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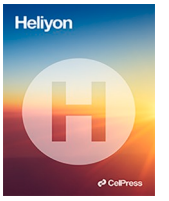

Associations between home environmental factors and childhood eczema and related symptoms in different cities in China

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ABSTRACT

Previous studies have shown significant associations between home environmental factors and childhood eczema. However, few studies have compared how associations differ in different regions. This study investigated associations between home environmental factors and childhood eczema ever, and related symptoms including itchy rash (IR) and being awakened by itchy rash at night (awake by IR) in 4 cities located in different regions of China, based on cross-sectional investigations during 2010–2012. We used two-step analysis to explore the associations between influencing factors and eczema/related symptoms: first, group Least Absolute Shrinkage and Selection Operator (LASSO) was conducted to identify important factors among a list of candidates; then, the associations in total study population and in each city were estimated using logistic regression. We found these home environmental factors to be risk factors for eczema or related symptoms: large residence size, shared room, air cleaner at home, abnormal smell, perceived dry air, visible mold or damp stains, cooking with coal or wood, painted wall, incense, mice, new furniture during pregnancy, abnormal smell at birth, window condensation at birth and environmental tobacco smoke at birth. Environmental protective factors were rural house location and window ventilation. Associations of factors with eczema/related symptoms differed across cities. For example, air conditioning was protective for eczema in Beijing and awakening by IR in Shanghai with ORs of 0.70 (95%CI: 0.52, 0.95) and 0.33 (95%CI: 0.14, 0.81) respectively, but not significant in other cities. Our results have implications for improving home environments to reduce the risk of childhood eczema/related symptoms in different regions of China.

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1. Introduction

Eczema is an acute or chronic allergic disease that causes dry, itchy and inflamed skin [1]. Eczema can occur at any age but is more common in young children [2]. Eczema may cause insomnia and severe distress and may negatively impact a person's life quality [3]. The Global Asthma Network (GAN) investigation from 2015 to 2020 estimated that the worldwide prevalence of eczema ever was 13.4 % among children 6–7 years old [4]. The International Study of Asthma and Allergies in Childhood (ISAAC) Phrase III study conducted in 2002–2003 reported that the prevalence of current eczema (in previous 12 months before survey) in children is much higher in developed countries (up to 20 %) than in China (less than 2 %) [5]. However, the prevalence of eczema has increased rapidly in China during recent decades [6]. Questionnaire-based investigations in ten China cities during 2010–2012 reported the prevalence of eczema had increased to 25.7 % [7]. The increasing trend is even more apparent in metropolises [6].

Eczema and its related symptoms have multi-factorial etiology, including immune dysfunction, genetic predisposition and environmental factors [1]. Previous studies have shown that higher risk for eczema was associated with changes due to industrialization and urbanization, especially environmental changes. Scholtz [8] and Adam et al. [9] found that the associations between eczema and environmental factors were larger than those with genetic factors. A number of studies have shown that both climatic factors and ambient air pollutants are significantly related to childhood eczema and related symptoms [10–12]. Specifically, precipitation and humidity have been found to be positively associated with eczema and its related symptoms (such as itchiness, rash on swollen skin), while temperature and UV exposure have been found to be protective; ambient air pollutants such as nitrogen oxides, carbon monoxide and inhalable particles (particulate matter, PM_{10}) may increase eczema risk [13–16]. These associations existed both inside and outside of China, both in northern hemisphere and southern hemisphere (like Australia). Since people spend the majority of time indoors, several studies have investigated associations between home environmental factors with eczema. The worldwide ISAAC study identified indoor pets [17], cooking fuels [18], tobacco smoke [19] as risk factors. Miyake et al.'s study [20] in Japan and Batlles et al.'s study [21] in Spain have shown that mold in the kitchen during pregnancy and in general the presence of fungi were positively associated with eczema. A cross-sectional study in Japan also found that visible mold, moldy odor, and condensation on the windowpanes were positively related to eczema [22].

In the past two decades, there have been substantial changes in indoor environments in China. Exposure to indoor pollutants in China are greater than in developed countries and still increasing [7,23]. The main causative factors are indoor sources such as building materials that contain formaldehyde and other Volatile Organic Compounds (VOCs) contaminants, Chinese style cooking, and tobacco smoke which generates particulate matter and volatile carcinogens (e.g., Benzene and Formaldehyde) [24]. In addition, under the concept of carbon neutrality, energy conservation has resulted in insufficient indoor ventilation rates, reducing the discharge of indoor pollutants to outdoors [25,26]. Another problem is that ambient pollutants, e.g., fine particles ($PM_{2.5}$) and ozone, are still at higher levels in China than in developed countries and hence also contribute to indoor exposure [27]. As indoor exposure levels and other home environmental factors (such as home type and home ventilation mode) in China are different than in developed countries, home environmental risk factors for eczema and other allergies may also be different in China [28]. In order to explore potential home environmental risk factors for children's allergies in China, a cross-sectional questionnaire-based study, the China, Children, Home, Health (CCHH) study was conducted in several research centers in 10 cities in China from 2010 to 2012 [7]. Previous CCHH studies have investigated risk factors in one or multiple cities, and have found that new furniture/renovation, home-dampness, living in urban area, buildings age and the presence of cockroaches/rats/mice were potential risk factors of childhood eczema [29–34], while exposing bed clothing to sunshine and breastfeeding were protective factors [30].

However, previous studies have some limitations. First, they have only estimated associations between one or several target factors and eczema, adjusting for limited covariates based on literature and experience, and may therefore have missed some important risk factors [35]. Second, to the best of our knowledge, no study has compared the differences among risk factors in different regions in China. A study that investigated risk factors for eczema in 7 cities simply combined the observations from different cities [34]. However, due to differences among indoor environments and lifestyles in different areas, risk factors differ in different cities. For example, moldy smell was identified as a risk factor of childhood eczema in Wuhan in Ref. [31] study, but not identified in Shanghai in Ref. [33] study.

In this study, the researchers assumed that many homes' environmental factors are in relation to childhood eczema and those associations might differ across different regions due to the difference of geological site, economic development and living habits. Therefore, the aims of the present study are to: (1) identify the associations between home environmental and other factors and eczema and its related symptoms by considering as many candidate factors as possible; (2) compare and explain the differences among risks for different cities based on the CCHH cross-sectional investigations during 2010–2012.

2. Methods

2.1. Study population

In 2010–2012, ten capital cities of provinces or municipalities were selected to conduct the cross-sectional CCHH study. The questionnaires were distributed to randomly selected kindergartens in each city and the children's parents were asked to complete the questionnaires. (Fig. S1).

Of the 10 cities, however, the author could only get access to eight cities (except Harbin and Xi'an), and four of them (Wuhan, Nanjing, Taiyuan, Urumqi) had poor data qualities. So, we targeted children in Beijing, Shanghai, Chongqing and Changsha as our

research subjects, because the completeness of the questionnaires from these cities was better than for others.

In the present study, we included children 3–6 years old, but not children aged 1–2 and 7–8, as both groups were low percentages of the whole (1.4 % and 3.0 % 125 respectively). The justifications were: (1) younger children are more susceptible to getting eczema than older children, (2) eczema prevalence was highest in 3–6 years old than in other age groups in Beijing (prevalence of eczema among 3–6 years old children was 26.3 % in 2009, while 20.6 % in 6–7 years old and 7.4 % in 13–14 years old children) [6], and (3) most kindergartners in China are aged from 3 to 6 years old; therefore questionnaires were distributed to kindergartens with most samples were aged 3–6 years old (95.6 %). We excluded: (1) observations that did not report information related to health outcomes (details in section 2.3), (2) observations with a missing rate of candidate influencing factors greater than 76 % (details in section 2.4); (3) children who live in different cities from their birth city. Finally, we included 5730 children from 4 cities in our study: 2143 children in Beijing, 1407 in Shanghai, 1230 in Chongqing and 950 in Changsha.

2.2. Questionnaire

Questionnaires were distributed in randomly selected kindergartens in each city, and then filled out by the students' parents. Our questionnaire, asking about demographic, health-related, home environmental, lifestyle factors and socio-economic factors was based on the ISAAC questionnaire that has been validated by of studies conducted in 236 centers in 98 countries [5,36]. The CCHH survey questionnaire has been published in a summary CCHH study [7].

