

ENVIRONMENTAL DETERMINANTS

Indoor environmental factors associated with wheezing illness and asthma in South Korean children: phase III of the International Study of Asthma and Allergies in Childhood

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Abstract

Background: The relationship between exposure to indoor environmental pollutants and incidence of asthma and wheezing illness in children is unclear. This study aimed to clarify this relationship by identifying the risk factors associated with these conditions in South Korean children aged 6–7 years. **Methods:** The parents or guardians of 3810 children aged 6–7 years who had participated in the International Study of Asthma and Allergies in Childhood and met the study criteria completed validated questionnaires regarding their children's asthma and wheezing illness, risk factors and exposure to indoor pollutants. The data were subjected to chi-square and multivariate logistic regression analysis to identify the factors significantly associated with asthma and wheezing illness. **Results:** Parental history of allergic disease (odds ratio [OR]: 1.729; 95% confidence interval [CI]: 1.447–2.066), living on the basement or semi-basement floor (OR: 1.891; 95% CI: 1.194–2.996) and living in housing that had been remodeled within the last 12 months (OR: 1.376; 95% CI: 1.101–1.720) were found to be significantly associated with wheezing illness. Parental history of allergic disease (OR: 2.189; 95% CI: 1.483–3.231), male sex (OR: 1.971; 95% CI: 1.369–2.838) and positive skin prick test (SPT) result (OR: 1.583; 95% CI: 1.804–3.698) were found to be significantly associated with current asthma. **Conclusions:** Although the risk factors for current asthma appear to be more related to the non-modifiable risk factors like sex, parental history of allergic diseases, SPT, the two groups are associated with exposure to modifiable indoor environmental factors.

Keywords

Asthma, indoor environmental factors, International Study of Asthma and Allergies in Childhood, South Korea, wheezing illness

History

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Introduction

The increasing prevalence of asthma over the past several decades, particularly in children, has led it to become the most common chronic disease in children and adolescents [1–3]. The risk of developing persistent asthma in childhood, which has been attributed to environmental exposure early in life and genetic susceptibility [4,5], appears to be compounded by factors associated with the modern unhealthy lifestyle, including exposure to an increasingly polluted indoor and outdoor environment, an unhealthy diet and psychological stress [6,7]. In the research into the effects

of these factors on respiratory health, most studies of air pollution have focused on exposure to outdoor pollutants, leading the effects of exposure to indoor pollutants to be less clearly understood [8]. Nevertheless, several indoor pollutants have been investigated and, based on the findings, implicated in respiratory morbidity in children, including mold/dampness, tobacco smoke, air pollution and formaldehyde [8–11]. Among these pollutants, chemical vapor has been found to increase the risk of physician-diagnosed asthma by 135% and the risk of suspected asthma by 114% after adjusting for confounding factors [12].

More recently, volatile organic compounds (VOCs), suspected irritants emitted by various sources that are often components of newly built dwellings, have been independently associated with respiratory symptoms [8,13]. The importance of this finding emerges with consideration of modern urban development in South Korea. Since the 1980s,

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when the provision of housing first became an important issue, the government has sought to increase the number of dwelling units, especially apartments in new city projects, to sustain property prices and stimulate the domestic housing market [14]. Therefore, South Koreans born after 1980 have a higher probability than older generations of living in newly built housing during infancy, and hence can be studied to determine the relationship between prevalence of allergies and related disorders. As a recent study that found that 49% of those moving into a newly built apartment undertake further remodeling to provide an additional space or for convenience [15], investigation of this relationship remains very pertinent. In accordance, the aim of this study was to identify the factors associated with the incidence of asthma and wheezing illness in South Korean children between 6 and 7 years of age. As this study focused on investigating the effects of factors associated with living in newly built housing, the findings have implications for those considering remodeling their housing and for South Korean housing policy.

Methods

Study population

Identification of potential participants was conducted by review of data collected by International Study of Asthma and Allergies in Childhood (ISAAC). Using a stratified two-stage cluster sampling design, the ISAAC had surveyed the parents or guardians of a representative sample of first-grade students aged 6–7 years attending 45 elementary schools in South Korea between October and November 2010. In the first stage, the schools had been stratified by geographic region (into 1 of 7 regions) and by location type (metropolitan, urban or rural). Within each stratum, sample schools had been selected using the systematic probability proportional to size sampling procedure, with the measure of size based on the number of classes in each school. Schools that had declined participation had been substituted with replacement schools to meet the predetermined sample size. The participation rate of the originally sampled elementary schools had been 82.0%.

