed to the writing of subsequent drafts of the paper.

Conflicts of interest

We declare that we have no conflicts of interest.

Acknowledgments

We thank the children and parents who participated in ISAAC phase three; the school staff for their assistance and help with coordination; the phase three principal investigators and their colleagues; the many funding bodies around the world that supported the individual ISAAC centres and collaborators and their meetings. The ISAAC International Data Centre was supported by the Health Research Council of New Zealand, the Asthma and Respiratory Foundation of New Zealand, the Child Health Research Foundation, the Hawke's Bay Medical Research Foundation, the Waikato Medical Research Foundation, Glaxo Wellcome New Zealand, the New Zealand Lottery Board, and Astra Zeneca New Zealand. Glaxo Wellcome International Medical Affairs supported the regional coordination and the ISAAC International Data Centre.

References

1 The International Study of Asthma and Allergies in Childhood (ISAAC) Steering Committee. Worldwide variation in prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema: ISAAC. *Lancet* 1998; **351:** 1225–32.

2 Asher MI, Montefort S, Björkstén B, et al. Worldwide time trends in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and eczema in childhood: ISAAC Phases One and Three repeat multicountry cross-sectional surveys. *Lancet* 2006; **368:** 733–43.

3 Hsien-Ho Lin, Megan Murray, Ted Cohen, Caroline Colijn, Majid Ezzati. Effects of smoking and solid-fuel use on COPD, lung cancer, and tuberculosis in China: a time-based, multiple risk factor, modelling study. *Lancet* 2008; **372:** 1473–83.

4 Salvi SS, Barnes PJ. Chronic obstructive pulmonary disease in non-smokers. *Lancet* 2009; **374:** 733–43.

5 Jarvis D, Chinn S, Luczynska C, Burney P. Association of respiratory symptoms and lung function in young adults with use of domestic gas appliances. *Lancet* 1996; **347:** 426–31.

6 Wong GW, Ko FW, Hui DS, et al. Factors associated with difference in prevalence of asthma in children from three cities in China: multicentre epidemiological survey. *BMJ* 2004; **329:** 486–89.

7 Jarvis D, Chinn S, Sterne J, Luczynska C, Burney P. The association of respiratory symptoms and lung function with the use of gas for cooking. European Community Respiratory Health Survey. *Eur Respir J* 1998; **11:** 651–58.

8 Smith KR, Mehta S, Maeusezahl-Feuz M. Indoor air-pollution from solid fuel use. In: Ezzatti M, Lopez AD, Rodgers A, Murray CJL, eds. Comparative quantification of health risks: global and regional burden of diseases attributable to selected major risk factors. Geneva: World Health Organization, 2004. 1435–93.

9 Eva Rehfuess. Fuel for life: household energy and health. Geneva: World Health Organization, 2006.

10 Smith KR. National burden of disease in India from indoor air pollution. *Proc Natl Acad Sci USA* 2000; **97:** 13286–93.

11 Kumar R, Nagar JK, Raj N, et al. Impact of domestic air pollution from cooking fuel on respiratory allergies in children in India. *Asian Pac J Allergy Immunol* 2008; **26:** 213–22.

12 Agrawal S. Effect of indoor air pollution from biomass and solid fuel combustion on prevalence of self-reported asthma among adult men and women in India: findings from a nationwide large-scale cross-sectional survey. *J Asthma* 2012; **49:** 355–65.

13 Barry AC, Mannino DM, Hopenhayn C, Bush H. Exposure to indoor biomass fuel pollutants and asthma prevalence in Southeastern Kentucky: results from the Burden of Lung Disease (BOLD) study. *J Asthma* 2010; **47:** 735–41.

14 Mohamed N, Ng'ang'a L, Odhiambo J, et al. Home environment and asthma in Kenyan schoolchildren: a case–control study. *Thorax* 1995; **50:** 74–78.

15 Azizi BH, Zulkifli HI, Kasim S. Indoor air pollution and asthma in hospitalized children in a tropical environment. *J Asthma* 1995; **32:** 413–18.

16 Melsom T, Brinch L, Hessen JO, et al. Asthma and indoor environment in Nepal. *Thorax* 2001; **56:** 477–81.

17 Mishra V. Effect of indoor air pollution from biomass combustion on prevalence of asthma in the elderly. *Environ Health Perspect* 2003; **111:** 71–78.

18 Schei MA, Hessen JO, Smith KR, et al. Childhood asthma and indoor woodsmoke from cooking in Guatemala. *J Expo Anal Environ Epidemiol* 2004; **14:** S110–17.

19 Ellwood P, Asher MI, Beasley R, Clayton TO, Stewart AW, ISAAC Steering Committee. The international study of asthma and allergies in childhood (ISAAC): phase three rationale and methods. *Int J Tuberc Lung Dis* 2005; **9:** 10–16.

20 Ellwood P, Asher MI, Stewart AW, ISAAC Phase III Study Group. The impact of the method of consent on response rates in the ISAAC time trends study. *Int J Tuberc Lung Dis* 2010; **14:** 1059–65.

21 Anderson HR, Gupta R, Kapetanakis V, et al. International correlations between indicators of prevalence, hospital admissions and mortality for asthma in children. *Int J Epidemiol* 2008; **37:** 573–82.

22 Crane J, Beasley R, Stewart B, Shaw R, Pearce N, Burgess C. The international asthma video questionnaire for measuring asthma prevalence in different populations. *Int Arch Allergy Immunol* 1995; **107:** 450–51.

23 ISAAC. 2009. Home page. Available: http://isaac.aucklandac.nz/ (accessed Dec 18, 2012).

24 Ellwood P, Williams H, Aït-Khaled N, Björkstén B, Robertson C; ISAAC Phase III Study Group. Translation of questions: the International Study of Asthma and Allergies in Childhood (ISAAC) experience. *Int J Tuberc Lung Dis* 2009; **13:** 1174–82.

25 World Bank. World Bank GNI per capita operational guidelines and analytical classifications. http://siteresources.worldbank.org/DATASTATISTICS/Resources/OGHIST.xls (accessed Dec 18, 2012).

26 Brunekreef B, Stewart AW, Anderson HR, Lai CK, Strachan DP, Pearce N. Self-reported truck traffic on the street of residence and symptoms of asthma and allergic disease: a global relationship in ISAAC phase 3. *Environ Health Perspect* 2009; **117:** 1791–98.

27 Beasley R, Clayton T, Crane J et al. Association between paracetamol use in infancy and childhood, and risk of asthma, rhinoconjunctivitis, and eczema in children aged 6–7 years: analysis from Phase Three of the ISAAC programme. *Lancet* 2008; **372:** 1039–48.

28 Lim SS, Vos T, Flaxman AD, et al. A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2012; **380:** 2224–60.

29 Ezzati M, Lopez AD, Rodgers A, Vander Hoorn S, Murray CJ; Comparative Risk Assessment Collaborating Group. Selected major risk factors and global and regional burden of disease. *Lancet* 2002; **360**: 1347–60.

30 Po JYT, FitzGerald JM, Carlsten C. Respiratory disease associated with solid biomass fuel exposure in rural women and children: systematic review and meta-analysis. *Thorax* 2011; **66:** 232–39.

31 Dherani M, Pope D, Mascarenhas M, Smith KR, Weber M, Bruce N. Indoor air pollution from unprocessed solid fuel use and pneumonia risk in children aged under five years: a systematic review and meta-analysis. *Bull World Health Organ* 2008; **86:** 390–98.

32 Ezzati M, Kammen DM. The health impacts of exposure to indoor air pollution from solid fuels in developing countries: knowledge, gaps, and data needs. *Environ Health Perspect* 2002; **110:** 1057–68.

33 Albalak R, Frisancho A, Keeler G. Domestic biomass fuel combustion and chronic bronchitis in two rural Bolivian villages. *Thorax* 1999; **54:** 1004–08.

34 Garrett MH, Hooper MA, Hooper BM, Abramson MJ. Respiratory symptoms in children and indoor exposure to nitrogen dioxide and gas stoves. *Am J Respir Crit Care Med* 1998; **158:** 891–95.

35 Melia RJ, Florey CD, Altman DG, Swan AV. Association between gas cooking and respiratory disease in children. *BMJ* 1977; **2:** 149–52.

36 Moran SE, Strachan DP, Johnston ID, Anderson HR. Effects of exposure to gas cooking in childhood and adulthood on respiratory symptoms, allergic sensitization and lung function in young British adults. *Clin Exp Allergy* 1999; **29:** 1033–41.

37 Kurmi OP, Semple S, Simkhada P, Smith WC, Ayres JG. COPD and chronic bronchitis risk of indoor air pollution from solid fuel: a systematic review and meta-analysis. *Thorax* 2010; **65:** 221–28.