2.3. Health outcomes

Our health outcomes were parent reported lifetime-ever eczema (abbreviated as eczema), and two eczema-related symptoms, itchy rash (abbreviated as IR) and awake at night by itchy rash in the last 12 month (abbreviated as awake by IR). Eczema was defined as dry cracked skin, rash on swollen skin, small, raised bumps or oozing and crusting found on children's face, torso, arms and legs. Three outcomes were all parent reported and thus they were not as precise as doctor diagnosed. The outcomes eczema, IR and awake by IR are all binary, that is, 1 = yes, 0 = no.

2.4. Candidates for influencing factors

Candidates for influencing factors include factors shown or suspected to be associated with eczema or related symptoms. These factors were chosen from: (1) demographic factors, i.e., age and gender; (2) health related factors, i.e., pregnant time, birth season, birth weight, family history of allergy and antibiotic medicine use; (3) home environmental factors, classified among 7 categories: basic home information, air ventilation/purification, perceived air quality factors, pollution sources, biological exposures, home renovation-related exposures and perinatal in-house exposures; (4) other factors: a lifestyle factor (who takes care of the child) and a socio-economic factor (ownership of the home). Details for the 56 candidate factors we considered are summarized in Table S1.

2.5. Statistical analysis

We explored influencing factors in a total study population of 4 cities (global analysis) (n = 5730), and in children of each city respectively (city-specific analysis). We applied a two-step analysis for both the global and city-specific analysis.

2.5.1. Global analysis

In the first step, we performed a group Least Absolute Shrinkage and Selection Operator (group LASSO) algorithm (package: "gepreg" in R) to identify important variables or variable groups, adjusting *a priori* for age and gender [37]. We used group LASSO instead of LASSO to select or exclude pre-specified groups of variables (e.g., cooking fuels such as gas, electric, coal or wood). In the second step, we used a mixed logistic regression to evaluate associations between selected variables and eczema and its related symptoms [38]. The random intercept in the mixed logistic model (package: "lme4" in R) captures those differences across cities, such as climatic, socioeconomic and lifestyle, that may have effects on eczema and related symptoms. The LASSO procedure can mitigate some multicollinearity concerns by performing variable selection and regularization. Through LASSO, certain coefficients are pushed to zero, effectively "selecting out" variables that might be redundant or highly correlated with others, which can indirectly address multicollinearity. We further computed the VIF for fixed effects in mixed models by fitting an equivalent linear model without the random effects.

2.5.2. City-specific analysis

To compare different results in different areas, we also identified influencing factors and assessed associations between these factors and eczema/related symptoms for each city. Similarly, in the first step, we conducted group LASSO to select important variables for each city. In the second step, we used multivariate logistic regression (function: "glm" in R) to evaluate associations between the selected factors and health outcomes for each city.

All statistical analysis was performed using R 4.1.2 software (a free software environment for statistical computing and graphics, https://www.r-project.org/). Associations between influencing factors and health outcomes were expressed as odds ratios (OR) with a 95 % confidence interval (CI). Differences were considered to be significant if $p < 0.05$.

2.5.3. Model validation

The accuracies of our models were evaluated by the area under the curve (AUC) of the receiver operating characteristic (ROC) curve [39,40]. A model can be considered to be predictive when AUC >0.6 [41].

This study was approved by the Medical Research Ethics Committee of School of Public Health, Fudan University (International Registered Number: IRB00002408&FWA00002399, approval no. 2013-06-0451. The original ethical issue was approved before the survey. But during the research, researchers applied the ethical approval again because researchers wanted to improve study design, and the approval date of final version was 2013–06-04 for CCHH I study.). All participants provided informed consent.

3. Results

3.1. Demographic characteristics of investigated children

We used inclusion and exclusion criteria for our study population as described in Methods Section 2.1. Finally, we included 5730 children in our analysis. Statistical information on health outcomes, demographic factors, health related factors, lifestyle and social-economic factors in our study population is shown in Table 1. Prevalences of eczema from greatest to lowest were Shanghai (36.7 %), Beijing (30.6 %), Changsha (24.3 %) and Chongqing (22.7 %); the highest prevalence of IR and awake by IR were in Shanghai, with values of 16.9 % and 9.1 % respectively. The prevalences of eczema in our study population (complete cases) in Beijing, Chongqing, and Changsha were close to the prevalences in all investigated children (all particitpants in the survey) (Fig. S2) with relative errors less than 8.5 %; however, the prevalence of eczema in Shanghai in our study population (complete cases) was less than that of the total study population (all participants). One possible reason is that parents of children with eczema were more interested in our study, thus more likely to answer the questionnaires completely.

The statistical description of home environmental factors is shown in Table 2. The percentage of home renovation-related factors were similar among all cities. Most of the home environmental factors showed differences among cities, due mainly to differences in climate, economy, and culture. For example, participants living in Shanghai, Chongqing and Changsha were more likely to frequently open the child's bedroom window in spring, autumn and winter than those living in Beijing，while no differences were found among

Table 1
Statistical description of health outcomes, demographic factors, health related factors, lifestyle and social-economic factors of our study population.

Variable Classification	Variable	Value	Total (N = 5730)	Beijing (N = 2143)	Shanghai (N = 1407)	Chongqing (N = 1230)	Changsha (N = 950)
Health outcomes	Eczema	Yes	1681 (29.3 %)	655 (30.6 %)	516 (36.7 %)	279 (22.7 %)	231 (24.3 %)
		No	4049 (70.7 %)	1488 (69.5 %)	891 (63.3 %)	951 (77.3 %))	719 (75.7 %)
	IR	Yes	657 (11.5 %)	243 (11.3 %)	238 (16.9 %)	86 (7.0 %)	90 (9.5 %)
		No	5073 (88.5 %)	1900 (88.7 %)	1169 (83.1 %)	1144 (93.0 %)	860 (90.5 %)
	Awake by IR	Yes	351 (6.1 %)	118 (5.5 %)	128 (9.1 %)	77 (6.3 %)	28 (3.0 %)
		No	5379 (93.9 %)	2025 (94.5 %)	1279 (90.9 %)	1153 (93.6 %)	922 (97.1 %)
Demographic factors	Gender	Male	2934 (51.2 %)	1105 (51.6 %)	697 (49.5 %)	631 (51.3 %)	501 (52.7 %)
		Female	2796 (48.8 %)	1038 (48.4 %)	710 (50.5 %)	599 (48.7 %)	449 (47.3 %)
	Age	3 years-old	1204 (21.0 %)	584 (27.3 %)	82 (5.8 %)	279 (22.7 %)	259 (27.3 %)
		4 years-old	2051 (35.8 %)	640 (29.9 %)	603 (42.9 %)	444 (36.1 %)	364 (38.3 %)
		5 years-old	1574 (27.5 %)	550 (25.7 %)	404 (28.7 %)	349 (28.4 %)	271 (28.5 %)
		6 years-old	901 (15.7 %)	369 (17.2 %)	318 (22.6 %)	158 (12.9 %)	56 (5.9 %)
Health related variables	Family history of allergy	Yes	1315 (23.0 %)	610 (28.5 %)	379 (26.9 %)	153 (12.4 %)	173 (18.2 %)
	Antibiotic	Yes	4284 (74.8 %)	1387 (64.7 %)	1111 (79.0 %)	1077 (87.6 %)	777 (81.8 %)
Lifestyle factors	Who takes care of the child before day nursery	Parents	2783 (48.6 %)	882 (41.2 %)	601 (42.7 %)	644 (52.4 %)	561 (59.1 %)
		Grandparents	845 (14.8 %)	1039 (48.5 %)	777 (55.2 %)	549 (44.6 %)	365 (38.4 %)
		Nanny or others	2102 (36.7 %)	222 (10.4 %)	29 (2.1 %)	37 (3.0 %)	24 (2.5 %)
Socio-economic factors	Owner	Yes	3976 (69.4 %)	1474 (68.8 %)	993 (70.6 %)	817 (66.4 %)	692 (72.8 %)

Table 2
Statistical description of home environmental factors in the 4 studied cities.