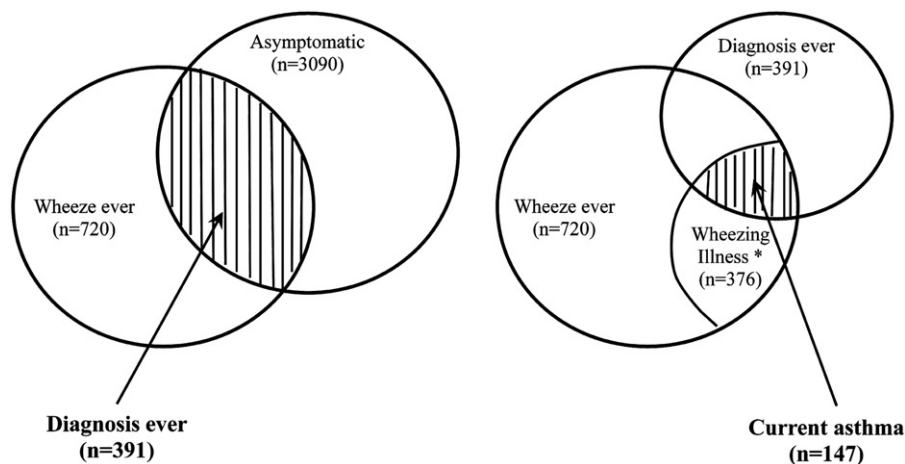
For the second stage of sampling, three classes had been randomly selected from the first grade of each sample school, and the parents or guardians of all the children in each class had been requested to participate. Among these students, the parents or guardians of 4348 children had provided informed consent for their child's participation, yielding a response rate of 92.1%. Among these 4348 children, 3810 met the study criteria of (1) having undergone a skin prick test (SPT) and (2) having ISAAC data available because their parents or guardians had completed the standard ISAAC questionnaire on their behalf were subjected to further examination by classification into the following three study groups: (1) an wheeze ever group ($n=720$), composed of subjects who had experienced wheezing at least once within their lifetimes; (2) a wheezing illness group ($n=376$) composed of subjects who had experienced wheezing unrelated to the common cold within the past year; and (3) a current asthma group ($n=147$) composed of subjects who had been diagnosed with asthma by a physician and had experienced wheezing unrelated to the common cold within the past year (Figure 1). Written informed consent from a parent or guardian was obtained at the time of enrollment. Approval for conducting the study was obtained by the Institutional Review Board of Dankook University (IRB approval number: DKUH IRB 2010-09-0260).

Measures

The parents or guardians of the participating children were requested to complete a validated questionnaire containing items regarding their children's asthma and risk factors. To keep translation bias to a minimum and allow for analysis of the possible consequences of data analysis and interpretation of outcomes, the questionnaire protocol was based on the protocol that had been used in ISAAC Phase III. In this study, questionnaire translations have been used within various cultural contexts, and back-translation into English had been performed [16,17].

The risk factor of exposure to environmental tobacco smoke was defined as exposure to secondhand tobacco smoke in the home and the risk factor of exposure to home dampness

Figure 1. Venn diagrams illustrating the classification of the subjects into the wheeze ever wheezing illness and current asthma groups. *Wheeze in the past year.



and mold as exposure to visible mold growth and/or wet or damp spots on indoor surfaces in the home. Residential floors were categorized as the basement floor, the semi-basement floor or the first floor and above, and determination of the age of a housing structure was based on the year of its construction.

Recent exposure to remodeling was scored based on the response to the question "Has any remodeling been performed over the last 12 months in the dwelling in which your child lives?" Recent exposure to newly built furniture was scored based on the response to the question "Have you placed newly built furniture in the area in which your child usually resides over the last 12 months?" Habitation in a new or remodeled house before one year of age based on the response to the question "Did you move to a new or remodeled house 1 year after your child's birth?"

All subjects underwent a standard SPT panel to detect exposure to the following 18 inhalant allergens: *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, *Tyrophagus putrescentiae*, cockroaches, cats, dog, alder, birch trees, oak trees, Japanese cedar (Lofarma, Milan, Italy), orchard grass, Bermuda grass, Timothy grass, mugwort, ragweed, Japanese hop, *Alternaria alternata* and *Aspergillus fumigatus*. Histamine was used as a positive control and normal saline as a negative control. A mean wheal diameter of 3 mm or above that of the negative control was considered a positive reaction. Atopy was defined as positive skin test reactivity to one or more of the allergens tested.