38 Willers SM, Brunekreef B, Oldenwening M, et al. Gas cooking, kitchen ventilation, and asthma, allergic symptoms and sensitization in young children: the PIAMA study. *Allergy* 2006; **61:** 563–68.

39 Fullerton DG, Bruce N, Gordon SB. Indoor air pollution from biomass fuel smoke is a major health concern in the developing world. *Trans R Soc Trop Med Hyg* 2008; **102:** 843–51.

40 Padhi BK, Padhy PK. Domestic fuels, indoor air pollution, and children's health. *Ann N Y Acad Sci* 2008; **1140:** 209–17.

41 Venn AJ, Krämer U, Sugiri D, et al. Eczema, respiratory allergies, and traffic-related air pollution in birth cohorts from small-town areas. *J Dermatol* Sci 2009; **56:** 99–105.

42 Bakke JV, Wieslander G, Norback D, Moen BE. Eczema increases susceptibility to PM10 in office indoor environments. *Arch Environ Occup Health* 2012; **67:** 15–21.

43 Pénard-Morand C, Raherison C, Charpin D, et al. Long-term exposure to close-proximity air pollution and asthma and allergies in urban children. *Eur Respir J* 2010; **36:** 33–40.

44 Lai CK, Chan JK, Chan A, et al. Comparison of the ISAAC video questionnaire (AVQ3.0) with the ISAAC written questionnaire for estimating asthma associated with bronchial hyperreactivity. *Clin Exp Allergy* 1997; **27:** 540–45.

45 Solé D, Vanna AT, Yamada E, Rizzo MC, Naspitz CK. International study of asthma and allergies in childhood (ISAAC) written questionnaire: validation of the asthma component among Brazilian children. *J Investig Allergol Clin Immunol* 1998; **8:** 376–82.

46 Gibson PG, Henry R, Shah S, et al. Validation of the ISAAC video questionnaire (AVQ3.0) in adolescents from a mixed ethnic background. *Clin Exp Allergy* 2000; **30:** 1181–87.

47 Mata Fernández C, Fernández-Benítez M, Pérez Miranda M, Guillén Grima F. Validation of the Spanish version of the Phase III ISAAC questionnaire on asthma. *J Investig Allergol Clin Immunol* 2005; **15:** 201–10.

48 Romieu I, Riojas-Rodríguez H, Marrón-Mares AT, Schilmann A, Perez-Padilla R, Masera O. Improved biomass stove intervention in rural Mexico: impact on the respiratory health of women. *Am J Respir Crit Care Med* 2009; **180:** 649–56.

Environment International 123 (2019) 61–69

Contents lists available at ScienceDirect

Environment International

journal homepage: www.elsevier.com/locate/envint

Onset and remission of childhood wheeze and rhinitis across China — Associations with early life indoor and outdoor air pollution

Dan Norbäck[a,b,c,*,1], Chan Lu[a,b,1], Yinping Zhang[d], Baizhan Li[e], Zhuohui Zhao[f], Chen Huang[g], Xin Zhang[h], Hua Qian[i], Yuexia Sun[j], Jan Sundell[a,j], Wang Juan[c,e], Wei Liu[d], Qihong Deng[a,b,**]

[a] XiangYa School of Public Health, Central South University, Changsha, Hunan, China
[b] School of Energy Science and Engineering, Central South University, Changsha, Hunan, China
[c] Department of Medical Sciences, Uppsala University, Uppsala, Sweden
[d] School of Architecture, Tsinghua University, Beijing, China
[e] Key Laboratory of Three Gorges Reservoir Region's Eco-Environment, Chongqing University, Chongqing, China
[f] Department of Environmental Health, Fudan University, Shanghai, China
[g] School of Environment and Architecture, University of Shanghai for Science and Technology, Shanghai, China
[h] Institute of Environmental Science, Shanxi University, Taiyuan, China
[i] School of Energy & Environment, Southeast University, Nanjing, China
[j] School of Environmental Science and Engineering, Tianjin University, Tianjin, China

A R T I C L E I N F O

Keywords:
Asthma
Rhinitis
Dampness
PM2.5
Traffic-related air pollution (TRAP)
Renovation

A B S T R A C T

Objective: Few longitudinal studies exist on childhood exposure to indoor and outdoor air pollution and respiratory illness in China. We studied associations between indoor and outdoor environment and prevalence, onset and remission of wheeze and rhinitis among children across China.
Methods: Children (3–6 y) were recruited from randomized day care centres in six cities. The main data analysis was restricted to children not moving since birth (N = 17,679). Data on wheeze, rhinitis and the home environment were assessed by a parental questionnaire. Prevalence in the first two years of life (baseline) and the last year (follow-up) was used to calculate onset and remission. Outdoor $PM_{2.5}$, PM_{10}, and NO_2 at the day care centre were modelled from monitoring station data. Associations were calculated by multilevel logistic regression.
Results: Prenatal NO_2 was associated with decreased remission of wheeze and increased prevalence and increased onset of rhinitis. Prenatal $PM_{2.5}$ was associated with increased prevalence of wheeze. Postnatal NO_2 and postnatal PM_{10} were associated with increased prevalence and lower remission of wheeze and rhinitis. Mould, window pane condensation, renovation and cockroaches at home were associated with increased prevalence and increased onset of wheeze and rhinitis. Gas cooking was associated with increased onset of rhinitis. Children of mothers with industrial work had more wheeze.
Conclusions: Outdoor $PM_{2.5}$, PM_{10} and NO_2 can increase childhood wheeze and rhinitis. Dampness and mould can increase onset and decrease remission. Crowdedness, cockroaches at home and emissions from new building materials and gas cooking can be risk factors for wheeze and rhinitis.

1. Introduction

There has been a global increase of asthma and rhinitis, especially in middle income countries (Asher et al., 2006). In China there has been a pronounced increase of asthma (Zhang et al., 2013 and allergic rhinitis (Zhang and Zhang, 2014) over the past decades. The priming of the immune system can occur in the prenatal period (Hehua et al., 2017) and in the first years of life (van der Velden et al., 2001). Thus, it is important to study early life effects of environmental exposure in the prenatal as well as in the postnatal period (Gehring et al., 2015; Yang et al., 2016).

Birth cohort studies have demonstrated association between NO_2,

---

* Correspondence to: D. Norbäck, Dept. of Medical Sciences, Uppsala University, Occupational and Environmental Medicine, University Hospital, SE-75185 Uppsala, Sweden.
** Correspondence to: Q. Deng, School of Energy Science and Engineering, Central South University, Changsha 410083, Hunan, China.
E-mail addresses: dan.norback@medsci.uu.se (D. Norbäck), qhdeng@csu.edu.cn (Q. Deng).

[1] These authors contributed equally to the work.

https://doi.org/10.1016/j.envint.2018.11.033
Received 29 May 2018; Received in revised form 13 November 2018; Accepted 14 November 2018

$PM_{2.5}$ and elemental carbon and the development of asthma (Gehring et al., 2015; Yang et al., 2016; Hsu et al., 2015; Clark et al., 2010). Moreover, panel studies from China have demonstrated associations between outdoor PM_{10}, $PM_{2.5}$, NO_2, SO_2 and elemental carbon and airway inflammation (Shi et al., 2016; Zhao et al., 2016; Lin et al., 2011). However, we found no previous study on incidence and remission of asthma or rhinitis among pre-school children in relation to outdoor air pollution in China.

Longitudinal studies have demonstrated associations between indoor exposure at home and childhood asthma or wheeze, including environmental tobacco smoke (ETS) (Burke et al., 2012, gas cooking (Lin et al., 2013), indoor dampness and mould (Quansah et al., 2012) and indoor chemical exposure (Patelarou et al., 2015). Chemical emissions from renovation have been suggested to be a risk factor for childhood allergic disease (Mendell, 2007) but few prospective studies exist on this topic.

The Chinese Children Health Home study (CCHH-study) is a large multi-centre study on environmental risk factors for respiratory health among pre-school children in China (Zhang et al., 2013). The CCHH-study is based on a parentally administered questionnaire with questions on the health of the child and the home environment. Data collection was performed in one wave (a cross-sectional questionnaire survey) but the questionnaire included questions covering different temporal aspects of environmental exposure and symptoms.

The main aim was to study associations between early life outdoor air pollution ($PM_{2.5}$, PM_{10}, and NO_2) and environmental factors the home environment and prevalence (in the first two years of life), onset and remission of wheeze and rhinitis within the CCHH-study. Investigated home environment factors included number of persons at home, environmental tobacco smoke (ETS), home renovation, type of cooking fuel, dampness and mould, presence of cockroaches, cleaning frequency and use of air conditioning units. In addition, we evaluated associations for two indicators of socioeconomic status (SES) of the family, namely size of the home and mother's occupation during pregnancy and two city level variables (outdoor temperature and GDP per capita).

