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Article

Interactions of Parents' Stress and Environmental Factors on Children's Eczema: Key Roles in Allergens and Air Pollution

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Keywords

childhood eczema;
parents' psychological stress;
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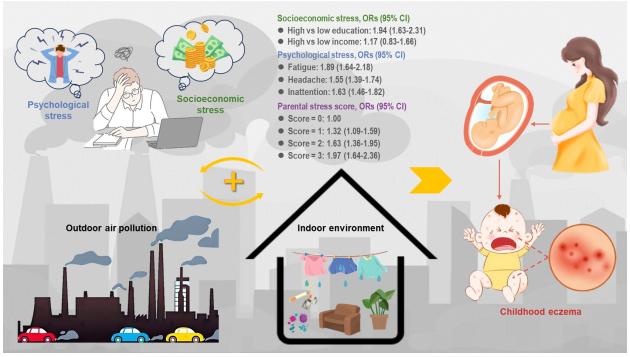
stress-environment interaction

Highlights

- Parental stresses are associated with children's physician-diagnosed eczema (PDE)
- High parental socioeconomic stress increased PDE risk of decoration and allergens
- High parental social stress elevated the impact of prenatal exposure to NO_2 on PDE
- Parental psychological stress enhanced PDE risk of $PM_{2.5–10}$ and PM_{10} exposure
- There is a "stress-environment interaction" on the development of childhood eczema

Abstract: Increasing evidence linked air pollution and social stress with eczema independently, yet their interactive effects on childhood eczema in early life are unknown. This study aimed to explore the effects of parental stresses and their interactions with interior and extraventricular environmental exposures on preschooler's physician-diagnosed eczema (PDE). We conducted a mixed cross-sectional and retrospective cohort study involving 8689 children at Changsha in China. Individual data for health information, parental stresses, and interior environments were collected through questionnaires. Individual exposure to temperatures and extraventricular pollutants were computed using the Inverse Distance Weighted (IDW) technique method. Multivariable logistic regression analyses were engaged in this research. We found that childhood PDE was markedly associated with higher education among parents (ORs [95% CI] = 1.94 [1.63–2.31]), while presence of fatigue, headache and distractibility amplified PDE risk (1.89 [1.64–2.18], 1.55 [1.39–1.74] and 1.63 [1.46–1.82]). Higher score of parental psychological stresses was related to elevated risks of PDE. Parents owning lower education or income had higher childhood PDE risk of moldy clothing/bedclothes, nonflowering plants, decoration throughout pregnancy till previous year. PDE risk from $PM_{2.5}$, NO_2 and O_3 exposure mainly before birth were higher in families with high social stress. PDE risk from early life exposure to $PM_{2.5}$, $PM_{2.5–10}$, PM_{10}, and NO_2 during preconception, first year, and entire postnatal stage was higher in parents with psychological stress. Our study indicates that early life exposures to parental stresses as well as their combinations with interior and outdoor pollution and allergen increased risk of childhood PDE, suggesting the "(pre-)fetal origin of eczema" hypothesis through stress-environment interaction.



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1. Introduction

Eczema is the most common chronic relapsing skin disease in children, characterized by pruritus, epidermal barrier dysfunction, and immunoglobulin E-mediated sensitization to environmental allergens. Approximately 40 million people suffer from eczema, affecting up to 15–30% of children worldwide [1]. Previously, the International Study of Asthma and Allergy in Children (ISAAC) conducted a survey of 700,000 children from 56 countries on allergic diseases, including eczema, and found that the prevalence of eczema in children ranged from 0.3–20.5% [2]. A recent national study reported a relatively high prevalence of eczema (12.94%) among children aged 1–7 years in 12 major cities in China [3]. Some of our recent work reported a rapid increase in preschooler's eczema in Chinese cities [4,5]. Eczema is a multifactorial and complex disease that can not only lead to abnormal development, but children who frequently suffer from eczema are also more prone to develop asthma, allergic rhinitis, and other allergic diseases later in life [6]. On the other hand, due to its high prevalence and atopic progression to respiratory allergy and a range of other complications, eczema in children may represent a significant economic and public health burden for families [7]. The development of eczema has been associated with both genetic factors and environmental changes, so it is important to explore the joint role of major genetic and environmental factors in childhood eczema for early prevention and effective control.

The development of eczema in children begins in utero, where the developing embryo is particularly vulnerable to toxic substances due to immature immune, neuroendocrine, and antioxidant system. Early studies traced adult's diseases back to the childhood environment [8]. On the other hand, theories of the origin of health and the development of disease suggest that many hereditary chronic diseases are related to poor lifestyles or environments, and that negative environmental factors experienced early in human life will have a certain impact on the onset of various diseases in future lives [9]. More and more studies show that the incidence of eczema is increasing rapidly in China [10–14], therefore, identifying environmental risk factors early in life is important for developing preventive measures to minimize childhood eczema. Parents' stress, mainly from socioeconomic and psychological perspectives, is an important factor in the development of allergic diseases in children [15,16]. On the one hand, the relationship between socioeconomic status and health begins in the early stages of life [17]. Economic stress affects the living environment and quality of life of the family, as well as daily dietary and living habits [18]. Many studies have shown that people with low socioeconomic status have higher odds and susceptibility to stress-related diseases [19–22]. On the other hand, early life exposure to psychosocial stress has been identified as a determinant of social differences in health that occur throughout life and is thought to be associated with a variety of diseases including atopic dermatitis (AD) [23]. Parents' stress can influence the development of eczema in early childhood through a number of pathways and may lead to a stressful home environment that further affects skin barrier function and immune system function [24], resulting in a more pronounced inflammatory skin response. Several studies have found that mothers' stress and anxiety levels in pregnancy are related with the incidence of eczema in children [25,26]. This suggests that early psychological states may have long-term impacts on the development of the child's immune system.

There is growing evidence that traffic-related air pollution (TRAP) exposure is associated with allergic diseases in children [27–30]. In addition, several research showed that the prevalence of eczema in early children is not only associated with postnatal exposure to TRAP, but also with prenatal exposure. A German birth cohort study [30] found that traffic pollutants exposure such as $PM_{2.5}$ and NO_2 during the period from birth to 6 years of age significantly increased the risk of asthmatic bronchitis, pollen allergy, eczema and other allergic diseases in children. A study from China showed that exposure to environmental NO_2 during pregnancy and throughout life is a risk factor for atopic eczema in children [31].

Increasing studies have characterized independent effects of parents' stress or environmental pollution exposure on childhood eczema, but their potential interactions are poorly understood. Several studies have suggested that psychological stress may alter susceptibility to physical exposures (e.g., air pollution) [32,33]. A systematic review of human and animal evidence suggests that chemical exposure has a stronger effect than stress, and that this effect is generally greater in the presence of stress [34]. Therefore, whether the "dual exposure" of high parents' stresses and heavy environmental pollution in China leads to a rapid increase in childhood eczema warrants further investigation. In this study, we propose that there is a potential interaction of parents' stress with outdoor air pollution and indoor environmental factors on the risk of children's eczema. To demonstrate this hypothesis, we conducted a retrospective cohort cross-sectional study, so as to assess the impacts of different types of parent's stresses as well as their synergy with indoor and outdoor environmental factors on children's eczema.

2. Materials and Methods

2.1. Study Protocol and Surveyed Participants

We conducted a population-specific retrospective cohort cross-sectional study in Changsha, China, between 2019 and 2020 (Figure S1). The detailed procedures of

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this study have been fully described in our previous academic papers [35–37], and we successfully obtained formal approval from the Institutional Review Boards of Fudan University and Central South University (IRB#2019-09-0778), as well as ethical approvals from all participating kindergartens. In order to ensure the scientific validity of the study in line with international standards, we designed the questionnaire with full reference to the standardized framework of the International Study of Asthma and Allergies in Childhood (ISAAC), as well as the Swedish International Guidelines on Building Health and Dampness (DBH). Based on this, we systematically collected comprehensive data on health status, basic personal information, interior environmental exposures, daily behaviours, and the life habits for the children and the family members.

A total of 36 kindergartens out of 220 kindergartens in nine administrative districts (Furong, Tianxin, Yuelu, Kaifu, Yuhua, Wangcheng, Liuyang, Ningxiang, and Changsha County) in Changsha, China, were randomly selected as the sample sites for the study, and the target respondents were children enrolled in these kindergartens [37]. The number and percentage of samples located in the nine administrative districts is listed in Table S1. To ensure the accuracy and reliability of the survey data, we first provided specialized training to kindergarten teachers who were responsible for distributing the questionnaires, with the aim of ensuring that they could properly understand and implement the process of questionnaire distribution and retrieval so as to maintain the quality of the questionnaires. The trained teachers then distributed the questionnaires to the parents or guardians of each child and gave them one week to complete them. First, we conducted a preliminary questionnaire survey in 9 kindergartens by distributing 180 questionnaires (20 questionnaires for each kindergarten). We accurately calculated the time required to fill out each questionnaire, and the average time used is 10–20 min which can ensure the quality of questionnaire filling very well. We further asked the questionnaire respondents about the problems they encountered during the questionnaire filling process and then made corresponding improvements to the questionnaire. Furthermore, 13,609 questionnaires were distributed to all the participanted kindergartens. After the questionnaires were returned, it was decided after careful review to exclude data from children under the age of 3 and over the age of 6 because of the small sample size and possible uncertainty about the diagnosis of health problems containing eczema, which might affect the overall validity and reliability of the data. After a series of screening and processing procedures, we finally collected 8,689 valid questionnaires, which formed the core basis of this study (Figure 1).

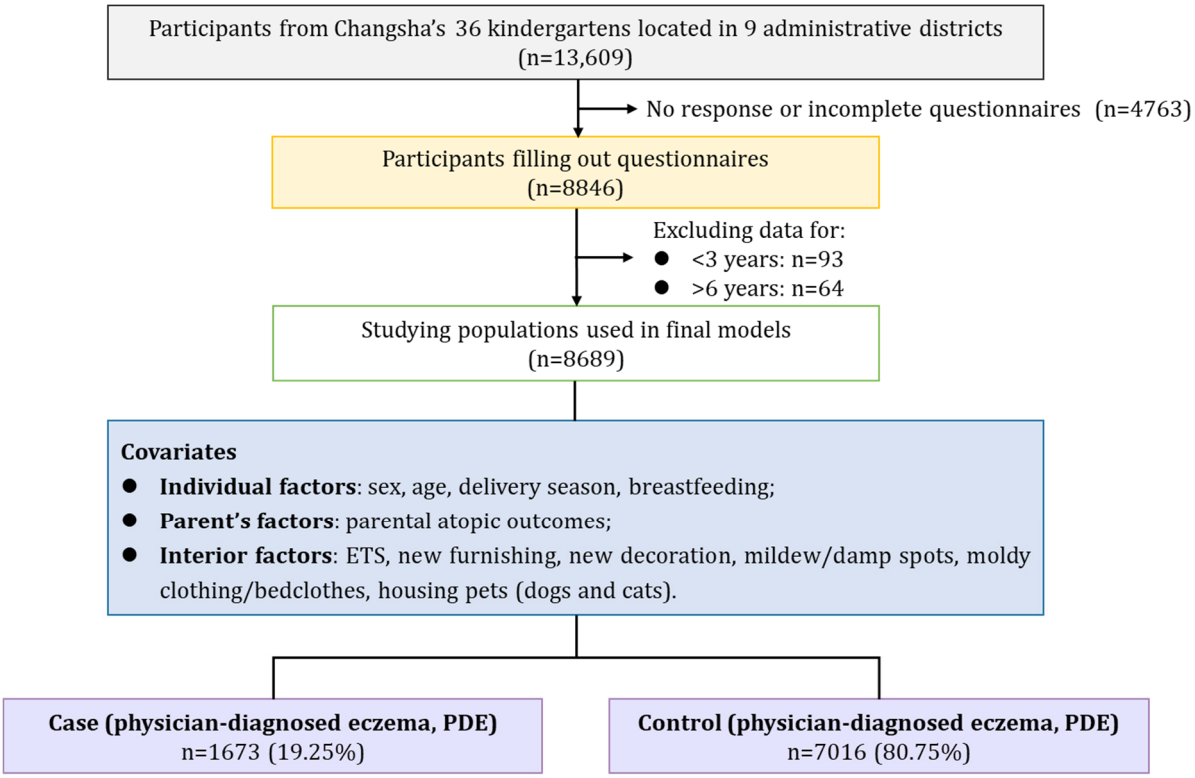

Figure 1. Flowchart showing the number and prevalence of PDE in the study population.

