DOCKETED	
Docket Number:	19-BSTD-03
Project Title:	2022 Energy Code Pre-Rulemaking
TN #:	235293
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 5:16:30 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 2

Additional submitted attachment is included below.

Science of the Total Environment 616–617 (2018) 1513–1523

Contents lists available at ScienceDirect

Science of the Total Environment

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

The role of the indoor environment: Residential determinants of allergy, asthma and pulmonary function in children from a US-Mexico border community

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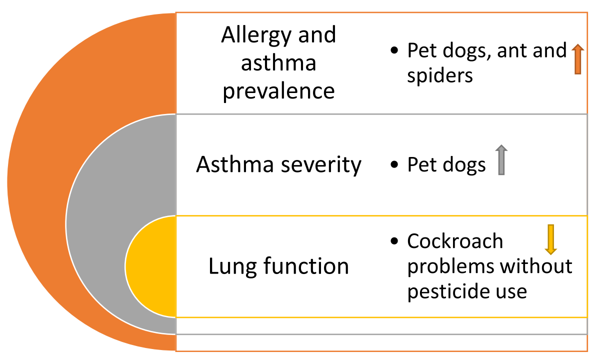
HIGHLIGHTS

- Several indoor environmental risk factors were positively associated with allergy and asthma prevalence
- Exposure to pet dogs increased monotonically with increasing asthma severity
- Lung function decreased among children who lived in homes with reported cockroach pest problems in the past year without concurrent use of pesticides
- Clinicians and public health professionals may need to look closely at indoor risk factors for pulmonary health outcomes

GRAPHICAL ABSTRACT



ARTICLE INFO

Article history:
Received 19 July 2017
Received in revised form 30 September 2017
Accepted 16 October 2017
Available online 6 November 2017

Editor: D. Barcelo

Keywords:
Asthma
Allergy
Indoor air quality
Environmental risk factors

ABSTRACT

The El Paso Children's Health Study examined environmental risk factors for allergy and asthma among fourth and fifth grade schoolchildren living in a major United States-Mexico border city. Complete questionnaire information was available for 5210 children, while adequate pulmonary function data were available for a subset of 1874. Herein we studied indoor environmental health risk factors for allergy and asthma. Several indoor environmental risk factors were associated with allergy and asthma. In particular, we found that ant and spider pest problems, pet dogs, fireplace heat, central air conditioning, humidifier use, and cooking with gas stoves were positively associated with both allergy and asthma prevalence. With regards to asthma severity, our analysis indicated that exposure to pet dogs increased monotonically with increasing asthma severity while the lack of any heat source and gas stove use for cooking decreased monotonically with increasing asthma severity. Lung function also decreased among children who lived in homes with reported cockroach pest problem in the past year without concurrent use of pesticides. These effects on pulmonary function were present even after excluding children with a current physician's diagnosis of asthma. Clinicians and public health professionals may need to look closely at the contribution of these indoor risk factors on pulmonary health and quality of life among susceptible populations.

Abbreviations: $FEV_{0.5}$, forced expiratory volume in first 0.5 s; FEV_1, forced expiratory volume in first second; FVC, forced vital capacity; $FEF_{25–75}$, MMEF, forced expiratory flow in the middle half of the expiration; PEF, peak expiratory flow; $FEV_{0.5}$/FVC, The ratio of $FEV_{0.5}$ to FVC; 95%, Ninety five %; CI, Confidence Interval.

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https://doi.org/10.1016/j.scitotenv.2017.10.162
0048-9697/

1. Introduction

There has been an upsurge of allergic respiratory diseases in the last few decades, with asthma noted as the most common such disease among children (D'Amato et al., 2010; Hollenbach and Cloutier, 2015). Indoor environmental conditions play significant roles in the onset and exacerbation of such chronic conditions (Braman, 2006; Ferkol and Schraufnagel, 2014). Increasing evidence of allergy and asthma morbidity and mortality have been attributed to allergen and irritant exposures in the modern indoor environment (Platts-Mills, 2015), and these risk factors are associated with decreased lung function, and adverse respiratory health in children (Carrer et al., 2001; Do et al., 2016).

Recently, chemical exposures in the indoor environment, such as phthalates, pesticides, and bisphenol-A (BPA), have been identified as important risk factors for asthma development and exacerbation (Hoppin et al., 2002; Jaakkola and Knight, 2008; Maffini et al., 2006). However, the associations between these chemicals and the pathogenesis of asthma are not clear. Several studies have revealed associations between phthalate exposures and the development of asthma and allergies (Bornehag et al., 2004; Bornehag and Nanberg, 2010; Jaakkola and Knight, 2008; Kolarik et al., 2008), while emerging evidence associates in utero and early life BPA exposures to the weakening of immature immune systems (Carraro et al., 2014; Unuvar and Buyukgebiz, 2012). What is currently less clear is the association between pesticide exposures and the development of respiratory disease, particularly, the link between pesticide exposures at the levels encountered in residential settings and asthma is vague (Duramad et al., 2006; Kanchongkittiphon et al., 2015). Further studies are needed to determine the contribution of these ubiquitous compounds on human health.

Most people spend a large fraction of their time indoors, particularly at home and are often exposed to numerous sources of allergens and irritants (Gaffin et al., 2014; Gaffin and Phipatanakul, 2009; Salo et al., 2008). The contribution of indoor environmental conditions to disease burden must be carefully delineated to inform sustainable interventions and policy measures that reduce the economic burden and improve overall quality of life (IOM, 2000; Sheehan et al., 2010; Wu and Takaro, 2007). We examined associations between multiple residential indoor environmental risk factors (hereafter termed indoor risk factors) and children's respiratory health, as assessed by questionnaire and spirometry, in a cross-sectional study of a predominantly Hispanic community in a major United States-Mexico border city.

To achieve this objective, we assessed two main questions:

1. Which indoor risk factors are associated with allergy and asthma prevalence, and with asthma severity?
2. Which indoor risk factors are associated with adverse pulmonary function measures?

For question 1 we evaluated trends in allergy and asthma prevalence by indoor risk factors in a large population of schoolchildren; and for question 2 we examined associations between pulmonary function measurements and indoor risk factors in a subset of children who underwent spirometry testing.

2. Materials and methods

2.1. Study population

The study population consisted of fourth and fifth grade students enrolled in 54 elementary schools of the El Paso Independent School District in February 2001. The full description of the El Paso Children's Health Study has been previously described (Gonzales et al., 2005; Svendsen et al., 2009). Herein we assess the effects of indoor rather than outdoor exposures on children's pulmonary health ($n = 5210$).

2.2. Exposure assessment

Our primary assessment for exposure to indoor risk factors was by parental questionnaire; the presence or absence of pets, pests, mold and water damage (mold problems were defined as the evidence of mold or mildew anywhere in the home – whether in the bathroom, bedroom(s), kitchen, living room, basement and/or attic. Answers to any of these were combined for subsequent analysis), type of home heating delivery system and air conditioning, as well as the use (or lack thereof) of pesticides, humidifiers, gas stoves and air cleaners were queried (Svendsen et al., 2009). There was also opportunity to elucidate the types of pests, pets, heat delivery system, type of heat and air conditioning and type of gas stove used for cooking.

2.3. Health outcome assessment

Children's health outcomes included prevalent allergy and asthma, also ascertained by the American Thoracic Society's respiratory questionnaire (Ferris, 1978). A subset of the study population underwent spirometry analyses ($n = 1874$) (Svendsen et al., 2012).

2.3.1. Allergy

A child had prevalent allergy if his or her parent reported either a physician's diagnosis of allergy or any specifically diagnosed allergy to one or more of the following: foods, house dust or house dust mites, pollens, molds, animal fur or dander, insect bites or stings, feathers, skin contact irritants (other than poison ivy, oak or sumac), or other allergens.

2.3.2. Asthma

Parents indicated whether or not their child had a physician's diagnosis of asthma. If a child had ever been diagnosed with asthma, then the parents answered further questions about medication use. Some parents believed their children may have outgrown their asthma; hence, we defined current asthma as prevalent asthmatics who had any asthma exacerbations or had taken any asthma medications during the previous year.

2.3.3. Pulmonary function measurements

Spirometry testing was performed between March and May 2001 at a subset of 20 elementary schools selected based on their geographic distribution and without prior knowledge of children's health conditions. Spirometry tests used American Thoracic Society certified spirometers (SensorMedics 922; Cardinal Health, Dublin, OH), and were performed during normal school hours using standardized protocols for children (American Thoracic Society, 1991; Miller et al., 1995) after child's weight and standing height were obtained. Three clinical teams and two separate sets of spirometry equipment were utilized due to a large sample size; selected schools were randomized to one of six study weeks and one of the three field teams. Informed assent of child and receipt of a signed parental consent form were confirmed before each pulmonary function testing session. Children who had smoked more than five cigarettes in their lifetime or had a respiratory infection within the previous two weeks were excused from testing.

Spirometry measures used include forced vital capacity (FVC), forced expiratory volume in the first 0.5 s and first second ($FEV_{0.5}$ and FEV_1 respectively), peak expiratory flow (PEF), forced expiratory flow in the middle half of the expiration ($FEF_{25–75}$), and the ratio of forced expiratory flow in the first 0.5 s to forced vital capacity ($FEV_{0.5}$/FVC). Deficits in $FEV_{0.5}$/FVC and $FEF_{25–75}$ were used as indicators of asthma development and the best spirometry values were calculated from an average of the two maneuvers with the first and second greatest FVC measurements. The study protocol was approved by the University of North Carolina School Of Medicine's Institutional Review Board and the Human Subjects Research Review Official for the US Environmental Protection Agency.

Table 1
a: Unadjusted prevalence of selected demographics and outcomes in 4th or 5th grade children, both the entire study population and the subset with pulmonary function exams: El Paso Independent School District, February 2001.
b: Unadjusted prevalence of selected exposures in 4th or 5th grade children, both the entire study population and the subset with pulmonary function exams: El Paso Independent School District, February 2001.

		EPISD	Subset
		%	%
		$n =$ 5210	$n =$ 1874
Demographics			
Ethnicity			
Non-Hispanic		20.0	24.4
Hispanic, English preferred		46.5	46.7
Hispanic, Spanish preferred		33.5	28.9
El Paso resident since			
Birth		62	60.6
Before entering 1st grade		17.5	19
After entering 1st grade		20.6	20.5
Maximum parental education			
Some secondary school		16.8	12.7
High school graduate		21.5	20.8
Some post-high school		22.3	22.9
College graduate or higher		39.4	43.7
Sex: female		50.6	49.9
Parental risk factors			
		$n =$ 5154	
Parental allergy		35.4	38.8
		$n =$ 5160	
Parental asthma		13.4	13.8
Smoker in household		31.8	29.9
Mother smoked in pregnancy		8.6	8.9
Perinatal risk factors			
Born premature		8.4	8.9
Severe chest illness before 2 years old		11.8	11.1
Outcomes			
			$n =$ 1870
Allergy		34.4	35.3
Current asthma		10.8	10.0
Asthma symptom level	Severity scale	$n =$ 5002	$n =$ 1806
No symptoms, though diagnosed	Asymptomatic	2.9	2.6
Some symptoms requiring little or no medication	Intermittent	5.7	5.4
Some symptoms requiring routine medication	Persistent	1.9	1.8
Indoor environmental exposures			
Pests within home			
Mice		6.5	6.8
Cockroaches		21.9	21.0
Ants		19.9	21.3
Spiders		9.2	11.3
None		54.9	52.8
Pesticides used in past year		$n =$ *5056*	$n =$ *1824*
		61.9	64.5
Pets			
Dog		49.4	54.4
Cat		15.4	16.1
Hamster		2.8	3.3
Bird		9.0	10.0
None		38.1	34.3
Heat delivery system		$n =$ 5207	$n =$ 1873
Forced air		59.7	63.8
Vented floor		11.7	8.9
Heat type			
Wood stove		0.6	0.5
Fireplace		18.0	23.5
Portable gas heater		3.2	3.0
Portable electric heater		12.4	12.0
None		62.0	58.7
Air conditioning type		$n =$ 5209	$n =$ 1873
Central		81.0	83.6
Room: living room		10.8	9.8
Room: this child's bedroom		6.9	6.1
Room: other		4.3	3.7
Mold problem in home		$n =$ 5197	$n =$ 1864
		91.4	92.1
Water damage		17.6	16.1
Humidifier used in home		$n =$ 4968	$n =$ 1777
		15.2	17.1
Gas stove for cooking		83.7	84.9
With pilot light		39.1	36.9
Air cleaners used		8.8	9.9

El Paso Independent School District (EPISD).