Variable Classification	Variable	Value	Total (N = 5730)	Beijing (N = 2143)	Shanghai (N = 1407)	Chongqing (N = 1230)	Changsha (N = 950)
Basic home information	House location	Urban	4722 (82.4 %)	1825 (85.2 %)	999 (71.0 %)	1002 (81.5 %)	896 (94.3 %)
		Rural	1008 (17.6 %)	318 (14.8 %)	408 (29.0 %)	228 (18.5 %)	54 (5.7 %)
	Residence size	<60 m^2	1267 (22.1 %)	488 (22.8 %)	421 (29.9 %)	246 (20.0 %)	112 (11.8 %)
		60–100 m^2	2328 (40.6 %)	787 (36.7 %)	534 (38.0 %)	584 (47.5 %)	423 (44.5 %)
		>100m^2	2135 (37.3 %)	868 (40.5 %)	452 (32.2 %)	400 (32.5 %)	415 (43.7 %)
	Shared room	Yes	5031 (87.8 %)	1856 (86.6 %)	1260 (89.6 %)	1062 (86.3 %)	853 (89.8 %)
	Living at the present residence during the whole life	Yes	4129 (72.1 %)	1645 (76.8 %)	935 (66.5 %)	838 (68.1 %)	711 (74.8 %)
Air ventilation/ purification	Window opening frequency in spring	No/ sometimes	1029 (18.0 %)	781 (36.4 %)	160 (11.4 %)	47 (3.8 %)	41 (4.3 %)
		Sometimes	2323 (40.6 %)	988 (46.1 %)	645 (45.8 %)	359 (29.2 %)	331 (34.8 %)
		Often	2378 (41.5 %)	374 (17.5 %)	602 (42.8 %)	824 (67.0 %)	578 (60.8 %)
	Window opening frequency in summer	No/ sometimes	1857 (32.4 %)	733 (34.2 %)	516 (36.7 %)	309 (25.1 %)	299 (31.5 %)
		Often	3873 (67.6 %)	1410 (65.8 %)	891 (63.3 %)	921 (74.9 %)	651 (68.5 %)
	Window opening frequency in autumn	No/ sometimes	854 (14.9 %)	643 (30.0 %)	140 (10.0 %)	40 (3.3 %)	31 (3.3 %)
		Sometimes	2358 (41.2 %)	1038 (48.4 %)	664 (47.2 %)	356 (28.9 %)	300 (31.6 %)
		Often	2518 (43.9 %)	462 (21.6 %)	603 (42.9 %)	834 (67.8 %)	619 (65.2 %)
	Window opening frequency in winter	No/ sometimes	2374 (41.4 %)	1486 (69.3 %)	521 (37.0 %)	191 (15.5 %)	176 (18.5 %)
		Sometimes	2262 (39.5 %)	543 (25.3 %)	640 (45.5 %)	590 (48.0 %)	489 (51.5 %)
		Often	1094 (19.1 %)	114 (5.3 %)	246 (17.5 %)	449 (36.5 %)	285 (30.0 %)
	Air conditioning at home	Yes	4460 (83.1 %)	1887 (88.1 %)	1359 (96.6 %)	1206 (98.1 %)	888 (99.2 %)
	Air cleaner at home	Yes	2036 (35.5 %)	1839 (85.8 %)	125 (8.9 %)	41 (3.3 %)	31 (3.3 %)
Perceived air quality factors	Visible mold or damp stains	Yes	544 (9.5 %)	134 (6.3 %)	221 (15.7 %)	77 (6.3 %)	112 (11.8 %)
	Abnormal smell	Yes	2669 (46.6 %)	1095 (51.1 %)	545 (38.7 %)	573 (46.6 %)	456 (48.0 %)
	Perceived dry air	Yes	3087 (53.9 %)	1620 (75.6 %)	545 (38.7 %)	470 (38.2 %)	452 (47.6 %)
	Perceived humid air	Yes	1638 (28.6 %)	278 (13.0 %)	618 (43.9 %)	399 (32.4 %)	343 (36.1 %)
Pollution source	Cooking fuels	Gas	4948 (86.4 %)	2028 (94.6 %)	988 (70.2 %)	1108 (90.1 %)	824 (86.7 %)
		Coal or wood	237 (4.1 %)	26 (1.2 %)	176 (12.5 %)	23 (1.9 %)	12 (1.3 %)
		Electric	1150 (20.1 %)	246 (11.5 %)	345 (24.5 %)	365 (29.7 %)	194 (20.4 %)
	Environmental tobacco smoke	Yes	1799 (31.4 %)	580 (27.1 %)	361 (25.7 %)	473 (38.5 %)	385 (40.5 %)
	Incense	Yes	880 (15.4 %)	248 (11.6 %)	156 (11.1 %)	214 (17.4 %)	262 (27.6 %)
	Wood or laminate floor	Yes	3989 (69.6 %)	1389 (64.8 %)	1256 (89.3 %)	671 (54.6 %)	673 (70.8 %)
	Wall materials	Paper	565 (9.9 %)	230 (10.7 %)	140 (10.0 %)	146 (11.9 %)	49 (5.2 %)
		Paint	3578 (62.4 %)	1140 (53.2 %)	1050 (74.6 %)	791 (64.3 %)	595 (62.6 %)
		Wood	291 (5.1 %)	246 (11.5 %)	20 (1.4 %)	9 (0.7 %)	16 (1.7 %)

(*continued on next page*)

Table 2 (*continued*)

Variable Classification	Variable	Value	Total (N = 5730)	Beijing (N = 2143)	Shanghai (N = 1407)	Chongqing (N = 1230)	Changsha (N = 950)
	Printer or photocopy machine at home	Yes	655 (11.4 %)	291 (13.6 %)	170 (12.1 %)	122 (9.9 %)	72 (7.6 %)
	Heating during winter	Yes	4812 (84.0 %)	2143 (100 %)	1272 (90.4 %)	767 (62.4 %)	630 (66.3 %)
	Heating districtly	Yes	–	1630 (76.1 %)	–	–	–
	Cleaning frequency	mean (sd)	4.238 (0.96)	4.26 (0.98)	4.413 (0.83)	4.019 (0.98)	4.155 (1.00)
	Cleaning due to allergies	Yes	1093 (19.1 %)	367 (17.1 %)	330 (23.5 %)	213 (17.3 %)	183 (19.3 %)
Biological exposures	Pets	Yes	1223 (21.3 %)	537 (25.1 %)	281 (20.0 %)	246 (20.0 %)	159 (16.7 %)
	Mice	Yes	1013 (17.6 %)	86 (4.0 %)	167 (11.9 %)	459 (37.3 %)	301 (31.7 %)
	Mosquitoes and flies	Yes	4694 (81.9 %)	1586 (74.0 %)	1188 (84.4 %)	1046 (85.0 %)	874 (92.0 %)
Home renovation-related exposures	New furniture 1 year before pregnancy	Yes	465 (8.1 %)	200 (9.3 %)	109 (7.8 %)	82 (6.7 %)	74 (7.8 %)
	New furniture during pregnancy	Yes	152 (2.6 %)	71 (3.3 %)	23 (1.6 %)	36 (2.9 %)	22 (2.3 %)
	New furniture during 0–1 year old	Yes	153 (2.7 %)	69 (3.2 %)	28 (2.00 %)	37 (3.0 %)	19 (2.0 %)
	New furniture after 1 year old	Yes	467 (8.2 %)	199 (9.3 %)	78 (5.5 %)	117 (9.5 %)	73 (7.7 %)
	Home renovated 1 year before pregnancy	Yes	679 (11.9 %)	255 (11.9 %)	190 (13.5 %)	107 (8.7 %)	127 (13.4 %)
	Home renovated during pregnancy	Yes	191 (3.3 %)	83 (3.9 %)	32 (2.3 %)	43 (3.5 %)	33 (3.5 %)
	Home renovated during 0–1 year old	Yes	172 (3.0 %)	72 (3.4 %)	29 (2.1 %)	43 (3.5 %)	28 (3.0 %)
	Home renovated after 1 year old	Yes	847 (14.8 %)	405 (18.9 %)	154 (11.0 %)	164 (13.3 %)	124 (13.1 %)
Perinatal in-house exposures	Environmental tobacco smoke at birth	Yes	1321 (23.1 %)	398 (18.6 %)	237 (16.8 %)	371 (30.2 %)	315 (33.2 %)
	Visible mold or damp stains at birth	Yes	664 (11.6 %)	182 (8.5 %)	160 (11.4 %)	175 (14.2 %)	147 (15.5 %)
	Perceived dry air at birth	Yes	1408 (24.6 %)	325 (15.2 %)	404 (28.7 %)	358 (29.1 %)	321 (33.8 %)
	Perceived humid air at birth	Yes	2258 (39.4 %)	1119 (52.2 %)	447 (31.8 %)	360 (29.3 %)	332 (35.0 %)
	Abnormal smell at birth	Yes	2054 (35.9 %)	769 (35.9 %)	403 (28.6 %)	502 (40.8 %)	380 (40.0 %)
	Window condensation at birth	Yes	2718 (47.4 %)	991 (46.2 %)	738 (52.5 %)	522 (42.4 %)	467 (49.2 %)
	Pets at birth	Yes	691 (12.1 %)	295 (13.8 %)	158 (11.2 %)	171 (13.9 %)	67 (7.1 %)