In addition, we conducted another double sampling inspection by randomly extracting 10% of formally completed questionnaires and checked their completion degree, missing data, and logic error. We observed that more than 98% extracted questionnaires were completed well without missing data in the double sampling

inspection and there were very few logic errors among these samples. Therefore, our questionnaire data are valid, accurate and completed, which can ensure our data and results reliable.

2.2. Health Outcome

Childhood eczema was defined based on responses to the following three questions (Table S2):

(1) Has the child ever been diagnosed by a doctor with eczema or atopic dermatitis?
(2) Has the child ever been diagnosed by a doctor with itching rashes that recurred for at least 6 consecutive months?
(3) Has the child been diagnosed by a doctor with recurrent itching rashes lasting for at least 6 consecutive months during the past 12 months?

Children who answered "yes" to any of these questions were classified as having eczema.

2.3. Exposure Time Stages

We considered each child's preconceptional, gestational and postnatal exposure stages [37]. Preconceptional stage was defined as one year before the date of mother's conception, comprising tenth to twelfth gestational months, seventh to nineth gestational months, fourth to sixth gestational months, first to third gestational months, and the whole year before conception date (the date of mother's last menstrual period before pregnancy). Prenatal stage was calculated from the conception date till the delivery date, including first trimester (first till twelfth gestational weeks), second trimester (thirteenth till twenty seventh gestational weeks), third trimester (twenty eighth gestational week till delivery day), and whole gestational days. Postnatal stage spanned from the first day of delivery till the day of completing questionnaire, containing the first year (delivery day till the 365th/366th day of life) and past year (365/366 days prior to the day of completing questionnaire).

2.4. Parent's Exposure for Stress Indicators

The stresses described in this study refer to parents' stress including socio-economic stress and mental stress, for which data were obtained from standardized questionnaires [37]. Parents' socio-economic stress can be described using the level of parents' education and the level of parents' gross annual income, due to that lower parental education and income levels are associated with greater social and economic stress [38–41]. Social stress (parents' education) was fixed by the questions of "What's the child's father's highest education level? (Elementary/junior high school/high school or vocational high school/undergraduate or specialist/master's degree/doctorate or above)" and "What's the child's mother's highest education level? (Elementary/junior high school/high school or vocational high school/undergraduate or specialist/master's degree/doctorate or above)". The related data on parental socio-economic stress and mental stress were obtained from the standardized questionnaires. To determine the social stress, we classify the social pressure into three levels: high (the father's or mother's highest education level as primary/junior high school/high school or vocational high school), middle (the father's or mother's highest educational level as undergraduate or specialized), and low (the father's or mother's highest educational level as master's degree/doctoral degree or above). We further classify the social pressure into two classifications: high/middle and low levels. Economic stress (parents' gross annual income) is fixed by the question "What is the average level of gross annual income of the child's parents in the local area (low/middle/high)". The levels of gross annual income of the parents were further categorized into two subgroups: low and high/middle levels. We believe that the lower the level of parent's education/income, the higher the level of social/economic stress. Since our questionnaires did not involve the issue of chronic psychosocial stress of parents, such as anxiety and depression, in this study, parental psychological stress was assessed via three self-reported symptoms: fatigue, headache, and distractibility, experienced over the past three months. Although these symptoms are subjective, prior studies suggest that they are common manifestations of psychological stress and have been widely used as proxy indicators in population-based research where clinical psychological tools (e.g., Psychological and Social Sciences [PSS] or General Health Questionnaire [GHQ]) are not feasible due to logistical constraints. In this study, we fixed the parent's psychological stress through the question that "In the past three months, have you had fatigue/headache/distractibility (never/sometimes/frequently)". Fatigue [42–45], headache [46–49], and distractibility [50] are typical indicators of chronic psychological stress or are demonstrated to be closely related to psychological stress in previous studies. According to the frequency of the above symptoms, we further categorized the mental stress into two levels: never and sometimes/frequently, with the heavier the symptoms, the greater the mental stress. Additionally, we calculated the score (from 0 to 5) of parents' stress by adding up two indicators of socio-economic stress and three indicators of psychological stress.

2.5. Child's Exposure for Interior Environmental Factors (IEFs)

Data on exposure to IEFs were obtained from household questionnaires collected at various time

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windows [37]. The study included twelve common interior environmental variables, as shown in Table S3.

2.6. Child's Exposure for Ambient Air Pollution and Temperature

We collected data on seven common outdoor air pollutants: $PM_{2.5}$, $PM_{2.5–10}$, PM_{10}, sulfur dioxide (SO_2), nitrogen dioxide (NO_2), carbon monoxide (CO), and ozone (O_3) [37]. The data were collected daily from 2011 to 2020 at 10 municipal air quality monitoring stations over nine districts in Changsha. The 24-h mean concentrations of the seven pollutants except $PM_{2.5–10}$ were recorded daily, covering the entire time period for all children in the study. We then calculated the daily concertation of $PM_{2.5–10}$ by subtracting the daily average concentration of $PM_{2.5}$ from the daily average concentration of PM_{10} at each station. This ranged from the earliest first day of the 1-year period before the date of the mother's last menstrual period (LMP) at the time of conception of the oldest child to the latest questionnaire completion date. We identified the four nearest meteorological monitoring stations for each child's home address based on longitude and latitude. Using the daily concentrations from these stations and the inverse distance weighting (IDW) method, we calculated the daily individual exposure concentrations for each pollutant at the home address [37]. Additionally, we assessed the average daily temperature at the eight monitoring stations. Finally, we calculated the average exposure levels for each stage using each child's daily exposure values of seven pollutants and temperatures.

2.7. Selected Covariates

The selected covariates were selected from the standardized questionnaire according to the magnitude of their influence on the development of eczema in children, containing: (1) Individual variables: sex of the child (male; female); age (3; 4; 5; 6 years); delivery season (spring: March–May; summer: June–August; fall: September–November; winter: December–February), breastfeeding (no; yes); (2) Parent's variables: parents' atopic outcomes (no; yes); (3) Interior variables: environmental tobacco smoke (ETS) (no; yes); new furnishing (no; yes); new decoration (no; yes); mildew/damp spots (no; yes); moldy clothing/bedclothes (no; yes); housing pets such as dogs and cats) (no; yes). All of the above confounding covariates were found to be associated with eczema [4,5,51–55].

2.8. Statistical Analysis

Statistical analysis included: numbers with percentages, mean and standard deviation, as well as interquartile range (IQR) (25%, 50%, and 75% percentiles). Chi-square and the t-tests were adopted to describe the covariates' distribution between controls and PDE cases. We adopted multiple logistic regression models to evaluate the associations of childhood PDE with parents' socioeconomic and mental stresses, with the adjustment of selected covariates and atmospheric temperature and typical traffic-related air pollutant NO_2 [5]. Stratifications according to different types of stresses were performed to investigate the associations of parents' stresses with individual air pollutants exposure.

Extraventricular air pollutants exposure was determined via two subgroups: low as <median; high as ≥median. Extra stratifications were performed by interior exposure (presence; absence) and extraventricular air pollutants exposure (low; high). This research evaluated the associations of PDE with parents' socioeconomic and mental stresses and the relationships of PDE with environmental pollution and allergens stratified by these stress indicators through estimating the IQR increment for extraventricular air pollutants and interior environments exposure (presence; absence) [37]. We further assessed the synergies of parents' socioeconomic and mental stresses with home and extraventricular environments on PDE.

We combined parents' stresses level (high/middle; low), household exposure levels (yes; no), and ambient air pollutants exposure levels (high; low) to estimate the associations of PDE with four sets [37]: (1) low parents' stresses together with low or no interior/extraventricular exposures; (2) low parents' stresses together with high or yes interior/extraventricular exposures; (3) high parents' stresses together with low or no interior/extraventricular exposures; and (4) high parents' stresses together with high or yes interior/extraventricular exposures. Subgroup's analysis was conducted to determine whether the special subjects who were more susceptible to PDE risk owing to parents' different types of stress from socioeconomic and mental status.

SPSS (version 27, SPSS Inc. in Chicago of US) was adopted for the statistical analyses. Associations are calculated as odds ratio (OR) with 95% confidence interval (95% CI). The *p*-values equal or smaller than 0.05 were considered for statistical significance. The *p*-values equal or smaller than 0.05 were considered for significant interactions. Python (version 3.1, JetBrains s.r.o. in Czech Republic) was adopted to estimate individual extraventricular pollutants and temperatures exposure.

3. Results

Table 1 shows the demographics and prevalence for childhood PDE stratified by covariates. A total of 1673 out of 8689 preschoolers report PDE, and the diagnostic rate is 19.3%. The prevalence of PDE was higher in younger subjects (3 and 4 years), subjects born in the fall, with parents' atopic outcomes, renovated pollution (new furnishing; new decoration), moisture allergen (mildew/damp spots; moldy clothing/bedclothes), and house pets than older subjects (5 and 6 years), those born

in the spring, without parents' atopic outcomes and these interior environmental factors ($p < 0.05$). In addition, gender, breastfeeding, and ETS were not related to childhood PDE.

Table 1. Demographics for the number and prevalence of physician-diagnosed eczema (PDE) in surveyed children (3–6 years) (n = 8689).

	Total		Eczema		
	Number (n)	(%)	Case (n)	(%)	*p*-Value
Total	8689	(100.00)	1673	(19.25)	
Sex					0.150
Boys	4667	(53.71)	925	(19.82)	
Girls	4022	(46.29)	748	(18.60)	
Age (years)					**0.002**
Three	1855	(21.35)	398	(21.46)	
Four	2965	(34.12)	597	(20.13)	
Five	2793	(32.14)	493	(17.65)	
Six	1076	(12.38)	185	(17.19)	
Delivery season (month)					**0.007**
Spring (March–May)	2168	(24.95)	374	(17.25)	
Summer (June–August)	2378	(27.37)	455	(19.13)	
Autumn (September–November)	2089	(24.04)	448	(21.45)	
Winter (December–February)	2054	(23.64)	396	(19.28)	
Breastfeeding					0.840
No	567	(6.53)	111	(19.58)	
Yes	8122	(93.47)	1562	(19.23)	
Parents' atopic outcomes					**<0.001**
No	6032	(69.42)	836	(13.86)	
Yes	2657	(30.58)	827	(31.13)	
Environmental tobacco smoke (ETS)					0.852
No	4235	(48.74)	812	(19.17)	
Yes	4454	(51.26)	861	(19.33)	
New furnishing					**<0.001**
No	5711	(65.73)	984	(17.23)	
Yes	2972	(34.20)	689	(23.18)	
New decoration					**<0.001**
No	6871	(79.08)	1261	(18.35)	
Yes	1812	(20.85)	412	(22.74)	
Mildew/damp spots					**<0.001**
No	6517	(75.00)	1096	(16.82)	
Yes	2166	(24.93)	577	(26.64)	
Moldy clothing/bedclothes					**<0.001**
No	7328	(84.34)	1301	(17.75)	
Yes	1355	(15.59)	372	(27.45)	
Housing pets (cats and dogs)					**<0.001**
No	4585	(52.77)	786	(17.14)	
Yes	4104	(47.23)	887	(21.61)	

Sum of the number is not 8689 due to missing data. The *p*-values < 0.05 were indicated as statistical significance in bold.

Table S4 presents the statistics for parents' socioeconomic and mental stress as well as the associations of parents' stresses with children's PDE. PDE prevalence was markedly higher for children having parents with high or middle education than low education ($p < 0.001$). Moreover, parents owing higher economic levels owned slightly higher risk for child's PDE compared to low economic level, in spite of an insignificant level. In addition, parents with mental stress (fatigue; headaches; and/or distractibility) prone to own a child with PDE ($p < 0.001$).

Table S5 displays summaries for interior environments and the associations with PDE in early children. Families holding new furnishing, mildew/damp spots, and moldy clothing/bedclothes across whole stages owned higher PDE prevalence ($p < 0.05$). During all stages except 1 year prior to conception, exposure to ETS and grandparents' smoking elevated the prevalence of childhood PDE ($p < 0.05$). Families with plants especially non-blooming plant owned higher PDE prevalence ($p \leq 0.001$). Table S6 displays individual seven extraventricular air pollutants, temperatures exposure and relative humidity exposure during the three stages as well as the associations with PDE risk. Children having PDE owned higher pollutants exposure except CO and O_3 to most of across all stages ($p < 0.05$). In addition, parents

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reported significant variations before delivery among the children with and without PDE ($p < 0.05$).