2.4. Statistical analysis

Descriptive statistics were generated for allergy, asthma prevalence and severity, together with indoor risk factors for both the entire study population and the subset with pulmonary function measurements. Cochran–Armitage tests for trends were performed to assess patterns between health outcome and categories of indoor risk factors. Data analyses were performed with SAS version 9.2 software (SAS Institute Inc., Cary, North Carolina). We used linear mixed-effects models (PROC MIXED) regression procedures with model-based standard error estimates. Mixed models with a random effect of clinical team ∗ equipment set were used in the final models to adjust for any unmeasured local neighborhood, technology, clinical team, or location of spirometry testing effects. All spirometry measurements were log transformed. Covariates associated with the outcomes at a $p < 0.1$ level were considered for inclusion in final models. Final parsimonious linear models included sex, race/ethnicity, respondent's sex, socioeconomic status, military base school, household smoker, duration of El Paso residence, allergy, current asthma, log of height, log of weight, age, interaction of sex with height, interaction of Hispanic ethnicity with height, interaction of Hispanic ethnicity with weight, and a random school effect. Figures were made with SigmaPlot (Systat Software Inc., San Jose, CA, USA).

3. Results

3.1. Characteristics of study population

Full characteristics of the study population are described elsewhere (Svendsen et al., 2009). There were few differences in selected demographics, outcomes, and indoor exposures between the pulmonary function testing subset and larger study sample student population (Table 1a & b). The subset had slightly fewer children who returned the Spanish language questionnaire and slightly more dog owners and fireplace heat users (Table 1b). Hence we concluded that the subset of children with pulmonary function testing reasonably represented the study population.

3.2. Prevalence of indoor risk factors

Pesticide use in the past 12 months was quite common (64.5%, Table 1b), and the majority of the households did not report any residential pest problems (52.8%, Table 1b). Of those that had pest problems in the past year, most had problems with ants or cockroaches (Table 2).

Table 2
Unadjusted prevalence of allergy and asthma strata by selected factors in 4th or 5th grade children: El Paso Independent School District, February 2001 ($n = 5210$).

	Allergy	No-allergy	Ever diagnosed asthma	No diagnosed asthma	Current asthma	No current asthma
	%	%	%	%	%	%
Pests within home						
Mice	7.9	5.8	7.2	6.4	7.7	6.4
Cockroaches	22.7	21.4	24.2	21.5	25.0	21.5
Ants	25.1	17.2	25.0	19.1	25.2	19.3
Spiders	11.5	8.0	12.1	8.8	12.7	8.8
None	49.6	57.7	50.6	55.6	50.7	55.4
Pesticides used in past year ($n = 5056$)	68.0	58.7	68.8	60.8	67.4	61.2
Pets						
Dog	54.3	46.9	53.9	48.7	53.6	48.9
Cat	17.4	14.4	18.4	15.0	18.0	15.1
Hamster	3.7	2.4	4.1	2.6	3.2	2.8
Bird	9.7	8.7	8.2	9.2	8.6	9.1
None	34.4	40.1	34.1	38.8	34.6	38.6
Heat delivery system: ($n = 5207$)						
Forced air	64.8	57.1	62.9	59.2	61.7	59.5
Vented floor	9.8	12.7	11.8	11.7	12.2	11.7
Heat type						
Wood stove	0.7	0.5	1.0	0.5	1.3	0.5
Fireplace	21.1	16.4	22.6	17.3	22.3	17.5
Portable gas heater	2.6	3.6	3.0	3.3	3.0	3.2
Portable electric heater	14.6	11.3	15.2	12.0	14.5	12.2
None	59.3	63.4	58.4	62.6	58.9	62.4
Air conditioning type: ($n = 5209$)						
Central	84.9	79.0	85.7	80.3	86.3	80.4
Room: living room	9.9	11.3	8.9	11.1	8.8	11.1
Room: this child's bedroom	6.5	7.0	4.9	7.2	5.2	7.1
Room: other	3.8	4.6	2.8	4.6	2.9	4.5
Mold problems in home ($n = 5197$)	90.7	91.8	88.8	91.9	88.3	91.8
Water damage	19.9	16.4	20.2	17.3	19.9	17.3
Humidifier used in home ($n = 4968$)	23.1	11.1	23.1	14.0	25.1	14.0
Gas stove for cooking	81.6	84.8	81.2	84.1	80.5	84.1
With pilot light ($n = 5196$)	39.7	38.8	40.3	38.9	40.5	38.9
Air cleaners used	9.4	8.5	10.3	8.6	11.0	8.5

Few families reported problems with rats or termites within the past 12 months (<1%). Over half of all the households had a pet dog (Table 1b). The majority of children lived in homes with central cooling systems and central air conditioning but without any heating system. Most homes used gas stoves, and over a third used continuous burning pilot lights (Table 2).

3.2.1. Which indoor risk factors are associated with allergy and asthma prevalence, and with asthma severity?

We found that ant and spider pest problems within the past year, pet dogs, fireplace heat, central air conditioning, humidifier use, and cooking with gas stoves were positively associated with both allergy and asthma prevalence (ever and current) (Table 2).

Asthma severity was categorized as follows: Asymptomatic (diagnosed asthmatic without reported symptoms in the past year), Intermittent (diagnosed asthmatic with little or no medication use), and Persistent (diagnosed asthmatic with routine medication use). These categories were then compared with non-asthmatics.

Exposure to pet dogs increased monotonically with increasing asthma severity while the lack of any heat source and gas stove use for cooking decreased monotonically with increasing asthma severity (Table 3). Among asthmatics (whether asymptomatic, intermittent or persistent), the presence of spiders, air conditioning in child's bedroom, the use of woodstoves, fireplaces, humidifiers and air cleaners increased with symptom severity, while the absence of pets and the use of air conditioning use in the living room decreased with asthma severity (Table 3). The presence of cats, mold in the home and use of air conditioning in rooms other than the child's bedroom were associated more with asymptomatic and persistent asthma while pesticide use was associated more with asthma, particularly asymptomatic and persistent symptoms (Table 3).

3.2.2. Which indoor risk factors are associated with adverse pulmonary health measures?

The asthma severity categories based on symptoms were accurate representations of increased asthma morbidity, as demonstrated by the decreasing trends in $FEF_{25-75\%}$ and $FEV_{0.5}$/FVC with increasing asthma severity ($n = 1874$) (Fig. 1). A cockroach pest problem in the past year without concurrent use of pesticides was associated with significantly decreased PEF, $FEV_{0.5}$, and $FEV_{0.5}$/FVC independent of any other pest problem or asthma prevalence or symptoms (Fig. 2). When children exposed to cockroach pest problems in the past year had their homes treated with pesticides, they had 8.6% higher PEF (CI: 3.1, 14.4). Similar results were found with $FEV_{0.5}$, and $FEV_{0.5}$/FVC but to a lesser degree (Fig. 2).

Pesticide exposure without concurrent exposure to cockroach pest problems had only 1% higher PEF (CI: −1.1, 3.1) (Fig. 2). Likewise, having had no pest problems in the past year without exposure to any pesticide was associated 2.4% higher PEF (CI: −0.06, 4.96) and 1.9% higher $FEV_{0.5}$ (CI: −0.07, 3.82). Neither pesticide nor cockroach exposure in the past year were associated with FVC. In models that included reported cockroach, ant, spider, and mouse pest problems without concurrent pesticide use within the past twelve months; only a cockroach pest problem was associated with 5.3% lower PEF (95% CI −9.9, −0.3).

When analyses were restricted to allergic and non-allergic or asthmatic and non-asthmatic models, similar patterns were detected in the association of reported cockroach exposure and pesticide use and pulmonary function measures (Fig. 3a & b). Similarly, a cockroach pest problem in the past year was associated with allergy and asthma-like symptoms, but not prevalence ($p > 0.05$). These patterns were robust to adjustment for other indoor environmental risk factors (gas stove, furry pets, and humidifier use).

Humidifier use, water damage in the home and the use of gas stoves (both with and without pilot lighting) were associated with decreased pulmonary function (Fig. 4). There was 3.1% lower PEF among children in homes which had gas stoves with pilot lighting (95% CI −0.5, −5.6) compared with homes without (−2.8%) (Fig. 5). The presence of water damage in the home was significantly associated with 2.5% lower PEF (95% CI −0.2, −4.8), and the use of humidifiers associated with 4.7%, 2.1% and 1% lower FEF_{25-75}, $FEV_{0.5}$ and $FEV_{0.5}$/FVC respectively (Fig. 6).

4. Discussion

We found that ant and spider pest problems, pet dogs, fireplace heat, central air conditioning, humidifier use, and cooking with wood stoves were positively associated with both allergy and asthma prevalence in our population of predominantly Hispanic schoolchildren living in a U.S.-Mexico border city. Our analysis indicated that exposure to pet dogs increased monotonically with increasing asthma severity while the lack of any heat source and gas stove use for cooking decreased monotonically with increasing asthma severity. Additionally, lung function measures decreased among children who lived in homes with a reported cockroach pest problem in the past year without concurrent use of pesticides. This finding was independent of any other pest problem or asthma prevalence or symptoms.

We previously evaluated the relationships between school and residential level traffic related air pollution exposures (Svendsen et al., 2012), ethnicity, language and duration of residence (Svendsen et al., 2009) on pulmonary health in this population, while accounting for certain indoor risk factors. The current analysis is a separate detailed investigation of the association between pulmonary health and the indoor residential environment.

In this arid community, only a fifth of the children lived in homes with reported cockroaches and 86% of these families reported pesticide use in the last year. The association between peak expiratory flow (PEF) and the presence of cockroaches in the home was further assessed by considering pesticide use. When cockroaches were observed in the home, recent pesticide use was associated with higher PEF; while in homes without reported cockroaches, pesticide use resulted in slightly higher PEF values that crossed the null. Our results suggest that the simple intervention of pesticide application concurrent with a reported cockroach pest problem may have prevented the adverse effects of exposure to insect allergen.