2. Material and methods

2.1. Study population

The study population consisted of pre-school children recruited from randomly selected day care centres in six major cities in China (Urumqi, Taiyuan, Nanjing, Shanghai, Chongqing and Changsha). Urumqi and Taiyuan were defined as northern cities since they are located north of the Yangtze River and the others were defined as southern cities. A questionnaire was distributed to the parents or other guardians from December 2010 to January 2012 (in different heating seasons in different cities). All children in the randomly selected day care centres (N = 48,372) were invited to join the study and 38,475 participated (79.5% participation rate). This paper was restricted to children 3–6 years old with information on age and sex of the child. Most of the questionnaires (91.2%) were answered by the parents, the rest (8.8%) were mainly answered by grandparents. Initially, we excluded all children living in rural areas (N = 1307) since they had to commute to reach the day care centres which were in urban or suburban areas. In the main analysis, we restricted the analysis to children who had lived in the same home since birth to get a better assessment of exposure to indoor and outdoor air pollution. A total of 17,679 children were included in the main analysis, and 3723 (21%) were from northern China. Additional data analysis was made including all children (movers and non-movers) living in urban or suburban areas (N = 29,428).

2.2. Study design and dependent variables

The study is based on a cross-sectional data collection where onset and remission of wheeze and rhinitis symptoms were estimated retrospectively. One yes/no question asked if the child ever had wheeze in the first two years of life. Another yes/no question asked about wheeze in the last 12 months. A third yes/no question asked if the child had rhinitis symptoms when not having a cold in the first two years of life. A fourth yes/no question asked about rhinitis symptoms when not having a cold in the last 12 months. These questions were from the large international ISAAC study (The International Study of Asthma and Allergies in Childhood) (Asher et al., 2006). The prevalence of wheeze and rhinitis in the first two years of life was defined as baseline prevalence. The prevalence of current wheeze and rhinitis (in the last 12 months) was defined as follow-up prevalence. Onset of wheeze was defined as not having wheeze at baseline (first 2 years of life) but having current wheeze (in the last 12 months) when the questionnaire was answered. Onset of rhinitis was defined in the same way as not having rhinitis at baseline but having current wheeze. Remission of wheeze was defined as having wheeze at baseline (first 2 years of life) but not having current wheeze (in the last 12 months) when the questionnaire was answered. Remission of rhinitis was defined in the same way as having rhinitis at baseline but not current rhinitis. A total of six dependent variables were analysed (baseline prevalence, onset and remission of wheeze and rhinitis).

2.3. Ethics

The study and the consent procedure were approved by the Medical Research Ethics Committee of School of Public Health, Fudan University, Shanghai. The participants and parents gave informed consent.

2.4. Assessment of demographic data and socioeconomic status (SES)

Data on gender, age, birth season, birth weight, breast feeding and parental asthma or rhinitis, were collected from the questionnaire. These six covariates were considered as potential confounders and were included all models. Moreover, two SES variables were included, size of the home (m^2) and mothers' occupation during pregnancy, number of persons living in the home, and life-time mean GDP per capita on city level. There was no question on father's occupation or family income. Size of the home has been demonstrated to be a good socioeconomic indicator related to family income in USA as well as in China (Juhn et al., 2011; Norbäck et al., 2018). Moreover, we calculated lifetime GDP per capita on city level as an indicator of the economic development level of the city. Annual data on income per capita from 2005 to 2012 was obtained from China Statistical Yearbook for each city. Due to the rapid economic development in China, GDP per capita is increasing year by year. For each child, a life-time mean GDP/capita value was calculated based on average values of GDP per capita (city level data) from year of birth of the child until the year when the questionnaire was answered.

2.5. Assessment of data on the home environment

Data on the home environment was obtained from the parental questionnaire. There were three yes/no questions on renovation of the home environment (a) during pregnancy, (b) when the child was 0–1 year old and (c) after first year of life. Three other yes/no questions asked about buying new furniture to the home (a) during pregnancy, (b) when the child was 0–1 year old and (c) after first year of life. These six questions were combined to one variable called renovation (Yes if at least one answer was eyes, or else no). There were two questions asking about visible mould: (a) at birth and (b) after birth. Two other questions asked about damp stains (a) at birth and (b) after birth. These four questions were combined to one variable called visible mould/damp stains (Yes if at least one answer was eyes, or else no). Moreover, there were two questions asking about window pane condensation in winter: (a) at birth and (b) after birth. These two questions were combined to one variable called window pane condensation (Yes if at least one answer was yes, or else no). One question asked about type of cooking fuels in the current home and was classified as only electricity, gas cooking but not biomass and any type of biomass (wood or coal). Moreover, there were four other questions asking about the situation in the current home: Number of persons living in the current home, environmental tobacco smoke (yes/no), daily cleaning (yes/no), presence of cockroaches (yes/no) and use of air conditioning units (yes/no). All home environment variables were included in all models. One additional question asked if the child had had moved to another home since birth. This variable was used to select children who had lived in the same home since birth (in the main analysis). Another question asked if the current home was located in (a) an urban area, (b) a suburban area and (c) a rural area. In this article we restricted all statistical analysis to children living in urban or suburban areas to get a better assessment of the outdoor air pollution exposure.

2.6. Assessment of personal exposure to outdoor air pollution and temperature

We calculated personal exposure to outdoor air pollution and temperature for each child during different pre-natal and post-natal periods based on birth month and location of the day care centre. We knew the location of their day care centre but not the children's home address or postal code of the home address. Since children in China live relatively close to their day care center, the day care centre air pollution level could be a reasonable approximation of their outdoor exposure. We used an inverse distance weighted (IDW) method (Bell, 2006) to estimate the monthly mean concentrations of air pollutants ($PM_{2.5}$, PM_{10}, NO_2, SO_2) at each day care centre by interpolation from modelled data for the closest four monitoring stations. The IDW approach to air pollution data modelling have been us by different research groups (Bell, 2006; Brauer et al., 2008; Marshall et al., 2008; Nishimura et al., 2013, Deng et al., 2016a, b). In the present study, the concentration of air pollutant in different kindergarten was calculated by the following formula using quadratic function:

$$C_k = (C_{S1}/d_1^2 + C_{S2}/d_2^2 + C_{S3}/d_3^2 + C_{S4}/d_4^2)$$
$$/(1/d_1^2 + 1/d_2^2 + 1/d_3^2 + 1/d_4^2)$$

where, C_k is the concentration of air pollutant ($PM_{10}/SO_2/NO_2$) in the kindergarten; C_{S1} to C_{S4} are the concentration of air pollutant in the first to the fourth nearest monitoring station of air pollution from the kindergarten; d1 to d4 are the distances from the kindergarten to the first to the fourth nearest monitoring station of air pollution.

We retrospectively modelled air pollution and temperature for the study period (2003 – 2013) using available measured data from all monitoring stations for the period 2014–2016 as well as official annual mean (city level) air pollution data for all years (2003–2013). Measurements at the monitoring stations followed the standard methods set by the Environmental Protection Agency of China: $PM_{2.5}$ and PM_{10} by a tapered element oscillating microbalance, and NO_2 by the chemiluminescent method. The annual concentrations of PM_{10} and NO_2 during 2003–2009 were obtained from the website of the National Bureau of Statistics of the People's Republic of China.

Modelled data on day care center level were calculated by regression equations based on annual mean city level air pollution data and daily mean air pollution data from 61 air pollution monitoring stations and 81 climate monitoring stations in the six cities. Each city had 7 to 17 air pollution monitoring stations and 8 to 33 climate monitoring stations (including temperature). The largest numbers of stations were for Shanghai and Chongqing, the largest cities. Data on SO_2 on day care center level were calculated but not used in this study due to strong correlation between PM_{10} and SO_2 ($r = 0.92$) and between ambient temperature and SO_2 ($r = -0.87$), we did not include SO_2 in the hypothesis testing in this article.

The modelled data of air pollutants on day care center level were calculated as follows: First, we downloaded the annual concentrations PM_{10}, SO_2, and NO_2 during 2003–2013 and calculated their annual concentrations by daily data in 2015 among six cities. We then calculated the ratios of the annual mean concentrations of PM_{10}, SO_2, and NO_2 in each year during 2003–2013 to the annual averaged data in 2015 at all the monitoring stations (supplemental materials, Table S1-a, Table S1-b, and Table S1-c). Secondly, the daily concentrations of the two pollutants in 2015 were multiplied by the ratio at each station for each year during 2003–2013, and thus we obtained the modelled daily data of PM_{10}, SO_2, and NO_2. This method ensured that the annual averaged values of modelled data were the same as the measured data. Thirdly, we calculated the ratio of daily concertation of each air pollutant at each monitoring station to the average daily concentration among all the monitoring stations in 2015 to obtain the concentration ratio of each station to the averaged value for all monitoring stations in the city. Fourthly, we multiplied the ratio for each station calculated in the third step by the daily concentration during 2003–2013 calculated in the second step, and thus we finally obtained the modelled daily concentration of the pollutant at each station during 2003–2013. Furthermore, we constructed a linear regression model for the daily measured data of $PM_{2.5}$ based on the measured PM_{10} data at different monitoring stations during 2014–2015. Finally, we used the regression functions to calculate the daily data of $PM_{2.5}$ based on the daily concentration of PM_{10} during 2003–2013 calculated above.