Figure 2 displays associations of parents' stresses with children's PDE. It indicates that high parents' social indicator (high or middle education) was related with childhood PDE (OR [95% CI]: 1.94 [1.63–2.31]). Nonetheless, parents' economic status (low/middle/high level of gross annual income) was not related to PDE. Parents' fatigue, headache and/or distractibility amplified PDE risk, ORs (95% CI): 1.89 (1.64–2.18), 1.55 (1.39–1.74) and 1.63 (1.46–1.82). Furthermore, PDE risk for both parents' socioeconomic and psychological stresses were higher among children with male gender and without breastfeeding. In addition, children with smaller age (three and four years), born in warm months (May to September), and without parents' atopic history were at higher PDE risk of socioeconomic stress, while PDE risk owing to parents' psychological stresses was higher for children with bigger age (4–6 years old), delivered during cold month (October throughout April), and owning parents' atopic history (Table S7). Associations between childhood PDE and parental stresses were stronger among families with non-daily cleaning habits, especially for parental education and psychological stress indicators (Table S8). Similarly, the associations were more evident under high relative humidity, particularly for education and psychological stress indicators (Table S9).

Table 2 reveals prevalence of parents' stress score and the associations of the score with children's PDE. PDE was forwardly associated with parents' total stress (TS) and psychological stress (PS) scores, but was inversely related with parents' socioeconomic stress (SS) score. For example, parents having higher TS (≥2) and PS (≥2) scores owned a child with higher PDE risk than lower TS (<2) and PS (<2) scores, ORs (95% CI): 1.35 (1.19–1.52) and 1.25 (1.18–1.32) respectively. Nevertheless, parents owning higher SS (≥1) score held a child with lower PDE risk than lower PS (=0) score, OR (95% CI): 0.73 (0.64–0.84).

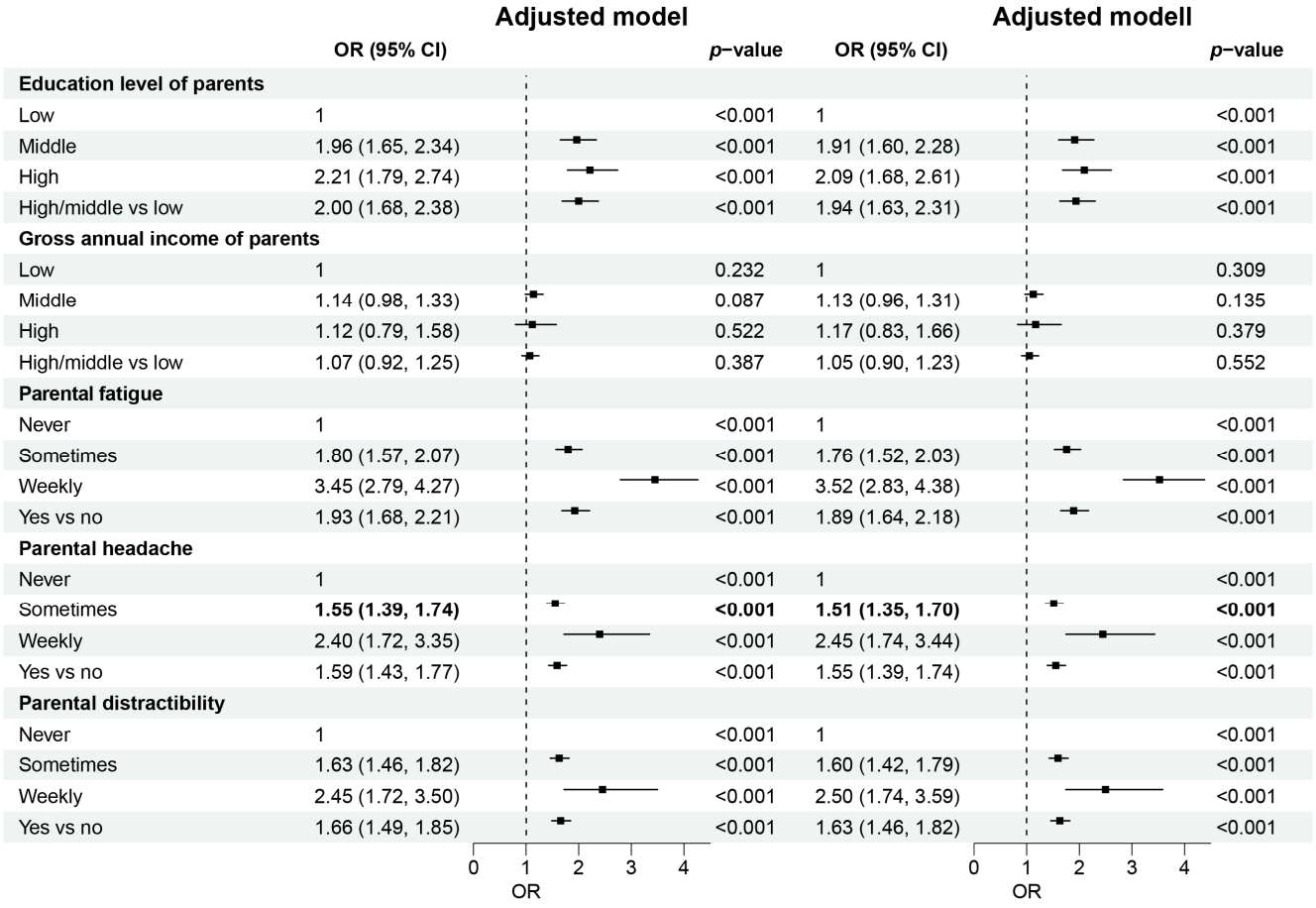

Figure 2. Odds ratio (95% CI) of children with PDE for the exposure to parents' stress among children aged 3 to 6 years. Adjusted model I was adjusted for covariates; Adjusted model II was also adjusted for extraventricular NO_2 and temperature during postnatal period according to adjusted model I; Parents' education level: low is defined as primary school, junior high school, and high school or vocational high school; middle is defined as undergraduate or college degree; high is defined as master's or doctoral degree. The p-value < 0.05 was indicated as statistical significance.

Table 2. The odds ratio (95% CI) for childhood PDE owning to score of parents' stresses.

Score of Parents' Stresses	Total		Childhood PDE	
	Number (n)	(%)	OR (95% CI)	*p*-Value
Score of total stress (TS)				
≤1	3435	39.53	1.00	
2	2380	27.39	1.26 (1.09, 1.45)	**0.002**
≥3	2874	33.08	1.42 (1.24, 1.64)	**<0.001**
High (≥2) vs. low (<2) TS score	5254 vs. 3435	60.47 vs. 39.53	1.35 (1.19, 1.52)	**0.001**
Score of socioeconomic stress (SS)				
0	6207	71.44	1.00	
1	2021	23.26	0.75 (0.65, 0.87)	**<0.001**
2	461	5.31	0.67 (0.50, 0.90)	**0.007**
High (≥1) vs. low (=0) SS score	2482 vs. 6207	28.56 vs. 71.44	0.73 (0.64, 0.84)	**<0.001**
Score of psychological stress (PS)				
0	2087	24.02	1.00	
1	2060	23.71	1.32 (1.09, 1.59)	**0.004**
2	2438	28.06	1.63 (1.36, 1.95)	**<0.001**
3	2104	24.21	1.97 (1.64, 2.36)	**<0.001**
High (≥2) vs. low (<2) PS score	4542 vs. 4147	52.27 vs. 47.73	1.25 (1.18, 1.32)	**<0.001**

Models are adjusted for covariates, extraventricular temperature and NO_2 in postnatal period. The *p*-values < 0.05 considered as statistical significance.

Figure 3 explored the associations of interior environments with children's PDE by stratified socioeconomic (Figure 3a) and mental stresses (Figure 3b). Parents owning high social stressor (low parents' education) held a child with higher PDE risk owning to exposure for moldy clothing/bedclothes in pregnant stage, as well as new decoration and moldy clothing/bedclothes in previous year (interaction p = 0.013, 0.088 and 0.007, respectively), yet those owning high economic stressor (low parents' gross annual income) held higher PDE risk owning to first-year non-blooming plants (interaction p = 0.025) (Figure 3a). Nevertheless, no positive interactions of parents' mental stressors with interior environments were displayed for PDE (Figure 3b).

Figure 4 assessed joint impacts of socioeconomic pressures and extraventricular air pollutants exposure throughout preconception (Figure 4a), pregnancy (Figure 4b), and postpartum (Figure 4c) on PDE. We detected that PDE risk owning to NO_2 exposure in the third trimester was higher for children having high parents' social pressure (low education) compared to low pressure (high/middle education), having significant interaction p of 0.025. Figure 4 illuminated the associations of extraventricular pollutants throughout preconception (Figure 4d), pregnancy (Figure 4e), and postpartum (Figure 4f) with PDE stratified parents' owning mental stress. Parents owning headache reported a higher PDE risk owning to exposure to PM_{10} in first year and $PM_{2.5–10}$ in entire postpartum (interaction p = 0.017 and 0.047 and 0.054).

We also explored the associations of parents' stresses with children's PDE stratified through interior environments (Table S10) and extraventricular pollutants (Table S11). Households owning mildew/damp spots in 1 year prior to conception day owned higher children's PDE risk of parents' social stress, interaction p = 0.004 (Table S10). In addition, early-life exposure for heavy extraventricular pollutants ($PM_{2.5}$/PM_{10}/SO_2/NO_2) in preconception and first trimester amplified PDE risk owning to high/middle social stress, while higher exposure to high level of the seven ambient pollutants over all the stages amplified PDE risk owning to mental stressors (Table S11), with all interaction p values < 0.1.

We interestingly observed positive interactions of parents' economic and mental stresses with early-life interior environments (new furnishing, mildew/damp spots, moldy clothing/bedclothes) 1 year prior to conception day and first year of life related to PDE, and parents owning both high stress and interior exposures reported the highest risk (Table S12). There were positive interactions of parents' mental stress with all the seven extraventricular pollutants in relation to PDE risk, and parents owning both mental stress and high pollutants exposure held the highest risk (Table S13).