Exposure to both cockroaches and their allergens has been associated with increased asthma morbidity (Kang et al., 1992; Kaur et al., 1998; Munir et al., 1994; Stelmach et al., 2002; Wegienka et al., 2013). Similarly, the use of pesticides in the home is associated with increased respiratory symptoms in children (Raanan et al., 2015; Salameh et al., 2003; Xu et al., 2012). Pesticide exposure alone has been reported as an occupational risk factor for asthma related outcomes (Beard et al., 2003; Boers et al., 2008; Hoppin et al., 2008; Hoppin et al., 2006; Hoppin et al., 2016; Senthilselvan et al., 1992). Yet still, others have demonstrated the efficacy of cockroach abatement measures, including pesticide use (Arbes et al., 2003; Arbes et al., 2004; Gergen et al., 1999; McConnell et al., 2003; Morgan et al., 2004; Sever et al., 2007; Wood et al., 2001). It is possible that integrated pest management may be have been implemented in study homes, for instance sealing holes and caulking, along with pesticide use, which could explain the protective association between pesticide use and lung function (Jhun et al., 2017). Further studies may be needed to highlight the risks and benefits of pesticide use and allergen reduction.

Our results are also consistent with those of others who found the reported presence of pests, and home pets such as dogs, and their associations with asthma and/or asthma-like symptoms and allergy (Apelberg et al., 2001; Bobolea et al., 2011; Brunekreef et al., 2012; Kim et al., 2001; McConnell et al., 2002). Reducing or eliminating ants, spiders and other pests may decrease asthma and allergy exacerbations (Jones, 1998; Platts-Mills et al., 1997). Allergens derived from pets are mostly associated with dander, hair, saliva and/or urine (Carrer et al., 2001) and may act as airway inflammation enhancers (Delfino et al., 2013; Delfino et al., 2002; Leavy, 2014); hence their removal is of great import.

Similarly, the use of fireplaces and woodstoves for heating has been associated with adverse respiratory health since they can contribute to indoor particulate matter and gaseous concentrations (Belanger et al., 2003; Belanger and Triche, 2008; Honicky et al., 1985; Koenig et al., 1993; McConnell et al., 2002; Noonan and Ward, 2012). Central air conditioning use is also associated with asthma and/or allergy in a meta-analysis of housing and asthma (Zock et al., 2002).

Humidifier use was associated with allergy, asthma and reduced pulmonary function in our study population, as has been reported by others (Dekker et al., 1991; Infante-Rivard, 1993; Nguyen et al., 2010). Microorganisms or particles from the water supply of the humidifier could have led to this result (Burge et al., 1985; Tyndall et al., 1995), or the general increase in indoor humidity as in the case of the air conditioning use, may have created a favorable climate that promotes increased allergen concentrations (Johnston et al., 2016). This observation could be a characteristic of indoor environments typical for homes with asthmatic children. For instance a child exhibiting

Table 3
Unadjusted prevalence of asthma severity strata by selected factors in 4th or 5th grade children: El Paso Independent School District, February 2001 ($n = 5210$).

	Non-asthmatic	Asthma: asymptomatic	Asthma: intermittent	Asthma: persistent
	%	%	%	%
Pests within home				
Mice	6.4	5.5	7.7	6.5
Cockroaches	21.6	22.1	26.9	17.2
Ants	19.3	20.0	28.3	25.8***
Spiders	8.8	8.3	15.0	17.2****
None	55.5	51.0	48.3	53.8*
Pesticides used in past year ($n = 5056$)	60.9	75.2	69.8	76.1****
Pets				
Dog	48.6	53.1	56.6	58.1***
Cat	15.1	17.9	20.6	17.2*
Hamster	2.7	6.2	3.5	2.2
Bird	9.1	6.2	9.1	8.6
None	38.7	35.9	32.9	30.1**
Heat delivery system: ($n = 5207$)				
Forced air	59.7	63.5	64.6	62.4
Vented floor	11.6	11.0	11.6	11.8
Heat type				
Wood stove	0.5	0.0	1.1	4.3****
Fireplace	17.4	20.7	25.2	23.7***
Portable gas heater	3.1	0.7	2.8	3.2
Portable electric heater	11.9	19.3	15.4	16.1**
None	62.8	60.0	57.3	57.0*
Air conditioning type: ($n = 5209$)				
Central	80.5	81.9	88.5	86.0***
Room: living room	11.0	8.3	8.0	5.4**
Room: this child's bedroom	7.0	2.8	4.9	5.4*
Room: other	4.5	3.5	2.1	3.2*
Mold problems in home ($n = 5197$)	92.4	91.0	88.4	89.3**
Humidifier used in home ($n = 4968$)	14.0	13.2	26.8	38.9****
Water damage ($n = 4778$)	17.4	16.6	17.8	25.8
Gas stove for cooking:	83.9	83.5	80.1	78.5*
with pilot light ($n = 5196$)	38.7	37.2	39.9	43.0
Air cleaners used	8.3	8.3	11.2	16.7**

Cochran-Armitage one-sided test for trend: *$p \le 0.05$, **$p \le 0.01$, ***$p \le 0.001$, ****$p \le 0.0001$.

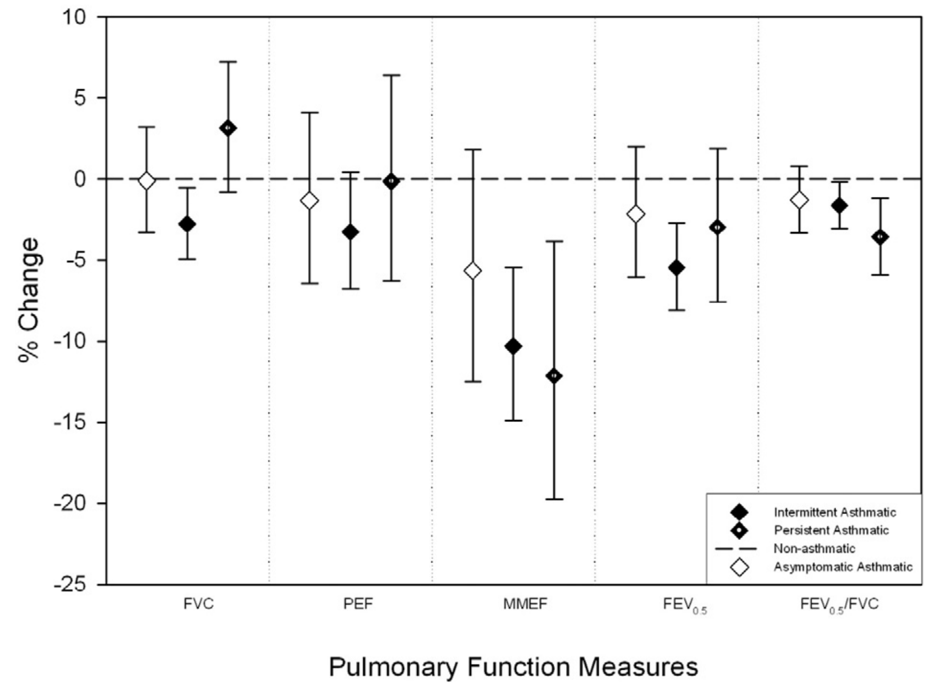

Fig. 1. Pulmonary function measures by asthma severity in 4th or 5th grade children: percent change in pulmonary function measures relative to non-asthmatic adjusted for sex, race/ethnicity, socio-economic status, log of height, log of weight, age, interaction of sex with height, interaction of Hispanic ethnicity with height, interaction of Hispanic ethnicity with weight, and a random school effect in multivariate mixed effect linear models. El Paso Independent School District, Spring 2001 ($n = 1874$). Definitions: non-asthmatic- never diagnosed with asthma, past asthmatic- diagnosed with asthma but without symptoms within the past 12 months, intermittent asthmatic- diagnosed asthmatic with some asthma symptoms in past 12 months, and persistent asthmatic- diagnosed asthmatic with routine medication use and had an episode requiring additional medical treatment within the past 12 months.

signs of asthma may have prompted parents to humidify the air in hopes of relieving the symptoms (Dekker et al., 1991).

Previous studies have reported relationships between dampness in the indoor environment and respiratory symptoms (Belanger et al., 2003; Jaakkola et al., 2002; Kercsmar et al., 2006; Mudarri and Fisk, 2007; Thorn et al., 2001). Appropriate steps to reduce or eliminate these risk factors (e.g. adequate ventilation to clean the home – after events which cause wetness) can improve overall indoor environmental quality. This is because excessive moisture creates conducive habitats for pests and microorganisms (Kercsmar et al., 2006; Krieger et al., 2002). House dust mites and fungi are prevalent in damp environments, and are capable of triggering allergic reactions, in both regular

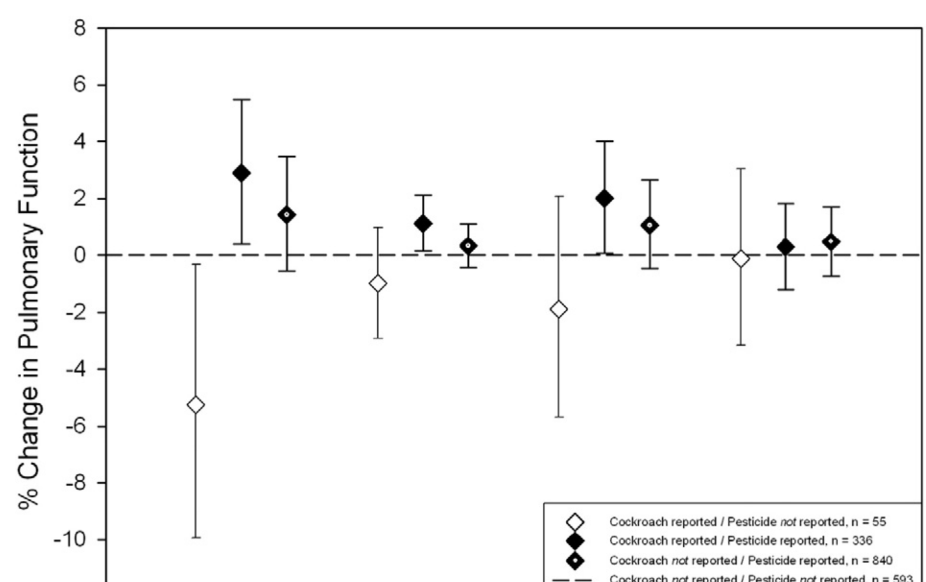

Fig. 2. The effect of pesticide use in the past year and cockroach pest problems in the past year on pulmonary function in 4th or 5th grade children: percent change in pulmonary function measures relative to unexposed adjusted for sex, race/ethnicity, socio-economic status, log of height, log of weight, age, interaction of sex with height, interaction of Hispanic ethnicity with height, interaction of Hispanic ethnicity with weight, and a random school effect in multivariate mixed effect linear models. El Paso Independent School District, Spring 2001 ($n = 1874$).

and sensitized individuals (Dekker et al., 1991; Delfino et al., 2002; Kilpeläinen et al., 2001; Nelson et al., 1999).

The use of air cleaners emerged as a risk factor for asthma prevalence and severity. This may be because families with known asthmatic children may have modified their homes and this observation may be characterizing the indoor environments of homes with asthmatic children. It is common for households to adopt preventative strategies such air filters, humidifiers in an effort to help in disease management (2). Further studies with detailed risk factor and exposure assessment may be needed to draw more definitive conclusions.