In accordance with the cutoff criteria used in the 2007 Korean growth charts, children with a body mass index (BMI) within 5%–85% of the mean BMI for their age were classified as normal weight, children with a BMI within 85% and 94% as overweight, children with a BMI within 95% or greater as obese and children with a BMI within 4% or lower as underweight [18]. Data regarding tobacco smoke exposure in the home; education level of the father and parental history of allergic disease, which were based on whether the child's mother and/or father reported ever having had asthma, allergic rhinitis, allergic conjunctivitis or atopic eczema, were obtained *via* administration of additional questionnaires. Based on the results of the chi-square test, sex, paternal education level, type of housing and region of residence were selected as co-variables to adjust in the analysis of the association between environmental exposure and asthma and/or wheezing illness.

Statistical analysis

Associations between exposure to environmental risk factors and health outcomes were assessed using the chi-square test of significance. Statistical analysis was analyzed by performing multiple logistic regression to determine the 95% confidence interval (CI) at a 5% level of significance. The adjusted odds ratio (OR) for development of wheezing illness or current asthma was determined controlling for sex, parental history of allergic diseases, type of housing, type of housing flooring and SPT results, the factors found to be significantly related to these conditions. As BMI, paternal educational level, household income, residential area and breast feeding

were not found to be significantly related to either wheezing illness or current asthma, these factors were not included in the model. The exposure variables of habitation in remodeled housing within the last 12 months, exposure to newly built furniture within the last 12 months and habitation in new or remodeled housing before one year of age were tested separately using the model adjusted by the co-variables and exposure variables. All statistical analyses were performed using SPSS version 19.0 (SPSS Inc., Chicago, IL). $p < 0.05$ was considered a level of statistical significance in the comparison of the groups and results.

Results

General characteristics

Of the 3810 children for whom completed questionnaire data sets were analyzed, the prevalence of current asthma and wheezing illness was found to be 3.9% and 9.9%, respectively. Among subjects with current asthma, a significantly higher percentage (5.2%) was found to be male compared to female (2.5%; $p < 0.05$). Compared to underweight and normal weight subjects, overweight subjects were found to have a higher prevalence of current asthma (1.7–3.3% vs. 6.8%, respectively; $p < 0.05$). No significant differences regarding paternal education level, household income, residential area or type of housing were found between subjects with wheezing illness and current asthma (Table 1).

Difference in prevalence of symptoms according to non-modifiable and modifiable environmental factors

Incidence of allergic disorders in parents was found to be significantly associated with both wheezing illness (12.0%) and current asthma (5.3%; Table 2). Among the subjects in the current asthma group, 6.2% obtained a positive SPT result and 2.2% a negative result ($p < 0.000$). Breast feeding and exposure to secondhand smoke, pets, dampness or carpeting were not found to be significantly associated with the prevalence of wheezing illness or current asthma. Among the subjects with wheezing illness, a significantly higher percentage were living on the basement or semi-basement floor compared to the first floor or above (16.0% vs. 9.6%, respectively; $p < 0.05$), and 14.4% were living in houses that had been remodeled within the last 12 months (Table 3).

Factors associated with wheezing illness and current asthma

The factors associated with wheezing were investigated by multivariate logistic regression of the independent variables identified in previous studies of asthma and the results of the chi-square test in this study (Table 4). Table 4 lists the adjusted OR and 95% CI for the modifiable environmental factors identified. As can be observed, male sex (OR: 1.515; 95% CI: 1.204–1.907), parental history of allergic disease (OR: 1.662; 95% CI: 1.309–2.112), living on the basement or semi-basement floor (OR: 2.003; 95% CI: 1.141–3.518), living in housing that had been remodeled house within

Table 1. General characteristics of study subjects.