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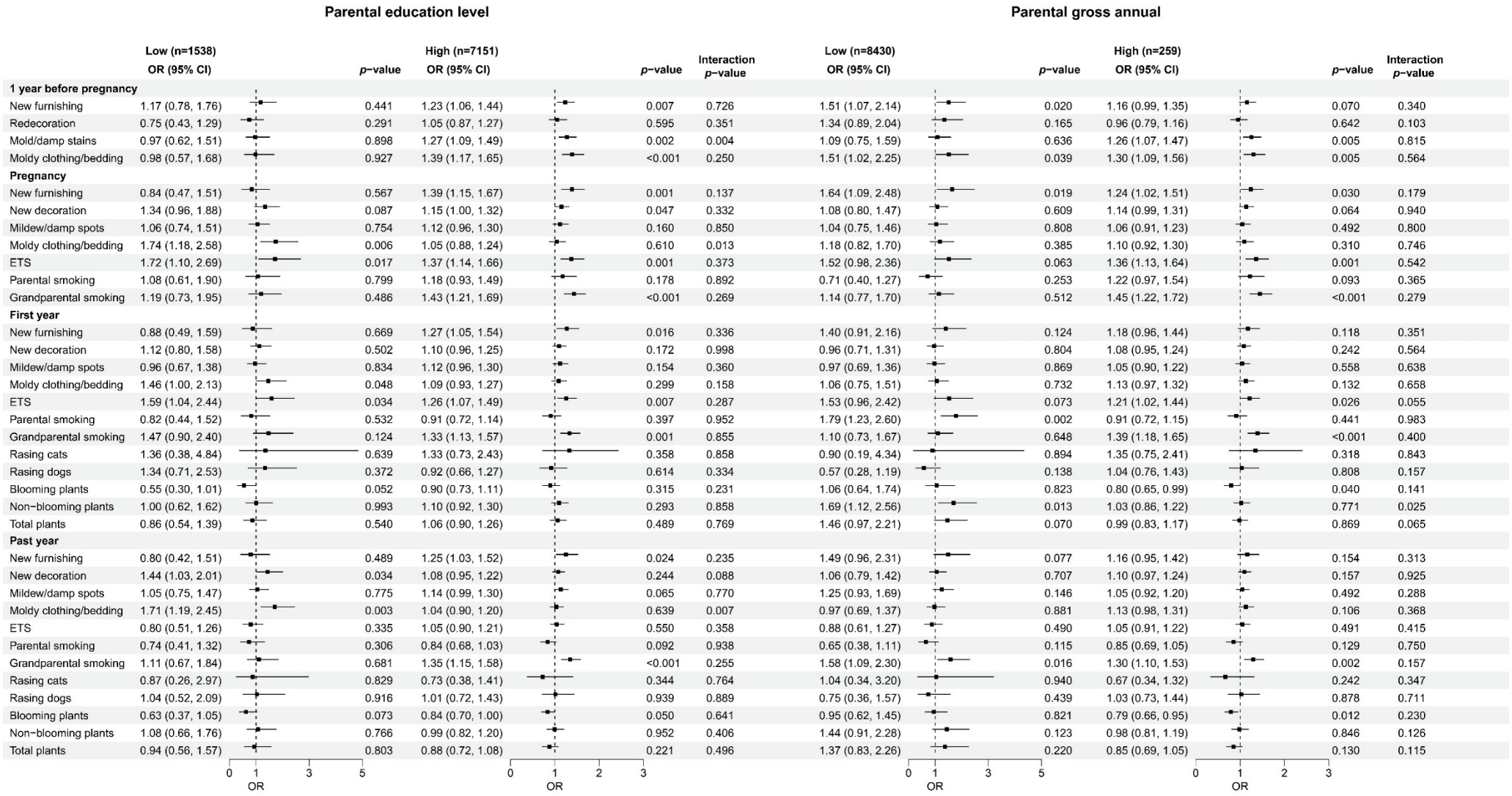
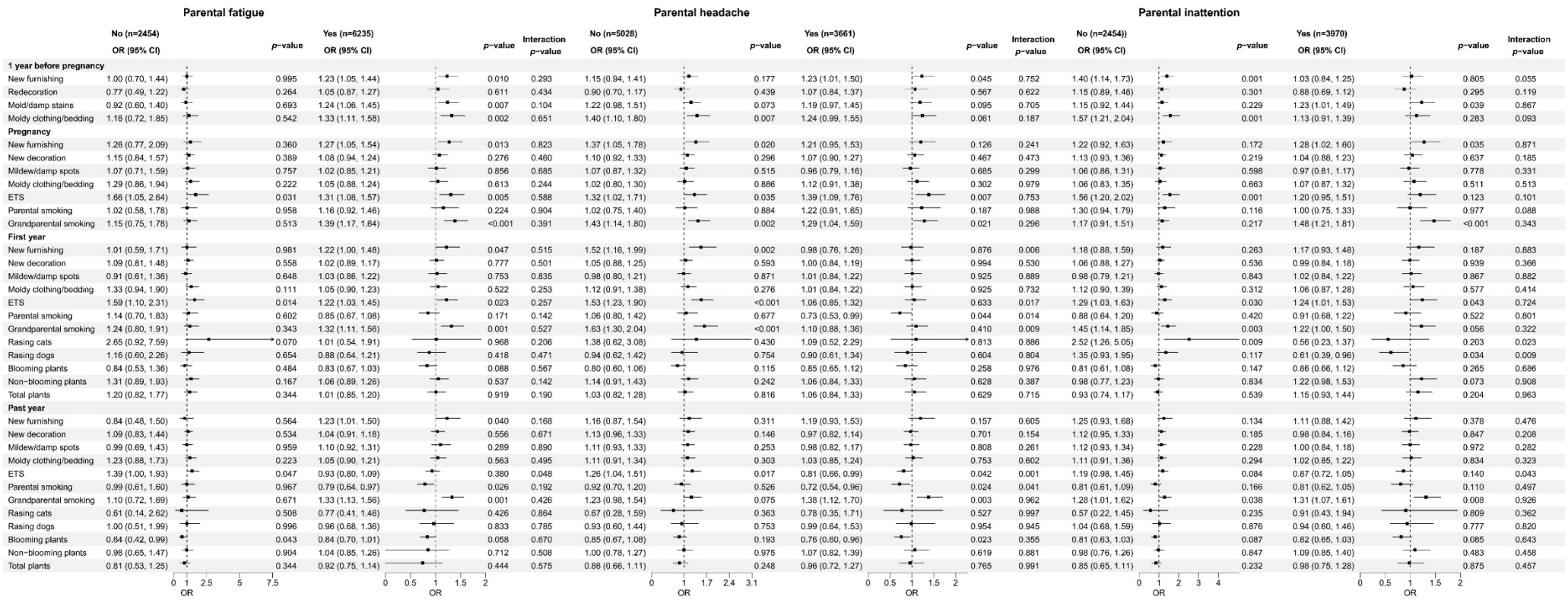


(a)

Figure 3. *Cont.*



(b)

Figure 3. (**a**) Interior environments concerned to children with PDE: ORs (95% CI) laminated by parents' socioeconomic stress. ORs were adjusted for covariates, extraventricular NO_2 and temperature exposure in different stages; significant interaction *p*-value < 0.05. (**b**) Interior environments concerned to children with PDE: ORs (95% CI) laminated by parents' psychological stress. ORs were adjusted for covariates, extraventricular NO_2 and temperature exposure in different stages; significant interaction *p*-value < 0.05.

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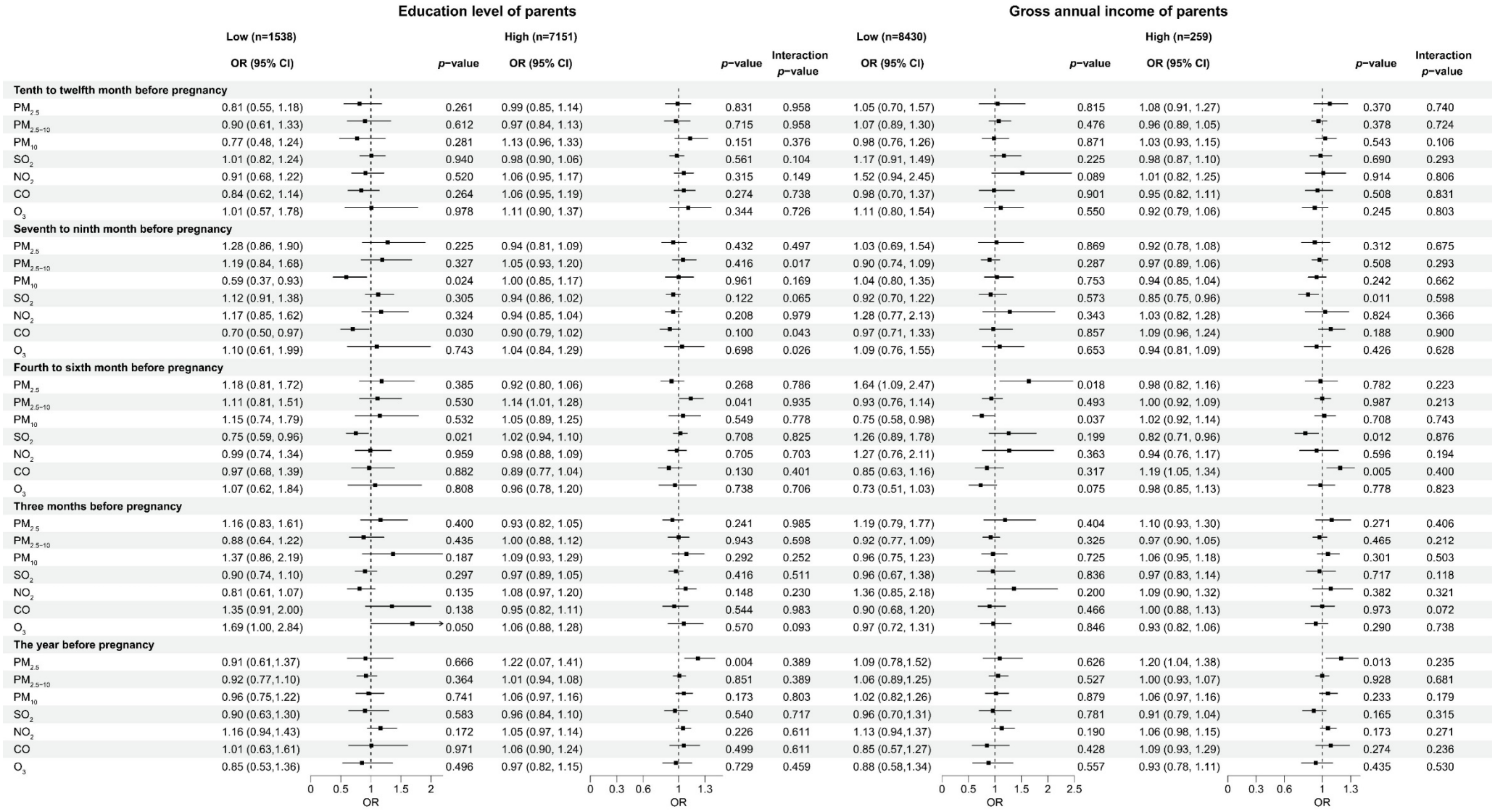
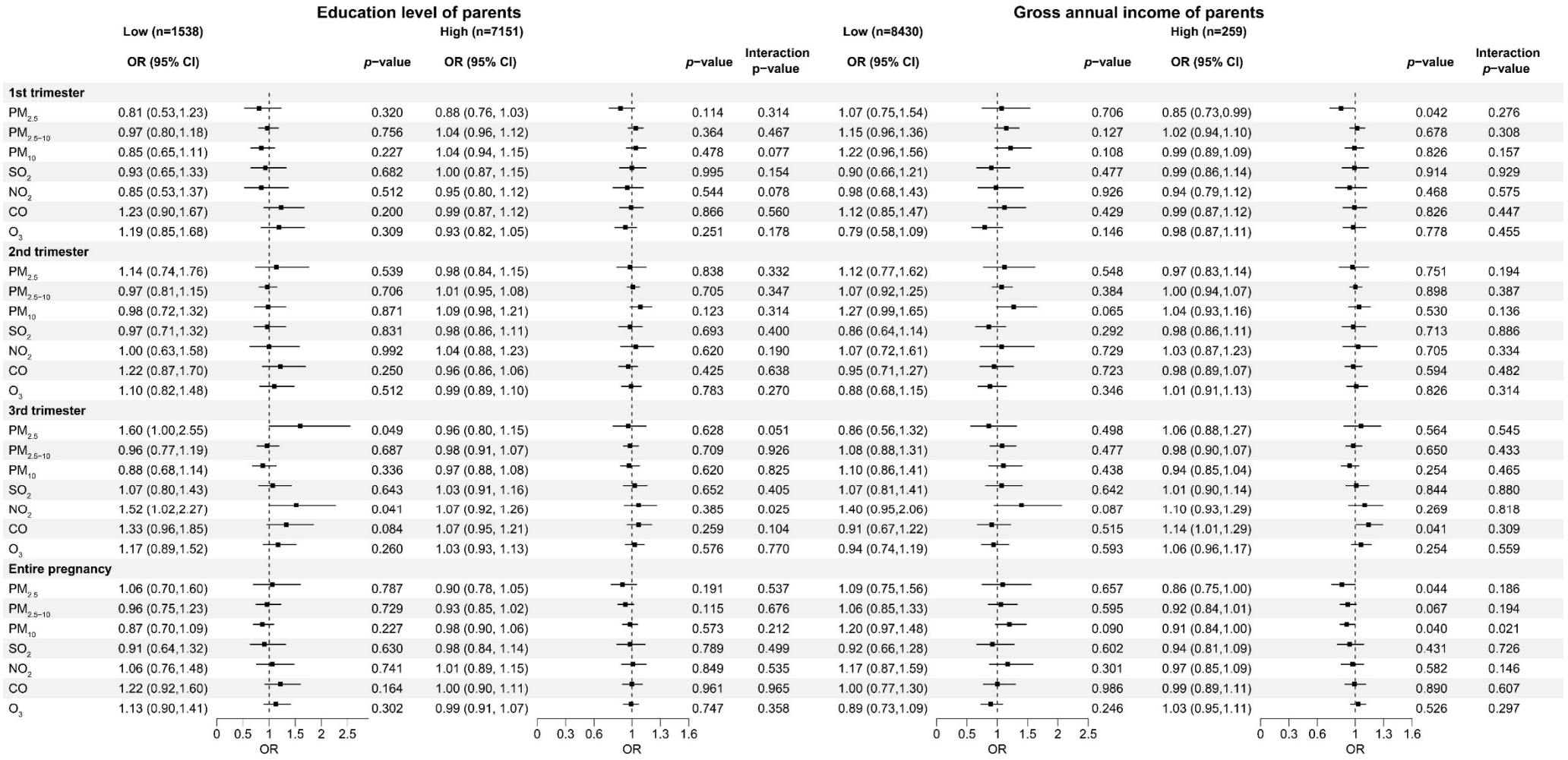