those cities in summer. More than 96 % families in the three southern cities, Shanghai, Chongqing and Changsha, had air conditioning at home while only 88.1 % families had air conditioning at home in Beijing. Nearly 25.1 % of families in Beijing kept pets at home while in the other three cities, the percentages of families keeping pets were less than 20.0 %.

3.2. Associations between home environmental and other factors with eczema and related symptoms in the total study population

Regression results for the LASSO selected variables are presented in Table S2 in Supplementary Materials. Fig. 2 shows estimated ORs for variables significantly associated with eczema/related symptoms. Fig. 2 shows that males were at higher risk for eczema and IR than females with OR values of 1.16 (95%CI: 1.03, 1.32) and 1.20 (95%CI: 1.01, 1.43) respectively. The 4-year-old children were at the lowest risk for eczema. A family history of allergy was positively associated with the risk for eczema, IR and awake by IR, with OR values of 1.87 (95%CI: 1.63, 2.15), 2.37 (95%CI: 1.98, 2.85) and 1.73 (95%CI: 1.36, 2.20) respectively. Antibiotic use was also associated with increased risk for eczema and IR, with OR values of 1.22 (95%CI: 1.06, 1.42) and 1.34 (95%CI: 1.06, 1.68) respectively.

Fig. 2 shows several home environmental factors that were significantly associated with eczema, IR, or awake by IR. For eczema, we found that large residence size, air cleaner, abnormal smell, perceived dry air, cooking with coal or wood, new furniture during pregnancy, environmental smoke at birth, abnormal smell at birth, and window condensation at birth had a significantly positive

association with risk while frequently opening the window in summer was protective. ORs for these factors are shown in Fig. 1. For example, we found cooking with coal or wood increased the risk by 40 % for eczema with OR values of 1.28 (95%CI: 1.03, 1.60) and 1.40 (1.01, 1.95) respectively.

For IR, larger residence size, visible mold, or stains at home, perceived dry air, a painted or wood wall, abnormal smell at birth and window condensation at birth had significantly positive associations with risk, while rural house location, sometimes opening window in spring, and printer or photocopy machines were significantly and negatively associated with the risk.

For awake by IR, incense, mice, window condensation at birth and cleaning due to allergy were risk factors.

The VIF for all predictors of each outcome showed no or very slight (<6) multicollinearity, and details were shown in Table S4.

3.3. Associations between home environmental and other factors with eczema and related symptoms in each city

The regression results for the group LASSO selected variables of each city are presented in Table S3. OR values for significant variables in each city are shown in Fig. 3. Fig. 3(a)–(d) show that associations between home environmental and other factors with eczema and related symptoms are different in different cities.

For eczema, a family history of allergy was significantly and positively associated with eczema in Beijing, Shanghai, and Chongqing, with OR values of 1.81 (95%CI: 1.46, 2.24), 2.09 (95%CI: 1.59, 2.74) and 1.79 (95%CI: 1.24, 2.59) respectively; however, it was not significantly associated with eczema in Changsha. Cleaning due to allergies was significantly and positively associated with eczema in Shanghai, Chongqing and Changsha with OR values of 1.85 (1.39, 2.47), 1.66 (1.17, 2.33) and 1.70 (95%CI: 1.17, 2.45) respectively but not Beijing. Shared room was identified as a risk factor in Beijing and Chongqing, with OR values of 1.43 (95%CI: 1.04, 1.97) and 1.89 (95%CI: 1.08, 2.73) respectively, but not identified as a risk factor in Shanghai or Changsha. Other home environmental factors like perceived air dry, air cleaner at home, perceived humid air at birth and window condensation at birth were positively associated with eczema in Beijing while air conditioning at home was identified as a protective factor in Beijing but not in other cities. Cooking with coal or wood, mosquito, and flies and new furniture in the year before pregnancy were risk factors of eczema in Shanghai but not in other cities. A rural house location, opening a window in winter, printer or photocopy machine at home were negatively associated with eczema only in Shanghai. Abnormal smell was identified as a risk factor only in Changsha.

For IR, family history of allergy were risk factors across all four cities, with OR values of 1.95 (95%CI: 1.45, 2.60), 2.55 (95%CI: 1.83, 3.56), 2.44 (95%CI:1.42, 4.11) and 3.32 (95%CI: 2.04, 5.36) respectively. Cleaning due to allergies was significantly and positively associated with IR in Beijing, Shanghai and Chongqing, with OR values of 1.41 (95%CI: 1.00, 1.97), 2.05 (95%CI: 1.45, 2.90) and 1.61 (95%CI: 1.07, 2.99) respectively but not significant in Changsha. Large residence size and painted wall were risk factors of IR while printer or photocopy machine at home were negatively related with IR in Beijing and Shanghai but were not identified as risk factors in Chongqing or Changsha. Antibiotic use was a risk factor in Beijing and Chongqing but not in Shanghai or Changsha. Paper and wood wall, new furniture during pregnancy, perceived dry air at birth, and window condensation at birth were risk factors for eczema in Beijing but not risk factors in other cities. Rural house location and living at the present residence during the whole life were protective factors against IR while cooking with coal, wood or electric; new furniture 1 year before pregnancy; and visible mold or

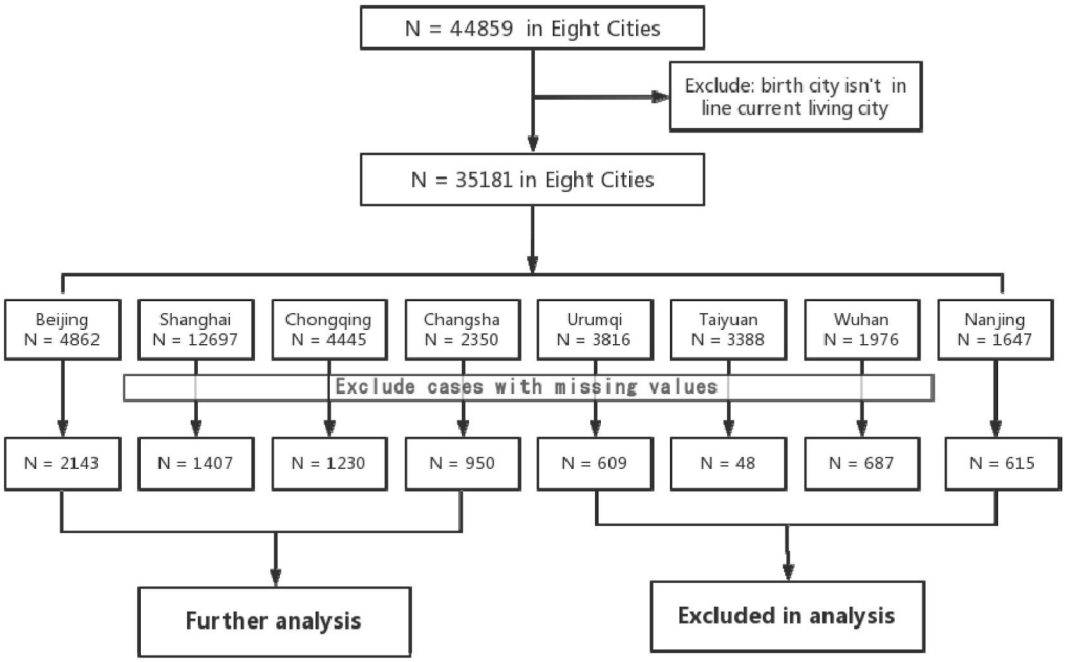


Fig. 1. Flow diagram. Flowchart showing the selection of study participants.