The literature has had conflicting findings on the relationship between adverse pulmonary health and the use of gas stoves (Eisner and Blanc, 2003; Garrett et al., 1998; Ostro et al., 1994). Several factors such as genetic susceptibilities, type of gas stoves, even cooking and ventilation practices can modify this relationship and help explain this inconsistency (Amaral, 2014; Dennekamp et al., 2001; Kile et al., 2014; Willers et al., 2006). In our study, the use of gas stoves may have contributed to increased indoor concentrations of combustion by-products, particularly nitrogen dioxide (Belanger et al., 2006; Belanger and Triche, 2008; Neas et al., 1991). Exposure to such an air

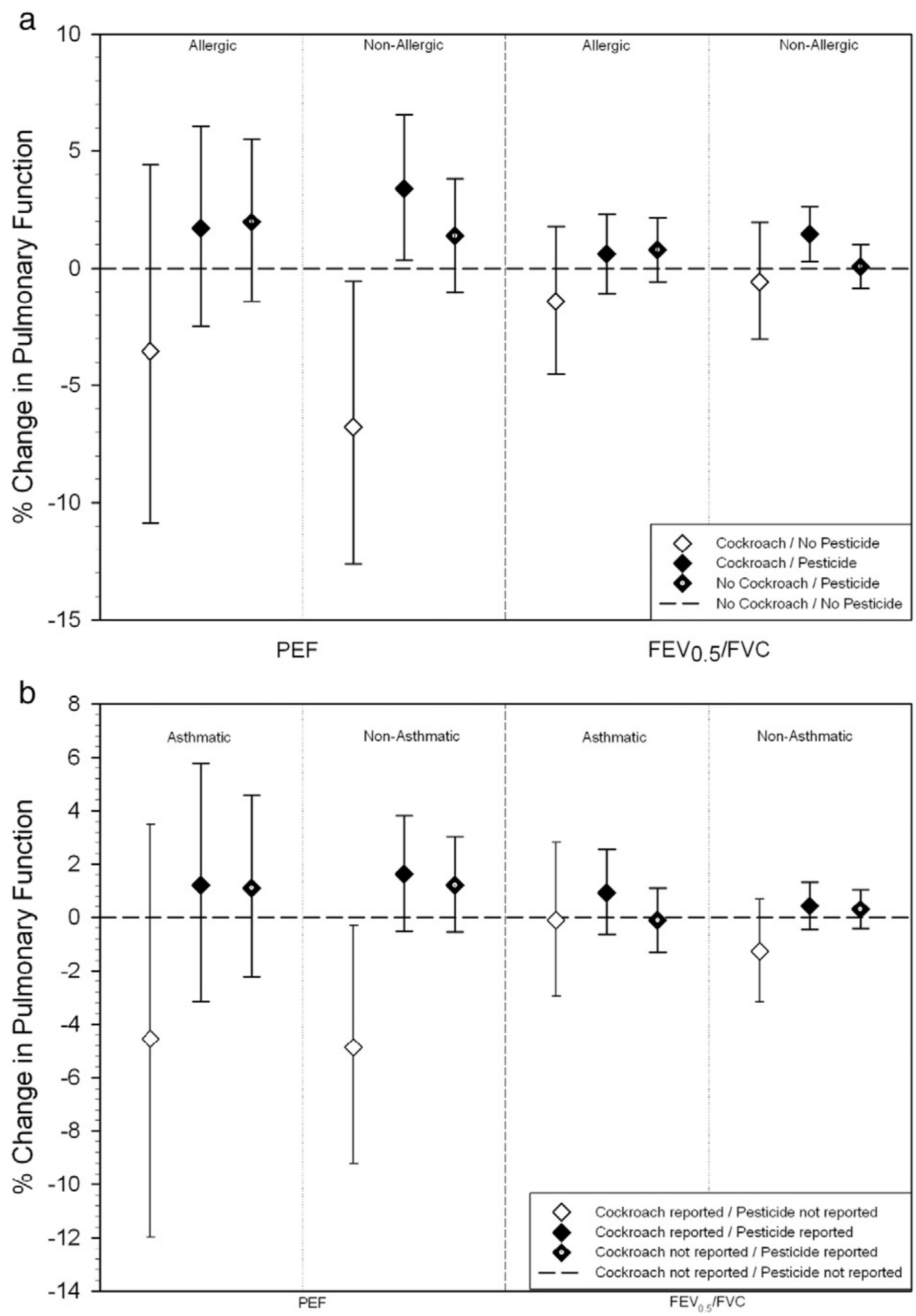

Fig. 3. a: The effects of pesticide and cockroach exposure on pulmonary function in 4th or 5th grade children, restricted by diagnosed allergy status: percent change in pulmonary function measures relative to unexposed adjusted for sex, race/ethnicity, socio-economic status, log of height, log of weight, age, interaction of sex with height, interaction of Hispanic ethnicity with height, interaction of Hispanic ethnicity with weight, and a random school effect in multivariate mixed effect linear models. El Paso Independent School District, Spring 2001 ($n = 1874$). b: The effects of pesticide and cockroach exposure on pulmonary function in 4th or 5th grade children, restricted by diagnosed asthma: percent change in pulmonary function measures relative to unexposed adjusted for sex, race/ethnicity, socio-economic status, log of height, log of weight, age, interaction of sex with height, interaction of Hispanic ethnicity with height, interaction of Hispanic ethnicity with weight, and a random school effect in multivariate mixed effect linear models. El Paso Independent School District, Spring 2001 ($n = 1874$). Asthma definition: reported current asthmatic or obstructed (PEF, $FEV_{0.5}$, or $FEF_{25–75}$ under 85% of predicted values).

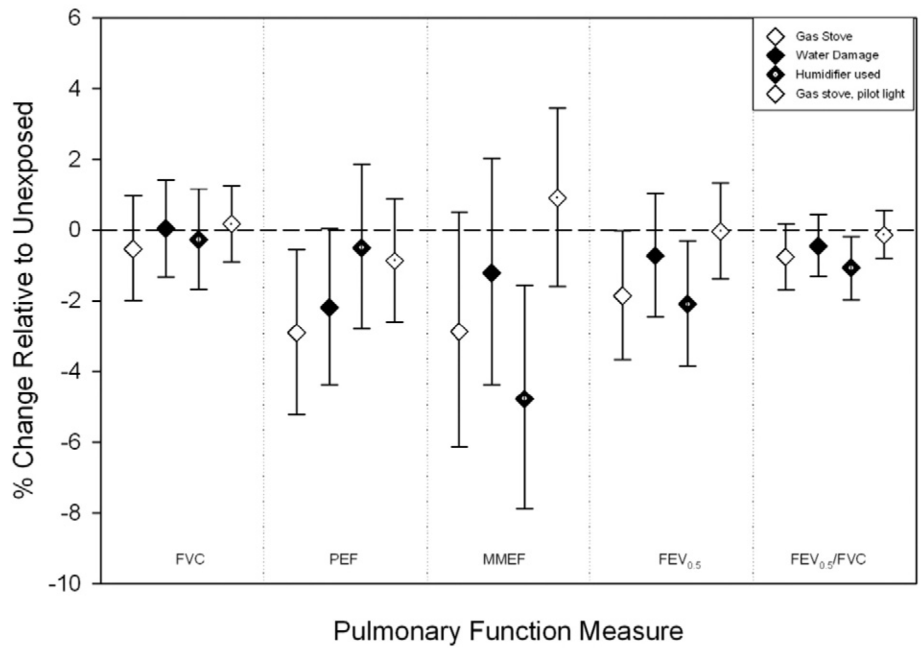

Fig. 4. The effects of indoor environmental exposures indicative of mold or indoor combustion sources on pulmonary function in 4th or 5th grade children: percent change in pulmonary function measures relative to the unexposed adjusted for sex, race/ethnicity, socio-economic status, log of height, log of weight, age, interaction of sex with height, interaction of Hispanic ethnicity with height, interaction of Hispanic ethnicity with weight, and a random school effect in multivariate mixed effect linear models. El Paso Independent School District, Spring 2001 ($n = 1874$).

pollutant, depending on the ventilation practices and genetic susceptibilities of families, can lead to airway inflammation and reduced pulmonary function (Al-Daghri et al., 2013; Ather et al., 2010; Delfino et al., 2002). Modifying cooking practices (e.g. adequate kitchen ventilation and secluding certain cooking activities to the outdoors when possible) could help reduce the effect of this risk (Dennekamp et al., 2001). A review of 20 intervention studies that targeted children and adolescents showed that asthma symptoms, school days missed and acute care visits were reduced by 21 symptom-days/year, 12.3 days/year and 0.57 visits/year respectively (Crocker et al., 2011). This is an indication that appropriate steps to reduce or eliminate these risk factors in the home can improve overall indoor environmental quality and health.

Additionally, a 2014 updated report on the scientific evidence for exposures and asthma exacerbations identified cat allergens, cockroach allergens and home dampness as exposures with sufficient evidence to

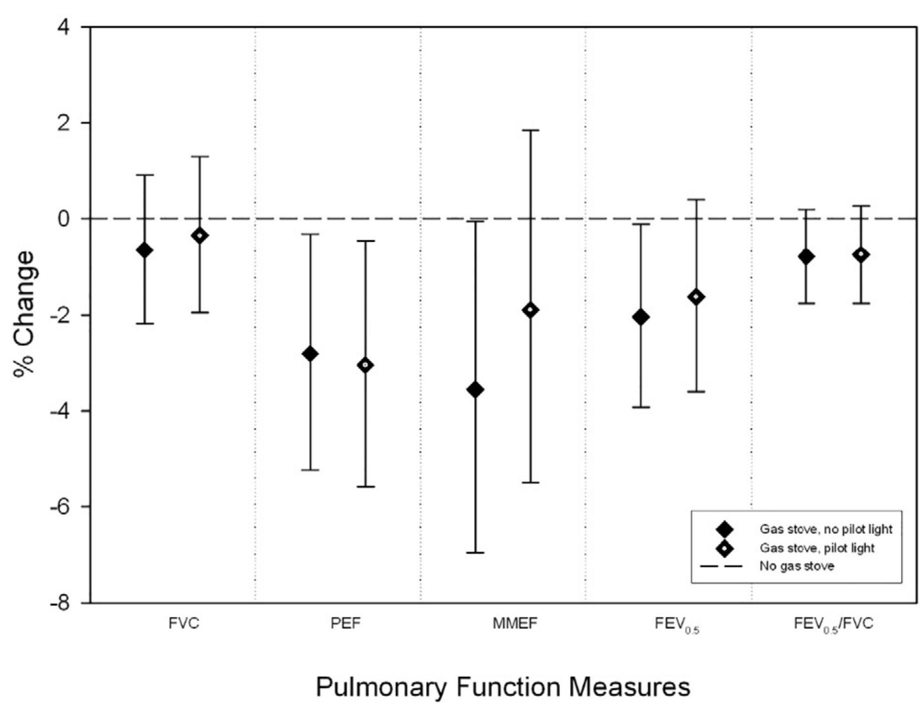

Fig. 5. The differential effects within a single model of pilot lights with gas stoves on pulmonary function in 4th or 5th grade children: percent change in pulmonary function measures relative to the unexposed adjusted for sex, race/ethnicity, socio-economic status, log of height, log of weight, age, interaction of sex with height, interaction of Hispanic ethnicity with height, interaction of Hispanic ethnicity with weight, and a random school effect in multivariate mixed effect linear models. El Paso Independent School District, Spring 2001 ($n = 1874$).