	Total	Wheeze ever (<i>n</i> = 720)		Wheezing illness (<i>n</i> = 376)		Current asthma (<i>n</i> = 147)	
		<i>n</i> (%)	<i>p</i> Value	<i>n</i> (%)	<i>p</i> Value	<i>n</i> (%)	<i>p</i> Value
Sex			0.000		0.000		0.000
Male	1925	417 (21.7)		225 (11.7)		100 (5.2)	
Female	1885	303 (16.1)		151 (8.0)		47 (2.5)	
Body mass index			0.360		0.080		0.013
Underweight	232	40 (17.2)		19 (8.2)		4 (1.7)	
Normal weight	2165	404 (18.7)		191 (8.8)		71 (3.3)	
Overweight	310	70 (22.6)		40 (12.9)		21 (6.8)	
Obese	296	56 (18.9)		33 (11.1)		11 (3.7)	
Paternal education level (years)			0.199		0.856		0.807
≤ 9	1346	243 (18.1)		135 (10.0)		48 (3.6)	
9–12	671	143 (21.3)		69 (10.3)		27 (4.0)	
> 12	1709	319 (18.7)		164 (9.6)		68 (4.0)	
Household income (\$US/month)			0.608		0.259		0.491
< 2000	523	91 (17.4)		58 (11.1)		18 (3.4)	
2000–4000	1851	341 (18.4)		168 (9.1)		68 (3.7)	
2000–6000	939	188 (20.0)		102 (10.9)		44 (4.7)	
≥ 6000	388	75 (19.3)		33 (8.5)		13 (3.4)	
Residential area			0.894		0.481		0.153
Metropolitan	1761	332 (18.9)		169 (9.6)		67 (3.8)	
Urban	1404	262 (18.7)		135 (9.6)		47 (3.3)	
Rural	645	126 (19.5)		72 (11.2)		33 (5.1)	
Type of housing			0.397		0.705		0.082
Detached house	413	79 (19.1)		46 (11.1)		11 (2.7)	
Townhouse	757	130 (17.2)		72 (9.5)		22 (2.9)	
Apartment	2504	480 (19.2)		241 (9.6)		110 (4.4)	
Other	112	26 (23.2)		13 (11.6)		2 (1.8)	

p Values were derived using the chi-square test.

Table 2. Prevalence of symptoms according to non-modifiable risk factors and indoor environmental factors.

	Total	Wheeze ever (<i>n</i> = 720)		Wheezing illness (<i>n</i> = 376)		Current asthma (<i>n</i> = 147)	
		<i>n</i> (%)	<i>p</i> Value	<i>n</i> (%)	<i>p</i> Value	<i>n</i> (%)	<i>p</i> Value
Parental history of allergic disease			0.000		0.000		0.000
No	1725	245 (14.2)		126 (7.3)		37 (2.1)	
Yes	2085	475 (22.8)		250 (12.0)		110 (5.3)	
Skin prick test result			0.000		0.000		0.000
Negative	2245	379 (16.9)		183 (8.2)		50 (2.2)	
Positive	1565	341 (21.8)		193 (12.3)		97 (6.2)	
Breast feeding			0.217		0.709		0.521
No	948	166 (17.5)		90 (9.5)		33 (3.5)	
Yes	2815	544 (19.3)		279 (9.9)		111 (3.9)	
Dampness or mold in the home			0.002		0.351		0.549
No	2761	490 (17.7)		264 (9.6)		103 (3.7)	
Yes	1011	224 (22.2)		107 (10.6)		42 (4.2)	
Carpeting in the home			0.061		0.587		0.275
No	3197	621 (19.4)		316 (9.9)		129 (4.0)	
Yes	526	84 (16.0)		48 (9.1)		16 (3.0)	
Pets in the home			0.188		0.244		0.407
No	3370	629 (18.7)		323 (9.6)		134 (4.0)	
Yes	328	71 (21.6)		38 (11.6)		10 (3.0)	
Tobacco smoke exposure in the home			0.020		0.027		0.204
No	1493	255 (17.1)		128 (8.6)		51 (3.4)	
Yes	2217	446 (20.1)		239 (10.8)		94 (4.2)	

p Values were derived using the chi-square test.

the last 12 months (OR: 1.575; 95% CI: 1.191–2.083) and habitation in new or remodeled housing before one year of age (OR: 1.425; 95% CI: 1.090–1.864) were found to be significantly associated with wheezing illness ($p < 0.05$). Male sex (OR: 1.971; 95% CI: 1.369–2.838), parental history of allergic disease (OR: 2.189; 95% CI: 1.483–3.231), positive SPT (OR: 1.583; 95% CI: 1.804–3.698) and habitation in new or remodeled housing before one year of age (OR: 1.575; 95%

CI: 1.064–2.330) were found to be significantly associated with current asthma and more strongly associated with current asthma than wheezing illness.

Discussion

To our knowledge, this study was the first nationwide, population-based investigation of the risk factors most

Table 3. Prevalence of symptoms according to indoor environmental factors.