(a)

Figure 4. *Cont.*



(b)

Figure 4. *Cont.*

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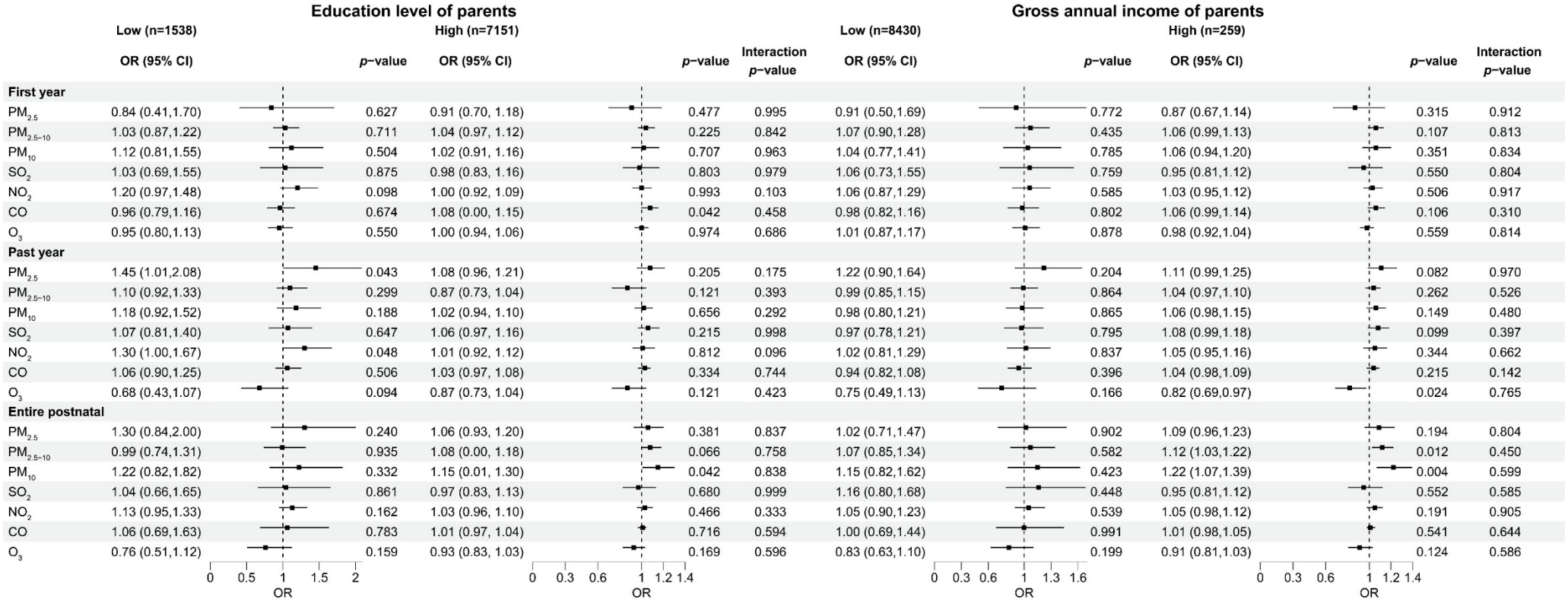

(**c**)

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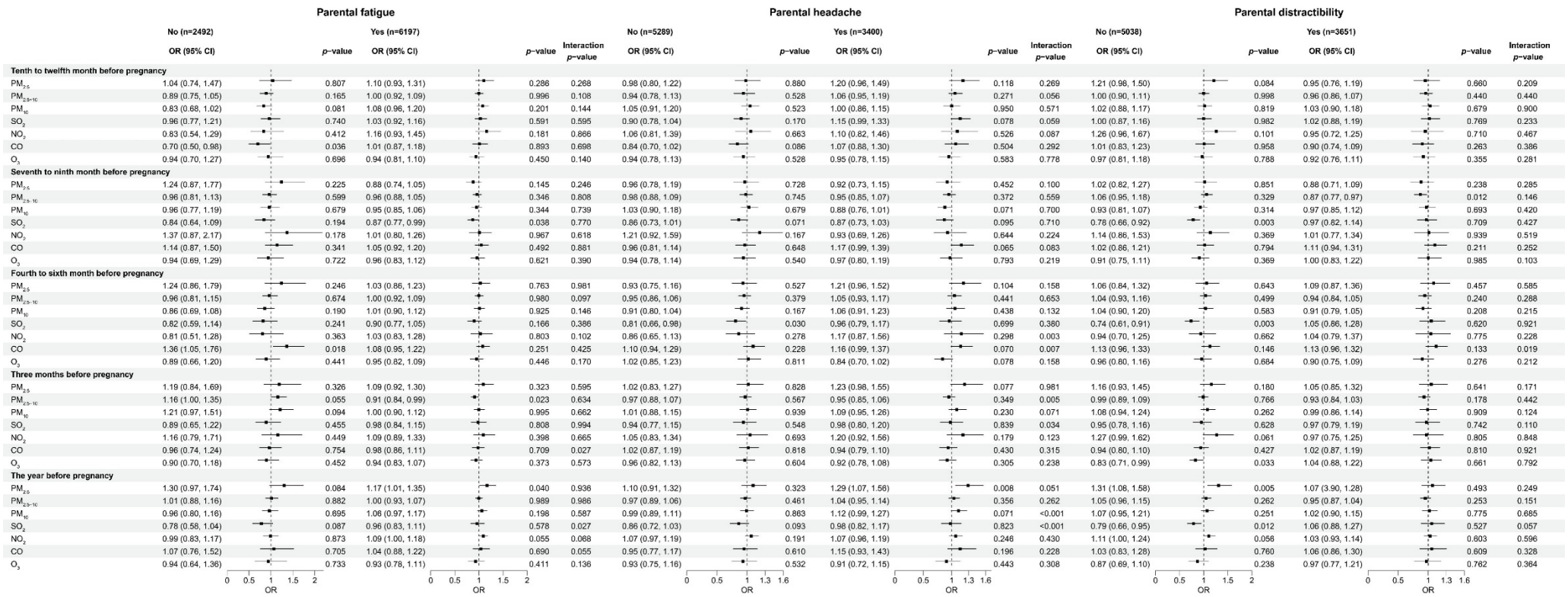

(d)

Figure 4. *Cont.*

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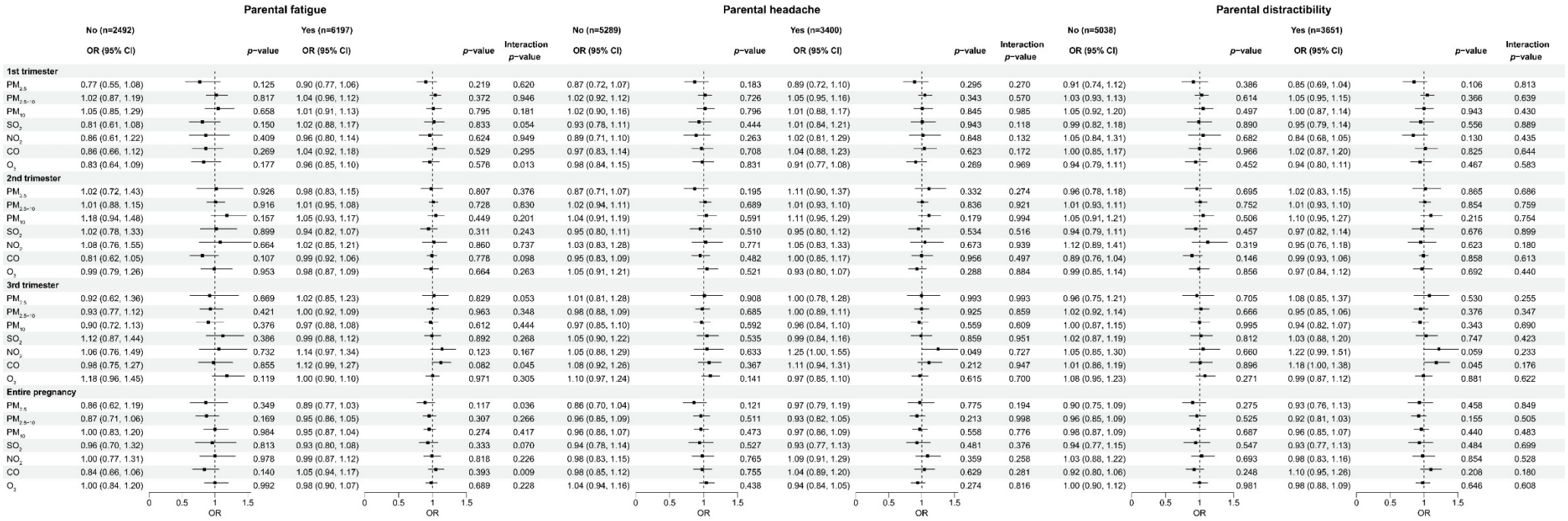
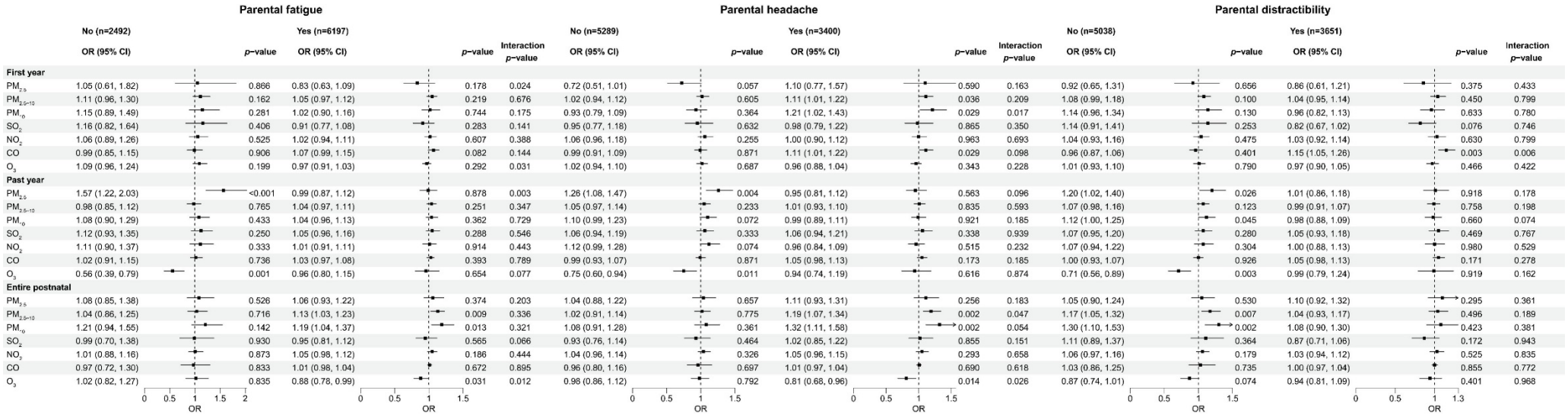


(e)

Figure 4. *Cont.*



(f)

Figure 4. (**a**) ORs (95% CI) of surveyed pre-primary children with PDE for extraventricular air pollutants exposure during the preconception period laminated by parents' socioeconomic stress. ORs were adjusted for covariates and extraventricular temperature exposure in different stages; significant interaction *p*-value < 0.05. (**b**) ORs (95% CI) of surveyed pre-primary children with PDE for extraventricular air pollutants exposure during gestation laminated by parents' socioeconomic stress. ORs were adjusted for covariates and extraventricular temperature exposure in different stages; significant interaction *p*-value < 0.05. (**c**) ORs (95% CI) of surveyed pre-primary children with PDE for extraventricular air pollutants exposure during the postnatal period laminated by parents' socioeconomic stress. ORs were adjusted for covariates and extraventricular temperature exposure in different stages; significant interaction *p*-value < 0.05. (**d**) ORs (95% CI) of surveyed pre-primary children with PDE for extraventricular air pollutants exposure during the preconception period laminated by parents' psychological stress. ORs were adjusted for covariates and extraventricular temperature exposure in different stages; significant interaction *p*-value < 0.05. (**e**) ORs (95% CI) of surveyed pre-primary children with PDE for extraventricular air pollutants exposure during the prenatal period laminated by parents' psychological stress. ORs were adjusted for covariates and extraventricular temperature exposure in different stages; significant interaction *p*-value < 0.05. (**f**) ORs (95% CI) of surveyed pre-primary children with PDE for extraventricular air pollutants exposure during the postnatal period laminated by parents' psychological stress. ORs were adjusted for covariates and extraventricular temperature exposure in different stages; significant interaction *p*-value < 0.05.