The modelled data of daily mean temperature on day care center level were calculated as follows: First, we downloaded the daily maximum and minimum temperature during 2011–2016 from the China Meteorological Agency (CMA) during different stations in each city and also the relative data during 2003–2016 (total city) from National Meteorological Information Center (NMIC). Secondly, we constructed a linear regression model between the data from NMIC and CMA in each station during 2011–2016 ($R^2 > 0.9$). Thirdly, we used the function from the regression model to calculate the daily maximum and minimum temperature at different stations in each city based on the data from the CMA during 2003–2013. Finally, we obtained the daily mean temperature by averaging the data of daily maximum and minimum temperatures at different stations in each city during 2003–2013 (the study period).

Finally, individual exposure at the co-ordinates of the current day care centre was assessed based on the monthly mean values as follows: (1) prenatal exposure during the full gestation length was calculated as the average of the monthly mean concentrations of the air pollutants and temperature during the full gestational months; and (2) postnatal exposure was calculated as the average of the monthly mean concentrations during the period from the first month of life until the past year.

Modelled data for air pollution and outdoor temperature were validated by comparing modelled data and real data (monthly mean values) for monitoring stations in one city (Changsha) where monitoring station data were available for the study period (2003–2013). The Pearson correlation coefficient (r) between modelled and real data was 0.75 for PM_{10}, 0.87 for SO_2, and 0.84 for NO_2 and 0.995 for outdoor temperature. Data on $PM_{2.5}$ was not available in Changsha during the study period.

2.7. Statistical analysis

We had questions about symptoms in the first two years of life and current symptoms (in the past 12 months) when the questionnaire was answered. Since the prevalence of wheeze or rhinitis during the first two year of life was defined as the baseline data, follow up time was defined as age (when the questionnaire was answered) minus two years. Mean follow-up time and total follow up time (person years) were calculated for each city. Onset was calculated excluding those with wheeze or rhinitis at baseline. Onset per year was calculated by dividing number of onset cases with number of person years. Remission was calculated including only those with wheeze or rhinitis at baseline. Remission per year was calculated by dividing number of remission cases with number of person years.

Multilevel logistic regression was used to study associations between exposure and incidence and remission of wheeze and rhinitis (two different dependent variables). Two levels were used (city and child). We included six personal factors (sex, age, birth season, birth weight, breast feeding, parental asthma or rhinitis), four SES variables (mothers occupation during pregnancy, house size, number of persons in the home, city GDP per capita), and nine home environment variables (ETS, renovation, type of cooking, visible mould/damp stains, window pane condensation, water damage/leakage, cleaning frequency, presence of cockroaches, air conditioning). Ambient temperature for the same period as the modelled air pollution (prenatal or postnatal) was included in all models. First, we analysed associations for prenatal and postnatal air pollution ($PM_{2.5}$, PM_{10}, and NO_2). Then we analysed associations for covariates, SEI variables and indoor factors, adjusting for NO_2 and ambient temperature. Moreover, we performed sensitivity analysis stratifying for sex. Odd ratios (ORs) with 95% confidence interval (95% CI) were calculated. Associations for air pollutants were expressed per interquartile range (IQR). A two-tailed p-value < 0.05 was considered as significant. All statistical analysis was performed by STATA11.0 (STATA Corp., Texas, and USA).

3. Results

There were no significant differences in the prevalence, onset or remission of wheeze or rhinitis symptoms when comparing answerers from parents with answers from other guardians (Table S2). Descriptive data on personal factors, the home environment and indicators of socioeconomic status (SES) are given in Table 1 and data on outdoor air pollution is given in Table 2. There were no co-linearity problems for the exposure variables included in the models (maximum $r = 0.74$). There was a significant association between the two SES variables (home size and mothers occupation during pregnancy ($p < 0.001$ by Chi^2 test) but the differences in prevalence were small when comparing mother living in smaller and larger homes (Table S3). To increase the relevance of our assessment of home environment factors, our main data analysis was based on a restricted dataset of children living in the same home since birth. Thus, it is relevant to see to what extent the home environment and indicators of SES differed between children moving and not moving to another home since birth. Non-movers tended to have slightly more persons living in the home, slightly more ETS at home, less renovation of the home and slightly more use of biomass for cooking. Moreover, non-movers had slightly more water damage, slightly more cockroaches and slightly more use of air conditioning units. Besides the difference regarding home renovation (38.8% vs 54.6%), the differences in home environment factors were small. None of the SES indicators differed between movers and non-movers (Table S4).

Baseline prevalence (0–2 y), onset and remission data of wheeze and rhinitis symptoms is given in Table 3. The mean follow-up time was 2.38 years (range 2.06–2.67 years). For wheeze, there was totally 15.8% onset (6.5%/year) and 48.5% remission (20.2% per year). For rhinitis, there was totally 38.9% onset (15.7%/year) and 29.1% remission (12.7%/year). Onset as well as remission per year of wheeze was highest in the two northern cities Urumqi and Taiyuan. Onset per year of rhinitis was highest in Nanjing and remission per year was highest in Urumqi and Taiyuan (Table 3).

Associations between outdoor air pollution and baseline prevalence, onset and remission of wheeze and rhinitis and are given in Table 4. Data on outdoor air pollution was calculated for the location of the current day care centre using the four closest air pollution monitoring stations by the IDW method. The mean distance from the day care centre to the closest monitoring station was 5.87 km and the mean distance to the 4th monitoring station (most far away) was 12.52 km. The overall mean distance to the monitoring stations was 9.38 km. The mean distance to the monitoring stations were longer in Shanghai as compared to the other cities (Table S5). $PM_{2.5}$ was associated with prevalence of rhinitis (OR 1.12 per IQR; 95% CI 1.03–1.22). Prenatal exposure to NO_2 was associated with prevalence (OR 1.21 per IQR; 95% CI 1.19–1.32) and increased onset of rhinitis (OR 1.18 per IQR; 95% CI 1.00–1.40) and lower remission of wheeze (OR = 0.63 per IQR; 95% CI

Table 1
Demographic information among Chinese children aged 3–6 y living in the same home since birth (n = 17,679).

	Number (n)	Percentage (%)
Total	17,679	100
Personal factors		
Sex		
Boys	9071	51
Girls	8608	49
Follow up time (from age-2) (years)		
1	3396	19
2	6552	37
3	5279	30
4	2452	14
Birth season		
Spring (March–May)	4311	24
Summer (June–August)	4549	26
Autumn (September–November)	4593	26
Winter (December–February)	4226	24
Birth weight (kg)		
< 2.5	417	2
≥2.5	16,902	96
Breast-feeding	15,341	87
Parental atopy	2153	12
Home environment factors		
Number of persons living in current home (n)		
< 3	2857	16
3–4	8933	51
> 4	4800	27
Environmental tobacco smoke (ETS) at home	10,197	58
Home renovation	6841	39
Cooking fuel in current home		
Only electricity	2088	12
Natural gas but no biomass	13,216	75
Any biomass cooking (coal/wood)	1305	7
Visible mould/damp stains at home	5317	30
Window pane condensation in winter	10,417	59
Water damage	2724	15
Cleaning every day	9586	54
Cockroaches noted	9405	53
Air conditioning use	2264	13
Indicators of socioeconomical status (SES)		
Size of the home (m^2)		
≤100	12,225	69
> 100	5210	29
Maternal occupation during pregnancy		
Not occupationally active*	6923	39
Farmer	173	1
Industrial worker	578	3
White-collar worker†	9929	56

City level data	Mean	SD
Lifetime gross domestic product (GDP) per capita (RMB) (on city level)	77,870	36,752

Sum of the number is not 17,679 due to missing data.

* House wife or unemployed.

† White-collar worker was defined as office staff, teacher, medical staff, student, shop assistant and other occupations.

Table 2
Prenatal and postnatal exposure to outdoor air pollution and outdoor temperature among children aged 3–6 (n = 17,679).