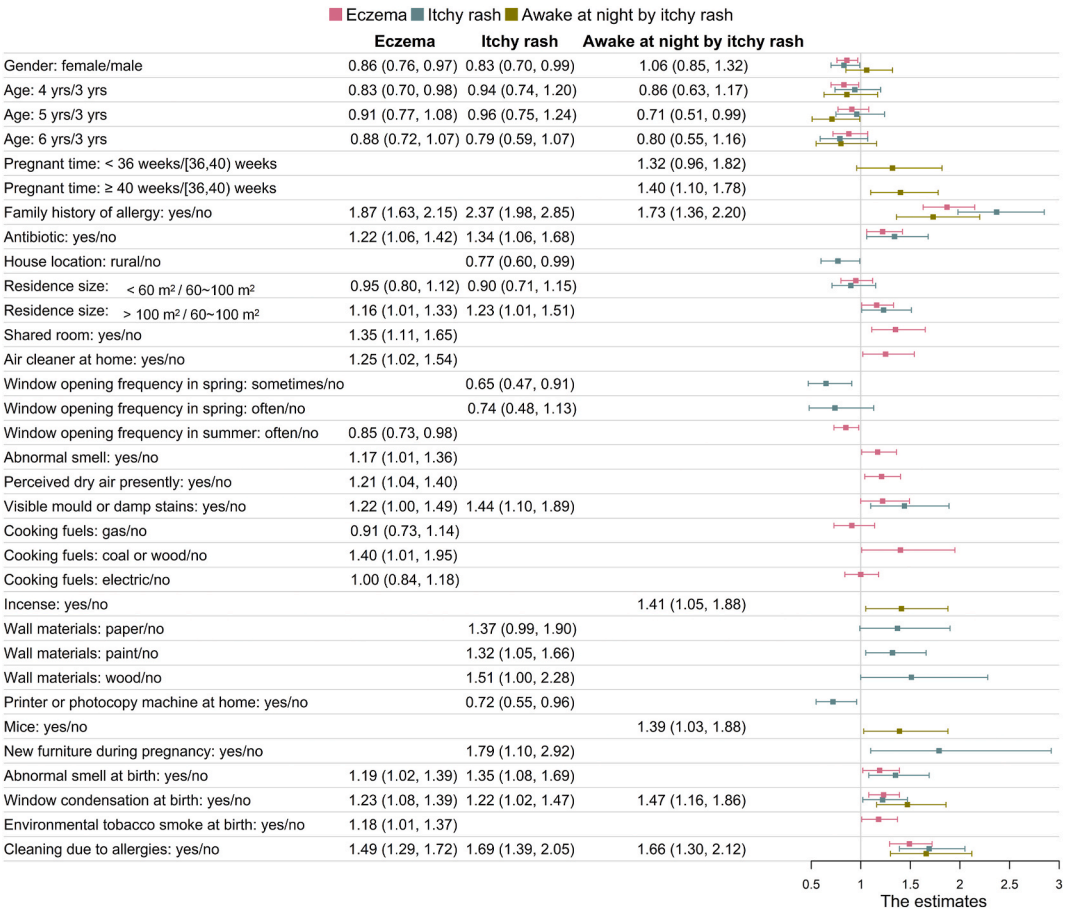


Fig. 2. Odds ratios of independent variables for eczema and related symptoms in total observations in 4 cities (n = 5730)
Footnote: In global analysis, we performed group LASSO to identify important variables or variable groups, adjusting *a priori* for age and gender. The random intercept in the mixed logistic model captures those differences across cities. Only those independent variables having significant associations with at least one of the 3 health outcomes are presented. The reference groups were shown in forms like "/[ref]".

damp stains at birth were risk factors for IR in Shanghai but not in other cities. Environmental tobacco smoke was a risk factor for IR in Changsha but not a risk factor in other cities.

For being awakened by IR, family history of allergy was a risk factor in Beijing and Shanghai but not in Chongqing or Changsha. Birth weight ≥4 kg, attached or semi-attached dwelling, paper wall, incense and cleaning due to allergies were risk factors for awake by IR in Beijing but not in other cities. Pregnancy ≥40 weeks, shared room, environmental tobacco smoke and window condensation at birth were risk factors for being awakened by IR while air conditioning was a protective factor in Shanghai but not in other cities. Abnormal smell, home renovation during pregnancy or after 1 year old, incense, and pets were risk factors for being awakened by IR in Chongqing but not in other cities. The OR values for the above influencing factors in each city are shown in Fig. 3. No variable was selected in Changsha for awake by IR, probably due to the relatively small sample size of Changsha (N = 950) or the prevalence of awakened by IR in Changsha (28 (2.95 %) cases), both of which were much lower than for other cities.

3.4. Model validation

The AUCs of the eczema models, IR and awake by IR were 0.67, 0.73 and 0.70 respectively in the total study population in 4 cities, which indicate that our model has greater accuracy than models in previous CCHH studies (AUCs ranged from 0.61 to 0.69) [29,30,32,33]. The AUCs of city-specific models ranged from 0.64 to 0.80, indicating that our city-specific models were also predictive.

Fig. 4 shows predicted probabilities of eczema, IR and awake by IR in total 4 cities, for different values of gender, age, as well as group LASSO selected variables that were significantly associated with two or more of any of the following health outcomes: family history of allergy, window condensation at birth, visible mold or damp stains, abnormal smell, perceived dry air and new furniture during pregnancy.

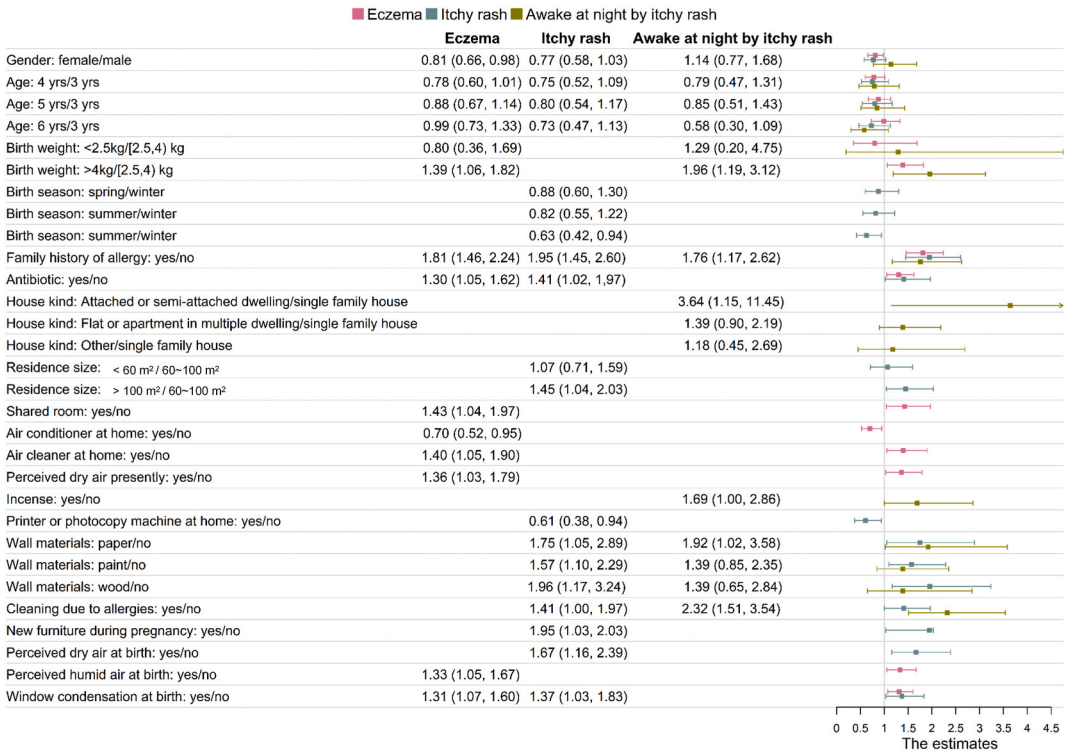


Fig. 3. Odds ratios of independent variables for eczema and related symptoms in observations in each city
Footnote: We conducted group LASSO to select important variables for each city. Then, we used multivariate logistic regression to evaluate associations between the selected factors and health outcomes for each city. Only those independent variables having significant associations with at least one of the 3 health outcomes are presented. Panel (d) only includes factors for eczema and IR. The reference groups were shown in forms like "/[ref]".