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4. Discussion

The present retrospective cohort cross-sectional study assessed the associations of parents' stresses and the interactions with household environments and ambient air pollutants exposures on PDE in preschool children throughout multiple temporal exposure stages (prior to conception day, during gestation and after delivery). Firstly, PDE was inversely associated with parents' social and economic pressures, yet was positively associated with parents' mental stressors. Household exposure for new decoration, moldy clothing/bedclothes, and non-blooming plants in pregnancy, first year of life and previous year exerted greater impacts on PDE in children owning high parents' social or economic stresses, but high parents' social stress amplified associations of extraventricular traffic-related air pollutant (NO_2) exposure with PDE from preconceptional stage till previous year. High parents' mental stress enhanced PDE risk owning to early-life coarser particulate matters ($PM_{2.5–10}$ and PM_{10}) exposure. There exist positive interactions of parents' stress with interior environments and extraventricular pollutants, markedly amplified PDE risk. Our results suggest that parents' stresses not only increase susceptibility to PDE in early children, but also modifies the effects of interior and extraventricular environments on eczema risk, elaborating and supporting the "(Pre-)Fetal Origin of Eczema Hypothesis" through stress-environment synergy.

The strengths of this study are manifold: firstly, the large sample size, covering nine administrative areas in Changsha, makes the sample of preschooler's representative and comprehensive for a medium-sized city. Secondly, the study innovatively utilized the inverse distance weighting (IDW) technique to accurately assess the exposure level of each child according to his/her residential location, thus realizing a detailed portrayal of the exposure level of atmospheric pollution. Thirdly, the study systematically examined the joint effects of parents' stresses, major household environmental factors and extraventricular pollutants on PDE in children during the key stages from preconception prior to conception day, pregnant to postnatal stages. Fourthly, the study took into account the diversity of interior environmental factors, including not only indicators related to smoke exposure (e.g., ETS, parents' and/or grandparents' smoking), but also multidimensional factors such as potential renovation pollution (e.g., pollutants introduced by new furnishing and new decoration), mildew/humid environments (e.g., mildew/damp spots, moldy clothing/bedclothes), as well as different patterns of housing pets and plants. Fifthly, the study was further spanned atmospheric pollution to comprehensively assess the important impacts of seven common pollutants ($PM_{2.5}$, $PM_{2.5–10}$, PM_{10}, SO_2, NO_2, CO, O_3) on children's PDE. Sixthly, the study pioneered the associations of parents' various stresses with childhood PDE, a novel perspective that may provide more targeted insights and recommendations for early risk prevention and treatment strategies.

In this study, we newly and comprehensively demonstrated the impacts of parents' social, economic, and psychosocial stresses on their child's PDE. A growing body of evidence emphasizes the importance of psychosocial stress as a determinant of human health [56], but the effect of psychological stress interacting with air pollution on the occurrence of eczema has rarely been studied. Many studies have shown that psychological disorders may increase susceptibility to eczema and other allergic diseases in children [57–59]. Some investigations have found that the severity of eczema may be influenced by high levels of perceived stress [60,61], which has a significant effect on the skin barrier, sebaceous gland secretion, skin inflammation, and immunity [62], and would therefore logically be involved in the development of inflammatory skin diseases. This has been demonstrated in psoriasis or AD. A UK study through Southampton Women's Survey (SWS) [63] found a positive correlation between maternal psychological stress and the development of childhood eczema in infants from 6 months of age to 1 year of age, which is in agreement with our findings. However, an earlier prospective birth cohort study conducted by Sausenthaler [61] in Germany showed that maternal stress during pregnancy was positively associated with the risk of children's eczema, but the significance of this positive association was only observed in young children under two years of age. This suggests that the association between maternal stressors and the risk of childhood eczema is more important in the early years of a child's life. Meanwhile, families with poor economic conditions may result in pregnant women not having access to quality medical services, inadequate nutrition, which may affect the normal development of the fetus, and may also cause psychological problems, such as anxiety and depression, etc. Some studies have confirmed that increased work-related stress during pregnancy is positively associated with the risk of childhood eczema [64]. Furthermore, our study indicates that children from families owing high socioeconmonic status are at higher risk of developing PDE. A large population-based study from 48 countries suggests that the migration early in life is often associated with an increased risk of childhood atopic diseases [65]. Epidemiology of migration shows a higher prevalence of AD in children under 4 years of age at the time of migration to Italy compared to children who migrated after the age of 4 years [65]. This confirms the importance of early life for the development of PDE in children, which is in line with our findings.

We acknowledge that cross-sectional designs cannot determine the directionality of "stress → eczema" or "eczema → stress." To approximate a time-series approach as closely as possible, this study included three

questions in the questionnaire about eczema onset during distinct periods diagnosed by doctors. Parents were instructed to use "from before pregnancy to the present" as the recall period, thereby extending the exposure window backward. Simultaneously, we referenced evidence from the CCHH retrospective cohort: indoor dampness, mold, and elevated postnatal NO_2 and PM_{10} levels were all significantly associated with "recurrent episodes/difficulty in resolution." This confirms that recurrent eczema is indeed associated with long-term exposure to both indoor and outdoor factors. Longitudinal studies further substantiate the bidirectional causality [4]. Parental psychological distress may worsen children's eczema by impacting disease management and stress-related immune responses [66]. During the prenatal period, high levels of maternal anxiety, depression, or adverse life events significantly elevate the risk of AD in offspring aged 0–3 years [67,68]. Conversely, recurrent or severe eczema episodes can heighten parental psychological distress and family tension. The UK's ALSPAC study found that the negative impact of childhood atopic dermatitis on maternal sleep quality persists throughout childhood (0–11 years) [69]. Taiwanese clinical controlled studies also demonstrate a dose-response relationship between a child's allergic burden and caregiver psychological stress [70]. Collectively, this evidence suggests that "stress ↔ eczema" can form a vicious cycle. Future research should therefore adopt prospective or repeated-measure designs, such as cross-lagged panel models, to disentangle temporal ordering and potential mediating mechanisms between parental stress, family functioning, and eczema outcomes.

Many previous studies have associated children's eczema with various interior environments. A study from Sweden found a dose-dependent relationship between childhood eczema and low ventilation in the home, especially in children's bedrooms [71], which is consistent with our findings. Several studies have also found an association between interior renovation activities (paint, floor coverings, and new furnishing) in the first few years of life and the lifetime prevalence of eczema in the first few years of life, which may be related to high levels of volatile organic compounds (VOCs) [72–74]. In contrast, environmental VOCs at concentrations below the threshold can lead to barrier defects in children, making them more susceptible to environmental factors [75] and triggering eczema-related symptoms [76]. In our study, we found that families with less educated parents had a significantly increased risk of PDE in children when the mother was exposed to environmental smoke during pregnancy and during the past year after the birth of the child. Several studies have shown that maternal smoking during pregnancy is significantly associated with the incidence of eczema in children [77,78], probably because smoke exposure affects children's humoral and cellular immunity via the placenta, and epigenetic modifications of the immune system in utero adversely affect skin barrier integrity [79], leading to oxidative damage and reduced skin barrier function [80], which makes the skin more susceptible to external stimuli and allergens. Passive smoking due to the smoking of family members has also been associated with the development of eczema in children [81,82], which triggers an imbalance in the immune system of children, making the skin more susceptible to irritation and inflammation, and possibly through skin contact and respiratory inhalation, which can alter the skin barrier function, thus exacerbating the symptoms of eczema [83].

Air pollutants have been found to increase the severity of eczema in children in previoys studies [84,85]. These ambient air pollutants may induce eczema by providing nonspecific stimuli and elevating total serum IgE levels [86]. In addition, earlier studies [87] suggested that NO_2 has the potential to disrupt the skin barrier in eczema patients by increasing trans epidermal water loss (TEWL). It has also been found that the compromised barrier promotes allergen sensitization and may lead to systemic allergic reactions [88,89]. A recent Chinese study evaluated the association between childhood eczema and air pollution exposure during pregnancy and the first year of life [90]. The results showed that high levels of NO_2, $PM_{2.5}$ and PM_{10} exposure in the first year of life were significantly associated with an increased risk of childhood eczema, which is consistent with our findings. Therefore, early pregnancy is a critical stage for air pollution exposure related to eczema development.

Atopic eczema, also known as AD, affects a large number of children, especially those under two years of age [91,92]. The immunologic theory focuses on the imbalance between T helper (Th) cell subpopulations, specifically the overactivity of Th2 cells relative to Th1 cells, which contributes to a significant increase in immunoglobulin E (IgE) via the interleukin-mediated pathway [93]. On the other hand, the skin barrier theory suggests that atopic eczema is closely related to mutations in the filipin gene. Filament are key protein that work together with keratinocytes to maintain the integrity and protective function of the skin surface. When filipin is defective, the skin barrier function is impaired, resulting in a decrease in the skin's ability to retain water, which in turn leads to dryness of the skin. This dry state makes it easier for external allergens to penetrate into the skin, thus inducing or exacerbating allergic reactions and eczema symptoms [94].

We need to address several limitations of this study: first and foremost, we acknowledge that, as a cross-sectional study, our analysis could not fully establish the temporal relationship between exposure and outcome. However, by incorporating multiple doctor-confirmed questions regarding eczema occurrence over different time periods, we attempted to capture the chronic and

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recurrent nature of the disease. Nevertheless, the exact timing of eczema onset was not available, which may lead to some uncertainty in aligning exposure periods with disease occurrence. Therefore, causal inference should be interpreted with caution. Second, it was a retrospective cohort cross-sectional study design based on questionnaires that were completed by parents of preschool-aged children. The relative accuracy and reliability of parents' recall of key information such as the child's delivery day, as well as the fact that all families kept detailed medical records covering key information from routine prenatal checkups to the child's birth record, and even the results of regular medical checkups during the kindergarten years, reduced the impact of recall bias to a certain extent, making it considered to be minimal. Third, the geographical limitation of this study should not be overlooked. The study was conducted only in Changsha, China, which limits the representativeness of the sample and makes it difficult to fully reflect the situation of children nationwide. In order to enhance the generalizability of the findings, future studies should consider expanding the sample size nationwide. Fourth, we relied on questionnaires rather than direct measurements of the exact concentrations of interior air pollutants (e.g., harmful gases such as VOCs, SVOCs, PMs, etc.) and interior environmental factors (e.g., mildew, pets, or plant) in our assessment of interior air pollution. This indirect assessment may have introduced bias into our analysis and limited the precision of the conclusions. While these symptoms are not diagnostic in a clinical sense, they have been recognized as biologically relevant responses to chronic psychological burden. Nonetheless, we acknowledge that future studies should consider incorporating standardized psychological scales to improve measurement precision. Fifth, there are missing data for several covariates and indoor environmental factors, which may bias the results. Multiple imputations should be performed to analyze the whole participants in multivariable analysis in the future study. Sixth, Self-reported measures of parental stress may be subject to recall and social desirability biases, and the absence of objective indicators limits the precision of stress assessment. Future studies should incorporate multimodal or repeated-measure designs to enhance the validity and temporal resolution of psychosocial stress evaluation. Lastly, this study did not consider the nutritional factors (i.e., dietary habits or nutritional additives) that may be related to eczema and allergic diseases [95]. Future study should also investigate the independent and joint effects of these factors and their interactions with stress and environment on allergic outcomes.