	Mean	25th Percentile	50th Percentile	75th Percentile	IQR
During entire pregnancy					
$PM_{2.5}$	69	63	67	76	13
PM_{10}	107	91	104	121	30
SO_2	68	55	60	77	22
NO_2	50	44	53	58	14
T	16.4	15.1	17.3	19.7	4.6
Postnatal period					
$PM_{2.5}$	62	58	60	67	9
PM_{10}	96	82	93	105	23
SO_2	53	41	47	61	20
NO_2	48	43	52	53	10
T	16.2	17.0	18.0	18.2	1.2

$PM_{2.5}$, $PM_{2.5-10}$, PM_{10} (μg/m^3) = particulate matter ≤2.5, between 2.5 and 10, and ≤10 μm in aerodynamic, SO_2 (μg/m^3) = sulphur dioxide, NO_2 (μg/m^3) = nitrogen dioxide, T (°C) = temperature.

0.49–0.81). Postnatal $PM_{2.5}$ was associated with prevalence of wheeze (OR 1.15 per IQR; 95% CI 1.00–1.31). Postnatal PM_{10} was associated with lower remission of wheeze (OR = 0.50 per IQR; 95% CI 0.30–0.84) and rhinitis (OR = 0.59 per IQR; 95% CI 0.41–0.84). Postnatal NO_2 was associated with prevalence of wheeze (OR 1.12 per IQR; 95% CI 1.03–1.22) and rhinitis (OR 1.18 per IQR; 95% CI 1.08–1.28) as well as lower remission of wheeze (OR = 0.70 per IQR; 95% CI 0.57–0.86) and rhinitis (OR 0.83 per IQR, 95% CI 0.71–0.97). Since the correlation between prenatal and post-natal NO_2 (on day care center level) was strong (r = 0.87) it was not possible to include prenatal and postnatal exposure in the same model. The accuracy of the pre-natal exposure assessment can be less if the mother moved to another area from pregnancy to the birth of the child. However, questionnaire data demonstrated that only 7% of the mothers had moved from pregnancy to birth.

Health associations for personal factors, indoor factors, indicators of socioeconomic status (SES) and city level GDP per capita are given in Table 5. Boys had higher prevalence of wheeze and rhinitis and higher incidence of rhinitis. Children with longer follow-up time (older children) had lower prevalence of wheeze, higher remission of wheeze and rhinitis and higher incidence of rhinitis. Children born in summer or autumn had higher incidence and lower remission of wheeze. Parental atopy was associated with higher prevalence and higher incidence and lower remission of wheeze and rhinitis.

Among the indoor environment factors, size of the family (> 4 persons in the home) was associated with higher incidence of wheeze. Recent renovation at home was associated with higher prevalence of wheeze and higher incidence of wheeze and rhinitis. Cooking with electricity only was associated with lower incidence of rhinitis, as compared to gas cooking (used as reference category). Visible indoor mould/damp stains in the child's bedroom was associated with higher prevalence and higher incidence of asthma and rhinitis and lower remission of wheeze. Window pane condensation in wintertime was associated with higher prevalence of wheeze and higher incidence and lower remission of wheeze and rhinitis. Presence of cockroaches was associated with higher prevalence and higher incidence of wheeze and rhinitis. Use of air conditioners were associated with higher prevalence and daily cleaning of the home was associated with lower prevalence of wheeze (Table 5).

Among the two indicators of socioeconomic status (SES-variables), living in a large home (> 100 m^2) was associated with lower incidence of rhinitis. Children of mothers with an industrial work during pregnancy had higher prevalence of wheeze. Children of mothers who did not work during pregnancy (housewife or unemployed) had higher incidence of rhinitis. Among the two city level exposure variables, a higher ambient temperature was associated with lower remission of wheeze and higher prevalence, lower incidence and lower remission of rhinitis. A higher GDP per capita (on city level) was associated with lower prevalence of wheeze, lower incidence of wheeze and a lower remission of wheeze and rhinitis (Table 5).

A sensitivity analysis was performed to study gender interaction for associations between onset and remission of wheeze and rhinitis and outdoor air pollution. No statistically significant gender interaction was observed (all p-values for interaction > 0.1).

To improve the relevance of the exposure assessment, we restricted the statistical analysis to children living in the same home since birth. This restriction could have created a selection of children with different home environment or a different socioeconomic status (SES). However, we found no major difference in the prevalence of home environment factors (except for renovation), and no significant difference in indicators of SES, when comparing movers and non-movers. Moreover, when analysing associations between outdoor air pollution (Table S6)

Table 3
Number of cases and percentage of onset and remission of wheeze and rhinitis symptoms (n = 17,679).

	Prevalence at baseline (%) (0–2 years)	Mean follow up time (yr)	Onset				Remission			
			N[a]	N[b]	%	No/yr (%)	N[c]	N[d]	%	No/yr (%)
Wheeze										
Urumqi	17.5	2.62	329	1309	25.1	9.19	202	275	73.5	26.17
Taiyuan	9.8	2.06	262	1845	14.2	7.21	154	199	77.4	39.71
Nanjing	9.2	2.67	209	1545	13.5	5.02	65	156	41.7	15.63
Shanghai	11.2	2.43	1061	6561	16.2	5.95	312	828	37.7	16.04
Chongqing	12.3	2.35	298	2147	13.9	5.83	132	301	43.9	16.28
Changsha	13.9	2.18	264	1912	13.8	5.84	137	309	44.3	20.40
Total	11.9	2.38	2423	15,319	15.8	6.52	1002	2068	48.5	20.17
Rhinitis symptoms										
Urumqi	21.1	2.62	627	1274	49.2	18.00	169	337	50.1	19.45
Taiyuan	18.4	2.06	468	1638	28.6	14.94	225	375	60.0	31.24
Nanjing	22.5	2.67	786	1325	59.3	21.94	63	383	16.4	6.94
Shanghai	25.2	2.43	2026	5489	36.9	12.98	414	1838	22.5	10.76
Chongqing	23.6	2.35	618	1882	32.8	14.11	171	584	29.3	11.82
Changsha	25.1	2.18	637	1676	38.0	16.78	145	567	25.6	13.71
Total	23.5	2.38	5162	13,284	38.9	15.74	1187	4084	29.1	12.71

[a] Number of onset cases of wheeze or rhinitis symptoms.
[b] Number of children without wheeze or rhinitis symptoms at baseline (0–2 y age).
[c] Number of remission cases of wheeze or rhinitis symptoms.
[d] Number of children with wheeze or rhinitis symptoms at baseline.

Table 4

Odd ratio (95% CI) of baseline prevalence, onset and remission of wheeze and rhinitis symptoms in relation to pre- and post-natal exposure to air pollution (n = 17,679).

	Wheeze			Rhinitis symptoms		
	Prevalence	Onset	Remission	Prevalence	Onset	Remission
Prenatal						
$PM_{2.5}$	1.06 (0.95, 1.18)	0.96 (0.86, 1.06)	0.86 (0.67, 1.09)	1.12 (1.03, 1.22)**	1.04 (0.96, 1.14)	1.01 (0.85, 1.20)
PM_{10}	0.96 (0.79, 1.17)	0.92 (0.77, 1.09)	0.70 (0.46, 1.05)	1.14 (0.98, 1.32)	1.06 (0.91, 1.23)	1.19 (0.89, 1.61)
NO_2	1.09 (0.97, 1.23)	1.04 (0.93, 1.17)	0.63 (0.49, 0.81)***	1.21 (1.10, 1.32)***	1.18 (1.00, 1.40)*	0.85 (0.68, 1.06)
Postnatal						
$PM_{2.5}$	1.15 (1.00, 1.31)*	0.96 (0.86, 1.07)	0.81 (0.63, 1.04)	1.08 (0.98, 1.20)	1.03 (0.90, 1.18)	0.95 (0.77, 1.17)
PM_{10}	1.05 (0.84, 1.31)	0.89 (0.71, 1.13)	0.50 (0.30, 0.84)**	1.03 (0.87, 1.21)	0.75 (0.48, 1.18)	0.59 (0.41, 0.84)**
NO_2	1.12 (1.00, 1.26)*	1.04 (0.95, 1.14)	0.70 (0.57, 0.86)***	1.18 (1.08, 1.28)***	1.18 (0.86, 1.62)	0.83 (0.71, 0.98)*

OR (95%CI) was estimated for IQR increase in air pollutants.

Models were adjusted for all the covariates in Table 1, GDP per capita, and air temperature within each time window.

* $p < 0.05$.

** $p < 0.01$.

*** $p < 0.001$.

and other co-variates (Table S7), including movers as well as non-movers, similar associations were obtained as in the restricted analysis (Tables 4 and 5).