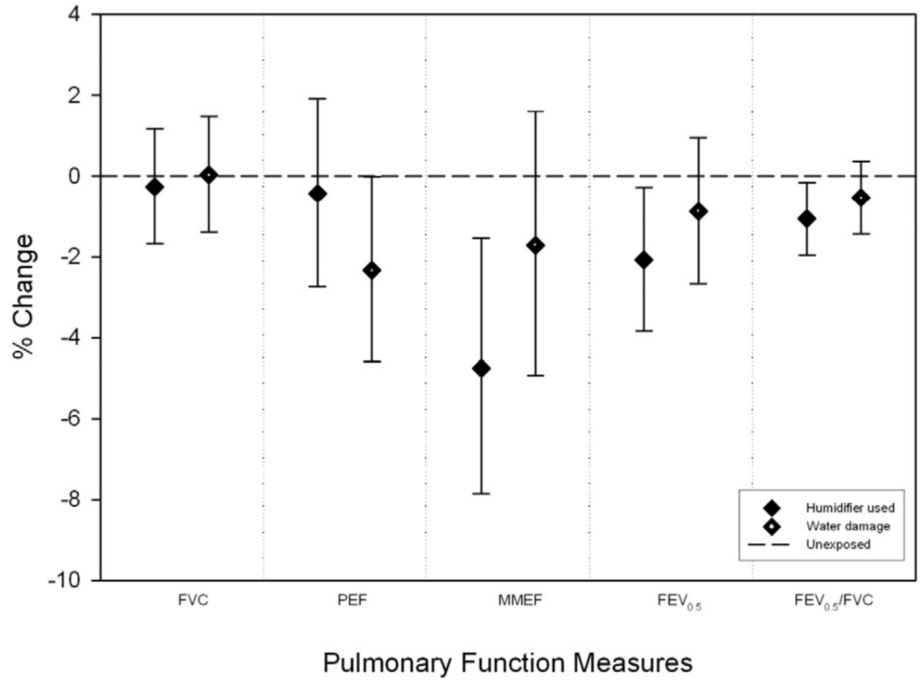

Fig. 6. The differential effects within a single model of indicators of household mold problems on pulmonary function in 4th or 5th grade children: percent change in pulmonary function measures relative to the unexposed adjusted for sex, race/ethnicity, socio-economic status, log of height, log of weight, age, interaction of sex with height, interaction of Hispanic ethnicity with height, interaction of Hispanic ethnicity with weight, and a random school effect in multivariate mixed effect linear models. El Paso Independent School District, Spring 2001 (n = 1874).

show causation of asthma exacerbations (Kanchongkittiphon et al., 2015). The report further indicated that dog allergen and nitrogen dioxide exposures were associated with asthma exacerbations but there was not enough evidence to establish causation. There is also currently inadequate or insufficient evidence for an association between pesticide exposures and asthma exacerbations (Kanchongkittiphon et al., 2015). Our results provide further evidence that some of these indoor risk factors may exacerbate asthma.

We did not obtain information on indoor conditions in subjects' former homes; however, asthma prevalence at the time of our study (2001) was comparable to national US estimates (CDC, 2012). Given the dry climate in El Paso, Texas, it is unlikely that the effects of former places of residences within El Paso would have changed the observed associations between indoor risk factors and respiratory health (CDC, 2016; Salo et al., 2014), as reported by other investigators of a large multisite cohort study (Gehring et al., 2013). In this study, exposure to indoor risk factors was ascertained by questionnaire derived responses from parents and we did not attempt to conduct exposure assessment in the homes of the children. Also, these analyses were cross-sectional and were based on current residences as opposed to conditions in former places of residence, and we did not evaluate cigarette smoking in the home and were unable to adjust for this indoor environmental contribution to poor air quality. There may also be residual confounding from other risk factors not captured through the questionnaire-based exposure assessment used. These are limitations of our study. Future studies may need to take these additional risk factors into consideration when assessing exposures.

Overall, our findings suggest that risk factors in the indoor environment can be assessed, via questionnaire, to determine their relative influence on children's respiratory health. Clinicians may need to look closely at the contribution of these indoor risk factors among patients who require recurring care to help prevent deteriorating pulmonary health (Puranik et al., 2016; Rabinovitch et al., 2011). Public health professionals may also need to improve surveillance to help identify communities which may be at risk for these indoor environmental factors (Bryant-Stephens, 2009; Gomez et al., 2017; Milligan et al., 2016). Further longitudinal studies with detailed indoor exposure assessment are needed to better estimate pulmonary health outcomes and implement effective intervention measures among different subpopulations and in different indoor environments such as schools and workplaces (Gruber et al., 2016; Huffaker and Phipatanakul, 2014; Jhun et al., 2017; Kanchongkittiphon et al., 2015).

5. Conclusions

We found that in the indoor residential environment in El Paso, Texas, reported pest problems, pet dogs, use of fireplaces, heating systems, central air conditioning, humidifier use, and cooking with gas stoves were positively associated with allergy and asthma prevalence among school aged children. Water damage, the use of humidifiers and gas stoves with pilot lighting were also associated with decreased lung function. Additionally, exposure to pet dogs increased asthma severity, and home cockroach pest problems within the past year led to decreased peak expiratory flow. These results, although cross-sectional in nature, add to the mounting literature needed to increase the strength of evidence linking specific indoor risk factors and adverse respiratory health.

Acknowledgement

This original research was supported by the EPA.

We would like to thank the study participants and their families. We would also like to acknowledge the US EPA team which performed the field data collection for this study: Debra Walsh, Scott Rhoney, Gina Andrews, and Lucas Neas. These findings do not necessarily represent EPA policy.

Conflict of interest

The authors declare that they have no conflict of interest.

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Environmental Pollution 256 (2020) 113426

Contents lists available at ScienceDirect

Environmental Pollution

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

Home environmental and lifestyle factors associated with asthma, rhinitis and wheeze in children in Beijing, China☆

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ARTICLE INFO

Article history:
Received 12 June 2019
Received in revised form
15 October 2019
Accepted 15 October 2019
Available online 22 October 2019

Keywords:
Home environment
Lifestyle
Allergy
Asthma
LASSO

ABSTRACT

Background: The prevalence of asthma and allergic diseases has increased rapidly in urban China since 2000. There has been limited study of associations between home environmental and lifestyle factors with asthma and symptoms of allergic disease in China.
Methods: In a cross-sectional analysis of 2214 children in Beijing, we applied a two-step hybrid Least Absolute Shrinkage and Selection Operator (LASSO) algorithm to identify environmental and lifestyle-related factors associated with asthma, rhinitis and wheeze from a wide range of candidates. We used group LASSO to select variables, using cross-validation as the criterion. Effect estimates were then calculated using adaptive LASSO. Model performance was assessed using Area Under the Curve (AUC) values.
Results: We found a number of environmental and lifestyle-related factors significantly associated with asthma, rhinitis or wheeze, which changed the probability of asthma, rhinitis or wheeze from −5.76% (95%CI: −7.74%, −3.79%) to 27.4% (95%CI: 16.6%, 38.3%). The three factors associated with the largest change in probability of asthma were short birth length, carpeted floor and paternal allergy; for rhinitis they were maternal smoking during pregnancy, paternal allergy and living close to industrial area; and for wheeze they were carpeted floor, short birth length and maternal allergy. Other home environmental risk factors identified were living close to a highway, industrial area or river, sharing bedroom, cooking with gas, furry pets, cockroaches, incense, printer/photocopier, TV, damp, and window condensation in winter. Lifestyle-related risk factors were child caretakers other than parents, and age<3 for the day-care. Other risk factors included use of antibiotics, and mother's occupation. Major protective factors for wheeze were living in a rural/suburban region, air conditioner use, and mother's occupation in healthcare.
Conclusions: Our findings suggest that changes in lifestyle and indoor environments associated with the urbanization and industrialization of China are associated with asthma, rhinitis, and wheeze in children.

☆ This paper has been recommended for acceptance by Payam Dadvand.

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https://doi.org/10.1016/j.envpol.2019.113426
0269-7491/

1. Introduction

Asthma, the most common chronic disease in children, is among the top 20 chronic conditions in the global ranking of childhood disability-adjusted life years, as well as among the top 10 in the mid-childhood ages of 5–14 years (Asher and Pearce, 2014). Asthma and allergy are rapidly increasing in many Chinese cities while the prevalence of childhood asthma and allergy appear to have plateaued in some western countries (Asher et al., 2006; Bai et al., 2010; Lai et al., 2009; Zhang et al., 2013a). A national survey of 438,000 children up to age 14 years in 43 Chinese cities in 2000 found that the prevalence of physician-diagnosed asthma was 1.97% (Chen, 2003). Although this was relatively low compared to the nearly 8.0% in US reported in 2001, it represented a 64% increase compared to a 1990 survey in China (Chen, 2003; Kemp and Kemp, 2001). In 2010, the prevalence of asthma in children from birth through age 14 in urban areas in China was 3.02%. Although this prevalence was still low compared to that in the US (8.4% in 2010) (Akinbami et al., 2012), the rate of increase was much steeper. Asthma in China increased by 52.8% during 2000–2010, over three times the increase of 15.1% in 2001–2010 in the US (Akinbami et al., 2012; Chen et al., 2016).

Allergic rhinitis is common in children with asthma (de Groot et al., 2012; Price, 2010). Concurrent with the increase of childhood asthma in China, allergic rhinitis, and wheeze, a symptom suggestive of asthma, have also been increasing recently among children (Guo et al., 2019). A survey of ten cities in different geographic regions of China found that the prevalence of rhinitis varied from 24.0% to 50.8%, while the prevalence of wheeze varied from 13.9% to 23.7% (Zhang et al., 2013a).

China has experienced great changes due to rapid modernization and urbanization. China's urban population in 1990 was about 29% urban, and by the end of 2017, it had increased to about 59% (Sun, 2017). Rapid modernization and urbanization brought dramatic changes to living environments and life styles (Zhang et al., 2013b). Tighter construction techniques leading to reduced ventilation, and extensive use of composite materials have resulted in a degrading of indoor air quality (Zhang et al., 2013b). In 2010, a multiple-centre epidemiological study (China, Children, Homes, Health, abbreviated as CCHH) was launched to explore potential home environmentally associated factors for children's allergic diseases in China. A cross-sectional questionnaire survey of 48,219 children aged 1–8 years old in 10 Chinese cities was conducted during 2010–2012 (Zhang et al., 2013a). Previous CCHH studies (Bu et al., 2016; Deng et al., 2016a, 2016b; Huang et al., 2015; Lynch et al., 1987; Sun and Sundell, 2011a; Wang et al., 2015; Wang et al. 2016; Wang et al., 2017; Qu et al., 2013) reported that several home environmental factors including living close to a main road or highway, new furniture, dampness, and the presence of cockroaches and mosquito/flies in the home were positively associated with asthma and rhinitis in children. However, these previous CCHH studies are limited since wheeze was not assessed and the analyses focused on only one or several environmental and life-style factors (Qu et al., 2013; Wang et al., 2015; Li et al., 2015). For example, Qu et al. (2013) focused on breastfeeding only and adjusted for age, gender and family history; Wang et al. (2015) considered indoor environmental factors only.

In this analysis, we investigate an expanded suite of factors associated with modernization and urbanization. Our aim is to identify those associated with asthma, rhinitis and wheeze in Chinese children in Beijing.