	Total	Wheeze ever (<i>n</i> = 720)		Wheezing illness (<i>n</i> = 376)		Current asthma (<i>n</i> = 147)	
		<i>n</i> (%)	<i>p</i> Value	<i>n</i> (%)	<i>p</i> Value	<i>n</i> (%)	<i>p</i> Value
Age of housing			0.973		0.879		0.691
> 2 years	3619	679 (18.8)		351 (9.7)		137 (3.8)	
≤ 2 years	159	30 (18.9)		16 (10.1)		7 (4.4)	
Floor of housing			0.009		0.033		0.935
First floor or higher	3671	682 (18.6)		352 (9.6)		141 (3.8)	
Basement or semi-basement	100	29 (29.0)		16 (16.0)		4 (4.0)	
Remodeling within the last 12 months			0.000		0.000		0.252
No	3094	554 (17.9)		271 (8.8)		116 (3.7)	
Yes	590	142 (24.1)		85 (14.4)		28 (4.7)	
Newly built furniture within last 12 months			0.229		0.258		0.805
No	2617	483 (18.5)		248 (9.5)		102 (3.9)	
Yes	1153	232 (20.1)		123 (10.7)		43 (3.7)	
Habitation in new or remodeled housing before one year of age			0.391		0.004		0.006
No	3102	578 (18.6)		284 (9.2)		106 (3.4)	
Yes	673	135 (20.1)		86 (12.8)		38 (5.6)	

p Values were derived using the chi-square test.

Table 4. Factors associated with wheezing illness and current asthma in children aged 6–7 years.

	Wheeze ever			Wheezing illness			Current asthma		
	OR	95% CI		OR	95% CI		OR	95% CI	
Sex									
Female	1.000			1.000			1.000		
Male	1.434	1.208	1.704	1.515	1.204	1.907	1.971	1.369	2.838
Parental history of allergic diseases									
No	1.000			1.000			1.000		
Yes	1.729	1.447	2.066	1.662	1.309	2.112	2.189	1.483	3.231
Skin prick test result									
Negative	1.000			1.000			1.000		
Positive	1.298	1.093	1.541	1.539	1.227	1.930	1.583	1.804	3.698
Floor of housing									
First floor or higher	1.000			1.000			1.000		
Basement or semi-basement	1.891	1.194	2.996	2.003	1.141	3.518	1.112	0.395	3.133
Tobacco smoke exposure in the home									
No	1.000			1.000			1.000		
Yes	1.207	1.013	1.438	1.230	0.974	1.553	1.307	0.916	1.866
Remodeling within the last 12 months									
No	1.000			1.000			1.000		
Yes	1.376	1.101	1.720	1.575	1.191	2.083	1.156	0.738	1.810
Newly built furniture within last 12 months									
No	1.000			1.000			1.000		
Yes	1.035	0.858	1.248	1.042	0.814	1.333	0.897	0.610	1.319
Habitation in new or remodeled housing before one year of age									
No	1.000			1.000			1.000		
Yes	1.059	0.852	1.318	1.425	1.090	1.864	1.575	1.064	2.330

strongly associated with the incidence of wheezing illness and asthma in children 6–7 years of age. In accordance with previous research indicating that asthma in young children is more common in boys than girls, the incidence of asthma was found to be greater in the boys in this study, suggesting the greater influence of hereditary mechanisms in males [2,4]. The study findings also suggest that asthma in children is more strongly related to parental history of allergic disease (OR: 2.189; 95% CI: 1.483–3.231) and greater sensitization, as indicated by a positive SPT (OR: 1.583; 95% CI: 1.804–3.698), compared to wheezing illness. Although the reason for

this difference remains unclear, both systemic and lung-specific factors likely play important roles [1]. As current asthma was found to be associated with male sex and atopic status (i.e. a positive SPT) but not with living in a house that had undergone remodeling before one year of age, current asthma is likely more strongly associated with non-modifiable than modifiable environmental factors.