4. Discussion

To our knowledge, this is one of few studies examining the effects of early life exposure to home environment factors and outdoor air pollution in relation to onset and remission of childhood respiratory symptoms in China. We found that prenatal NO_2 was associated with lower remission of wheeze and increased onset of rhinitis. Postnatal NO_2 and postnatal PM_{10} were associated with decrease remission of wheeze and rhinitis. Crowdedness, dampness or mould, window pane condensation in winter, renovation and cockroaches at home were associated with increased onset of wheeze and rhinitis. Gas cooking was associated with increased onset of rhinitis. A lower economic development level of the city, measured as GDP per capita, was associated with increased onset of wheeze. Moreover, children living in smaller homes (< 100 m^2 area) and children of mothers not being occupationally active during pregnancy had a higher onset of rhinitis.

The study has some strengths. It is a large study including six cities in China with different climate and different development level. By calculating onset and remission during the pre-school period we could get a more valid estimation of health effects of the indoor and outdoor air pollution, as compared to analysing only the prevalence of wheeze and rhinitis. Another strength is that we adjust for many potential confounds in mutually adjusted models. To increase the precision of the exposure assessment, we restricted the main statistical analysis to children living in the same home since birth.

The study has a number of limitations. One limitation is that we assessed onset and remission of wheeze and rhinitis symptoms retrospectively. Another limitation is that we did not included clinical assessment or doctor diagnosis of asthma and rhinitis. Since we did not have access to the home address, outdoor air pollution was calculated by IDW models for the location of the day care centre. Since children in Chinese cities usually go to a day care centre near the home, and the mean distance from the day care centre to the air pollution monitoring stations used in the IDW models were about 10 km, this would not be a major limitation of the study.

Outdoor NO_2 is mainly an indicator of traffic-related air pollution (TRAP) and the mean personal outdoor exposure in our study was 50 $\mu g/m^3$ (prenatal exposure) and 48 $\mu g/m^3$ (postnatal exposure). This is well above the WHO limit value of 40 $\mu g/m^3$ for NO_2 (WHO, 2005). We found that pre-natal exposure to NO_2 was associated with onset of rhinitis. This agrees with a previous publication from Changsha, China (Deng et al., 2016a). Moreover, NO_2 exposure was associated with lower remission of wheeze (pre-natal) and lower remission of rhinitis (prenatal and post-natal). A recent meta-analysis of 18 studies concluded that prenatal exposures to NO_2 can increase the risk of childhood wheeze (Hehua et al., 2017). Another meta-analysis of 12 studies found that childhood exposure to NO_2 can increase the onset of wheeze and childhood asthma (Takenoue et al., 2012).

In our study, prenatal $PM_{2.5}$ was associated with higher prevalence of rhinitis and postnatal $PM_{2.5}$ was associated with higher prevalence of wheeze. Moreover, postnatal PM_{10} was associated with lower remission of wheeze and rhinitis. One recent article from the CCHH study found associations between kindergarten-level $PM_{2.5}$ concentrations, obtained from satellite data, and rhinitis and doctor diagnosed asthma among pre-school children Chen et al., 2018). Some previous studies exist from East Asia on associations between exposure to outdoor PM_{10} and prevalence of wheeze (Gao et al., 2014) and rhinitis (Siwarom et al., 2017; Teng et al., 2017).

Six indoor factors at home were associated with wheeze and rhinitis. Children in crowded homes, with > 4 persons, had a higher onset of wheeze. Renovation (including indoor painting or buying new furniture) was associated with prevalence and onset of wheeze and rhinitis. Our results agree with previous prevalence studies showing associations between renovation/new furniture and wheeze (Franck et al., 2014; Fan et al., 2017) and rhinitis (Deng et al., 2016a; Li et al., 2014). However, we found no previous study on renovation and onset of childhood wheeze and rhinitis.

We found that children living in homes with gas cooking, as compared to homes using only electricity for cooking had a higher onset of rhinitis. This agrees with a previous prevalence study from China (Wong et al., 2004).

Mould or damp stains in the bedroom of the child was associated with prevalence and onset of wheeze and rhinitis and lower remission of wheeze. This agrees with previous review articles concluding that dampness and indoor mould are risk factors for incidence of asthma symptom (Quansah et al., 2012) and prevalence of rhinitis (Jaakkola et al., 2013).

Window pane condensation in winter was the most consistent indoor risk factor in our study, associated with prevalence of wheeze, onset of wheeze and rhinitis and lower remission of wheeze and rhinitis. To our knowledge, our study is the first to demonstrate associations between window pane condensation and onset or remission of wheeze and rhinitis. However, previous prevalence studies have found that window pane condensation at home in wintertime is a risk factor for wheeze (Deng et al., 2016a; Takaoka and Norbäck, 2011) and rhinitis (Deng et al., 2016a; Wang et al., 2014). Window pane condensation in wintertime is an indicator of high air humidity, low ventilation flow and higher levels of house dust mite allergens in dust (Emenius et al., 2000).

Table 5

Associations (OR, 95% CI) between personal factors, SES, indoor environment and baseline prevalence, onset and remission of wheeze and rhinitis symptoms (n = 17,679).