2. Material and methods

2.1. Study population

This survey was performed in 11 of Beijing's 16 administrative districts (Dongcheng, Xicheng, Chaoyang, Fengtai, Haidian, Shijingshan, Tongzhou, Changping, Daxing, Mengtougou and Fangshan) as described in Qu et al. (2013). The questionnaires were delivered to randomly selected kindergartens from January to May 2011. The response rate was 64.9%: a total of 9047 questionnaires were distributed by teachers for children to bring home to parents, and one week later, the children returned 5876 questionnaires to their teachers. The Medical Research Ethical Committee of the School of Public Health, Fudan University, Shanghai, China granted approval for the study, as part of China, Children, Health and Homes (CCHH) Phase I (International Registered Number: IRB00002408&FWA00002399). Each child's parents provided informed consent.

2.2. Questionnaire

Our questionnaire was based on the Dampness in Buildings and Health (DBH) questionnaire previously used in Sweden, Bulgaria, Singapore, Taiwan, Denmark, South Korea, and the US (An and Yamamoto, 2016; Bornehag et al., 2005; Harving et al., 1993; Naydenov et al., 2008; Sun and Sundell, 2011b; Tham et al., 2007; Yang et al., 1997). We modified some questions to be appropriate for China's home environments. The questionnaire includes demographic questions about the child and family as well as questions on the child's and the family's health, information on the child's residence, and information concerning lifestyle habits. The entire questionnaire is available in Zhang et al. (2013a).

2.3. Asthma, rhinitis and wheeze

We obtained the following information from the questionnaire reported by parents regarding their child: (1) asthma diagnosed by a doctor (asthma); (2) hay fever or allergic rhinitis diagnosed by a doctor (rhinitis); (3) parent-observed wheezing or whistling in the chest without respiratory infection in the last 12 months (wheeze). In the questionnaire, we asked about any wheeze in the past 12 months, with additional questions on when the wheeze took place (e.g., when having a cold, during exercise, playing or being outdoors, laughing or crying, in contact with furry animals). We excluded children with wheeze reported only with a cold in efforts to account for wheeze unassociated with a respiratory infection (Castro-Rodríguez et al., 2000).

2.4. Candidate factors

Important associations may not have been identified in previous studies due to focus on a limited set of potential risk factors and manual variable selection. In order to overcome this problem, we considered a more comprehensive range of possible explanatory variables associated with China's modernization and urbanization. Factors which have been demonstrated or suspected to be associated with allergic diseases or associated symptoms were the candidates in our model. Pregnancy (Erkkola et al., 2009) and family health history factors included paternal and maternal allergy, feeding, nutrition in infancy and early childhood, and medicine use (Qu et al., 2013). Factors related to family residence were dwelling location (Wieringa et al., 1997; Margolis et al., 2009) and construction characteristics including flooring, wall covering and furniture materials, heating, ventilation, and air conditioning; and dwelling-related behaviors such as window opening (Bornehag et al., 2005). Potential factors in the home environment included environmental tobacco smoke, mold, dampness, furry pets (e.g., cat, dog, rabbits, rats), non-furry pets (e.g., fish, bird), air conditioner, air cleaner, TV and computer (Zhang et al., 2013a). Factors related to the family's socio-economic status and lifestyle included the mother's occupation; and which persons were caretakers of the child (Lynch et al., 1987). Details for all home environmental and lifestyle factors (n = 64) are summarized in Table S1 in the Supplementary Material.

2.5. Statistical methods

We used a two-step hybrid Least Absolute Shrinkage and Selection Operator LASSO algorithm following the strategy described in Meinsausen (2007) and Meier et al. (2008). Specifically, the first step was group LASSO which identified important variables or variable groups, and screened out unimportant ones. In the second step, we used adaptive LASSO to zoom in on the selected variables and determine the effect estimates.

2.5.1. Variable selection

We adjusted for age and gender *a priori*, including age as a categorical variable. As there are a large number of potential factors associated with each outcome, we used a group LASSO approach for logistic regression (R package “grpreg”). LASSO’s variable selection and regularization method reduces estimate variances by shrinking regression coefficients towards zero (Tibshirani, 1996). Group LASSO is an extension of LASSO that allows pre-specified groups of covariates to be selected or excluded from a model (Yuan and Lin, 2006). Similar to LASSO, group LASSO applies a λ (i.e., the summation of absolute values of all of a vector’s components) penalty to the component regression coefficients, which essentially minimizes the sum of squared errors subject to the sum of the absolute values of the coefficients being less than a given value. We used cross-validation (CV) criteria for variable selection (function “cvfit.glasso” in R package “grpreg”).

We used group LASSO instead of plain LASSO or induced smoothed LASSO (Cilluffo et al., 2019) as there are a number of environmental and variables in our data that are reported in categories (Table S1). Using group LASSO ensures that all the dummy variables of each categorical variable of interest are included or excluded in the model.

2.5.2. Model regression

After variable selection, we further applied adaptive LASSO (R packages “glmnet” and “glmpath”) (Zou, 2006) to determine the regression coefficients from the set of predictors selected in the first step. The final model can be expressed as:

$$\mathrm{logit}(Y) = \beta_0 + \sum_{i=1}^{k} \beta_i X_i \tag{1}$$

where logit represents the adaptive LASSO for logistic regression; Y is whether the observation is of asthma, rhinitis or wheeze; Y = 1 represents “Yes” and Y = 0 represents “No”; X_i (i = 1, 2, …k) represents LASSO selected variables; β_i represents the regression coefficient of X_i; β_0 is the intercept of the logistic model.

Variances of the regression coefficients with *p*-values were estimated by a bootstrap-based procedure (Tibshirani, 1996). A *p*-value of less than 0.05 was accepted as indicating significance.

2.5.3. Missing data

About half of the returned CCHH questionnaires had missing information for at least one factor. The proportions of missing variables ranged from 0.5% to 16.6% (median = 3.0%; IQR = 2.3%). The sample of respondents who provided completed questionnaires (2,214) is large enough relative to the number of candidate predictors (65) to have sufficient power to discern differences among covariates using a LASSO approach (Tibshirani, 1996). To determine whether bias would result from not including incomplete questionnaires, we compared the relative frequencies of variables in the 2214 completed questionnaires with those in the excluded dataset (n = 5876−2214).

2.5.4. Model evaluation

Once β_0 *and* β_i (i = 1, 2, …k) have been determined, the probabilities for asthma, rhinitis, or wheeze (π) can be calculated by equation (2):

$$\pi = \exp\left(\beta_0 + \sum_{i=1}^{k} \beta_i X_i\right) \Big/ \left\{1 + \exp\left(\beta_0 + \sum_{i=1}^{k} \beta_i X_i\right)\right\} \tag{2}$$

The accuracy of our model equation (1) was estimated by plotting the area under the curve (AUC) of a receiver operating characteristic (ROC) curve, that is, the plot of true positive rate versus false positive rate for each outcome. The AUC represents the probability that the model correctly ranks the pairs (with and without the disease or symptom) of observations (Bradley, 1997). In addition, we used 10-fold cross validation to avoid an over-fitting bias (Efron and Tibshirani, 1997). The original sample was randomly partitioned into 10 equal sized subsamples. One subsample was retained for model validation, and the other 9 subsamples were used as training data. The cross-validation process was repeated 10 times and the estimate was the average of the 10 results. All analyses were performed with R software (R Development Core Team, Version 3.3.1).

3. Results

3.1. Sample characteristics

Descriptive information is summarized in Table 1 for 2214 completed questionnaires. In the analytic sample (n = 2214), the prevalence of asthma, rhinitis and wheeze were 6.0%, 8.0% and 16.7%, and there was overlap among each outcome (Fig. 1). Twenty-four percent of the children had at least one of the conditions, and 5.1% had two or three of the conditions.

3.2. Associated factors

The regression coefficients and *p*-values for the LASSO selected variables for asthma, rhinitis and wheeze are summarized in Table S3. We accepted results with *p*-value<0.05 as significant; and marginally significant when 0.05≤*p*-value<0.1. Odds ratios of factors significantly associated with at least one of the diseases are presented in Table 2. Significant values are in bold.

We found that boys were at higher risk than girls for all three conditions, and significantly so for asthma and rhinitis. The probabilities of asthma and rhinitis increased with age, while the probability of wheeze decreased with age.

Several risk factors were associated with all or with two of the conditions: short birth-length (all), use of antibiotics ever (all), paternal allergy (asthma and rhinitis), maternal allergy (rhinitis and wheeze), living close to highway (asthma and rhinitis), window condensation in winter (rhinitis and wheeze), carpet floor compared to cement floor (asthma and wheeze).

Other factors significantly associated with at least one’ outcome included: day-care <3 years old with asthma (positive and significant) and wheeze (positive and marginally significant); living close to industrial area with rhinitis (positive and significant) and wheeze (positive); gas cooking (compared to electric cooking) with asthma (positive and significant) and wheeze (positive); furry pets with asthma (positive and significant), and rhinitis and wheeze (positive); printer/photocopier in the home with rhinitis (positive

Table 1
Demographic and other information for 2214 children.

Variable		n	P (%)
Asthma	Yes	133	6.0
Rhinitis	Yes	177	8.0
Wheeze	Yes	370	16.7
Gender	Male	1129	50.8
	Female	1085	49.2
Age	3	578	26.1
	4	669	30.2
	5	587	26.5
	6	379	17.1
Birth weight (kg)	<2	20	0.9
	[2,2.5)	55	2.5
	[2.5,4)	1895	85.6
	[4,5)	148	6.7
	≥5	95	4.3
Birth length (cm)	<40	53	2.4
	[40,46)	69	3.1
	[46,52)	1665	75.2
	[52,58)	339	15.3
	≥58	89	4.0
Family history of allergy	Yes	6539	29.5
Antibiotic	Yes	1468	16.3
House location	urban	1853	83.7
	Rural/suburban	361	16.3

Footnote: n is the number; P is the percentage.

and significant) and wheeze (positive).

Other factors associated with at least one outcome included: day-care <3 years old with asthma (positive and significant) and wheeze (positive and marginally significant); living close to industrial area with rhinitis (positive and significant) and wheeze (positive); gas cooking (compared to electric cooking) with asthma (positive and significant) and wheeze (positive); furry pets with asthma (positive and significant), and rhinitis and wheeze (positive); printer/photocopier in the home with rhinitis (positive and significant) and wheeze (positive).

Living in a rural/suburban area (compared to an urban area), shared bedroom, use of air conditioning, presence of cockroach in the home, use of incense, TV in the home, damp for clothing and bedding at home, mother's occupation in healthcare (compared to housewife) were significantly associated with wheeze, but not with asthma or rhinitis. In contrast, some risk factors for asthma or rhinitis e.g., mother smoking during pregnancy, caretakers other than parents, living close to river, were not associated with wheeze.

3.3. Risk of asthma, rhinitis and wheeze due to associated factors

We calculated the probabilities of asthma, rhinitis and wheeze using equation (2) with the LASSO selected factors. Fig. 2 shows predicted probabilities of asthma, and rhinitis and wheeze for common variables selected by LASSO, including gender, age, birth height, antibiotic use, paternal allergy, maternal allergy, living close to highway and furry pets.

We summarized probability changes due to associated factors in Table 2. Our results show that these home environmental and lifestyle associated factors increased the probability of asthma, rhinitis, or wheeze from −5.8% (95%CI: −7.7%, −3.8%) to 27.4% (95% CI: 16.6%, 38.3%). For example, maternal smoking during pregnancy increased the probability of rhinitis by 25.6% (95CI%: 8.3%, 43.1%); carpeted floor increased the probability of asthma by 13.4% (95CI: 4.3%, 22.4%) compared to cement floor, and 27.4% (95%CI: 16.6%, 38.3%) for wheeze; antibiotics use ever increased the probabilities of asthma, rhinitis and wheeze by 6.3% (95CI%: 5.8, 6.8), 5.4% (95CI %: 4.8%, 6.0%) and 9.5% (95CI%: 8.6%, 10.4%) respectively.