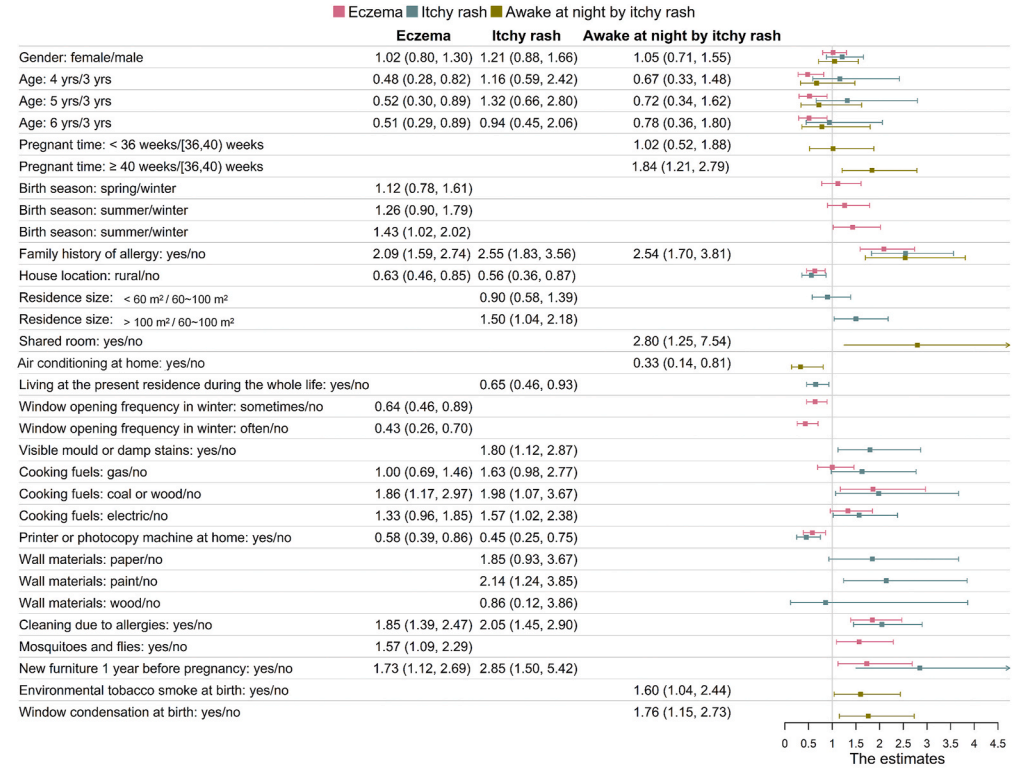
4. Discussion

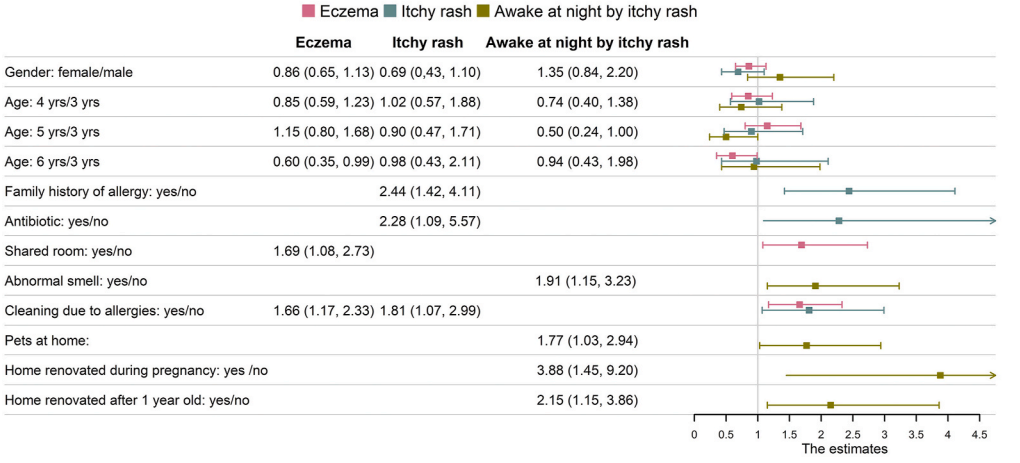
We investigated associations between home environmental factors and childhood eczema, IR and awake by IR, both in the total study population of four cities in China and individually in each city. We first employed group LASSO to screen for important factors; then, we applied logistic regression to determine associations between selected factors and health outcomes.

The prevalence of eczema during 2010–2012 was 29.3 % in the total study population of 4 cities (n = 5730), with the highest value in Shanghai (36.7 %), followed by Beijing (30.6 %), Changsha (24.3 %), Chongqing (22.7 %). Different prevalences in different cities can be attributed to several different factors: climate, indoor and ambient environmental conditions, lifestyles, diet, and socioeconomic factors in these cities [42,43]. As shown in Fig. S2, Beijing, the capital city, is in northern part of China with four distinctive seasons, and the city provided central heating for majority of its citizens while in other three cities heating in winter comes in a private way like air conditioning. Shanghai is also a metropolis, located in the estuary of the Yangtze River. People in Beijing and Shanghai live a more prosperous and delicate life than those in Chongqing and Changsha, and thus may have a high risk of eczema.

Consistent with previous studies, we found health related factors (i.e., family history of allergy and antibiotics) and home environmental factors (i.e., visible mold, incense, abnormal smell, perceived dry air presently, perceived dry air at birth, perceived humid air at birth, Environmental Tobacco Smoke at birth, window condensation at birth, shared room, home renovation and new furniture) were risk factors for eczema and related symptoms, while rural house location and window ventilation were protective [2,30,44–47]. We found that more frequent window opening was protective for eczema and its related symptoms. This finding is consistent with a previous case-control study that found that increased natural ventilation in single family houses significantly reduced the risk of eczema [45]. We identified current ETS as a risk factor for IR in Shanghai, and ETS at birth as a risk factor for IR in Changsha, which is consistent with findings in previous studies [48–51]. ETS exposure adversely affects immune function and induces oxidative disorders and can therefore damage skin barrier function, which may be the mechanism by which it can be a causative factor for eczema [52]. Apart from direct contact-damage of ETS to the skin-barrier, ETS at birth may affect expression of microRNA and DNA methylation, thus inducing immune dysregulation and leading to allergic sensitization or exacerbation of allergic disease [53]. Antibiotic use, identified as a risk factor, has been shown to alter host microbiota, which could further affect a child's immune system, as for example by stimulating immune responses to environmental allergens [2].