		Wheezing			Rhinitis-like symptoms		
		Prevalence	Onset	Remission	Prevalence	Onset	Remission
Personal factors							
Sex	Male vs. female	1.49 (1.33, 1.68)***	1.05 (0.94, 1.17)	0.96 (0.76, 1.22)	1.18 (1.08, 1.29)***	1.14 (1.05, 1.25)**	0.91 (0.76, 1.09)
Follow up time (from age-2) (years)	1	1.00	1.00	1.00	1.00	1.00	1.00
	2	0.84 (0.71, 0.98)*	0.92 (0.79, 1.08)	1.82 (1.31, 2.52)***	0.79 (0.70, 0.88)***	1.17 (1.01, 1.35)*	1.32 (1.04, 1.67)*
	3	0.82 (0.69, 0.97)*	0.97 (0.82, 1.14)	2.24 (1.59, 3.16)***	0.59 (0.52, 0.68)***	1.30 (1.09, 1.55)**	1.40 (1.08, 1.81)*
	4	0.77 (0.62, 0.95)*	0.88 (0.71, 1.08)	2.29 (1.50, 3.52)***	0.46 (0.39, 0.55)***	1.12 (0.88, 1.42)	1.34 (0.93, 1.91)
Birth season	Spring (reference)	1.00	1.00	1.00	1.00	1.00	1.00
	Summer vs. spring	0.88 (0.75, 1.05)	1.19 (1.02, 1.40)*	0.68 (0.49, 0.95)*	1.03 (0.91, 1.17)	1.00 (0.88, 1.14)	0.97 (0.76, 1.24)
	Autumn vs. spring	1.05 (0.89, 1.23)	1.17 (1.00, 1.37)*	0.69 (0.50, 0.96)*	1.09 (0.96, 1.23)	1.05 (0.92, 1.19)	0.85 (0.66, 1.09)
	Winter vs. spring	1.05 (0.89, 1.24)	1.15 (0.97, 1.35)	0.89 (0.64, 1.24)	1.01 (0.89, 1.15)	1.03 (0.90, 1.17)	1.00 (0.78, 1.30)
Birth weight (kg)	< 2.5 vs. ≥2.5	1.53 (1.08, 2.16)*	1.05 (0.72, 1.53)	1.41 (0.73, 2.71)	0.97 (0.72, 1.31)	0.96 (0.71, 1.30)	1.01 (0.55, 1.84)
Breast-feeding	Yes vs. no	0.89 (0.74, 1.07)	0.97 (0.82, 1.16)	1.26 (0.88, 1.82)	0.91 (0.80, 1.05)	1.01 (0.87, 1.17)	1.02 (0.77, 1.34)
Parental atopy	Yes vs. no	2.13 (1.85, 2.46)***	1.94 (1.68, 2.25)***	0.66 (0.50, 0.87)**	1.69 (1.50, 1.91)***	2.29 (2.00, 2.62)***	0.45 (0.35, 0.60)***
Home environment factors							
Number of persons living in the home (n)	< 3	0.96 (0.74, 1.25)	0.90 (0.70, 1.16)	0.69 (0.41, 1.15)	1.15 (0.95, 1.38)	1.15 (0.94, 1.41)	1.23 (0.85, 1.78)
	3–4	1.00	1.00	1.00	1.00	1.00	1.00
	> 4	1.06 (0.93, 1.21)	1.18 (1.04, 1.34)**	0.81 (0.63, 1.05)	0.96 (0.87, 1.06)	1.04 (0.94, 1.15)	1.06 (0.86, 1.30)
ETS	Yes vs. no	0.98 (0.86, 1.11)	1.11 (0.99, 1.24)	0.84 (0.66, 1.07)	0.99 (0.90, 1.08)	1.08 (0.99, 1.19)	0.92 (0.77, 1.11)
Home renovation	Yes vs. no	1.14 (1.01, 1.28)*	1.16 (1.04, 1.30)**	0.89 (0.70, 1.12)	1.03 (0.94, 1.13)	1.17 (1.07, 1.28)***	0.88 (0.73, 1.05)
Type of cooking fuel	Only electricity	0.91 (0.75, 1.10)	0.97 (0.82, 1.16)	1.05 (0.71, 1.54)	1.06 (0.92, 1.21)	0.87 (0.75, 1.00)*	1.09 (0.82, 1.43)
	Natural gas but no biomass	1.00	1.00	1.00	1.00	1.00	1.00
	Any biomass (coal/wood)	1.13 (0.91, 1.41)	0.98 (0.80, 1.22)	0.83 (0.54, 1.28)	1.08 (0.92, 1.27)	1.04 (0.87, 1.24)	1.13 (0.80, 1.60)
Visible mould/damp stains at home	Yes vs. no	1.22 (1.03, 1.44)*	1.31 (1.12, 1.54)***	0.71 (0.51, 1.00)*	1.22 (1.07, 1.38)**	1.30 (1.14, 1.49)***	0.81 (0.62, 1.05)
Window pane condensation	Yes vs. no	1.24 (1.09, 1.40)***	1.45 (1.29, 1.64)***	0.77 (0.60, 0.99)*	1.09 (0.99, 1.19)	1.23 (1.12, 1.35)***	0.81 (0.67, 0.97)*
Water damage	Yes vs. no	1.18 (0.97, 1.44)	1.03 (0.85, 1.24)	1.40 (0.95, 2.07)	0.94 (0.81, 1.10)	0.99 (0.84, 1.17)	1.24 (0.90, 1.71)
Cleaning every day	Yes vs. no	0.83 (0.74, 0.94)**	0.90 (0.81, 1.01)	0.93 (0.74, 1.19)	1.02 (0.93, 1.11)	0.98 (0.89, 1.07)	1.19 (0.99, 1.43)
Cockroaches noted	Yes vs. no	1.20 (1.05, 1.36)**	1.12 (1.00, 1.26)*	0.82 (0.63, 1.05)	1.11 (1.01, 1.22)*	1.16 (1.05, 1.27)**	1.03 (0.84, 1.24)
Air conditioning use	Yes vs. no	1.25 (1.00, 1.55)*	0.99 (0.84, 1.18)	1.08 (0.78, 1.50)	1.01 (0.89, 1.15)	0.72 (0.49, 1.05)	1.30 (0.92, 1.82)
Indicators of socioeconomical status (SES)							
Size of the home (m^2)	≤100 vs. > 100	0.98 (0.86, 1.11)	1.12 (0.99, 1.27)	1.24 (0.96, 1.59)	1.02 (0.92, 1.12)	0.84 (0.76, 0.92)***	1.18 (0.97, 1.44)
Maternal occupation	Not occupationally active	1.02 (0.91, 1.16)	1.07 (0.95, 1.20)	1.04 (0.82, 1.33)	1.02 (0.93, 1.12)	1.17 (1.07, 1.29)***	1.05 (0.88, 1.27)
	Farmer	1.08 (0.55, 2.11)	0.76 (0.36, 1.59)	1.93 (0.47, 7.92)	0.79 (0.46, 1.37)	1.13 (0.69, 1.84)	1.95 (0.70, 5.41)
	Industrial worker	1.41 (1.03, 1.93)*	1.07 (0.77, 1.49)	0.87 (0.47, 1.62)	1.06 (0.81, 1.37)	1.26 (0.97, 1.64)	0.94 (0.55, 1.60)
	White-collar worker	1.00	1.00	1.00	1.00	1.00	1.00
City level data							
Gross domestic product (GDP) per capita (RMB)	Continuous (per 10,000)	0.96 (0.93, 0.99)**	0.96 (0.93, 0.98)***	1.00 (0.96, 1.05)	0.99 (0.97, 1.00)	0.96 (0.87, 1.05)	0.99 (0.94, 1.03)
Day care center climate data							
Outdoor T	Continuous (per 1 °C)	0.99 (0.96, 1.02)	1.00 (0.98, 1.02)	0.84 (0.80, 0.89)***	1.04 (1.02, 1.06)***	0.87 (0.76, 0.99)*	0.86 (0.82, 0.90)***

Models were adjusted for all the 19 covariates in Table 1, city, lifetime mean GDP per capita, mean outdoor temperature, and outdoor NO_2.

* $p \le 0.05$.

** $p \le 0.01$.

*** $p \le 0.001$.

Children in homes with cockroaches had higher prevalence and higher onset of wheeze and rhinitis. Cockroach allergy is common among allergy patients in China. A nationwide study on allergy clinic patients across China found that 22% of the children with asthma and rhinitis had cockroach allergy (Li et al., 2009) and presence of cockroaches at home has been associated with prevalence of wheeze (Salo et al., 2004) and rhinitis (Wang et al., 2014) in population studies in China.

We found that daily cleaning at home could reduce the prevalence of wheeze and that use of air conditioners was associated with a higher prevalence of wheeze. Frequent cleaning can reduce the exposure to allergens, microbial compounds from mould and bacteria and chemicals from settled dust. Air conditioners can contain microbial compounds from mould and bacteria that can contaminate indoor air (Hatayama et al., 2018). Thus, frequent cleaning of indoor surfaces at home and regular cleaning of the air conditioning units is important.

In our study we included two indicators of the socio-economic status (SES) of the family. Size of the home has been demonstrated to be a good indicator of SES in USA (Juhn et al., 2011) and a good indicator of family income China (Norbäck et al., 2018). We found that children of mothers with industrial work had a higher prevalence of wheeze a 2 y age, but found no association between size of the home and respiratory health. The association between wheeze in the offspring and maternal industrial work during pregnancy could be due to chemical exposure during pregnancy rather than a general effect of low SES.

We found less onset of rhinitis and less remission of wheeze and rhinitis in a warmer climate, in mutually adjusted models. China is a large country with different economic development level and different climate in different parts of the country. Our data suggests that the turnover of symptoms among pre-school children is higher in a cold climate (higher incidence and higher remission). Our result is partly in agreement with a previous study from China demonstrating a higher aggravation of allergic rhinitis in a cold climate (He et al., 2017). However, our results do not agree with a global ecological analysis of data from the IAAC phase III study, suggesting an increased prevalence of intermittent rhinitis in warmer climate zones (Fuertes et al., 2014).

Prevalence and onset of wheeze was inversely associated with GDP per capita (on city level) in mutually adjusted models. This indicates that there could be factors related to the economic development of the society that reduces the risk of wheeze among pre-school children. Further studies are needed to identify these beneficial factors, but one explanation could be better access to health care and medicine or a better diet.

Our study is an epidemiological questionnaire study which limits the possibility to draw conclusions on biological mechanisms behind observed statistical associations. However, it is well know that there are critical time windows before birth and after birth that can influence the programming of the immune system (Hehua et al., 2017; van der Velden et al., 2001). Our study supports the view of an early life programming of the immune system. Details on the biological mechanisms behind these effects need to be clarified in more detailed studies measuring biomarkers and genetic information. Other studies have demonstrated the significance of inflammation as a biological mechanism behind respiratory effects of outdoor and indoor air pollution. In some cases, e.g. for respiratory symptoms in relation to presence of cockroaches at home, allergic sensitisation could be another biological mechanism.

In conclusion, prevalence, onset and remission of wheeze and rhinitis among pre-school children across China can be influenced by the outdoor and the indoor environment. The most consistent results for outdoor air pollution was observed for NO_2, an indicator of traffic related air pollution (TRAP) but we also found health associations for PM_{10} and $PM_{2.5}$. The respiratory effects could be linked to increased prevalence, increased onset as well as decreased remission. Risk factors in the indoor environment can include emission of chemicals from new materials, emissions from gas cooking, dampness (visible mould and window condensation), cockroaches and use of air conditioning. Daily cleaning of the home and regular cleaning of the air conditioning units could be beneficial for respiratory health. There is a clear need for more prospective studies on risk factors for childhood asthma and rhinitis in China. Future work is needed to reduce the outdoor air pollution in China, especially TRAP. Moreover, there is a need to improve the home environment, by increasing the ventilation, avoiding dampness and indoor mould growth, reducing chemical emissions from renovation materials and new furniture, eradicating cockroaches, encouraging use of electricity for cooking and by improving the cleaning frequency.

Conflicts of interest

None of the authors declare any conflict of interest.

Acknowledgements

The research was supported by the National Natural Science Foundation of China (No. 51576214, No. 51178466, No. 21777193 and No. 81861138005) and the Swedish Research Council.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envint.2018.11.033.

References

Asher, M.I., Monteford, S., Bjorksten, B., et al., 2006. Worldwide time trends in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis and eczema in childhood: ISAAC phases one and three repeat multicountry cross-sectional surveys. Lancet 368, 733–743.