3.4. Bias due to missing

The were no significant difference of relative frequencies of the three outcomes and risk/protective factors between included

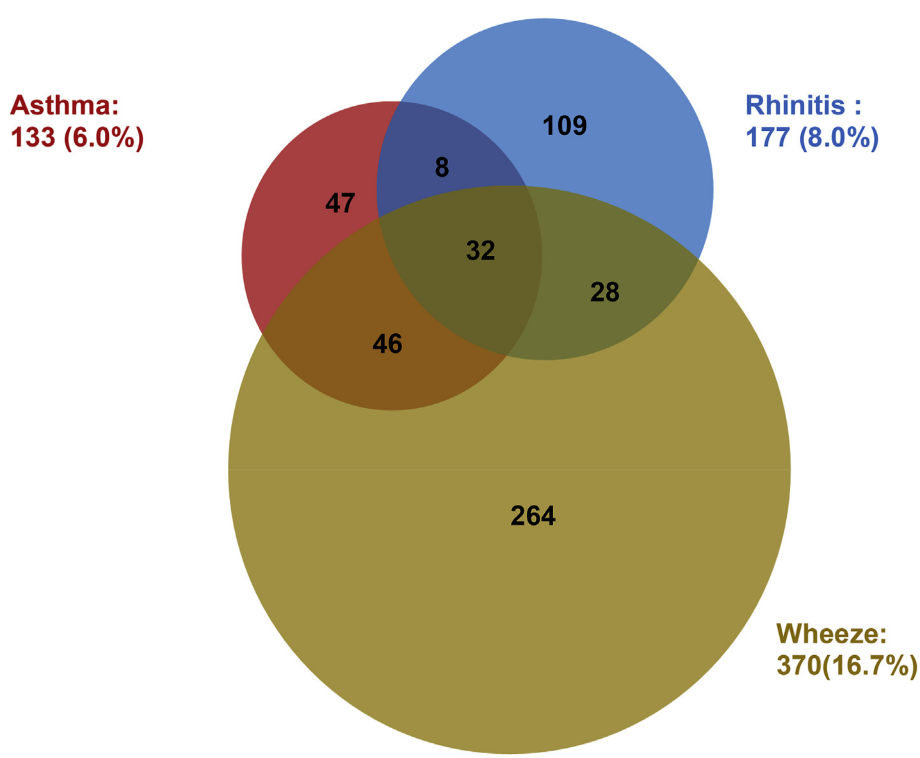


Fig. 1. Prevalence and overlap of asthma, rhinitis and wheeze. The number with each condition and the number that overlap is provided within each circle.

Table 2
Regression results and predicted probability changes for asthma, rhinitis and wheeze based on LASSO selected variables (n = 2214).

	Asthma		Rhinitis		Wheeze	
Variable	**OR (95%CI)**	**% Difference (95%CI)**	**OR (95%CI)**	**% Difference (95%CI)**	**OR (95%CI)**	**% Difference (95%CI)**
Gender: male (ref=female)	**1.63 (1.08, 2.48)***	**2.82 (2.13, 3.51)**	**1.63 (1.15, 2.32)****	**3.38 (2.64, 4.11)**	1.22 (0.96, 1.57)	3.31 (2.27, 4.34)
Age 4 (ref=3)	1.40 (0.78, 2.56)	1.40 (0.69, 2.11)	**1.99 (1.21, 3.29)****	**1.43 (0.59, 2.27)**	**0.58 (0.42, 0.79)****	**-2.16 (-3.26, -1.07)**
Age 5 (ref=3)	1.52 (0.84, 2.75)	1.51 (0.66, 2.35)	**1.82 (1.09, 3.03)***	**2.24 (1.29, 3.18)**	**0.53 (0.38, 0.75)*****	**-1.46 (-2.67, -0.24)**
Age 6 (ref=3)	**2.36 (1.27, 4.39)****	**3.52 (2.33, 4.72)**	1.48 (0.83, 2.64)	2.54 (1.55, 3.54)	**0.50 (0.34, 0.75)****	**-5.21 (-6.36, -4.06)**
Mother smoking during pregnancy: yes (ref=no)	-		**10.3 (1.63, 64.7)***	**25.6 (8.26, 43.1)**	-	
Birth height (cm): 40 (ref=[46, 52))	**4.35 (1.73, 10.8)****	**18.6 (11.34, 25.9)**	**2.94 (1.30, 6.69)***	**18.2 (11.6, 24.8)**	**2.08 (1.03, 4.18)***	**14.8 (9.42, 20.1)**
Paternal allergy: yes (ref=no)	**2.80 (1.68, 4.66)*****	**9.22 (7.26, 11.2)**	**2.20 (1.39, 3.49)****	**8.84 (7.02, 10.7)**	1.45 (0.99, 2.12)	7.54 (5.40, 9.68)
Maternal allergy: yes (ref=no)	1.42 (0.79, 2.56)	5.41 (3.59, 7.22)	**3.19 (2.05, 5.00)*****	**13.2 (11.1, 15.4)**	**1.73 (1.17, 2.53)****	**11.0 (8.71, 13.3)**
Caretaker other than parents: yes (ref=no)	**1.62 (1.06, 2.46)***	**2.87 (2.18, 3.55)**	**-**		**-**	
Day-care <3 years old: yes (ref=no)	**1.73 (1.14, 2.61)***	**3.49 (2.57, 4.40)**	-		1.28 (0.90, 1.67)	4.15 (2.97, 5.34)
Ever antibiotic use: yes (ref=no)	**5.21 (2.64, 10.3)*****	**6.26 (5.75, 6.77)**	**1.95 (1.28, 3.00)****	**5.38 (4.77, 5.99)**	**2.32 (1.72, 3.12)*****	**9.51 (8.59, 10.4)**
Home location: rural/suburban (ref=urban)	**-**		**-**		**0.69 (0.49, 0.98)***	**-3.96 (-5.56, -2.37)**
Living close to highway: yes (ref=no)	**1.80 (1.20, 2.72)****	**3.23 (2.46, 4.00)**	**1.55 (1.11, 2.18)***	**3.15 (2.35, 3.94)**	1.23 (0.96, 1.58)	3.57 (2.48, 3.67)
Living close to industrial area (ref=no)	**-**		**3.71 (1.67, 8.33)****	**15.1 (9.30, 20.8)**	1.08 (0.53, 2.23)	12.3 (7.4, 17.3)
Living close to river: yes (ref=no)	**2.77 (1.12, 6.82)***	**5.29 (2.23, 8.35)**	**-**		-	
Shared bedroom: yes (ref=no)	-		-		**1.88 (1.17, 3.00)****	**9.19 (8.15, 10.2)**
Window condensantion in winter: yes (ref=no)	-		**1.57 (1.12, 2.23)***	**2.50 (1.76, 3.25)**	**1.38 (1.07, 1.79)***	**4.57 (3.53, 5.62)**
Air conditioner: yes (ref=no)	-		-		**0.70 (0.51, 0.99)***	**-5.62 (-7.49, -3.75)**
Cooking with gas: yes (ref=no)	**2.39 (1.01, 5.64)***	**3.68 (3.16, 4.20)**	-		1.36 (0.92, 2.03)	2.61 (1.19, 4.03)
Floor: carpet (ref=cement)	**30.9 (2.56, 376)****	**13.4 (4.33, 22.4)**	-		**6.17 (1.62, 23.3)****	**27.4 (16.6, 38.3)**
Cockroach: yes (ref=no)	**-**		**-**		**1.27 (1.05, 1.52)***	**3.00 (1.90, 4.10)**
Incense: yes (ref=no)	-		**-**		**1.36 (1.00, 1.88)***	**3.50 (1.59, 5.41)**
Furry pets: yes (ref=no)	**2.12 (1.15, 3.9)***	**6.62 (4.15, 9.09)**	1.27 (0.74, 2.20)	5.87 (3.45, 8.30)	0.70 (0.44, 1.12)	0.26 (-2.05, 2.56)
Damp for clothing or bedding: yes (ref=no)	-		**-**		**1.42 (1.01, 2.01)**	**7.72 (5.63, 9.82)**
TV: yes (ref=no)	**-**		**-**		**1.31 (1.01, 1.70)***	**4.74 (3.61, 5.88)**
Printer/photocopier: yes (ref=no)			**1.60 (1.06, 2.44)***	**7.21 (5.48, 8.94)**	1.32 (0.94, 1.86)	6.39 (4.47, 8.32)
Mother's occupation: healthcare (ref=housewife)	-		-		**0.39 (0.18, 0.84)***	**-5.76 (-7.74, -3.79)**

Footnotes: OR represents the Odds Ratio which euqals to e^{β}, β is the regression coefficient; Significant results are in **blue bold font**; "-" represents a variable not selected by LASSO; * represents 0.01≤ p-value<0.05, ** represents 0.001≤ p-value<0.01, *** represents p-value<0.001, detailed p-values were in Table S3 in the Supplementary Material; % Difference is the difference (%) in predicted probabilities between exposure and reference groups; 95%CI is the 95% confidence interval; ref represents the reference value (no "ref" for ordinal variables).

questionnaires (n = 2214) and the excluded questionnaires (n = 5876−2214) (most of the p-values of Welch's two-sample t-test were greater than 0.05) (Table S2 in Supplementary Material), affirming that the missingness was random (Welch, 1947). Therefore, bias was not introduced by using the subset of questionnaires with no missing data.

3.5. Model strength

To show the predictive strength of the factors selected by LASSO, the ROC curves for asthma, rhinitis, and wheeze are provided in the Supplementary Materials Fig. S1. An AUC ≥0.70 is generally accepted as indicating a meaningful model (Godil et al., 2013). The AUCs were 0.81 for asthma, 0.77 for rhinitis and 0.75 for wheeze, indicating strong model predictions and associations.