Some of our findings do not agree with those of previous studies. Previous studies identified living close to a highway or industrial





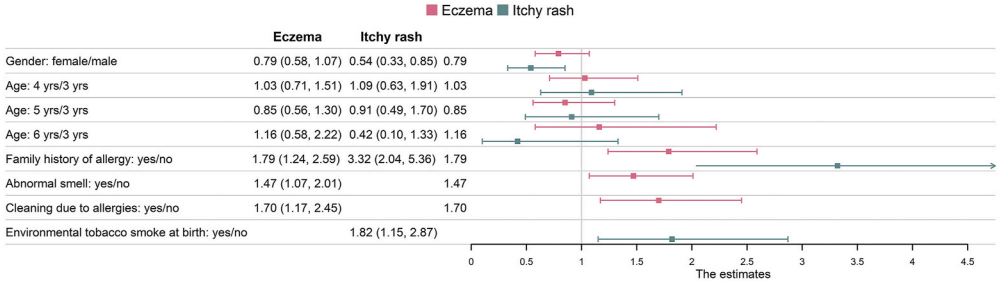
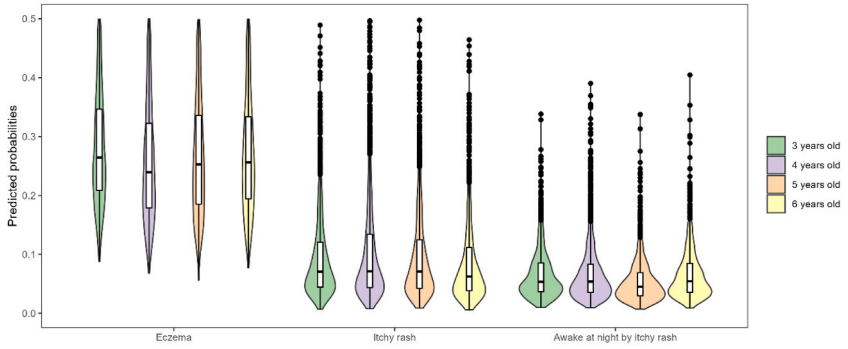
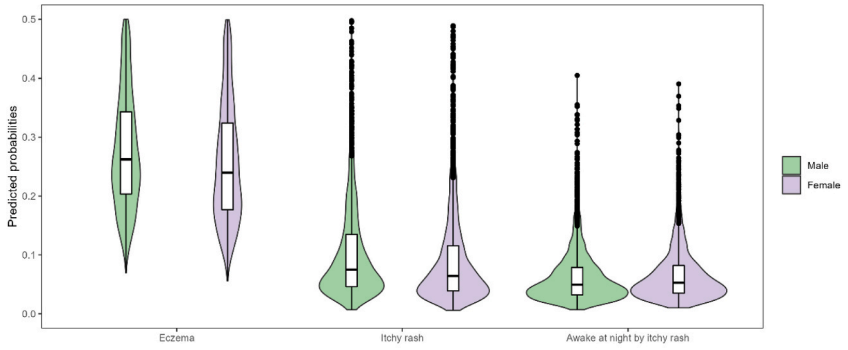


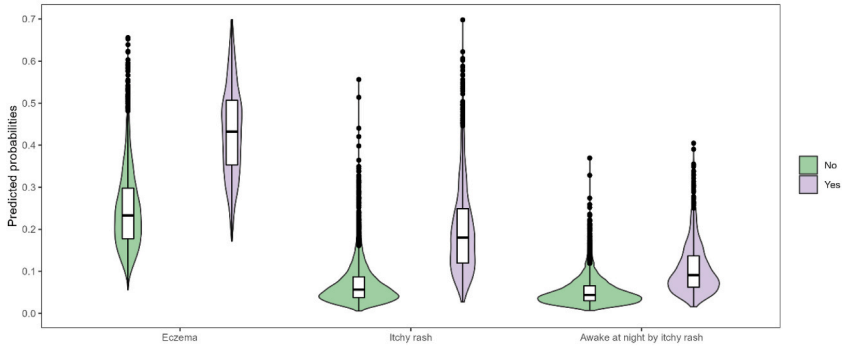
Fig. 3. (*continued*).



(a) Age



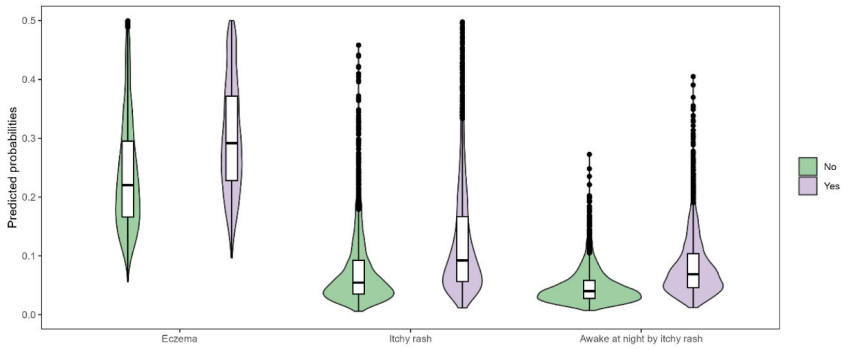
(b) Gender



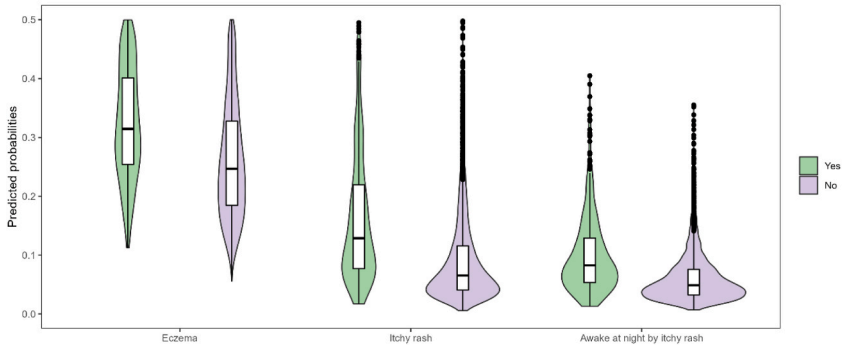
(c) Family history of allergy

Fig. 4. Predicted probabilities of eczema, itchy rash and awake at night by itchy rash for each condition of influencing factors.
Footnote: Variables selected by group LASSO for each outcome - eczema, Itchy rash and awake at night by itchy rash - are included. Inside the violin plot, the horizontal lines represent median values, the top and bottom of the boxes represent 25th and 75th percentiles, and the whiskers extend to the 5th and 95th percentile; the black plots represent the outliers.

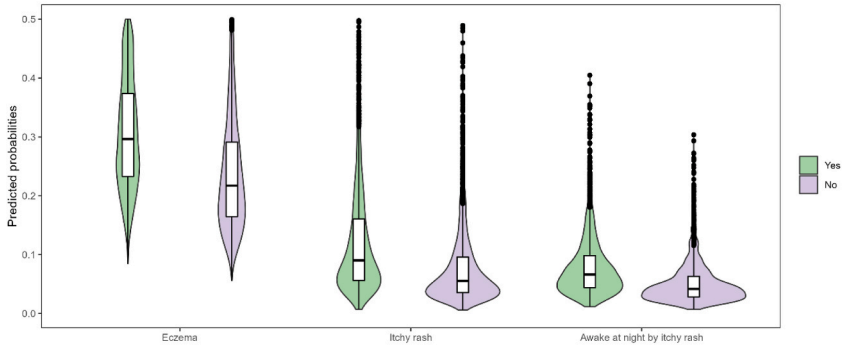
area, mice, mosquitoes, and flies as independent risk factors for eczema [7,54], but these factors were not significantly associated with eczema in our study. Contrary to previous studies conducted by Ponsonby et al. in Australia among infants during 2010–2013, which found larger residence size to be protective against allergic disease at 12 months age [55], we found larger residence size to be a risk factor for eczema and awakening by IR. It is possible that a larger house area is positively related to less ventilation, a factor that merits further study. Also, the cited study was conducted in an Australian birth cohort study of 1074 infants during 2010–2013, nearly the same time with CCHH survey in China. The economic status is associated closely with allergic disease and there was economic difference between Australia and China back to that time. Probably the economic difference is the reason why association between



(d) Window condensation at birth



(e) Visible mold or damp stains



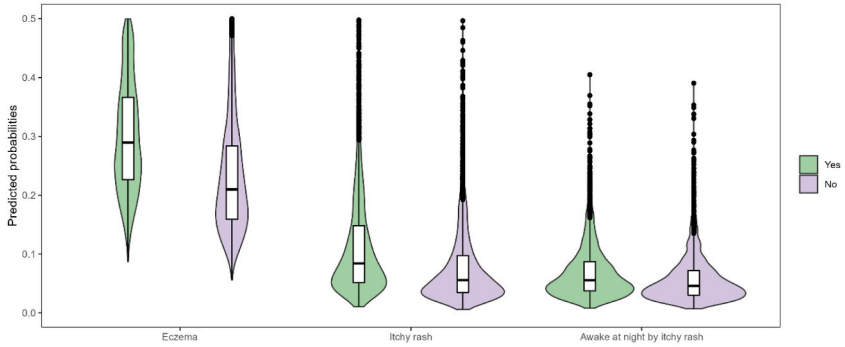
(f) Abnormal smell

Fig. 4. (*continued*).