During the first 12 months of habitation in remodeled housing, occupants are exposed to large quantities of chemical substances, especially formaldehyde and VOCs, which can stimulate the mucous membranes of the eyes, nose and

throat [19]. As they generally spend many hours indoors and are more susceptible to environmental pollutants, children are particularly vulnerable to the effects of these substances. Based on these observations and the assumption that the level of formaldehyde indoors is at least as high as the level outside, the effects of living in remodeled housing, living in new housing and living in housing with newly built furniture were examined as proxy factors for VOC exposure in this study. The analysis of these and other risk factors for wheezing illnesses and asthma revealed that they differ to some extent. Parental history of allergic diseases was found to be a risk factor for both diseases, with children with a parental history of allergic diseases found to have a high OR (OR: 2.189; 95% CI: 1.483–3.231) for current asthma. Likewise, a randomized clinical trial for primary prevention of asthma found that maternal, paternal and/or sibling history of asthma is associated with high risk of asthma in seven-year-olds [20]. In accordance, Chan-Yeung et al. [20] found a higher prevalence of asthma in male children and in those with inherent risk factors for asthma, such as atopic predisposition and family history of asthma, factors that cannot be modified by intervention. These findings, taken together with the data presented in this study, suggest that current asthma is more strongly associated with non-modifiable risk factors compared to wheezing illness.

Unlike Simoni et al. [9] and Venn et al. [8], who reported an increased risk, specifically an OR of 5.1 and 1.8, respectively, no association was found between presence of mold and dampness, and the incidence of asthma or wheezing illness in this study. These differing results may be attributed to several factors, including use of different means of measuring mold and dampness. For example, Jaakkola et al. [21] and Rydjord et al. [22] based their measurement on self-reported exposure data, whereas Hyvärinen et al. [23] used a standardized home inspection kit to determine the presence of mold in homes of newly diagnosed asthma patients. In other studies, mold exposure quantification was performed or levels of visible mold were measured. This study collected self-reported data on the presence of mold and dampness, a method that Simoni et al. [9] suggested could underestimate the presence of dampness compared with objective inspection, independent of the presence of asthmatic children.

Most studies reporting a relationship between asthma and dampness in the home have investigated geographic regions with consistently high levels of air humidity, which increases the risk of mold growth and mite infestation. In contrast, a study conducted in northern latitudes found the levels of air humidity and prevalence of mites to be low, indicating that these factors may not be equally important in other countries [24]. As this study was conducted in the South Korean autumn, during which high atmospheric pressure results in low levels of humidity, exposure to dampness and mold growth was likely low compared to that in studies conducted in other countries.

The study findings also indicate a strong association between living in housing that had undergone remodeling within the last 12 months and living on the basement or semi-basement floor was found to be highly associated with

wheezing illness (OR: 2.003; 95% CI: 1.141–3.518), it was not found to be associated with current asthma. A significant difference in the incidence of exposure to dampness and mold between children living on the basement or semi-basement floor (61.0%) and children living on the first floor or above (25.9%) suggests that living on an underground floor is associated with greater dampness and mold exposure [8,9], and thus a higher risk of developing wheezing illness or asthma.

As described in the above method, we divided into three study groups (Figure 1), the current asthma and wheezing illness was included in wheeze ever group. But, the current asthma groups were clinically severe than wheezing illness in aspect of wheezing time; wake up during night due to wheezing; chest tightness due to wheezing; absences the school due to wheezing in the last 12 months in additional analysis. So even if we classified the group by a questionnaire, there were clinically different group.

This study has several limitations that should be considered when reviewing the findings. First, as the parents and guardians completed the items in the ISAAC survey regarding past events based on memory, their responses may have been affected by recall bias. In particular, the extent of their child's environmental exposure to such factors as dampness and mold, chemicals in newly built housing during infancy and secondhand tobacco smoke was measured retrospectively. The fact that mold growth on indoor surfaces is seldom present in housing in South Korea owing to a low level of relative humidity during the autumn should also be considered. Second, the prevalence of asthma and wheezing illness and symptoms was determined by the review of questionnaire responses, which may have led to overestimation or underestimation compared to the true values. However, this risk was averted to the greatest possible extent by the use of validated symptom-based written questionnaires and estimation of the overall prevalence of wheezing illnesses and current asthma using a randomized, stratified, two-stage cluster sampling design based on the ISAAC protocol. Use of these methods decreased the likelihood of major recall bias, particularly as participants were asked to remember only events that had occurred during the study period. Third, it is important to consider that the prevalence of current asthma was only 147. The minor differences of the odds ratios among the three groups, especially in the tobacco smoke exposure, was noted. Thus, the lack of environmental differences between the groups might be due to small sample size in the current asthma.

Conclusions

In conclusion, we identified that the effect of indoor environment was different in the prevalence of wheeze and asthma among Korean children. Regardless of the major risk factors, certain modifiable environmental factors, particularly living in remodeled housing within the last 12 months, appear to increase the incidence of wheezing illness but not current asthma, indicating the need to focus on modifying the indoor environment.

Declaration of interest

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