5. Conclusions

We are the first to evaluate the associations of parents' social, economic, and mental stresses, as well as the interactions with early-life interior environments and extraventricular pollution exposures, with early childhood PDE. Associations were detected between parents' stresses and children's PDE. Moreover, interactions were found between parents' stress and household/extraventricular environments over early stages. High parents' social and economic stresses increased the amplified associations of early-life and current household moldy clothing/bedclothes, new decoration, and non-blooming plants, as well as traffic-related air pollutant (NO_2) exposure in preconception, third trimester, and previous year with PDE. High parents' mental stress amplified PDE risk owing to ambient coarser PMs ($PM_{2.5–10}$ and PM_{10}) exposure in preconceptional and postnatal stages. Our research supports the "fetal origin of PDE" hypothesis through stress-environmental interaction. The findings may service for the public policy in order to decrease PDE through avoiding early-life adverse family experiences, improving household ventilation, and avoiding crucial air pollutants (such as TRAP and PMs) exposure. This finding emphasizes the importance of targeted preventive measures at different life stages, such as improving the interior environments, reducing exposure to traffic pollution, and focusing on parents' stress conditions, particularly for mental health, as well as building a harmonious community, to early prevent and reduce the risk of children's PDE.

Supplementary Materials

The additional data and information can be downloaded at: https://media.sciltp.com/articles/others/2511060951277627/GES-25090113-SI-FC.pdf. Figure S1. The locations of kindergartens (n = 36), ambient air quality surveillance points (n = 10), and meteorological observation posts (n = 8) across Changsha's nine administrative districts. Table S1. Statistics of number and percentage of surveyed children. Table S2. Health outcomes, questions and answer options set in the questionnaire. Table S3. Descriptions and questions on exposure to indoor environmental factors during different time windows. Table S4. Statistics of parents' stress and its associations with childhood physician-diagnosed eczema (PDE) (n = 8689). Table S5. Statistics of exposure to interior environmental factors (IEFs) during pre-birth and post-birth periods among surveyed children (3–6 years) (n = 8689). Table S6. Statistics of extraventricular air pollution during preconceptional, prenatal, and postnatal periods among surveyed children (3–6 years) (n = 8689). Table S7. Sensitivity analysis of the association (ORs [95% CI]) between childhood PDE and parents' stresses stratified by individual, parents', and interior factors. Table S8. The association (ORs [95% CI]) between childhood PDE and parents' stresses stratified by clean habits (n = 8689). Table S9. The association (ORs [95% CI]) between childhood PDE and parents' stresses stratified by relative humidity (n = 8667). Table S10. Odds ratio (95% CI) of children PDE for the exposure to parents'

stress stratified by interior environment factors among surveyed children (3–6 years). Table S11. ORs (95% CI) of children PDE for parents' stress stratified by extraventricular air pollutants. Table S12. Parents' stress and interior environmental factors interactions on childhood PDE adjusted odds ratios (95% CI) (n = 8689). Table S13. Parents' stress and extraventricular air pollutant interactions on childhood PDE adjusted odds ratios (95% CI) (n = 8689).

Author Contributions

C.L. conducted the study, conceptualized, designed, and performed the study, collected the data, supervised the data analysis, and drafted the initial manuscript and revised the manuscript. Y.C. and J.Y. collected and analyzed the data, drew the figures, and drafted the initial manuscript. J.M. collected and analyzed the data, and drew the figures. W.S. revised the manuscript. W.D. and X.X. collected the data. All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement

This work has received approval for research from Fudan University and a proof/certificate of approval (IRB # 2019-09-0778) is available upon request.

Informed Consent Statement

A written consent was obtained from all the surveyed kindergartens, parents or guardians for all individual participants included in the study.

Data Availability Statement

Not applicable.

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Conflicts of Interest

The authors declare no conflict of interest.

Use of AI and AI-assisted Technologies

No AI tools were utilized for this paper.

References

1. Ridd, M.J.; Wells, S.; Edwards, L.; et al. Best emollients for eczema (BEE)—comparing four types of emollients in children with eczema: protocol for randomised trial and nested qualitative study. *BMJ Open* **2019**, *9*, e033387.
2. Beasley, R. Steering Committee. Worldwide variation in prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema: ISAAC. *Lancet* **1998**, *351*, 1225–1232.
3. Guo, Y.; Li, P.; Tang, J.; et al. Prevalence of Atopic Dermatitis in Chinese Children aged 1–7 ys. *Sci. Rep.* **2016**, *6*, 29751.
4. Lu, C.; Norbäck, D.; Zhang, Y.; et al. Onset and remission of eczema at pre-school age in relation to prenatal and postnatal air pollution and home environment across China. *Sci. Total Environ.* **2021**, *755*, 142467.
5. Lu, C.; Li, Q.; Qiao, Z.; et al. Early and late onset childhood eczema: Role of preconceptional, pre-natal and post-natal environmental exposures. *Build. Environ.* **2024**, *258*, 111626.
6. Ramírez-Del-Pozo, M.E.; Gómez-Vera, J.; López-Tiro, J. Risk factors associated with the development of atopic march. Case-control study. *Rev. Alerg. Mex.* **2012**, *59*, 199–203.
7. Chamlin, S.L.; Frieden, I.J.; Williams, M.L.; et al. Effects of atopic dermatitis on young American children and their families. *Pediatrics* **2004**, *114*, 607–611.
8. Kermack, W.O.; McKendrick, A.G.; McKinlay, P.L. Death-rates in Great Britain and Sweden. Some general regularities and their significance. *Int. J. Epidemiol.* **2001**, *30*, 678–683.
9. Gluckman, P.D.; Hanson, M.A.; Cooper, C.; et al. Effect of in utero and early-life conditions on adult health and disease. *N. Engl. J. Med.* **2008**, *359*, 61–73.
10. Bai, J.; Zhao, J.; Shen, K.L.; et al. Current trends of the prevalence of childhood asthma in three Chinese cities: a multicenter epidemiological survey. *Biomed Environ. Sci.* **2010**, *23*, 453–457.
11. Lee, S.L.; Lau, Y.L.; Wong, H.S.; et al. Prevalence of and Risk Factors for Childhood Asthma, Rhinitis, and Eczema in Hong Kong: Proposal for a Cross-Sectional Survey. *JMIR Res. Protoc.* **2017**, *6*, e7252.
12. Li, F.; Zhou, Y.; Li, S.; et al. Prevalence and risk factors of childhood allergic diseases in eight metropolitan cities in China: a multicenter study. *BMC Public Health* **2011**, *11*, 437.
13. Zhang, Y.; Li, B.; Huang, C.; et al. Ten cities cross-sectional questionnaire survey of children asthma and other allergies in China. *Chin. Sci. Bull.* **2013**, *58*, 4182–4189.
14. Zhao, T.; Wang, H.J.; Chen, Y.; et al. Prevalence of childhood asthma, allergic rhinitis and eczema in Urumqi and Beijing. *J. Paediatr. Child. Health* **2000**, *36*, 128–133.
15. Shalowitz, M.U.; Mijanovich, T.; Berry, C.A.; et al. Context matters: a community-based study of maternal mental health, life stressors, social support, and children's asthma. *Pediatrics* **2006**, *117*, e940–e948.
16. Yamamoto, N.; Nagano, J. Parental stress and the onset and course of childhood asthma. *Biopsychosoc. Med.* **2015**, *9*, 7.
17. Dohrenwend, B.S. Social status and stressful life events. *J. Pers. Soc. Psychol.* **1973**, *28*, 225-235.
18. Lewis-Jones, S. Quality of life and childhood atopic

dermatitis: the misery of living with childhood eczema. *Int. J. Clin. Pract.* **2006**, *60*, 984–992.
19. Seeman, T.E.; Crimmins, E.; Huang, M.H.; et al. Cumulative biological risk and socio-economic differences in mortality: MacArthur studies of successful aging. *Soc. Sci. Med.* **2004**, *58*, 1985–1997.
20. Miller, G.; Chen, E. Unfavorable socioeconomic conditions in early life presage expression of proinflammatory phenotype in adolescence. *Psychosom. Med.* **2007**, *69*, 402–409.
21. Kubzansky, L.D.; Kawachi, I.; Sparrow, D. Socioeconomic status, hostility, and risk factor clustering in the Normative Aging Study: any help from the concept of allostatic load? *Ann. Behav. Med.* **1999**, *21*, 330–338.
22. Silverberg, J.I.; Hanifin, J.M. Adult eczema prevalence and associations with asthma and other health and demographic factors: a US population-based study. *J. Allergy. Clin. Immunol.* **2013**, *132*, 1132–1138.
23. Arndt, J.; Smith, N.; Tausk, F. Stress and atopic dermatitis. *Curr. Allergy Asthma Rep.* **2008**, *8*, 312–317.
24. Peters, E.M. Stressed skin?—A molecular psychosomatic update on stress-causes and effects in dermatologic diseases. *J. Dtsch. Dermatol. Ges.* **2016**, *14*, 233–252.
25. Flanigan, C.; Sheikh, A.; DunnGalvin, A.; et al. Prenatal maternal psychosocial stress and offspring's asthma and allergic disease: A systematic review and meta-analysis. *Clin. Exp. Allergy* **2018**, *48*, 403–414.
26. Andersson, N.W.; Hansen, M.V.; Larsen, A.D.; et al. Prenatal maternal stress and atopic diseases in the child: a systematic review of observational human studies. *Allergy* **2016**, *71*, 15–26.
27. Min, K.D.; Yi, S.J.; Kim, H.C.; et al. Association between exposure to traffic-related air pollution and pediatric allergic diseases based on modeled air pollution concentrations and traffic measures in Seoul, Korea: a comparative analysis. *Environ. Health* **2020**, *19*, 6.
28. Yi, S.J.; Shon, C.; Min, K.D.; et al. Association between Exposure to Traffic-Related Air Pollution and Prevalence of Allergic Diseases in Children, Seoul, Korea. *Biomed. Res. Int.* **2017**, *2017*, 4216107.
29. Deng, Q.; Lu, C.; Li, Y.; et al. Exposure to outdoor air pollution during trimesters of pregnancy and childhood asthma, allergic rhinitis, and eczema. *Environ. Res.* **2016**, *150*, 119–127.
30. Bråbäck, L.; Forsberg, B. Does traffic exhaust contribute to the development of asthma and allergic sensitization in children: findings from recent cohort studies. *Environ. Health* **2009**, *8*, 17.
31. Liu, W.; Cai, J.; Huang, C.; et al. Associations of gestational and early life exposures to ambient air pollution with childhood atopic eczema in Shanghai, China. *Sci. Total Environ.* **2016**, *572*, 34–42.
32. Bose, S.; Chiu, Y.M.; Hsu, H.L.; et al. Prenatal Nitrate Exposure and Childhood Asthma. Influence of Maternal Prenatal Stress and Fetal Sex. *Am. J. Respir. Crit. Care. Med.* **2017**, *196*, 1396–1403.
33. Perera, F.P.; Wang, S.; Rauh, V.; et al. Prenatal exposure to air pollution, maternal psychological distress, and child behavior. *Pediatrics* **2013**, *132*, e1284–e1294.
34. Vesterinen, H.M.; Morello-Frosch, R.; Sen, S.; et al. Cumulative effects of prenatal-exposure to exogenous chemicals and psychosocial stress on fetal growth: Systematic-review of the human and animal evidence. *PLoS ONE* **2017**, *12*, e0176331.
35. Lu, C.; Yang, W.; Wang, F.; et al. Effects of Intrauterine and post-natal exposure to air pollution on children's pneumonia: key roles in different particulate matters exposure during critical time windows. *J. Hazard. Mater.* **2023**, *457*, 131837.
36. Lu, C.; Deng, W.; Qiao, Z.; et al. Childhood Helicobacter pylori infection: Impacts of environmental exposures and parental stress. *J. Hazard. Mater.* **2024**, *478*, 135584.
37. Lu, C.; Xiao, X.; Deng, W.; et al. Parental stress modifies effects of early life exposure to interior environmental factors and extraventricular air pollution on childhood otitis media. *Build. Environ.* **2025**, *269*, 112440.
38. Noble, K.G.; Houston, S.M.; Brito, N.H.; et al. Family income, parental education and brain structure in children and adolescents. *Nat. Neurosci.* **2015**, *18*, 773–778.
39. Gyamfi, P.; Brooks-Gunn, J.; Jackson, A.P. Associations between employment and financial and parental stress in low-income single black mothers. *Women Health* **2001**, *32*, 119–135.
40. Fujiwara, T.; Ito, J.; Kawachi, I. Income inequality, parental socioeconomic status, and birth outcomes in Japan. *Am. J. Epidemiol.* **2013**, *177*, 1042–1052.
41. Hakulinen, C.; Mok, P.L.; Horsdal, H.T.; et al. Parental income as a marker for socioeconomic position during childhood and later risk of developing a secondary care-diagnosed mental disorder examined across the full diagnostic spectrum: a national cohort study. *BMC Med.* **2020**, *18*, 323.
42. Chaudhuri, A.; Behan, P.O. Fatigue in neurological disorders. *Lancet* **2004**, *363*, 978–988.
43. Grossoehme, D.H.; Friebert, S.; Baker, J.N.; et al. Association of religious and spiritual factors with patient-reported outcomes of anxiety, depressive symptoms, fatigue, and pain interference among adolescents and young adults with cancer. *JAMA Netw. Open* **2020**, *3*, e206696.
44. Lock, A.M.; Bonetti, D.L.; Campbell, A.D. The psychological and physiological health effects of fatigue. *Occup. Med.* **2018**, *68*, 502–511.
45. Pawlikowska, T.; Chalder, T.; Hirsch, S.R.; et al. Population based study of fatigue and psychological distress. *BMJ* **1994**, *308*, 763–766.
46. Holroyd, K.A.; O'Donnell, F.J.; Stensland, M.; et al. Management of chronic tension-type headache with tricyclic antidepressant medication, stress management therapy, and their combination: a randomized controlled trial. *JAMA* **2001**, *285*, 2208–2215.
47. McGeary, D.D.; Resick, P.A.; Penzien, D.B.; et al. Cognitive behavioral therapy for veterans with comorbid posttraumatic headache and posttraumatic stress disorder