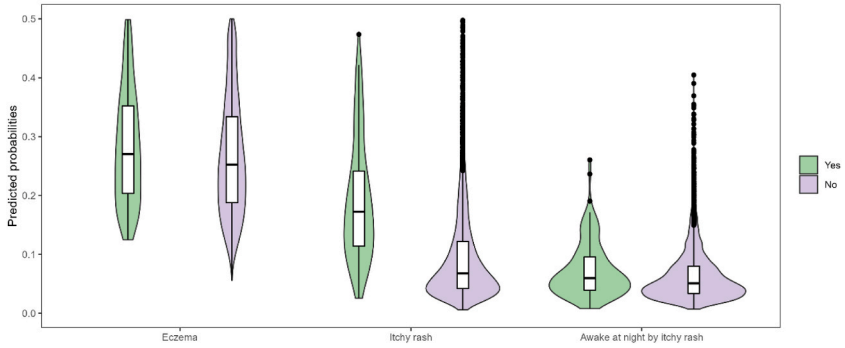
residence size and eczema differs in two countries. Or it is because China and Australia located in different geological site, one in east Asia and the other in Oceania, the geological and other environmental factors may contribute to the variation of studies' result.

We found that perceived humid air and perceived dry air at birth were both positively associated with the risk of eczema and IR in Beijing. An explanation is the U-shaped effects of air humidity on atopic skin: lower humidity might increase trans epidermal water loss which correlated with eczema severity, while higher humidity might provoke perspiration and further irritated or aggravated pruritus [54,56,57]. Previous CCHH studies reported only the monotonic relationship between indoor relative humidity with eczema or related symptoms. For example, Cai et al. [29] found a positive association between home dampness-related factors and children's eczema in Shanghai.

The uniqueness of the present study is that we found that a given factor had different associations with eczema/related symptoms in different cities.



(g) Perceived dry air presently



(h) New furniture during pregnancy

Fig. 4. (*continued*).

(1) We found air humidity related perception (i.e., perceived dry air, perceived humid air at birth and perceived dry air at birth) were positively associated with higher risk for eczema and IR in Beijing; however, perceived humid or dry air did not significantly affect the risk for eczema or related symptoms in other cities. The explanation may be different humidities in different cities: the annual average values for relative humidity during 2010–2012 in Beijing, Shanghai, Chongqing, Changsha were 50.8 %, 69.2 %, 77.2 % and 69.2 % respectively [58]. Humid air can be perceived more than 5 months per year in Shanghai, Chongqing and Changsha, three southern cities in China. However, in the northern city of Beijing, that time can be limited to 3 months [59]. It is probable that the children in southern cities (Shanghai, Chongqing and Changsha) are more tolerant of humid air because they were exposed to higher humidity since birth. Current air or perceived dry air at birth were not identified as risk factors in southern cities due to the lack of experiencing dry air.

(2) We found the use of air conditioning was negatively associated with the risk of awakening by IR in Shanghai and eczema in Beijing, while it had no significant associations with eczema or related symptoms in the other two cities. The effects of air conditioning on the risk of eczema or related symptoms could be two-sided. Because air conditioning regulates air temperature and humidity, it could reduce the risk of eczema. However, air conditioning can also release dust and fungi from a contaminated filter, which could be a risk for eczema [60,61]. Another possible explanation of different findings for air conditioning in different cities could be that usage habits for air conditioning such as cleaning frequency are different in different cities.

(3) Ownership of a printer or photocopy machine at home was associated with lower risk of eczema and related symptoms in Beijing and Shanghai, the most developed metropolitan cities in China, but had no significant associations with eczema or related symptoms in Chongqing or Changsha. It is possible that printer or photocopy machine ownership are related to the family's socioeconomic level, which may in turn be negatively associated with eczema.

(4) We found that the use of an air cleaner was associated with higher prevalence of eczema in Beijing. Although previous studies have shown that an air cleaner can significantly reduce indoor PM concentrations and in turn reduce asthma symptom-days and mortality among asthmatic children [62,63], it is possible that the family had an air cleaner at home because their children had eczema or allergic symptoms and the air cleaner was aimed to ease the allergic symptoms by purifying the indoor air.

(5) The associations between home renovation and new furniture with eczema/related symptoms were stronger in Shanghai than in Beijing. Renovation-associated risk may have been caused by artificial synthetic materials related pollutants (e.g., formaldehyde, volatile organic compounds, and phthalate esters) [64]. Eczema, as a type I-allergic reaction, may perhaps be caused or

exacerbated by pollutants that induce and stimulate the production of blood immunoglobulin E (IgE) [65–67]. Higher temperatures in Shanghai leads to stronger emissions of harmful chemicals [68], which in turn worsen eczema or related symptoms.

This study has some limitations. First, there were no direct measurements of environmental factors, no physical examinations, no allergy screening tests. It has been shown that perception of dry air does corresponds more to air pollutants than to relative humidity [69]. Health outcomes and possible influencing factors were reported by parents, which might result in errors. Nonetheless, our questionnaire was based on the ISAAC questionnaire (ISAAC) that has been shown to agree well with standard clinical diagnosis (sensitivity of 0.87 and specificity of 0.98) [70]. Second, because we selected important factors from 56 candidates, we deleted observations with missing rate$\geq$30 %. Therefore, our study population may differ from the total investigated population, as parents of children with eczema or related symptoms might be more interested in our study and accordingly more likely to fill out questionnaires completely, which may result in the higher prevalence of eczema or related symptoms than they really are. Third, of all ten cities in CCHH, we could only get access to eight of them and excluded 4 cities due to poor data quality, which would limit our results' generalizability across China. Fourth, the uneven sample size might induce unmeasured bias to our result. Fifth, we did not consider ambient pollutant exposures [16]. However, children spend about 90 % of their time indoors, and their exposure to ambient outdoor pollutants mostly occurs indoors [71]; as well, we also considered the home location.

Our study also has specific strengthens. First, the four cities we studied are in different climate zones in China, such that our study population is more representative of Chinese children. To the best of our knowledge, this is the first study to compare different influencing factors of children's eczema/related symptoms in different locations in China. In addition, we used group LASSO, a variable selection method, to identify influencing factors using a more comprehensive set of possible factors. This increased the predictive power of our model compared to models in previous studies.

5. Conclusion

This study explored associations between home environmental and other factors with lifetime-ever eczema and related symptoms in children aged 3–6 years old in four cities in China. Home environmental factors are in relation to childhood eczema and those associations differ across different regions. For the total study population, home environmental risk factors included larger residence size, shared room, air cleaner, abnormal smell, perceived dry air, visible mold or damp stains, cooking with coal or wood, incense, and wallpapered or painted or wooden walls, mice, new furniture during pregnancy, abnormal smell at birth, ETS at birth and window condensation at birth. Protective factors included rural house location and window ventilation in spring and summer. Other risk factors are age, gender, family history of allergy, antibiotic use and length of pregnancy. The associations between home environmental and other factors with eczema and related symptoms differed across cities. These findings may help parents reduce the risk of eczema/related symptoms by adopting strategies to improve home environments. Further studies regarding home environmental factors and childhood allergic diseases should have quantitative measurement of home environmental parameters (i.e., humidity, temperature, and pollutants) and health outcome (i.e., biomarkers in blood or urine, diagnose from doctors), adequate sample size in multicenter, and high-quality control procedures.

Data availability statement

According to Informed Consent, CCHH researchers need to keep the data confidential. So data associated with our study weren't deposited into a publicly available repository. The authors do not have permission to share data.

CRediT authorship contribution statement

Ruosu Zhang: Writing – original draft, Formal analysis, Data curation. **Louise B. Weschler:** Writing – original draft. **Jin Ye:** Data curation. **Zhaokun Wang:** Data curation. **Qihong Deng:** Data curation. **Baizhan Li:** Data curation. **HuaQian:** Data curation. **Zhuohui Zhao:** Data curation. **Yinping Zhang:** Data curation. **Shaodan Huang:** Writing – original draft, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Chuan Hong:** Data curation.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2023.e21718.

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