4. Discussion

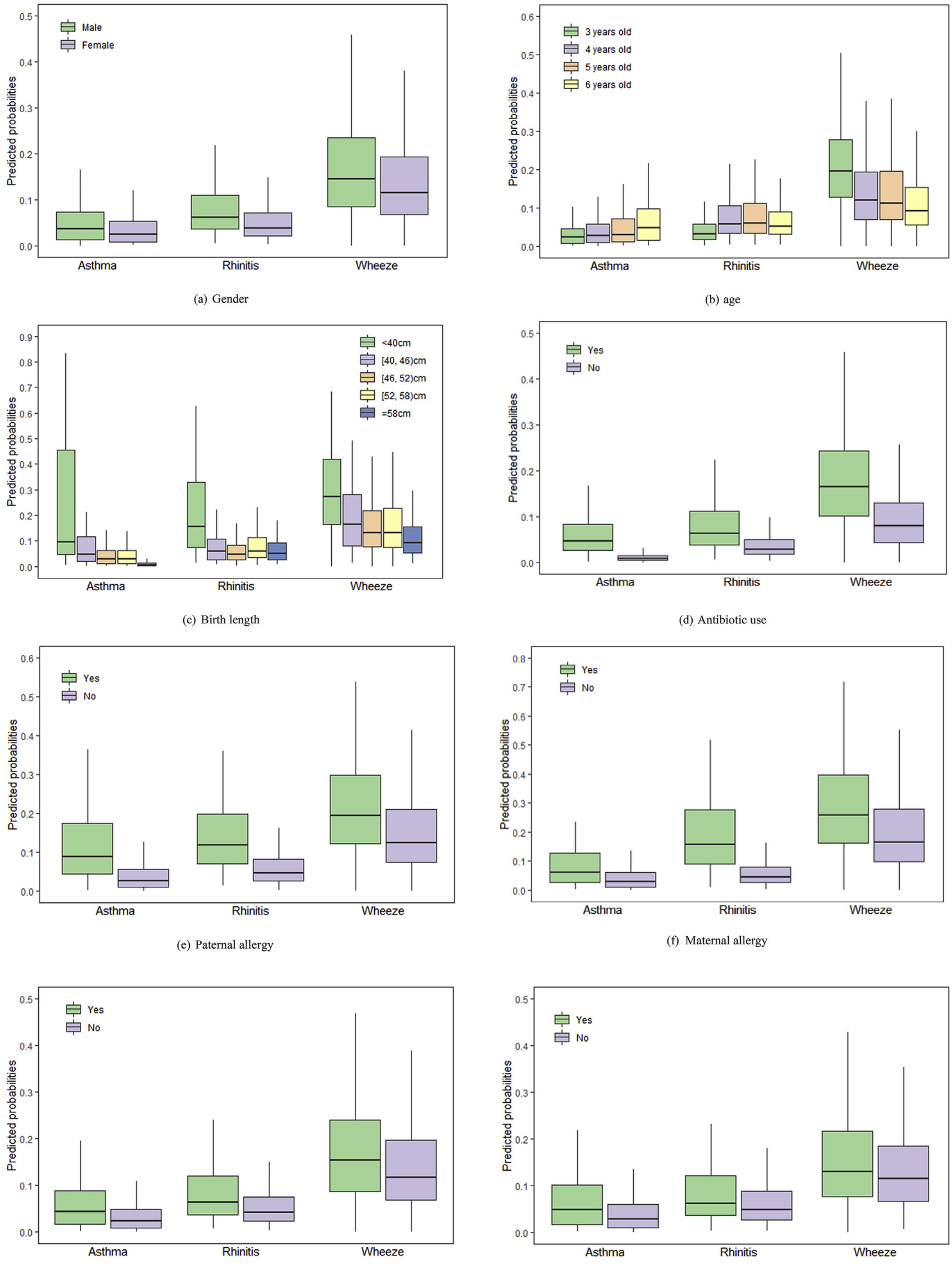
For 2214 completed questionnaires, we first used group LASSO to select the most important factors associated with asthma, rhinitis and wheeze for children aged 3−6 in Beijing. We then used adaptive LASSO regression to determine associations between selected factors and these allergies.

We found that the prevalence of asthma in 2010−2011 among children aged 3−6 in Beijing was 6.0%, an increase compared to earlier surveys (Ma et al., 2002; NCGCA, 1993; Zhao et al., 2010). The prevalence of wheeze in the absence of a respiratory infection within the previous 12 months was 16.7%, or slightly higher than the 12.3% reported by Zhao et al. (2010). In contrast, the prevalence (8.0%) of rhinitis in the present study was lower than the 14.9% reported by Zhang et al. (2013c). It is possible that the finding by Zhang et al. (2013c) is attributable to the use of medical record review that included diagnostic tests for the assessment of allergic symptoms, while our result is from self-reported data.

Our results show that asthma, rhinitis and wheeze had several common risk factors (e.g., shorter birth length and antibiotic use). While this finding may be consistent with a common etiology (Bjerg et al., 2015), we note that some factors associated with wheeze were not associated with asthma or rhinitis and that the converse is also true. It is possible that differences may be due to a greater prevalence of parent-reported wheeze than doctor-diagnosed disease, or it is possible that children who have asthma or rhinitis may take medicine that controls associated wheeze. It is also possible that some children may have had asthma or rhinitis, but were not examined by a doctor. In addition, the diagnosis of asthma in younger children is not as reliable as at older ages, as many children with recurrent asthma-like symptoms no longer experience symptoms by age 6 years (van de Kant et al., 2009). All the above possibilities may contribute to uncertainties in the assessment of our outcomes.

To the best of our knowledge, we are the first to describe the positive association between caretakers other than parents with asthma. One past study has suggested a causal relationship between positive parenting attitude and less childhood asthma (Nagano et al., 2010). Modernization in China impacts family structure and relationships (Xu and Xia, 2014). It is also noteworthy that attending a day-care nursery at <3 years old had a significant positive association with asthma, a finding that agrees with Sun and Sundell (2011a) study in Northeast Texas.

Early antibiotic use has been reported to be positively associated with allergy (Lapin et al., 2014; Marra et al., 2009; Risnes et al., 2011). China historically has overused antibiotics with physicians



(a) Gender

(b) age

(c) Birth length

(d) Antibiotic use

(e) Paternal allergy

(f) Maternal allergy

(g) Living close to highway

(h) Furry pets

Fig. 2. Predicted probabilities of asthma, rhinitis and wheeze for the Lasso selected risks. The risks are (a) gender, (b) age, (c) birth height, (d) antibiotic use, (e) paternal allergy, (f) maternal allergy, (g) living close to highway and (h) furry pets. (a) Gender. (b) age. (c) Birth length. (d) Antibiotic use. (e) Paternal allergy. (f) Maternal allergy. (g) Living close to highway. (h) Furry pets. Footnote: Only variables selected by group LASSO for each disease – asthma, rhinitis and wheeze – are included. The horizontal lines represent median values and boxes represent 25th-75th percentile range, and the whiskers extend to the 5th and 95th percentiles.

commonly prescribing them to as many as half of all outpatients (Hvistendahl, 2012). We note that worsening asthma may be associated with some infections (Custovic et al., 2005); however, it is also possible that doctors prescribe antibiotics in response to non-specific signs of either allergy or infection.

Consistent with many previous studies conducted both inside and outside of China (Beasley, 1998; Pearce et al., 2007; Wang et al., 2015; Qu et al., 2013; Xu et al., 2014), we found that male gender, age, and birth length were significantly associated with asthma, rhinitis and wheeze. We found that paternal allergy was positively and significantly related to asthma and rhinitis, while maternal allergy was positively and significantly related to rhinitis and wheeze, which have been found in previous studies (Litonjua et al., 1997; Paaso et al., 2014). Home environmental factors, including dwelling location and in-dwelling exposure factors and ventilation were also related to asthma, rhinitis or wheeze, similar to previous reports (Li et al., 2013; Margolis et al., 2009; Patel et al., 2011; Vastardi et al., 2012; Lee et al., 2013; Litonjua et al., 2001; Bu et al., 2016; Andersen et al., 1974; Naclerio et al., 1995; Nielsen, 1991; Strom-Tejsen et al., 2008; Sundell and Lindvall, 1993). A recent study in Italy (Cilluffo et al., 2018) found that children living in an urbanized setting had a higher symptom score for symptoms such as red or itching eyes, itching nose, and wheezing compared to children in a less urbanized environment. Between 1978 and 2016, more than 550 million Chinese people have moved to urban from rural/suburban areas because of rapid industrialization (Zhang, 2017). Rapid urbanization has resulted in a 2.6% decrease of vegetated areas in urban locations per decade, and a 1.5% decrease in suburban areas in China during 1998–2012 (Jin et al., 2018). The changes may have contributed the increase of children's asthma and allergies in China. A home environmental factor significantly protective against wheeze was air conditioner use, consistent with less exposure to outdoor allergens (Solomon et al., 1980).

In contrast to previous CCHH studies (Bu et al., 2016; Liu et al., 2013; Wang et al., 2015), we found no significant protective association between breastfeeding and no significant risk association between environmental tobacco smoke (ETS) and allergic diseases or symptoms in our study. Associations of both breastfeeding and ETS with allergies are inconsistent in previous studies (Qu et al., 2013; Arif and Racine, 2017; Lebowitz and Quackenboss, 1990; Leung et al., 2016; Lodge et al., 2015; Miyake et al., 2008; Vargas et al., 2007). We found that maternal smoking during pregnancy was significantly associated with rhinitis, consistent with reports from Ferrante et al. (2014) and Kulig et al. (1999). According to Xu et al (2017) investigation, the prevalence of maternal smoking in 5 provinces in China is 3.8%. The prevalence of smoking among young women has increased and is predicted to keep increasing due to China's economic growth and growing independence of women (https://www.ncbi.nlm.nih.gov/pubmed/?term=Sansone%20N%5BAuthor%5D&cauthor=true&cauthor_uid=26240136 Snansone et al., 2015).

Our study has a number of strengths. First, we considered a comprehensive suite of candidate predictors compared to previous CCHH studies. We included 64 candidate variables that included demographic information on the child and family, home environmental characteristics, and life habits. Secondly, our two-step LASSO approach had strong model predictive performance as evidenced by all AUCs $\geq$0.75. For comparison, we assessed the strength of the risk predictors for rhinitis detected by Wang et al., (2015) Beijing CCHH study based on the same dataset. The AUC for Wang et al.'s model was below 0.60. Larger AUC of our model suggests improved risk identification. In addition, as asthma, wheeze and rhinitis may have similar but not exactly the same etiology, we assessed risk factors in common and risk factors that differed for asthma, rhinitis and wheeze, which have not been evaluated in previous CCHH studies.

A main limitation of the present study is that it is based on a questionnaire survey without physical examinations, allergy screening tests, or environmental measurements such as temperature, humidity, levels of allergens and chemicals in the home. There may be recall errors for both children's health status and exposure history. However, our analysis did indicate that the missing values were randomly distributed, so that we were able to exclude incomplete questionnaires without introducing error. Secondly, exposures to outdoor pollutants (e.g., NO_2) or exposures in school/daycare environment may be potential influencing factors (Deng et al., 2016b; Salo et al., 2009) were not directly considered in our study. However, we did ask questions that can partly characterize outdoor exposure, such as home location and the traffic time very day. Thirdly, we were not able to assess some potential risk factors, such as the family income, which was found to a risk factor for allergies in a previous study (Chen et al., 2018). Finally, we used "in-sample" validation to evaluate the predictive ability of the observed associations; it would be valuable to investigate whether this model can retain high accuracy when it is applied to other data sets or assessed prospectively.

5. Conclusions

Starting with a relatively large comprehensive suite of home environmental and lifestyle factors, we used LASSO to select key factors associated with asthma, rhinitis and wheeze in children based on 2214 completed questionnaires in Beijing. Indoor environmental factors associated with increased risk of asthma, rhinitis, and wheeze in children include residence in an urban area, near a highway or an industrial area, carpeted floor, gas cooking, perceived indoor odor, perceived dryness, furry pets, cockroaches. Lifestyle-related factors associated with increased risk of asthma, rhinitis, and wheeze in children include antibiotic use, caretakers other than parents, starting day-care before 3 years old, shared bedroom, maternal smoking, and a printer/photocopier and TV in the home. We note that many of the home environmental and lifestyle factors identified have accompanied rapid modernization and urbanization in China.

Competing financial interests

The authors do not have any competing financial interests.

Funding

Natural Science Foundation of China (51420105010 and 51521005), the NIH (R01 ES019853) and USEPA (RD-83479801 and RD-83587201).

Acknowledgements

This study was made possible by the findings from Natural Science Foundation of China (51420105010 and 51521005), the NIH (R01 ES019853) and U.S. EPA (RD-83479801 and RD-83587201). We thank the kindergarten teachers, children and their parents for participating in the survey.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envpol.2019.113426.

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