Bell, M.L., 2006. The use of ambient air quality modelling to estimate individual and population exposure for human health research: a case study of ozone in the Northern Georgia Region of the United States. Environ. Int. 32, 586–593.

Brauer, M., Lencar, C., Tamburic, L., et al., 2008. A cohort study of traffic-related air pollution aspects on birth outcomes. Environ. Health Perspect. 116, 680–686.

Burke, H., Leonardi-Bee, J., Hashim, A., et al., 2012. Prenatal and passive smoke exposure and incidence of asthma and wheeze: systematic review and meta-analysis. Pediatrics 129, 735–744.

Chen, F., Lin, Z., Chen, R., et al., 2018. The effects of PM2.5 on asthmatic and allergic diseases or symptoms in preschool children of six Chinese cities, based on China, Children, Homes and Health (CCHH) project. Environ. Pollut. 232, 329–337.

Clark, N.A., Demers, P.A., Karr, C.J., et al., 2010. Effect of early life exposure to air pollution on development of childhood asthma. Environ. Health Perspect. 118, 284–290.

Deng, Q., Lu, C., Ou, C., et al., 2016a. Preconceptional, prenatal and postnatal exposure to outdoor and indoor environmental factors on allergic diseases/symptoms in preschool children. Chemosphere 152, 459–467.

Deng, Q., Lu, C., Yu, Y., et al., 2016b. Early life exposure to traffic-related air pollution and allergic rhinitis in preschool children. Respir. Med. 121, 67–73.

van der Velden, V.H., Laan, M.P., Baert, M.R., et al., 2001. Selective development of a strong Th2 cytokine profile in high-risk children who develop atopy: risk factors and regulatory role of IFN-gamma, IL-4 and IL-10. Clin. Exp. Allergy 31, 997–1006.

Emenius, G., Korsgaard, J., Wickman, M., 2000. Window pane condensation and high indoor vapour contribution — markers of an unhealthy indoor environment? Clin. Exp. Allergy 30, 418–425.

Fan, X.J., Yang, C., Zhang, L., et al., 2017. Asthma symptoms among Chinese children: the role of ventilation and PM10 exposure at school and home. Int. J. Tuberc. Lung Dis. 21, 1187–1193.

Franck, U., Weller, A., Röder, S.W., et al., 2014. Prenatal VOC exposure and redecoration are related to wheezing in early infancy. Environ. Int. 73, 393–401.

Fuertes, E., Butland, B.K., Ross Anderson, H., et al., 2014. Childhood intermittent and persistent rhinitis prevalence and climate and vegetation: a global ecologic analysis. Ann Allergy Asthma Immunol 113, 386–392.

Gao, Y., Chan, E.Y., Li, L., et al., 2014. Chronic effects of ambient air pollution on respiratory morbidities among Chinese children: a cross-sectional study in Hong Kong. BMC Public Health 14, 105.

Gehring, U., Wijga, A.H., Hoek, G., et al., 2015. Exposure to air pollution and development of asthma and rhinoconjunctivitis throughout childhood and adolescence: a population-based birth cohort study. Lancet Respir. Med. 3, 933–942.

Hatayama, K., Oikawa, Y., Ito, H., 2018. Bacterial community structures in air conditioners installed in Japanese residential buildings. Antonie Van Leeuwenhoek 111, 45–53.

He, S., Mou, Z., Peng, L., Chen, J., 2017. Impacts of meteorological and environmental factors on allergic rhinitis in children. Int. J. Biometeorol. 61, 797–806.

Hehua, Z., Qing, C., Shanyan, G., et al., 2017. The impact of prenatal exposure to air pollution on childhood wheezing and asthma: a systematic review. Environ. Res. 159, 519–530.

Hsu, H.H., Chiu, Y.H., Coull, B.A., et al., 2015. Prenatal particulate air pollution and asthma onset in urban children. Identifying sensitive windows and sex differences. Am. J. Respir. Crit. Care Med. 192, 1052–1059.

Jaakkola, M.S., Quansah, R., Hugg, T.T., et al., 2013. Association of indoor dampness and molds with rhinitis risk: a systematic review and meta-analysis. J. Allergy Clin. Immunol. 132, 1099–1110.

Juhn, Y.J., Beebe, T.J., Finnie, D.M., et al., 2011. Development and initial testing of a new socioeconomic status measure based on housing data. J. Urban Health 88, 933–944.

Li, J., Sun, B., Huang, Y., et al., 2009. A multicentre study assessing the prevalence of sensitizations in patients with asthma and/or rhinitis in China. Allergy 64, 1083–1092.

Li, C.W., Chen, D.H., Zhong, J.T., et al., 2014. Epidemiological characterization and risk factors of allergic rhinitis in the general population in Guangzhou City in China. PLoS One 9, e114950.

Lin, W., Huang, W., Zhu, T., et al., 2011. Acute respiratory inflammation in children and black carbon in ambient air before and during the 2008 Beijing Olympics. Environ. Health Perspect. 119, 1507–1512.

Lin, W., Brunekreef, B., Gehring, U., 2013. Meta-analysis of the effects of indoor nitrogen dioxide and gas cooking on asthma and wheeze in children. Int. J. Epidemiol. 42, 1724–1737.

Marshall, J., Nethery, E., Brauer, M., 2008. Within-urban variability in ambient air pollution: comparison of estimation methods. Atmos. Environ. 42, 1359–1369.

Mendell, M.J., 2007. Indoor residential chemical emissions as risk factors for respiratory and allergic effects in children: a review. Indoor Air 17, 259–277.

Nishimura, K.K., Galanter, J.M., Roth, L.A., et al., 2013. Early-life air pollution and asthma risk in minority children. The GALA II and SAGE II studies. Am. J. Respir. Crit. Care. Med. 1888, 309–318.

Norbäck, D., Lu, C., Zhang, Y., et al., 2018. Lifetime-ever pneumonia among pre-school children across China — associations with pre-natal and post-natal early life environmental factors. Environ. Res. 167, 418–427.

Patelarou, E., Tzanakis, N., Kelly, F.J., 2015. Exposure to indoor pollutants and wheeze and asthma development during early childhood. Int. J. Environ. Res. Public Health 12, 3993–4017.

Quansah, R., Jaakkola, M.S., Hugg, T.T., et al., 2012. Residential dampness and molds and the risk of developing asthma: a systematic review and meta-analysis. PLoS One 7, e47526.

Salo, P.M., Xia, J., Johnson, C.A., et al., 2004. Indoor allergens, asthma, and asthma-related symptoms among adolescents in Wuhan, China. Ann. Epidemiol. 14, 543–550.

Shi, J., Chen, R., Yang, C., et al., 2016. Association between fine particulate matter chemical constituents and airway inflammation: a panel study among healthy adults in China. Environ. Res. 150, 264–268.

Siwarom, S., Puranitee, P., Plitponkarnpim, A., et al., 2017. Association of indoor air quality and preschool children's respiratory symptoms. Asian Pac. J. Allergy Immunol. 35, 119–126.

Takaoka, M., Norbäck, D., 2011. The home environment of Japanese female university students-association with respiratory health. Indoor Built Environ. 20, 369–376.

Takenoue, Y., Kaneko, T., Miyamae, T., et al., 2012. Influence of outdoor NO_2 exposure on asthma in childhood: meta-analysis. Pediatr. Int. 54, 762–769.

Teng, B., Zhang, X., Yi, C., et al., 2017. The association between ambient air pollution and allergic rhinitis: further epidemiological evidence from Changchun, Northeastern China. Int. J. Environ. Res. Public Health 14, 226.

Wang, J., Li, B., Yu, W., et al., 2014. Rhinitis symptoms and asthma among parents of preschool children in relation to the home environment in Chongqing, China. PLoS One 9, e94731.

WHO, 2005. WHO Air Quality Guidelines Global Update 2005. World Health Organization, Denmark.

Wong, T.W., Yu, T.S., Liu, H.J., et al., 2004. Household gas cooking: a risk factor for respiratory illnesses in preschool children. Arch. Dis. Child. 89, 631–636.

Yang, A., Janssen, N.A., Brunekreef, B., et al., 2016. Children's respiratory health and oxidative potential of PM2.5: the PIAMA birth cohort study. Occup. Environ. Med. 73, 154–160.

Zhang, Y., Zhang, L., 2014. Prevalence of allergic rhinitis in China. Allergy, Asthma Immunol. Res. 6, 105–113.

Zhang, Y.P., Li, B.Z., Huang, C., et al., 2013. Ten cities cross-sectional questionnaire survey of children asthma and other allergies in China. Chin. Sci. Bull. 58, 4182–4189.

Zhao, Z., Chen, R., Lin, Z., et al., 2016. Ambient carbon monoxide associated with alleviated respiratory inflammation in healthy young adults. Environ. Pollut. 208 (Pt A), 294–298.