symptoms: a randomized clinical trial. *JAMA Neurol.* **2022**, *79*, 746–757.
48. Schramm, S.H.; Moebus, S.; Lehmann, N.; et al. The association between stress and headache: A longitudinal population-based study. *Cephalalgia* **2015**, *35*, 853–863.
49. Sic, A.; Bogicevic, M.; Brezic, N.; et al. Chronic stress and headaches: the role of the HPA axis and autonomic nervous system. *Biomedicines* **2025**, *13*, 463.
50. Espay, A.J.; Aybek, S.; Carson, A.; et al. Current concepts in diagnosis and treatment of functional neurological disorders. *JAMA Neurol.* **2018**, *75*, 1132–1141.
51. Möhrenschlager, M.; Schäfer, T.; Huss-Marp, J.; et al. The course of eczema in children aged 5–7 years and its relation to atopy: differences between boys and girls. *Br. J. Dermatol.* **2006**, *154*, 505–513.
52. Ek, W.E.; Karlsson, T.; Hernándes, C.A.; et al. Breast-feeding and risk of asthma, hay fever, and eczema. *J. Allergy Clin. Immunol.* **2018**, *141*, 1157–1159.
53. Calov, M.; Alinaghi, F.; Hamann, C.R.; et al. The association between season of birth and atopic dermatitis in the northern hemisphere: a systematic review and meta-analysis. *J. Allergy Clin. Immunol. Pract.* **2020**, *8*, 674–680.
54. Lee, Y.L.; Li, C.W.; Sung, F.C.; et al. Environmental factors, parental atopy and atopic eczema in primary-school children: a cross-sectional study in Taiwan. *Br. J. Dermatol.* **2007**, *157*, 1217–1224.
55. Nafstad, P.; Magnus, P.; Gaarder, P.I.; et al. Exposure to pets and atopy-related diseases in the first 4 years of life. *Allergy* **2001**, *56*, 307–312.
56. Acabchuk, R.L.; Kamath, J.; Salamone, J.D.; et al. Stress and chronic illness: The inflammatory pathway. *Soc. Sci. Med.* **2017**, *185*, 166–170.
57. Bockelbrink, A.; Heinrich, J.; Schäfer, I.; et al. Atopic eczema in children: another harmful sequel of divorce. *Allergy* **2006**, *61*, 1397–1402.
58. Calam, R.; Gregg, L.; Simpson, A.; et al. Behavior problems antecede the development of wheeze in childhood: a birth cohort study. *Am. J. Respir. Crit. Care. Med.* **2005**, *171*, 323–327.
59. Sandberg, S.; Paton, J.Y.; Ahola, S.; et al. The role of acute and chronic stress in asthma attacks in children. *Lancet* **2000**, *356*, 982–987.
60. Wen, H.J.; Wang, Y.J.; Lin, Y.C.; et al. Prediction of atopic dermatitis in 2-yr-old children by cord blood IgE, genetic polymorphisms in cytokine genes, and maternal mentality during pregnancy. *Pediatr. Allergy Immunol.* **2011**, *22*, 695–703.
61. Sausenthaler, S.; Rzehak, P.; Chen, C.M.; et al. Stress-related maternal factors during pregnancy in relation to childhood eczema: results from the LISA Study. *J. Investig. Allergol. Clin. Immunol.* **2009**, *19*, 481–487.
62. Stefanovic, N.; Irvine, A.D.; Flohr, C. The Role of the Environment and Exposome in Atopic Dermatitis. *Curr. Treat. Options Allergy* **2021**, *8*, 222–241.
63. El-Heis, S.; Crozier, S.R.; Healy, E.; et al. Maternal stress and psychological distress preconception: association with offspring atopic eczema at age 12 months. *Clin. Exp. Allergy* **2017**, *47*, 760–769.
64. Wang, I.J.; Wen, H.J.; Chiang, T.L.; et al. Maternal employment and atopic dermatitis in children: a prospective cohort study. *Br. J. Dermatol.* **2013**, *168*, 794–801.
65. Garcia-Marcos, L.; Robertson, C.F.; Ross Anderson, H.; et al. Does migration affect asthma, rhinoconjunctivitis and eczema prevalence? Global findings from the international study of asthma and allergies in childhood. *Int. J. Epidemiol.* **2014**, *43*, 1846–1854.
66. Chang, H.Y.; Suh, D.I.; Yang, S.I.; et al. Prenatal maternal distress affects atopic dermatitis in offspring mediated by oxidative stress. *J. Allergy Clin. Immunol.* **2016**, *138*, 468–475.
67. Ai, Y.; Huang, J.; Zhu, T.T. Early exposure to maternal stress and risk for atopic dermatitis in children: a systematic review and meta-analysis. Clin. *Transl. Allergy* **2024**, *14*, e12346.
68. Chan, C.W.; Law, B.M.; Liu, Y.H.; et al. The association between maternal stress and childhood eczema: a systematic review. *Int. J. Environ. Res. Public Health* **2018**, *15*, 395.
69. Ramirez, F.D; Chen, S.; Langan, S.M.; et al. Assessment of Sleep Disturbances and Exhaustion in Mothers of Children With Atopic Dermatitis. *JAMA Dermatol.* **2019**, *155*, 556.
70. Kuo, H.C.; Chang, L.S.; Tsai, Z.Y.; et al. Allergic diseases do not impair the cognitive development of children but do damage the mental health of their caregivers. *Sci. Rep.* **2020**, *10*, 13854.
71. Bornehag, C.G.; Sundell, J.; Hägerhed-Engman, L.; et al. Association between ventilation rates in 390 Swedish homes and allergic symptoms in children. *Indoor Air* **2005**, *15*, 275–280.
72. Herbarth, O; Fritz, G.J.; Rehwagen, M.; et al. Association between indoor renovation activities and eczema in early childhood. *Int. J. Hyg. Environ. Health* **2006**, *209*, 241–247.
73. Lee, J.H.; Suh, J.; Kim, E.H.; et al. Surveillance of home environment in children with atopic dermatitis: a questionnaire survey. *Asia Pac. Allergy* **2012**, *2*, 59–66.
74. Lee, J.Y.; Seo, J.H.; Kwon, J.W.; et al. Exposure to gene-environment interactions before 1 year of age may favor the development of atopic dermatitis. *Int. Arch. Allergy Immunol.* **2012**, *157*, 363–371.
75. Carson, C.G.; Rasmussen, M.A.; Thyssen, J.P.; et al. Clinical presentation of atopic dermatitis by filaggrin gene mutation status during the first 7 years of life in a prospective cohort study. *PLoS ONE* **2012**, *7*, e48678.
76. Kim, E.H.; Kim, S.; Lee, J.H.; et al. Indoor air pollution aggravates symptoms of atopic dermatitis in children. *PLoS ONE* **2015**, *10*, e0119501.
77. Neuman, Å.; Hohmann, C.; Orsini, N.; et al. Maternal smoking in pregnancy and asthma in preschool children: a pooled analysis of eight birth cohorts. *Am. J. Respir. Crit. Care Med.* **2012**, *186*, 1037–1043.
78. Lee, J.H.; Son, S.W.; Cho, S.H. A Comprehensive Review of the Treatment of Atopic Eczema. *Allergy Asthma Immunol. Res.* **2016**, *8*, 181-190.
79. Ständer, S. Atopic Dermatitis. *N. Engl. J. Med.* **2021**, *384*, 1136–1143.

80. Egawa, M.; Kohno, Y.; Kumano, Y. Oxidative effects of cigarette smoke on the human skin. *Int. J. Cosmet. Sci.* **1999**, *21*, 83–98.
81. Krämer, U.; Lemmen, C.H.; Behrendt, H.; et al. The effect of environmental tobacco smoke on eczema and allergic sensitization in children. *Br. J. Dermatol.* **2004**, *150*, 111–118.
82. Wickman, M.; Melén, E.; Berglind, N.; et al. Strategies for preventing wheezing and asthma in small children. *Allergy* **2003**, *58*, 742–747.
83. Leung, D.Y.; Guttman-Yassky, E. Deciphering the complexities of atopic dermatitis: shifting paradigms in treatment approaches. *J. Allergy Clin. Immunol.* **2014**, *134*, 769–779.
84. Kim, J.; Kim, E.H.; Oh, I.; et al. Symptoms of atopic dermatitis are influenced by outdoor air pollution. *J. Allergy Clin. Immunol.* **2013**, *132*, 495–498.
85. Guo, Q.; Liang, F.; Tian, L.; et al. Ambient air pollution and the hospital outpatient visits for eczema and dermatitis in Beijing: a time-stratified case-crossover analysis. *Environ. Sci. Process Impacts* **2019**, *21*, 163–173.
86. Gref, A.; Merid, S.K.; Gruzieva, O.; et al. Genome-Wide Interaction Analysis of Air Pollution Exposure and Childhood Asthma with Functional Follow-up. *Am. J. Respir. Crit. Care Med.* **2017**, *195*, 1373–1383.
87. Ushio, H.; Nohara, K.; Fujimaki, H. Effect of environmental pollutants on the production of pro-inflammatory cytokines by normal human dermal keratinocytes. *Toxicol. Lett.* **1999**, *105*, 17–24.
88. Huss-Marp, J.; Eberlein-König, B.; Breuer, K.; et al. Influence of short-term exposure to airborne Der p 1 and volatile organic compounds on skin barrier function and dermal blood flow in patients with atopic eczema and healthy individuals. *Clin. Exp. Allergy* **2006**, *36*, 338–345.
89. Kim, B.E.; Leung, D.Y.M. Significance of Skin Barrier Dysfunction in Atopic Dermatitis. Allergy Asthma Immunol. *Res.* **2018**, *10*, 207–215.
90. Deng, S.; Huang, D.; Wang, W.; et al. Associations of gestational and the first year of life exposure to ambient air pollution with childhood eczema in Hubei, China. *Environ. Sci. Pollut. Res. Int.* **2019**, *26*, 23842–23849.
91. Boguniewicz, M.; Leung, D.Y. Recent insights into atopic dermatitis and implications for management of infectious complications. *J. Allergy Clin. Immunol.* **2010**, *125*, 4–13.
92. Joshi, P.A.; Smith, J.; Vale, S.; et al. The Australasian Society of Clinical Immunology and Allergy infant feeding for allergy prevention guidelines. *Med. J. Aust.* **2019**, *210*, 89–93.
93. Thomsen, S.F. Atopic dermatitis: natural history, diagnosis, and treatment. *ISRN Allergy* **2014**, *2014*, 354250.
94. Maintz, L.; Novak, N. Getting more and more complex: the pathophysiology of atopic eczema. *Eur. J. Dermatol.* **2007**, *17*, 267–283.
95. Lu, C.; Jiang, Y.; Deng, W.; et al. Early-life nutritional additives, household environment, and air pollution in relation to childhood food allergies: A multi-city mother–child study in China. *Environ. Int.* **2025**, *203*, 109774.